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Preface

Basic Clinical Anesthesia is designed as an all-in-one resource for medical students, residents, and practitioners who seek comprehensive and up-to-date coverage of fundamental information and core clinical topics in anesthesiology. The book comprises 57 chapters organized into five parts and addresses ambulatory and non-operating room anesthesia, pain management and regional anesthesia, preoperative evaluation and intraoperative management, specialty anesthesia, and critical care. It encompasses the full range of anesthetic knowledge from clinically relevant basic science including system physiology and pharmacology to the anesthetic management of very sick patients. Experts have written each chapter to enable new and seasoned anesthesia practitioners alike to keep abreast of the latest information.

A great effort has been made to present information in a succinct and easy-to-read style, and numerous tables and color images and illustrations enhance the text. Multiple choice questions at the end of each chapter allow readers to test themselves and quickly review important facts.

We are pleased to present this brand new textbook and hope that it proves useful to anesthesiology residents, practitioners, and medical students as a core text, a clinical refresher, and/or an examination preparation tool. The editors gratefully acknowledge the contributions of the chapter authors and the editorial staff at Springer Science+Business Media. We welcome readers' constructive suggestions to improve the book in future editions and can be reached at the email below.

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Part I

The Basics

History of Anesthesia

1

Paul K. Sikka

"Gentlemen this is no humbug"

The desire to relieve pain has been a never-ending quest for humans and is, therefore, responsible for the birth of the specialty "anesthesiology." From the earliest records when opium sponges were used to relieve pain until today, the desire to relieve human pain and suffering has been second to none.

Inhalational Anesthetic Agents

The road to developing modern inhalational anesthetic agents started with ether (Table 1.1). The abovementioned words were used by John Warren, a surgeon, to describe a successful "public" demonstration of ether anesthesia administered by William Morton (Figs. 1.1 and 1.2) at the Massachusetts General Hospital on October 16, 1846. The patient was Edward Gilbert Abbott. Warren performed a painless surgery on Abbott's neck tumor, even though Abbott was aware that the surgery was proceeding. This marked the inauguration of the specialty "anesthesiology."

The quest for a pleasant and rapid-acting inhalational agent leads to the discovery of chloroform which was first used by J. Y. Simpson for obstetric anesthesia. However, the administration of chloroform for obstetrics was brought into fame by John Snow who administered the agent for Queen Victoria's deliveries. Ether (unpleasant) and chloroform (liver and cardiac toxicity) were replaced by ethylene gas (high concentration requirement and explosive potential), which was in turn replaced by cyclopropane (more stable). Finally, came the era of fluorinated inhalational agents (increased stability, decreased toxicity). Trifluoroethyl vinyl ether (toxic metabolite) was the first fluorinated anesthetic agent to be used which was followed by halothane (hepatitis), methoxyflurane (nephrotoxicity), enflurane (cardiac depression, convulsant properties), and finally isoflurane (synthesized by Ross Terrell in 1965, clinically used in 1971).

John Snow (1813–1858, England) was popularly known as "the first anesthesiologist" (Fig. 1.3). His research leads to the development of the concept of minimum alveolar concentration (MAC). He administered ether and chloroform in various concentrations to anesthetize animals and determined the concentration to prevent movement to a sharp stimulus. He also described the stages of ether anesthesia and invented the ether face mask. Joseph Clover (1825–1882, England) was a leading anesthesiologist in London after Snow's death. He favored a nitrous oxide-ether sequence for anesthesia and introduced pulse monitoring during anesthesia. He designed the Clover-respirator bag (to deliver known quantities of chloroform), introduced airway management skills and use of airway cannulas, and designed a portable anesthesia machine.

The Story of Nitrous Oxide

Joseph Priestly, an Englishman and one of the greatest pioneers of chemistry, first prepared nitrous oxide in 1773. Horace Wells (Fig. 1.4) of Hartford, CT, was one of the first to recognize the anesthetic potential of nitrous oxide. On December 10, 1844, while attending an exhibition where nitrous oxide was made available to the audience for inhalation, he noticed that Samuel Cooley, one of the guests, was unaware that his leg was injured while dancing. The next day Horace Wells allowed Gardner Colton, a dentist, to extract his tooth under nitrous oxide inhalation. Horace Wells described his procedure as a success. A few weeks later Wells tried to simulate the same procedure for dental extraction in a medical student in Boston. The medical student screamed and Wells was labeled as a failure. He finally committed suicide in 1848. After his death, Colton led the revival of nitrous oxide, one of the oldest anesthetic agents, which is still being used.

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Table 1.1 Ether milestones

William E. Clarke	January 1842, Rochester, NY	Teeth extraction of Ms. Hobbie by dentist E. Pope
Crawford W. Long	March 1842, Jefferson, Georgia	Neck tumor excision of Mr. Venable. Fee charged $2.00
James Y. Simpson	November 1847, Edinburgh, Scotland	Among the first to use ether and then chloroform for labor pain relief

Fig. 1.1 William T. G. Morton 1819–1868 (courtesy of the Wood Library-Museum of Anesthesiology, Park Ridge, Illinois)

Fig. 1.2 A replica of William Morton's ether inhaler as used at the first public demonstration of ether anesthesia on October 16, 1846 (courtesy of the Wood Library-Museum of Anesthesiology, Park Ridge, Illinois)

Fig. 1.3 John Snow 1813–1858, the first anesthesiologist (courtesy of the Wood Library-Museum of Anesthesiology, Park Ridge, Illinois)

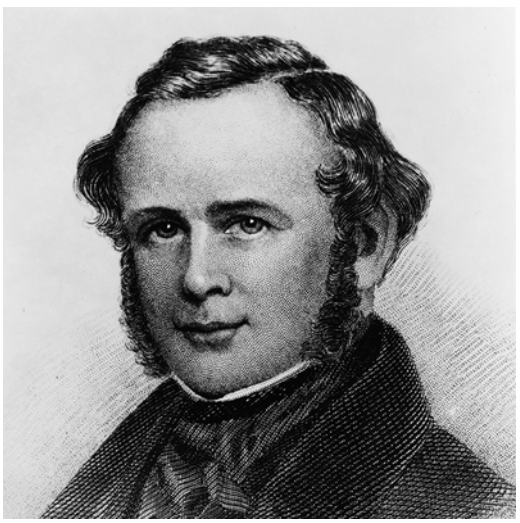

Fig. 1.4 Horace Wells 1815–1848 (courtesy of the Wood Library-Museum of Anesthesiology, Park Ridge, Illinois)

Intravenous Anesthetics

Phenobarbital, a barbiturate, was the first intravenous induction agent developed. It was synthesized by Emil Fischer and Joseph von Mering in 1903. Phenobarbital caused prolonged periods of unconsciousness and was associated with slow

emergence. Hexobarbital, a short-acting barbiturate, was clinically introduced in 1932. This was replaced by a more potent and rapidly acting barbiturate, thiopental, which was first clinically used in 1934.

Curare was the first muscle relaxant to be used by Harold Griffith in 1942 for an appendectomy. Succinylcholine was synthesized by Daniel Bovet in 1949 and till today is one of the most widely used muscle relaxants. In 1960s muscle relaxants with steroidal nucleus, pancuronium and vecuronium, were synthesized. The opioid "fentanyl" (chemical R4263) was synthesized in 1960 by Paul Janssen and remains one of the most popular pain-relieving agents used today. In 1977, propofol was synthesized by Imperial Chemical industries and is widely in use at present for sedation or induction and maintenance of anesthesia.

Airway and the Anesthesia Machine

Jay Heidbrink, Samuel White, and Charles Teter (American dentists) were the first to develop instruments in order to use compressed cylinders of nitrous oxide and oxygen. Then came the Boyle machines (Henry Boyle, England) and the Draeger machines (Heinrich Draeger, Germany). The first use of carbon dioxide absorbers occurred in 1906 (Franz Kuhn, Germany), which were made simpler and less bulky by Ralph Waters. In 1930, Brian Sword created an anesthesia machine with a circle system and an in-circuit carbon dioxide absorber. Airway milestones are listed in Table 1.2.

Local and Regional Anesthesia

Carl Koller was one of the pioneers in discovering the local anesthetic properties of cocaine (an extract of the coca leaf). He used it extensively in his practice to anesthetize the eyes for ophthalmic surgery. William Halsted and Richard Hall used cocaine to perform blocks of the sensory nerves of the face and arms. Both ended up becoming addicted to cocaine (a phenomenon which was not understood until later). Leonard Corning coined the term spinal anesthesia in 1885 (administered cocaine to produce blockade of the lower extremity). August Bier (credited for spinal anesthesia) and Theodore Tuffier were the first to describe spinal anesthesia with the mention of escape of cerebrospinal fluid. August Bier was also the first to report the technique of intravenous regional anesthesia with procaine, a procedure later modified by Mackinnon Holmes. Regional anesthesia milestones are listed in Table 1.3.

Finally, it is worth mentioning that Ralph Waters was the first president of the American Society of Anesthesiologists (ASA) in 1945. He is credited to raise the academic standards in anesthesia and launched extensive anesthesia residency training programs.

Table 1.2 Airway milestones

William Macewan, 1878	First orotracheal intubation with flexible metal tubes, technique advanced by Franz Kuhn, 1900, Germany
Alfred Kirstein, 1895	First direct vision laryngoscope
N. Korotkoff, 1905	Blood pressure measurement
M. Neu, 1910	First to apply rotameters in anesthesia
Sir Ivan Magill, 1920	Technique for blind nasal intubations, Magill's airway tubes, and angulated forceps
Arthur Guedel, 1926	Cuffed airway tubes
Phillip Ayre, 1937	Ayre's T-piece (reduce work of breathing)
Lucien Morris	Copper Kettle, first temperature-compensated vaporizer
British engineers	Tecota (temperature-compensated trichloroethylene air vaporizer), Fluotec, the first series of agent-specific vaporizers
Robert Miller, 1941	Miller straight blade
Sir Robert Macintosh, 1941	Macintosh curved blade
Glen Millikan, 1945	Developed the first pulse oximeter
F. Robertshaw, 1953	Double lumen tubes
Bain-Spoerel apparatus, 1972	Light weight breathing apparatus
A. Brain, 1981	Laryngeal mask airways (LMA)

Table 1.3 Regional anesthesia milestones

Heinrich Quincke, 1899	Described the technique of lumbar puncture
Dudley Tail and Guidlo Caglieri, 1899	Advocated use of small needles to prevent CSF escape
Heinrich Braun, 1900	Used epinephrine to prolong the effect of local anesthetics, first to use procaine, "father of conduction anesthesia"
Arthur Barker, 1907	Concept of hyperbaric solutions
Achille Dogliotti, 1931	Loss of resistance technique
William Lemmon, 1940	Concept of continuous spinal anesthesia
Lofgren and Lundquist, 1943	Synthesis of lidocaine
Edward Tuohy, 1944	The famous "Tuohy" needle
Labat and Wertheim	First American Society for regional anesthesia
Rovenstein	First American chronic pain clinic
John Bonica	Multidisciplinary pain clinic

Further Reading

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Preoperative Evaluation

2

Ursula A. Galway

Preoperative evaluation of patients undergoing anesthesia is a mandatory requirement as per the American Society of Anesthesiologists (ASA) and the Joint Commission for the Accreditation of Healthcare Organizations (JCAHO). Goals of preoperative evaluation are summarized in Fig. 2.1. Preoperative evaluation should include a detailed patient's history, medications and allergies, previous surgeries including anesthetic problems, physical and airway examination, NPO status, and formulation of an anesthetic plan. A basic anesthetic pre-evaluation is summarized in Table 2.1.

Preoperative System Review

Cardiovascular

In general, history should include questions about hypertension (diastolic BP < 110 mmHg), angina, myocardial infarction, congestive cardiac failure, arrhythmias (atrial fibrillation on warfarin), valvular disease, lipids status, and the presence of a pacemaker/AICD. Specific guidelines for preoperative cardiac evaluation for noncardiac surgery were initially developed in 1980 by the American Heart Association and American College of Cardiology. This included an algorithm to assist in clinical decision making for cardiac evaluation. The most recent revision of this was in October 2007. The algorithm (Table 2.2) is now based on several factors:

- Need for surgery
- Presence of active cardiac conditions
- Surgical risk
- Functional capacity
- Clinical indicators/risk factors

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Need for Surgery

During emergency surgeries, cardiac complications are significantly increased, up to 2–5 times more frequent when compared to similar elective procedures. Due to the nature of emergency surgery, it is not possible to optimize the patient with significant cardiac comorbidities that are currently not under control. In addition, the nature of the surgery and the insult to the system that has already occurred may make perioperative precautions (i.e., maintenance of blood pressure, avoidance of anemia, use of invasive monitors, etc.) all that one can do to decrease perioperative morbidity and mortality.

If the surgery is emergent, then surgery needs to happen regardless of the patient's comorbidities. The physician should determine cardiac status and tailor anesthetic management based on that. However, if the surgery is not an emergency, the physician needs to determine the surgical risk, whether or not the patient has active cardiac conditions, clinical risk factors, and what the patient's functional capacity is, and tailor preoperative workup based on this.

Active Cardiac Conditions

If a patient has any active cardiac conditions, this mandates further evaluation and intensive management, which may result in surgical delay. Active cardiac conditions are listed in Table 2.3. If a patient has active cardiac conditions involving the coronary arteries, then one must take into consideration how long the surgery can wait. This timing is related to the period that the patient needs to be on antiplatelet medication after revascularization:

- Balloon angioplasty—delay surgery 2–4 weeks
- Bare metal stent—delay surgery 4–6 weeks to allow endothelialization of stent. Administer aspirin and Plavix for 4 weeks.
- Drug-eluting stent—need to complete 12 months of dual antiplatelet therapy

Surgical Risk

Surgical risk is divided into three categories—high (vascular), intermediate, and low (Table 2.4). The evaluating

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Fig. 2.1 Goals of preoperative evaluation

clinician must also take into account the type of surgery the patient is scheduled to undergo. Factors related to the type of surgery are a function of the degree of invasiveness. Therefore, the amount of expected blood loss, duration of the procedure, potential patient-related stress, and fluid shifts associated with the procedure all need to be taken into account. Once all of these factors are evaluated, a final decision can be made as to the patient's potential for experiencing a perioperative cardiac complication. Patients undergoing low-risk surgery do not need any additional cardiac testing, unless of course active cardiac conditions are present.

Functional Capacity

Functional capacity involves assessing metabolic equivalent of task (MET) (Table 2.5). If the patient is unable to obtain an exercise level of 4 MET or MET cannot be obtained, further testing may be warranted depending on the patient's clinical risk factors and the invasiveness of surgery. Patients who can achieve more than 4 MET rarely need any additional cardiac testing.

Table 2.1 Basic preoperative evaluation

Patient particulars	Age	Sex	Height	Weight
Allergies	Drug and type of allergy: rash/anaphylaxis			
Medications	List of medications and those taken in AM			
Previous surgeries	List of surgeries			
Anesthesia problems	PONV	MH	Other	
System review	See below			
Airway examination	Class 1–4	Neck movements	Dentition (dentures/caps/crown)	
Physical examination	Cardiac	Pulmonary	Neurological	Vitals/others
Laboratory values	CBC	Chemistry	Coagulation	ECG/chest X-ray/others
NPO status	Full stomach precautions?			
Anesthetic plan	General	Regional	TIVA	MAC
Regional anesthesia	Spinal	Epidural	Nerve block: single shot/continuous	
Invasive monitoring	Arterial line	Central venous catheter	Pulmonary artery catheter	
ASA classification	1–6 (E)			

Table 2.2 Cardiac evaluation algorithm

Active cardiac conditions	Surgical risk	Functional capacity	Clinical risk factors	Surgical class	Plan
Yes					Testing and treatment
No	Low				Surgery
	Intermediate or high	>4 MET			Surgery
		<4 MET	3 or more	Vascular	Testing/surgery
				Intermediate	Surgery/beta-blockers or testing
			1–2	Vascular	Surgery/beta-blockers or testing
				Intermediate	Surgery/beta-blockers or testing
			None	Vascular	Surgery
				Intermediate	Surgery

MET metabolic equivalent of task

Table 2.3 Active cardiac conditions

Unstable coronary syndromes	Unstable angina
	Acute myocardial infarction within 30 days
Congestive heart failure	Decompensated
Arrhythmias	Heart block
	Atrial fibrillation
	Ventricular tachycardia
	Symptomatic bradycardia
Severe valvular disease	Severe aortic stenosis (mean pressure gradient greater than 40 mmHg, valve area less than 1 cm^2, presence of symptoms)
	Symptomatic mitral stenosis

Table 2.4 Surgical risk

High—vascular (cardiac risk >5 %)	Intermediate (cardiac risk 1–5 %)	Low (cardiac risk <1 %)
Aortic	Orthopedic	Endoscopy
Major vascular	Head and neck	Breast
Peripheral vascular	Prostate	Eye
	Intraperitoneal or intrathoracic	
	Carotid endarterectomy	

Table 2.5 Assessing metabolic equivalent of task (MET)

MET	Activity	Perioperative cardiac risk
1–3 MET	Taking care of yourself (eating, desk work), walking 1–2 blocks	High
4–9 MET	Climb stairs, walk briskly, running short distance, moderate sports	Intermediate to low
10 MET or greater	Active sports (swimming, ski, jogging)	Low

Table 2.6 Clinical risk factors

Heart disease	Myocardial infarction >1 month
	Positive stress test
	Nitroglycerin use
	Angina
	Q waves on EKG
Congestive heart failure (CHF)	History of CHF
	Positive chest X-ray (pulmonary vascular redistribution)
	Peripheral edema, presence of third heart sound (S3) and rales on chest auscultation, dyspnea
Cerebrovascular disease	History of stroke or transient ischemic attack (TIA)
Diabetes mellitus	Insulin therapy
Renal insufficiency	Serum creatinine > 2

Clinical Risk Factors

If the patient is undergoing intermediate-risk surgery and has an activity level of less than 4 MET, one must establish how many clinical risk factors the patient has (Table 2.6). If there are no clinical risk factors then one may proceed with surgery. If one or more risk factors are present, then additional cardiac testing may be considered if it will change management. If no cardiac testing is decided, then one may proceed with surgery with heart rate control.

If the patient is undergoing high-risk surgery and has an activity level of less than 4 MET, one must establish how many clinical risk factors the patient has. If there are no clinical risk factors, then it may be fine to proceed with surgery. If there are 1–2 clinical risk factors, then consider additional cardiac testing if it will change management, or proceed to the operating room with heart rate control. If there are three or more clinical risk factors, then proceed with additional cardiac testing.

Pulmonary

Asthma and COPD

Both asthma and COPD increase the risk of postoperative respiratory failure. The history should include questions about the type of therapy including steroid use, severity (ER visits, intubation), and any aggravating factors, such as aspirin use or exercise. The patient should be instructed to continue their inhalers as usual and to bring them with them on the day of surgery. If the patient has worsening symptoms or poorly controlled COPD/asthma, a pulmonary consult may be warranted.

Sleep Apnea

The evaluating physician should inquire about snoring (confirmed by a partner), hypertension, chronic fatigue, and obesity. Patients that wear continuous positive airway pressure (CPAP) masks should be instructed to bring their machines on the day of surgery.

Smoking

Patients should be instructed to stop smoking before surgery. Smoking increases airway reactiveness, inhibits ciliary motility to remove secretions, causes poor wound healing, and increases the rate of complications after surgery. The maximal beneficial effects occur if smoking is stopped for at least 8 weeks prior to surgery. However, carboxyhemoglobin (carbon monoxide—CO) levels decrease in the first 12–24 h after stopping smoking (improves oxygenation). Both nicotine and CO have negative effects on the heart (increase oxygen demand, decrease contractility). It should be noted that in some patients, airway reactiveness and secretions might increase paradoxically for about a week after smoking cessation.

Neurological

In general, one should inquire about diseases such as multiple sclerosis, myasthenia gravis and muscular disorders, and spinal cord injury (level of lesion—risk of hypertensive crisis in lesions above T_6). The evaluating physician should inquire about the type of seizure type, frequency, and medications. Antiseizure medications should be continued throughout the perioperative period. If the patient cannot take oral medications postoperatively, then intravenous formulations should be substituted. Any baseline functional and neurological impairments (any residuals) should be documented. If the patient has advanced dementia, the evaluating physician may need to take history or to get informed consent from a family member or health care proxy.

Renal

Chronic kidney disease is a complex systemic disease that results commonly from conditions, such as diabetes mellitus, hypertension, and glomerulonephritis. For patients on hemodialysis, the frequency and route of administration of dialysis should be documented, including a plan for timing of dialysis perioperatively. A potassium level should be obtained preoperatively. Volume control is a critical issue in dialysis patients, and these patients may be prone to hypotension.

Hepatic

Etiologies of liver disease include alcoholic, infectious, autoimmune, or neoplastic processes. End-stage liver disease may manifest with ascites, coagulopathies, and encephalopathy with alterations in drug distribution and metabolism. Platelet count and coagulation profile should be evaluated preoperatively in these patients.

Endocrine

For patients with diabetes mellitus (DM), history should include the type of DM (I/II), insulin or oral medications, and presence of associated diseases, such as hypertension, coronary, vascular, cerebrovascular, or renal disease. A history of hemoglobin A1-C results can be used to establish the degree of blood glucose control. Patients with a history of thyroid disease should be euthyroid before surgery.

Gastrointestinal

A positive history of gastroesophageal reflux may result in a change in the anesthetic plan (endotracheal intubation may have to be used instead of a laryngeal mask airway). Patients may be given aspiration prophylaxis preoperatively. Obesity increases anesthesia risks. Documentation of body mass index (BMI) (weight in kg/height in m^2), airway difficulties, and presence of comorbid conditions such as hypertension, diabetes, and sleep apnea is important. These patients may require special equipment in the operating room, such as a large blood pressure cuff, adequate padding, wide stretchers, and larger operating room beds.

Pregnancy

Childbearing age women should be asked if there is any chance of pregnancy. A pregnancy test should be performed on all women of childbearing age. Usually, the test is valid for 2 weeks.

Family History

One should evaluate for a history of malignant hyperthermia (presence or family history), pseudocholinesterase deficiency (history of unexplained prolonged weakness or postoperative intubation in otherwise healthy patients), and other neuromuscular disorders.

Prior Anesthetic History

Patients should be questioned on their prior surgeries—type and approximate dates. They should also be questioned on whether they had any history of difficult intubation, postoperative nausea or vomiting, poor venous access, mask "phobia" or claustrophobia, and any other problems perioperatively.

Allergies and Social Habits

A history of alcohol intake, smoking, and illegal drug use should be obtained. These patients may experience an increased tolerance to anesthetic agents and the potential for unexpected withdrawal following the surgery.

Medications

All medications and their dosages, including medications taken in AM of surgery, should be documented. The following instructions should be given to patients preoperatively:

- Medications to be taken on the day of surgery include beta-blockers, asthma medications, antihypertensives (except ACE inhibitors and diuretics), antiseizure medications,

Table 2.7 Preoperative diabetic instructions

Medication	Day before surgery	Day of surgery
Oral hypoglycemics	• Continue oral hypoglycemic medications	• Hold oral hypoglycemic medications
Insulin	• Continue to take their usual dose of insulin • If prone to nocturnal or AM hypoglycemia, decrease night time dose by 20–30 %	• Take half to one-third dose of intermediate- or long-acting insulin (Lantus, Levemir, NPH) • 70/30 mix—replace it with intermediate-acting insulin and take half to one-third of morning insulin dose • Short-acting insulin should not be taken
Insulin pump	• Continue as usual	• Continue basal rate

narcotic pain medications, H2 and proton pump blockers, and cholesterol-lowering drugs.
- Medications to be held on the day of surgery—oral hypoglycemic agents, diuretics, ACE inhibitors.
- Stop vitamin E 10–14 days and herbals 7 days before surgery.
- Anticoagulants—aspirin (hold for 7 days), clopidogrel (hold for 5 days, 7 days if planning neuraxial block), and NSAIDs (hold for 3 days, some NSAIDs may need to be held for up to 7 days).
- Management of patients on warfarin should be discussed with their primary physician or cardiologist.
- Diabetics—please refer to Table 2.7.

Preoperative Testing and Examination

Physical Examination

Points to evaluate include the following:
- General assessment of the patient—is the patient healthy looking or frail and cachectic?
- Is the patient anxious or combative?
- Can the patient give his or her own history?
- Airway examination for potential difficulties or dentition.
- Record of vitals—includes record of blood pressure, heart rate, respiratory rate, resting oxygen saturation, temperature, and the height and weight of the patient.
- Auscultation of the heart and lungs should be done to document the presence or absence of murmurs, abnormalities in cardiac rhythm, and abnormal lung sounds.
- Baseline neurological examination.
- Examination of the site for regional anesthesia and presence of scoliosis or kyphosis.
- An automatic implantable cardioverter defibrillator (AICD) or a pacemaker needs to be interrogated preoperatively.

Preoperative Laboratory Testing

Laboratory testing should be directed by findings on history and physical exam. Age-based criteria are controversial as test abnormalities are common in older patients but are not as predictive of complications as information gained from the history and physical. Routine and age-based preoperative tests may not be reimbursed by Medicare and Medicaid. Patients over 70 years have a 10 % chance of having abnormal serum creatinine, hemoglobin, or glucose and a 75 % chance of having at least one abnormality on EKG. These factors were found not to be predictive of postoperative complications; however, physicians often like to be aware of what these baseline abnormalities are before proceeding with surgery.

Generally, test results within 6 months are acceptable if the patient's history has not changed. If the patient's condition has changed in the interim, lab tests within 2 weeks are more favored. The following points should be kept in mind:
- Routine labs are not good screening devices and should not be used to screen for diseases.
- Repetition should be avoided.
- Healthy patients may not need tests.
- Patients undergoing minimally invasive procedures may not need tests.
- A test should only be ordered if its result will influence management.

Pregnancy Testing

A history and physical exam are insufficient to determine early pregnancy, and patients are often unreliable in suspecting that they may be pregnant. Importantly, management usually changes if it is discovered the patient is pregnant, even in emergency situations. All premenopausal women of childbearing age who have not had tubal ligation or hysterectomy should have a preoperative pregnancy test.

Blood Count

White cell count should be considered in patients suspected to have infection, patients on chemotherapy, and patients with myeloproliferative disorders. Platelet counts are indicated in patients with a history of low platelets, pregnancy, liver disease, or preeclampsia. Bleeding time is usually not performed as a preoperative screening indicator of platelet function. Hemoglobin/hematocrit should be considered in the following situations:
- Anticipated blood loss >500 ml
- Suspicion of anemia
- Recent chemotherapy or radiation (within 2 months)
- Renal disease
- Active cardiac symptoms
- Recent blood loss
- Sickle-cell anemia or thalassemia
- Recent autologous blood donation

Blood Glucose, Renal Function, and Electrolytes

BUN, creatinine, and electrolytes should be tested in patients with chronic kidney disease, cirrhosis of the liver, certain medications (diuretic, ACE inhibitor, digoxin), diabetes mellitus, and certain perioperative indications (surgery on the kidney, aortic clamping). Renal dialysis patients should have their potassium tested immediately prior to surgery.

Blood glucose should be ordered on patients with diabetes mellitus, steroid use, and cirrhosis of the liver. Urinalysis should be performed for patients with permanent implants at risk of seeding (artificial joints, heart valves), certain urological procedures, and active symptoms of urinary tract infection (UTI).

Liver Function and Coagulation Profile (PT/PTT/INR)

Liver function tests (LFTs) should be ordered on patients with cirrhosis, jaundice, alcohol abuse, easy bleeding and bruising, and malnutrition. The following patients should have preoperative coagulation studies drawn:

- Patients with current or recent anticoagulation use
- Patients with history of bleeding disorders
- Patients with liver disease or abnormal liver function profile
- Patients with a history of clotting disorders, multiple miscarriages, autoimmune disorders
- Coagulation testing may be recommended in procedures with high risk of bleeding such as coronary artery bypass graft (CABG) and liver resections, in the absence of above indications

Neuraxial block for surgery (spinal/epidural/nerve block) is *not* an indication for INR and aPTT testing unless the patient was recently on anticoagulants. INR and aPTT testing are not recommended prior to the procedure with low risk of bleeding. Patients on warfarin (prothrombin time) or heparin (partial thromboplastin time) should have coagulation studies generally repeated on the morning of the surgery. The aim is to document normal coagulation parameters after stopping these medications.

Type and Screen/Type and Crossmatch

A type and screen/cross should be ordered if you expect a blood transfusion may be required. They should be based on the degree of expected blood loss and the presence of any blood-forming disease. "Jehovah's witness" patients may refuse blood products for religious reasons. In these instances, the reasons and options must be carefully reviewed. Alternatives, such as the use of a cell saver and administration of plasma expanders (albumin, hetastarch), can be explicitly discussed and documented.

Chest X-Ray (CXR)

Patients with significant risk factors for postoperative pulmonary complications may warrant preoperative CXR irrespective of age. For asymptomatic patients older than 50 years with no risk factors, there is insufficient evidence for or against ordering CXR. Without symptoms or pertinent medical history, abnormal CXRs do not predict a worse clinical outcome. Congestive heart failure and pneumonia have been found to be the only conditions that appear to affect postoperative outcomes, and these can be predicted preoperatively by a thorough history and physical exam. CXR should *not* be considered as unequivocal indication for extremes of age, smoking, stable COPD, stable cardiac disease, and recent resolved upper respiratory tract infection. CXR should be ordered on patients with the following conditions:

- Severe or uncontrolled COPD
- Active pulmonary disease or symptoms
- Abnormal lung sounds on physical exam
- Recent pneumonia
- Patients undergoing thoracic, upper abdominal, or AAA surgery

Electrocardiogram (EKG)

Important characteristics to consider when deciding whether to order an EKG include cardiovascular disease, respiratory disease, and the type and invasiveness of surgery. EKG abnormalities may be higher in older patients: however, currently there is no consensus regarding a minimum age for which to order an EKG. Patients over 70 years have a 75 % chance of having at least one abnormality on EKG, which may not be predictive of postoperative complications. According to the ACC/AHA 2007 guidelines, an EKG should be performed on the following patients. An EKG is not indicated for patients undergoing low-risk surgery:

- Patients undergoing vascular surgery
- Patients with known coronary artery disease, peripheral vascular disease, or cerebrovascular disease who are undergoing intermediate-risk surgery
- Patients with episode of angina or ischemic equivalent
- Patients undergoing intermediate-risk surgery and who have at least 1 clinical risk factor

Echocardiography and Pulmonary Function Tests (PFTs)

An echocardiogram may be indicated for patients with dyspnea of unknown origin or a history of heart failure with progressive symptoms. It is not indicated for patients with clinically stable cardiomyopathy. PFTs may be considered for type and invasiveness of surgery (specifically CAGB and lung resection), severe asthma, symptomatic COPD, scoliosis, and restrictive lung function diseases.

Preoperative Premedication

Preoperative medication is usually administered up to 1 h or immediately before taking the patient to the operating room. Drugs can be administered intravenously or orally with a sip of water (not exceeding 150 ml).

Anxiolysis

Benzodiazepines produce sedation, relief of anxiety, and anterograde amnesia (suppression of recall of events after their administration). They have minimal cardiorespiratory depressant effects. Commonly used drugs are midazolam (1–2 mg) or lorazepam (0.5–2 mg), usually given intravenously.

Analgesia

Opioids are commonly used if the patient is experiencing pain in the preoperative area (fractures, abdominal pain, etc.). Fentanyl 12.5–25 mcg may be administered at appropriate intervals. Alternatively, if the patient is already on opioids (morphine or hydromorphone), those may be continued in the preoperative area. It is important to remember that opioids when combined with benzodiazepines have synergistic effects, causing their cardiorespiratory depressant effects to be enhanced.

Acid Suppression

Commonly used drugs for acid suppression are antacids (nonparticulate sodium citrate), prokinetic agents (metoclopramide), histamine (H_2)-receptor antagonists (famotidine, ranitidine), and proton pump inhibitors (omeprazole, pantoprazole). The two commonly prescribed agents are metoclopramide (10 mg orally/IV) and either famotidine (20 mg IV) or ranitidine (150 mg orally/50 mg IV). Sodium citrate 30 ml is typically used 15–30 min before a cesarean section to neutralize (raises the pH > 2.5) the acid present in the stomach.

Antisialagogue Effect

Glycopyrrolate (0.2–0.4 mg IV) can be administered especially before bronchoscopy or lung surgery to dry up the secretions. In addition, it may act as a prophylactic agent against the oculocardiac reflex (cataract surgery) and negate the antivagal effects of propofol and fentanyl.

Antiemetics

Prophylactic antiemetics may be administered before surgery in the preoperative area. These drugs include a combination of drugs that suppress gastric acid effects and those which have direct antinausea effects. Commonly used drugs are metoclopramide, H_2 antagonists (famotidine/ranitidine), ondansetron (4–8 mg IV), and dexamethasone (4–8 mg IV). In addition, a scopolamine (anticholinergic drug) patch placed behind the ear is also beneficial. The patch is removed by the patient the next day. The patient should be instructed to wash their hands after touching the patch so that the medication does not affect their eyes (pupillary dilation), etc. It is important to remember that scopolamine can cause sedative and amnesic effects, especially in the elderly.

Antiallergic Prophylaxis

Patients undergoing radiographic studies with dyes who have a history of allergies can be pretreated with diphenhydramine (H_1 blocker, 25–50 mg orally/IV) and a steroid such as hydrocortisol (100 mg IV). However, pretreatment does not guarantee protection against an allergic reaction.

Table 2.8 NPO guidelines for fasting before surgery

Food material	Minimum fasting (h)[a]
Clear liquids (water, pulp-free juice—apple/cranberry, black coffee, carbonated beverages)	2
Breast milk	4
Infant formula/nonhuman milk	6
Light meal (toast)	6
Fried, fatty foods	8

[a]It is important to remember that patients with anxiety, on opioids, and with gastric problems may have a prolonged gastric emptying time

Nil per Oral

The term "nil per oral (NPO)" comes from a Latin phrase "non per os" meaning nothing by mouth. It is important that patients fast before arriving to the hospital for surgery. Patients are usually instructed to fast after midnight. The presumption is that fasting will lead to a decrease in gastric volume, so that with induction of anesthesia, there will be a decreased risk of pulmonary aspiration of gastric contents. Guidelines for fasting are summarized in Table 2.8.

Aspiration

Pulmonary aspiration involves the regurgitation of gastric contents into the respiratory tract. The incidence of pulmonary aspiration of gastric contents during general anesthesia is about 1 in 5,000 anesthetics. However, with advances in modern pulmonary care and the availability of newer antinausea drugs, the aspiration of gastric contents is fortunately associated with minimal morbidity and negligible mortality. Patient populations prone to aspiration include pregnancy, obesity, and trauma patients. The two modalities of regurgitant material are the particulate matter and a pH < 2.5. This may lead to acute lung injury manifested as pneumonitis, aspiration pneumonia, respiratory failure, or acute respiratory distress syndrome.

Risk Factors for Pulmonary Aspiration

- Increased gastric volume—delayed gastric emptying, diabetic gastroparesis, labor, pain, stress
- Increased gastric regurgitation—decreased lower esophageal sphincter tone, achalasia, esophageal or abdominal surgery, increased intra-abdominal pressure

Table 2.9 American Society of Anesthesiologists classification of physical status

ASA	Description	Medical conditions
1	Healthy patient	–
2	Patient with mild systemic disease	HTN, DM, asthma, mild obesity, extremes of age, smoker, pregnancy
3	Patient with severe systemic disease	Uncontrolled HTN or DM, angina pectoris, MI, controlled CHF, COPD, renal failure, morbid obesity
4	Patient with severe systemic disease which is a constant threat to life	Unstable angina, symptomatic CHF, advanced COPD, hepatorenal failure
5	Patient who is not expected to survive 24 h without surgery	Ruptured AAA, head injury
6	Brain dead patient for organ removal	–
E	Any patient undergoing emergency surgery	Healthy patient for appendectomy, patient for ruptured AAA repair

HTN hypertension, *DM* diabetes mellitus, *MI* myocardial infarction, *CHF* congestive cardiac failure, *COPD* chronic obstructive pulmonary disease, *AAA* abdominal aortic aneurysm

- Decreased laryngeal competence—general anesthesia, head injury/decreased conscious level, neuromuscular disorders

Strategies to Reduce/Prevent Pulmonary Aspiration

- Strict adherence to NPO guidelines.
- Anesthetic techniques—rapid sequence intubation and the application of cricoid pressure.
- Pharmacologic intervention—preoperative administration of nonparticulate antacids, histamine H_2 antagonists, proton pump inhibitors, and prokinetic agents. For routine prophylaxis, metoclopramide (10 mg) and either famotidine (20 mg IV) or ranitidine (50 mg IV) may be administered.

ASA Classification

Once the preoperative evaluation is completed, the anesthesiologist then assigns an ASA classification number to denote how healthy/sick the patient is (Table 2.9). Hospitals, law firms, and health groups use this classification as a scale to predict perioperative risk. Although the ASA classification of a patient is not a measure of risk per se, patients with higher ASA classifications in general have an increased risk from surgery. An "E" is added to the physical classification to designate a patient in whom surgery is emergent. ASA-5 is usually an emergency (E), while for ASA-6 "E" is not applicable. The ASA physical classification system is a simpler and useful way to communicate about patients across other medical disciplines as well. Other classification systems, such as APACHE II, are much more cumbersome, are complex, and lack ease of communication between anesthetists, surgeons, and health insurers.

Clinical Review

1. A 65-year-old patient is to undergo a total knee replacement. He has a history of hypertension (140/90 mmHg), smoking, and diabetes mellitus (blood sugar 160 mg/dl). His ASA classification is:
   A. I
   B. II
   C. III
   D. IV
2. A 54-year-old patient can climb stairs, walk briskly, and take care of himself (eating/drinking) but cannot take part in active sports like swimming or skiing. His metabolic equivalent of task (MET) is most likely:
   A. 1
   B. 3
   C. 5
   D. 10
3. Maximal beneficial effects occur if smoking is stopped for at least:
   A. 4 weeks
   B. 6 weeks
   C. 8 weeks
   D. 12 weeks
4. Body mass index (BMI) is calculated as:
   A. Weight in pounds/height in in.^{2}
   B. Height in in./weight in kg^2
   C. Weight in kg/height in in.^{2}
   D. Weight in kg/height in m^2
5. All of the following medications may be taken on the day of surgery, except:
   A. Metoprolol
   B. Simvastatin
   C. Metformin
   D. Omeprazole

6. A 70-year-old patient had an inguinal hernia repair. Perioperative medications included midazolam, fentanyl, ondansetron, and a scopolamine patch. The next day the patient is found to be confused. The medication most likely causing the confusion is:
   A. Midazolam
   B. Fentanyl
   C. Ondansetron
   D. Scopolamine
7. All of the following can be used for acid suppression, except:
   A. Particulate antacid
   B. Metoclopramide
   C. Famotidine
   D. Pantoprazole
8. A 76-year-old patient is scheduled for cataract surgery. He had toast and apple juice 2 h back. The following is true:
   A. One can proceed with surgery as the procedure is to be done with monitored anesthesia care (MAC).
   B. Surgery can be scheduled in 4 h from the time of eating.
   C. Surgery can be scheduled in 6 h from the time of eating.
   D. Surgery can be scheduled in 8 h from the time of eating.
9. Patients on dialysis should at least have the following tested on the day of surgery:
   A. Serum potassium
   B. Serum sodium
   C. Serum creatinine
   D. Blood urea nitrogen
10. True statement is:
   A. An EKG is indicated for all patients over 50 years.
   B. A chest X-ray is indicated for all patients above 50 years.
   C. A Chest X-ray is indicated in a patient who smokes regularly.
   D. An EKG is indicated in a patient undergoing vascular surgery.

Answers: 1. B, 2. C, 3. C, 4. D, 5. C, 6. D, 7. A, 8. C, 9. A, 10. D

Further Reading

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Approach to Anesthesia

3

Paul K. Sikka

Anesthesia can be of several types, general, regional (epidural/spinal), peripheral nerve blocks, or monitored anesthesia care (MAC). The type of anesthesia administered depends on the choice of the patient, choice of the surgeon, and the type of surgery being performed. Each type of anesthesia involves a logical sequence of steps with which the practitioner needs to get familiar. This chapter will describe the basic steps involved in the administration of general anesthesia and MAC/TIVA (total intravenous anesthesia).

Administration of General Anesthesia

General anesthesia is a pharmacologically (drug) induced reversible state of unconsciousness. In general, anesthesia is a reversible state of amnesia, analgesia, loss of responsiveness, loss of skeletal muscle reflexes (varying degree), and decreased stress response. The primary goal of anesthesia administration is to provide patient comfort and safety during surgery. Mortality from general anesthesia is about 1:250,000, while morbidity related to anesthesia includes dental, soft tissue and nerve injury, and postanesthesia respiratory and cardiac complications. Common intraoperative problems are described in Table 3.1.

Steps involved in administration of general anesthesia include *preoperative preparation, monitoring, induction of anesthesia, airway management, maintenance of anesthesia, reversal of anesthesia, and postoperative management.*

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Preoperative Preparation

- Evaluating the patient—history and physical, airway evaluation, laboratory tests, NPO status—and formulating an anesthetic plan.
- Preparing the patient for the OR—obtain consent, type and screen/crossmatch, preoperative medication, and line placement (IV, arterial/central line). Side of IV placement for breast surgery/AV fistula is usually opposite to the side of surgery.
- Preparing anesthesia equipment—anesthesia machine, airway equipment, monitors, fluid warmer, and medications.

[Preoperative medication may include midazolam (sedative), metoclopramide and famotidine/ranitidine (acid prophylaxis), and opioid (if pain relief is required)].

Monitoring

After adequate preoperative preparation, the patient is transported to the operating room and monitors are applied.

- Basic monitoring—pulse oximeter, noninvasive blood pressure monitoring, and electrocardiogram (rhythm, heart rate). Additional monitors include end-tidal CO_2 monitoring, temperature monitoring (skin/esophageal/other), and urine output (if Foley catheter is inserted).
- Specialized monitoring—nerve stimulator (facial/ulnar nerve, if muscle relaxants are used), inspired oxygen monitor, airway pressure monitor, and inhalational agent monitoring.
- Arterial line—sites include radial/brachial/femoral/dorsalis pedis arteries. Indications include surgeries associated with significant blood loss and fluid shifts, patients with severe systemic disease, and drawing of repeated samples for blood gas/hematocrit.
- Central venous pressure line and pulmonary artery catheter—sites include internal jugular/subclavian/femoral veins (the latter mainly for venous access). Indications

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Table 3.1 Common intraoperative problems and their management

Problem	Cause	Treatment
Difficulty/failure to ventilate	Circuit disconnection	Check circuit attachments
	Obstruction—mucus plug, biting ETT	Suction of ETT, if biting ETT—insert oral airway, deepen anesthesia
	Pneumothorax (no breath sounds)	Auscultate patient, inform surgeon
	Bronchospasm (wheezing, high airway pressure)	Auscultate patient, 100 % O_2, increase depth of anesthesia, beta-2 agonists, epinephrine
	Right main stem intubation (low O_2 saturation)	Auscultate patient, ETT at lip is usually 23 cm in males and 21 cm in females
	Hypoventilation (anesthetic agents—opioids, inhalational agents, muscle relaxants)	Treat accordingly (opioid reversal—naloxone, check for adequate muscle strength recovery, controlled ventilation)
	Pulmonary edema (fluid overload)	O_2, diuretics
Hypotension	Anesthetic drugs, spinal/epidural anesthesia, blood loss	Vasopressors—phenylephrine (40–100 mcg IV), ephedrine (5–10 mg IV), norepinephrine, dopamine, fluids/blood
Hypertension	Pain	Opioids
	Light anesthesia	Deepen anesthesia—propofol, inhalation agent
	Increased sympathetic response (increased BP)	Labetalol, metoprolol, esmolol, hydralazine, nitroglycerine, nitroprusside
	Tourniquet pain	Deflate tourniquet in consultation with surgeon
Arrhythmias	Anesthetic drugs, spinal anesthesia, venous air embolism, pulmonary embolus, myocardial ischemia	Treatment described in the chapter on cardiac arrhythmias
Anaphylaxis	Antibiotic, muscle relaxants	Epinephrine, O_2, fluids
Hypothermia	Use of unwarmed IV fluids or unwarmed irrigation fluid for TURP, general/spinal anesthesia, convective, conductive, radiative, or evaporative fluid loss from the patient	Use of warmed fluids, fluid warmer, forced-air warming device, maintain OR temperature, radiant heat for pediatric patients, humidifier
Hyperthermia	Malignant hyperthermia	Stop the offending agent (inhalational/succinylcholine), dantrolene IV, fluids, supportive care
	Sepsis	Antibiotics, vasopressors if needed
	Blood transfusion reaction	Stop the transfusion, acetaminophen, diphenhydramine, steroids, fluids
Bradycardia	Increased vagal stimulation-surgical vagal stimulus (cranial, bladder surgery), anesthetic drugs (propofol, fentanyl), spinal anesthesia	Inform the surgeon to stop the surgery momentarily, glycopyrrolate IV
	Hypoxia	Correct the ventilation, treat the cause
	Myocardial infarction, heart block	See the chapter on cardiac arrhythmias

include patients with significant systemic disease (cardiac/renal) undergoing major surgery, anticipated large fluid shifts and blood loss, and measurement of central venous pressure/cardiac output.

- Transesophageal echocardiogram (TEE)—to evaluate cardiac function in patients undergoing cardiovascular surgery or in patients with reduced cardiac function undergoing major surgery. It can be also used to evaluate volume status in a patient and thus can be used together/instead of a pulmonary artery catheter.
- Bispectral index (BIS) monitor—to monitor depth of anesthesia so as to decrease incidence of patient awareness under anesthesia. It processes electroencephalogram (EEG) to give a number (up to 100). The higher the number, the more awake the patient. A number below 60 is aimed for adequate depth of anesthesia.

Induction of Anesthesia

Once the monitors are applied to the patient, the preinduction vital signs are measured (BP, HR, O_2 saturation). The next step is to preoxygenate the patient with 100 % O_2 via the anesthesia circuit. In emergency, trauma, or cesarean section patients, additional preinduction considerations may include full stomach precautions, possibility of alcohol and drug intoxication, and cervical spine and hemodynamic instability.

- Techniques of induction—intravenous (used commonly) or inhalational (children, adults without IV access)
- Drugs used for IV induction—propofol (1–2 mg/kg), thiopental (5–7 mg/kg), etomidate (0.3 mg/kg), ketamine (1 mg/kg), or midazolam (0.1 mg/kg)
- Drugs used for inhalational induction—O_2, N_2O with sevoflurane (nonpungent)

Airway Management

Once the patient is asleep, the next step is to control the airway. Airway control can be achieved via the following:

- Insertion of laryngeal mask airway (LMA)—different sizes are available by weight/age. It is important to establish an IV access before inserting an LMA, if induction is done via inhalational agents.
- Insertion of endotracheal tube (ETT)—once the patient is asleep the patient is ventilated via a face mask. Muscle relaxants are used to facilitate intubation, either succinylcholine (1–2 mg/kg) or a nondepolarizing muscle relaxant—rocuronium (0.6–0.9 mg/kg)/vecuronium (0.1 mg/kg). The next step is to intubate the patient via an appropriate size of ETT using a laryngoscope (Macintosh/Miller blade).
- Rapid sequence intubation—patients on full stomach precautions (trauma, bowel obstruction) and acid reflux disease can be intubated via this technique (to prevent pulmonary aspiration). The premedication is omitted (no midazolam/fentanyl), the patient is preoxygenated with 100 % O_2, and the anesthesia is induced with an IV induction agent followed immediately with the administration of succinylcholine. The patient is not given any positive pressure breaths via the face mask, a cricoid pressure is applied gently, and the patient is intubated to secure the airway.
- Difficult airway patients—patients with known and anticipated difficult airway may be intubated with the help of specialized intubating equipment (instead of direct laryngoscopy), such as fiber-optic intubation and use of a Glidescope or Airtraq.

Positioning

Proper patient positioning and padding are required while the patient is asleep under general anesthesia, to avoid pressure on the peripheral nerves and soft tissues (eyes, breasts, AV fistula). Besides the supine position, surgery may be carried out in the prone, lateral, lithotomy, or jack-knife positions. The ulnar nerve is the most common nerve to be injured under anesthesia. It is important to remember that a sudden change from the supine position may lead to hemodynamic effects.

Maintenance

- Gases—oxygen, nitrous oxide or air, and an inhalational agent (isoflurane, sevoflurane, or desflurane). Nitrous oxide is contraindicated in patients with bowel obstruction, pneumothorax, and tympanoplasty as it leads to dilation of closed air spaces.
- Analgesics—narcotics such as fentanyl, morphine, or hydromorphone.
- Muscle relaxants—required to provide muscle relaxation for bowel surgery and used in patients who should not move during surgery (cardiac or neurosurgery). Nondepolarizing muscle relaxants, such as rocuronium, vecuronium, or cisatracurium, are used. Cisatracurium is beneficial for patients with renal failure as it is eliminated by Hoffman degradation (not dependent on liver/renal routes for metabolism).
- Adjuncts—epidural anesthesia/nerve blocks are commonly used in addition to general anesthesia for intraoperative/postoperative pain management.
- Monitor patient's vital signs and ventilation, assess blood loss, and communicate with the surgeon.
- Fluid management—4 ml/kg/h for the first 10 kg of weight, 2 ml/kg/h after first 10 kg up to 20 kg of weight, and 1 ml/kg/h thereafter. When calculating fluid requirements under anesthesia, one needs to consider fluid deficit from NPO status, maintenance fluid requirements, additional fluid requirements secondary to blood loss, and losses through the gastrointestinal and respiratory systems. Replacement of blood loss by crystalloid is done by a ratio of 1:3 and for colloid by a ratio of 1:1. This means that every milliliter of blood loss should be replaced with 3 ml of crystalloid or 1 ml of colloid.
- Blood components—blood (packed RBCs), platelets, and fresh frozen plasma. Blood transfusion is required when excessive blood loss leads to hemodynamic instability or a hemoglobin of less than 7 g/dl (note: with rapid blood loss, the measured hematocrit may not be accurate).

Emergence and Extubation

- Discontinue inhalational agents.
- Reverse muscle relaxants (with neostigmine plus glycopyrrolate).
- Criteria for extubation—these include stable vital signs, adequate ventilation (tidal volume >5 ml/kg, respiratory rate of 7–35 per minute), negative inspiratory force < −20 mmHg, reversal of muscle relaxant (sustained head lift for 5 s, good grasp strength), and preferably an awake and cooperative patient. Occasionally, the anesthesiologist may perform a deep extubation (unawake patient but with stable parameters), so as to prevent coughing and bucking during emergence, or in a patient with reactive airway disease.
- Problems with tracheal extubation—include laryngospasm, hypoventilation, pulmonary aspiration, negative pressure pulmonary edema (patient attempting to breathe with an obstructed airway), and patient agitation (hypoxia, hypercarbia, full bladder, pain).

Postoperative Management

- Transport—after emergence from anesthesia in the OR, patients are transported to postanesthesia care unit (PACU) or the intensive care unit (ICU). Patients are transported to the ICU if they are kept intubated (cardiac or neurosurgery) or if they are hemodynamically unstable. Patients are always transported with supplemental oxygen and with a monitor (for ICU).
- Patient report is given to the receiving nurse (history, intraoperative events, medications, fluids).
- Postoperative care includes maintaining adequate patient ventilation, pain management, antinausea medications, administration of fluids/blood, and treating any complications. Pain management includes IV narcotics/PCA, ketorolac, or pain control via an epidural infusion.

Anesthesia Equipment Preparation

The following protocol may be followed to prepare anesthesia equipment in the operating room:

- Suction—make sure the suction is connected and working adequately.
- Circuit—perform a circuit leak test, correct circuit size for pediatric patients.
- Oxygen—the anesthesia machine is turned ON, and gas flow is adequate.
- Monitors—pulse oximetry, ECG, blood pressure cuff, temperature monitor, $ETCO_2$ monitor, and nerve stimulator.
- Airway—two endotracheal tube sizes (with/without stylet, cuff tested for leak), oral/nasal airway, nasal cannula/face mask, and appropriate-size LMAs.
- Laryngoscope—Macintosh and Miller blades with adequate illumination.
- IV—an intravenous line prepared if an IV has to be started and an IV start kit (tourniquet, alcohol swab, 1 % lidocaine for local infiltration, IV needle, gauze, tape).
- Drugs—all drugs labeled with concentration and date/time multidose vials (Table 3.2).
- For major surgeries—arterial line setup, central line/pulmonary artery catheter setup, fluid warmer, availability of heparin, protamine, beta-blockers, drug infusions (epinephrine, nitroglycerine, nitroprusside, dopamine), etc.
- For special cases
- —malignant hyperthermia—change soda lime, run oxygen at high flows for about 20 min, remove or put tape on inhalational vaporizers, and remove succinylcholine from the anesthesia cart.

  Difficult airway
  - —bring airway cart in room, fiber-optic scope (tip cleaned with alcohol swab and focused), or alternate method of intubation—LMA Fastrach (intubating), Glidescope, and Airtraq. Appropriate-size airways, endotracheal tubes, and lubricant jelly.
  - Drugs for airway blocks—4 % lidocaine.
  - Antisialogogue drug—glycopyrrolate (0.2–0.4 mg IV)—depending on the heart rate.
  - Drugs for sedation—midazolam, fentanyl, ketamine, propofol, and dexmedetomidine.
- Miscellaneous—forced-air warming device, tape (regular, eye tape, endotracheal tube fixation tape), lubricant jelly, two poles hooks for the drape, and arm restraints.

Table 3.2 Drugs to be prepared (*not dosages*) for anesthesia administration

Premedication/opioids	Midazolam 2 ml (1 mg/ml)
	Fentanyl 2 ml or 5 ml (50 mcg/ml)
Induction agents	Propofol 20 ml (10 mg/ml) or thiopental 20 ml (25 mg/ml) or etomidate 10 ml (2 mg/ml)
Neuromuscular blocking agents	Succinylcholine 10 ml (20 mg/ml) and rocuronium 5/10 ml (10 mg/ml) or vecuronium 10 ml (1 mg/ml)
Opioids	Morphine 10 ml (1 mg/ml), hydromorphone 10 ml (0.2 mg/ml)
Vasopressors	Ephedrine 10 ml (5 mg/ml), phenylephrine 10 ml (100 mcg/ml—dilute 10 mg in 100 ml of saline bag)
Emergency drugs	Lidocaine 5 ml (20 mg/ml), atropine 1 ml (0.4 mg/ml)
Reversal agents	Neostigmine (0.05 mg/kg), glycopyrrolate (0.2 mg = 1 ml for each ml of neostigmine)

Monitored Anesthesia Care

Monitored anesthesia care (MAC) involves monitoring a patient's vital signs while caring for the patient's comfort and safety. MAC involves administering a combination of drugs for anxiolytic, amnestic, and analgesic effect. The surgeon may/may not administer local anesthesia in addition. MAC results in less physiologic disturbance and allows for more rapid recovery than general anesthesia.

Indications

- Minor surgeries, such as breast biopsy, Port-a-Cath placement, and cataract surgery
- Patient with severe systemic disease
- Surgeon's and patient's preference

MAC Involves

- Performance of a preanesthetic examination and evaluation.
- Basic monitoring of patient's vital signs.

- Ability of the patient to remain still and cooperate with the surgeon. Ability to communicate with the patient assists in monitoring the level of sedation and cardiorespiratory function and is a means of explanation/reassurance to the patient.
- Ability of the patient to lie supine for the duration of time.
- Facilities to secure the airway should be immediately available.

MAC/Conscious Sedation

While MAC is provided by a fully trained anesthesiologist, "conscious (moderate) sedation" (Table 3.3) is provided for patients where the physician performing the procedure (surgeon) is also directing and supervising the administration of sedation by another provider (nurse). Conscious sedation is usually provided because of scheduling issues, convenience, or lack of availability of anesthesiologists. Most institutions request anesthesiologists to provide MAC for high-risk patients (patients with morbid obesity, sleep apnea, and severe cardiac, pulmonary, hepatic, renal or central nervous system disease).

Total Intravenous Anesthesia

Total intravenous anesthesia (TIVA) is defined as a technique of general anesthesia using a combination of agents given solely by the intravenous route. No inhalational agents including nitrous oxide are used. Indications for TIVA include any general anesthetic and patients with a history or family history of malignant hyperthermia or muscular dystrophy.

- Advantages of TIVA include no operating room pollution, decreased incidence of postoperative nausea and vomiting, and earlier discharge to home, thereby reducing costs.
- Awareness under anesthesia can be an issue while administering TIVA.

Drugs Used for MAC/TIVA

The aim is to have a rapid return to baseline status and facilitate early discharge. Various techniques of MAC include administering a combination of drugs (Table 3.4) with intermittent boluses and/or continuous infusions. The ideal drug used during MAC should have:

- Quick onset of action
- Short duration of action
- Minimal side effects
- High therapeutic index
- Rapid elimination (noncumulative)

Drugs commonly used for TIVA include propofol, midazolam, opioids, dexmedetomidine, and ketamine. Propofol has become the hypnotic drug of choice for the TIVA as it has a shorter context-sensitive half-life than either thiopental or etomidate. Use of dexmedetomidine causes sedation, analgesia, anxiolysis and amnesia, and hence decreased usage of narcotics and decreased incidence of PONV.

Commonly used opioids include fentanyl, alfentanil, and remifentanil. While the context-sensitive half-life of fentanyl increases markedly with prolonged infusion, remifentanil on

Table 3.3 Various types of sedation techniques and their characteristics

Parameter	Minimal sedation	Moderate/conscious sedation	Deep sedation	General anesthesia
Responsiveness	Normal response to verbal stimulation	Intermediate response to verbal stimuli	Varying response to painful stimuli	Unarousable
Airway	Unaffected	No intervention required	Intervention may be required	Intervention required
Spontaneous ventilation	Good	Adequate	May be inadequate	May have to be controlled
Cardiac function	Maintained	Usually maintained	Usually maintained	May be impaired

Table 3.4 Commonly used drugs for MAC/TIVA

Drug	Effect	Dosage	
		Intermittent boluses	Maintenance infusion
Midazolam	Sedation, amnesia	0.5–2 mg	–
Fentanyl	Analgesia	25–50 mcg	0.01–0.03 mcg/kg/min
Alfentanil	Analgesia	25–50 mcg	0.25–1 mcg/kg/min
Remifentanil	Analgesia	10–25 mcg	0.025–1 mcg/kg/min
Propofol	Hypnotic	10–30 mg	10–200 mcg/kg/min
Ketamine	Hypnotic, analgesia	10–30 mg	1–10 mcg/kg/min
Dexmedetomidine	Sedation	10–30 mcg	0.2–0.7 mcg/kg/h

the other hand has a short context-sensitive half-life. Ketamine is a dissociative anesthetic with sedative, hypnotic, and analgesic properties. Ketamine can be used with continuous infusions of propofol and help reduce opioid requirement.

Postoperative Care/Discharge Criteria

For patients receiving MAC or TIVA, the discharge criteria are similar to any patient undergoing general anesthesia (stable vital signs, awake and oriented, no nausea/vomiting, can ambulate, adequate pain control). Written discharge instructions and an emergency phone number should be given to all patients. The patient should be instructed not to operate machinery or sign legal documents for at least 24 h. A responsible adult must be available to escort the patient home.

Clinical Review

1. The following monitor may not be used during administration of general anesthesia:
   A. Pulse oximeter
   B. Noninvasive blood pressure cuff
   C. Electrocardiogram
   D. Bispectral index
2. For rapid sequence intubation, the correct statement is:
   A. No premedication is given
   B. Midazolam or fentanyl are given as premedication as required
   C. Ventilation is tested before succinylcholine is administered
   D. Application of cricoid pressure reliably prevents pulmonary aspiration
3. All of the following are criteria for extubation, except:
   A. Respiratory rate less than 35 breaths/min
   B. Respiratory rate greater than 7 breaths/min
   C. Tidal volume > 5 ml/kg
   D. Blood pressure of 80/54 mmHg
4. All of the following may trigger malignant hyperthermia, except:
   A. Sevoflurane
   B. Isoflurane
   C. Ketamine
   D. Succinylcholine
5. A 75-year-old patient comes to the hospital for an inguinal hernia repair. The patient had coffee with milk and a toast 1 h ago. The following statement is true:
   A. Since the patient has a full stomach, one can proceed with surgery under spinal anesthesia
   B. Since the patient has a full stomach, one can proceed with surgery under conscious sedation with local anesthesia
   C. One can proceed with surgery under general anesthesia in another 3 h
   D. One can proceed with surgery under general anesthesia in another 5 h
6. The true statement about total intravenous anesthesia (TIVA) when compared to complete general anesthesia is:
   A. Increased operating room pollution
   B. Increased probability of awareness under anesthesia
   C. Increased incidence of postoperative nausea and vomiting
   D. Longer stay in postoperative anesthesia care unit
7. The following anesthetic drug has analgesic properties:
   A. Propofol
   B. Ketamine
   C. Etomidate
   D. Thiopental

Answers: 1. D, 2. A, 3. D, 4. C, 5. D, 6. B, 7. B

Further Reading

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Perioperative Airway Management

4

Samuel Irefin and Tatyana Kopyeva

Airway management remains the fundamental part of anesthesia practice. Over the past two decades, many advances in technology, devices, and techniques for airway management have been made. It is extremely important for the clinician to be proficient in basic techniques and become familiar with new developments since airway management literally remains a "life or death" issue.

Airway Assessment

Airway management is an essential part of anesthesia practice. Problems with airway management carry significant risk of morbidity and mortality. The preoperative evaluation of the airway aims at predicting difficulties in airway management and allows the anesthesiologist to be prepared to deal with the "difficult airway," "Difficult airway" is a somewhat broad definition and can be divided into difficult ventilation by traditional face mask, difficult direct- or videolaryngoscopy, difficult intubation, difficult supraglottic airway placement, or a difficult surgical airway.

Patient History

Numerous congenital or acquired diseases have strong associations with difficulties in airway management (Tables 4.1 and 4.2). Thus a focused history concerning diseases or symptoms related to airway is of outmost importance.

A prior history of airway management should be carefully reviewed for any difficulties with mask ventilation, laryngoscopy, intubation, or supraglottic airway placement. It has been reported that a history of difficult or failed intubation by direct laryngoscopy, as a stand-alone test, has a likelihood ratio of approximately 6 and 22, respectively, for the prediction of subsequent difficult or failed intubation. For the test to be regarded as a powerful discriminator, a likelihood ratio over 10 should be present, which means that a history of failure is a better predictor of subsequent problem with intubation than a history of difficulty. Nonetheless, any prior difficulties should be taken very seriously, and an anesthesia provider should formulate a plan for airway management. It is also important to document any encountered airway problem and notify the patient.

If there are additional studies available, such as chest X-ray, CT scan, or flexible laryngoscopy, the results should be carefully reviewed to identify possible problems: deviation and compression of the trachea, degree of airway compression and its localization, evidence of distorted laryngeal anatomy, etc.

Physical Examination

An anesthesia provider should be aware and look for signs and symptoms of airway obstruction: marked respiratory distress, intolerance of supine position, altered voice, dysphagia, odynophagia, and the hand-to-throat choking sign. Stridor is a sign of imminent airway obstruction and indicates that the airway diameter has been reduced to 4 mm or less.

Physical examination should start with the basics: consciousness level, presence of any intoxication, and language barrier. This piece of information may profoundly influence the choice for airway management from the beginning. Any facial abnormalities, presence of facial trauma, beard, and the body habitus should be noted. A focused airway examination should be part of the evaluation of any patient presenting for anesthesia. The LEMON criteria can be used for simple airway assessment (Table 4.3).

1. Mallampati score

The patient should be in sitting position (if possible), with the neck in neutral position for proper assessment.

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Table 4.1 Acquired disease states associated with a difficult airway

Acromegaly	Thick mandible, large tongue and epiglottis, overgrowth of mucosa and soft tissues of the pharynx, larynx and vocal cords, as well as arthritis at the temporomandibular joint may make mask ventilation and laryngoscopy difficult. Glottic and subglottic narrowing may require a smaller endotracheal tube size. Nasal intubation or placement of a nasal airway may be impossible due to nasal turbinate enlargement
Angioedema	Progressive swelling of the tongue and pharyngeal mucosa may make mask ventilation and laryngoscopy difficult or impossible
Ankylosing spondylitis	Flexion deformity of cervical spine may make direct laryngoscopy extremely difficult, if at all possible, and involvement of the temporomandibular joint (TMJ) will compound the problem further
Burns of the head and neck	Massive mucosal edema within 2–24 h from thermal damage to the upper airway may cause severe airway compromise and difficult laryngoscopy and intubation. Scars developing, as the burns heal, may limit mouth opening and neck mobility
Cervical spine limitations	Osteoarthritis, degenerative changes, fusion, etc. Limitations of cervical spine mobility (both extension and flexion) may render mask ventilation, laryngoscopy, and intubation difficult
Diabetes mellitus	Long-term diabetes may reduce atlanto-occipital joint mobility and make laryngoscopy difficult
Hypothyroidism	Development of myxedema and macroglossia make mask ventilation and laryngoscopy difficult
Infections	Epiglottitis, retropharyngeal and submandibular abscess, Ludwig's angina. Airway may be severely distorted making mask ventilation and laryngoscopy and intubation extremely difficult
Irradiation	To the head and neck (fibrosis) may make mask ventilation and laryngoscopy difficult to impossible
Obstructive sleep apnea	Anatomical and physiological features of obstructive sleep apnea (OSA) reduce the skeletal confines of the tongue, change the shape of the airway, and predispose to both difficult mask ventilation (DMV) and difficult intubation (DI). DI is related to the severity of OSA: patients with apnea-hypopnea index > 40 have a higher incidence of difficult intubation
Pregnancy	DI is reported to be 1.3–16.3 % in parturients, with an incidence of failed intubation around 1:300 to 1:800, which is higher than the general population. Difficulties in airway management are attributed to generalized soft tissue swelling, which may cause macroglossia, supraglottic edema, and increased tissue friability. Laryngeal edema worsens during labor and pushing. Weight gain with deposition of fat around the neck, breast engorgement, positioning requirements, cricoid pressure may all interfere with laryngoscopy
Rheumatoid arthritis	TMJ involvement leads to limited mouth opening, cervical spine arthritis, impaired neck mobility with subsequent DMV and DI. Atlantoaxial subluxation compounds the problem and increases the risk of spinal cord injury
Scleroderma	Small mouth with decreased opening and tight facial skin, hardening of the submandibular tissues make laryngoscopy difficult
Trauma	Maxillary or mandibular injury, cervical spine injury, neck trauma or surgery with edema, hematoma, airway disruption
Tumors	Maxillofacial region, oropharyngeal, laryngeal, or neck malignancies distort the anatomy
Miscellaneous	Lingual tonsil hypertrophy, laryngeal papillomatosis, laryngeal sarcoidosis, foreign bodies may lead to airway obstruction and difficult mask ventilation and intubation

Table 4.2 Congenital syndromes associated with a difficult airway

Down's	Obstructive sleep apnea, small mouth opening, large tongue, subglottic stenosis, atlantoaxial instability
Goldenhar	Hemifacial microsomia, cervical vertebral anomalies, scoliosis
Klippel-Feil	Congenital synostosis of some or all of cervical vertebrae resulting in neck rigidity
Pierre Robin	Micrognathia, cleft palate, glossoptosis, small mouth
Treacher Collins	Maxillary, zygomatic, and mandibular dysplasia
Turner	Short neck with limited mobility, contracture of the temporomandibular joint, maxillary and mandibular hypoplasia

Table 4.3 LEMON score for airway assessment

L = Look externally	Facial trauma, narrow mouth, short thick neck, large incisors, presence of a beard, protruding jaw, large tongue
E = Evaluate	The 3-3-2 rule Inter-incisor distance (mouth opening)—normal >3 fingerbreadths Hyoid-mental distance—normal >3 fingerbreadths Thyroid cartilage-mouth floor distance—normal >2 fingerbreadths
M = Mallampati score	Class I–IV
O = Obstruction	Presence of any condition that could cause an obstructed airway (abscess, hematoma, epiglottitis, tumor)
N = Neck mobility	Check for neck flexion, extension, and limited neck mobility (avoid in patients with neck injury)

The mouth should be opened maximally and the tongue protruded without phonation. An observer grades the view depending on oropharyngeal structures seen (Fig. 4.1).

Class I—soft palate, fauces, uvula, and tonsillar pillars (anterior and posterior) visible

Class II—soft palate, fauces, and uvula visible

Class III—soft palate and base of the uvula visible

Class IV—soft palate is not visible at all

Although Mallampati classes III and IV correlate with almost sixfold increase of difficult intubation, only about 35 % of the patients with difficult intubation are correctly identified using the score.

2. Jaw protrusion test or its modification—upper lip bite test (ULBT). ULBT evaluates the presence of mandibular subluxation and buckteeth at once. Additionally, one should look for a recessed mandible or protruding jaw.

   Class I—lower incisors can bite above the vermilion border of the upper lip

   Class II—lower incisors cannot reach vermillion border

   Class III—lower incisor cannot bite upper lip

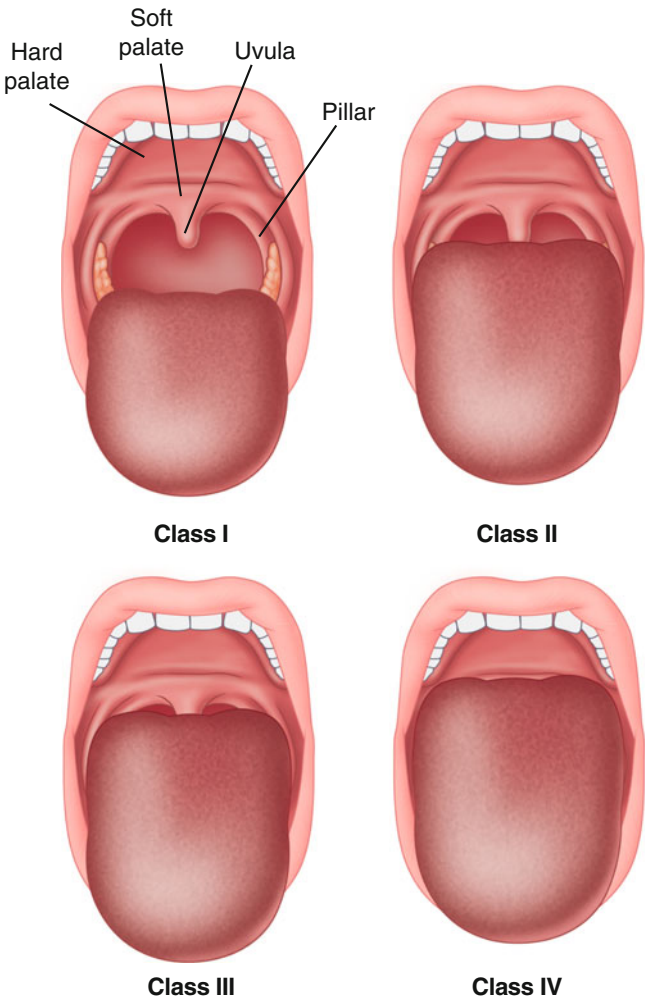

Fig. 4.1 Mallampati airway classification

3. Dentition should be assessed and findings documented: prominent upper incisors (protruding teeth), loose or missing teeth, dentures.
4. Neck range of motion: both flexion and extension are checked, and any neurological changes with the movement of the cervical spine noted. Normal neck extension at atlanto-occipital joint is 35°.
5. Mouth opening: normal inter-incisor distance is 4–6 cm (>3 finger breadths).
6. Thyromental distance: mentum to upper border of thyroid cartilage is measured (normal >3 ordinary finger breadths, corresponds to 6 cm).
7. Compliance of submandibular space should be checked: it is the space where the tongue is displaced during direct laryngoscopy.
8. Miscellaneous: large tongue, short and thick neck, deviated trachea.
9. Presence of any airway pathology (tumor, abscess).

Prediction of Difficult Mask Ventilation

Standard definition of difficult mask ventilation (DMV) is lacking at present, which may be related to the very subjective and operator-dependent nature of the skill. Risk factors for DMV are listed in Table 4.4. The acronym "OBESE" can be used to remember the predictors of DMV (O-obese, B-bearded, E-elderly, S-snorers, E-edentulous). The incidence of DMV has been reported to be 1.4–2.2 %, while that of impossible mask ventilation 0.15 %. Although DMV does not necessarily mean difficult intubation, there is a relationship between the two. Patients with DMV have a fourfold increase in the incidence of difficult intubation and a 12-fold increase in the incidence of impossible intubation. ASA definition for DMV is as follows:

> It is not possible for the anesthesiologist to provide adequate ventilation because of one or more of the following problems: inadequate mask or SGA seal, excessive gas leak, or excessive resistance to the ingress or egress of gas. Signs of inadequate ventilation include (but are not limited to) absent or inadequate chest movement, absent or inadequate breath sounds, auscultatory

Table 4.4 Risk factors for difficult mask ventilation

BMI ≥ 30 kg/m^2
Presence of a beard
History of snoring/obstructive sleep apnea
Age ≥ 55 years
Mallampati III or IV
Limited mandibular protrusion test
Airway masses/tumors
Male gender
Edentulous state
Neck radiation changes (strong predictor)

signs of severe obstruction, cyanosis, gastric air entry or dilatation, decreasing or inadequate oxygen saturation (SpO_2), absent or inadequate exhaled carbon dioxide, absent or inadequate spirometric measures of exhaled gas flow, and hemodynamic changes associated with hypoxemia or hypercarbia (e.g., hypertension, tachycardia, arrhythmia).

The use of Han's Mask Ventilation and Description Scale may be recommended for clinical description of mask ventilation:

Grade 0—ventilation by mask not attempted
Grade 1—ventilated by mask
Grade 2—ventilated by mask with oral airway or other adjuvants
Grade 3—difficult mask ventilation (inadequate, unstable, or requiring two practitioners)
Grade 4—unable to mask ventilate

Prediction of Difficult Intubation

To date there is no international agreement on the definition of "difficult intubation." The American Society of Anesthesiologists defines difficult intubation as tracheal intubation requiring multiple attempts, in the presence or absence of tracheal pathology. Often the terms "difficult intubation" and "difficult laryngoscopy" are used interchangeably, though difficult laryngoscopy does not always lead to difficult intubation. With difficult laryngoscopy, it is not possible to visualize any portion of the vocal cords after multiple attempts at conventional laryngoscopy (Cormack-Lehane Grade 3 and Grade 4 view of glottic opening). The reported incidence of DI varies and may be as high as 10.3 % for emergent intubation, with the incidence of failed intubation from 0.05 to 0.35 %. Generally accepted predictors of difficult intubation are listed in Table 4.5.

Conventional teaching requires establishing mask ventilation after induction of anesthesia before giving muscle relaxants in fear of not returning to spontaneous ventilation and the ability to wake up a patient in case of difficulties with airway management. Some data suggests that avoidance of neuromuscular blocking agents may actually increase the risk of difficult tracheal intubation. That may especially be the case with high-dose opioids sometimes producing vocal cord adduction. The continuing practice of mandatory conformation of ventilation before administration of muscle relaxants contradicts the widely accepted practice of rapid sequence induction, where total muscle paralysis is achieved without any such conformation.

Since none of the current tests can reliably predict difficult airway in patients whose airway looks "normal," it is imperative for the anesthesia provider to be prepared to deal with unforeseen difficulties at any time.

Table 4.5 Predictors of difficult intubation

History of prior difficult intubation
Long, protruding upper incisors
Prominent "overbite" (maxillary incisors override mandibular incisors)
High ULB test scores (failed TMJ translation)
Inter-incisor distance less than 3 cm
Mallampati Class III or IV
Noncompliant submandibular space
Thyromental distance less than 6 cm (three ordinary finger breadths)
Highly arched or very narrow hard palate
Short thick neck
Limited cervical spine range of motion (flexion or extension)
BMI > 35 kg/m^2

Prediction of Difficult Insertion of Supraglottic Airway Devices

In spite of the worldwide use of numerous supraglottic airway devices (LMA Classic used in about 200 million anesthetics), data on predictors of difficult insertion and predictors of failure of such airway devices are lacking. Supraglottic airway devices are incorporated in the ASA Difficult Airway Algorithm as rescue devices in the "cannot intubate, cannot ventilate" situation and have been shown to be effective in such scenarios on multiple occasions.

Limited mouth opening and restricted atlanto-occipital joint range of motion insertion (especially fixed flexion deformity of the neck) may present difficulties during laryngeal mask airway (LMA) insertion. LMA is also not recommended for use in patients with oropharyngeal pathology. One large retrospective study identified four independent risk factors of LMA Unique failure (defined as an acute airway event requiring LMA Unique removal and rescue intubation): surgical table rotation, male sex, poor dentition (missing teeth), and increased BMI.

Prediction of Difficult Videolaryngoscopy

Videolaryngoscopy is a rapidly developing technique in airway management with continuous addition of new and improved devices. But as with the supraglottic airway devices, data on prediction of difficulties with videolaryngoscopy is lacking. It is possible that predictors may be somewhat different for different groups of the videolaryngoscopes (Macintosh-type blades vs. highly curved blades vs. devices with tube-guiding channels).

It has been shown, however, that for the GlideScope most of the standard predictors of difficult laryngoscopy, with the possible exception of high ULB test score, are not predictors of intubation difficulties. The strongest predictor of the GlideScope failure is altered neck anatomy with presence of a surgical scar, radiation changes, or mass.

Prediction of Difficult Surgical Airway

Emergent surgical airway usually is the last resort for the anesthesiologist, but occasionally it may be the only option for airway management. Data on the predictors of difficult emergent tracheostomy or cricothyrotomy is very limited since the occurrence of the event is rare. Most of the difficulties are related to inaccurately localizing the trachea or a cervical spine flexion deformity.

A short thick neck, obesity, neck masses (hematoma, infectious process, goiter, packets of lymphatic nodes), burns, or radiotherapy can make localization of the trachea difficult, especially in an emergency. In such cases real-time ultrasonography of the neck may be helpful. Ultrasonography may be used to identify and mark the trachea or cricothyroid membrane or place a transtracheal catheter before attempting airway management in cases of suspected difficult airway and/or difficult surgical airway.

Airway Management

Nonintubation Airway Management Techniques and Equipment

Management of the airway during anesthesia does not always call for tracheal intubation or supraglottic airway device placement. In cases of regional anesthesia, procedural sedation, and total intravenous anesthesia with spontaneous respiration, it may be sufficient for the anesthesiologist to provide supplemental oxygen and ensure an unobstructed airway. It is important to know that any type of oxygen therapy is a potential fire hazard, especially when the surgical site is close to the airway or an oxygen source and cautery is being used.

Management of nonintubated patients with spontaneous respirations includes continuous monitoring of end-tidal CO_2, respiratory pattern, and oxygen saturation. While nonintubated, the anesthesia provider must be aware of the potential for partial or total upper airway obstruction and treat it accordingly. Obstruction can happen at the pharyngeal level (loss of pharyngeal muscle tone, anatomic airway abnormalities, space-occupying lesions, foreign bodies), at the hypopharyngeal level (epiglottis obstructing the airway), and at the laryngeal level (laryngospasm, foreign bodies, secretions).

Partial airway obstruction often manifests with noisy expiration or inspiration (snoring, stridor). Complete airway obstruction is a medical emergency and manifests with absence of chest expansion with inspiratory effort, inaudible breath sounds, absence of perceivable air movement, use of accessory muscles, and sternal, epigastric, and intercostal retractions with inspiration. Airway patency may be established with simple maneuvers: head tilt-chin lift and jaw thrust. Some describe "the triple maneuver": head tilt, jaw thrust, and mouth opening or head tilt, flexion at lower cervical spine, and jaw thrust. Head tilt-chin lift is contraindicated in patients with cervical spine instability and basilar artery syndrome; jaw thrust is contraindicated in patients with a fractured or dislocated mandible and awake patients. All secretions should be suctioned.

Oxygen Delivery Systems

Oxygen delivery systems may be divided into low-flow systems (most commonly used perioperatively) and high-flow systems. Flow systems should not be confused with delivered oxygen concentration: high-flow devices (such as a Venturi mask) can deliver FiO_2 (fraction of inspired oxygen) as low as 0.24, while low-flow devices (such as a nonrebreathing mask) can deliver an FiO_2 of 0.9 or more. With high-flow systems the patient's ventilatory demand is completely met by the system, but if a system fails to meet the ventilatory demands of the patient, it is classified as a low-flow system.

Low-Flow Systems/Devices

They include nasal cannulas, simple face masks, partial rebreathing masks, nonrebreathing masks, face tent, tracheostomy collar, and transtracheal catheter.

Nasal cannulas

These are simple, easy tolerated by patients, and require that the nasal passages be patent. Nasal cannulas allow an FiO_2 delivery of approximately 0.24–0.44, with oxygen flow rates from 1 to 6 L/min. For each 1 L/min increase in flow, the FiO_2 increases approximately by 4 %, though the FiO_2 can be inaccurate and inconsistent depending on the inspiratory demand of the patient (variable amount of room air entrained with different tidal volumes). Increasing the oxygen flow rate above 6 L/min does not increase the FiO_2 much further than 0.44. The use of >4 L/min O_2 flow requires a humidifier to prevent the mucous membranes from drying and crusting, epistaxis, or causing laryngitis.

Simple face masks

These allow a higher FiO_2 due to increase in the size of the O_2 reservoir (100–200 mL as additional O_2 reservoir volume). An FiO_2 of 0.4–0.6 can be achieved with O_2 flows of 5–8 L/min. O_2 flow should be at least 5 L/min to prevent CO_2 accumulation and rebreathing. Gas flows >8 L/min do not increase FiO_2 significantly over 0.6.

Partial rebreathing masks

These are simple masks with a reservoir bag (600–1,000 mL). An FiO_2 of 0.6–0.8+ can be achieved with an oxygen flow of 6–10 L/min. Partial rebreathing occurs because the first 33 % of the exhaled volume derived from anatomic dead space fills the reservoir bag and subsequently gets inhaled

with the fresh gas during the next respiratory cycle. To minimize rebreathing, the O_2 flow should be kept at 8 L/min or more, sufficient to keep the reservoir bag 1/3 to 1/2 inflated during the entire respiratory cycle.

Nonrebreathing masks

These have three unidirectional valves allowing venting of exhaled gas and preventing room air entrainment. Oxygen flows of 10–15 L/min are used to deliver an FiO_2 of 0.8–0.9. If room air is not entrained from around the mask, an FiO_2 of 1.0 can be potentially achieved with 15 L/min of oxygen flow.

High-Flow Devices

They include Venturi masks, high-flow nasal cannulas, air entrainment nebulizers, and air-oxygen blenders.

Venturi masks

Two types of Venturi masks are available: a fixed FiO_2 model with color-coded specific attachments and a variable FiO_2 model with a graded adjustment. Venturi masks use the Bernoulli principle and constant-pressure jet mixing to entrain air and provide the needed FiO_2. Alterations in the gas orifice or entrainment port size change the FiO_2. The oxygen flow determines the total gas flow by the device, not the FiO_2. The minimum recommended O_2 flows for a certain FiO_2 should be used with the standard air-O_2 ratios. Venturi masks provide reliable FiO_2 of 0.24–0.5 and are very useful in patients in respiratory distress, as delivered FiO_2 is not dependent on the patient's inspiratory demand. As FiO_2 increases, the total gas flow decreases due to reduction in air entrainment.

High-flow nasal cannulas

Oxygen gas flow through regular low-flow nasal cannulas is limited to 16 L/min. High gas flows through regular nasal cannulas can cause patient discomfort, frontal sinus pain, irritation, and drying of the nasal mucosa because of lack of humidification. High-flow nasal cannulas (HFNC) have the advantages of providing warmed and humidified gas flows up to 50 L/min with FiO_2 0.72–1.0. HFNCs offer independent adjustments of FiO_2 and gas flow, a design feature which allows greater flexibility to match the needs of acutely ill patients. In addition, they generate moderate level of continuous positive airway pressure (CPAP), thereby improving pulmonary dynamics. HFNCs can be useful in patients with marginal oxygenation, for whom removing a face mask for eating, drinking, or the need to frequently expectorate to clear pulmonary secretions could precipitate hypoxemia.

Pharyngeal Airways

Oropharyngeal and nasopharyngeal airways of different sizes (correct size—distance from lip to ear lobe) are available to assist in establishing the upper airway patency in the nonintubated patient (Fig. 4.2). Oropharyngeal airways, if used in lightly anesthetized patients with intact pharyngeal and laryngeal reflexes, may lead to airway hyperreactivity (coughing, gagging with emesis, laryngospasm, bronchospasm). Oropharyngeal airways can cause trauma to oropharyngeal structures, including dental trauma.

Nasopharyngeal airways are inserted with adequate lubrication and are better tolerated than oral airways by awake or lightly anesthetized patients. They may be preferable in cases of oropharyngeal trauma. Complications of nasopharyngeal airways include epistaxis, submucosal tunneling, avulsion of the turbinates, and pressure ulcers. There are some contraindications (absolute and relative) to the use of nasopharyngeal airways: nasal fractures, known nasal airway occlusion, coagulopathy, cerebrospinal fluid rhinorrhea, known or suspected basilar skull fracture, adenoid hypertrophy, and prior transsphenoidal hypophysectomy.

Mask Ventilation

A proper bag-mask ventilation technique is one of the fundamental skills required for every anesthesiologist (Fig. 4.3).

Uses

Mask ventilation technique is minimally invasive and is used for assisted or controlled ventilation during resuscitation, for preoxygenation with spontaneous ventilation; during sedation with inadequate spontaneous ventilation, as a transitional airway technique after induction; and before intubation or after extubation, for general anesthesia by mask, and in case of failed endotracheal intubation. It is minimally stimulating and can be performed even on an awake patient and does not require neuromuscular blockers.

Characteristics of a face mask

The standard face mask has three parts: a body, an air-filled cushion rim, and a connector. The most common style of mask used nowadays is a disposable, transparent plastic mask (allows to see the condensation from exhalation, the presence of any secretions or vomiting, and the patient's color). Masks come in different sizes, are designed to fit different contours of the patient's face, and provide adequate seal for leak-free ventilation (spontaneous and controlled). Some masks still come with a collar around the connector and hooks to allow attachment of straps for hands-free airway maintenance. With the wide use of supraglottic airway devices, such a technique is now largely of historical interest. Most of the masks are made to cover both the nose and the mouth of the patient, but there are also nasal masks covering only the nose and potentially creating a better seal and causing less obstruction during controlled ventilation even in the neutral position.

Prerequisites for mask ventilation

Mask ventilation requires a few things for success: the airway must be patent, the seal between the mask and the patient's face must be effective, and the mask should be

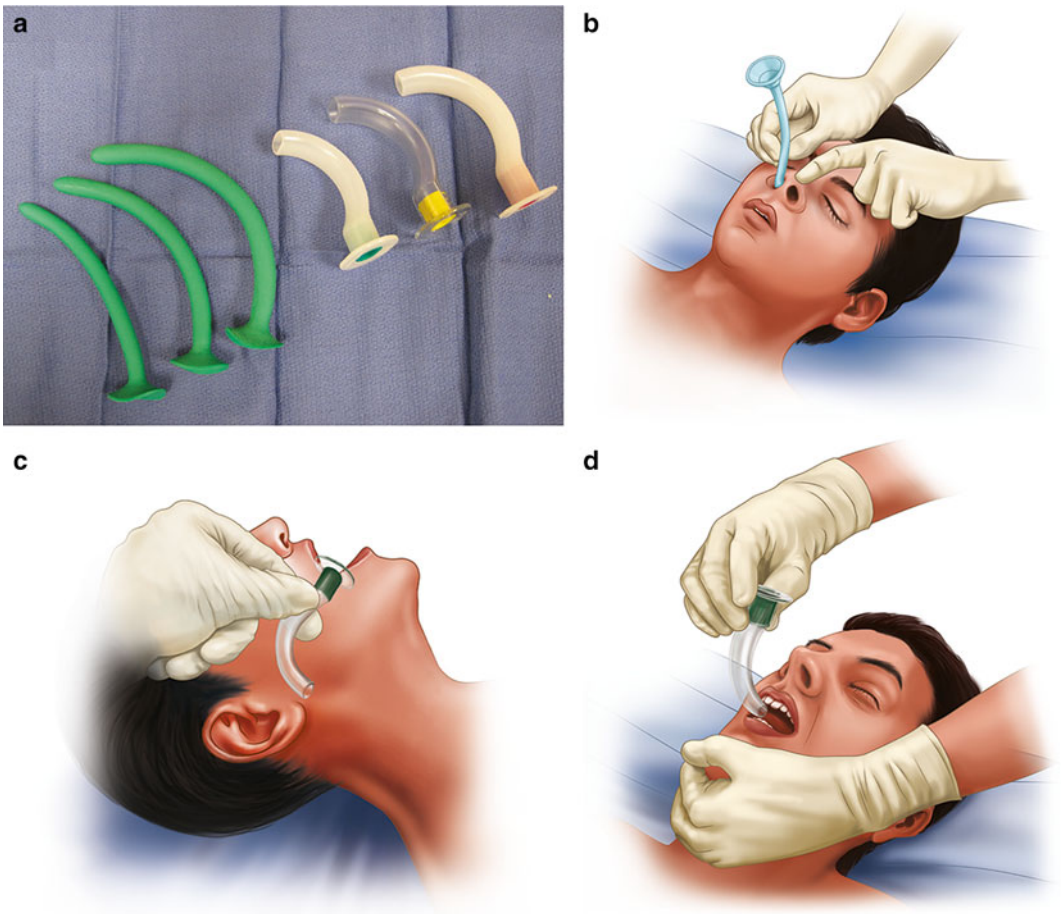

Fig. 4.2 (**a**) Nasal and oral airways of different sizes. (**b**) Insertion technique of a nasal airway. The nasal airway is always lubricated prior to insertion. (**c**) Sizing of an oral airway (distance from lip to ear lobe). (**d**) Insertion technique of an oral airway. Once the airway touches the hard palate, it is rotated 180° and seated in the mouth. If a tongue depressor is used to insert an oral airway, then the oral airway is inserted with the airway's curvature following the curvature of the patient's airway

attached to a bag-valve system (anesthesia circle system in the operating room or air-mask-bag unit; "Ambu" bag outside the operating room).

Techniques of mask ventilation

There are two techniques for mask ventilation: the "one person" technique and the "two person" technique. With the one-person technique, an anesthesia provider uses one hand to hold the mask while the second hand squeezes the bag to provide positive pressure ventilation. Usually, the thumb and index finger are placed on the body of the mask to apply downward pressure to achieve a good seal, at the same time using the middle and ring fingers to lift the chin and pull the mandible toward the mask, while the little finger hooks under the angle of the mandible to lift it anteriorly. These maneuvers lead to upper cervical extension as well. With the two-person technique, one person applies the mask and establishes a patent airway with a good seal using both hands, while the second person squeezes the bag.

Assessment of ventilation

During mask ventilation constant attention should be paid to assess the effectiveness of the technique: monitoring chest excursion, exhaled tidal volumes, presence of breath sounds, signs of airway obstruction, presence of leaks, pulse oximetry data, and capnography (if available).

Contraindications and complications

Mask ventilation is relatively contraindicated in patients with increased risk of aspiration (full stomach, hiatal hernia, esophageal motility disorders, pharyngeal diverticula); however, even in such patients, with failed intubation, it is more important to oxygenate the patient than to prevent aspiration. Mask ventilation is impractical for surgeries lasting longer than 60 min and should be used with extreme caution in surgeries requiring a position other than supine or when it is difficult to easily access the head of the patient. During mask ventilation the ventilatory pressure should generally not exceed 20 cm H_2O as gastric insufflation is

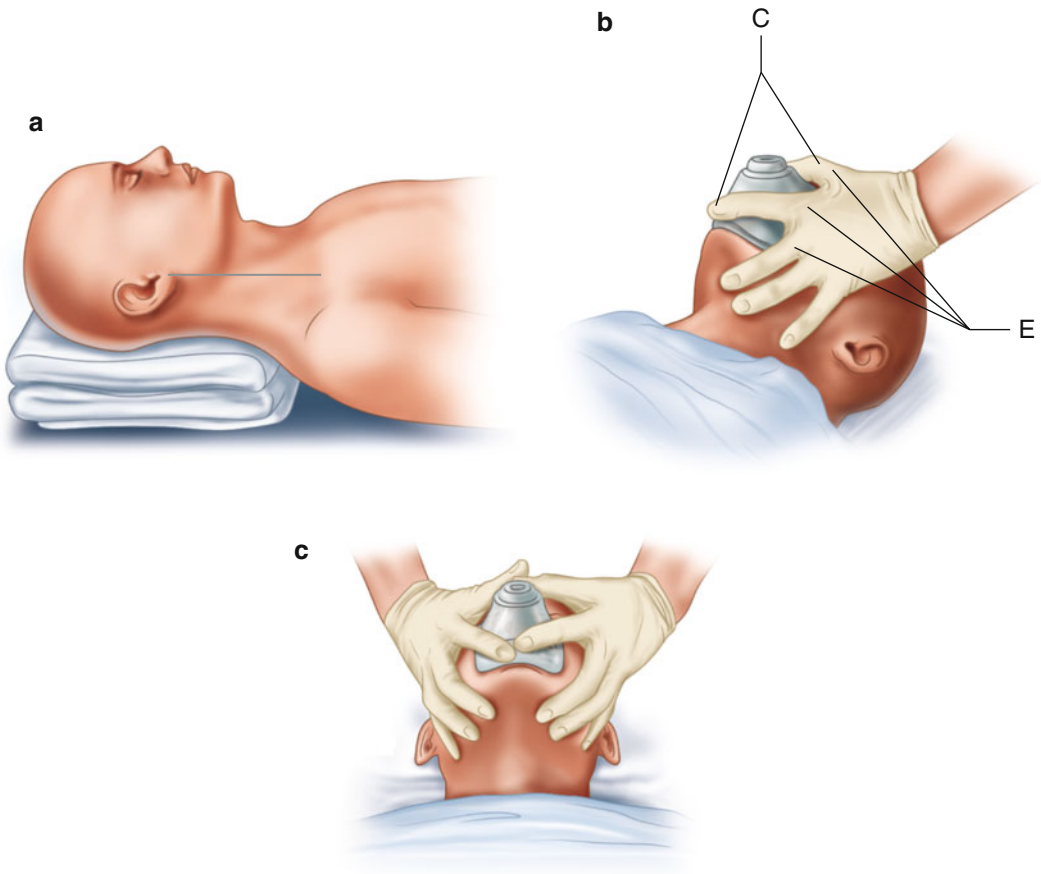

Fig. 4.3 Bag-mask ventilation. (**a**) Aligning the external auditory meatus with the sternal notch. (**b**) One-provider technique: the "EC" hand position sealing the mask on the face. (**c**) Two-provider technique: one provider holds the mask with both hands, while the second provider squeezes the bag

common with higher pressures and leads to increased risk of aspiration and/or regurgitation. Complications of mask ventilation include aspiration, airway obstruction, lip or dental trauma, and facial or ocular pressure injury.

Supraglottic Airway Devices

Supraglottic airway devices (SADs) represent a group of airway devices designed to be inserted into the oropharynx to establish and maintain a clear, unobstructed airway without entering the larynx. Some prefer the term "extraglottic airway devices" since many of these devices have components that are positioned in the hypopharynx and upper esophagus (i.e., infraglottic), but SAD is the more widely accepted and used term.

Uses and advantages

SADs are used for temporary airway management during anesthesia, for airway rescue after failed intubation and mask ventilation, as a conduit for tracheal intubation and during cardiopulmonary resuscitation in and out of hospital. There are several advantages of SAD use over endotracheal intubation and mask ventilation: rapid learning curve, improved hemodynamic stability on induction and emergence, and lower incidence of coughing on emergence. In the past 10–15 years, more than 40 SADs have been introduced, but not all of them remain in clinical practice.

The indications for safe use of SADs are continuously growing as more and more anesthesia providers become familiar and confident with their use. They are being used during anesthesia in spontaneously breathing patients as well as with positive pressure ventilation. They are being increasingly used in the operating room as well as for procedures outside the operating room, such as in radiology and magnetic resonance imaging, radiation therapy, cardiologic procedures, diagnostic and invasive endobronchial procedures, and ophthalmologic procedures.

SADs have became part of airway management during various procedures, such as tonsillectomy and adenoidectomy, dental and oral surgeries, and awake craniotomies. It still remains highly controversial to use SADs for routine use due to very limited data on safety in morbidly obese patients, during laparoscopic surgeries, in positions other than supine (prone, lateral), or in elective C-sections. However, in case of emergency (i.e., inability to intubate for emergent C-section, intraoperative loss of airway), SADs can be and should be used either for the entire procedure if feasible or until a definite airway can be established.

If SADs are used for positive pressure ventilation, the following may be considered:

- Patients should have normal lung compliance and airway resistance.
- Limit tidal volumes to 8 mL/kg with constant vigilance for adequacy of ventilation and amount of leak. Do not exceed airway pressures recommended for the specific SAD to prevent gastric insufflation.
- Select the largest SAD size appropriate for the patient.
- Follow correct insertion and fixation technique.
- Always auscultate over the stomach to ensure that there is no gastric insufflation.
- Maintain an adequate level of anesthesia and muscle relaxation if muscle relaxants are being used.
- If leaking occurs, and the leak is substantial and ventilation is inadequate, investigate the cause and try to correct it before considering endotracheal intubation.

Classification of SADS

There have been several attempts to classify the SADs. Practically, one may classify SADs on the basis of specific design features to improve safety (Table 4.6). SADs designed to prevent or decrease the risk of aspiration have either a gastric access channel (ProSeal LMA, LMA Supreme, Laryngeal Tube Suction II or Gastro-Laryngeal Tube, i-gel, Baska Mask) or a chamber for accepting some regurgitant content (streamlined liner of the pharynx airway—SLIPA) or have a double-lumen tube with one lumen used as a gastric port for venting or suctioning (Combitube, EasyTube).

The Laryngeal Mask Airway Classic (cLMA) was the first commercially available SAD. Note that LMA is a protected term and is used to refer to laryngeal mask airways produced by the LMA Company (now part of Teleflex). LM refers to laryngeal masks manufactured by anyone other than the original manufacturer.

Table 4.6 Classification of supraglottic airway devices (SAD)

SAD with an inflatable periglottic cuff:
Ultra CPV (Cuff Pilot Valve) family (AES)
Ambu Aura family (Ambu)
Air-Q/Intubating Laryngeal Airway (ILA) (Cookgas)
Vital Seal (GE Healthcare)
King LAD family (King Systems)
Laryngeal Mask Airway (LMA) device family (LMA Company)
Soft Seal Laryngeal Mask (Portex)
Sheridan Laryngeal Mask (Teleflex)
SADs with no inflatable cuff:
I-gel (Intersurgical)
Slipa (Slipa Medical)
Baska Mask
SADs with two inflatable cuffs:
Laryngeal Tube family (King Systems)
Esophageal Tracheal Combitube (Nellcor)
Rusch EasyTube (Teleflex)
SADs with single pharyngeal inflatable cuff:
Cobra Perilaryngeal Airway (PLA) family (Pulmodyne)
Tulip Airway Device (Marshall Medical)

The cLMA is designed to form end-to-end seal against the periglottic tissues with the cuff encircling the laryngeal inlet once it is inserted correctly and the cuff is inflated. It is composed of a teardrop-shaped laryngeal mask with an inflatable cuff, airway tube, two bars at the junction of the airway tube and the mask to prevent the epiglottis from obstructing the ventilation lumen, pilot tube with the balloon, and a standard 15 mm connector.

Types of LMAs

There are eight sizes for cLMA: six full and two half sizes, for use in pediatric and adults patients. Several types of somewhat differently designed LMAs are available (Fig. 4.4):

- LMA Unique—cLMA with its disposable version
- LMA Flexible—with a flexible reinforced airway tube which allows the anesthesiologist to share the airway with the surgeon
- LMA Fastrach—or intubating LMA designed to facilitate blind or fiberoptically guided tracheal intubation
- LMA ProSeal—which has a gastric port for gastric venting, allowing use with higher pressures for positive pressure ventilation
- LMA Supreme—which combines the features of LMA ProSeal and Fastrach and is disposable like the LMA Unique
- Reusable LMA Classic Excel—designed to assist in tracheal intubation while retaining all the features of cLMA

Technique of insertion

In order to achieve better success with the insertion and less troubleshooting, a proper technique should be used (Fig. 4.5, Table 4.7). The basic insertion technique is applicable for insertion of all LMA models. It provides a reliable airway with lesser chance of failure and results in minimal stress response and has a low complications risk.

Complications

The majority of complications from SADs are from minor mucous membrane injuries and manifest as a dry mouth and sore throat, which usually resolve quickly. More serious complications have been described but are rare. They include trauma to the epiglottis and larynx, dysphonia, hypoglossal and lingual nerve palsy, and tongue cyanosis secondary to vascular compression. Esophageal rupture with the use of Combitube has been reported as well. With such a wide variety of SADs currently in clinical use, it would be strongly advised to study manufacturer's recommendations for use and at least some available literature before incorporating the device in everyday clinical practice.

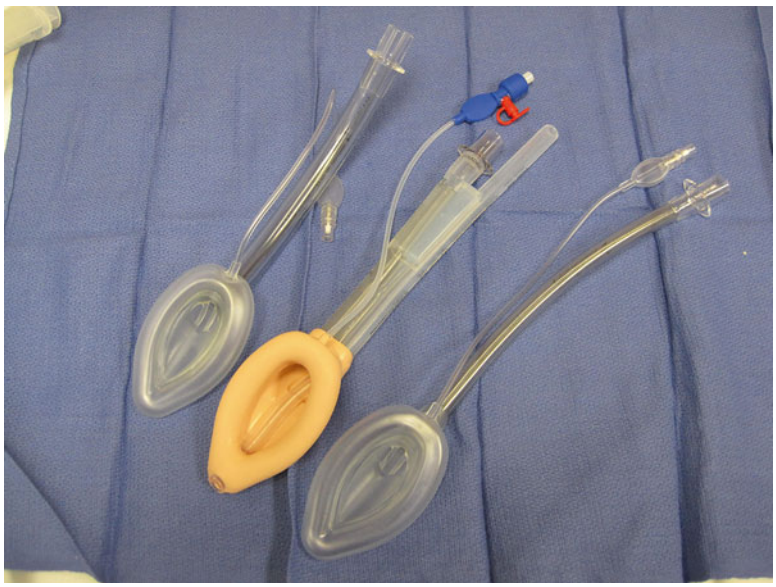

Fig. 4.4 Common types of laryngeal mask airways (LMAs), from *left* to *right*: Classic, ProSeal (port for insertion of orogastric tube), Flexible (wire reinforced)

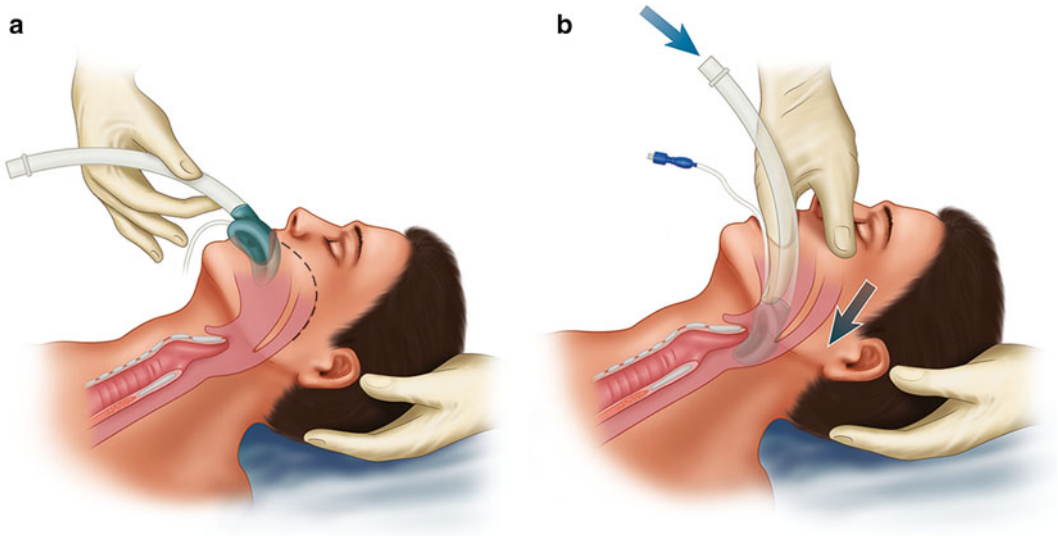

Fig. 4.5 LMA insertion technique

LMAs and Aspiration Risk

Of all the SADs, the laryngeal mask airways have been studied the most since their introduction. The LMA Classic remains the benchmark against which all other SADs are judged. Although cLMA is not designed to protect against pulmonary aspiration, with proper selection of patients (excluding non-fasted patients for emergency surgeries and patients at high risk of aspiration), its safety is comparable to endotracheal intubation in patients for elective procedures.

Pulmonary aspiration during elective surgeries is a rare event. It is also unknown if the design of LMA ProSeal truly decreases the incidence of aspiration. If regurgitation or aspiration occurs during the surgery despite proper selection of the patient, correct insertion technique, and adequate depth of anesthesia, the following plan of action should be strongly considered:

- Notify the surgeon immediately.
- Do not attempt to remove the LMA: removing may worsen the situation since the LMA still provides some protection and shields from more fluid entering the larynx.
- Put the patient in Trendelenburg position while temporarily disconnecting the circuit to allow the fluid to drain passively.
- Suction the LMA and administer 100 % O_2.
- Deepen the anesthetic (e.g., with propofol) if necessary.
- Ventilate the patient manually with low fresh gas flow and small tidal volumes to minimize the distal spread of the aspirated fluid.

Table 4.7 Insertion technique for laryngeal mask airway (LMA)

• Correct mask deflation is important: the laryngeal mask should be fully deflated with the tip not following the curvature of the palate. Deflating the mask such that it follows the curvature makes the leading edge of the mask more prominent during the insertion, and it is more likely to catch on the tongue or epiglottis
• The posterior part of the deflated mask should be well lubricated just before insertion with water-soluble jelly
• LMA is held like a pen with the index finger at the anterior junction of the airway tube and the mask
• The nondominant hand maintains firm caudal pressure on the occiput from the start of insertion. This maneuver achieves head extension, neck flexion (as in sniffing position), and mouth opening at the same time. It widens the oropharyngeal angle and lifts the larynx away from the posterior pharyngeal wall facilitating LMA insertion. An assistant may apply chin lift or jaw thrust to facilitate the insertion
• The mask needs to be flattened against the hard palate so that the hollow form of the mask will invert
• The index finger is advanced toward the occiput and is inserted to its fullest extent until resistance is felt
• The nondominant hand at this moment should move from behind the head to grasp the proximal end of LMA, before removing the index finger to prevent the LMA from sliding out of position. If the LMA is not fully inserted at this point, the nondominant hand can press it down further
• The cuff of the mask is then inflated. When correctly inserted the LMA will come out 1–2 cm during inflation. Recommended cuff pressure is <60 cm H_2O and can be measured with a manometer. Usually, adequate seal is achieved with the cuff pressure <30 cm H_2O, after the first 10 mL of air are inserted into the cuff. High cuff pressures may cause mucosal and nerve damage if the LMA is kept for a long period
• Once the cuff is inflated, the anesthesia circuit is connected to confirm adequate ventilation
• The LMA is fixed into position using tape. A bite block may be inserted to prevent the patient from biting on the LMA

- Before making a decision to intubate the patient, consider the evaluation of the tracheobronchial tree with a fiberoptic scope to confirm aspiration below the vocal cords and suction any aspirated fluid.

Intubation Techniques for Perioperative Airway Management

Endotracheal intubation is the placement of an endotracheal tube (ETT) into the trachea via the nasal, oral, or tracheal route. It provides a patent protected airway and allows controlled ventilation with high airway pressure, removal of tracheobronchial secretions, lung isolation, and administration of medications.

Indications for Endotracheal Intubation

The indications for perioperative intubation may be broadly divided into surgical and patient related. An anesthesia provider should be always prepared for intubation during anesthesia: surgical plans may change, ventilation with SADs may become inadequate, and complications during surgery (massive blood loss, anaphylaxis) and regional anesthesia (inadequate regional anesthesia, high spinal, local anesthetic toxicity) may arise and so the need for resuscitation.

- Elective endotracheal intubation is indicated for major surgeries when there is a need for controlled ventilation or lung isolation and for cases with unusual positioning, long duration of the surgery, or the need for airway access.
- Endotracheal intubation is indicated for protection against aspiration in patients at high risk for resuscitation, when the gas exchange is likely to be impaired, when there is possible use of high pressures for ventilation, and in patients who will require prolonged postoperative intubation.

The Endotracheal Tube

Essential equipments for intubation include the endotracheal tubes (ETT). Besides the standard single-lumen endotracheal tubes, double-lumen tubes, reinforced flexible tubes, pre-shaped tubes (oral and nasal RAE), laser tubes, and microlaryngeal tubes are available. The choice of the tube is mostly dictated by the surgery.

ETTs are commonly made of polyvinyl chloride (PVC) and consist of a tube, cuff (sometimes uncuffed for pediatric patients), pilot balloon, self-sealing valve, and standard 15 mm adapter (Fig. 4.6). The size of the ETT refers to the inner diameter of the tube in millimeters. Standard ETTs are shaped to follow the airway contour, and if necessary, the shape can be altered by inserting a stylet. A line of radiopaque material runs throughout the ETTs to make them visible on a chest X-ray. Standard ETTs have an asymmetric left-facing bevel that can be cut straight, rounded, or have a ski-tip design, as in the Parker tube. At the end of many ETTs, there is a secondary side opening, the Murphy eye, to ensure ventilation in case the proximal opening becomes obstructed.

The barrel-shaped cuffs ensure the proper seal in the trachea to allow positive pressure ventilation and prevent the trachea from soiling with oral secretions and gastric contents. ETTs come with two types of cuffs: the high-pressure low-volume cuff (which can cause mucosal ischemia, especially with prolonged use) or a low-pressure high-volume cuff. The TaperGuard Evac ETT has a bulbous, conically shaped cuff, designed to decrease the incidence of microaspiration to help prevent ventilator-associated pneumonia.

Proper ETT selection is important: larger-size ETTs provide less resistance to gas flow, while smaller-size ETTs cause less trauma during insertion. Usually, ETTs size 7.0 or

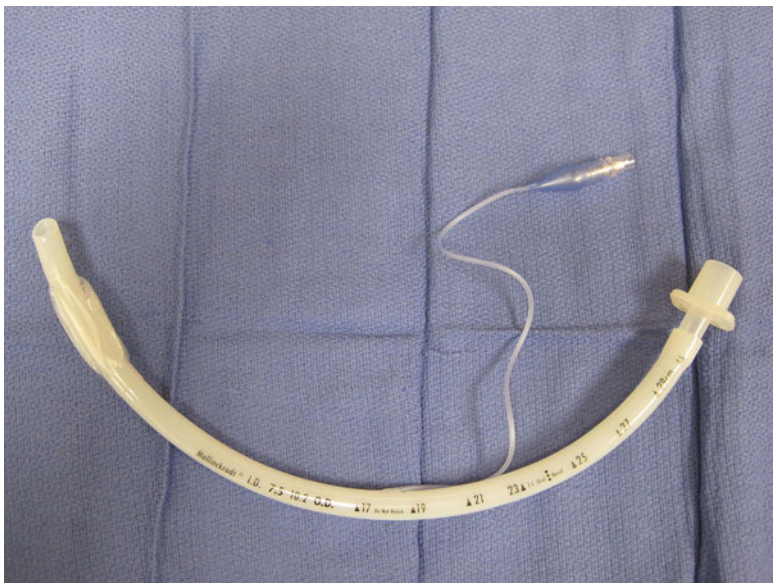

Fig. 4.6 The endotracheal tube

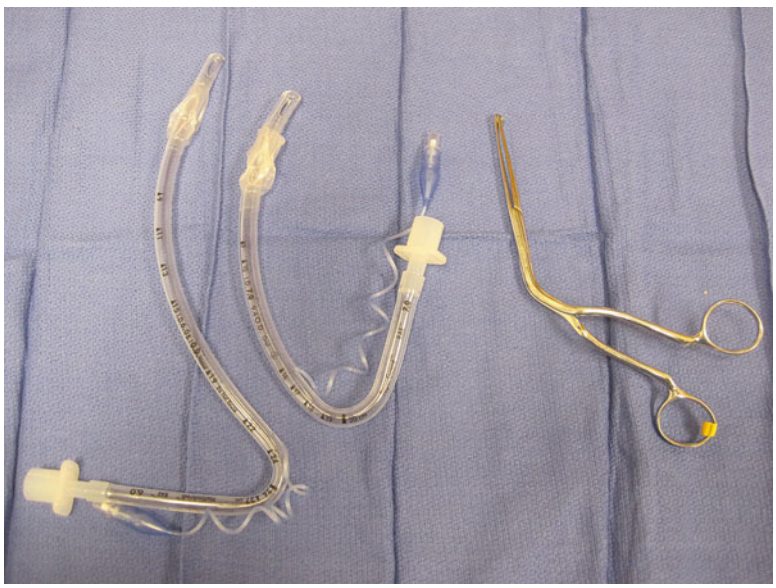

Fig. 4.7 Right-angle endotracheal tubes (RAE), nasal (*left*), oral (*center*), and Magill's forceps (*right*). Note that the nasal RAE tube has a curve toward the head, while the oral RAE tube has the curve toward the foot. A Magill's forceps is used to guide a nasotracheal ETT during nasotracheal intubation. A regular stylet can be inserted in the oral RAE tube to shape it for the intubation procedure. The tube retains its shape after the stylet is removed

7.5 are used for adult females, and size 7.5 or 8.0 are used for adult males. Certain procedures call for smaller- (laryngeal surgeries) or bigger-size (endobronchial procedures) ETT. Right-angle ETTs (RAE), shaped for nasal and oral intubation, are available for special situations (Fig. 4.7). They are useful for directing ETT and circuit away from surgical field. The nasal RAE is often used for oral surgery or mandibular fracture surgery, while the oral RAE is used in any surgery to facilitate directing the tubes away from the surgical field above the neck (ophthalmology, ENT-T and A, or facial surgery).

Techniques for Endotracheal Intubation

Laryngoscopic Intubation

Preoxygenation

Airway instrumentation mostly is done after induction of anesthesia on an apneic patient and requires some time during which the patient is at risk of arterial oxygen desaturation and hypoxia. To minimize the risk of hypoxia, preoxygenation is done before the instrumentation to increase the oxygen reserves of the body and allow longer time for instrumentation without arterial desaturation. It is accomplished by administration of high flow of 100 % O_2 through

a tight-fitting face mask in a spontaneously breathing patient or can be done with positive pressure ventilation in some cases. The goal is to fill the functional residual capacity with O_2 and achieving an end-tidal oxygen level of at least 90 %, instead of an SpO_2 of 100 % as the end point. In healthy adults, after preoxygenation, the duration of apnea without desaturation (DAWD—time between the onset of apnea and the time when SpO_2 reaches 90 %) is around 6–7 min.

Preoxygenation before induction of anesthesia is recommended for all patients, including those with full stomach (mask ventilation is relatively contraindicated), those with anticipated difficult mask ventilation, when intubation may take longer time, or when patients are expected to desaturate quickly (pregnant, obese, patients with pulmonary disease).

The "slow" preoxygenation technique takes about 3 min in normally tidal volume breathing patients. The "fast" technique involves vital capacity breathing (8 deep breaths over 60 s) and requires patient cooperation. Obese patients are better preoxygenated in a 25° head-up position or in an upright sitting position and with the application of continuous positive airway pressure. When a high leak around the mask is likely, or the patient is claustrophobic and does not accept the mask, the patient is asked to do the "fast" technique with the patient's mouth sealed directly around the circuit connector. A nose clip may be necessary if the patient is breathing with tidal volumes.

Apneic oxygenation may be employed after induction of anesthesia to prolong the DAWD in obese and nonobese patients. The method is based on the principle that, if the airway is patent, continuous O_2 consumption from alveoli creates the pressure difference that causes mass movement of gas from the upper airway into the alveoli. Insertion of a nasopharyngeal or oropharyngeal catheter connected to an oxygen source with O_2 flow of 2–5 L/min will increase the DAWD during difficult laryngoscopy. It is expected that $PaCO_2$ will rise (12 mmHg in first minute and then 6 mmHg/min thereafter) without ventilation.

Position for Intubation

For successful direct laryngoscopy and intubation, proper positioning of the patient is essential. There are three major positions for the intubation, the difference being in the position of the lower cervical spine: extended, neutral, or flexed. The atlanto-occipital joint remains extended for all positions. The "sniffing" position (flexed lower cervical spine at 35° and extended head at the atlanto-occipital joint at 15°) is the most widely used position with the highest success rate for intubation. According to the three axes alignment theory, the oral, pharyngeal, and laryngeal axes are brought into better alignment with the sniffing position to facilitate visualization of the glottic opening during direct laryngoscopy.

The height of an uncompressible head support for optimal sniffing position (to achieve lower neck flexion of 35°) may vary in patients, depending on the head and neck anatomy, but in most individuals it is 7–9 cm. It may be advisable to start with the sniffing position and adjust it if the visualization is poor: elevating the head higher, convert to simple extension by removing the head support, or convert to extension-extension position by lowering the head of the table.

In obese patients simple elevation of the head is not enough for optimal positioning. The optimal position can be accomplished by placing a stack of blankets or one of the commercially available elevation pillows under the upper back, shoulders, and head to elevate the back and head to 25° (so-called ramped position). This position can be achieved by reconfiguring the operating room table by flexing the table at the trunk-thigh hinge and raising the trunk portion of the table. With proper position the external auditory meatus and the sternum will be aligned horizontally.

Direct Laryngoscopy

With direct laryngoscopy the glottic opening is visualized to allow placement of ETT into the trachea (Fig. 4.8, Table 4.8). Two basic blades for laryngoscope are the curved blade (Macintosh, Fig. 4.9) and the straight blade with curved tip (Miller, Fig. 4.10). There are other blades available with different curvature, length, optical components, and angulation, with channels for oxygen insufflation and suction, levering tip, and a mirror-image version of Macintosh blade.

The Macintosh (curved blade) is considered to be less stimulating and less traumatic to the patient and provides more room for ETT passage. On the other hand, the Miller (straight blade) provides better exposure of the glottic opening in patients with an anterior larynx or with a long, floppy epiglottis. A system for grading the laryngoscopic view of patients was introduced by Cormack and Lehane. It consists of four grades (Fig. 4.11):

Grade 1: full view of the glottis
Grade 2: partial view of glottis or only arytenoids
Grade 3: only epiglottis visible
Grade 4: neither glottis nor epiglottis visible

The scoring system above is somewhat subjective and skill dependent. Attempts have been made to improve the system, and although they did not gain wide acceptance, one may find them helpful: Grade 2 was suggested to be divided into 2a (partial view of the glottis) and 2b (arytenoids or posterior part of the vocal cords only just visible). This grading system correlates more with difficult intubation. The laryngeal view may be improved with external maneuvers: optimal external laryngeal manipulation (OELM) or backward upward rightward pressure (BURP) performed by the laryngoscopist with the right hand and maintained by the assistant after obtaining the best possible view.

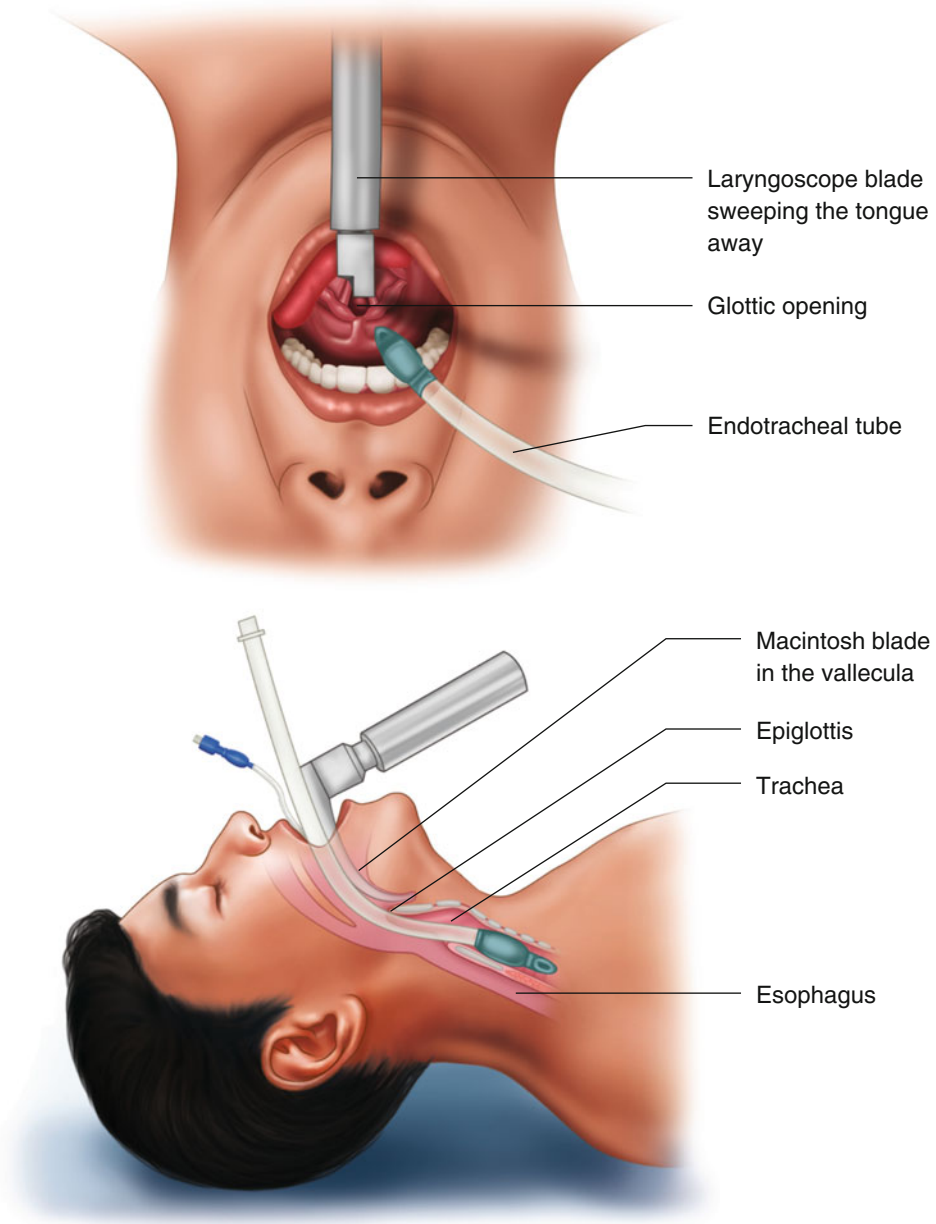

Fig. 4.8 Endotracheal intubation

Table 4.8 Technique for direct laryngoscopy

• The mouth is opened either with head extension or a scissors maneuver (the right thumb presses down on the right molars and the right index finger presses up on the right upper molars) to facilitate the insertion of the blade
• The laryngoscope is held in the left hand and inserted into the right side of the patient's mouth
• The laryngoscope is advanced toward the base of the tongue with the tip directed toward the midline so the tongue is being displaced completely to the left by the flange of the blade
• To expose the epiglottis the laryngoscope is lifted along a 45° straight line above the long axis of the patient, with the laryngoscopist's left arm and shoulder. The tongue and pharyngeal soft tissue is displaced in an anterior and caudal direction. The left wrist should remain straight to prevent dental trauma
• After the epiglottis is exposed, the Macintosh blade is placed into the vallecula. If using the Miller blade, the Miller blade lifts up the epiglottis to expose the glottic opening with continuous forward and upward movement of the blade
• The ETT is inserted through the vocal cords from the right hand side to avoid obstruction of the view during the insertion. The insertion is complete as the tube is inserted an additional 2 cm after the cuff passes the vocal cords. Another way to insure proper depth of ETT insertion is by the cm marks on the tube: 20–21 cm at the teeth for females and 22–23 cm for males
• The laryngoscope is gently removed after ETT insertion
• The tube is then fixed by tape, and the ventilation is resumed

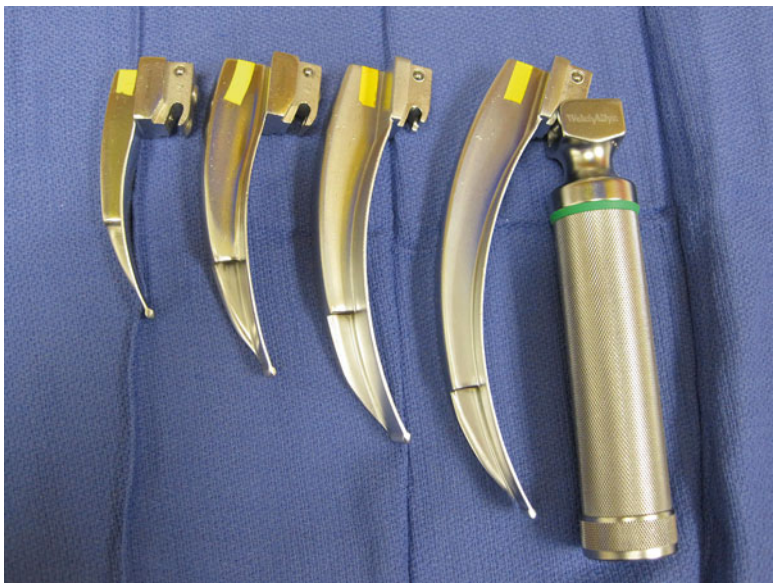

Fig. 4.9 Macintosh laryngoscopy blades

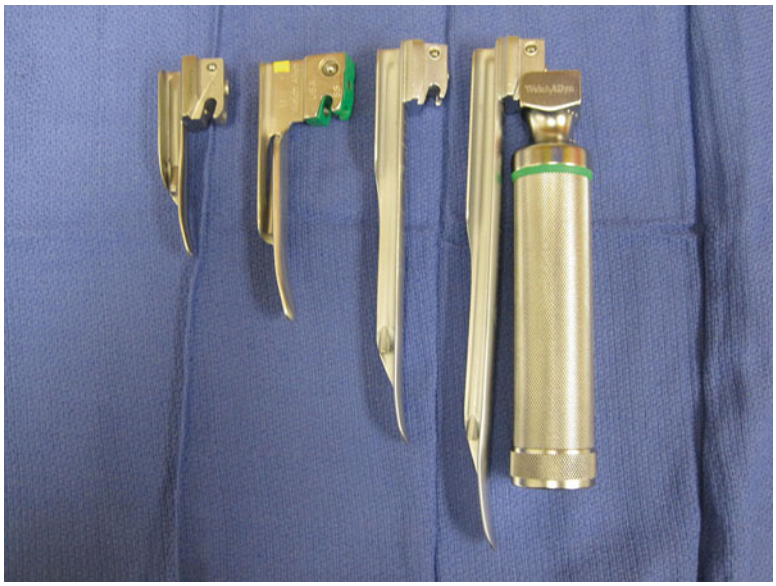

Fig. 4.10 Miller laryngoscopy blades

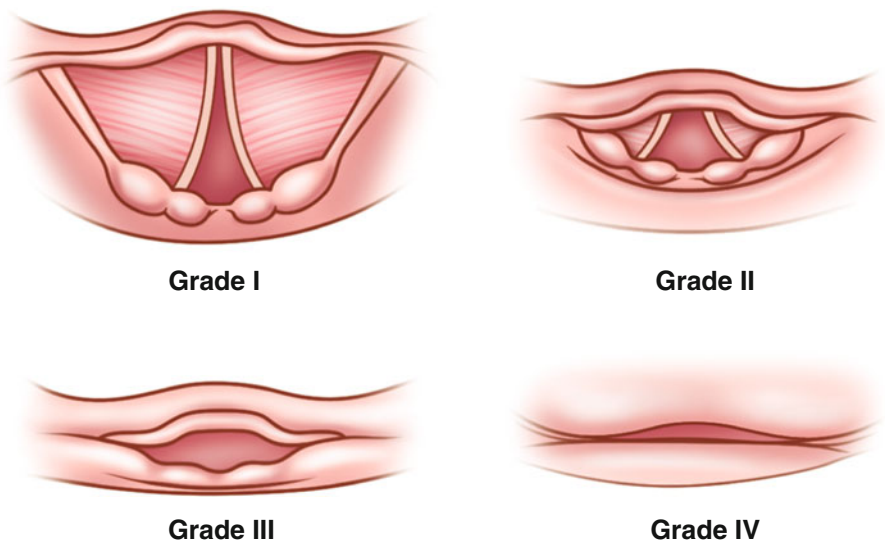

Fig. 4.11 Grades of laryngoscopic views

Nasotracheal Intubation

Nasotracheal intubation is usually reserved for surgeries requiring access to the oropharynx. The ETT is inserted into a nostril (usually the right or into the one which the patient thinks is more patent). The nostrils are prepared with the application of a vasoconstrictor to reduce the risk of epistaxis. One may introduce lubricated nasal airways of increasing size prior to inserting the ETT in the nostril. After the ETT is passed into the oropharynx, conventional direct laryngoscopy is performed, and the tube is guided into the trachea under direct vision. A Magill's forceps is commonly used to guide the ETT into the trachea.

ETT Placement Verification

Proper placement of the ETT can be verified by different methods. The most reliable signs (gold standard) include direct visualization of the ETT between the vocal cords or fiberoptic visualization of the tracheal rings and carina. Sustained detection of normal end-tidal CO_2 waveform and rapid expansion of a large rubber tracheal indicator bulb are also reliable signs. Less reliable signs include chest rise and fall with ventilation, breath sounds in the axillary chest wall, absence of breath sounds over the stomach, absence of gastric distension, large and spontaneous exhaled tidal volumes, condensation in the ETT, appropriate compliance of the reservoir bag, and maintenance of arterial saturation.

The anesthesia provider must be aware that if under any circumstance any one of the latter signs is false-positive or false-negative, then the ETT placement should be promptly confirmed with laryngoscopy or fiberoptic bronchoscopy. Ultrasonography (US) may offer some advantages: the proper placement of the ETT can be confirmed with the observation of the tube entering the trachea or esophagus during the intubation (it is a dynamic process and cannot be used to confirm the position of the ETT already in the trachea). Ultrasonography can also confirm ventilation by observing the lungs sliding bilaterally.

If an esophageal intubation is suspected, the ETT should be removed, and the patient should be ventilated with bag-mask following which another intubation attempt should be carried out with improved position, different intubating device, or different operator.

Complications of Endotracheal Intubation

Complications of intubation include airway injury (laryngeal trauma, damage to the vocal cords, edema with postextubation stridor or croup, massive tongue swelling, pharyngeal mucosal damage), injury to temporomandibular joint, lip injury, dental injury, and esophageal injury. In patients with an unstable cervical spine, excessive neck extension during laryngoscopy may lead to spinal cord injury (maintain in-line neck stabilization). Nasal intubation may cause epistaxis, dislodgement of nasal polyps or turbinates, or injury to the septum. Repeated attempts or a difficult intubation is associated more often with injury.

Videolaryngoscopy

In the past decade, advances in technology have changed the field of airway management. Some see videolaryngoscopy as the next evolutionary step in intubating technology. Numerous devices have been introduced into clinical practice allowing better visualization of the glottic opening, image capture and video documentation, and even remote real-time transfer of the image that may be very important in out-of-hospital airway management (Fig. 4.12).

Although airway pathology, difficult airway (non-emergent and emergent), and immobilization of the cervical spine are important indications for the use of videolaryngoscopes (VL), they also can be and are used for routine intubations and for education and teaching. Videolaryngoscopy systems are available in reusable and disposable forms and with an external or internal monitor (gives unrestricted mobility but at the expense of more difficult visual orientation with smaller monitor). Videolaryngoscopes may be divided into the following groups:

- Videolaryngoscopes with Macintosh-based blades: A.P. Advance, DCI Video Laryngoscope System, C-MAC VL System, McGRATH MAC VL, GlideScope Direct, Truview Picture Capture Device
- Videolaryngoscopes with highly curved blades: GlideScope, McGRATH Series 5
- Videolaryngoscopes with tube-guiding channel: King Vision, Pentax Airway Scope, Airtraq

The role of videolaryngoscopy in the management of difficult airway is well recognized, and it is included in the Difficult Airway Algorithm. VLs have different technical requirement and handling conditions, making it mandatory to train practitioners with each device in elective situations before using in airway emergencies.

Awake Fiberoptic and Flexible Endoscopic-Aided Intubation Techniques

When approaching any patient requiring endotracheal intubation for anesthesia and surgery, a very important question should first be answered: is it safe to induce anesthesia and then secure the airway or should the airway be secured before the induction of anesthesia? The ASA Difficult Airway Algorithm is depicted in Fig. 4.13. Awake intubation in a spontaneously breathing patient is the safest way to secure the airway in case of a known or suspected difficult airway. Awake endotracheal intubation can be accomplished with any technique (direct laryngoscopy, videolaryngoscopy, blind intubation), but awake fiberoptic intubation is considered to be the gold standard. Fiberoptic bronchoscope (FOB) or a non-fiberoptic flexible bronchoscope (Ambu aScope) can be used.

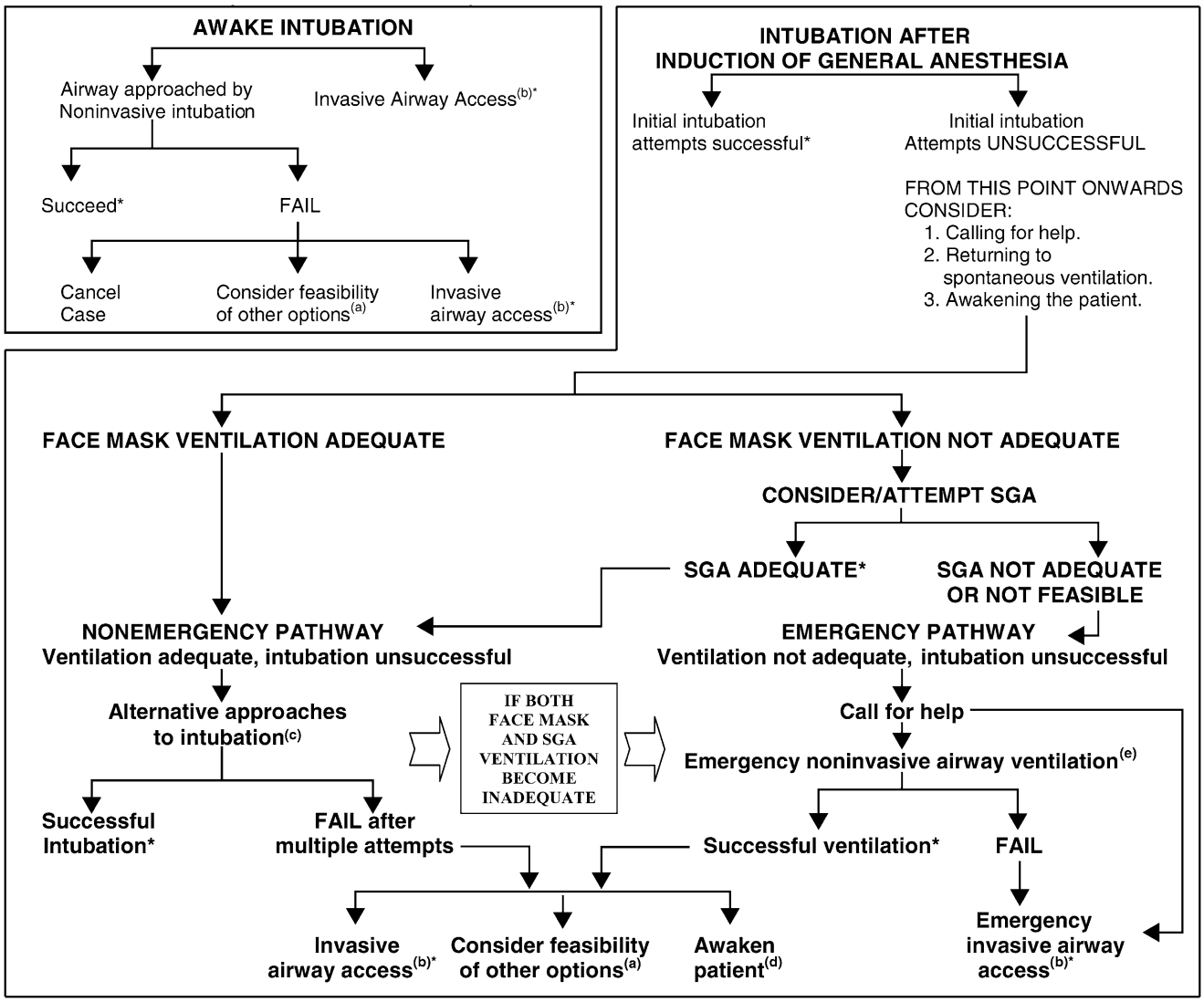

Fig. 4.12 Difficult airway algorithm

Indications of Fiberoptic Intubation

Besides for a difficult airway, FOB awake intubation is indicated in patients with an unstable cervical spine, since the technique is less likely to cause cervical spine movements. In patients with severe flexion deformity of the neck, it may be the only option for securing the airway. Awake FOB intubation is also recommended for patients with a blunt or penetrating upper airway injury to avoid creation of a false passage at the level of tissue disruption. FOB intubation may be recommended to avoid aspiration in high-risk patients.

Contraindications of Fiberoptic Intubation

Lack of time for preparation; lack of skill, assistance, or equipment; and massive airway trauma are absolute contraindications for awake FOB intubation. The technique requires cooperation from the patient and becomes impossible to

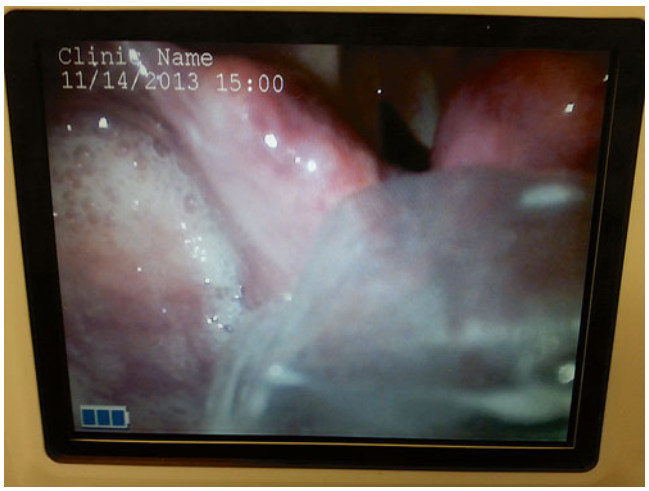

Fig. 4.13 Videolaryngoscopy showing the endotracheal tube entering the glottic opening

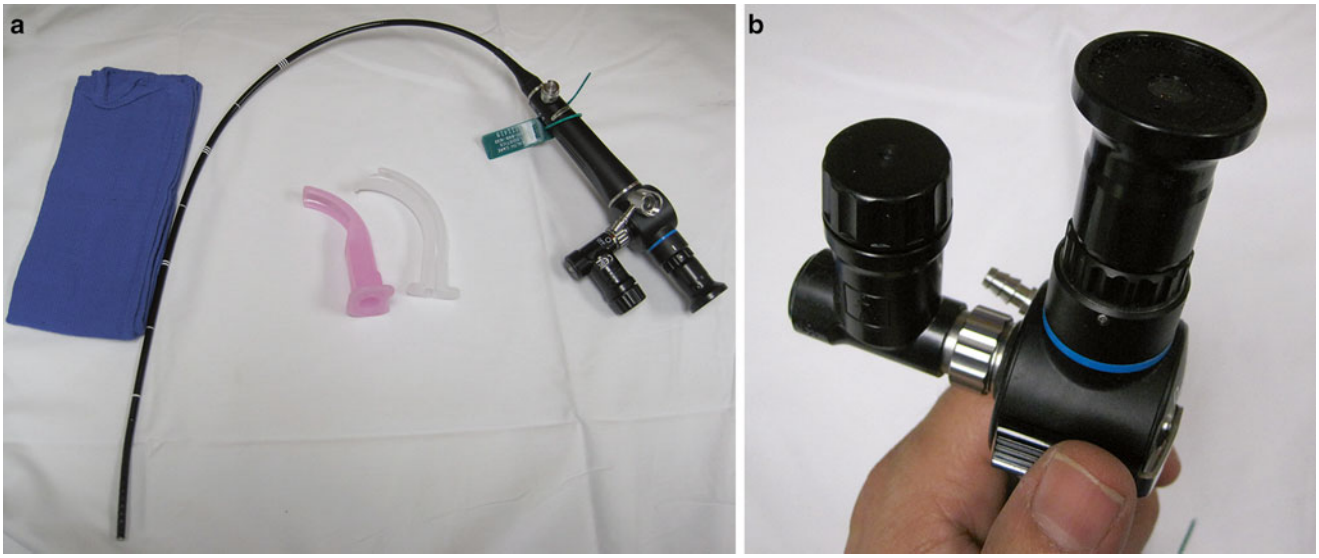

Fig. 4.14 (**a**) Fiberoptic bronchoscope with two types of oral airways. (**b**) Eye piece, battery compartment, side port for suction or oxygen, and thumb on the control lever, which is used to move the tip of the scope up or down (vertically)

perform in a completely uncooperative patient. Relative contraindications include blood or excessive secretions in the upper airway that can obscure the view, very small entry space, and presence of pharyngeal abscess that can be disrupted during ETT passage soiling the lower airway. Since the insertion of the ETT is done blindly over the FOB, FOB is associated with the risks of damage to the vocal cords and "corking out" of some perilaryngeal masses. The latter should be discussed with the ENT surgeon prior to intubation.

Equipment

Preparation for awake FOB intubation starts with equipment check. The FOB scope diameter should be closest in size to ETT diameter to prevent encroachment of ETT onto the arytenoids or vocal cords during railroading the tube into the trachea. A defogger can be applied or the FOB can be inserted into a warm irrigation bottle alongside with the ETT (softening of ETT). Softening of the ETT helps with insertion, making it less traumatic. If using a standard ETT, it is advisable to load it onto the FOB with the Murphy eye facing anteriorly, to prevent encroachment of the tube tip onto the arytenoids. Oral airways specifically designed to accommodate the FOB scope should be readily available (Fig. 4.14).

Sedation and Antisialogogues

Patient preparation starts with the application of standard monitors and administration of supplemental O_2. If there are no contraindications, an antisialogogue (usually glycopyrrolate 0.2–0.4 mg IV) is administered 15–20 min beforehand to reduce the amount of secretions that might interfere with the application of the local anesthetic and obscure the optics.

Sedation choices are numerous. Sedation must be titrated with caution to avoid respiratory depression and collapse of the upper airway soft tissues. In patients with a severely compromised airway, sedatives should be avoided. Most commonly opiates and benzodiazepines are used, but ketamine, dexmedetomidine, or remifentanil can also be used to provide sedation.

Local Anesthesia for the Airway

Local anesthesia of the upper airway prevents discomfort and makes FOB intubation easier and more successful.

Nasotracheal

For nasotracheal FOB intubation vasoconstrictors must be applied to the nasal mucosa to decrease the risk of epistaxis. Commonly used vasoconstrictors include phenylephrine 0.25–0.5 % spray and oxymetazoline 0.005 % spray. Cocaine 4 % (maximum dose 1.5 mg/kg) may be used, which provides both vasoconstriction and local anesthesia. A mixture of local anesthetic (4 % lidocaine) and vasoconstrictor (epinephrine/phenylephrine) can also be used for simultaneous vasoconstriction and local anesthesia. Local anesthetic and vasoconstrictors can be applied to the nasal mucosa on soaked Q-tip swabs or pledgets, as a spray, or as a gel coating short nasal airways.

Orotracheal

For orotracheal FOB intubation the soft palate, posterior tongue, posterior wall of the pharynx, vallecula, periglottic area, larynx, and the trachea are anesthetized. All these structures are innervated by the glossopharyngeal nerve and two

branches of the vagus nerve: the superior laryngeal and recurrent laryngeal nerves. In a vast majority of the cases, complete anesthesia may be achieved just with topical application of local anesthetics. Topical orotracheal anesthesia may be performed via several techniques: use of atomizer, aerosol, "spray as you go," gargle, "lollipop," and "toothpaste" techniques.

The local anesthetic with these techniques may reach the laryngeal area and even trachea as the drugs are inhaled or aspirated. Lidocaine is the most widely used local anesthetic for topicalization, having a better safety profile than benzocaine and tetracaine. However, it should be remembered that topicalization alone in the absence of any sedation may lead to airway collapse in patients with tenuous airway. Commonly used local anesthetics/modes of administration include:

- Cetacaine spray (mix of 14 % benzocaine and 2 % tetracaine); toxic dose (100 mg each) may cause methemoglobinemia, which is treated by administering methylene blue
- 4 % lidocaine/0.5 % tetracaine nebulizer for 5 min
- 10 % lidocaine spray
- 2 % viscous lidocaine, 2–4 mL via gargles/tongue coating

Airway Blocks

Nerve blocks that are performed include the superior laryngeal, the transtracheal (recurrent laryngeal nerve), and sometimes the glossopharyngeal nerve blocks (Figs. 4.15 and 4.16). The superior laryngeal and the recurrent laryngeal nerves are branches of the vagus nerve.

Superior laryngeal nerve block

The superior internal laryngeal nerve supplies sensation between the epiglottis and the vocal cords, while the external branch supplies motor innervation to the cricothyroid muscle (adducts cords). Using the thumb and index finger, the cornu (cartilage) of the hyoid bone is palpated transversally immediately beneath the angle of the mandible and anterior to the carotid artery. Next the one hand displaces the carotid artery laterally and posteriorly, while with the other hand a 22/25G 1 in. needle is "walked off" the cornu of the hyoid bone in an anterior caudad direction. The needle is aimed in the direction of the thyroid ligament and passed through it. At a depth of about 1–2 cm, 2–3 mL of 1 % lidocaine with epinephrine is injected (after negative aspiration of air/blood) into the space between the thyrohyoid membrane and the pharyngeal mucosa. The block is repeated on the other side.

Transtracheal nerve block

The recurrent laryngeal nerve supplies sensory innervations below the vocal cords and supplies motor innervations (abducts the cords) for all muscles, except the cricothyroid

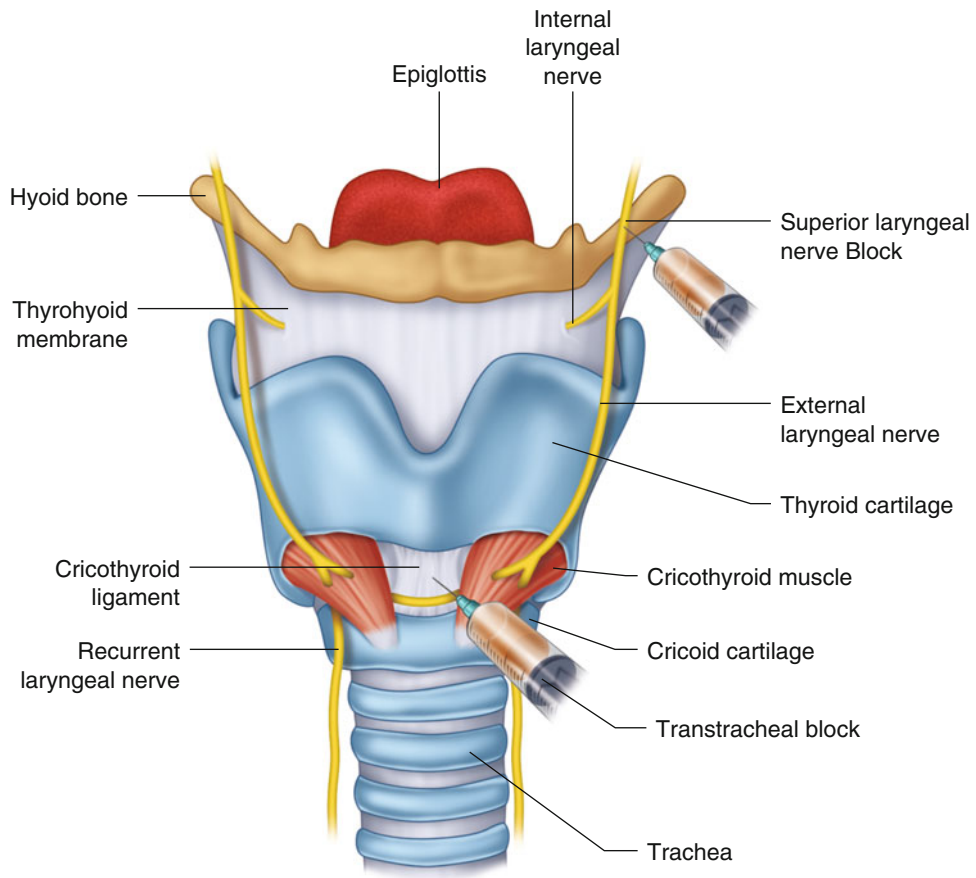

Fig. 4.15 Superior laryngeal nerve and transtracheal nerve blocks

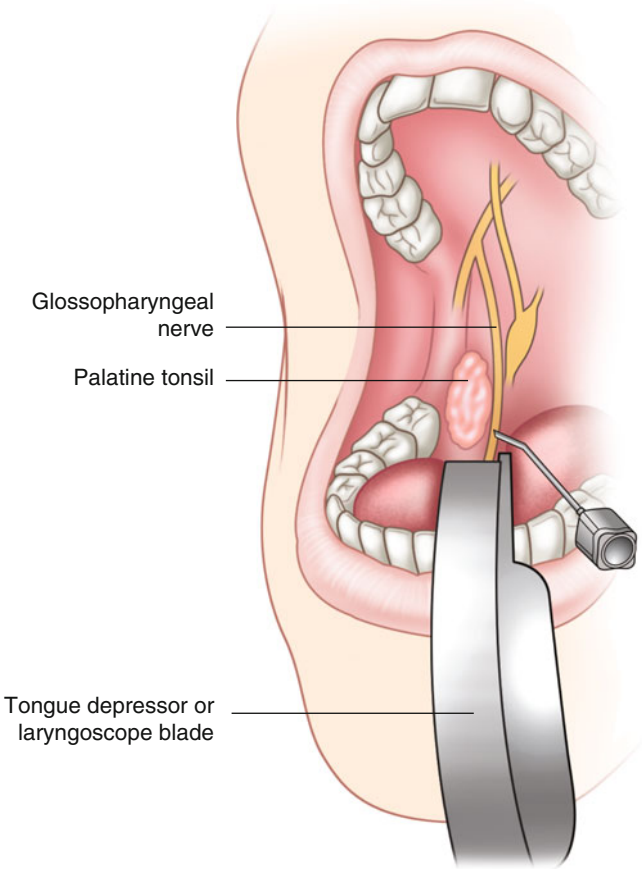

Fig. 4.16 Glossopharyngeal nerve block

muscle. The anesthesiologist places the index and third fingers of the nondominant hand in the space between the thyroid and cricoid cartilages, identifying the cricothyroid membrane. The skin over the midline is anesthetized with local anesthesia (25G needle). Next a 10 mL syringe containing 4 mL of 4 % lidocaine is attached to a 22G intravenous cannula. The needle is then introduced into the trachea through the cricothyroid membrane. Placement of the needle into the trachea is confirmed by loss of resistance and aspiration of air. Then only the flexible cannula is advanced caudally, after which the needle is removed. Next the patient is asked to take a deep breath and exhale forcefully, and at the end of the expiratory effort, about 4 mL of the local anesthetic solution is rapidly injected into the trachea. This will usually cause the patient to cough, causing spreading of the lidocaine over the trachea.

Glossopharyngeal nerve block

The glossopharyngeal nerve is responsible for sensory supply to the posterior tongue and the gag reflex. With the patient's mouth wide open, the palatopharyngeal fold (posterior tonsillar pillar) is identified. Using a tongue blade, the tongue is displaced to the contralateral side creating a gutter between the tongue and the teeth. A 25G spinal needle is inserted into the tonsillar membrane near the floor of the mouth at the base of the cul-de-sac and advanced slightly (0.25–0.5 cm). After negative aspiration, about 2 mL of 2 % lidocaine is injected (0.5 cm lateral to the base of the tongue).

Technique of FOB Intubation

The patient may be positioned supine with the anesthesia provider standing behind the patient's head, or for the patient's comfort, the backup bed position may be employed with the anesthesia provider facing the patient. Intubating oral airways (Berman Intubating Pharyngeal Airway, Ovassapian Fiberoptic Intubating Airway, Williams Airway Intubator) may be used to facilitate the FOB navigation and prevent damage to the FOB from the patient's teeth (biting). The ETT, with the connector removed, is lubricated and loaded onto the lubricated FOB scope. It is advisable to have a trained assistant during FOB intubation to help with patient's monitoring and application of some simple maneuvers such as jaw thrust, neck flexion, or gentle tongue retraction if needed.

Correct positioning of the FOB in the trachea should be confirmed not just by identifying the tracheal rings but the carina as well. As the correct position of the FOB is confirmed, the ETT should be railroaded over the FOB into the trachea. If the ETT is not entering the trachea, some simple maneuvers may help: withdraw the ETT 1–2 cm, rotate it 180° counterclockwise, and advance quickly while the patient is taking deep breath. That maneuver may be repeated with clockwise rotation of the tube.

Rapid Sequence Induction and Intubation

Rapid sequence induction and intubation (RSII) is the most commonly used anesthetic technique to reduce the chance of pulmonary aspiration of gastric contents in surgical patients at high risk: non-fasted patients for emergency surgery and patients with delayed gastric emptying, bowel obstruction, incompetent lower esophageal sphincter, and esophageal strictures. The term RSII is more meaningful than rapid sequence induction (RSI) alone since the technique involves both induction and intubation. The current protocol of RSII includes:

- Mandatory preoxygenation, no premedication
- Induction of anesthesia with predetermined amounts of intravenous anesthetic and muscle relaxant
- Application of cricoid pressure
- Avoidance of mask ventilation
- Intubation with cuffed ETT
- Then establishing lung ventilation. The teaching about not ventilating until the ETT is placed is controversial, since it makes hypoxemia more likely. Modified RSII allows for gentle mask ventilation before intubation while applying cricoid pressure.

Cricoid pressure (CP) is part of the expected standard of care for patients at high risk for aspiration, but at the same time, it is a controversial practice. Sellick, who originally described it in 1961, argued that backward pressure on the cricoid cartilage, the only complete cartilaginous tracheal ring, would occlude the upper esophagus between the cricoid cartilage and the cervical vertebrae and thus prevent regurgitation of gastric content into the pharynx. The concept has now been questioned with the finding that in many patients the esophagus is not located directly behind the trachea at the level of the cricoid cartilage but is displaced laterally, especially with cricoid pressure.

Another study found that application of CP could occlude the hypopharynx. CP may also worsen the laryngoscopic view in some patients and make the intubation more difficult. The timing of CP application, the amount of force applied, and the correct identification of the cricoid cartilage all play a role in the ultimate success of RSII. There are no large randomized studies, which arguably would be unethical to conduct, and hence, the actual efficacy of CP at the present time remains questionable.

Extubation

The data from the American Society of Anesthesiologists (ASA) Closed Claims Project showed that 17 % of brain injuries and deaths occurred after extubation in the operating room or postanesthesia care unit (PACU). After the introduction of guidelines for the management of difficult intubation, claims of airway-related injury at the induction of anesthesia significantly decreased, while the claims arising from airway injury at extubation remain unchanged.

Complications during or after extubation include coughing or breath-holding, hypoventilation or apnea (desaturation <90 %, residual anesthetics, inadequate muscle relaxant reversal), airway obstruction (laryngospasm, bronchospasm, negative pressure pulmonary edema), vomiting with subsequent aspiration, and hemodynamic disturbances such as hypertension and tachycardia.

Patients may be extubated awake or deep. Deep extubation is performed in a spontaneously breathing anesthetized patient, when the depth of anesthesia is sufficient to obtund laryngeal reflexes. It offers smoother extubation with less chances for coughing, bronchospasm, hemodynamic disturbances, and increases in intraocular or intracranial pressure. But all these advantages come at a higher risk of airway obstruction and potential aspiration. Consequently, this extubation technique should be avoided in patients with a difficult airway, patients at risk for aspiration, and obese patients.

Awake extubation is the choice for majority of adult patients undergoing general anesthesia (Table 4.9). For routine extubation, the patient must regain consciousness and follow simple commands, have an intact gag reflex, display adequate spontaneous respirations, have adequate pain control, and be hemodynamically stable, requiring no vasopressors. Any neuromuscular blockade must be fully reversed. Unfortunately, none of the clinical signs used to judge the adequacy of muscle tone reliably detects residual neuromuscular blockade. One objective method to quantify and judge the adequacy of muscle tone is a train-of-four (TOF) ratio. A TOF ratio of 0.9 or more is desired, since pharyngeal dysfunction can be demonstrated in volunteers with a TOF ratio under 0.9.

Table 4.9 Common extubation criteria

Respiratory	Negative inspiratory force more than −25 cm H_2O
	Forced vital capacity > 10 mL/kg
	Tidal volume > 5 mL/kg
	Minute volume < 10 L/min
	Respiratory rate 7–35 breaths/min
	PaO_2 > 80 mmHg, $PaCO_2$ < 45 mmHg, pH 7.35–7.45
	SpO_2 > 92 %
	Adequate protected airway reflexes (cough, gag, swallowing)
	Minimal secretions
Cardiovascular	Stable cardiovascular status (BP, HR, ±20 %)
	Stable rhythm
Neurological	Alert, cooperative, able to follow commands
Temperature	Normothermia (T > 35.5 °C)
Muscular strength	TOF ratio > 0.9
	Sustained head lift > 5 s
	Sustained tetany > 5 s

Routine extubation should be carried out after administration of 100 % O_2 for a few minutes and adequate suctioning of the oropharynx. A bite block may be inserted before extubation. The ETT cuff is then deflated; while applying positive pressure to the breathing system, the ETT is removed. The oropharynx is then suctioned again, the circuit face mask is applied, and the patient is assessed for adequate spontaneous respiration. A face mask with high-flow O_2 (6–8 L/min) is then applied, and airway patency and adequate ventilation are confirmed again.

Clinical Review

1. For the following nerve block, the needle is inserted through the cricothyroid membrane:
   A. Superior laryngeal
   B. Transtracheal
   C. Glossopharyngeal
   D. Hypoglossal

2. The nerve that is responsible for the sensory afferent limb of the gag reflex is:
   A. Superior laryngeal
   B. Recurrent laryngeal
   C. Trigeminal
   D. Glossopharyngeal
3. Laryngospasm is caused by stimulation of the following nerve:
   A. Superior internal laryngeal
   B. Superior external laryngeal
   C. Recurrent laryngeal
   D. Glossopharyngeal
4. A patient's mouth is sprayed with a local anesthetic prior to performing a fiberoptic intubation. You notice that the patient becomes cyanotic. The most likely agent causing the cyanosis is:
   A. Tetracaine
   B. Lidocaine
   C. Benzocaine
   D. Oxymetazoline
5. The most common adverse perioperative event in the ASA Closed Claims review was:
   A. Hypotension
   B. Hypoventilation
   C. Upper airway obstruction
   D. Pulmonary aspiration
6. Sniffing position involves aligning the following axis:
   A. Oral, laryngeal, and pharyngeal
   B. Oral and laryngeal
   C. Oral and pharyngeal
   D. Laryngeal and pharyngeal
7. All of the following are criteria for extubation, except:
   A. Negative inspiratory force more than −25 cm H_2O
   B. Tidal volume > 5 mL/kg
   C. Respiratory rate of 7 breaths/min
   D. Sustained head lift for 4 s
8. All of the following are risk factors for difficult mask ventilation, except:
   A. BMI of 28 kg/m^2
   B. Presence of a beard
   C. Obstructive sleep apnea
   D. Age 60 years
9. Predictor/s of difficult intubation is/are:
   A. History of prior difficult intubation
   B. Long, protruding upper incisors
   C. Highly arched hard palate
   D. All of the above
10. The correct sequence of rapid sequence induction and intubation is:
    A. Premedication, preoxygenation, propofol, cricoid pressure, succinylchloine, no ventilation, intubation
    B. Preoxygenation, propofol, cricoid pressure, succinylchloine, no ventilation, intubation
    C. Preoxygenation, premedication, propofol, cricoid pressure, succinylchloine, no ventilation, intubation
    D. Premedication, preoxygenation, propofol, cricoid pressure, succinylchloine, gentle ventilation, intubation

Answers: 1. B, 2. D, 3. A, 4. C, 5. B, 6. A, 7. D, 8. A, 9. D, 10. B

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Anesthesia Machine

5

Preet Mohinder Singh, Dipal Shah, and Ashish Sinha

The anesthesia machine has evolved from simple Boyle's apparatus to a complex integrated anesthesia workstation (Fig. 5.1), which includes the anesthesia machine, vaporizers, ventilator, breathing system, scavenging system, monitors, drug delivering system, data management system, and suction equipment.

The anesthesia machine is designed to supply medical gases from a gas supply, then mix the gases with inhalational agents at desired concentrations, and deliver the final mixture at a desired and safe/reduced pressure to the breathing circuit that is connected to the patient's airway. Newer machines are being manufactured, which are smaller and lighter, provide enhanced patient safety features and advanced ventilation modes, and allow automated record keeping and new monitoring capabilities.

Components of the Anesthesia Machine

The anesthesia machine functions with pneumatic as well as electrical components (Fig. 5.2a, b).

Pneumatic Components

The pressures in the machine can be used to classify the system into three parts:

- *High-pressure system:* This starts from the cylinders and ends at the primary pressure regulator and receives gases at cylinder pressure. This system includes the hanger yoke (including filter and unidirectional valve), yoke block, cylinder pressure gauge, and cylinder pressure regulator.
- *Intermediate-pressure system*: This starts from the pipeline inlet or downstream of cylinder pressure regulator (above) to the flow control valve and includes components that receive gases at reduced and constant pressures (37–55 psi), which is the pipeline pressure. This system includes the pipeline inlets and pressure gauges, ventilator power inlet, oxygen pressure-failure device (fail-safe) and alarm, flowmeter valves, oxygen and nitrous oxide second-stage regulators, and the oxygen flush valve.
- *Low-pressure system*: This starts from the flow control valve (above) to the common gas outlet and receives gases slightly above atmospheric pressure (but less pressure than the intermediate-pressure system). This system includes flowmeter tubes, vaporizers, check valves, and the common gas outlet.

Electrical Components

- Master switch: In most machines both electrical and pneumatic functions are activated by the master switch.
- Power failure indicator: It warns the administrator of the failure of main power. Alarms may be visual and/or audible.
- Reserve power: This is "backup" power, which is available (for at least 30 min) in case of loss of main power and needs to be checked regularly. Individual monitors may have their own reserve batteries or may draw from the reserves of the machine.
- Automated machine checkout: if available, should be done before the cases are started in the morning. A manual check should be done before starting every case and a full logout and recheck should be done at least every 24 h. Bypass for automated checkout is available; however, bypassing the automated checkout should be avoided.
- Electrical outlets and circuit breakers on the machine: The electrical outlets should be used for anesthesia monitors only. When the circuit breakers are activated,

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the electrical load should be reduced and the breakers should be reset
- Data communication ports: provide information between the machine, monitors, and data management system.

Medical Gases

"Medical gases" are undoubtedly the most commonly used drugs throughout the world. On an average a 300 bedded hospital in USA consumes at least around 450 gallons of oxygen daily. To deliver medical gases to "point of care," the supply systems use cylinders or pipeline system.

Physics Governing Gas Storage

The primary aim of medical gas storage systems is to store maximal amount of usable gas in minimal volume. For this the gases need compression or even conversion to liquid form by alterations in storage pressure, temperature, or both. The expansion ratio (volume of gas generated per mL of cryogenic liquefied gas) for medical gases is around 800 mL of gas/mL of liquid. The following principles/gas laws affect medical gas storage:

Critical temperature: It is the temperature of a gas above which it cannot be liquefied, irrespective of the amount compression pressure applied on it. Thus for any gas whose critical temperature exceeds that of operating room (OR) temperature (around 20 °C), it cannot be stored in liquid form in the OR. Alternatively these gases are stored in pressurized cylinders.

Boyle's Law: The absolute pressure exerted by a given mass of an ideal gas is inversely proportional to the volume it occupies, if the temperature and amount of gas remain unchanged within a closed system.

$$P\alpha \frac{1}{V} \quad \text{(temperature being constant)}$$

Fig. 5.1 Anesthesia workstation

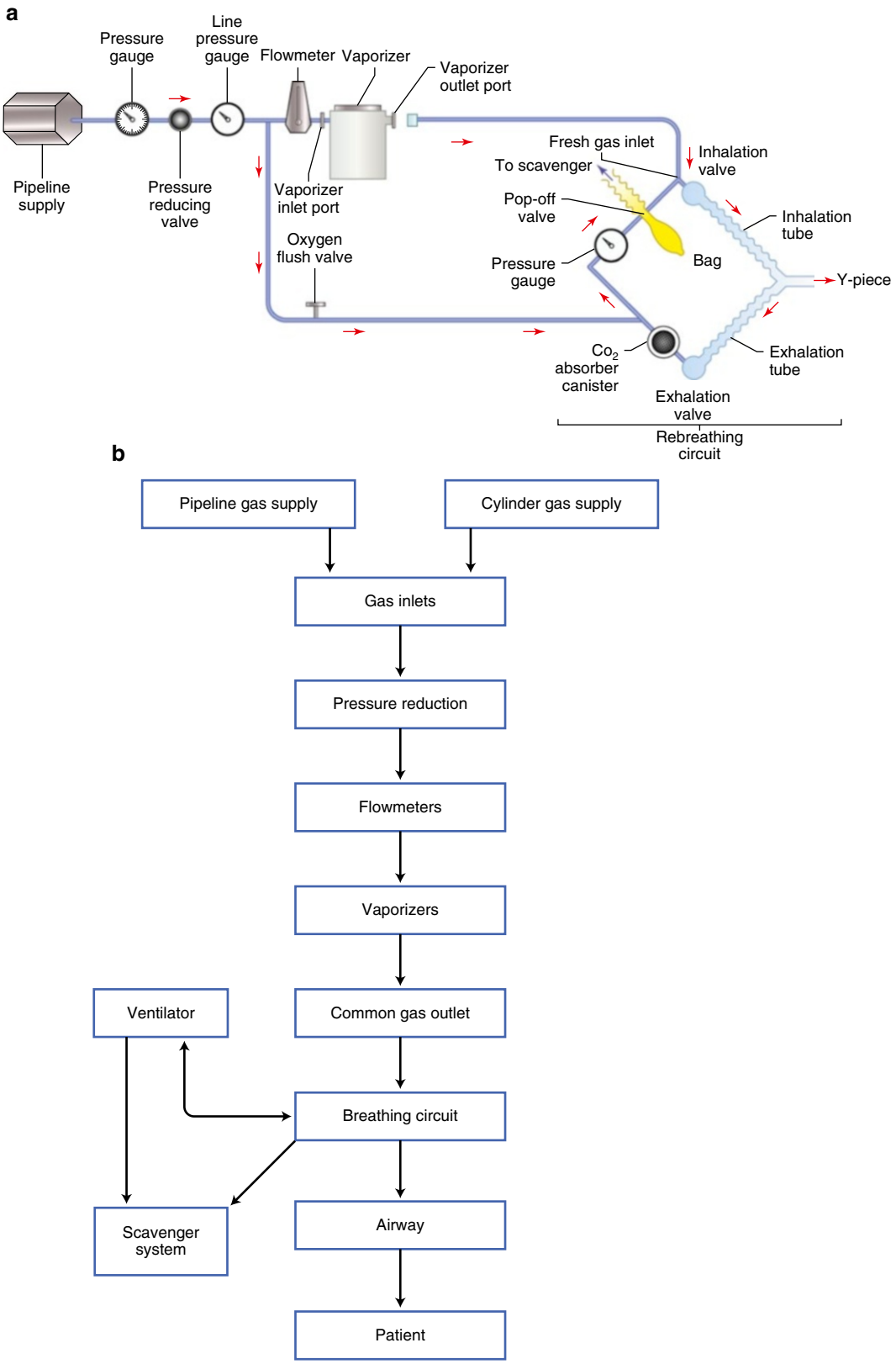


Fig. 5.2 Anesthesia mechanic circuit diagram, (**a**) and (**b**)

In simple terms it means the higher the pressure applied on the gas, the lower the volume it occupies. For medical cylinders the highest applicable pressure is limited by the tensile strength of medical cylinders. The safety of peak pressures, once gases are compressed in cylinders, is dependent upon their ambient temperature.

Gay-Lucca's Law: In a fixed volume (cylinder), an increase in gas temperature increases its pressure. Thus if cylinder is in a hotter climate, its pressure can increase significantly crossing the safety limit.

Medical Gas Supply Source

Medical gases are delivered to the anesthesia machine either by pipeline or via cylinders.

Pipeline Supply

This is the primary source of gas supply in the hospital. A central piping system is used to deliver oxygen, nitrous oxide, and air, usually at pressures of about 50 psi. Both oxygen and nitrous oxide are stored as liquids in large tanks. The pipelines are gas specific and coded with the gas name and specific color. In addition, for correct connections, the diameter index safety system (DISS) at the machine end and noninterchangeable quick coupler's (NIST) or Schrader's probe at the terminal wall units are incorporated to prevent accidental crossing of gases.

A check valve distal to the pipeline inlet prevents backflow of gases (reverse flow from the machine to the pipeline) or leaks to the atmosphere. The pipeline pressure indicator indicates the gas inlet pressures. To minimize pressure fluctuations when the oxygen flush valve or the ventilator is in use, two-stage pressure regulators further reduce the pressures (both pipeline and cylinder pressures) to 20 psi for oxygen and 38 psi for nitrous oxide.

Gas Distribution and the Pipeline System

Maintaining large cylinders, gas reservoirs, and cryogenic liquid gases at the point/site where these gases are used (operating room) is neither safe nor practical. Components of the gas distribution system that deliver these gases at "point of care" are:

- *Gas source:* Cylinder manifold, cryogenic liquid gas reservoirs, as per National Fire Protection Agency (NFPA) standards, must be located in open remote areas with bulk (liquid) oxygen reservoir having at least a 2-day hospital supply and a backup high-pressure H-cylinder manifold supply of at least one day. Each H-cylinder holds up to 6,000 L of oxygen or 16,000 L of nitrous oxide.
- *Connecting pipeline system:* Copper-based piping system receives gases at a pressure of 50–55 psi and should be capable of withstanding at least 150 psi for safety purposes. Recommended outer diameter of oxygen pipeline must be ½ an inch, whereas for all other gases, it should be 3/8 of an inch. Additional safety features in this system include:
  - *Pressure relief valves:* If the pressure exceeds by 50 % of the working pressure, the valve allows a deliberate leak to prevent buildup of pressure in the system.
  - *Shutoff valves:* These prevent pressure transmission downstream, thus allowing for pipeline maintenance/cleaning or preventing gas-related hazards by shutting off gas supplies.
- *Terminal outlet units:* These are units to which the user connects the medical devices that use the gas supplies. Common terminal outlets include wall-mounted outlets, ceiling-mounted pendants (as in intensive care units), or ceiling-mounted hoses (in OR). The safety features of these units include:
  - *Automatic shutoff valves:* These are self-sealing valves that shut off gas flow when no device is connected to them. Inserting the connecting male probe of concerned device into the terminal socket allows gas flow automatically. They prevent any gas wastage/leakage when the system is not in use.
  - *Gas-specific connectors:* The terminal unit of specific gas outlet has a unique configuration (female connector) that only allows connection to the corresponding male inlet connector from the medical device. Thus the possibility of wrong gas inflow to the patient is prevented. The two systems of specific connectors (socket assembly) used in most hospitals are:

    Diameter index safety system (DISS) (Fig. 5.3a): was developed as a standard to provide noninterchangeable connections, which are removable, exposed, and threaded connections. The DISS can be used in conjunction with individual gas lines delivering gas at pressures of up to 200 psi. Each DISS connection consists of a body adaptor, nipple, and nut. As the inner diameter of the body adaptor increases or decreases, the diameter of its mating nipple increases or decreases proportionally. In this way, only the properly mated and intended parts fit together (because of a unique thread engagement).

    Quick connectors (Fig. 5.3b)—Like the DISS system, they also allow a unique male probe from the equipment to fit into the specific female socket of the gas outlet. The advantages of these connections are that they are easier to engage and disengage, requiring minimum force, and can be done by a single hand.

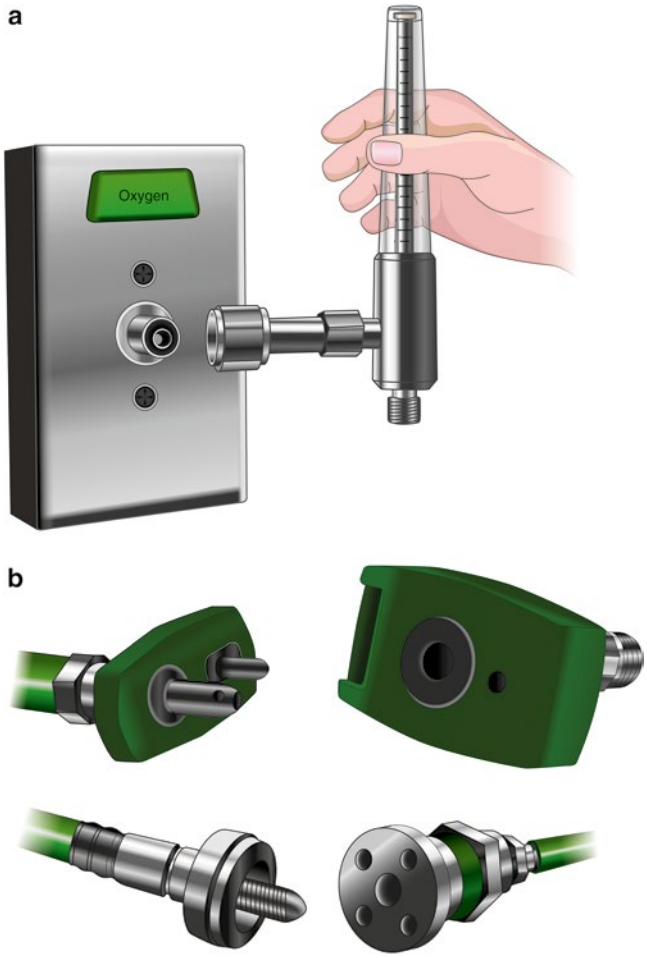


Fig. 5.3 (**a**) Diameter index safety system, (**b**) quick connectors

These connectors are, however, associated with a higher incidence of gas leaks when compared to DISS. The mechanism preventing a wrong connection is quite simple; the male probe either has a gas-specific shape or has two different mating portions with specific distance or orientation for each gas. The corresponding female socket has a configuration that allows only one specific complimentary male probe to be inserted.

Cylinder Supply

Gas cylinders are available for oxygen, nitrous oxide, and air (Table 5.1). These cylinders are color coded with cylinder labels and the Pin Index Safety System (PISS) to prevent gas delivery errors. Additionally, a safety relief valve opens in case of extreme pressures within the cylinder. A check valve prevents gas transfer between empty cylinders and minimizes leakage of gas to the atmosphere. The hanger yoke assembly orients the cylinders and maintains a unidirectional gas flow.

The cylinder contains gases at high and variable pressures which are inappropriate for direct use. Therefore, the pressure is reduced to a lower and constant pressure by the primary pressure regulator. Bourdon's pressure gauge is used to measure the pressure of gas inside the cylinder. This has a flexible curved tube that proportionately straightens out when exposed to gas pressure.

A full oxygen cylinder has a pressure of 2,200 psi, while a full nitrous oxide cylinder has a pressure of 745 psi. The pressures reflected are true indicators of residual gas pressure in oxygen cylinders but not in nitrous oxide cylinders, since nitrous oxide is in the liquid form. The pressure in a nitrous oxide cylinder will read 745 psi until it is 1/4 (400 mL) full. If both the cylinders and the pipeline supplies are kept open, the slightly lower pressure in the cylinder pipeline (45 psi) facilitates the preferential use of main pipeline supply. However, the cylinders should be kept closed after daily checks to prevent their unnoticed use in the event of pipeline gas supply failure, since cylinders are mainly a backup source.

Safe Practices for Handling Cylinders

- Regular checkup of cylinders for leaks, erosions, or any physical damage.
- Store cylinders in cool, dry places away from any possible inflammable source.
- When using the anesthesia workstation, check "pin index" match and also use "Bodok seal" (a washer preventing leaks at contact cite between yoke and cylinder nipple).
- Cylinder gas must be free from any moisture; otherwise the escaping gas can lead to icing and occlusion of the nipple (especially nitrous oxide).
- Avoid damage to outlet valve—cylinders with "bull nose" (output valve with side "L" angulation, cylinder type F, G, H) should be stored in vertical position, whereas cylinders with "pin index" valves (without any angulation) can be stored in horizontal position.
- Quality assurance tests must be performed as per manufacturer's recommendations (usually at 5-year intervals).

Types of Medical Gases

Oxygen

Commercially available oxygen is produced either by fractional distillation of liquefied air or by using oxygen concentrators. Modern zeolite-based oxygen concentrators are capable of producing up to 10 L/min of oxygen with 99 %

Table 5.1 Medical gas cylinders

Medical gas	Form in cylinder	E cylinder capacity	Color	Maximum pressure (at 20 °C)
Oxygen	Gas	600–700	Green	1,800–2,200
Air	Gas	600–700	Yellow	1,800–2,200
Nitrous oxide	Liquid	1,600	Blue	745

purity. Oxygen can be stored in high-pressure cylinders as a gas for mobile use or in the liquid form for hospital use. The "E"-type manifold cylinder is the commonly used mobile/rescue oxygen source. Estimation of residual time for oxygen supply in an "E" cylinder can be calculated as:

$$\text{Time left (min)} = \frac{0.3 \times \text{Pressure (psi)}}{\text{Flow } (L/\text{min})}$$

A full oxygen cylinder (600–700 L) at 18–2,200 psi will run for approximately 1 h at a 10 L/min flow. So if flow is halved, the time doubles, or if pressure is halved (half-full cylinder), the time will be halved. Recently, high-pressure oxygen cylinders (pressures up to 3,000 psi) have been made available, especially for remote locations. A pressure-reducing valve reduces cylinder pressure to a standard working pressure of about 45–50 psi.

For hospital pipeline supply, oxygen is stored in the liquid form and used via the "vacuum insulated evaporator system." This is considered as the most efficient and cost-effective method of storing oxygen. Using cryogenic, high-pressure principle (−160 °C, 5–10 atmospheres), oxygen is stored in the liquid form and capable of generating 842 mL of gas/mL of liquid. In contrast, a regular cylinder delivers only 137 mL of gas/mL of cylinder volume. Thermal insulation is a prime requirement, which is maintained by creating a vacuum between the inner steel and outer carbonated steel vessel.

Nitrous Oxide

Nitrous oxide (N_2O) is produced by controlled heating of ammonium nitrate to a temperature of 250 °C. Hospitals store N_2O in high-pressure and high-capacity (16,000 L each) H-cylinders, which are connected by a manifold. Owing to its high critical temperature (36.4 °C), which is above OR room temperature, N_2O is stored in cylinders as a liquid at OR temperature. Thus, the pressure in a nitrous oxide cylinder is not proportional to the volume of gas and will always read 745 psi until it is 1/4 (400 mL) full. The estimation of residual amount of N_2O can only be done by weighing the cylinder and subtracting it from the tare weight (weight of empty cylinder) stamped on the cylinder.

As a safety feature, nitrous oxide cylinders are not fully filled with the liquid, as any accidental increase in temperature can lead to vaporization of liquid, increasing pressures tremendously to a dangerous level. However, all cylinders are equipped with a pressure relief valve, which is designed to open at 3,300 psi, well below the "E" cylinder's maximum pressure threshold of 5,000 psi.

Medical Air

Air is being more commonly used during anesthesia to offset the side effects of N_2O or developing oxygen toxicity. Atmospheric air on compression, after passing through a series of driers and filters to remove impurities, is labeled as medical grade air. As per US pharmacopeia, it must contain 19.5–23.5 % oxygen and less than 0.001 % carbon monoxide. Special considerations are given to remove moisture, particulate matter, bacteria, and oil (a contaminant from the compressor system). Recently, synthetic medical air has been developed by using a mixture of liquid oxygen and nitrogen. Synthetic medical air has the advantage of being free from impurities, with the manufacturing process being easy without the need of using special compressors.

Heliox

Heliox is a mixture of oxygen and helium in varying proportions. Because of its low density, it is useful in airway obstruction as it provides laminar flow. The mixture is named on the basis of its oxygen concentration. For example, a 20 % oxygen and 80 % helium mixture is labeled as heliox-20. Approved mixtures are the heliox-20 and heliox-30, which have a density of almost 1/3 of air. Heliox is stored as a compressed gas, and oxygen flowmeters are used to measure its flow/output.

Xenon

Xenon is a recent addition into the list of medical gases, but it is yet to be licensed for its use for anesthesia maintenance. It is almost five times denser than air and is supplied in a low-pressure compressed gas cylinder.

Fail-Safe Safety Devices: Oxygen Supply Pressure Failure

These fail-safe safety devices are linked either mechanically, pneumatically, or electronically and proportionately reduce or completely shut off supply of all other gases, except air, when the oxygen pipeline pressure falls to below 50 % of "normal" supply or usually less than 30 psi, in order to provide a minimum oxygen concentration of 23–25 % at the

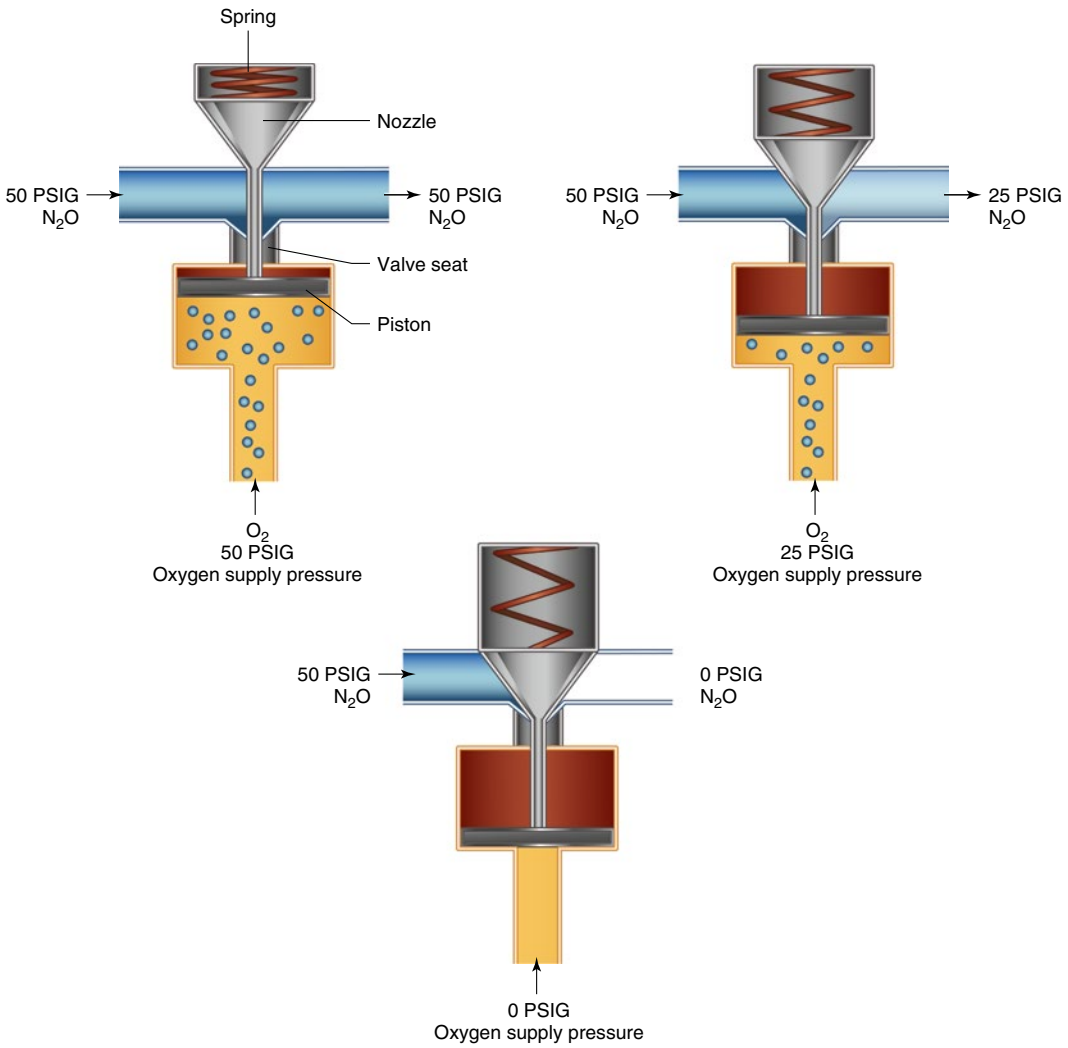


Fig. 5.4 Fail-safe valve

common gas outlet. These safety devices are present in gas line supplying all flowmeters, except the one for oxygen. Gases such as air and helium may not be linked with these systems.

Fail-safe safety devices can prevent the delivery of a hypoxic gas mixture to the patient, only if it is confirmed that the correct gas is flowing through the pipeline, as they only sense the loss of pipeline pressure. The administration of a hypoxic mixture can occur in spite of these safety devices in the following instances: if there is supply of wrong gas, use of inert gases, leak downstream of flowmeters, defective mechanics, or addition of low-potent gases in high concentration:

1. The *fail-safe valve* (Fig. 5.4) is located downstream of nitrous oxide supply source and is controlled by the oxygen supply pressure. In Datex-Ohmeda machines, the fail-safe valve is also called *pressure sensor shutoff valve* and has a threshold of 20 psi to shut off other gases. North American Dräger has an *oxygen failure protection device* (OFPD), which is based on a variable flow-type proportionating principle, to interface the oxygen pressure with that of other gases.
2. Newer Datex-Ohmeda machines have a *Link 25 proportion-limiting control system* (Fig. 5.5), which maintains a minimum 1:3 O_2:N_2O concentration or prevents delivery of less than 25 % of oxygen. Also, a pressure sensor shutoff valve is present with a threshold of 26 psi for oxygen, at which it completely shuts off N_2O flow.
3. Newer Dräger machines have an *oxygen ratio monitor controller* (ORMC), which shuts off nitrous oxide when oxygen pressure falls below 10 psi. Other Dräger machines have a *sensitive oxygen ratio controller* (S-ORC), which shuts off nitrous oxide when oxygen flow drops below 200 mL/min.
4. The Penlon machines have a *paramagnetic oxygen analyzer* which gives off an audible alarm when the oxygen concentration falls below 25 % and also simultaneously cuts off nitrous oxide supply.

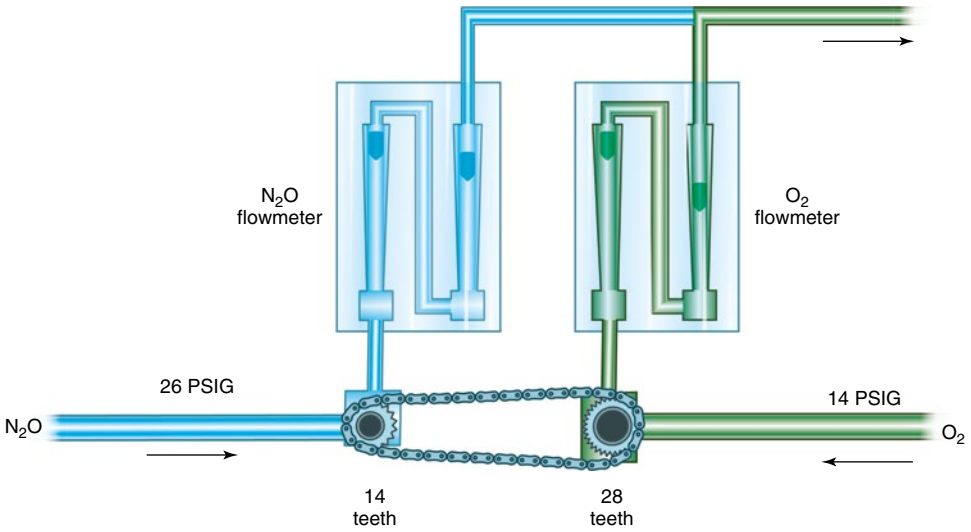


Fig. 5.5 Ohmeda Link-25 proportion-limiting control system

5. Some machines are equipped with the *minimum mandatory oxygen flow* sensor of 50–250 mL/min.
6. *Oxygen supply failure alarms* are medium priority alarms, which can be audible, visual, or both, and activated within 5 s of oxygen supply pressure failure and cannot be disabled. Some machines have a Ritchie whistle, which is an audible alarm that gets activated when the pressure drops below 38 psi and sounds till the pressure falls to 6 psi.
7. A *gas selector switch* installed in some machines prevents simultaneous use of air and nitrous oxide.
8. The *oxygen flush* valve receives gases from the cylinders or pipeline at 45–55 psi and is directly connected to the common gas outlet, bypassing the flowmeter and vaporizers. It is a self-closing device, can be operated with single hand, used for rapid refill or flushing of the breathing circuit, and provides 100 % oxygen at flows of 35–55 L/min. If the oxygen flush valve is faulty, it can cause barotrauma or dilution of inhaled anesthetic gases, potentially leading to intraoperative awareness.

Flowmeters

Flowmeters are deigned to precisely control and deliver gases to the common gas outlet over a range of flows. The flowmeters can be either an electronic type or the constant-pressure variable-orifice type. They are calibrated for specific gases at 20 °C at an ambient pressure of 760 mmHg. The flow rate through the vaporizer can be low and laminar (depends on the viscosity of the gas) or high or turbulent (depends on the density of the gas).

The flowmeter (Fig. 5.6) is composed of the body, stem, seat, and the control knob. Flowmeters consist of either a single- or double-tapered glass tube in series (Thorpe tube), mounted on a panel of fluorescent coating. Flowmeters are color coded, have an interior antistatic coating, and have knobs with a high torque to prevent changes from casual contact.

The oxygen knob may be larger, fluted, and protrude further and is positioned the last in sequence or farthest to the right (nearest to the outlet) to prevent delivery of a hypoxic mixture in the event of a leak (Fig. 5.7). The flow rate is measured with either a plumb bob-type float (read at the top) or the ball-type float (read at the center), which rotates with the flow of gas. The float is also coated with antistatic material to prevent sticking and has float stop which stops in full on/off position.

Near the bottom of the flowmeter tube, the diameter is small, and as the flow of gas is initiated, it creates pressure to lift the bobbin/float up. As the float rises, the tube orifice widens (tapering tube) allowing more gas to pass around the float. The float will rise until the pressure above and under the float equilibrates and supports its weight. If gas flow is increased further, the float will rise again until its weight is supported (Fig. 5.8). Therefore, gas flow in the flowmeter not only depends on the diameter of the tube but also on the weight and cross-sectional area of the float.

In electronic flowmeters, gas flows across a needle valve in a fixed volume chamber. As the flow increases, the pressure increases, and the solenoid valve opens to let out the gas when a specific pressure limit is reached. The flow/min is related to the number of times the valve opens.

Air may directly reach the flowmeters to allow its administration in the absence of oxygen. However, for other gases, the flow is permitted only if there is sufficient oxygen pressure. Most anesthesia machines also have an auxiliary O_2

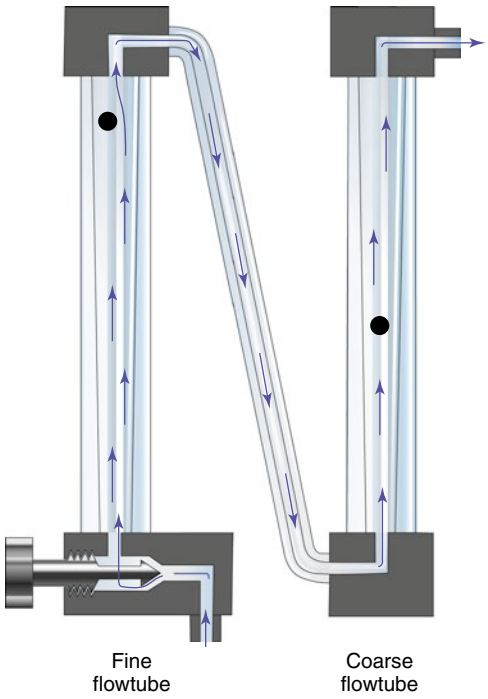


Fig. 5.6 Flowmeter

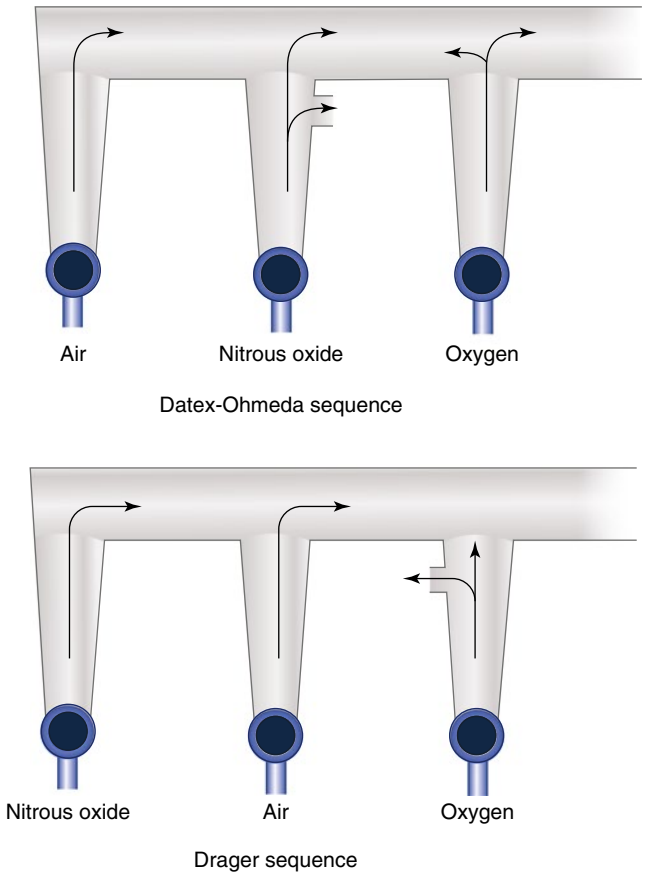


Fig. 5.7 Flowmeter arrangement

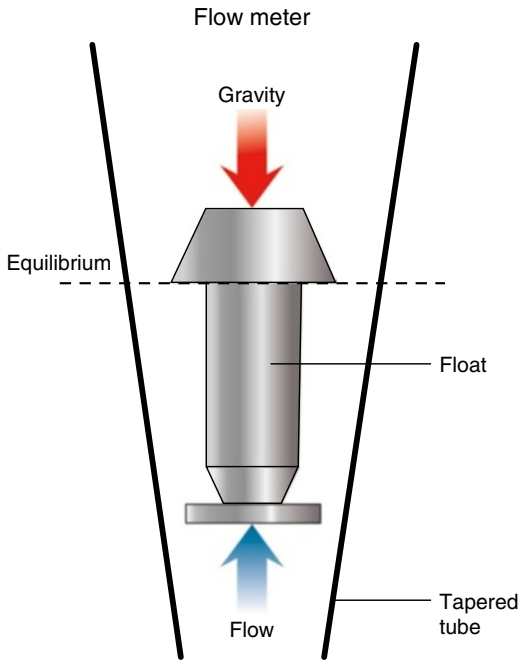


Fig. 5.8 Workings of a flowmeter

flowmeter with its own flow control valve, flow indicator, and outlet, providing a maximum flow of 10 L/min. The auxiliary oxygen port can be used to provide oxygen to the patient, for driving the ventilator, or for jet ventilation, and can be used without turning the anesthesia machine on.

Anesthesia Breathing Circuits

An "anesthesia circuit" is defined as an assembly of components that connect the patient's airway to the anesthesia machine, creating an artificial atmosphere from and to which the patient ventilates. They are designed for either spontaneous or positive pressure ventilation, while simultaneously allowing a safe and convenient method to deliver inhaled anesthetic agents. Over the last two centuries, these circuits have evolved from the simple Schimmelbusch's mask to the modern circle system.

Requirements of a Breathing System

The requirements, both essential and desirable, of an ideal breathing system are described below. The circuit must be capable of:

(a) *Delivering the gases from the machine to the alveoli*: to the nearest possible concentration that is set manually. In the process of delivery, it must be capable of rapid changes in the concentration. If the circuit volume is large, alterations made in fresh gas flow rate may take a

long time to reach equilibrium with that being delivered, and it may fail to meet the target concentration in an optimal time frame. The factors that add to discrepancy between the set and delivered concentration are rebreathing, air dilution, leaks, anesthetic agent uptake, and agent expired by the lung.

(b) *Eliminating carbon dioxide effectively*: from the gases being breathed in. This forms the basis of "efficiency of the circuit."

(c) *Minimal dead space:* Dead space of a circuit is defined as "the volume of the breathing system from the patient-end to the point up to which to and fro movement of expired gas takes place." Dead space is responsible for not only increasing rebreathing in the circuit but also increasing the work of breathing in a spontaneously breathing patient. In a circle system, the dead space is limited to beyond the point where the inspiratory and expiratory limbs unite (Y piece) and includes the endotracheal tube (Y piece to the ETT). The circuit tubing length does not affect the dead space.

(d) *Minimal possible resistance*: Increase in circuit resistance offers resistance to deflation of lungs (expiration), which is a passive process. The overall resistance offered by a circuit can be estimated by Hagen-Poiseuille's equation, that is,

$$\text{Pressure gradient across a circuit} = \frac{K \times \text{Flow rate} \times \text{Fresh gas viscosity} \times \text{Length of circuit}}{\text{Radius of circuit}^4}$$

where k is a constant. The above equation forms the basis of designing an optimal anesthesia circuit with the aim of lowering the work of breathing. The above equation also highlights that the radius of the tubing is the most substantial determinant of overall resistance, and a mere reduction of the radius to half increases the resistance to 16 times. Additional factors that can cause an increase in circuit resistance are valves in the circuit, acute bends, and turbulent gas flows (at high gas inflow rates).

(e) *Fresh gas economy*: The anesthesia circuit must use the lowest possible volume of fresh gas inflow to eliminate CO_2 and prevent rebreathing.

(f) *Heat and moisture conservation*: An ideal breathing circuit must try to conserve the heat and humidity in the expired gas, which helps to maintain physiological function and ciliary motility of respiratory mucosa. The inspired gas is often dry and cold, which can lead to significant heat and water loss.

(g) *Light weight*: Lighter circuits add to portability and also prevent drag on the patient's "airway device" or mask. This property adds significantly to convenience and safety in use of a circuit.

(h) *Universal for age*: If the breathing circuit can be used over a wide range of ages, it will add to user acceptability significantly.

(i) *Scavenging*: An anesthesia circuit should be free from leaks and allow for collection of exhaled gases effectively by providing a common accessible exit point.

Classification of Breathing Systems

Breathing systems can be classified depending on the amount of rebreathing of gases as open, semi-open, semi-closed, and closed (Table 5.2). In the semi-open system there is no rebreathing of gases, but it requires high fresh gas flows, while in the semi-closed and closed systems, there is rebreathing of exhaled gases after absorption of carbon dioxide. The use of carbon dioxide absorbent prevents the rebreathing of carbon dioxide, while allowing rebreathing of inhaled agents and other gases. In a closed system the inflow of gas exactly matches the take-up or consumption. The semi-closed circle breathing system is the most common type of circuit used (see below).

Non-rebreathing Circuits Without a CO_2 Absorber

In 1954, with assistance from William Mushin, Mapleson described non-rebreathing systems and classified them into five types (Fig. 5.9, Table 5.3). Mapleson labeled these breathing circuits from A through E, based upon fresh gas requirements. Later, Jackson and Rees made modifications to the Mapleson E circuit, which is now called the Mapleson F system/Jackson-Rees circuit.

Functional Basis of Mapleson Systems

The general principles of prevention of rebreathing in these systems are:

- The breathing cycle is divided into three phases—inspiratory phase, expiratory phase, and an end-expiratory pause.
- Gases move en bloc, i.e., they maintain their identity as fresh gas, dead space gas, and alveolar gas. There is no mixing of these gases.
- During expiration, fresh gas flow (FGF) pushes exhaled gas down the expiratory limb, where it collects in the reservoir (breathing) bag and opens the pop-off (APL) valve.
- The next inspiration draws on the gas in the expiratory limb. The expiratory limb will have less carbon dioxide (less rebreathing) if the FGF inflow is high, tidal volume (TV) is low, and the duration of the expiratory pause is long (a long expiratory pause is desirable as exhaled gas will be flushed out more thoroughly).

Table 5.2 Classification of breathing systems

Circuit type	Reservoir bag	Rebreathing of exhaled gases	Examples
Open	No	No (No valves/CO_2 absorber)	Nasal cannula, insufflation, open drop induction
Semi-open	Yes	No	Circle system at very high flows, Mapleson circuits (A, B, C, D, E, Bain, Jackson-Rees)
Semi-closed	Yes	Partial (incorporates valves + CO_2 absorber)	Circle system with flows less than minute ventilation (commonest system used on present-day anesthesia machines)
Closed	Yes	Complete (incorporates valves + CO_2 absorber)	Circle system at metabolic flows causing total rebreathing; fresh gas only adds consumed oxygen/vapors per minute

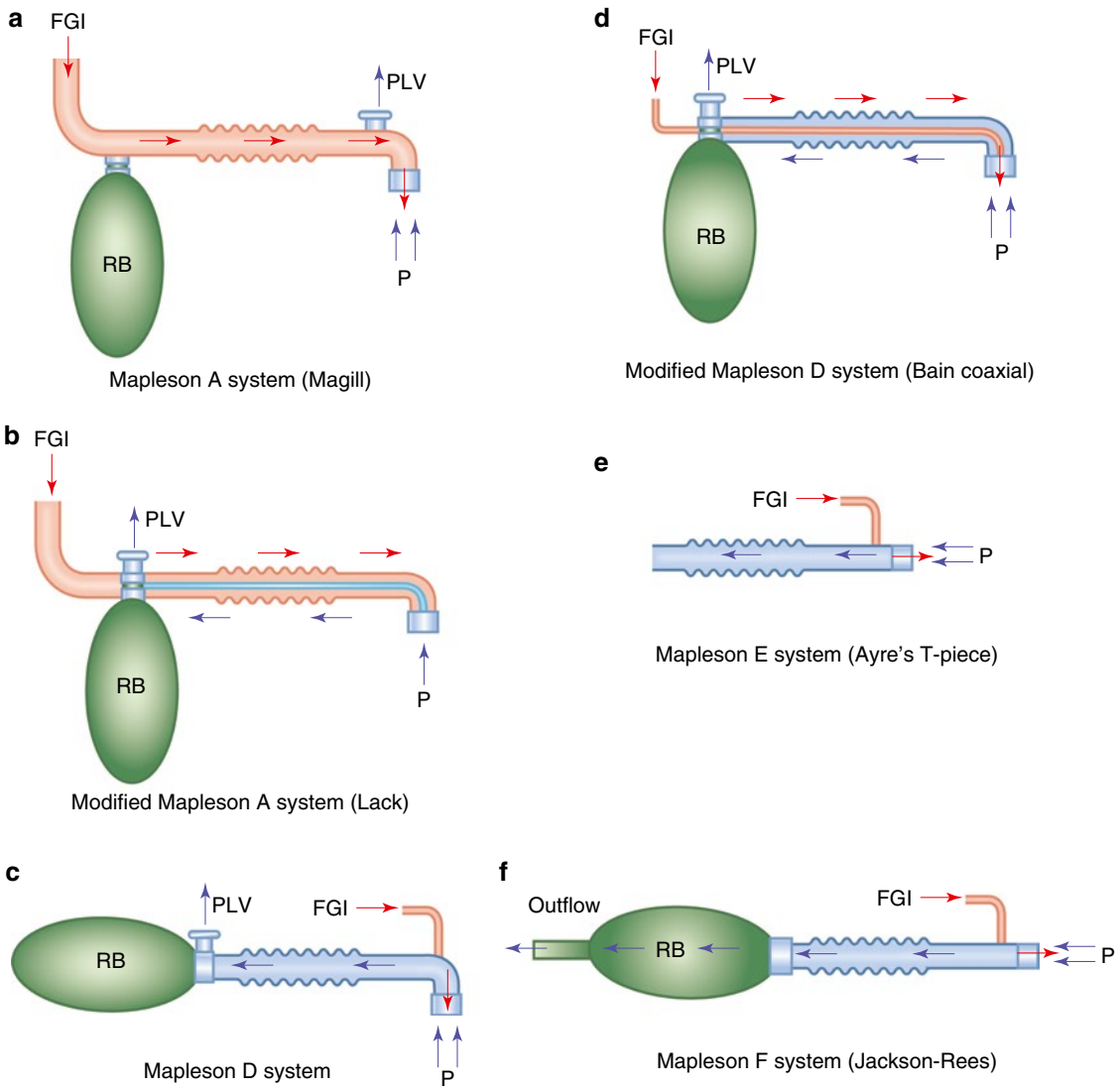


Fig. 5.9 Mapleson breathing circuits (FGI, fresh gas inlet; RB, reservoir bag; PLV, pressure-limiting valve; P, patient end; *red arrows*, fresh gas flow; *blue arrows*, waste gas)

- The reservoir bag continues to fill up, without offering any resistance, until it is full.
- The expiratory valve opens when the reservoir bag is full and the pressure inside the system increases above the atmospheric pressure. The valve remains open throughout the expiratory phase without offering any resistance to gas flow and closes completely at the start of next inspiration.

Table 5.3 Characteristics of Mapleson breathing systems

Mapleson class	Example	Fresh gas requirement		Notes
		Spontaneous	Controlled	
A	Magill's circuit	Equal to minute ventilation (80 mL/kg/min)	Very inefficient, some degree of rebreathing despite high flows	Magill's system is a modification of Mapleson A, allows for waste gas scavenging, preferred for spontaneous ventilation, avoids controlled ventilation
B		2 × minute ventilation	2–2.5 × minute ventilation	
C	Water's to and fro system	2 × minute ventilation	2–2.5 × minute ventilation	Was used for labor analgesia
D		2–3 × minute ventilation	1–2 × minute ventilation	Bain is a coaxial modification of Mapleson D system, fresh gas flow independent of tubing length
E	Ayre's T piece	2–3 × minute ventilation	2.5–3 × minute ventilation	High environmental pollution, low resistance, expiratory limb acts as a reservoir, scavenging not possible
F	Jackson-Rees circuit	2–3 × minute ventilation	2.5–3 × minute ventilation	Mapleson E system with a breathing bag with open end, manually control the leak, low resistance, scavenging difficult

Mapleson Circuits in Clinical Use

Over the years several modifications were made in the various Mapleson systems and eventually their practical use is now limited. Despite multiple advancements made in the circle system (see below), the Mapleson circuits are still in clinical use because they are cost-effective, easy to assemble, portable, and sterile, offer low resistance, and can be used with anesthesia ventilators. The systems in present use include:

a. Bain Circuit

Bain and Spoerel originally modified the "Mapleson D" system into a coaxial circuit in 1972, called as the Bain circuit (Fig. 5.10a). The fresh gas inlet tubing was incorporated inside the breathing tube, which decreased the bulkiness of the circuit and retained heat and humidity. The original circuit length proposed by Bain was 180 cm with the outer tube diameter of 22 mm and inner tube diameter of 7 mm. It is, in true sense, a universal circuit and can be efficiently used in both adult and pediatric patients and for spontaneous and controlled ventilation. It is a preferred breathing system used during patient transport and for anesthesia in remote locations. A unique feature of Bain system is that its function is independent of the circuit length, with longer lengths of Bain circuit available, presently. Bain originally recommended the following parameters for high efficacy of the circuit:

- 2 L/min FGF in patients weighing <10 kg
- 3.5 L/min FGF in patients between weighing 10–50 kg
- 70 mL/kg/min FGF in patients weighing more than 60 kg
- Respiratory rate at 12–16 breaths/min
- Minute ventilation of 100–140 mL/kg/min

b. Magill's Circuit

This is a modified form of "Mapleson A" system originally described by Evan Magill (Fig. 5.10b). The dimensions were planned such that its volume would be close to tidal volume in an adult (550 mL). The suggested length was 110–180 cm with an APL valve at the patient end and a reservoir bag at the machine (or fresh gas inflow port) end. This system is primarily used for patients on spontaneous ventilation due to its high efficacy.

The system is very inefficient for controlled ventilation and requires flows as high as 20 L/min to prevent rebreathing. The system has a very large dead space, and thus, it should not be used in patients below 25–30 kg. Also, the APL valve located at the patient end adds "drag" to the circuit making it inconvenient to use.

c. Lack System

This is a coaxial modification of "Mapleson A" system with the outer tube diameter of 30 mm and inner tube diameter of 14 mm (Fig. 5.10c). The advantage, besides conservation of heat and moisture, is that the APL valve is now shifted to machine end, and thus, the drag during the use of circuit is minimized. The rest of functional analysis remains the same as that of Mapleson A/Magill's system.

d. Jackson and Rees Modification

This is a modified "T piece" with a reservoir bag attached to the expiratory limb end (Fig. 5.10d). The pressure relief mechanism is either an adjustable valve at the end of the reservoir bag or a hole made on the side of the bag. Newer modifications have incorporated an APL valve just prior to the reservoir bag. This APL valve is fixed to release pressure above 30 cm H_2O, thereby adding safety.

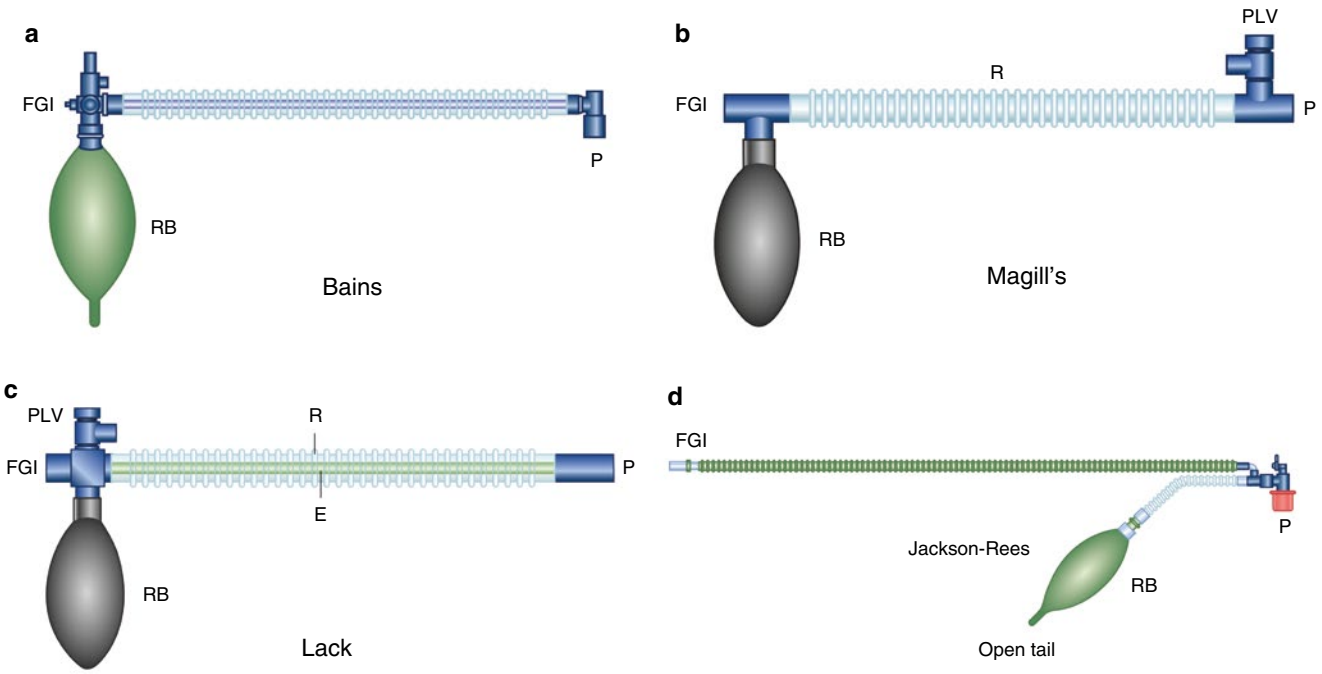


Fig. 5.10 (**a**) Bain circuit, coaxial modification of Mapleson D system, (**b**) Magill's breathing circuit, (**c**) lack modification of Mapleson A system, (**d**) Jackson and Rees modification of T piece (RB, reservoir bag; FGI, fresh gas inlet port; R, corrugated outer tubing (inspiratory); E, inner tubing (expiratory); PLV, adjustable pressure valve; P, patient end)

The ideal fresh gas requirement for spontaneous and controlled ventilation is similar and is around two to three times the minute ventilation. The circuit is particularly suited for pediatric patients as it is extremely light, lacks valves that increase circuit resistance, and has minimal dead space. Potential limitations of this modification are that it requires high fresh gas flows, which cannot be warmed or humidified.

Circle Breathing System

These are called circle systems because they deliberately rebreathe the expired gases after removing CO_2 using chemical absorbers. These systems are highly economical in terms of low fresh gas requirements and simultaneously conserve heat and moisture of expired gases. These systems allow easy monitoring and maintaining of inspired gas concentrations, as sampling errors due to high fresh gas flow being sampled (like in Mapleson systems) are eliminated. These circuits are environmentally friendly and prevent operating room pollution by allowing effective use of scavenging systems.

The potential problems with these systems are that they are prone to leaks and compensate for the leaks very poorly, due to the low fresh gas flows used with the system. The circle system is also bulky and prone to disconnections and obstruction. Moreover, the CO_2 chemical absorber can generate toxic compounds on interaction with volatile anesthetic agents and may itself be a source of circuit contamination.

Principles Guiding the Construction of an Efficient Circle System

- There should be two unidirectional valves on either side of the "y" or the common limb to prevent cross contamination of inspiratory or expiratory limb.
- APL (pressure relief) valve should be positioned in the expiratory limb downstream from the reservoir bag, allowing venting of expired gases, while conserving fresh gas.
- Fresh gas flow should enter the system proximal to the inspiratory unidirectional valve; thus it bypasses the CO_2 absorber, and all the fresh gas added to circuit is utilized during inspiration.
- The CO_2 absorber should be placed before the fresh gas flow inlet. This ensures that the gas being breathed by the patient is free of CO_2.
- The reservoir breathing bag should be located in the expiratory limb with the two unidirectional valves on either side of the bag. This will allow gases to move only in one direction (inspiratory) when bag is compressed.

Components of Circle System

The various components of the circle system are depicted in Fig. 5.11. It consists of a fresh gas flow inlet, unidirectional valves, a reservoir bag, an APL valve, and inspiratory and expiratory limbs. Other components that are housed in the circle system are a selector switch to alternate between the ventilator and reservoir bag, a peep valve at the expiratory

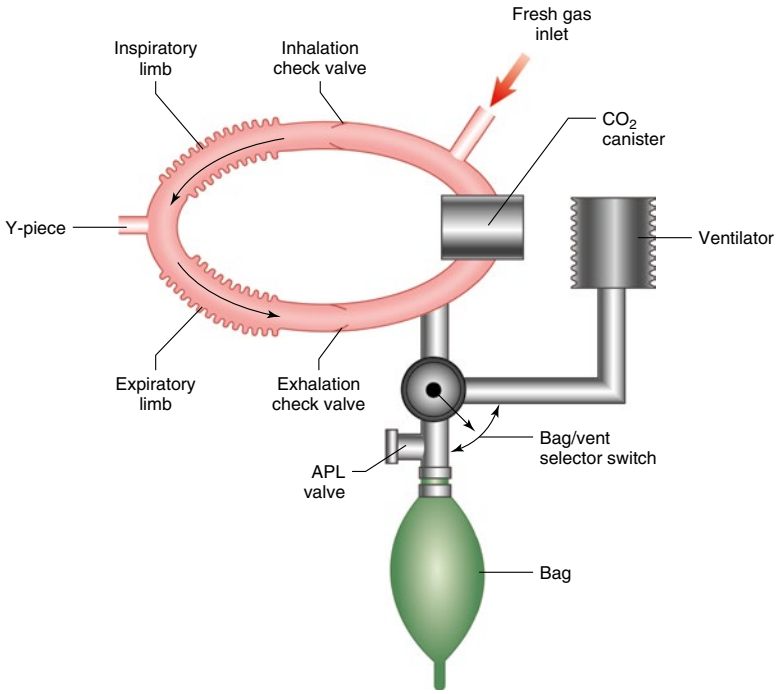


Fig. 5.11 Components of circle breathing system

port, a scavenging system, an oxygen analyzer, a spirometer, a humidifier, and a port to return the sampled gases used for analysis:

(a) *Fresh gas entry port*: The breathing circuit connects to the source of fresh gas with a leak proof connection, for allowing entry of gas into the circuit.

(b) *Gas reservoir* bag: The breathing gas is indrawn by the patient from the reservoir bag. The size of the bag should be larger than the inspiratory capacity of the patient, approximately equal to the vital capacity, or 3 times the tidal volume. Available bag sizes are from 0.25 to 6 L. For safety, the reservoir bag should withstand a maximum pressure of 50 cm H_2O.

(c) *Expiratory* port: This is most often an adjustable pressure-limiting (APL) valve that at a particular set pressure induces a leak in the circuit. During spontaneous breathing it allows leak in expiratory phase at a much lower pressure. Additionally, the valve acts as a safety device for preventing barotrauma to the lungs by preventing circuit pressure to rise past physiological limits. Modern valves allow a scavenging system to be attached to the expiratory port allowing waste gases to be diverted to the scavenging system. Some low-resistance pediatric circuits may have an open expiratory end or connect to the reservoir bag with an open end (Jackson and Rees modification of T piece) that allows manual control of allowable leak with each breath.

(d) *Corrugated connection tubes*: Universal standards have been set for size (diameter) of connection tubes. For adults, an internal diameter of 22 mm, and in children (pediatrics) a diameter of 15 mm, is recommended. The corrugations allow this tubing to bend without kinking. A potential disadvantage of corrugation is an increase in circuit compliance (change in volume produced by a specific change in pressure), which makes the circuit expand with each breath. This loss of volume during expansion can be significant for tidal volume breaths in pediatric patients.

An ideal adult circuit should have no more than 400–500 mL volume and a compliance of less than 0.5 mL/m/mmHg of pressure applied. The maximum allowable resistance offered by the circuit should be less than 1 mm H_{2O}/unit flow of fresh gas (L/min). For example, if the compliance of the circuit is 4 mL gas/cm H_{2O}, and the patient is receiving a tidal volume at a pressure of 22 cm H_{20}, then 88 mL (4 × 22) of tidal volume will be lost to the circuit.

(e) *Carbon dioxide absorber and flow-directing valves*: The mechanism of prevention of rebreathing determines which one of these two is present in the circuit. Carbon dioxide absorbers, by utilizing a series of chemical reactions, selectively remove CO_2 from the circuit/rebreathing gas. The flow-directing valves tend to isolate the expiratory gases out of the circuit preventing their re-inspiration. Generally, carbon dioxide absorber-based circuits are much more efficient in terms of low fresh gas flows required and preservation of heat and moisture in the exhaled gases.

Carbon Dioxide Absorption

The circle system allows rebreathing of gases but requires an absorbent for CO_2 absorption to prevent hypercarbia. Rebreathing the gases conserves heat and humidity in the circle system. Rebreathing is minimal at fresh gas flows greater than 5 L/min, which makes the presence of a CO_2 absorber unnecessary. Absorption of CO_2 is based on the principle of a base neutralizing an acid. CO_2 reacts with water to form carbonic acid, which is neutralized by hydroxides to generate the end products, namely, carbonate, water, and heat:

1. $CO_2 + H_2O \rightarrow H_2CO_3$
2. $H_2CO_3 + 2NaOH(\text{or } KOH) \rightarrow Na_2CO_3(\text{or } K_2CO_3) + 2H_2O + \text{Energy / Heat}$
3. $Na_2CO_3(\text{or } K_2CO_3) + Ca(OH)_2 \rightarrow CaCO_3 + 2NaOH(\text{or KO}$

The various absorbents and their compositions are mentioned in Table 5.4. Absorbent canisters maybe either single or in series, disposable, or reusable. The granules are generally 4–8 mesh in size, which gives maximum absorptive surface area with minimum resistance to flows. Mesh size refers to the number of openings per linear inch in a sieve through which the granular particles can pass.

Absorbents are held in transparent canisters to monitor their color change. Exhaustion of absorbent is indicated by the color conversion of a pH indicator dye. With rest, the granule color may return to normal, but not the absorbent capacity. The absorptive capacity of the granules is about 25 L of CO_2 per 100 g. Exhaustion of soda lime canister is reduced by channeling (space between the granules), smaller size of absorber, increased CO_2 production, high fresh gas flows, and relative position in the circle system.

Volatile inhalational agents react with the absorbent material to produce carbon monoxide (CO). Strong base content (NaOH/KOH) of the absorbents is implicated in the generation of CO. The agents potentially producing the highest to the lowest amount of CO: desflurane > isoflurane > sevoflurane = halothane. CO production increases when using dryer absorbent material (baralyme > soda lime), low fresh gas flows, or with high temperature. In addition, sevoflurane can react with the absorbent to produce a nephrotoxic "compound A" (fluoromethyl-2,2-difluoro-1-trifluoromethylvinylether). Compound A formation is generally increased with using low fresh gas flow rate (<1 L/min for 2 h), higher concentrations of sevoflurane, longer duration of anesthesia, higher temperatures, and dry absorbents (less water content).

Newer absorbents include:

- Lithium hydroxide lime (Litholyme): It is free of the strong bases (NaOH, KOH), contains LiCl as a catalyst to accelerate the formation of $CaCO_3$, and contains ethyl violet as the indicator. The CO_2 absorbing capacity is similar to Sodasorb and more than Amsorb. Litholyme does not produce CO and compound A from breakdown of volatile agents, when exhausted undergoes a permanent color change which does not revert upon resting the absorbent, and generates less heat than soda lime.
- Amsorb: It is free of the strong bases but perhaps has less carbon dioxide absorption efficacy as compared to soda lime.
- Others: Drägersorb 800 Plus, Drägersorb Free, Medisorb (by GE) with decreased amounts of NaOH/KOH to prevent production of CO, and compound A on interaction with volatile agents. Baralyme was withdrawn from the market in 2005.

Vaporizers

A vaporizer converts liquid anesthetic agent to its vapor form and adds it in measured concentrations to the fresh gas flow or the breathing system. When a liquid is enclosed in a container, molecules of liquid exist in the liquid and/or gaseous form (vapor) at a given temperature. The molecules in the vapor form and exert pressure on the walls of the container, which is called the saturated vapor pressure. Increasing the temperature increases the vapor pressure.

The temperature at which the liquid's vapor pressure is equal to the atmospheric pressure is called as the boiling point of that liquid. At lower atmospheric pressures (high altitude), the boiling point will be lower since the vapor pressure remains the same. Concentration of gases can be expressed as either partial pressure or volume percent. In a mixture of gases, the part of total pressure due to any one gas is called the partial pressure of that gas, which is affected by temperature changes. Volume percent is the number of units of volume of a gas in relation to total gas mixture. Partial pressure/total pressure = volume percent.

The number of calories required to convert 1 g of liquid to vapor is called the "heat of vaporization" for that liquid. As a liquid vaporizes, its temperature falls and so does the vapor pressure, unless externally supplied heat maintains the temperature equilibrium. Specific heat is defined as the quantity of heat required to raise the temperature of 1 g of substance by 1 °C. Thermal conductivity is the speed with which heat flows through a substance. Vaporizers are built with materials of high thermal conductivity for better thermostabilization. Properties of common anesthetic agents are listed in Table 5.5.

Table 5.4 Various CO_2 absorbents

Additive	Soda lime	Litholyme	Amsorb	Drägersorb 800+	Medisorb
Calcium hydroxide %	95	>75	85	80	70–80
Sodium hydroxide %	3			2	2
Potassium hydroxide %	2			2	0.003
Lithium chloride %		<3			
Calcium chloride and sulfate %, each			1		
Water %	15	15	15	15	17
Mesh size	4–8	4–8	4–8	4–8	4–8
Indicator dye (ethyl violet)	Yes	Yes	Yes	Yes	Yes

Table 5.5 Properties of volatile anesthetic agents

Agent	Boiling point (°C, 760 mmHg)	Vapor pressure (torr, 20 °C)	Minimum alveolar concentration (MAC)
Halothane	50.2	243	0.75
Isoflurane	48.5	238	1.15
Sevoflurane	58.6	157	2.0
Desflurane	22.8	669	6.4

Classification of Vaporizers

Vaporizers are commonly classified based upon:

- Method of regulating the output: variable bypass or measured flow
- Method of vaporization: flow over types (with or without wick), bubble through, or injection type
- Temperature compensation: thermo-compensated (by altered flow/heat or both) or non-compensated
- Specificity: agent specific or multi-agent
- Resistance: plenum type (high resistance) or draw over
- Location of the vaporizer: in circuit or out of circuit.

Most modern vaporizers are variable bypass, flow over, thermo-compensated, agent specific, plenum type, and out of circuit (for halothane, isoflurane, sevoflurane, but not for desflurane).

Working Principle

For conventional modern vaporizers (Fig. 5.12), the volatile liquid anesthetic is held in the vaporizing chamber, filled in via a filler port to a maximum "safe" fill level. The gases enter the vaporizer through an inlet from the flowmeters. Based on the dial settings, the flow gets distributed to the bypass chamber (where the gas, usually more than 80 %, directly flows to the vaporizer outlet without any addition of the inhaled anesthetic) or to the vaporizing chamber (where the volatile anesthetic vapor gets added to the fresh carrier gas, usually less than 20 %, depending on the temperature and vapor pressure of that particular inhaled anesthetic). A concentration control dial, which is a variable restrictor, regulates the relative flows to the two chambers.

The gas passing through the vaporizing chamber gets saturated with vapors of the volatile anesthetic as it flows over it. The gases from the two chambers thus exit the outlet of the vaporizer, carrying the inhaled anesthetic in a concentration that is the ratio of the flow of inhaled anesthetic to the total gas flow. Temperature compensation is necessary for variations in ambient temperatures, which is achieved by a bimetallic strip (of differential contraction) that changes resistance (according to temperature fluctuations) to the flow of gases through the bypass chamber, thus maintaining a relative constant vapor output. Wicks or baffle system is incorporated into the vaporizers to provide more surface area for vaporizing and prevent tipping, pumping, and pressuring effects. Modern vaporizers are designed for a single anesthetic agent (agent specific) and located outside the breathing circuit.

Factors Affecting Vaporizer Output

(a) *Flow rate*—vaporizer output is fairly constant between fresh gas flows of 250 mL/min to 15 L/min. However, at low flow rates (<250 mL/min) and at extremely high flow rates (>15 L/min), the vaporizer output is actually less than the dial setting due to the relatively high density of volatile inhaled anesthetics causing insufficient vapor and failure to saturate the carrier gas in the vaporizing chamber. It is important to know that the output from a sevoflurane vaporizer, when using high fresh gas flows (>10 L/min), is lower than the dial setting because of the lower vapor pressure of sevoflurane. This tendency is accentuated by a relatively empty vaporizer than a fully filled vaporizer. This is relevant when using sevoflurane for inhalational induction.

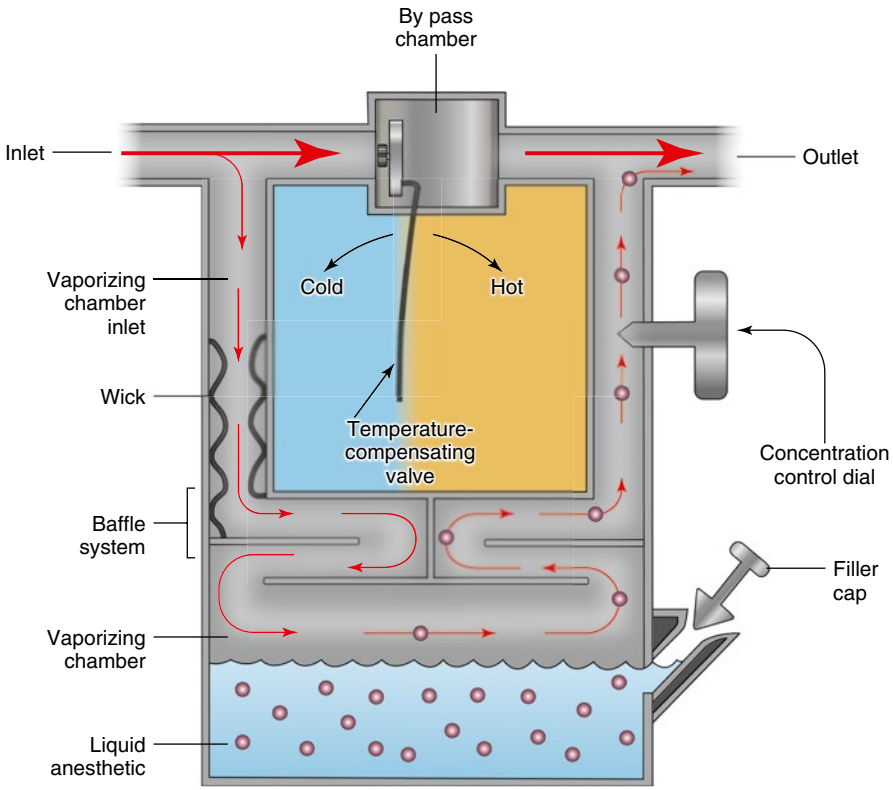


Fig. 5.12 Working principle of a vaporizer

(b) *Temperature*—output of modern vaporizers is linear from 20 to 35 °C due to automatic temperature compensation that increases carrier gas flow as the temperature of the liquid volatile agent decreases. Also, the vaporizer is constructed of metals with high specific heat and thermal conductivity. However, at very high temperatures, the bypass chamber flow increases and the vaporizing chamber flow decreases, leading to a decreased vapor output. The opposite occurs at very low temperatures.

(c) Intermittent back pressure

Pumping effect (Fig. 5.13)—at low dial settings, low flow rates, and low levels of liquid anesthetic in the vaporizing chamber, intermittent back-pressure changes from either positive pressure ventilation (rapid respiratory rates, high peak airway pressures) or the use of the oxygen flush valve may lead to higher than expected vaporizer output. The compression of gas molecules in the bypass and vaporizing chambers, which are suddenly released during the expiratory phase of positive pressure ventilation, and the retrograde flow of the vapor in the bypass chamber cause the increased output. This phenomenon is known as the pumping effect. However, modern vaporizers are immune to this effect due to a smaller vaporizing chamber, long spiral tubes at the inlet to the vaporizing chamber, extensive baffle system, and a one-way check valve at the common gas outlet, which prevents retrograde vapor flow.

Pressurizing effect: Lower than expected vaporizer outputs have been observed at high fresh gas flows and at low vaporizer settings. Increased pressure at the vaporizer outlet compresses the carrier gas but with no effect on the vapor pressure in the vaporizing chamber or the bypass gas. Hence, subsequent vapors get diluted producing lower than expected output.

(d) *Carrier gas composition*—when nitrous oxide is added to 100 % oxygen as a carrier gas, there is a sudden but transient decrease in the vaporizer output, followed by a slow increase to a new steady-state value since nitrous oxide is more soluble than oxygen in the halogenated volatile liquid anesthetic. Once the anesthetic liquid is totally saturated with nitrous oxide, the vaporizing chamber output further increases transiently, and a new steady state is established.

(e) *Rebreathing*—rebreathing of inhaled agents occurs more at lower fresh gas flows with a set high minute ventilation, as the exhaled gases contribute more to the percentage of inspired gases causing a discrepancy in vaporizer setting and delivered output.

The various hazards associated with the vaporizers are misfiling, contamination, tipping (>45°), obstructing the valves, overfilling or underfilling, simultaneous administration of inhaled anesthetics, and leaks. Various safety features incorporated to prevent these are agent-specific vaporizers, keyed filling devices to prevent misfiling, filler port located

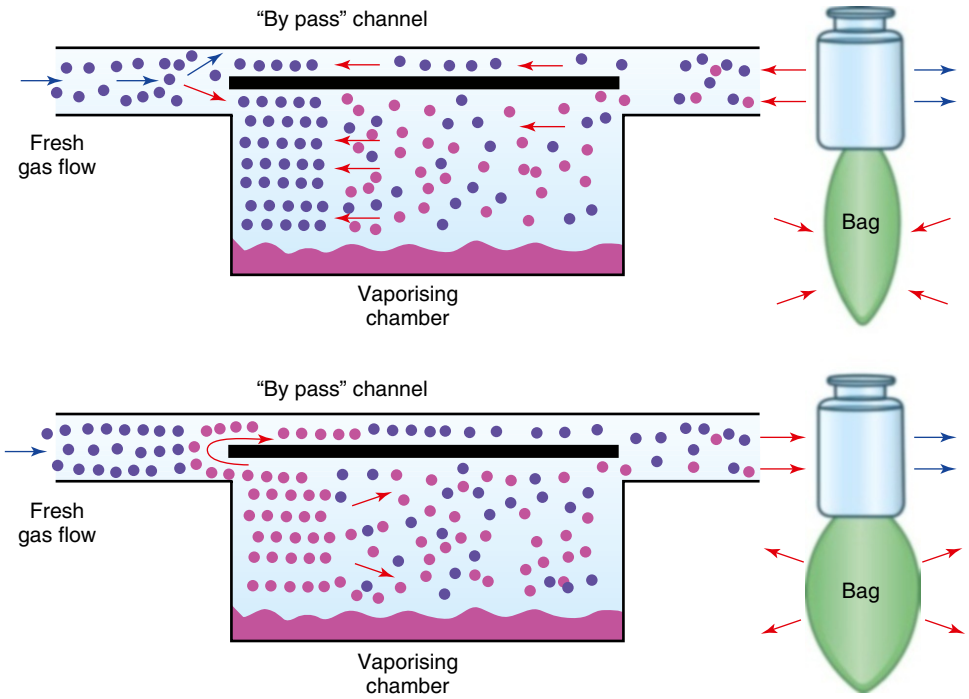


Fig. 5.13 Pumping effect in a vaporizer

at the maximum safe liquid level to prevent overfilling, firm securing of vaporizers on anesthesia machines to prevent tipping, interlock systems, or select-a-tec mechanism to prevent simultaneous administration of more than one inhaled anesthetic.

Desflurane Vaporizer

The Tec 6 or the desflurane vaporizer is an electrically heated, thermostatically controlled, constant-temperature, pressurized, electromechanically coupled dual-circuit, gas-vapor blender. Desflurane is an inhalation agent with high volatility, low potency (1/5 of other volatile agents), and high vapor pressure along with a low boiling point (boils at room temperature at sea level), which necessitates a specially constructed vaporizer to overcome certain delivery problems.

The desflurane vaporizer has two independent gas circuits arranged in parallel, one for the fresh gas flow and the other containing desflurane in a sump that is electrically heated and controlled at 39 °C to create a vapor pressure of two atmospheres. The pressures in the two circuits are pneumatically and electronically controlled and are related. A shutoff valve downstream of the sump opens when the concentration dial is switched on and allows the desflurane vapor from the sump reservoir to pass to the pressure regulating valve at 1.1 atmosphere absolute, at a fresh gas flow rate of 10 L/min. Desflurane output is thus regulated by the control dial (variable constrictor) and the fresh gas flow rate.The desflurane vaporizer is filled in a closed system with a special filler called "Safe-T-Fill." As a safety feature, the shutoff valve closes to produce no output in case of power failure, with less than 20 mL of anesthetic liquid left, disparity of pressures in the vaporizer, or during tipping. Desflurane is calibrated at 100 % oxygen and when other gases of low viscosity are used (nitrous oxide), or at low fresh gas flow rates, the working pressure gets reduced, reducing the vapor output proportionately.

For conventional vaporizers and not the Tec 6, atmospheric pressure changes inversely affect the vaporizer output in terms of volume percent with minimal effect on partial pressure and anesthetic potency. However, since the desflurane vaporizer maintains a constant vapor output and not a constant partial pressure, the dial settings need to be increased with increase in altitude (drop in atmospheric pressure).

Aladin Cassette Vaporizer

This is an agent-specific, color-coded cassette recognized by the anesthesia machine through magnetic labeling. It is used in Datex-Ohmeda S/5 ADU and similar machines. The cassettes are available for isoflurane, halothane, desflurane, and sevoflurane. A digital potentiometer adjusts agent concentra-

tion according to the number of output pulses from the agent wheel. The flow control valve is controlled by a central processing unit, which receives input from the concentration control dial, pressure, and temperature sensors in the vaporizing chamber, and the flowmeters to precisely regulate the vapor concentration.

Other Components of Anesthesia Machine

Ventilators

Ventilators provide positive pressure breaths to the patient. They can be classified as follows:

- Based on power source: pneumatic, electric, or both.
- Based on driving mechanism: Double circuit ventilators are pneumatically driven by either oxygen, air, or both. Single circuit ventilators are piston-driven mechanical ventilators, the piston being controlled by computer software to deliver various modes of ventilation and accurate tidal volumes.
- Based on cycling mechanism: Ventilators can be time cycled, volume cycled, or pressure cycled. Most ventilators are time cycled and electronically controlled. In advanced ventilators, various modes of ventilation and secondary cycling mechanisms are available, which allow for pressure support and adjustment for pressures based on triggers provided by pressure sensors.
- Based on type of bellows: The direction of movement of bellows during the expiratory phase classifies the ventilators as ascending or descending types. Ascending bellows are commonly used and are safer since disconnections are identified earlier with non-filling of bellows (collapse). A descending bellow may continue to entrain air by gravity in case of a disconnection. Generally, anesthesia workstations have an integrated apnea alarm that cannot be disabled while the ventilator is in use.

Working Principle

The basic principle of ventilator function is generation of a positive pressure gradient between the patient and the machine. In double circuit type of ventilators, a clear plastic box encases the bellows and the driving gas. The bellows separate the driving gas outside from the fresh gas inside it. During the inspiratory phase, the driving gas enters the bellows chamber and causes the pressure within it to increase resulting in closure of the ventilator relief valve and compression of the bellows to deliver the gases to the patient. A ventilator flow control valve regulates drive gas flow into the pressurizing chamber (Fig. 5.14).

During the expiratory phase, the driving gas exits the bellows housing, pressure drops within the bellows housing, and the ventilator relief valve opens. The bellows are then refilled with exhaled patient gases. Once the bellows are refilled and the pressure inside exceeds the threshold of 2–3 cm of H_2O, the ventilator relief valve opens allowing the gases to exit for scavenging during the expiratory phase. Exhalation is a passive process, where airway pressures are reduced to atmospheric levels or preset values of PEEP during the expiratory phase of ventilation. In piston-type ventilators, the bellows are replaced by an electrically driven piston and a negative pressure relief valve, which can terminate the downstroke of the piston.

Common hazards of using ventilators include misconnections, disconnections, leaks, loss of tidal volume to circuit compliance, excessive tidal volumes due to lack of fresh gas decoupling, barotrauma, hypoventilation due to incompetent ventilator relief valve, undesired PEEP (especially with ascending type of bellows), power supply problems, incorrect ventilator settings, and ventilator malfunction.

Spirometer

Spirometers or respirometers are used to measure the exhaled tidal volume and in some cases also the inspiratory tidal volumes. The flow of gas within the spirometer causes rotation, which is measured electronically, photoelectronically, or mechanically. Various types of spirometers are the anemometer (Wright's spirometer), hot-wire anemometer, ultrasonic flow sensors, or pneumotachograph.

Circuit Pressure Sensor

A pressure gauge or electronic sensor is used to measure breathing-circuit pressure. The measured pressure reflects the patient's airway pressure. Increase in pressure suggests worsening pulmonary compliance, an increase in tidal volume, or an obstruction in the breathing circuit, tracheal tube, or the patient's airway, while a decrease in pressure may indicate an improvement in compliance, a decrease in tidal volume, or a leak in the circuit.

Adjustable Pressure-Limiting Valve

The adjustable pressure-limiting (APL) valve or pressure relief or pop-off valve limits the pressure in the breathing system to 70–80 cm of H_2O. During spontaneous ventilation, it can be kept either fully open or partially closed (for assisted bag ventilation). Improper use can result in either excessive leak or barotrauma.

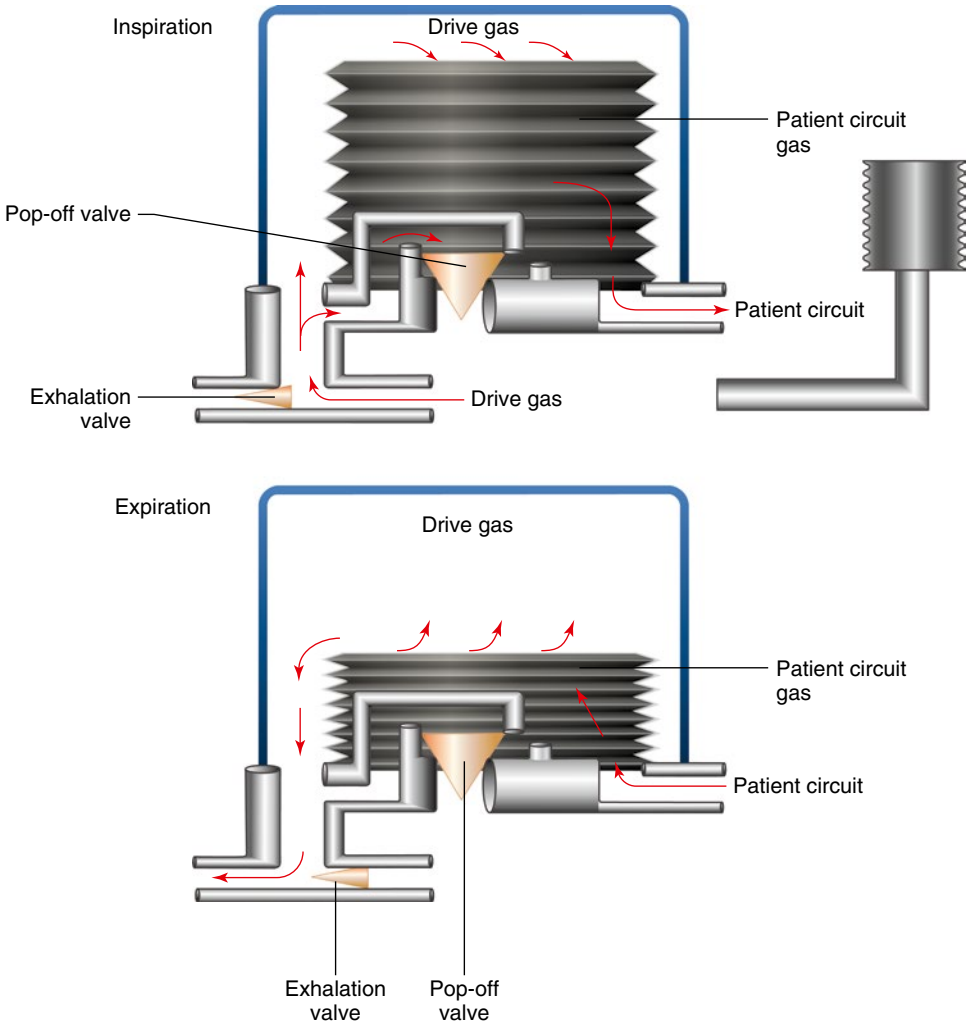


Fig. 5.14 Working of ventilator bellows

Humidifiers

Humidifiers warm inspired gases to body temperature and saturate them with water vapor prior to administration to the patient. Humidifiers minimize water and heat loss. The method of humidification can be either passive or active. Passive humidifiers, such as HME, retain the exhaled water vapor via a hygroscopic material. However, they can increase resistance and dead space or cause obstruction. Active humidifiers add heat and water to the inspired gases either via a passover, wick, bubble through, or vapor phase humidifier. They can, however, cause nosocomial infections, thermal lung injury, circuit disconnection, or increased resistance. Active humidifiers are more useful in pediatric patients, while passive humidifiers are more commonly used in patients with communicable respiratory diseases.

Electrical Safety

Since the operating room contains a variety of electronic equipment, both patients and healthcare professionals are exposed to the risk of electrical shocks. The maximum amount of leakage allowed for any electrical equipment is 10 microamps. Microshock is said to occur when the heart is directly exposed to a current of 100 microamps. An isolation transformer isolates operating room power supply from the grounds, while a line isolation monitor measures the potential for current flow from the isolated power supply to the ground. If an unacceptably high current flow occurs to the ground, the alarm of the line isolation monitor is activated, which denotes the presence of a single fault. Power will still flow unless the ground leakage circuit breaker is tripped. When the line isolation alarm is activated, the last piece of

equipment that was plugged in should be checked out. Two faults are needed to cause a shock.

Surgical cautery uses a high current that flows from the cautery tip, through the patient, and exits via the grounding pad/return electrode. A conductive gel prevents burns at the site of pad contact with the patient's skin. The grounding pad should be placed as far away from the heart and as near to the surgical site. Malfunction of the grounding pad can lead to the current passing to metal contacts, like cardiac pacing wires and ECG electrodes, causing burns at points of contact.

Operating Room Scavenging System

Scavenging is the collection and subsequent removal of vented gases from the operating room. Inadequate scavenging leads to operating room pollution with waste gas contamination and can be due to leaks, anesthetic techniques like flushing of circuits or failure to turn off gases, equipment issues like using uncuffed endotracheal tubes, during filling of vaporizers, or use of Jackson-Rees circuit (which cannot be scavenged).

The National Institute for Occupational Safety and Health (NIOSH) sets the standards for maximum allowable exposure limits for the health professionals. Thus in other words, it sets the targets for scavenging system efficiency. Exposure standards are time-weighted average (TWA) concentrations that represent mean concentration exposure in an 8-hour time period. For preventing decrement in performance, cognition, and audiovisual ability, a TWA of up to 25 parts per million (ppm) is suggested for nitrous oxide. When halogenated inhalation agents are used in combination with nitrous oxide, a TWA of up to 0.5 ppm is acceptable, whereas when halogenated agents are used alone, a value of 2 ppm is permissible.

The scavenging system transports excess/waste gases from anesthesia machines or circuits to the outside atmosphere at a remote location. The parts of a standard scavenging system include (Fig. 5.15):

>):*Collecting system*—these are a series of pipelines that directly receive waste gases from the OR environment, i.e., from the adjustable pressure release (APL) valve or the anesthesia machine. A unique safety feature of this system is that it uses 30 mm male and female connectors, unlike 22 mm standard connections used universally in breathing circuits. This prevents any accidental direct connection between the patient and the scavenging system. Additionally a pop-off valve set at around 10 cm H_2O is incorporated into the collecting system, which, in the event of an obstruction of the scavenging system, releases excess gas preventing backpressure buildup in the patient circuit.

- *Transfer systems*—these are kink-resistant tubings that act as a transit between the collecting system and the receiving system.
- *Receiving system*—it consists of a non-collapsible chamber capable of air entrapment when negative pressure is generated in the scavenging system as a result of excess gas vented out. The scavenging system continues to expel out gases at a constant rate irrespective of breathing phase, but it only receives waste gases in the expiratory phase of breathing cycle.

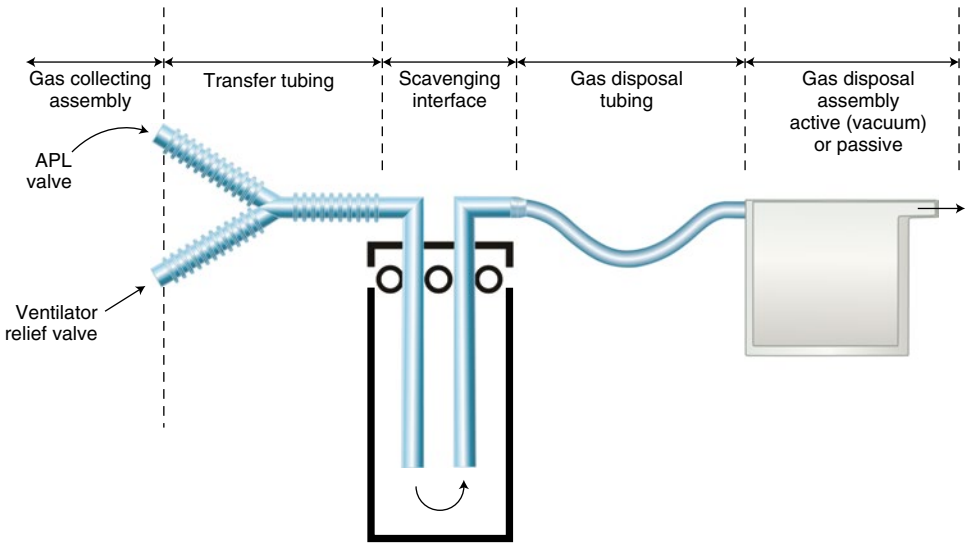


Fig. 5.15 Schematic of a scavenging system

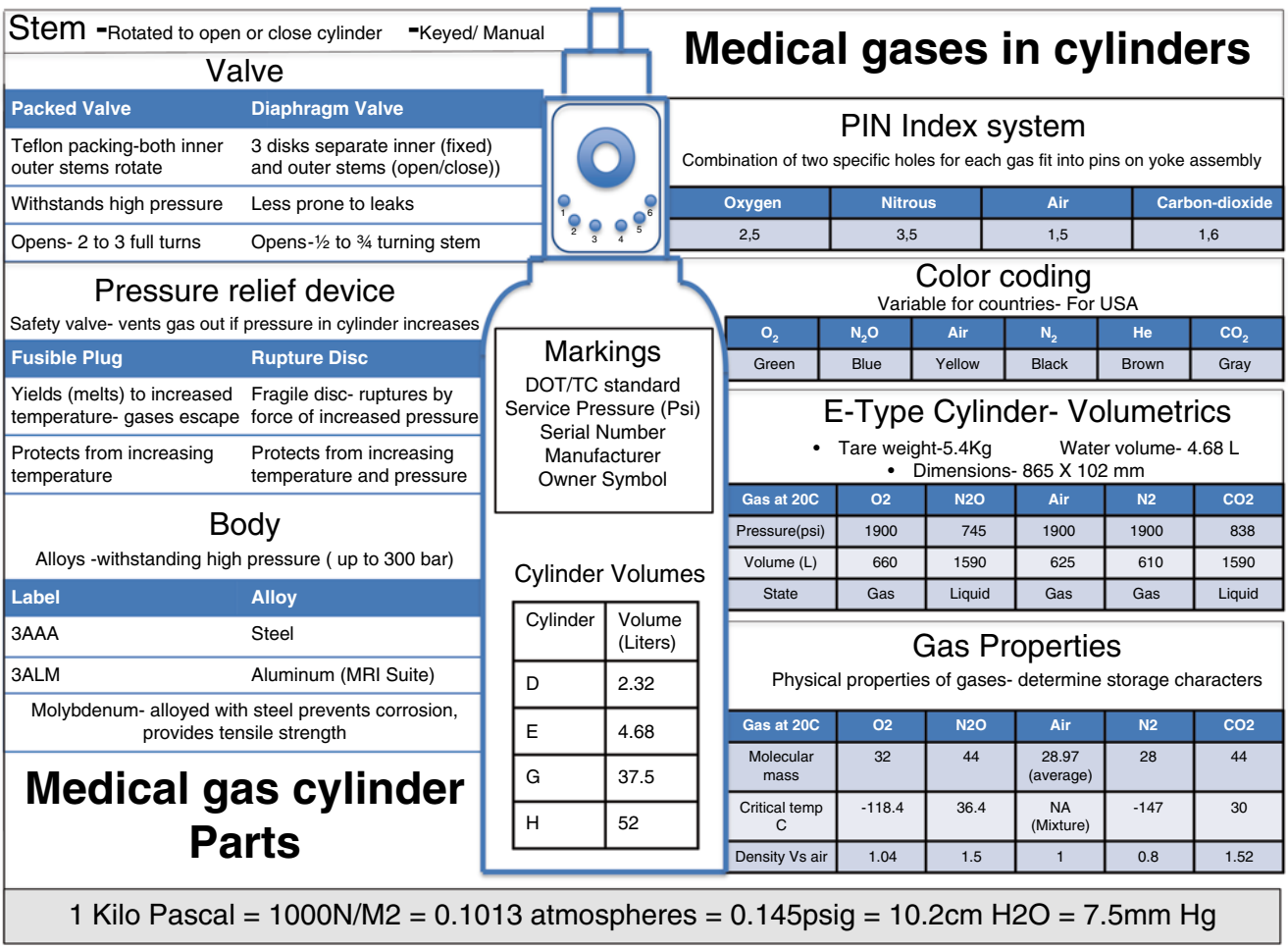
- *Disposal unit*—this is the terminal unit of scavenging system which disposes of the waste gases into the environment. It also uses a water trap to accumulate condensate from the exiting gases. This unit forms the basis of division of scavenging system into:

Active scavenging system—it caters to hospitals with large volumes of waste gases and generates negative pressure in the scavenging system by the use of an active exhaust/vacuum, where the vacuum control valve is set at 10–15 L of waste gas/min. Gases are pushed out into a remote environment.

Passive scavenging system—this is infrequently used nowadays and serves ORs with a small case load. Gases are discharged into a wide bore tubing opening into the outside environment. It relies upon negative pressure generated by the environmental wind to entrain the waste gases. Some of these units employ charcoal-based adsorption to dispose off the scavenged gases. However, the efficacy of these units is questionable and passive systems are not recommended anymore.

Newer Anesthesia Workstations

As technology is developing, newer anesthesia workstations are being incorporated with various features, such as fresh gas decoupling to provide more accurate/corrected tidal volumes, return of sampled gas to the fresh gas allowing low-flow anesthesia, electronic PEEP, electronic ventilation parameters, reduced external connections, compact CO_2 absorbent canisters that can be changed during ventilation without the loss of circle system integrity, and vertical orientation of the unidirectional valves to reduce resistance for spontaneous respiration.



Anesthesia Machine Checklist

Complete anesthesia workstation checkout or guidelines for preanesthesia checkout are listed in Appendices 1 and 2. The specific component check should be done as follows:

(a) *Calibration of the oxygen analyzer*—the oxygen sensor, which is placed either in the inspiratory or expiratory limb, is temporarily disconnected and exposed to room air to be calibrated at 21 %. Once the calibration is done, the sensor is reinstalled. Oxygen analyzers have a low-level alarm that is automatically activated by turning on the anesthesia machine.

(b) *Low-pressure circuit leak test*—it checks for leaks in the low-pressure system downstream from all safety devices except the oxygen analyzer. The leak test is chosen depending on the presence or absence of the check valve near the common gas outlet. A negative pressure leak test is performed on machines with a check valve, while a positive pressure test is performed on machines without a check valve near the common gas outlet.

Positive pressure leak test: The low-pressure system and the breathing circuit are pressurized with the oxygen flush or high gas flows from the flowmeter to a pressure of about 30 cm of H_2O. The flow necessary to maintain a steady pressure should not be greater than 350 mL/min.

Negative pressure leak test (universal leak test): The machine's master switch, flow control valves, and vaporizers are turned off, and a suction bulb is attached to the common gas outlet and squeezed repeatedly until it is fully collapsed. A vacuum is created in the low-pressure circuitry, and the leak is considered minimal if the hand bulb remains collapsed for at least 10 s. An unacceptable leak is present if the bulb reinflates during this period. The test is repeated with each vaporizer individually turned to the "on" position because internal vaporizer leaks can be detected only with the vaporizer turned on.

(c) *Circle system tests*—this has two components for check, a positive pressure leak test (above) and the flow test. The flow test checks the integrity of the unidirectional valves. The Y piece is removed from the circle system, and breathing is performed on each hose individually while the valves are checked for unidirectional movement. It should be possible to inhale but not exhale through the inspiratory limb and to exhale but not inhale through the expiratory limb.

(d) *Workstation self-tests*—newer anesthesia machines are incorporated with technology to check the various components of the anesthesia machine, either automatically or manually. Logs are kept automatically for the checks performed.

Appendix 1: Anesthesia Machine Checkout Recommendations

To be accomplished daily
Item 1: Verify that an auxiliary oxygen cylinder and self-inflating manual ventilation device are available and functioning
Item 2: Verify that patient suction is adequate to clear the airway
Item 3: Turn on the anesthesia delivery system and confirm that AC power is available
Item 4: Verify the availability of required monitors, including alarms
Item 5: Verify that pressure is adequate on the spare oxygen cylinder mounted on the anesthesia machine
Item 6: Verify that piped gas pressures are ≥50 psi
Item 7: Verify that vaporizers are adequately filled and, if applicable, that filler ports are tightly closed
Item 8: Verify that there are no leaks in the gas supply lines between the flowmeters and the common gas outlet
Item 9: Test the scavenging system function
Item 10: Calibrate or verify calibration of the oxygen monitor and check the low-oxygen alarm
Item 11: Verify that the carbon dioxide absorbent is not exhausted
Item 12: Check for proper breathing system pressure and leaks
Item 13: Verify that gas flows properly through the breathing circuit during both inspiration and expiration
Item 14: Document completion of checkout procedures
Item 15: Confirm ventilator settings and evaluate readiness to deliver anesthesia care (anesthesia time-out)

Appendix 2: Anesthesia Machine Checkout Recommendations

To be completed before each procedure
Item 2: Verify that patient suction is adequate to clear the airway
Item 4: Verify the availability of required monitors, including alarms
Item 7: Verify that vaporizers are adequately filled and, if applicable, that filler ports are tightly closed
Item 11: Verify that the carbon dioxide absorbent is not exhausted
Item 12: Check for proper breathing system pressure and leaks
Item 13: Verify that gas flows properly through the breathing circuit during both inspiration and expiration
Item 14: Document completion of checkout procedures
Item 15: Confirm ventilator settings and evaluate readiness to deliver anesthesia care (anesthesia time-out)

Clinical Review

1. All of the following are components of the low-pressure system of the anesthesia machine, except:
   A. Flowmeters
   B. Vaporizers
   C. Fail-safe valve
   D. Common gas outlet
2. The pressure gauge of an oxygen "E" cylinder shows 1,000 psi. How long will it take for the tank to get empty if using flows of 10 L/min?
   A. 15 min
   B. 30 min
   C. 1 h
   D. 1.5 h
3. The fail-safe valve:
   A. Senses pressure
   B. Senses flow
   C. Senses both pressure and flow
   D. Prevents delivery of a hypoxic gas mixture
4. If the fresh gas flow is 2 L/min, the volume of gas exiting via the scavenging system should be (L/min):
   A. 0.5
   B. 1
   C. 1.5
   D. 2
5. Characteristic of a circle system is that:
   A. It is light weight.
   B. It conserves heat and humidity.
   C. Disconnections are rare.
   D. It is not environmental friendly.
6. End products of the reaction in a CO_2 absorbent are:
   A. Carbonates
   B. Water and heat
   C. Sodium hydroxide
   D. All of the above
7. Hazards of vaporizer include:
   A. Tipping
   B. Pumping effect
   C. Incorrect agent
   D. All of the above
8. If the volume of gas is 500 L at 1,520 mmHg pressure, what would be the volume of gas at 760 mmHg, temperature being constant?
   A. 250 L
   B. 500 L
   C. 1,000 L
   D. 2,000 L
9. During manual ventilation, with the APL valve fully open, on squeezing the reservoir bag:
   A. All the gas is delivered to the patient.
   B. All the gas is leaked to the atmosphere.
   C. All the gas is collected by the scavenging system.
   D. The pressure in the reservoir bag increases.
10. On the anesthesia machine, the oxygen flowmeter should be arranged:
    A. Last in the sequence, on the right.
    B. First in the sequence, on the left.
    C. In the middle, between the other flowmeters.
    D. The order of arrangement is of insignificant consequence.

Answers: 1. C, 2. B, 3. A, 4. D, 5. B, 6. D, 7. D, 8. C, 9. C, 10. A

Further Reading

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Patient Monitoring

6

Benjamin Grable and Theresa A. Gelzinis

Modern monitoring devices have markedly improved anesthesia safety. However, it is important to realize that even as technology advances, the most important aspects of monitoring are vigilance and interpretation of the data by the anesthesiologist. The American Society of Anesthesiologists (ASA) has implemented a protocol for standards in anesthesia monitoring (Table 6.1). This chapter describes these standards, along with a description of the methodology of the most common invasive and noninvasive monitors used in anesthesia practice today.

Arterial Blood Pressure Monitoring

Maintaining arterial blood pressure within a physiologic range is of paramount importance to the anesthesiologist. Arterial hypotension can precipitate numerous adverse outcomes such as stroke, renal failure, and organ hypoperfusion. Conversely, arterial hypertension can lead to increased risk of myocardial infarction, surgical bleeding, and rupture of a preexisting vascular aneurysm leading to cerebral or aortic hemorrhage. Some basic information is described below.

- Systolic blood pressure (SBP) is the peak pressure generated during systolic contraction of the left ventricle. Normal SBP ranges from 90 to 140 mmHg (Table 6.2).
- Diastolic blood pressure (DBP) is the trough pressure during diastolic relaxation of the left ventricle. Normal DBP ranges from 60 to 90 mmHg.
- Mean arterial pressure (MAP) is the average arterial pressure during a single cardiac cycle and signifies the perfusion pressure of the organs in the body. Normal MAP ranges from 70 to 110 mmHg. MAP can be calculated by the formula MAP = DBP + 1/3 PP, where PP is the pulse pressure. Pulse pressure is the difference between SBP and DBP. Low MAP (<60 mmHg) can lead to ischemia of the organs in the body.

Noninvasive Blood Pressure Monitoring

Noninvasive blood pressure (NIBP) monitoring is accomplished by *placing* an inflatable cuff around an upper or lower extremity. Traditionally, the upper arm has been utilized, but depending on the patient's body habitus or the surgical procedure, the forearm and the calf are suitable alternatives. The blood pressure cuff is not placed over arteriovenous fistulas, infective sites, and wounds.

Selecting the appropriate *cuff size* is critical in achieving reliable results. An appropriately sized cuff should have a width of approximately 40 % of the circumference of the extremity and a bladder length that encircles at least 60 % of the extremity. A cuff that is too small or tight will produce falsely elevated blood pressure readings, while a cuff that is too large or loose will produce falsely low blood pressure readings.

The blood pressure reading is usually taken at 3–5 min *intervals. Complications* are rare with the use of NIBP monitoring. The two major complications are (1) venous congestion (leading to hematoma formation under and distal to the cuff and causing extravasation of intravascular fluid and edema) and (2) neuropathy from ulnar nerve ischemia. Both of these complications occur most commonly when NIBP monitoring is used for long procedures and at short intervals.

Methods of NIBP Monitoring

NIBP monitoring can be accomplished by using several different methods. The palpatory method involves palpation of a peripheral pulse, inflating the blood pressure cuff placed proximally to the artery to occlude the artery, then slowly releasing the cuff, and palpating the artery for return of pulsations. The latter point denotes the systolic pressure.

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Table 6.1 ASA standards for basic anesthetic monitoring

An anesthesia provider will be present in the operating room throughout the entire anesthetic course
Oxygen delivery will be measured using an oxygen analyzer placed in the inspiratory limb of the anesthesia circuit. This analyzer will contain a low inspired oxygen concentration alarm to prevent the delivery of a hypoxic oxygen mixture
Blood oxygenation will be monitored quantitatively using a device such as a pulse oximeter and qualitatively by assessing patient skin color
During general anesthesia, adequacy of ventilation shall be assessed by observing chest rise and by auscultation of breath sounds and continuous quantitative end-tidal carbon dioxide ($ETCO_2$) monitoring. During moderate and deep sedation, ventilation shall be assessed by qualitative clinical signs
Circulation shall be assessed using continuous electrocardiography (ECG) to monitor heart rate and blood pressure measurement at least once every five minutes. In addition, circulation shall be continuously monitored, either through the use of pulse oximetry or invasive monitoring
Body temperature will be measured when body temperature changes are expected

Table 6.2 Normal and abnormal blood pressures

Category	Systolic (mmHg)	Diastolic (mmHg)
Hypotension	<90	<60
Normal	90–140	60–90
Mild hypertension	141–160	91–100
Moderate hypertension	161–180	101–110
Severe hypertension	>180	>110

Diastolic blood pressure cannot be measured by this method. A Doppler probe, if available, can be substituted for the anesthesiologist's fingers, which will give a more accurate reading of the systolic blood pressure.

The most simplistic method of NIBP measurement is manual auscultation (via a stethoscope and sphygmomanometer) of the brachial artery (Korotkoff sounds) as the blood pressure cuff is slowly deflated (Fig. 6.1). The first sound auscultated represents SBP, and the last sound auscultated represents the DBP. While reasonably accurate, manual auscultation has a number of limitations. It is time consuming and cumbersome, cannot be performed during procedures that require the upper extremities to be tucked next to the patient, and is inaccurate in the presence of low flow states (hypotension) and with increased deflation speed, which underestimates the blood pressure.

In the operating room, an automated NIBP monitor, the oscillonometer, is the most commonly used method. This device has a transducer which is connected to a blood pressure cuff. The cuff is inflated until there is no oscillation present in the transduced pressure. This occurs at a pressure above the patient's systolic blood pressure. As the cuff slowly deflates, the oscillations increase in amplitude as shown in Fig. 6.2. The pressure at the peak oscillatory amplitude is the MAP.

There are two methods used to calculate the SBP and DBP, the maximal slope method and the set ratio method. With the maximal slope method, the SBP is defined as the point at which the oscillations decrease in amplitude most rapidly and the DBP as the point where the oscillations increase in amplitude most rapidly. With the set ratio method, a set ratio of oscillation amplitude to the maximum amplitude is utilized to estimate SBP and DBP. Each manufacturer maintains a proprietary microprocessor algorithm used to perform this calculation. Because of differences between algorithms, the most reliable measurement is the MAP. Limitations of using oscillonometers are similar to those of the auscultatory method. In addition, oscillonometers underestimate MAP in patients with increased pulse pressure (atherosclerosis and decreased arterial compliance) and should not be used during cardiopulmonary bypass (lack of pulsatile flow).

Although less frequently used intraoperatively, there are several other methodologies for noninvasive arterial blood pressure monitoring. Arterial digital photoplethysmography obtains blood pressure measurements through monitoring the artery of a digit. Concerns about this method include its inaccuracy and its inability to detect abrupt changes in blood pressure. Arterial tonometry measures blood pressure using sensors placed on an artery, thereby externally measuring the arterial pressure. For this device to work, a palpable artery must be present and it has been demonstrated that arterial tonometry, rather than measuring absolute systolic or diastolic blood pressures, is more accurate in detecting pulse pressure.

Invasive Blood Pressure Monitoring

Many surgical procedures require close monitoring and manipulation of arterial pressure to assist the surgeon during specific procedures, such as carotid endarterectomy, aortic cannulation, and orthopedic procedures, where significant blood loss is anticipated (Table 6.3). It is important for the anesthesiologist not only to monitor the blood pressure, but also to understand how the device measures and interprets data so that he/she will be able to determine whether a blood pressure reading is reliable or not.

Invasive blood pressure monitoring is the gold standard for the intraoperative measurement of arterial blood pressure. A normal arterial pulse waveform is shown in Fig. 6.3. Normal components of the waveform are:

- Upstroke: the upstroke (anacrotic limb/anacrotic rise) begins at the opening of the aortic valve in early systole. The steepness or rate of ascent and height of this initial upswing is related to the contractility and stroke volume of the left ventricle.

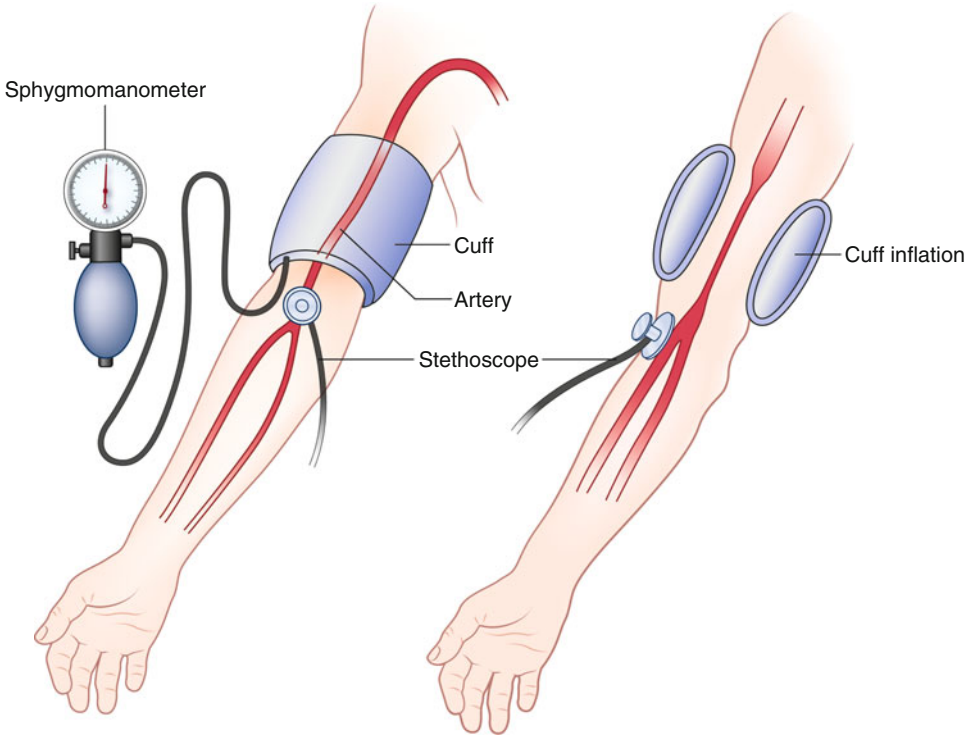

Fig. 6.1 Auscultatory method of blood pressure monitoring

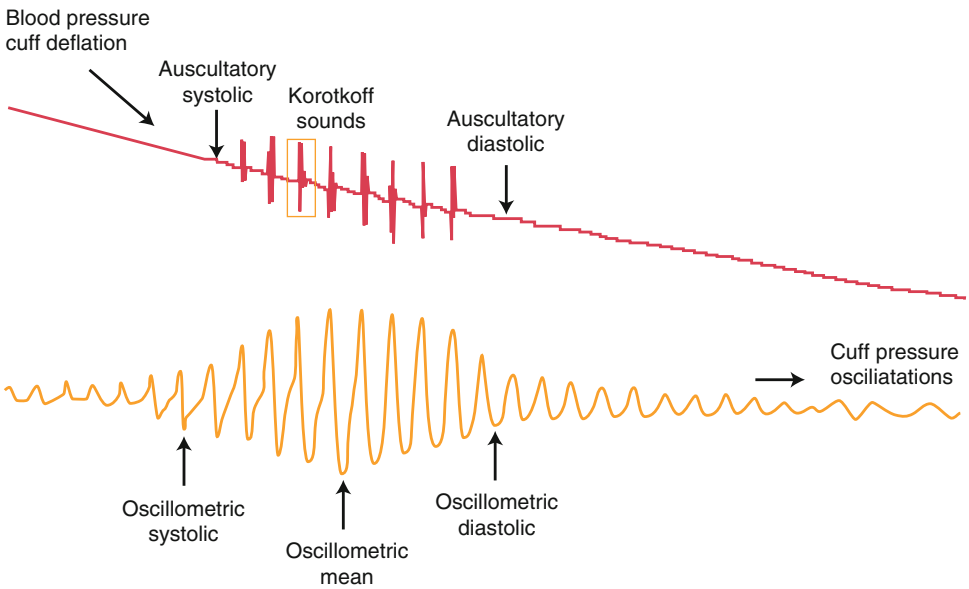

Fig. 6.2 Blood pressure measurement via an automated oscillonometer

Table 6.3 Indication and contraindications of invasive blood pressure monitoring

Indications	Contraindications
Major surgery requiring beat-to-beat monitoring of blood pressure	Severe peripheral vascular disease with lack of adequate collateral blood flow
Clinical conditions—hypotension, sepsis, vasopressor therapy, anticipated wide swings in blood pressure	Coagulopathies or bleeding disorders
Inability to accurately measure noninvasive blood pressure—obese patients	Infected sites
Repeated blood sampling—arterial blood gas, hematocrit	Extremity burns

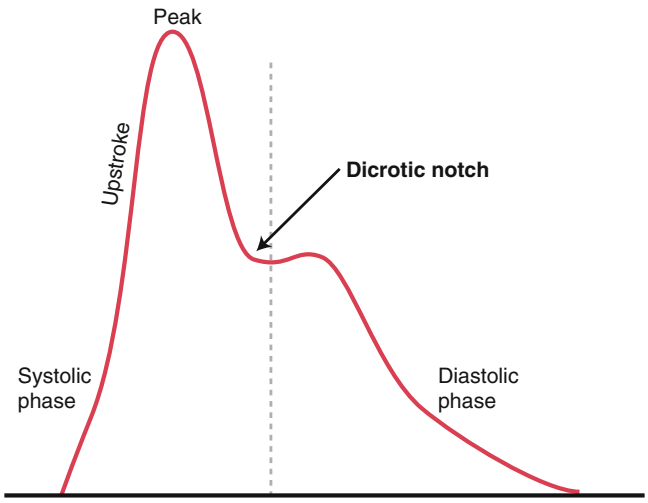

Fig. 6.3 Normal arterial pulse waveform

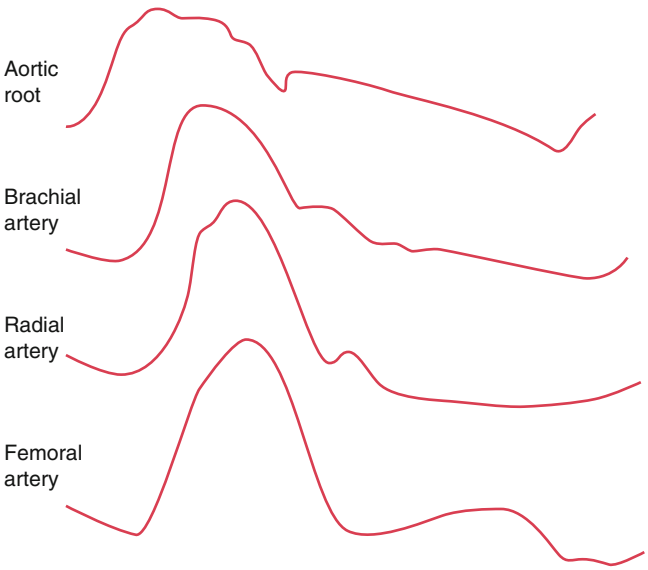

Fig. 6.4 Arterial pulse waveform change from central to the periphery. Pressures are higher in the more distal arteries than central arteries

- Systolic peak: the systolic peak represents the highest pressure generated by the left ventricle during cardiac contraction. This peak point marks the actual systolic blood pressure of the patient.
- Dicrotic limb: the dicrotic limb begins during late systole as the flow of blood out of the left ventricle starts to decrease.
- Dicrotic notch: the dicrotic notch represents the closure of the aortic valve and the beginning of diastole.
- Diastolic pressure: the end diastole pressure landmark is the location at which the patient's actual diastolic blood pressure is measured.

Radial artery pressures are higher than aortic pressure because of the distal location of the radial artery. Pressure waveforms from the aortic root (central) to the radial artery (peripheral) are shown in Fig. 6.4. However, it should be noted that during cardiovascular bypass, aortic pressures are higher than radial artery pressures because of decreased vascular resistance of the extremities. Secondly, in patients with severe peripheral vascular disease, there may be a difference in the blood pressure reading in the two extremities, in which case the higher blood pressure reading should be used.

Technique of Radial Artery Catheterization

Invasive arterial blood pressure monitoring is accomplished through the insertion of a catheter into an artery. Each arterial site has its own advantages and disadvantages (Table 6.4). If the radial artery is used for arterial catheterization, a modified Allen test can be performed prior to cannulation to ensure that the ulnar artery provides adequate circulation to the hand to prevent tissue ischemia or necrosis. To perform the Allen test, pressure is applied to occlude both the radial and ulnar arteries. The patient then opens and closes the fist several times until the hand blanches. The pressure is then maintained on the radial artery while releasing pressure from the ulnar artery. The hand is observed for the return of blood flow or flushing. If the hand color does not return within 5–10 s, the radial artery should not be used for arterial catheterization. The technique of radial artery catheterization is shown in Fig. 6.5.

- The wrist is positioned in the supine and dorsiflexed position supported by a roll of gauze over a board.
- Sterile technique is maintained throughout the procedure.
- The skin is prepared with a Betadine or a chlorhexidine preparation.
- The artery is palpated using the index and middle fingers of the nondominant hand.
- The skin over the artery is infiltrated with 0.5–1 ml of 1 % lidocaine with a 25–30G needle.
- A 20G arterial catheter with the needle in it is introduced into the skin at a 45° angle.
- As soon as flash of blood is seen, the catheter angle is dropped to 30°, and the needle and the catheter are advanced 1–2 mm further into the artery.
- The catheter is then advanced into the artery after which the needle is completely withdrawn. Alternatively, a wire is passed through the needle into the artery, over which the catheter is passed into the artery.
- The catheter is connected to a saline-filled transducer tubing, which transmits the arterial pressure waveform to a pressure transducer. The transducer then converts this physical energy to an electrical signal, which is then processed, filtered, and amplified before being displayed as an arterial waveform.
- The catheter is then fixed firmly to the skin by adhesive tape or may be sutured.

Table 6.4 Sites of insertion on arterial catheters

	Characteristics
Arteries commonly used	
Radial	Superficial location, good collateral blood flow via ulnar artery, most commonly used site
Brachial	Large artery, easily identifiable, less waveform distortion, end artery, kinking of catheter at elbow
Femoral	Large artery, good accessible site, site prone to infection and thrombosis, hematoma formation, avoid site in children (aseptic necrosis of femoral head)
Arteries less commonly used	
Dorsalis pedis	Most distortion of waveform (overestimates systolic blood pressure), avoid site in patients with peripheral vascular disease
Ulnar	Deep and tortuous artery, blood supply to the hand may be compromised, do not use if repeated attempts were made to cannulate the radial artery of the same hand
Axillary	Risk of nerve injury, emboli (air or thrombi) to brain, hematoma formation

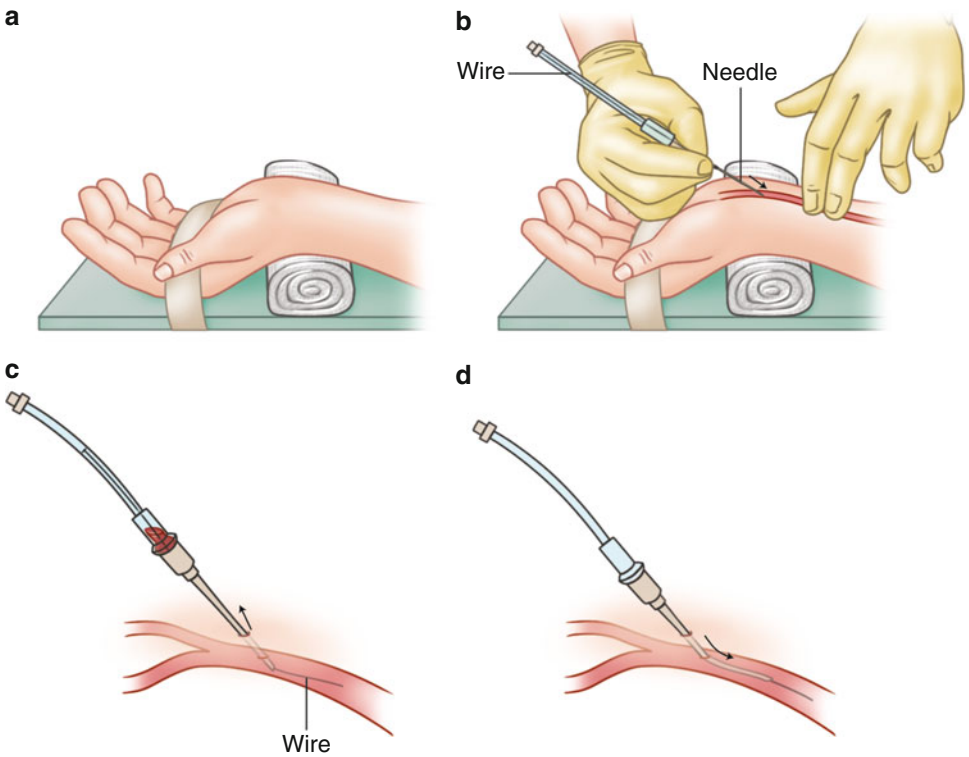

Fig. 6.5 Radial artery catheterization. (**a**) The wrist is positioned supine and dorsiflexed supported by a roll of gauze and stabilized over a board. The skin is then anesthetized with lidocaine. (**b**) A 20G catheter over a needle is inserted at a 45° angle, and as soon as a blood flash is seen, the angle is dropped to 30°. (**c**) A wire is passed through the catheter into the artery. (**d**) The catheter is advanced over the wire into the artery and the needle is completely withdrawn. The catheter is then attached to transducer tubing

Natural Frequency and Damping

The accuracy of the transducer is dependent on two physical properties of the system: the natural frequency and damping. The natural frequency is the frequency at which a system freely oscillates. The natural frequency of the arterial system ranges from 1 to 30 Hz, while the natural frequency of arterial transducer systems exceeds 30 Hz. This is done to prevent the development of a resonant frequency occurring between the arterial and transducer systems. A resonant frequency occurs when a force with a similar frequency is applied to the system, causing the system to oscillate at its maximum amplitude. If the natural frequency of the transducer is similar to that of the arterial waveform, the system will resonate, causing excessive amplification and distortion of the electrical signal, manifesting as erroneously elevated systolic and widened pulse pressures. The natural frequency of the system is also determined by the properties

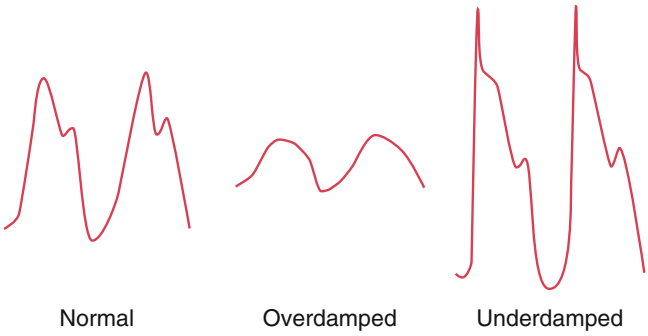

Fig. 6.6 Arterial waveform: normal, overdamped, and underdamped

of its components and may be increased by air in the tubing, the increased tubing length, and the addition of three-way stopcocks.

Damping occurs when there is a condition present that reduces/increases the energy in an oscillating system, thereby reducing/increasing the amplitude of the oscillations. The system can either be overdamped or underdamped. The transducer system is overdamped when there is excessive energy loss, which prevents the system from oscillating. With an overdamped system there is a blunted waveform tracing, with a falsely low SBP and elevated DBP. The transducer system is underdamped when there is excessive energy producing an increase in oscillations. With an underdamped system, there is an overshoot of the pressure waves, with excessively elevated SBP and low DBP (Fig. 6.6). In both scenarios, the MAP remains relatively accurate. Factors that cause overdamping include increased number of stopcocks; air or clots in the tubing; arterial vasospasm; narrow, low, or compliant tubing; narrow arterial cannulas; and kinks in the arterial cannula or tubing. Damping also reduces the natural frequency of the system, allowing resonance, and distortion of the arterial waveform.

Zeroing the Transducer

To obtain accurate IABP measurements, the transducer must be properly zeroed and leveled. To zero a transducer, the transducer is exposed to atmospheric pressure by turning the stopcock to air and calibrating the pressure reading to zero. This subtracts the atmospheric pressure from the total pressure measurement. Transducers must be leveled with the patient's heart at the 4th intercostal space in the midaxillary line, to measure blood pressure accurately. Failure to level will result in the hydrostatic pressure of the fluid in the tubing being added to or subtracted from the real blood pressure. A transducer that is higher than the level of the heart will produce a falsely low blood pressure reading, whereas a transducer that is lower than the level of the heart will produce a falsely elevated blood pressure reading. Every 10 cm error in leveling results in a 7.4 mmHg error in the pressure measured.

Table 6.5 Complications of arterial catheterization

Bleeding (disconnection) and hematoma formation
Infection—bacteremia, cellulitis
Thromboembolism (air bubbles, thrombi)
Management errors—disconnection, measurement errors, unintended intra-arterial drug injection
Nerve damage
Vasospasm
Limb ischemia

Complications of Arterial Catheterization

Though a relatively safe procedure, arterial cannulation is not without the risk of complications (Table 6.5). Thrombotic complications, leading to limb ischemia, although rare, may be minimized by using a catheter with the smallest diameter possible, limiting the duration of its use, and by suctioning the catheter during removal. Infectious complications are also rare but increase with duration of the indwelling catheter. Aseptic technique should be used for insertion at any site. Other complications include air embolism, fistula formation, skin necrosis, and aneurysm formation. A pulse oximeter can be placed on the same hand as the radial artery catheter to monitor perfusion.

Pulse Oximetry

The pulse oximeter is one of the standard ASA monitors for any type of anesthetic care from light sedation to general endotracheal anesthesia. A pulse oximeter monitors the oxygen saturation of a patient's blood (as opposed to measuring oxygen saturation directly through a blood sample). Prior to its use, anesthesiologists had to rely on qualitative assessments of oxygen saturation such as color of the skin or blood. Pulse oximetry first became available in the 1970s, and today it is widely used, making anesthesia care much safer.

Commonly used *sites* for pulse oximetry are the finger, toe, or the earlobe. SaO_2 readings above 95 % are considered normal, while readings below 90 % demand immediate investigation. Additionally, a pulse oximeter reading of 90 % may indicate a PaO_2 of less than 60 mmHg. Pulse oximeters become increasingly inaccurate with SaO_2 below 75–80 %. It is important to know that pulse oximetry measures solely oxygenation, not ventilation, and is not a substitute for blood gas analysis.

Pulse oximetry relies on the principle that as light passes through a substance, certain wavelengths of light will penetrate

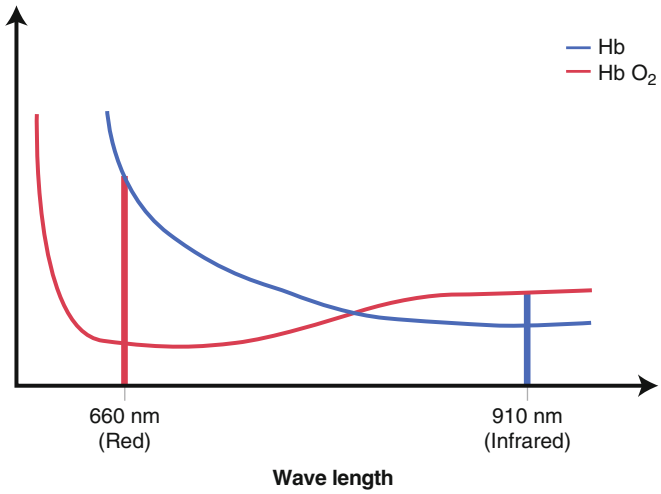

Fig. 6.7 Absorbance red and infrared light by oxy- and deoxyhemoglobin. Oxyhemoglobin absorbs more infrared light, whereas deoxyhemoglobin absorbs more red light

Table 6.6 Factors affecting pulse oximeter reading

Factor	Notes
Decreased perfusion	Hypotension, use of vasoconstrictors, hypothermia, low cardiac output states
Nail polish	Blue, green, pink, black
Dyes	Methylene blue, indigo carmine
Methemoglobin	SaO_2 of 85 % (falsely elevated/depressed)
Carboxyhemoglobin	Co-oximeter needed to differentiate carboxyhemoglobin from oxyhemoglobin

the substance and others will get absorbed. Modern pulse oximeters consist of two light-emitting diodes (LEDs) that emit light containing wavelengths in the red (660 nm) and infrared (940 nm) spectra. This light penetrates tissue, typically of a digit or an earlobe, and light that is not absorbed is captured by a photoreceptor on the opposite side of the tissue.

Oxyhemoglobin absorbs more infrared light and allows more red light to pass through, while deoxygenated hemoglobin absorbs more red light and allows more infrared light to pass through (Fig. 6.7). The transmitted light is processed to eliminate scatter and absorbance by tissues other than blood, the red/infrared (R/IR) ratio is analyzed, and the oxygen saturation (SaO_2) is then calculated by the microprocessor from an empiric formula based on calibration curves derived from healthy individuals. The SaO_2 is displayed as a waveform produced by the contraction and relaxation of digital arteries during a cardiac cycle. To ensure accuracy the displayed SaO_2 is an average of data collected from the prior 5–15 s. Because of this delay, hypoxemia or its treatment may not be immediately recognized.

The waveform of the pulse oximeter display is important in determining the accuracy of the displayed SaO_2. Any situation (Table 6.6) that reduces the amount of pulsatile blood flow in the area being measured will affect waveform and SaO_2 accuracy. This can be seen with hypotension, use of vasoconstrictors, hypothermia, and low cardiac outputs. The waveform can also be affected by nail polish and fluorescent and xenon light. Another factor that can affect SaO_2 measurements is the administration of dyes, such as methylene blue, indocyanine green, and indigo carmine, which transiently cause a falsely decreased SaO_2 reading. Hyperbilirubinemia, fetal hemoglobin, and acrylic fingernails do not affect the accuracy of pulse oximetry.

Presence of abnormal hemoglobin variants will also affect pulse oximetry readings. Carboxyhemoglobin (COHb) is frequently encountered in smokers and in those who have suffered smoke inhalation. COHb absorbs light of the same wavelength (660 nm) as oxyhemoglobin producing misleading SaO_2 readings. Methemoglobin (MetHb) absorbs equal amounts of light at both 660 nm and 940 nm. Since the ratio of the red and infrared absorbances is equal to 1 at an oxygen saturation of 85 %, the presence of significant methemoglobinemia will produce an SaO_2 of 85 %. This will be falsely elevated in the presence of hypoxia and falsely depressed in the presence of adequate oxyhemoglobin concentrations. If the presence of abnormal hemoglobin variants is suspected, co-oximetry can be used. A co-oximeter is a device that can measure more than two wavelengths of light at a time and can be used to determine the presence of carboxyhemoglobin or methemoglobin.

Electrocardiography

Electrocardiography (ECG), which measures the electrical activity of the heart, is a standard ASA monitor that is continuously displayed in every patient undergoing anesthesia. It can be used as both a cardiac monitor, to detect the presence of myocardial ischemia or arrhythmias, and a physiologic monitor, to assess excessive autonomic activity. ECG is commonly used to measure the rate and regularity of heartbeats, the size and position of the chambers, the presence of any damage to the heart, and the effects of drugs or devices used to regulate the heart, such as a pacemaker.

ECG Waveform

A cardiac cycle is composed of a P wave, corresponding to atrial depolarization, the QRS complex, corresponding to ventricular depolarization, and a T wave, corresponding to ventricular repolarization. The PR interval represents the signal delay caused by impulse conduction through the AV node, the ST segment represents the period between ventricular depolarization and repolarization, and the QT segment represents the entire period of ventricular depolarization and repolarization (Fig. 6.8, Table 6.7).

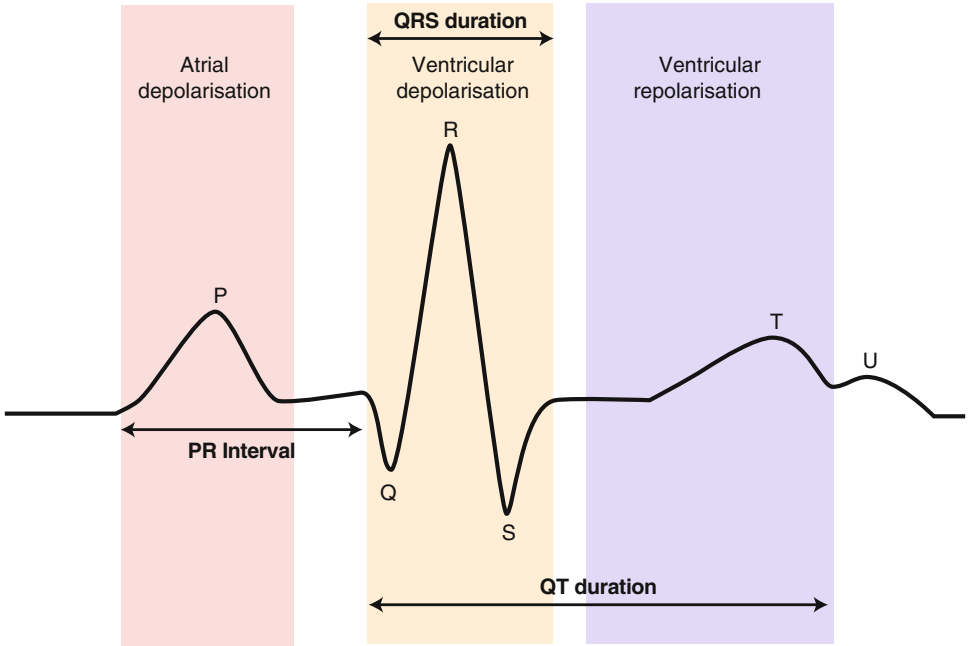

Fig. 6.8 A normal ECG tracing

Table 6.7 Significance of ECG waves and intervals

ECG	Characteristics	Duration
P wave	Electrical impulse during atrial depolarization traveling from the SA node toward the AV node, spreading from the right atrium to the left atrium	0.08–0.1 s
PR interval	It denotes AV node function. The PR interval is measured from the beginning of the P wave to the beginning of the QRS complex and is the time interval the electrical impulse takes to travel from the SA node to reach the ventricles via the AV node	0.12–0.2 s
QRS complex	Rapid depolarization of the right and left ventricles. Duration greater than 0.12 s signifies bundle branch block	<0.1 s
J point	This point denotes the ending of the QRS complex and beginning of the ST segment	
ST segment	The time period when the ventricles are depolarized	0.8–0.12 s
T wave	Repolarization of the ventricles, usually less than 10 mm in amplitude	0.16 s
QT interval	Prolonged interval increases risk for ventricular arrhythmias and sudden death	0.35–0.42 s
U wave	Usually follows T wave, has low amplitude, or may be absent. May be caused by repolarization of the interventricular system. Prominent U waves are seen in hypokalemia and hypercalcemia	

In the operating room, either a three-lead or five-lead ECG is utilized. With the five-lead ECG, the most commonly displayed leads are II and V_5. Lead II is chosen because it is approximately 60° from the right arm to the left leg and is most parallel to the atria, which makes it the most useful lead for accessing the P wave, heart rhythm, and inferior wall ischemia (Table 6.8). Lead V_5 is chosen because it lies at the fifth intercostal space over the anterior axillary line making it the most sensitive for detection of anterior and lateral ischemia. When using a three-lead ECG, V_5 can be obtained by placing the left arm lead in the V_5 position and selecting lead I on the monitor.

An ECG is obtained by placing gel-infused pads or needle electrodes on the patient. Needle electrodes are used in patients with extensive burns or scars (difficult standard electrode placement). The ECG tracing can be affected by several patient and surgical factors. Shivering can cause motion artifact. Obesity, COPD and other causes of lung hyperinflation, less-than-optimal electrode placement due to the surgical procedure, and fluid in the chest (pericardial or pleural effusions) can all decrease ECG signal amplitude. Surgical sources of interference include electrocautery and the monitoring of somatosensory evoked potentials.

Table 6.8 ECG leads corresponding to areas of the heart

Inferior leads	II, III, aVF
Anterior leads	V_3 and V_4
Septal leads	V_1 and V_2
Lateral leads	I, aVL, V_5 and V_6

Current ECG monitors have programs that allow continuous monitoring of ST segments to detect myocardial ischemia

Table 6.9 Sites of temperature monitoring

Site	Characteristics	Notes
Skin	Most accessible site (forehead, axilla)	Unreliably measures core body temperature
Tympanic probe	Measures brain temperature (external carotid artery)	Probe can cause tympanic membrane perforation
Nasopharynx probe	Measures core body (respiratory gas) temperature	Probe can cause epistaxis
Rectum or bladder probe	Measures core body temperature	Delayed rate of change if the core temperature is changing rapidly
Pulmonary artery catheter	Measures core body temperature	Invasive method
Esophageal probe	Most commonly used method to measure core body temperature under general anesthesia	Probe is inserted via the mouth into the distal 1/3 of the esophagus, can be used to listen to heart/breath sounds too

and to monitor pacemaker spikes in patients with implanted pacemakers. Approximately 80 % of significant ST segment changes are detected by leads II and V_5. This sensitivity increases to 96 % with the addition of V_4. Besides ischemia (ST segment depression exceeding 1 mm in conjunction with T-wave inversion) and arrhythmias, ECG can be used to diagnose electrolyte abnormalities, such as hyperkalemia (increased QRS amplitude and peaked T waves followed by progressive QRS widening and P-wave flattening, ultimately evolving into a sinusoidal wave and ventricular fibrillation), hypokalemia (inverted T waves, prominent U waves larger than the T waves, prolonged PR interval, and premature atrial or ventricular contractions), and hypocalcemia (prolonged QT interval).

Temperature Monitoring

Patient temperature should be monitored for every patient undergoing general anesthesia. Normal body temperature is 37 °C ± 0.5 °C (98.6 °F ± 0.9 °F). The site of temperature monitoring, and whether it is continuous or intermittent, is dependent on the patient and the surgical procedure. Short, minimally invasive procedures may only require intermittent measurements of temperature, whereas a patient undergoing a general anesthetic requires continuous temperature monitoring.

The *sites* of temperature monitoring include the skin (forehead, axilla), esophagus, nasopharynx, tympanic, blood, bladder/urine, and rectum (Table 6.9). Core body temperature is the temperature of the central body/blood compartment.

Phases of Heat Loss Under General and Regional Anesthesia

Core temperature is maintained under tight control by the hypothalamus. Anesthetic agents inhibit the ability of the hypothalamus to compensate for temperature changes and heat loss making the anesthetized patient particularly vulnerable to hypothermia. Heat loss under general/regional anesthesia generally occurs under three phases.

- Phase 1: the core temperature decreases by 1–2 °C during the first hour of anesthesia (general/regional). This is due to redistribution (minimal true heat loss) of heat from the warm central compartment of the body to the cooler peripheral tissues due to anesthetic-induced vasodilation and inhibition of hypothalamic function.
- Phase 2: gradual decline of temperature (0.5–1 °C) for the next 3–4 h due to continued heat loss to the environment. General anesthetics inhibit thermoregulation by inhibiting hypothalamic function, whereas regional anesthesia (spinal/epidural) causes an altered perception of temperature by the hypothalamus in the blocked dermatomes.
- Phase 3: or steady state equilibrium, where heat loss equals metabolic heat production.

Hypothermia (body temperature of less than 36 °C) has a multitude of deleterious effects. In the awake patient hypothermia can lead to postoperative delirium and can precipitate myocardial ischemia by increasing oxygen consumption by as much as 200 % (shivering) while shifting the oxyhemoglobin dissociation curve to the left. Hypothermia also sensitizes the heart to arrhythmias. Coagulation is affected by inhibition of platelet function. The immune response is depressed causing an increased risk of infection and delayed wound healing. There is an increased stress response with increased stress hormone secretion and hyperglycemia. Drug metabolism is slowed leading to increased sensitivity to sedative and neuromuscular-blocking drugs.

Hypothermia can be minimized or avoided by increasing the ambient operating room temperature, minimizing patient exposure to the cold operating room environment, prewarming the patient to avoid phase I heat loss, using warm intravenous fluids, heating and humidifying inspired gases, and using a forced-air warming blanket. Not all heat loss can be prevented, but through careful monitoring and by anticipating the stages of heat loss, significant hypothermia can nearly always be avoided.

Capnography

Capnography is the monitoring of the carbon dioxide content of expired gases ($ETCO_2$), measured through the use of infrared light absorption by CO_2. A beam of infrared light is passed through the gas sample. The presence of CO_2 causes less light to fall on the sensor, which is rapidly and accurately measured by the sensor.

Types of Capnographs

There are two types of capnography monitors found in anesthesia circuits, flow through (mainstream) and diverting (aspirating). Flow-through capnographs are integrated into the breathing circuit. They are more accurate when very small tidal volumes are used but have the disadvantage of being unable to detect the presence of CO_2 in the inspiratory limb of the circuit. Diverting capnographs are the most commonly used capnographs and measure CO_2 by continuously aspirating anesthetic gases distal to the joining of the inspiratory and expiratory limbs. Accuracy of CO_2 concentration depends on the rate of sampling, respiratory rate, and tidal volume. A sampling volume of 250 ml/min will maximize accuracy except during periods of low minute ventilation, where $ETCO_2$ will be underestimated. Also, low sampling rates will underestimate $ETCO_2$ especially when there is a high respiratory rate.

The measured $ETCO_2$ will always underestimate the arterial carbon dioxide concentration ($PaCO_2$). This is due to the sampling of a gas mixture composed of gas from the alveoli that participate in gas exchange and the physiologic dead space, which does not participate in gas exchange. The end-tidal to arterial carbon dioxide gradient is typically 3–5 mmHg but may be significantly higher in conditions that increase dead space. A rapid decrease in $ETCO_2$ can be seen with profound hypotension leading to decreased perfusion, pulmonary embolism, and circuit disconnection. Increasing $ETCO_2$ can be seen with hypoventilation, an exhausted CO_2 absorbent or a hypermetabolic state such as malignant hyperthermia or thyroid storm.

Uses of Capnography

One of the most common uses of capnography is to detect an esophageal intubation. Although the first two or three breaths may contain CO_2, esophageal CO_2 is rapidly eliminated. The capnograph waveform can also provide valuable information. The normal capnogram is a measure of the varying amounts of carbon dioxide excretion during exhalation (Fig. 6.9). The first part is of the graph is the baseline, which should read zero. Any increase in the baseline is due to the presence of inspired CO_2, caused by increased production, an exhausted absorbent, or an incompetent inspiratory valve. The next portion of the capnograph is the respiratory upstroke, followed by the expiratory plateau, and the inspiratory phase. $ETCO_2$ is measured at the end of the expiratory plateau.

Besides detecting CO_2, the capnograph can also be used to diagnose any obstruction to exhalation, seen with bronchospasm, patient-initiated respiratory effort, and acute loss of pulmonary blood flow, seen in massive pulmonary embolism or cardiac arrest (Fig. 6.10).

Neuromuscular Monitoring

Neuromuscular blockage through the use of neuromuscular-blocking drugs (NMBD) is a common practice during anesthesia to facilitate endotracheal intubation and to promote optimal surgical conditions for many procedures. To ensure adequate muscle relaxation and adequate recovery prior to emergence, the degree of neuromuscular blockade is monitored throughout the surgical procedure.

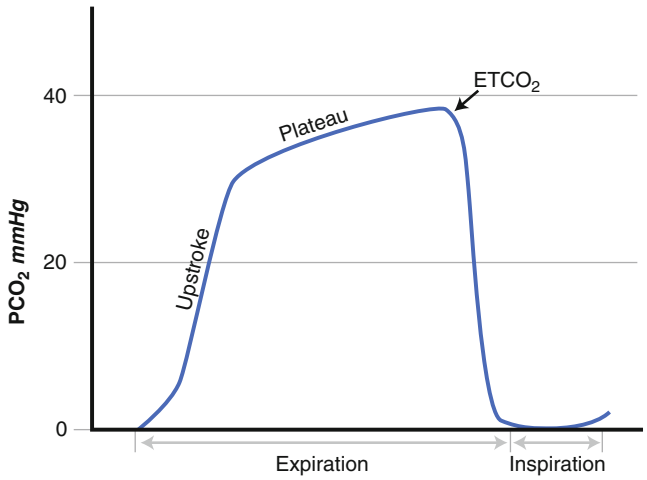

Fig. 6.9 A normal capnogram $ETCO_2$ is measured at the end of the expiratory plateau

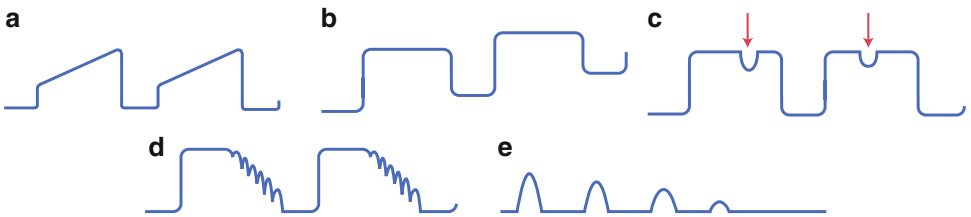

Fig. 6.10 Capnograms in various clinical situations. (**a**) Respiratory obstruction. (**b**) Rebreathing of CO_2. (**c**) Recovery from neuromuscular blockade. (**d**) Cardiac oscillations (the pressure of the heart beating against the lungs). (**e**) Esophageal intubation

Neuromuscular function can be monitored through both qualitative and quantitative methods. Quantitative methods include electromyography, mechanomyography, and accelerography. Though these methods provide more reliable and consistent results than qualitative methods, they are cumbersome and require bulky equipment and more elaborate monitoring procedures, making them impractical for the operating room environment.

The qualitative assessment of neuromuscular function can be performed using clinical tests of muscle strength and with nerve stimulation. Clinical tests include hand grip strength and the ability to sustain a head lift or to keep an arm raised for 5 s. The advantages of clinical tests include their simplicity, their ease of use, and their cost-effectiveness, but they are notoriously unreliable and require patient compliance and cooperation, which can be difficult during anesthetic emergence. Because of this, clinical testing is most often used in conjunction with nerve stimulation.

Nerve stimulation is accomplished by placing two electrodes over a nerve, applying an electrical stimulus that causes nerve depolarization, and evaluating for distal muscle contraction. Typical sites include the facial nerve stimulating the orbicularis oculi muscle, the ulnar nerve stimulating the adductor pollicis muscle, and the posterior tibial nerve stimulating the flexor hallucis brevis (Fig. 6.11). Of these sites, the ulnar nerve correlates most accurately with return of neuromuscular function. Multiple stimulation methods can be used to assess neuromuscular function.

- Single-twitch stimulation: can be used to assess twitch amplitude as compared to baseline. When the twitch amplitude begins to decrease, more than 70 % of receptors are occupied by NMBD. When 90 % of receptors are occupied, no twitch is detectable. Because human visual and tactile senses cannot accurately differentiate a decrease in twitch amplitude, electromyography is required to establish a baseline response amplitude to compare subsequent responses.
- Double burst suppression: consists of two bursts of three stimuli separated by a short time interval. In a non-paralyzed patient, both bursts will elicit an equal response. When recovering from non-depolarizing neuromuscular blockade, the second burst will elicit a weaker contraction than the first burst, also known as fade. Although double burst suppression is more reliable than train-of-four stimulation, it produces a much more noxious stimulus and should not be administered to an awake patient.
- Train-of-four stimulation: is the most commonly used method for monitoring neuromuscular blockade. This type of stimulation applies four individual stimuli of a given length over a set period of time. Clinically, these are 200-microsecond stimuli given over a 2 s period. The ratio of the amplitude of the first twitch to the fourth twitch predicts recovery from non-depolarizing neuromuscular blockade. A ratio of 0.75 predicts adequate recovery. Clinically, it is most useful to observe the strength and presence of the four twitches. When three twitches are present, there is a 75 % blockade of receptors, with two twitches, 80 % blockade, and with one twitch, 90 % blockade.
- Tetanic stimulation: involves a tetanic stimulus that is applied for 5 s. The presence of sustained muscle contraction without fade is consistent with adequate, but not necessarily complete, neuromuscular recovery. A tetanic stimulus can also be used to determine the presence of neuromuscular recovery when no twitches are present. If a tetanic stimulus of greater than 50 Hz is administered, muscle fatigue and acetylcholine release occur. When a double burst suppression or train-of-four stimulus is applied after the tetanic stimulation, post-tetanic potentiation can occur, which manifests as a return of twitches. Post-tetanic twitches indicate that neuromuscular recovery has begun. The problem with repeated tetanic stimulation is that it can cause the muscle being stimulated to recover more quickly from non-depolarizing neuromuscular blockade than the remainder of the body, which can lead to a false assessment of recovery.

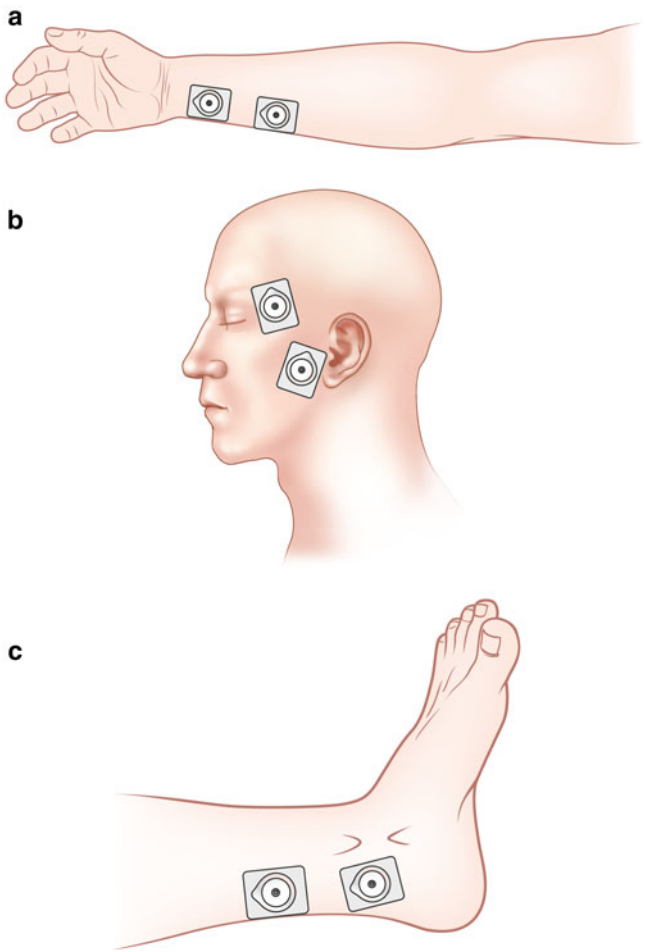

Fig. 6.11 Placement of electrodes for monitoring neuromuscular blockade. (**a**) Ulnar nerve. (**b**) Facial nerve. (**c**) Posterior tibial nerve

Neurophysiologic Monitoring

Neurophysiologic monitoring is utilized when there is a specific nerve or area of nervous tissue within the surgical field that could be misidentified and cut or damaged through manipulation and compression or become ischemic. Surgeries which employ neuromonitoring include spine instrumentation, intracranial surgery, carotid surgery, and face and neck surgery. The types of neuromonitoring available include encephalography (EEG), bispectral index (BIS), sensory evoked potentials [including somatosensory evoked potentials (SSEPs), visual evoked potentials (VAPs), brainstem auditory evoked potentials (BAEPs)], and motor evoked potentials (MEPs).

Electroencephalography

The electroencephalograph (EEG) is a useful monitor of cerebral oxygenation and is commonly employed when a period of ischemia is anticipated, as with carotid surgery, and when cortical electrical silence is desired to minimize ischemic damage, as with intracerebral aneurysm clipping. On the EEG, ischemia first manifests as activation and later by a change to low-frequency and high-voltage activity. Unfortunately these changes can also be seen with volatile and intravenous anesthetics, hypocapnia, hypotension, and electrolyte abnormalities making EEG accuracy questionable and abnormalities difficult to interpret. Also, EEG monitoring in patients with a prior stroke can be unreliable.

Inhalational anesthetics at high doses cause a burst suppression pattern on the EEG. Isoflurane, an inhalational anesthetic, causes electrical silence at high doses. Intravenous anesthetics typically produce a biphasic EEG pattern with initial activation followed by depression that is dose dependent. The exception to this is ketamine which produces an atypical pattern of activation.

Bispectral Index

The bispectral index (BIS) is a device which monitors EEG signals, which are then processed and filtered by a proprietary algorithm and then displayed as both an EEG tracing and a two-digit number that predicts level of consciousness. By definition, the awake state correlates with a digital number of 100, while a flat line EEG correlates with zero. An appropriate plane of anesthesia is maintained when the two-digit number is between 40 and 60.

There are a number of controversies regarding the BIS. Initially, it was hoped that the use of this monitor would decrease the incidence of intraoperative awareness. Though some studies have supported this conclusion, others have shown either no benefit or are inconclusive. One benefit of BIS monitoring is a decrease in anesthetic drug dosage to maintain the appropriate anesthetic depth. Avoidance of increased anesthetic dose has been shown to have several beneficial effects including decreased incidence of postoperative delirium, shorter wake-up time and PACU discharge time, and decreased nausea and vomiting and cost of anesthetic drugs. By basing anesthetic dosing on the BIS number, perhaps anesthetic drug overdose can be avoided.

Somatosensory Evoked Potentials

Somatosensory evoked potentials (SSEPs) monitor the ability of a peripheral nerve to receive a signal and transmit that signal through the dorsal columns of the spinal cord and be received by the cerebral cortex. These are most commonly used during spinal and thoracoabdominal aortic aneurysm surgeries. Monitoring typically consists of electrodes placed on the median nerve for upper extremity and the posterior tibial nerve for lower extremity monitoring with scalp electrodes to detect signal transmission. The signals as received by the cerebral cortex are monitored for amplitude and latency (length of time for signal to reach cerebral cortex) and compared to baseline values that are established after induction of anesthesia but prior to surgical incision. Neural compromise can be signaled by an increase in latency and/or a decrease in the amplitude of the signal.

SSEP amplitude and latency are affected by most anesthetic agents. Volatile inhalational anesthetics appear to affect SSEPs the most and can increase latency in a dose-dependent fashion. At steady state concentrations of 0.5 MAC or less, the increased latency is generally considered to be acceptable. To avoid increase in SSEP latency with volatile inhalational anesthetics, total intravenous anesthesia (TIVA) can be used alternatively. Nitrous oxide has no affect on latency but can decrease amplitude of SSEP signal. When combined with a volatile anesthetic, these effects are additive. Anesthetic agents such as propofol and opioids will increase latency but to a lesser extent than volatile anesthetics. When these agents are used as a continuous infusion rather than intermittent boluses, their depressive effects are minimized. The overall goal is to establish a baseline level of anesthesia from which the baseline SSEP study is performed and then avoid changes or boluses of the anesthetic agents chosen. If boluses or changes must be made, it is prudent to inform the neurophysiologist prior to drug administration.

SSEPs are plagued by issues of reliability. Their sensitivity is relatively low, leading to many false positives. These false changes can be seen because of drug administration, hypotension, and changes in body temperature. SSEPs are purely a monitor of sensory function and lack the ability to

detect an intact motor pathway, thus leading to false negatives. False negatives can be seen during cases of anterior spinal artery syndrome.

Visual evoked potentials (VEP) monitor the optic nerve and may be a useful monitor during transnasal intracranial surgery and surgery involving the pituitary gland. They are the most sensitive to volatile anesthetic agents. Brainstem auditory evoked potentials (BAEPs) monitor cranial nerve VIII and are useful during intracranial surgeries involving the posterior fossa. BAEPs are the least sensitive to volatile anesthetics.

Motor Evoked Potentials

Motor evoked potentials (MEPs) monitor the motor pathway from the level of the motor cortex to the effector muscle. These are commonly used for spinal and thoracoabdominal aortic aneurysm surgeries. A stimulatory electrode is placed on the scalp which produces electrical stimulation to the motor cortex. The signal is transmitted through the *ventral* spinal cord, the nerve root, and the peripheral nerve and received through the neuromuscular junction at the effector muscle. The signal is monitored at the level of the muscle for both amplitude and latency. Ischemic and mechanical compromise is detected in the same way as for SSEPs, as a decrease in amplitude and an increase in latency compared to a baseline signal.

Initially, MEPs were difficult to interpret due to the use of volatile anesthetics because the MEPs are very sensitive to these agents than SSEPs. The advent of TIVA or use of less than 0.5 MAC of volatile anesthetic in combination with IV maintenance has dramatically increased MEP use and the accuracy of its data. Since MEPs involve monitoring muscle contraction, neuromuscular-blocking drugs are not used. This presents a challenge for the anesthesiologist to perform an anesthetic that is deep enough to prevent movement and yet not produce profound vasodilation leading to hypotension and decreased spinal cord perfusion. Since the use of volatile agents is limited or contraindicated, a TIVA using propofol, remifentanil, and dexmedetomidine, with a vasoconstrictor to maintain mean arterial pressure, is commonly used to provide anesthesia for these patients.

Central Venous Monitoring

Central venous cannulation (CVC) is an invasive procedure and carries significant morbidity and mortality. Indications and contraindications for central venous cannulation are listed in Tables 6.10 and 6.11, respectively.

Many *sites* are used for CVC with each site having its own advantages and disadvantages. The sites most commonly used are the internal jugular vein (IJ), subclavian vein (SC), and the femoral vein (FV). Of these, the most commonly used intraoperative site is the IJ because of its superficial location and relative ease of cannulation. The right IJ is most frequently cannulated due to its more consistent anatomic location and more direct path to the right atrium as compared to the left IJ (Fig. 6.12).

Table 6.10 Indications for central venous catheterization

Rapid volume resuscitation
Blood product transfusion
Administration of vasoactive drugs
Measurement of central venous pressure
Lack of sufficient peripheral venous access
Aspiration of venous air embolism

Table 6.11 Contraindications for central venous catheterization

Uncorrected coagulopathy
Combative or uncooperative patients
Cellulitis over the insertion site
Central venous obstruction by renal cell tumor extending to the right atrium
Fungating tricuspid valve vegetations
Presence of pacemaker/AICD wires

Technique of IJ insertion

- Full aseptic technique with sterile gown, gloves, mask and hair cap, bactericidal skin preparation, and the area draped.
- With the patient in a Trendelenburg position, which decreases the risk of air embolism and distends the vein, the site of cannulation is identified by the apex of the triangle formed by the overlapping of the medial and lateral heads of the sternocleidomastoid muscle, immediately lateral to pulsations of the carotid artery.
- In awake patients the skin is infiltrated with 1 % lidocaine using a 25G needle.
- A finder needle, usually a 22G needle attached to a 3 or 5 ml syringe, is directed laterally toward the ipsilateral nipple at a 30° angle until venous blood return is obtained.
- An 18G needle/catheter over a needle is then introduced along the same path as the finder needle until blood return is obtained.
- A J wire is introduced and advanced through the needle/catheter, at the same time watching the ECG for any arrhythmias. The wire is withdrawn slightly if arrhythmias occur.
- The needle is then removed, and a vein dilator is introduced after making a nick in the skin with a scalpel.
- The dilator is removed, and the central venous catheter is introduced over the wire, with the wire coming out of the brown hub.
- The wire is then removed and all ports of the CV catheter are flushed with saline.

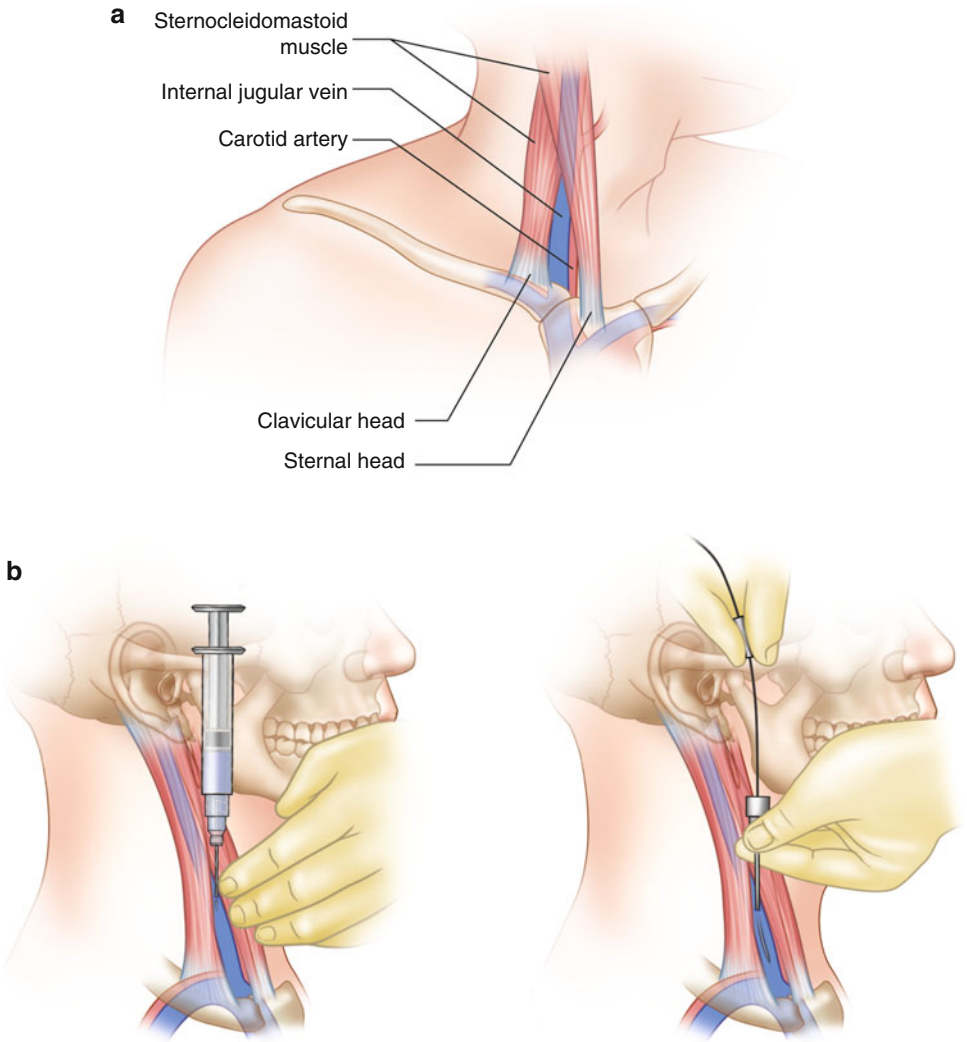

Fig. 6.12 The internal jugular (IJ) vein. (**a**) Anatomy. Note that the IJ lies just lateral to the carotid artery. (**b**) Cannulation, B1—the carotid artery is palpated, and the needle with the attached syringe is directed at a 30° angle toward the ipsilateral nipple; B2—after obtaining venous blood, the syringe is removed, and a wire is inserted through the needle into the vein

- The CV catheter is then sutured to the skin, and a sterile dressing with date and time is applied.
- Catheter placement is checked with a chest radiograph, with the catheter tip lying just above or at the junction of the superior vena cava and the right atrium.

Confirmation of Venous Puncture

Confirmation of venous puncture can be done by several ways:

- Noticing the blood color and flow: typically venous blood is more darker than arterial bright red blood. In addition, arterial blood flow is pulsatile.
- Manometry: venous puncture can be confirmed by manometry. Manometry is performed after initial vascular puncture and prior to vessel dilation. A length of IV tubing is connected to the catheter or needle, and blood is aspirated 12–15 cm into the tubing. The tubing is then held upward and venous system access is confirmed by the blood column falling to a level corresponding with central venous pressure. If the column does not fall or continues to rise, arterial puncture may have occurred. The needle or catheter is then removed and pressure held on the puncture site. Error may occur with severe hypotension, which can lead to misidentification of an arterial puncture, or elevated CVP, which may appear to be arterial. If there is any doubt, the tubing should be attached to a transducer, and the actual pressure measured.
- Ultrasound: ultrasound guidance for CVC is now widely used in the operating room, critical care unit, and emergency department (Fig. 6.13). Ultrasound images have demonstrated considerable anatomic variations in the location of the IJ, including an IJ that is medial to the

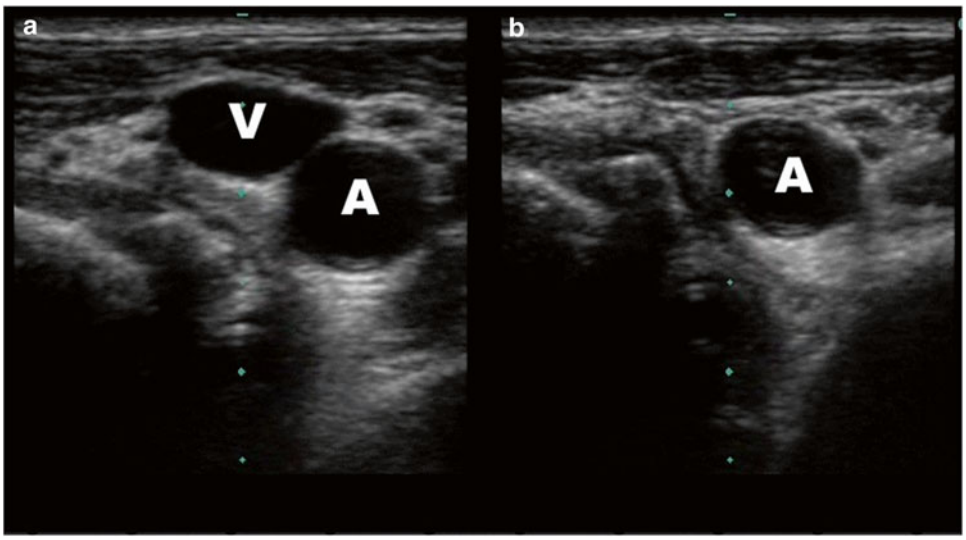

Fig. 6.13 Ultrasound image showing (**a**) the internal jugular vein lying lateral to the carotid artery, and (**b**) the vein (not the artery) is compressed by applying pressure on the transducer

carotid artery in up to 5 % of the population. Vascular structures can be identified by using color flow Doppler imaging. An artery can be differentiated from a vein by anatomic location and can be confirmed by applying downward pressure on the ultrasound transducer while maintaining the image of interest. A venous structure will easily compress under this pressure while an arterial structure will be much more difficult to compress. Studies have shown that the benefits of ultrasound-guided CVC include decreased time of procedure, decreased failure rate, decreased number of needle passes, and decreased incidence of complications such as arterial puncture.

Other Sites for CVC

The subclavian vein is the most common nonoperative site for CVC. Although the left and right subclavian veins can be cannulated, if a pulmonary artery catheter is necessary, it is easier to thread through a left subclavian vein, because of a less acute angle to the right atrium. The subclavian vein is cannulated by identifying the angle of the clavicle and the sternal notch (Fig. 6.14). With the patient supine and in Trendelenburg position, the needle is inserted just lateral to the angle of the clavicle. The needle is directed superficially toward the sternal notch until contact is made with the clavicle. The needle is then slightly withdrawn and redirected just posteriorly until it is able to slip underneath the clavicle and advanced until blood is aspirated. There is a significant risk of pneumothorax when the subclavian site is selected. In addition, due to the deep location of the subclavian veins, hemothorax can develop due to the inability to hold pressure on a venous puncture site, which is especially problematic in an anticoagulated patient.

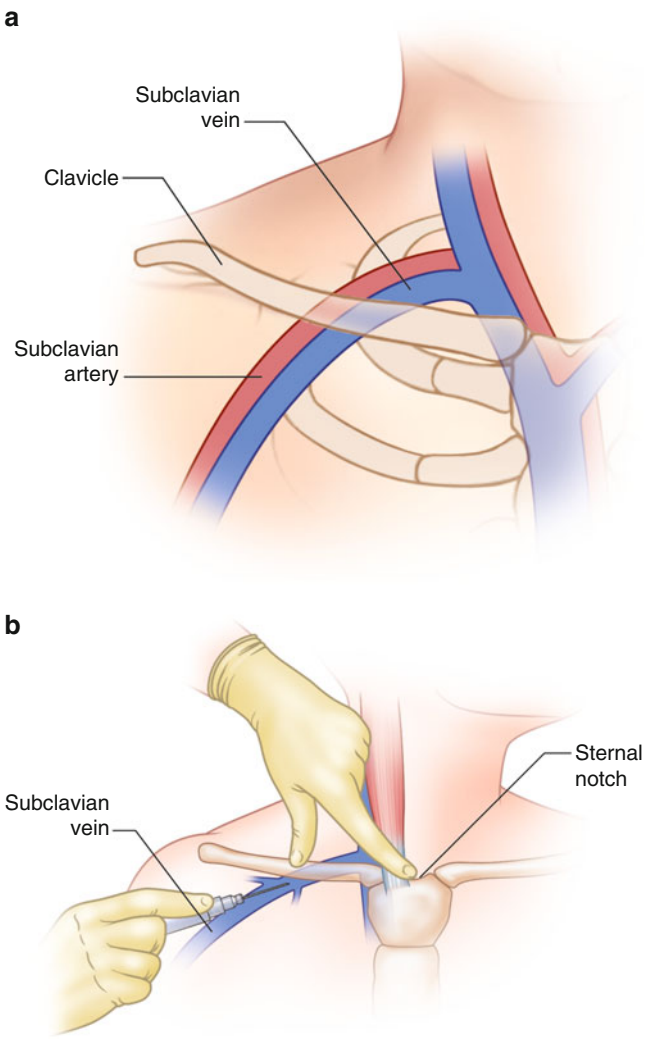

Fig. 6.14 The subclavian (SC) vein. (**a**) Anatomy. (**b**) Cannulation. The needle is directed toward the sternal notch just below the clavicle

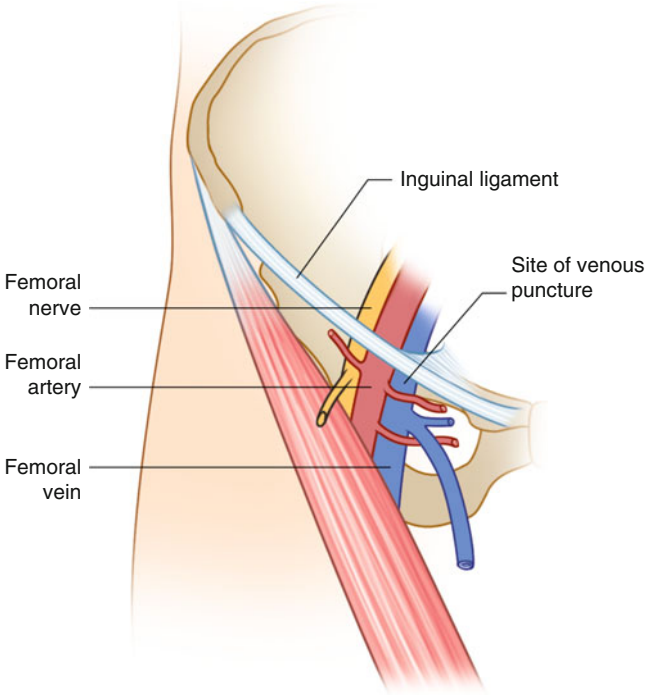

Fig. 6.15 The femoral vein lying medial to the femoral artery just below the inguinal ligament

Table 6.12 Complications of central venous catheterization

Type	
Mechanical	Arrhythmias, carotid artery puncture (IJ), chylothorax (left IJ), pneumothorax (IJ and SC), retroperitoneal hematoma (FV), pseudoaneurysm (FV)
Infectious	Most common with FV and least with SC cannulation
Thromboembolic	Air, fibrin clots, thrombi

IJ internal jugular vein, *SC* subclavian vein, *FV* femoral vein

The easiest central vein to cannulate is the femoral vein. The FV is accessed in the inguinal crease, caudal to the inguinal ligament and medial to the femoral artery (Fig. 6.15). The needle is advanced in the cephalad direction until blood return is achieved. After confirmation of venous blood, a wire is inserted and the catheter is placed using Seldinger's technique. The FV is often the site of choice in trauma resuscitation because of its ease of cannulation and it allows the initial trauma examination to occur with minimal interruptions. In addition, the femoral vein is often the site of CVC choice for patients requiring craniotomy and for patients with superior vena cava syndrome.

Complications of CVC are listed in Table 6.12. To prevent venous air embolism, all IV tubing needs to be flushed with saline prior to connecting it to the catheter, with CVC access points never left open to air prior to connecting to the IV tubing. This is particularly important in spontaneously breathing patients who generate negative intrathoracic pressures with each inspiration, even when they are in a Trendelenburg position.

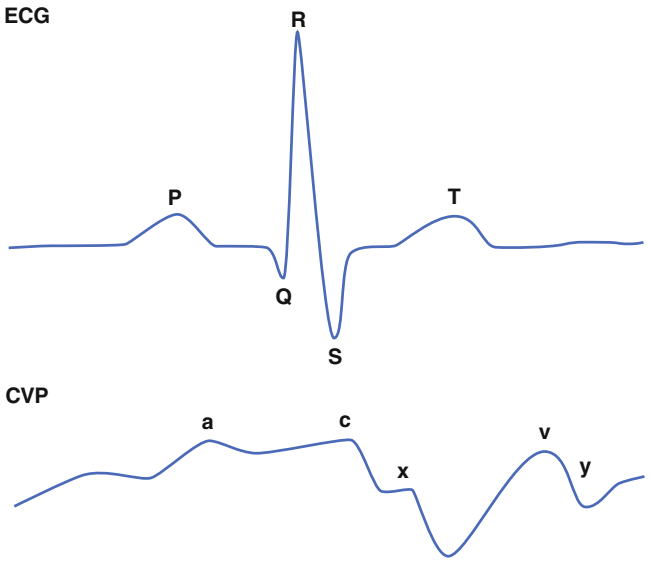

Fig. 6.16 A normal central venous pressure tracing and its relation to the ECG

Information from Central Venous Catheterization

- Volume status: the central venous pressure (CVP), normal being 2–6 mmHg, can be used to ascertain volume status and right ventricular function. Although accepted as an indicator of volume status, the accuracy of the absolute CVP has been questioned due to variables such as anesthetic-induced vasodilatation and the use of positive pressure ventilation. A better estimate of volume status using the CVP is following the trend, rather than the absolute number, throughout the course of the anesthetic.
- Filling pressures: in the patient with a normally functioning heart, the CVP can be used as an estimate of right atrial pressure (RAP). RAP is the filling pressure for the right ventricle (RV) and is, therefore, an estimate of the RV end-diastolic pressure and volume. Since the heart consists of two parallel circuits (pulmonary and systemic), right-sided pressures reflect left ventricular filling pressure and end-diastolic volume in the absence of significant heart disease.
- Waveform characteristics: the CVP waveform displayed has several characteristic waves (Fig. 6.16). The *a* wave corresponds to atrial systole and is absent in heart rhythms lacking atrial contraction such as extrinsic ventricular pacing and atrial fibrillation. Cannon *a* waves can be seen in junctional rhythms. The *c* wave corresponds to early

ventricular systole and the bulging of the tricuspid valve into the atrium. The *x* descent is due to the downward displacement of the closed tricuspid valve during late systole, and the *y* descent is due to the opening of the tricuspid valve in early diastole.

Pulmonary Artery Monitoring

A pulmonary artery catheter (PAC) is placed through a central line introducer for use as an invasive hemodynamic monitor. This catheter measures cardiac output, pulmonary artery systolic, diastolic and wedge pressures, central venous pressure, and temperature. It contains a port for sampling of mixed venous blood. Information from the PAC can be used both in the diagnosis and management of critical hemodynamic derangements (Table 6.13). Besides monitoring CVP and PA pressures and measuring cardiac output, there are multiple types of PA catheters that contain extra infusion ports and that allow pacing, continuous cardiac output, and mixed venous oximetry measurements. There are significant risks associated with PAC use and therefore, it is reserved for patients in whom the benefit is likely to outweigh the risks.

Contraindications to PAC placement are the same as for central line insertion, as well as conditions where a brief arrhythmia would not be tolerated, such as severe aortic stenosis or left bundle branch block and endocarditis involving the tricuspid or pulmonary valve. One of the most significant pitfalls in the use of a PAC is misinterpretation of the data produced. Some studies have reported up to a 45 % incidence of inappropriate management when intervention was based on PAC data, leading some to argue that the increased morbidity and mortality reported with PAC use may be due to misinterpretation of data.

The PAC is inserted under sterile conditions, through a sheath placed in a central vein. Before insertion, the PAC is prepared by flushing the air out of the catheter and testing the balloon to ensure proper inflation. With the balloon deflated, the PAC catheter is inserted to a depth of 18–20 cm (right atrium). The balloon is then inflated while observing the central venous waveform. The PAC is advanced slowly until a right ventricular pressure tracing is encountered (30–35 cm), evidenced by an increase in systolic pressure. As the catheter is further advanced, there will be a step-up in the diastolic pressure tracing as the pulmonary artery is entered. At this point the catheter is further advanced by 1–2 cm and the balloon is deflated (40–45 cm). If a wedge pressure is desired, with the balloon still inflated, the catheter is advanced (about 50 cm) until the PA pressure waveform mimics a CVP tracing. A PAC should never be left in the wedge position and also should never be left with the balloon inflated. Continuous monitoring of the pulmonary artery pressure tracing ensures that no distal migration into a wedge position has occurred. A PAC pressure tracing is depicted in Fig. 6.17.

Table 6.13 Indications for pulmonary artery catheter insertion

Cardiac	• Complicated MI producing acute mitral regurgitation, papillary muscle rupture, ventricular septal rupture, or pericardial tamponade • Assess volume status • Shock (hypovolemic, cardiogenic, septic) • Decompensated CHF
Pulmonary	ARDS, pulmonary HTN, hemodynamically significant PE
Intraoperative	High-risk surgery/patient
Pharmacologic	Assess response to pharmacologic interventions, fluid challenges

MI myocardial infarction, *CHF* congestive cardiac failure, *ARDS* acute respiratory distress syndrome, *HTN* hypertension, *PE* pulmonary embolus

Complications of PAC placement include pulmonary infarction, pulmonary embolism, sepsis, endocarditis, and catheter knotting. The most serious complication of PAC insertion is pulmonary artery rupture, which, though rare, carries a 50–70 % mortality. During catheter insertion, the most common complication is the development of arrhythmias, which can be as benign as occasional premature ventricular contractions or as severe as ventricular tachycardia, fibrillation, or complete heart block. When hemodynamically significant arrhythmia occurs, the balloon should be deflated and the catheter withdrawn until the arrhythmia subsides.

Values directly measured by the PAC include the pulmonary artery (PA) systolic, diastolic, and wedge pressures (Table 6.14). Starling's law identifies the relationship between left ventricular muscle fiber length and left ventricular function. In the normal heart, left ventricular muscle fiber length correlates with left ventricular end-diastolic volume. Left ventricular end-diastolic volume is directly related to pressure in the ventricle with normal diastolic relaxation. Left atrial pressure is an estimate of left ventricular end-diastolic pressure which is directly related to end-diastolic volume and, therefore, predicts left ventricular filling. Left atrial pressure can be estimated by placing a PAC into the wedge position, which isolates pulmonary arterial pressures from right ventricular pressures. Diastolic dysfunction and aortic insufficiency will underestimate left ventricular end-diastolic pressure, while mitral stenosis, elevated airway pressures, and obstructing left atrial myxomas will overestimate left ventricular end-diastolic pressure.

PA pressures are often elevated in patients with cardiac and pulmonary disease, and it is important to monitor PAP in these patients to avoid further elevation due to hypoxia, hypercapnia, acidosis, excessive airway pressures, and administration of vasoconstrictors such as phenylephrine.

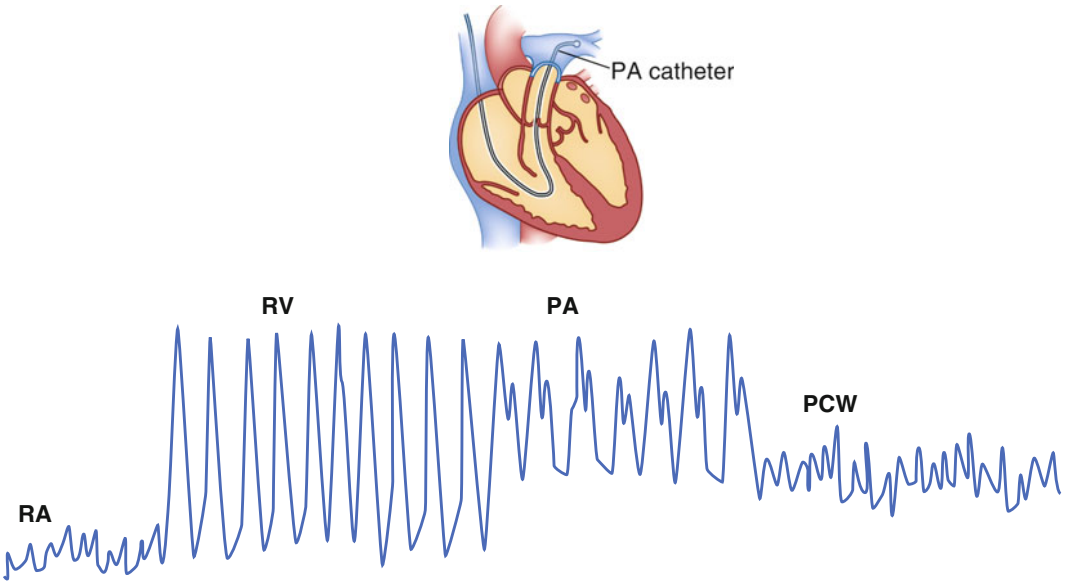

Fig. 6.17 A pulmonary artery catheter pressure tracing as it is passed through the right atrium, right ventricle, pulmonary artery, and wedge pressure

Table 6.14 Normal cardiac parameters

Parameter	Value
Central venous pressure/right atrial pressure (RAP)	2–6 mmHg
Right ventricular pressure	15–30/2–8 mmHg (systolic/diastolic)
Pulmonary artery pressure	15–30/8–15 mmHg (systolic/diastolic)
Mean pulmonary artery pressure (MPAP)	9–18 mmHg
Pulmonary artery occlusion pressure	6–12 mmHg
Left atrial pressure	4–12 mmHg
Cardiac output = heart rate × stroke volume	4–8 L/min
Cardiac index = cardiac output/body surface area	2.5–4 L/min/m^2
Stroke volume = 1,000 × cardiac output/heart rate	60–100 ml/heart beat
Systemic vascular resistance = 80 × (mean arterial pressure − RAP)/cardiac output	800–1,200 dynes-s/cm^{-5}
Pulmonary vascular resistance = 80 × (MPAP − PAOP)/cardiac output	<250 dynes-s/cm^{-5}

Cardiac Output

Cardiac output can be measured with a PAC using the technique of thermodilution, which plots a change in temperature over change in time. Catheters that measure intermittent cardiac output do so by injecting a known volume of saline at a known temperature into the proximal (CVP) port. A distal thermistor at the tip of the catheter measures the change in temperature over time after injection. Integration of the area under the curve gives a cardiac output. Continuous cardiac output catheters produce proximal pulses of heat through coils placed near the proximal port and measure the change in blood temperature sensed by a distal thermistor. The quantity of heat introduced and the change in blood temperature are analyzed by a computer and the cardiac output calculated. However, any situation where the right ventricular output (which is measured) does not equal left ventricular output, as with intracardiac shunts or tricuspid regurgitation, invalidates the thermodilution-determined cardiac output.

Newer devices are able to derive a cardiac output estimate through less invasive methods. One such device is connected to an arterial transducer. The cardiac output is estimated by measuring peak-to-peak changes in the systolic phase of the arterial waveform. Reliability of data produced from such devices has been controversial but does appear to be improving as the analysis program is further refined and modified. Additionally, cardiac output can also be determined by using TEE.

The cardiac output can also be calculated using the Fick equation, which is based on the Fick principle stating that the amount of oxygen that is consumed must be equal to the difference between the arterial and venous oxygen content.

With a PAC a true mixed venous blood sample can be drawn and oxygen content determined by blood gas analysis. An arterial sample can be drawn from an arterial catheter and the oxygen content also determined. The cardiac output is then calculated using the equation:

$$VO_2 = CaO_2 - CvO_2 \times CO \text{ or } CO = VO_2 / (CaO_2 - CvO_2)$$

(where CO = cardiac output, VO_2 = oxygen consumption, CaO_2 = arterial oxygen content, CvO_2 = venous oxygen content).

In addition, the mixed venous oxygen content is valuable in the overall assessment of organ perfusion. With no change in VO_2 or arterial oxygen content, a decrease in the mixed venous oxygen content is due to a decrease in CO and thus a decrease in end organ perfusion.

Transesophageal Echocardiography

Transesophageal echocardiography (TEE) is a commonly applied tool for both diagnosis and monitoring in the operating room. It can be used to diagnose ventricular and valvular function, aortic pathology, presence of emboli, and hemodynamic derangements and can be used to monitor fluid status. It is the most sensitive monitor for detecting myocardial ischemia.

Clinical Review

1. Appropriate cuff size for measuring blood pressure noninvasively should have the following width circumference of the extremity and a bladder length that encircles the extremity:
   A. Width 20 %, bladder length 30 %
   B. Width 30 %, bladder length 40 %
   C. Width 40 %, bladder length 60 %
   D. Width 30 %, bladder length 60 %
2. Pressures in radial artery when compared to aortic pressures are:
   A. Higher
   B. Lower
   C. The same
   D. Either higher or lower
3. All of the following factors cause decreased pulse oxygen saturation readings, EXCEPT:
   A. Hypotension
   B. Blue nail polish
   C. Administration of methylene blue
   D. Presence of carboxyhemoglobin
4. The following leads on the ECG correspond to the inferior region of the heart:
   A. I, aVL, V_3
   B. II, III, aVF
   C. I, aVF, V_3
   D. II, III, aVL
5. Core body temperature can be measured at all of the following sites, EXCEPT:
   A. Nasopharynx
   B. Rectum
   C. Tympanic
   D. Esophagus
6. Pneumothorax is most common with cannulation of:
   A. Internal jugular vein
   B. Subclavian vein
   C. Femoral vein
   D. Basilic vein
7. Infection is most common with cannulation of:
   A. Internal jugular vein
   B. Subclavian vein
   C. Femoral vein
   D. Basilic vein
8. In the central venous tracing, absent a waves indicate:
   A. Junctional rhythm
   B. Supraventricular tachycardia
   C. Bulging of the tricuspid valve into the atrium
   D. Atrial fibrillation
9. The most common complication when inserting a pulmonary artery catheter is:
   A. Pulmonary embolism
   B. Endocarditis
   C. Catheter knotting
   D. Arrhythmia
10. The most sensitive monitor to detect myocardial ischemia is:
    A. Electrocardiography
    B. Pulmonary artery monitoring
    C. Measuring cardiac enzymes
    D. Transesophageal echocardiography

Answers: 1. C, 2. A, 3. D, 4. B, 5. C, 6. B, 7. C, 8. D, 9. D, 10. D

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Fluid and Electrolyte Balance

7

Patrick Hackett and Michael P. Mangione

The goal of anesthesia providers when caring for surgical patients or the critically ill is to ensure adequate tissue perfusion and thus tissue oxygenation. Surgery and the stress of being ill result in an increased oxygen requirement, and if one does not have the ability to increase oxygen delivery, then the likelihood of infection, multiorgan failure, and death rises. Therefore, fluid therapy to maintain adequate hydration, oxygen delivery, renal perfusion, and electrolyte balance is a cornerstone to hemodynamically manage surgical and nonsurgical patients.

Fluid Compartments

Total body water (TBW) as a percentage of body weight varies between individuals (males 60 %, females 50 % of TBW). In adult males and newborns, TBW is greatest, while it is lowest in adult females and the obese. TBW is distributed between intracellular and extracellular compartments (Fig. 7.1). Intracellular fluid (ICF) is 2/3 of TBW, where the major cations are potassium and magnesium (Table 7.1) and the anions are phosphates, either adenosine triphosphate (ATP), adenosine diphosphate (ADP), or adenosine monophosphate (AMP). The extracellular fluid (ECF) constitutes the other 1/3 of TBW where the major cation is sodium and the anions are bicarbonate (HCO3−) and chloride (CL−). Furthermore, plasma accounts for ¼ of ECF, while interstitial fluid accounts for ¾ of ECF.

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Electrolytes are readily exchanged between intracellular and extracellular fluids in order to support cell metabolism. A membrane-bound ATP-dependent pump exchanges sodium for potassium in a ratio of 3:2. Intravascular pressure continuously forces fluid toward the interstitial space, but the equilibrium is maintained by the oncotic pressure created by large molecules, such as proteins and colloids. These large molecules cannot cross the barrier between compartments and thus maintain intravascular volume, thereby effectively maintaining circulation. Tonicity of a solution is usually expressed in terms of osmolarity (number of osmoles/liter of solution) or osmolality (number of osmoles/kg of solution). For nondissociative substances an osmole equals 1 mole, and for dissociative (ionized) substances, each mole results in "*n*" moles (e.g., NaCl produces 2 osmoles). A mole of a substance equals 6.02×10^{23} molecules. Normal plasma osmolality is 280–290 mosm/kg and can be calculated by the following formula:

$$\text{Plasma osmolality} = \text{sodium concentration}\,(\text{meq}/1) \times 2 + \text{BUN}\,(\text{mg}/\text{dl})/2.3$$

Perioperative Fluid Management

The practice of perioperative fluid therapy has been under scrutiny for the past 50–60 years. In the late 1950s–1960s, two men began the debate with Francis Moore first arguing for a more restricted regimen, while Tom Shires supported a liberal administration of fluid. The latter's theory was then supported during the Korean War where large amounts of fluid were infused to trauma patients resulting in improved survival. Tom Shires' recommendation for excessive administration of fluids was then a common practice for decades, until the past 5–10 years where the deleterious effects of such management have been illustrated in the literature and a new approach to perioperative fluid management has been developed.

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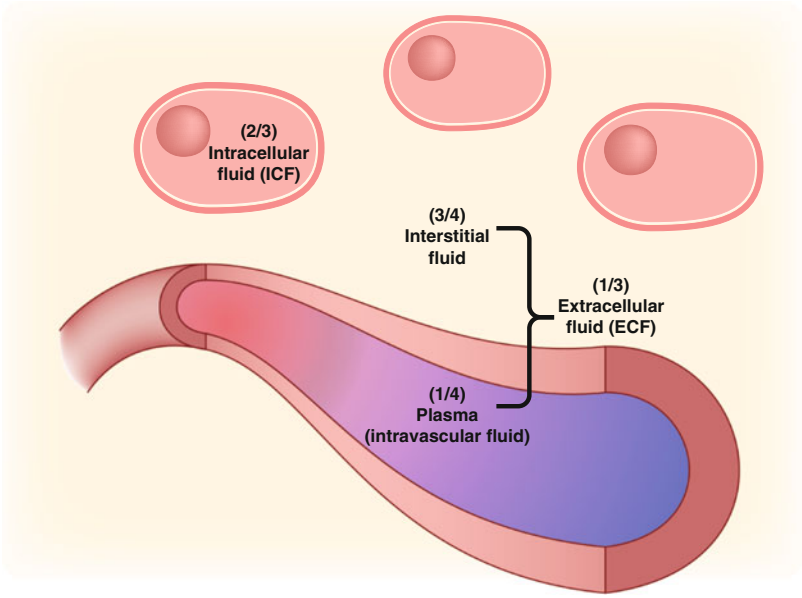

Fig. 7.1 Fluid compartments in the human body

Table 7.1 Electrolyte concentrations, plasma and intracellular

Ion	Plasma (meq/l)	Intracellular (meq/l)
Sodium	140	12
Potassium	4	150
Calcium	5	1
Magnesium	2	40
Chloride	105	4
Bicarbonate	24	7

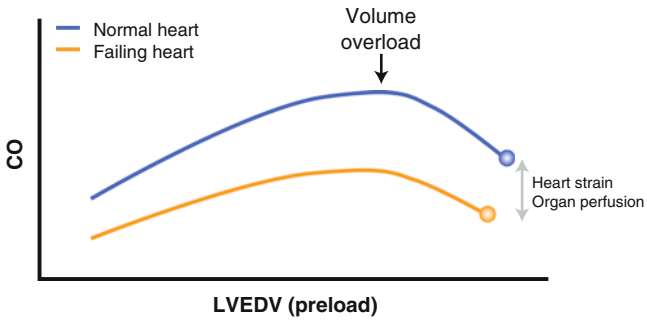

Fig. 7.2 Frank–Starling relationship between CO and LVEDV. Increasing volume initially leads to improved myocardial performance, but volume overload eventually leads to decreased organ perfusion and increased heart strain. *CO* cardiac output, *LVEDV* left ventricular end diastolic volume

Hypovolemia

Hypovolemia can result from prolonged preoperative fasting, vasodilation caused by anesthesia drugs or neuraxial blockade, or acute bleeding. To understand when and how to manage fluid therapy, it is important to distinguish dehydration from intravascular hypovolemia. Dehydration affects the extravascular space and is a result from urine production and perspiration. This leads to a colloid-free fluid loss from the extracellular space and is treated by administering crystalloid solution. On the other hand, acute hypovolemia results from a loss of colloid-rich solution (plasma) from the intravascular space which lowers oncotic pressure and leads to interstitial edema. Using crystalloids to replace these losses may exacerbate the already low oncotic pressure and worsen edema. Therefore, using colloid solutions may be preferable when treating acute hypovolemia.

Hypervolemia

Various negative effects of excessive administration of fluid before, during, and after surgery have been well illustrated. Marked hypervolemia is defined as weight gain of at least 10 % over the preoperative weight. When volume overloading, there is the potential to impair left ventricular stroke volume or cause myocardial ischemia. Pulmonary function can also be impaired with accumulation of fluid in the interstitium leading to pulmonary edema, atelectasis, pneumonia, or respiratory distress. Furthermore, volume overload can lead to impaired tissue oxygenation resulting in impaired wound healing. Paralytic ileus may be worsened by excessive fluid administration. Finally, liberal fluid management can exacerbate the sodium and water-conserving effects of the surgical stress response and can result in electrolyte and acid–base disturbances.

The source of these side effects has been credited to various physiological responses within the body. Excessive fluid administration leads to shifting a patient along their Frank–Starling performance curve to the extreme right, leading to left ventricular strain, a decrease in stroke volume, and thus low cardiac output (Fig. 7.2). The myocardial dysfunction can result in pulmonary or peripheral edema and decreased oxygen delivery. Another aspect of volume overload leading to system dysfunction arises from “third spacing,” which

results from fluid seeping from the intravascular space. This is believed to result from damage to two different layers of the endothelium—the endothelial surface layer (EDL) and the overlying glycocalyx. The EDL acts as a barrier between the intravascular space and the interstitial space. Positive hydrostatic pressure continuously forces fluid toward the interstitium. However, the glycocalyx contains large proteins which cannot cross the EDL, effectively increasing the oncotic pressure and keeping the majority of fluid within the intravascular space. Unfortunately, many factors such as surgical stress, ischemia/reperfusion injury, and circulating mediators such as TNF-alpha, cytokines, proteases, and atrial natriuretic peptide lead to thinning of the EDL and breakdown of the glycocalyx, and thus worsening the edema.

The current goal of fluid management is to support the cardiovascular system in maintaining cardiac output and thus adequate oxygen-carrying capacity to equal the metabolic demand. Both hypovolemia and hypervolemia decrease tissue perfusion and can result in end organ failure; consequently *optimizing* volume status does not mean *maximizing*. Therefore, prior practices of administering excessive levels of fluid to replace preoperative fasting and overestimated insensible losses during the surgical procedure may not be prudent. Rather an individualized fluid regimen, which includes replacing the intravascular and extravascular losses as demanded, should be used.

Measuring and Monitoring Fluid Losses

Accurately measuring the amount of fluid in these compartments is not easily performed; therefore, physical examination, laboratory measurements, and hemodynamic monitoring are utilized to determine a patient's volume status. Physical examination of hypovolemia include examining the hydration of mucous membranes (dryness), loss of skin turgor, low urine output (<0.5 ml/kg/h), heart rate (tachycardia, >100 beats/min), hypotension (measuring orthostatic blood pressure, if possible), tachypnea, and altered mental state (drowsiness, lethargy). However, under anesthesia often these exam findings are not reliable, as the stress of surgery and many of the medications used for anesthesia alter their relationship with intravascular volume. When the physical exam is unreliable, laboratory measurements such as rising hematocrit, metabolic acidosis, mixed venous oxygen saturation (SvO_2), increasing lactate, increasing specific gravity, urinary sodium less than 20 meq/l, urinary osmolality >450 mosm/kg, rising plasma sodium levels, and a BUN-to-creatinine ratio more than 10:1 may be signs of volume depletion.

Invasive monitoring used to determine volume status includes central venous pressure (CVP) monitoring, pulmonary artery catheters (PACs), and arterial lines. CVP is the most widely used invasive technique for measuring intravascular volume in critically ill patients. The CVP is measured by placing a catheter within a central vein at the junction of the superior vena cava and the right atrium. The best time to record CVP is at end expiration, unless the patient is mechanically ventilated in which case true CVP is best measured at the beginning of expiration. The Society of Critical Care Medicine's Surviving Sepsis protocol recommends a goal of CVP between 8–12 mmHg and 12–15 mmHg for patients on mechanical ventilation. PACs are used to measure both right and left heart pressures by "floating" a balloon-tipped catheter through the right heart to within the proximal branches of the pulmonary artery—preferably the West Lung Zone III. However, multiple studies have shown inconsistencies of PAC measurements in the critically ill. Over the last decade this form of monitoring has fallen from favor with CVP becoming a valid replacement.

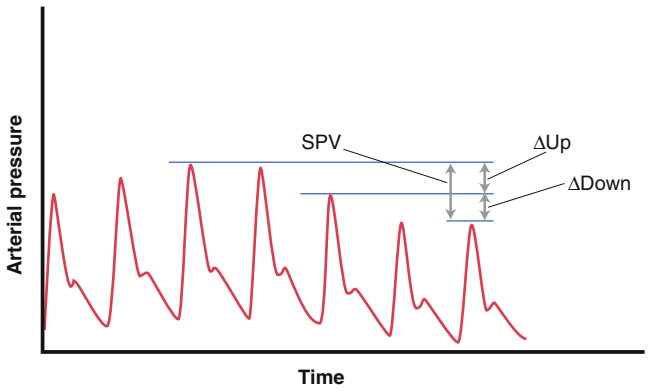

Fig. 7.3 Determination of systolic pressure variation (SPV)

Furthermore, arterial line placement can be utilized to determine systolic pressure variability (SPV) within the tracing displayed on monitor (Fig. 7.3). In a mechanically ventilated patient, the baseline pressure is taken during an apneic period. Then the two components of SPV can be measured from the change in peak amplitude with expiration (delta up) and inspiration (delta down). The sum of delta up and delta down equals SVP with a value less than 5 mmHg signifying the absence of hypovolemia. All in all, while CVP, PACs, and arterial lines are useful, they should only be used in conjunction with physical examination and laboratory data to accurately determine volume status and fluid responsiveness.

New literature describes less invasive monitoring of volume status via echocardiography and esophageal Doppler monitoring (EDM) with increasing popularity. Echocardiography when available can be used to visualize the inferior vena cava (IVC) via a subcostal view. A decrease in IVC diameter more than 50 % with respirations correlates with hypovolemia. Furthermore, in the mechanically ventilated patients, an IVC variation of more than 12 % with respirations represents those who would respond to fluid boluses. Esophageal Doppler monitoring (EDM) consists of a small, thin, flexible probe, much like a nasogastric tube, with a Doppler transducer located at the tip, which is placed

approximately 35 cm into the esophagus. EDM is used to measure the length traveled by an erythrocyte within the descending aorta during a single cardiac cycle. This correlates to a wave tracing representing flow time and peak velocity. The area under the curve correlates with stroke distance (Fig. 7.4). From this data, the stroke volume can be calculated by multiplying stroke distance and the diameter of the aorta, which is calculated via nomograms based on the patient's weight and height. Furthermore, cardiac output can be roughly calculated by multiplying the stroke volume by heart rate. These data can be used to determine the appropriate timing and amount of fluid to administer.

Fluid Therapy

Fluid resuscitation is a major aspect of managing the care of critically ill patients, whether as a result of burns, trauma, surgery, or from sepsis. There are many different options when it comes to replacing this deficit including crystalloid or colloid solutions, or both. Largely, the difference between crystalloid and colloid is that crystalloids are made from low-molecular-weight salts, while colloids contain larger-molecular-weight proteins or glucose polymers.

Crystalloid solutions include varying concentrations of normal saline (sodium and chloride), lactated ringers (sodium chloride, potassium, calcium, lactate), and dextrose in water (Table 7.2). Normal saline is usually the initial fluid choice for resuscitation. However, excessive amounts of normal saline administered (>3–4 l) can lead to hyperchloremic metabolic acidosis. Lactated ringer's (LR) solution is slightly hypotonic, providing 100 ml of free water per liter, and the most physiologic solution when a large amount of fluid is required. However, LR is not an ideal solution to use as a Dilutent for administering packed red cells as it contains calcium (antagonizes citrate). Additionally, LR contains potassium, which may not be preferable for patients with kidney disease, and also lactate, which is metabolized to bicarbonate leading to metabolic alkalosis. Dextrose in water is mainly used for replacement of pure water deficits and for hypernatremia but is also useful in preventing ketosis and hypoglycemia during fasting. Dextrose solutions are not used in neuroanesthesia, as hyperglycemia has been found to be detrimental to injured neuronal tissue. Crystalloid solutions, because of their lower molecular weight, lack the ability to maintain the oncotic pressure of the intravascular space and largely (80 %) redistribute throughout the entire extracellular space.

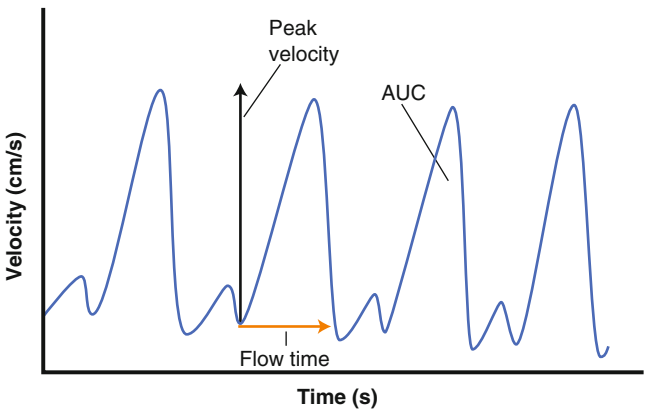

Fig. 7.4 Determination of cardiac output by analyzing flow tracing of an esophageal Doppler probe. The area under the curve is calculated (AUC), which shows the stroke distance (the length traveled by an erythrocyte during the cardiac cycle). By multiplying stroke distance by aortic cross-sectional area, the stroke volume is calculated. Cardiac output = stroke volume × heart rate

Colloids are organized into naturally occurring albumin and artificial solutions containing starches (dextran, hetastarch) and gelatins. Human albumin is a protein mainly responsible for sustaining intravascular osmotic pressure and should theoretically be the ideal colloid for restoring protein loss from the vasculature. Albumin is prepared by heating it to 60 °C for 10 h, and therefore, an albumin solution does not cause allergic reactions or immunological complications. Furthermore, albumin (5 and 25 % solutions) can add a survival benefit when used to correct hypoalbuminemia in patients with cirrhosis, ascites, and hepatorenal syndrome.

Hydroxyethyl starches are similar to gelatins in that they are artificial, but these are derived from amylopectin which is a glucose molecule found in waxy maize or potatoes. Hetastarch solution (6 % Hespan in isotonic saline) is usually given in a dose of 500–1,000 ml (20 ml/kg). However, it should be noted that hetastarch solutions, by using thromboelastography, were found to cause coagulopathies, specifically depleting von Willebrand factor and factor VIII and prolonging PTT and INR. In 2013, the FDA issued a black box warning for use of Hetastarch in critically ill patients, and in patients with pre-existing renal and severe liver dysfunction (causing excessive bleeding and increased mortality). Dextrose starches (dextran) improve blood flow in the microcirculation by

Table 7.2 Composition of commonly used crystalloids

Crystalloid	Tonicity (mosm/l)	Na^+ (meq/l)	Cl^- (meq/l)	K^+ (meq/l)	Ca^{2+} (meq/l)	Lactate (meq/l)	Glucose (g/l)
Normal saline	308 (isotonic)	154	154				
Lactated ringers	274 (slightly hypotonic)	130	109	4	3	28	
5 % Dextrose in water	253 (hypotonic)						50
$D_5$1/2NS	432 (hypertonic)	77	77				50
3 % NS	1,026 (hypertonic)	513	513				

decreasing blood viscosity. However, dextrans have antiplatelet effects (inhibition of aggregation), prolong bleeding time, interfere with blood typing, and cause allergic reactions. Gelatins are polydispersed polypeptides created from degraded bovine collagen, have the potential to cause allergic reactions (including anaphylaxis), and are not available in the United States. Furthermore, Hespan, gelatins, and dextran solutions were shown in multiple studies to cause nephrotoxicity.

There has been a debate through the years as to which solution is superior for resuscitation strategies, crystalloid or colloid. A Cochrane review published in 2011 looked at 65 trials and determined that there was no evidence from randomized control trial's (RCT) that colloids provided any mortality benefit over crystalloids for patients suffering from trauma, burns, or following surgery. Furthermore, the SAFE trial disproved the belief that larger infusions of crystalloids are required to reach the same resuscitation goals as can be achieved by smaller volumes of colloid. Therefore, because colloids provide no mortality benefit and are considerably more expensive than crystalloid solutions, the value of their continued use in resuscitative guidelines and intensive care management algorithms is not clear.

Preoperative oral hydration

In the 1990s long preoperative fasting strategies were used in patients undergoing elective surgery to avoid emesis and pulmonary aspiration during the induction of general anesthesia. This practice was later questioned, and in 1999 the American Society of Anesthesiologists (ASA) issued new guidelines (see Chap. 2) in which patients were allowed to have clear fluids until 2 h before surgery. Subjectively, the majority of subjects reported to feel more comfortable leading up to their procedure, feeling less thirsty and hungry. All in all, oral rehydration up to 2 h before surgery has shown to increase patient satisfaction without causing any detrimental affects when compared to prolonged fasting in patients.

Strategies for intraoperative fluid replacement

(i) Traditional method of fluid replacement

Hourly maintenance rate: the 4/2/1 formula:

- 0–10 kg—4 ml/kg/h
- 11–20 kg—add 2 ml/kg/h
- For each kg above 20 kg—add 1 ml/kg/h for each kg above 20 kg

For example, a 70 kg patient will have an hourly maintenance rate of 110 ml/h (40 + 20 + 50). Therefore, a patient who has been fasting for 10 h has a preexisting fluid deficit of 1,100 ml.

Intraoperative fluid loss: these include evaporative and redistributive (internal redistribution of fluids) fluid losses. These are added to the hourly maintenance rate:

- Minor surgery—2 ml/kg/h
- Intermediate surgery—4 ml/kg/h
- Major surgery—8 ml/kg/h

Replacement of blood loss: intraoperative blood loss can be roughly estimated by measuring the blood in the surgical suction canister (deduct irrigation fluid), fully soaked sponges (10 ml/4 × 4 sponge), and laparotomy pads (100–150 ml). Serial hematocrits can be helpful in estimating blood loss, but are unreliable due to rapid fluid shifts; therefore, serial hematocrits represent more of a ratio of red blood cells to the plasma:

- Replace 1 ml of blood loss with 3 ml of crystalloid (half-life of crystalloids = 0.5–1.5 h).
- Replace 1 ml of blood loss with 1 ml of colloid (half-life of colloid = 4–6 h).
- Replace 1 ml of blood loss with 1 ml of packed red blood cells.

Trigger for blood transfusion is a hemoglobin of 7 mg/dl (10 mg/dl in elderly patients, and in those with significant cardiac/pulmonary disease). However, the decision to transfuse should also take into account the physiologic state of the patient, blood pressure, heart rate, and presence of any acidosis. Approximately, one unit of packed red cells transfused increase the hemoglobin by 1 mg/dl (hematocrit by 3 %).

(ii) Goal-directed fluid therapy

This pertains to administration of fluid to maintain certain goals. Most importantly, maintaining stroke volume is the primary aim. Changes in stroke volume (trends) are continuously monitored, and a fluid bolus is administered when the stroke volume falls by 10–15 %. This form of fluid therapy is particularly useful for patients undergoing major surgery or with significant cardiac disease. Studies have shown that goal-directed fluid therapy, when compared to traditional fluid therapy, has a lower risk of pulmonary and renal complications, shorter length of hospital stay, earlier return of bowel function, and a decreased incidence of postoperative nausea and vomiting. For goal-directed fluid therapy, in addition to stroke volume and cardiac output, other parameters should also be maintained. These include a heart rate <100 beats/min, normal blood pressure (within 20 % of baseline), urine output of 0.5–1 ml/kg/h, CVP between 8 and 12 mmHg, hemoglobin of at least 7 g/dl (10 g/dl in elderly and patients with cardiac disease), normal pH, PaO_2, and serum lactate.

Electrolytes

Sodium

Serum sodium concentration and thus serum osmolality are tightly regulated by water homeostasis, which itself is controlled by thirst, vasopressin, and the kidneys. In addition, sodium balance is maintained by the renin–angiotensin–aldosterone system (aldosterone enhances sodium resorption in the distal nephron) and also by the atrial natriuretic peptide, which is released following atrial distention and

causes arterial vasodilation and increased urinary sodium and water excretion in the renal collecting tubules. A disruption in any of these mechanisms can lead to abnormalities in serum sodium concentration. This sodium ion is an impermeable solute that contributes to tonicity, which causes the movement of water across cell membranes.

Hypernatremia

Hypernatremia is defined as a serum sodium level greater than 145 meq/l. The causes of hypernatremia can be from a net loss of water (more common) or from a hypertonic sodium gain, the latter being usually iatrogenic or from accidental sodium loading. Sustained hypernatremia occurs when the thirst regulation is impaired or access to water is not available. This can be seen in intubated patients, patients with altered mental status, the elderly, and infants. The elderly usually develop hypernatremia via febrile illnesses or because they have impaired thirst regulation or depend on others to supply water. Infants are usually suffering from diarrheal illness when they present with abnormally high sodium.

The signs and symptoms of hypernatremia are largely associated with central nervous system dysfunction and are most severe when the serum levels of sodium are extreme or rise rapidly. Common symptoms in infants include tachypnea, weakness, restlessness, high-pitched cry, insomnia, lethargy, and even coma. The elderly typically aren't symptomatic until serum sodium rises above 160 meq/l. At this point, intense thirst may present, but later in the progression confusion predominates, causing lack of thirst response. No matter the age, if the patient is hypovolemic, orthostatic hypotension and tachycardia will manifest. Brain shrinkage is a morbid side effect of hypernatremia and is the result of water being pulled out of cells by the increased osmotic gradient produced by high sodium levels. This shrinkage can lead to vascular rupture, cerebral bleeding, subarachnoid hemorrhage, and even death. The brain can adapt by increasing the amount of solute which enables restoration of intracranial water levels. If hypernatremia develops slowly, this adaptation has ample time to respond and leads to milder symptoms. However, it is important to realize that patients with chronically high sodium shouldn't be treated aggressively with hypotonic fluids. This can lead to cerebral edema and potentially coma, seizures, and death.

The management of hypernatremia is twofold. One is correcting the underlying cause, while the other is correcting the hypertonicity. In patients with hypernatremia that has developed acutely (hours), rapid correction of 1 meq/l/h is appropriate and has little risk of cerebral edema. For patients with chronic hypernatremia, a slower correction should be implemented with a maximal rate of 0.5 meq/l/h. The end goal should be to decrease the serum sodium concentration to 145 meq/l. In addition to normalizing sodium levels, patients with seizures require early intervention with anticonvulsants and secured airways.

The required rate of infusion can be derived by first using the following formula to determine the rate of change in serum sodium caused by 1 l of the respected infusate [see Eq. below]. Then by dividing this value into the goal sodium concentration (usually 145), the infusion rate is given, usually over 48 h. Fluids administered via an oral route or a feeding tube are preferred, which when not possible, intravenous fluids can be utilized. Hypertonic saline should not be used to treat hypernatremia. Only hypotonic fluids are appropriate, including pure water, 5 % dextrose, and ¼ or ½ normal saline. The more hypotonic the solution, the quicker the sodium levels will fall:

$$\text{Change in serum } Na^+ = (\text{infusate } Na^+ - \text{serum } Na^+) \div (\text{TBW} + 1)$$

or

$$\text{Free water deficit} = \text{TBW} \times [1 - (140/[Na^+])],$$ administered over 48 h

Hyponatremia

Hyponatremia is defined as serum sodium concentration of less than 136 meq/l. Unlike hypernatremia which is always hypertonic, hyponatremia can be associated with low, normal, or high tonicity. Dilutional hyponatremia, accounting for the vast majority of cases, results from an intake of water that exceeds the capacity of the kidneys to excrete. This leads to dilution of the body's solutes, causing hypoosmolality and hypotonicity. Other forms of hyponatremia include hypertonic (translocational) hyponatremia, isotonic hyponatremia, and pseudohyponatremia. Hypertonic or translocational hyponatremia is caused by extraction of water from cells by extracellular solutes, which are unable to leave the extracellular space. Examples include hyperglycemia and hypertonic mannitol. An increase in glucose levels by 100 mg/dl can decrease serum sodium by 1.7 meq/l. Isotonic hyponatremia is a result of retention of large volumes of isotonic fluids devoid of sodium (isotonic mannitol) within the extracellular space. Pseudohyponatremia is caused by high levels of triglycerides and proteins within the plasma causing false measurements of sodium using primitive photometers. This has nearly been eliminated due to more accurate measurements by using ion-specific electrodes.

Like hypernatremia, the signs and symptoms of hyponatremia are a result of central nervous system dysfunction. These include headache, nausea, vomiting, muscle cramps, lethargy, restlessness, disorientation, and hyporeflexia. Most patients are asymptomatic until serum sodium concentrations reach below 125 meq/l or with sudden extreme decreases of sodium concentration. Severe complications can occur with serum sodium concentration below 120 meq/l and include seizure, coma, brain damage, respiratory failure, brainstem herniation, and death. These are a result of water entry into the brain, the resulting cerebral edema against an unimpeded cranium, and brain injury.

Fortunately, similar to hypernatremia, the brain can adapt to chronically low levels of hyponatremia by quickly excreting solutes, thereby inducing water loss and reducing swelling. Therefore, patients can be asymptomatic if decreases in serum sodium are slow. Furthermore, if corrections to sodium concentrations are too aggressive, osmotic demyelination can occur. This is found with corrections exceed 12 meq/l/day. Shrinkage of the brain triggers demyelination of pontine and extrapontine neurons that can lead to quadriplegia, pseudobulbar palsy, seizures, coma, and death.

Sodium deficit can be calculated by using the following equation:

$$\text{Sodium deficit} = \text{TBW} \times \left(\text{Desired sodium} - \text{present sodium}\right)$$

There are specific guidelines for treating hyponatremia. Patients with symptomatic hyponatremia with concentrated urine need fluid resuscitation with hypertonic saline. This is usually combined with furosemide to limit the expansion of extracellular fluid volume. This diuretic results in the loss of fluid equivalent to ½ normal saline which aids in the correction of hyponatremia. Furthermore, patients with hyponatremia and dilute urine usually only require restriction of water intake and observation. If symptomatic, these patients will require treatment with hypertonic saline. Correction of hyponatremia should be sufficient enough to correct any potential symptoms but not rapid enough to pose a risk for osmotic pontine demyelination. Studies illustrate that merely increasing sodium concentrations by 5 % are sufficient to reduce cerebral edema. Therefore, it is recommended to target a correction not exceeding 8 meq/l/day.

Potassium

Potassium is the most abundant intracellular ion and is primarily stored in skeletal muscle, and to a lesser extent in the liver. Normal potassium levels are 3.5–5.0 meq/l. Resting membrane potential is determined primarily by the ratio of extracellular to intracellular potassium. This gradient is regulated primarily by Na+/K+ ATPase pump, which is located on the plasma membrane of most cells. The excretion of potassium depends primarily on renal function, and to a much lesser extent on intestinal excretion. While only 2 % of serum potassium is located in the extracellular space, any small change in this value can affect the resting membrane potential.

Hyperkalemia

Hyperkalemia, which is defined as serum potassium levels greater than 5.5 meq/l, is caused by an imbalance of intake versus excretion, or from transcellular shift. In patients with normal renal function, excessive intake of potassium is needed to cause a significant increase in potassium levels. However, in patients with renal failure, any increase in potassium consumption can lead to hyperkalemia. In terms of impaired elimination, medications that interfere with urinary potassium excretion include potassium-sparing diuretics such as amiloride or spironolactone, as well as NSAIDs, and ACE inhibitors. Hypoaldosteronism either in Addison's disease, congenital adrenal hyperplasia, or chronic renal failure results in hyperkalemia with urinary salt wasting, which leads to hypovolemia and hypotension. Furthermore, pseudohypoaldosteronism refers to a disorder resulting in hyperkalemia, metabolic acidosis, and normal GFR. Congestive heart failure and lowered renal function can also lead to decreased potassium excretion. Constipation can lead to decreased potassium elimination as well. Transcellular potassium shifts can be caused by acidosis, diabetes mellitus (reduced insulin), acute increases in osmolality (hyperglycemia), and acute cellular breakdown (hemolysis). Succinylcholine can increase plasma potassium by about 0.5 meq/l, which can be further increased in the presence of burns or spinal cord injuries.

Symptoms of hyperkalemia are largely due to hyperpolarization of cells making them less able to depolarize when needed. This is especially important in the myocardium and manifests through changes in EKG. Mild hyperkalemia (5.5–6.5 meq/l) can be associated with peaked T waves. Moderate hyperkalemia (6.5–8.0 meq/l) leads to prolonged PR intervals, flattened P waves, and widening of the QRS complex. Severe hyperkalemia (>8 mmol/l) is associated with an absence of P waves, AV block, fascicular block, and bundle branch block. It should be pointed out that the above phenomena are not entirely specific and should not be used to rule out life-threatening hyperkalemia if the particular EKG tracings are not present. Other symptoms of hyperkalemia include weakness, paresthesias, and paralysis.

Immediate therapy for hyperkalemia involves stabilization of myocardium through administration of calcium salts, either calcium gluconate or calcium chloride. Increasing serum calcium levels will lead to increased thresholds for cardiac muscle action potentials, leading to decreased excitability. Next, potassium needs to be shifted into cells. This can be performed by using 10 units of insulin with 50 ml of 50 % dextrose, beta-2 agonists, bicarbonate, and diuretics. Finally, removal of potassium either through GI losses or renal excretion is the only permanent treatment for hyperkalemia. For mild to moderate levels of hyperkalemia, cathartics such as Kayexalate can be used. However, Kayexalate has been associated with intestinal necrosis in some studies indicating that it is not a benign medication. For severe life-threatening hyperkalemia that is refractory to initial therapy, hemodialysis can be used, which is the definitive treatment in end-stage renal disease.

Hypokalemia

Hypokalemia is defined as serum K^+ level less than 3.5 meq/l. The kidneys can avidly reabsorb potassium when needed. Therefore, low serum potassium levels are mostly due to potassium depletion and abnormal losses from the intestines or urine. Other processes that can cause a transcellular shift of potassium into cells include beta-2 agonists (can lower serum K^+ levels by 0.5–1.0 meq/l), catecholamines, insulin therapy, verapamil, theophylline (increased action of Na^+/K^+ ATPase pump by inhibiting cAMP), hypothermia, and hyperventilation or alkalosis (promotes potassium entry into the cell in exchange for hydrogen ions). Plasma K^+ concentration approximately decreases 0.6 meq/l for every 0.1 unit increase in arterial pH.

Hypokalemia is often asymptomatic. It increases the risk of cardiac arrhythmias in patients with ischemic heart disease or who are given digoxin therapy. Severe hypokalemia (less than 3 meq/l) can present with fatigue, skeletal muscle weakness (quadriceps), and constipation and can precipitate rhabdomyolysis and impair urinary concentrating mechanisms. EKG findings include prominent U waves, flattened T waves, and widened QRS.

Treatment of hypokalemia includes preventing continued loss of potassium, whether through diarrhea, emesis, hyperglycemia, alkalosis, or diuretic use. Also, hypomagnesemia should be corrected as this can impede correction of potassium levels. Supplementation includes oral and intravenous potassium. When using IV forms, rates of potassium administration should not exceed 20 meq/h. If administering through a peripheral vein, the potassium concentration should be below 50 meq/l as higher concentrations are often painful. Furthermore, potassium should be diluted in normal saline and not dextrose solutions as the latter can cause worsening of hypokalemia and increase the risk for life-threatening arrhythmias. There are many forms of supplementation: potassium chloride, potassium phosphate, potassium bicarbonate, and potassium citrate. For the most part, potassium bicarbonate or citrate should be used in patients with hypokalemia and metabolic acidosis. Potassium phosphate can be used when there is an accompanied hypophosphatemia. For all other settings, potassium chloride should be used to correct hypokalemia.

Calcium

Calcium has a wide range of intra- and extracellular functions including nerve conduction, muscle contraction, and maintenance of membrane potentials, hormone secretion and responsiveness, and enzyme activity. Additionally, calcium functions as structural support for mineralized bone. Serum calcium levels are tightly controlled with a narrow range of 8.5–10.5 mg/dl (2.1–2.6 mmol/l). Ninety percent of the body's total calcium is stored within bone, while the other 10 % is divided between the extra- and intracellular space. Of note, total serum calcium includes both the protein-bound and the ionized form of calcium (normal serum ionized calcium level = 4–5.6 mg/dl) and can be misleading. Thus low serum protein can lead to falsely low levels of calcium. Therefore, it can be assumed that for every 1.0 mg/dl decrease in albumin, 0.8 mg/dl of calcium can be added to the measured value. The ionized form of calcium is the "active" form and represents the portion of calcium that is hormonally regulated and associated with the signs and symptoms of hypo- and hypercalcemia.

Hypercalcemia

High serum level of calcium is defined as any value greater than 10.5 mg/dl. The causes of this disorder are many, with the most common for hospitalized patients being malignancy. Approximately 20–30 % of all cancer patients develop hypercalcemia at some point and this is seen as a poor prognostic indicator. The mechanism causing this is mainly increased parathyroid hormone activity causing increased osteoclastic activity resulting in release of calcium from bone, increased renal absorption of filtered calcium, and conversion of 25-hydroxyvitamin D to the active form, 1,25-dihydroxyvitamin D, which increases gut absorption of calcium.

Other causes of hypercalcemia include primary hyperparathyroidism. This can be found in as many as 3 in every 1,000 outpatient visits. Immobilization can cause increased bone resorption and decreased bone formation. Excessive ingestion of vitamin D and vitamin A can both lead to increased osteoclastic activity, while vitamin D can also cause increased gut absorption. Furthermore, hypercalcemia can be associated with medications such as lithium, thiazides, theophylline, estrogens, retinoic acid, growth hormone, and also parenteral nutrition.

As stated before, albumin plays a large role in determining the serum level of calcium through binding and inactivation. Therefore, high or low levels of albumin can cause reciprocal changes in serum calcium. In patients with alkalemia, albumin binds with higher affinity to ionized calcium, therefore decreasing the level of active calcium without altering the total value of serum calcium. This can cause symptoms even when total serum levels are normal. Decreased levels of ionized calcium can also be seen in hyperphosphatemia. Furthermore, acidemia causes decreased binding of albumin with calcium and thus increasing the ionized form of calcium.

Signs of hypercalcemia include anorexia, constipation, abdominal pain, nephrolithiasis, diabetes insipidus, anxiety, depression, headache, confusion, lethargy, and muscle weak-

ness. In addition, EKG changes can include shortened QT interval, broadened T waves, and even first-degree AV block.

Treatment for hypercalcemia begins with addressing the underlying cause. For mild hypercalcemia, often dietary restriction of 1,000–1,200 mg/day of calcium with 400–600 IU/day of vitamin D will suffice. In patients with adequate cardiac and renal function, fluid administration with normal saline will dilute calcium levels and decrease renal reabsorption. In severe cases, as much as 200–500 ml/h of IV fluids may be required. After volume resuscitation, furosemide or other loop diuretics should be given. If treatment remains refractory to fluids and diuresis, pharmacotherapy using bisphosphonates (alendronate or pamidronate) is indicated. These agents block osteoclast activity and require 2–4 days to create a clinical response. Calcitonin can rapidly reduce calcium levels, but its use is limited due to its short duration of action and association with tachyphylaxis.

Hypocalcemia

Hypocalcemia, defined as serum levels less than 8.5 mg/dl, is found in patients of all ages with variable causes depending on the age. In neonates, calcium is in high demand due to rapidly developing bones. A fetus is hypercalcemic relative to the mother, but after birth is abruptly disconnected from its calcium source. When a newborn is premature, has a low birth weight, or maternal diabetes is present, PTH levels are low. Furthermore, infants that are fed cow's milk-based infant formulas have excessive levels of phosphate which binds and lowers serum calcium. Congenital defects, such as DiGeorge's syndrome, can be associated with hypocalcemia. In adults, the most common cause of hypoparathyroidism is surgical excision of parathyroid glands or damage during thyroidectomy. Other causes include vitamin D deficiency whether acquired or congenital, chelation after transfusion, renal insufficiency, fluid overload, alkalosis, hungry bone syndrome, and pancreatitis.

Neuromuscular dysfunction is a common manifestation of low serum calcium levels. This includes tetany, numbness, and muscle cramps. When severe, hypercalcemia can also cause bronchospasm or laryngospasm and can lead to seizures. The underlying mechanism of these symptoms is that hypocalcemia causes hyperexcitable voltage-gated sodium channels, which then cause nerve fibers to spontaneously discharge. Cardiac dysfunction, including heart failure and cardiomyopathy, can also occur.

Treatment of hypocalcemia involves supplementation with 10 % calcium gluconate or 10 % calcium chloride. Calcium chloride has three times the level of elemental calcium (272 mg) than calcium gluconate (90 mg). These medications are hyperosmolar and should therefore be administered through a central vein. If one is not accessible, calcium gluconate can be given peripherally over 5–10 min. Bolus doses cause transient increases in calcium and can be followed by a calcium infusion. In adults, an appropriate treatment includes 100–200 mg of elemental calcium gluconate given over 10–20 min, followed by 0.5–1.5 mg of elemental calcium/kg/h. While this regimen will increase calcium levels, no study has illustrated a clear improvement in morbidity and mortality for critically ill patients. Regardless, serum calcium levels should be monitored continually during calcium infusions. Furthermore, maintaining therapeutic levels of magnesium and vitamin D will help correct calcium imbalance.

Phosphate

Phosphorus plays a major role in several processes within the body, including bone development, energy transfer, platelet aggregation, and cell membrane integrity and function. Bone contains 85 % of total body stores of phosphorous, while the remaining 14 % is intracellular, and 1 % is extracellular. Similar to calcium, a small percentage (0.15 %) of total body phosphorous is freely circulating and "active." Phosphorous homeostasis is dependent on intestinal absorption and renal regulation. Furthermore, significant and sustained alterations in phosphorous levels often are not seen without underlying kidney dysfunction. Normal values of serum phosphate are 2.5–4.5 mg/dl (0.8–1.45 mmol/l).

Hyperphosphatemia

Hyperphosphatemia can occur from increased gut absorption, decreased renal excretion, or cellular release or translocation of phosphate from the intracellular to the extracellular space. Increased gut absorption results from excessive intake of phosphate laxatives or enemas which can be seen in patients undergoing a colonoscopy who have just completed a bowel preparation. Furthermore, vitamin D overdose can lead to high serum phosphate levels. Acute tumor lysis syndrome, rhabdomyolysis, hemolysis, hyperthermia, and catabolic states such as cancers can lead to increased release of phosphate from cells.

Overt signs and symptoms of hyperphosphatemia are lacking. Rather, the interaction between high serum phosphate and calcium can lead to precipitation and deposition in bones and soft tissues. This has been shown to lead to kidney failure. Hypocalcemia should be ruled out whenever high levels of phosphate are discovered. Treatment for acutely elevated serum phosphate includes volume expansion, dialysis, and oral phosphate binders. In the setting of normal or even moderately decreased renal function, hyperphosphatemia is self-limiting as the kidney possesses a high capacity for phosphate excretion. Generally, phosphate-binding antacids such as aluminum hydroxide or aluminum carbonate can be used to treat hyperphosphatemia.

Hypophosphatemia

Hypophosphatemia can be caused by decreased intestinal absorption, increased renal excretion, or internal redistribution of phosphate. The majority of patients with severe hypophosphatemia possess both decreased total phosphate stores and redistribution of phosphate to the intracellular space. Redistribution is the most common cause of this disorder and can be found in many different processes. Respiratory alkalosis increases intracellular pH and causes influx of phosphate ions to stimulate glycolysis. Glucose and insulin administration stimulates carbohydrate metabolism, which then causes phosphate and glucose to enter cells. Catecholamines, such as epinephrine and norepinephrine, either endogenous or administered, cause a decrease in serum phosphate.

Specific disease processes that result in phosphate uptake into cells include hungry bone syndrome, acute leukemia, and metabolic acidosis. Serum phosphate levels are inversely related to inflammatory messengers like tumor necrosis factor and interleukin-6. This is supported by the finding that sepsis, especially when caused by gram-negative rods, is associated with hypophosphatemia. Therapies such as aminoglycosides, glucocorticoids, diuretics, antiretroviral, and cancer drugs also lead to low serum phosphate levels. Furthermore, a refeeding syndrome sometimes caused by initiation of parenteral feeding in a patient who has chronically been without nutrition can cause influx of phosphate into cells and cause low serum levels. Specific patient populations are most susceptible to hypophosphatemia. One study showed that up to 45 % of all hospital hypophosphatemia cases occur in the ICU population. Trauma patients, especially burn and head trauma patients, have shown a relationship to low serum levels of phosphate.

The total body deficit of phosphate is not always represented by measured serum levels. Thus, the degree of hypophosphatemia does not always correlate with symptoms. Low phosphate level impairs energy utilization and can lead to failure in various organ systems. Dysfunction in respiratory muscles can result in respiratory failure and difficulty weaning from mechanical ventilation. Low phosphate level depletes 2,3-diphosphoglycerate (2,3-DPG) stores and shifts the oxygen dissociation curve to the left, lowering oxygen delivery to peripheral tissues. Hypophosphatemia in cardiac myocytes can lead to decreased contractility and arrhythmias. This phenomenon is illustrated in studies showing the correlation between hypophosphatemia and inotropic requirements, as well as ventricular tachycardia after myocardial infarction. Other detrimental effects from hypophosphatemia include insulin resistance, rhabdomyolysis, and central pontine myelinolysis.

Treatment of hypophosphatemia causes much debate, but what is generally agreed upon is treating patients who are symptomatic or with serum levels < 1.0 mg/dl (0.32 mmol/l). Phosphate can be administered orally or intravenously. Moderate hypophosphatemia can be treated with oral supplements, but vitamin D should be added to facilitate intestinal absorption. Oral regimens include doses ranging from 2.5 to 3.5 g (80–110 mmol) divided over two to three doses. Care should be taken when utilizing IV routes as phosphate can precipitate calcium and lead to hypocalcemia. Intravenously, phosphate can be given in doses up to 45 mmol with an infusion rate of 20 mmol/h.

Magnesium

Second to potassium, magnesium is the most prevalent intracellular cation. It is required for all reactions involving ATP, illustrating the need of magnesium in various organ systems. Furthermore, calcium channels are regulated by magnesium, and therefore, reactions such as muscle contractions and insulin release can be affected negatively by the deficiency of magnesium. Normal serum level of magnesium is 1.8–2.3 mg/dl. Abnormal reactions to altered magnesium levels are more dependent on tissue levels rather than serum, making it difficult to associate symptoms with blood levels.

Hypermagnesemia

Hypermagnesemia is rarely seen due to the ability of the kidneys to increase the amount of excretion from a baseline of 3–4 % to 100 % if needed. One study showed only 8 patients out of 20,000 that had significant hypermagnesemia (greater than 6 mg/dl). Signs and symptoms of hypermagnesemia include lethargy, confusion, and even coma. Blockage of synaptic nerve impulses can lead to loss of deep tendon reflexes, flaccidity, and apnea. Hypermagnesemia can also result in ileus, urinary retention, and fixed dilated pupils. From a cardiac standpoint, magnesium acts as a calcium and potassium channel blocker causing bradycardia, hypotension, and EKG findings such as prolongation of PR, QRS, and QT intervals. Potassium excretion can also be blocked in the kidney causing hyperkalemia.

Renal insufficiency is the most common cause of hypermagnesemia. However, magnesium levels stay normal until the GFR decreases to less than 30 ml/min. This again illustrates the great reserve the kidney possesses for excreting magnesium. Other causes include increased intake in the setting of treatment for preterm labor or preeclampsia/eclampsia; overconsumption of antacids, laxatives, and magnesium cathartics; and ingestion of Epsom salts. As stated before, hypermagnesemia can cause an ileus, which then leads to increased absorption and worsening clinical picture.

Treatment of hypermagnesemia includes withholding all magnesium-containing medications in the setting of renal failure. If needed, calcium can be used to counteract cardiogenic and pulmonary depression. A reasonable dose is 100–200 mg of calcium given over 10 min. Although no studies have definitely shown to support the practice, diuretics,

calcium supplements, and isotonic saline infusions are thought to augment renal clearance of magnesium. Lastly, if needed, renal dialysis can be used to rapidly and safely lower serum magnesium levels.

Hypomagnesemia

Hypomagnesemia is common among geriatric and ICU patients. Mortality rates are inversely proportional to magnesium levels. This is hard to interpret given that hypomagnesemic patients also have associated electrolyte abnormalities such as hypokalemia, hypocalcemia, and hyponatremia, which contribute to the mortality risk. Neuromuscular symptoms of hypomagnesemia include vertical nystagmus, weakness, fatigue, muscle cramps, seizure, and associated rhabdomyolysis. Hypomagnesemia can also cause arrhythmias, both atrial and ventricular. EKG changes include flattening of the T waves, appearance of U waves, and prolongation of QT interval.

Causes of hypomagnesemia include extrarenal causes, such as decreased intake or increased losses from GI tract, NG tube suctioning, or emesis. Serum magnesium levels of alcoholics are commonly low given that they take in less food and are prone to malabsorption issues. Decreased absorption can also be seen in GI illnesses such as steatorrhea, diarrhea, or short bowel syndrome. Furthermore, hungry bone syndrome following parathyroidectomy can cause low levels of magnesium, calcium, and potassium. Renal losses include congenital wasting syndromes such as Gitelman's or Bartter's syndromes or from medications such as loop diuretics, which can also cause hypokalemia. Other medications that cause renal magnesium losses include cisplatin, amphotericin B, aminoglycosides, cyclosporine, and tacrolimus. Lastly, renal tubule dysfunction from acute tubular necrosis can cause the renal tubules to waste magnesium.

Treatment of hypomagnesemia commonly involves administration of magnesium sulfate (MgSO4), where one gram also contains 0.1 g of elemental calcium. To adequately replete magnesium stores, regimens include 8–12 g of MgSO4 in the first 24 h, followed by 4–6 g/day for up to 4 days of treatment. For the treatment of torsades de pointes, the American Heart Association recommends 1–2 g of MgSO4 as an IV bolus.

Total Parenteral Nutrition

Total parenteral nutrition (TPN) is a mixture of dextrose, amino acids, vitamins, minerals, electrolytes, trace elements, and fluids administered via a parenteral route. TPN is administered to supplement or replace the caloric needs of a patient who is unable to consume adequate amount of calories via an oral or enteral route. TPN solution is best prescribed by a team of practitioners usually consisting of a dietitian, physician, and pharmacist. Literature has suggested that a team approach to TPN can lead to a decrease in the duration of mechanical ventilation and more patients able to reach their energy consumption needs. *Perioperatively, it is recommended that TPN be continued*. In case the decision is made to stop or decrease the rate of TPN, it is important to monitor the patient for hypoglycemia, and other electrolyte abnormalities. The patient's blood sugar may be monitored every 30 min, and a dextrose (10 %) solution may have to be started.

Central venous access is required for most forms of parenteral nutrition due to high osmotic strength of the solutions. For short-term parenteral nutrition, subclavian, internal jugular, or femoral central venous catheters can be used. Peripherally inserted central catheters (PICC) or tunneled central venous catheters are utilized for long-term therapy either from subclavian, internal jugular, or femoral sites. The TPN composition consists of:

- Dextrose as a base, commonly a 40–70 % solution, which contributes 3.4 kcal/g.
- Amino acids add 4 kcal/g and act as a buffer solution for electrolytes.
- Lipids (20 % emulsion) can be added to the stock or infused separately, supplying 2 kcal/g.
- Vitamins and trace elements, such as selenium, copper, etc.

Regardless of the composition, TPN solution is a complex mixture and can lead to various metabolic derangements. While patients can undoubtedly benefit from TPN, it is not without risk. Patients are at a higher risk of contracting bloodstream infections when receiving parenteral nutrition. This can be minimized with good hand hygiene, maximal barrier precautions during line insertion, and minimizing the use of emergently placed lines. Additionally, while obtaining central access, there is risk of bleeding, vascular trauma, pneumothorax, thrombosis, arrhythmia, and air embolism.

Metabolic derangements associated with parenteral nutrition include hyperglycemia, electrolyte abnormalities, nutrient excess or deficiency, Wernicke's encephalopathy, hepatic dysfunction, and refeeding syndrome. To monitor these changes, it is recommended to measure serum electrolytes, glucose, calcium, magnesium, and phosphate daily and measure aminotransferases, bilirubin, and triglyceride at least weekly. A meta-analysis illustrated that patients receiving TPN were two times more likely to become hyperglycemic than patients receiving enteral nutrition. Refeeding syndrome is regarded as a potentially fatal derangement of fluid and electrolyte balance that can occur from feeding a chronically malnourished patient. The hallmark is hypophosphatemia but can also show any electrolyte or nutrient abnormality, leading to multiorgan system impairment, such as Wernicke's encephalopathy. This syndrome, which is characterized by ataxia, confabulation, and ophthalmoplegia, occurs as a result of thiamine deficiency and has been associated with TPN preparations lacking thiamine.

Clinical Review

1. The major cation that exists extracellularly is
   A. Potassium
   B. Sodium
   C. Magnesium
   D. Calcium
2. Administration of excessive amounts of normal saline intravenously may lead to
   A. Hyperchloremic metabolic acidosis
   B. Hyperchloremic metabolic alkalosis
   C. Hypochloremic metabolic acidosis
   D. Hypochloremic metabolic alkalosis
3. Administration of the following colloid may interfere with blood clotting
   A. Albumin
   B. Dextran
   C. Hetastarch
   D. Gelatin
4. Aggressive correction of low serum sodium levels may most likely lead to
   A. Brain herniation
   B. Ataxia
   C. Respiratory failure
   D. Cerebral pontine demyelination
5. A serum potassium level of 8 mg/dl may be best treated with
   A. Calcium chloride
   B. Kayexalate
   C. Glucose and insulin
   D. Hemodialysis
6. A decrease in serum albumin levels will lead to
   A. Increase in serum ionized calcium level
   B. No change in serum ionized calcium level
   C. Decrease in serum ionized calcium level
   D. Increase in total serum calcium level
7. Patients receiving total parenteral nutrition (TPN) may show
   A. Hyperglycemia
   B. Hypoglycemia
   C. Hypophosphatemia
   D. All of the above

Answers: 1. B, 2. A, 3. C, 4. D, 5. D, 6. A, 7. D

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Transfusion Medicine

8

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More than 60 % of all blood product transfusions in the United States occur during the perioperative period. It is, therefore, incumbent upon the anesthesiologist to rationally transfuse blood products, maximizing benefit and minimizing harm to patients. The goal is to strike a balance between the risks of anemia and the risks of transfusion. This chapter will attempt to help guide the clinician in formulating a rational transfusion algorithm, as well as provide an understanding of blood therapy and the appropriate utilization of the myriad guidelines available to the clinician. The reader is also encouraged to review both the American Society of Anesthesiologists Practice Guidelines for Perioperative Blood Transfusion and the Perioperative Blood Transfusion and Blood Conservation in Cardiac Surgery Guidelines.

Pretransfusion Testing

The time required to receive blood after it is ordered depends on the amount of pretransfusion testing required and laboratory processing. Pretransfusion testing can reduce or eliminate the risk of transfusion reactions. In an emergency, uncrossmatched type O or type-specific blood can be given. The risk of hemolytic reaction is low, but rises with history of transfusion, age, and female sex. FFPs require about 30 min to defrost in a 37 °C water bath and do not require compatibility testing. Apheresis platelets are ready immediately, while pooled whole blood-derived platelet concentrates take about 30 min. No compatibility testing is required for platelet transfusion. Cryoprecipitates require about 45 min to defrost and pool, and again no compatibility testing is required.

Type and screen

This is done to determine the ABO blood groups and Rh type (Tables 8.1 and 8.2). Patients may be of either type A, B, O, or AB blood groups. In addition, patients may be Rh positive or negative. This phase takes about 10 min and involves mixing the patient's red blood cells with commercially available anti-A and anti-B antibody preparations. The patient's serum is also tested by mixing it with commercially available reagent type O RBCs that collectively express about 20 antigens most commonly associated with hemolytic transfusion reactions. The latter is done to detect the presence of unexpected RBC antibodies to clinically significant red cell antigens. Type and screen requires about 45 min to complete. If unexpected antibodies are discovered, further testing is performed to identify and locate appropriate antigen-negative units, which may require a number of hours.

Type and cross

In type and cross, the recipient's blood is mixed with the donor RBCs. Crossmatching confirms compatibility between a donor unit of RBCs and the patient's sera. Type and cross adds an additional 15 min to the type and screen. If unexpected RBC antibodies are identified on the type and screen, serologic crossmatching must be performed, which takes an additional 30 min.

Red Cells and Non-erythrocyte Blood Components

Control of ongoing blood loss not only requires impeccable surgical technique but also potentially the institution of red and non-red cell blood component therapy. An outline of the indications, risks, benefits, and complications of the different types of blood products available to transfuse follows.

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Table 8.1 Blood type frequencies

ABO type	Rh type	Percentage	
O	+	37	44
O	–	7	
A	+	36	42
A	–	6	
B	+	8	10
B	–	2	
AB	+	3	4
AB	–	1	

Table 8.2 Compatible donors' blood types

Recipient blood type	PRBC donors	FFP donors
O	O	AB
A	A, O	A, AB
B	B, O	B, AB
AB	AB, A, B, O	AB
Rh+	Rh+, Rh–	Rh+
Rh–	Rh–	Rh+, Rh–

PRBC packed red blood cells, *FFP* fresh frozen plasma

Packed Red Blood Cells

Packed red blood cells (PRBCs) are ideal for transfusion in the presence of anemia (increase oxygen carrying capacity), but not volume replacement. The PRBCs red cells can be reconstituted with normal saline to provide volume, which also reduces the unit's viscosity to facilitate rapid transfusion. Lactated Ringers solution should not be used because of the presence of calcium. Blood is transfused through a blood warmer (37 °C) to prevent hypothermia. Also, a transfusion tubing with a 170 μm filter is used to trap any clots or debris.

A unit of whole blood is collected from the donor (about 450 ml). To this unit 63 ml of a citrate phosphate dextrose (CPD) anticoagulant is added as preservative. The donated whole blood unit is processed to produce one unit each of the RBCs, platelet concentrate, and fresh frozen plasma (FFP). To generate a unit of RBCs, a whole blood unit is centrifuged to separate the RBCs from the plasma. Such a unit has a volume of about 250 ml and a hematocrit of about 70 % and may be stored for up to 21 days at 1–6 °C. To increase the shelf life for up to 35–42 days, about 100 ml of an additive solution [e.g., CPDA-1 (A is adenine), AS-1, AS-3, or AS-5] is added to CPD-RBC units. The final volume of a unit of PRBCs is about 350 ml with a hematocrit of 55–65 %.

Patients who have a history of nonhemolytic febrile transfusion reactions, and who require cytomegalovirus-negative blood, are transfused with leukocyte-reduced RBCs. These RBC units are prepared with special filters that remove ≥99.99 % of WBCs prior to storage. Leukoreduction does not prevent graft-versus-host disease, which requires irradiated RBC units. Cryoprecipitate and fresh frozen plasma do not contain significant numbers of viable leukocytes.

Fresh Frozen Plasma

Clinical scenarios facing the anesthesiologist necessitating the transfusion of plasma include major hemorrhage (after transfusion of one blood volume), postpartum hemorrhage, complex surgical procedures such as liver transplantation and major cardiothoracic surgeries, patients with advanced liver disease, and associated coagulopathies (clotting factor deficiencies, warfarin associated). Reversal of warfarin should be done by injections of vitamin K. FFP should be only transfused for warfarin reversal in case of emergencies (like before surgery).

FFP contains all clotting factors and plasma proteins, but no platelets. FFP is prepared by centrifuging a unit of whole blood. ABO-compatible FFP transfusion units are desirable, but not required. FFP units are stored at −18 to −30 °C and thawed to 37 °C prior to transfusion. The thawed units should be used within 24 h of thawing. Deficiency of clotting factors can be diagnosed by measuring PT (INR) and PTT. This is usually the case when PT > 1.5, INR > 2.0, or PTT > 2 times the normal.

FFP is administered in a dose of about 10–15 ml/kg. One ml of FFP/patient weight in kilogram will raise most clotting factors by 1 %. Since the volume of each FFP unit is about 200 ml, a 70 kg patient will have his/her clotting factors increase by about 3 % per unit of FFP transfused.

Platelets

The decision to transfuse platelets must be contextualized for a particular patient and surgery. Platelet transfusions are indicated to prevent or treat bleeding in patients with qualitative or quantitative platelet deficiencies. Generally, platelet counts greater than 50–80 k/mm^3 are the acceptable standards for most procedures. In the case of neurosurgical operations, a number generally greater than 100 k/mm^3 is the usual accepted practice. Although transfusion practices vary, a prophylactic transfusion trigger of 10 k/mm^3 has been widely adopted in otherwise stable patients. In hemorrhaging patients, it is recommended that the transfusion trigger be 50 k/mm. Furthermore, a numeric trigger does not take into account platelet dysfunction, and clearly, without testing such as thromboelastogram interpretation, the platelet qualitative function is unknown. This issue is of particular importance when patients presenting for surgery have been receiving antiplatelet therapy such as aspirin or clopidogrel.

Platelet concentrates are derived from donated whole blood. Most platelet units used in the United States are actually obtained via plateletpheresis from a single donor. Platelet units usually contain some RBCs and the Rh antigen; hence, type-specific and crossmatched platelets should be transfused, whenever possible. Platelet concentrates are stored at room temperature (20–24 °C) with continuous gentle agitation (facilitates gas exchange and enhances survival) for up to 5 days. Because platelets are stored at room temperature, bacterial growth can occur during storage. Septic transfusion reactions may be observed, especially in immunocompromised patients.

Typically, one unit of platelets contains between 5 and 10 k/mm^3 cells. By convention the usual dose of platelets is 4–6 units (6 pack), which will characteristically raise the platelet count 40–60 k/mm^3 in the average-sized adult (70 kg). If lower than expected posttransfusion platelet count results, it may indicate a refractory state, either due to immune or nonimmune causes. The causes for the latter include fever, sepsis, certain medications, DIC, splenomegaly, hepatic veno-occlusive disease, and graft-versus-host disease (GVHD).

Cryoprecipitate

Cryoprecipitate is typically administered in hemorrhaging patients with presumed fibrinogen deficiency (<150 mg/dl). Examples of hypofibrinogenemic states encountered by the anesthesiologist include patients receiving massive transfusions and patients with disseminated intravascular coagulopathy (DIC). Cryoprecipitate is obtained from slow thawing of plasma (1–6 °C) into a cryoglobulin fraction.

Cryoprecipitate is rich in factor VIII and hence can be used for the treatment of hemophilia A. Each unit of cryoprecipitate contains about 80 units each of factor VIII and von Willebrand factor, about 200 mg of fibrinogen, and lesser quantities of fibronectin and factor XIII. Ten units of cryoprecipitate will typically raise the fibrinogen level to 80–100 mg/dl. Cryoprecipitate is administered in pooled units, which are administered within 4 h of thawing. ABO compatibility testing is not required before administration.

Erythropoietin

Erythropoietin is secreted by the kidney in the body to increase red cell mass. Manufactured recombinant human erythropoietin can be administered to increase red cell mass. It is administered in patients with anemia and chronic renal failure. It can also be used in patients who refuse blood transfusions. Its effect starts in about 2 weeks (therefore, not useful in acute situations) and it is expensive.

Recombinant Activated Factor VII

Recombinant activated factor VII (RVII) is administered in life-threatening hemorrhage and coagulopathy when other measures have failed. It is used to control bleeding in patients with hemophilia A or B. RVII binds to tissue factor to augment thrombin formation via the intrinsic clotting pathway and directly activating factors IX and X. Its dose is 50–100 mg/kg IV, which can be repeated in 2 h, though only one dose is usually administered. The administration of RVII is not associated with a risk of transfusion-transmitted diseases. However, it is expensive to use and is associated with thrombotic events (cerebrovascular accidents, myocardial infarction, pulmonary embolism, clotting of indwelling catheters).

Strategies for Perioperative Blood Conservation

It has been well established that the transfusion of allogeneic blood can potentially lead to a range of clinically significant complications, which can vary from mild to life-threatening. Therefore, conserving and reinfusing autologous blood in an attempt to minimize exposure to allogeneic blood appears to be an attractive option. Strategies for perioperative blood conservation include autologous pre-donation of blood, acute normovolemic hemodilution (ANH), which is initiated before the beginning of the surgical procedure, or cell salvage (utilized intraoperatively).

(i) Autologous blood donation

The decision for autologous donation is made by the surgeon in consultation with the anesthesiologist. The donation of blood should be made by the patient at 1-week intervals (maximum 2–3 units) and not within 72 h of the anticipated surgery. Autologous blood should not be collected if the likelihood of transfusion is low or the patient is at risk of developing perioperative anemia. The patient must meet certain criteria for autologous donation, which include a hemoglobin of 11 g/dl and absence of bacterial infection and severe cardiopulmonary, cerebrovascular (epilepsy), renal, or liver diseases.

The advantages of autologous blood donation include prevention of transfusion-transmitted diseases, reassurance to patients who are concerned of blood transfusion risks, and supplementation of blood supply to the patient (in addition to allogeneic units). Disadvantages of autologous blood donation include risks of bacterial contamination, error in storage leading to ABO incompatibility, more cost than allogeneic blood, and wastage of blood if not transfused.

Oral iron supplementation should be started prior to initial unit donation. Erythropoietin can be used in autologous

donation programs to increase red cell production. The blood units are collected in standard collection bags with added preservative solution. The collected units are usually stored as whole blood, with a refrigerated shelf life of 35 days.

(ii) Acute normovolemic hemodilution

ANH can be utilized in patients who have a high likelihood of blood transfusion or an estimated blood loss of at least 1.5 l. The aim of ANH is that the removal of blood decreases then concentration of RBCs, leading to decreased blood loss during the surgical procedure. For ANH, patients should have a hemoglobin of at least 12 g/dl and absence of infection, coagulation abnormalities, and severe coronary, pulmonary, kidney, or liver disease. Advantages of ANH include decreased risk of human error, as no compatibility testing is required, and lower cost than banked blood. The disadvantages of ANH include its cost and decreased oxygen delivery to the tissues if hemoglobin is reduced drastically.

For ANH, blood is collected from the patient (usually via a large-bore IV) before the anticipated blood loss, which is usually before the surgical incision. The allowable blood loss is calculated by the formula

$$\text{Blood collected} = \text{estimated blood volume} \times (\text{Hct(i)} - \text{Hct(f)}/\text{Hct(avg)})$$

Where

Hct(i) = the initial hematocrit before the start of the procedure

Hct(f) = the final hematocrit after hemodilution

Hct(avg) = the hematocrit average during the hemodilution process

The volume of blood removed is replaced with crystalloids/colloids just prior to the surgical process, such that the patient remains normovolemic with a minimum hematocrit of about 25 %. Crystalloids are replaced in a ratio of 3:1 (crystalloid/blood) and colloids in a ratio of 1:1. Though ANH will decrease the total oxygen carrying capacity of blood, compensatory mechanisms for oxygen delivery include an increase in cardiac output and oxygen extraction by the tissues. The removed blood is stored in CPD bags at room temperature for up to 6 h and then given back to the patient, when desired.

(iii) Cell salvage

An effective method of blood conservation is intraoperative collection of blood from the surgical field, called as cell salvage. Cell salvage is utilized when a high degree of intraoperative blood loss is anticipated (>1.5–2 l) and includes procedures such as surgery for trauma and vascular, cardiac, orthopedic, transplantation, urologic, and gynecologic surgery. The advantages of using cell salvage are that blood compatibility is not required, with little risk of human error, and the cost is lower. Cell salvage, however, is contraindicated in patients with malignancy (risk of cancer dissemination), infection, clotting abnormalities, or contamination with urine, fat, or bowel contents. Studies of cell saver use show minimal bacterial load in the returned blood, which is further reduced or eliminated altogether by antibiotic prophylaxis and by the use of the leukoreduction filter. The disadvantages of using cell salvage include availability of trained personnel, specialized equipment, and associated costs.

Blood is suctioned by the surgeon into the container of the cell salvage device. Heparin is then added to the blood by the perfusionist or a specially trained nurse to provide anticoagulation. Typically after approximately 500 ml of blood has been collected, the cell salvage machine is activated, which centrifuges the blood to separate out the RBCs. The RBCs are then washed, suspended in saline, and reinfused to the patient, when desired, in a packaging very similar to that of a blood bank unit of blood. The reinfusate has a hematocrit of 50–70 %.

Excessive use of cell salvage blood has its own complications. These include dilution of clotting factors and platelets, causing coagulopathy, since only the RBCs are reinfused to the patient. Moreover, the salvaged blood can be contaminated with bacteria and debris from the surgical field.

Perioperative Transfusion Criteria

Quantification of the blood loss

Quantification of blood loss is done by visual inspection. Blood loss is calculated by measuring the blood collected in the suction canister, sponges, and pads and by visual inspection of the surgical field. A 4×4 sponge holds about 10 ml of blood, while a pad holds about 100–150 ml of blood. Serial estimation of hematocrit reflects the ratio of the blood cells to the plasma and is affected by sudden fluid shifts; therefore, do not reliably estimate the actual blood loss.

Monitoring the vital signs

The parameters utilized to measure fluid status and blood loss include urine output, arterial blood pressure, and heart rate. Additional parameters include analysis of arterial blood gases, central venous pressure, mixed venous saturation, and echocardiography. Significant fluid or blood loss may be indicated by a decrease in urine output, hypotension, tachycardia, acidosis, low CVP (<6 mmHg), and low mixed venous saturation and cardiac output. The patient, if not adequately resuscitated, progresses from normovolemia to hypovolemia and finally to hypovolemic shock (hypoperfusion of the organs and tissues).

Transfusion triggers

Morbidity and mortality are associated with unnecessary transfusion, as healthy patients with a hemoglobin of 10 g/dl rarely require a transfusion. Transfusions should be administered when the benefits are thought to outweigh the risks. It should be remembered that there is not one specific laboratory value,

or transfusion trigger, that is appropriate to transfuse all patients. The clinician must take into account the entire picture: the estimated blood loss, patient's vital signs, comorbid illnesses of the patient, and laboratory valves when deciding to transfuse. The three most common parameters that are taken into consideration for transfusing are the degree of anemia, coagulopathy, and thrombocytopenia.

(i) Degree of anemia
The amount of hemoglobin in the RBCs reflects the oxygen carrying capacity of the blood. As blood is lost, the viscosity of the blood decreases, and this may in fact increase the delivery of oxygen to the tissues. This is considered to optimally happen at a hemoglobin of around 10 g/dl. However, a further decline in hemoglobin has to be closely monitored. Most patients tolerate hemoglobin levels between 7 and 9 g/dl. Below a hemoglobin level of 7 g/dl, patients experience impaired cognition and an increase in postoperative mortality. Therefore, most clinicians consider a hemoglobin level of 7 g/dl as an automatic trigger for blood transfusion. In patients with ST changes on the electrocardiogram, blood transfusion is initiated at a higher hemoglobin level (10 g/dl).

(ii) Coagulopathy
Presence of acute coagulopathy may require administration of both FFP (provides clotting factors) and platelets (to correct thrombocytopenia). About 10–15 ml of FFP per kg of body weight can be transfused to rapidly correct anticoagulation with warfarin. About 30 % level of clotting factors is required to achieve hemostasis. Intraoperatively, FFPs are administered when the PT or aPTT is prolonged >1.5 times the reference values or when blood loss exceeds one blood volume (70 ml/kg or when >6 units of PRBCs have been transfused). During massive transfusion, FFPs are administered in a 1:1 ratio with PRBCs. Cryoprecipitate contains concentrated clotting factors VIII, XIII, von Willebrand factor, and fibrinogen and is commonly used for the treatment of hypofibrinogenemia (fibrinogen <150 mg/dl). Commercially available factor VIII concentrates are available for treating hemorrhage due to hemophilia A or von Willebrand disease. In addition, recombinant activated factor VII concentrate can be used in acute hemorrhage.

(iii) Thrombocytopenia
To form an effective clot, platelets are required in sufficient number and adequate function. Platelet transfusions are administered to treat thrombocytopenia. However, in the presence of platelet dysfunction (antiplatelet drugs, cardiopulmonary bypass), it is more effective to treat the cause of the platelet dysfunction. In the surgical setting, thrombocytopenia without platelet dysfunction should be treated with platelet transfusions for a count less than 50,000/μl. In presence of platelet dysfunction, perioperative platelet transfusion is indicated even when the count is greater than 50,000/μl. For neurosurgical/ophthalmologic operations, where small bleeding can create complications, the minimum threshold for platelet transfusion is 80,000–100,000 platelets/μl.

Complications of Transfusion

Human Error

The most common cause resulting in complications from blood transfusion is human error. This can occur during collection of blood sample (labeling error), incorrect patient ID band, or faulty checking before transfusion.

Acute Hemolytic Reaction

This is the most serious complication usually resulting from ABO compatibility, causing an immune reaction in the patient. The transfused cells are lysed by the antibodies present in the patient's serum. Signs of hemolytic reaction include chills, fever, urticaria, chest and flank pain, hypotension, tachycardia, and hemoglobinuria (red urine). This can progress to shock, renal failure, or DIC. Many of these signs are masked by general anesthesia.

When a hemolytic reaction is suspected, the transfusion is immediately stopped, and supportive care instituted. Blood pressure and renal function are supported by administration of fluids and vasopressors. Diuretics may be administered to initiate diuresis. A blood sample from the patient and the blood being used are sent to the blood bank for confirmation of incompatibility. Additionally, coagulation studies, platelet count, and urinary hemoglobin should be measured.

Delayed Hemolytic Reaction

This type of reaction is called extravascular hemolytic reaction, where there is extravascular hemolysis of donor erythrocytes. The reaction is usually mild, occurs about 3 days–3 weeks after transfusion, and occurs to non-D antigens of the Rh system. Pregnancy can also lead to formation of these antibodies. Following transfusion, antibodies are formed by the patient against the non-D antigens. Subsequent transfusion leads to the antibody response against the antigens. The symptoms are self-limiting and include mild fever, jaundice (increased bilirubin), hemoglobinuria, and spherocytosis on blood smear. Diagnosis of the delayed hemolytic reaction can be confirmed by a Coombs (antiglobulin) test.

Febrile Nonhemolytic Reaction

Febrile reactions can occur as part of an acute hemolytic reaction or due to nonhemolytic causes. The latter occur due to white cell or platelet sensitization. Febrile nonhemolytic reactions are relatively common (1–3 %) and are characterized by an increase in temperature (usually by 1 °C), without hemolysis. Antipyretics should be administered with continuation of the blood transfusion. However, when the febrile reaction is severe, the transfusion may have to be discontinued. Such patients should receive red cells with low white cell count, which are removed by washing, filtration, or centrifugation. Platelets are stored at room temperature, and units are prone to bacterial contamination, which can lead to a febrile reaction and even sepsis.

Allergic Reactions

Allergic reactions may include urticaria or severe anaphylactic reaction. Urticarial reactions are relatively common (1 %) and due to sensitization of the patient to plasma proteins. Signs of an urticarial reaction include itching, hives, and erythema, without any fever. Urticarial reactions can be treated by administering an antihistaminic (diphenhydramine) and then continuing the transfusion. However, anaphylactic reactions, though rare, are life-threatening and require aggressive treatment. These reactions typically occur in patients with IgA deficiency, who have IgA antibodies and receive IgA-containing blood transfusions. Treatment of anaphylaxis includes stopping the transfusion, administering epinephrine, and supportive care. Such patients should receive IgA-free blood units.

Transfusion-Related Acute Lung Injury

Within 3–6 h of transfusion (PRBCs/FFP), an acute respiratory syndrome can develop, which is characterized by noncardiogenic pulmonary edema, dyspnea, hypoxia, and bilateral chest infiltrates on a chest radiograph and a PaO_2/FiO_2 ratio <200. Transfusion-related acute lung injury (TRALI) is supposed to occur in 1:5,000 blood transfusions and is considered as the leading cause of death. Most cases of TRALI appear to be caused by donor plasma anti-leukocyte or anti-HLA antibodies that recognize recipient leukocytes or recipient HLA cell surface markers and then activate an inflammatory response. TRALI is more common with FFP transfusions. Treatment is supportive and includes stopping the transfusion, mechanical ventilation, and maintaining the vital signs (correction of any associated hypotension).

Immunosuppression

Blood transfusion causes immunosuppression, which predisposes the patients to infections. Similarly, in patients with cancer, suppression of cell-mediated immunity by blood transfusion may cause tumor recurrence. These effects are, however, difficult to prove because patients receiving blood transfusions may be sicker to start with. Logically, administration of FFPs is more prone to cause immunosuppression than PRBCs.

Graft-versus-host disease reaction usually occurs in immunocompromised patients, where the donor lymphocytes initiate an immune response and attack the recipient's tissues. This is a very rare but often fatal complication. Use of leukocyte reduction filters reduce but not eliminate the risk of the reaction. Such patients should receive irradiated blood products (RBCs, platelets).

Metabolic Abnormalities

Stored blood contains an increased concentration of hydrogen ions, which increase as the erythrocytes metabolize further. However, acidosis is rarely seen with transfusion. Similarly, the potassium concentration is higher in stored blood, but it rarely leads to hyperkalemia in patients. This is because stored blood contains only 4–7 meq/unit. Additionally, stored blood contains decreased amounts of 2,3-DPG, which shifts the Hb-O_2 dissociation curve to the left (decreased unloading of oxygen due to increased affinity of hemoglobin for O_2). Citrate in the CPD bag binds to calcium and may cause hypocalcemia. Hypocalcemia, however, is rarely seen due to mobilization of calcium stores from the bone. Hypocalcemia is treated only when there is decreased plasma-ionized calcium levels and prolonged QT interval on the ECG. Calcium supplementation is commonly required during massive transfusion.

Infections

Bacterial contamination

This occurs rarely, but more commonly with platelet transfusion, as they are stored at room temperature. Bacteria that commonly contaminate blood products are the gram-positive *Staphylococcus aureus* and the gram-negative *Yersinia enterocolitica* and pseudomonas. The incidence of bacterial contamination is 1:30,000 transfusions. Patients may develop fever and even sepsis after the transfusion. Treatment of bacterial infection is starting antibiotic therapy.

Viral infections

Because of rigorous testing, the incidence of viral infections has decreased substantially. The incidence of contamination is approximately 1:1.8 million for HIV, 1:220,000 for hepatitis B virus, and 1:1.6 million for hepatitis C virus. Currently, screening of the donor blood for hepatitis B, hepatitis C, HIV 1 and 2, human T cell lymphotropic virus, syphilis, and cytomegalovirus (CMV) is mandatory. Immunocompromised patients should receive CMV-negative units. However, disease transmission might happen in the "window period," that is, the time after infection when the donor is infectious, but screening tests are negative. Other agents that can cause infections are malaria, West Nile virus, and Creutzfeldt–Jakob and Chagas diseases.

Massive Transfusion

Massive transfusion is defined as the need to transfuse more than 10 units of packed red blood cells (PRBCs), approximately one blood volume, in 24 h. Other less commonly used definitions include transfusion of more than 6 PRBC units in 12 h or more than 4 units of PRBCs in 1 h with ongoing need for transfusion. Massive hemorrhage causes shock (decreased circulating blood volume, cardiac output) leading to decreased oxygen delivery to the tissues. Progressive shock leads to systemic inflammation and acidosis, further impairing oxygen delivery to the tissues.

Indications

Massive trauma resulting in severe hemorrhage is the commonest indication of massive blood transfusion. Other indications include GI bleeding, hepatic surgery and transplantation, extensive cardiovascular and aortic surgical procedures, and major obstetric hemorrhage. Unlike simple blood loss causing anemia, massive hemorrhage leads to a complex state of shock and coagulopathy.

Monitoring

Monitoring of a patient in need of massive blood transfusion includes large-bore peripheral intravenous access, central venous access for fluid administration and CVP monitoring, intra-arterial line for blood pressure monitoring, and frequent blood draw for laboratory analysis. In addition, a urinary catheter is inserted for measuring urine output, which should be >0.5 ml/kg/h. Since hypothermia can worsen the acidosis and coagulopathy, core temperature is also measured. Patient should be adequately ventilated and oxygenated; therefore, the airway is usually secured with an endotracheal tube.

Resuscitation

Massive transfusion protocols coordinate the logistics of providing large amounts of blood products, in an appropriate ratio, to the patient with severe hemorrhage. These protocols have been shown to improve survival and decrease blood usage and cost. Due to the resources involved, implementation of such protocols has been largely limited to institutions where massive transfusion occurs frequently, such as level one trauma centers. Resuscitation of the patient begins with activation of the massive transfusion protocol. The surgeon should achieve hemostasis and control of bleeding, as soon as possible. Adequate personnel should be available to resuscitate the patient, and additionally, the blood bank and the laboratory are notified. The goals of resuscitation are to restore circulating volume, maximize oxygen delivery, and prevent coagulopathy.

Administration of PRBCs increases circulating blood volume and oxygen carrying capacity. Often blood loss is difficult to estimate in massive hemorrhage. Therefore, the amount of blood that is administered is guided by clinical parameters, such as urine output, blood pressure, CVP, hemoglobin/hematocrit, and acid–base status. Coagulation parameters need to be frequently performed to assess the patient's coagulopathy. Point of care coagulation tests, such as thromboelastography, may be helpful during resuscitation to guide product usage, but they are not always universally available. If active hemorrhage is occurring, transfusion of products should not be delayed for the results of laboratory testing.

Every attempt is made to administer type-specific crossmatched blood, but often this may not be available. The second best option is, therefore, to administer type-specific uncrossmatched blood. The third best option is to administer type O, Rh-negative blood. It is important to know that once enough O-negative blood has been administered (one blood volume), further transfusion should be continued with the O-negative blood and not with type-specific crossmatched blood. This is because at this point the patient's serum will have enough anti-A and anti-B antibodies, which can cause hemolysis.

Administering a large volume of PRBCs leads to dilution of the clotting factors and the platelets. Once one blood volume of PRBCs has been administered, FFPs are transfused to replace coagulation factors, and platelets are transfused to correct the dilutional thrombocytopenia. Several studies have shown that transfusion of these products (after one blood volume of PRBCs) in a 1:1:1 ratio of RBC/FFP/

platelet units is more successful in controlling coagulopathy and hemorrhage and hence in improving outcomes. The United States Army has shown that improving the ratio of plasma to RBC from 1:8 to approximately 1:1 was an independent predictor of survival by reducing death from hemorrhage. These products are more effective if given proactively and aggressively to prevent a worsening cycle of coagulopathy, hemorrhage, and shock.

Complications of Massive Transfusion

Early and aggressive resuscitation is clearly needed in patients receiving massive transfusion. A conservative transfusion strategy should be used once active bleeding is controlled and coagulopathy normalized. Correcting the coagulopathy and metabolic and electrolyte disturbances is required for optimal treatment. Complications of massive transfusion include:

- Transfusion associated—acute and delayed hemolytic reactions, acute lung injury, and transmission of infectious diseases.
- Volume overload—leading to pulmonary edema. Fluid resuscitation should be guided by monitoring urine output and CVP.
- Dilutional coagulopathy—dilutional of clotting factors and platelets (thrombocytopenia). At least 20–30 % levels of coagulation factors are required for hemostasis to occur. The prothrombin time should be kept below 1.5. Dilutional thrombocytopenia usually occurs after replacement of 1.5–2 blood volumes. If cell salvage is used, the washed blood returned to the patient is also deficient in coagulation factors and platelets.
- Decreased 2,3-diphosphoglycerate—decrease in 2,3-DPG shifting the hemoglobin dissociation curve to the left causing decreased oxygen delivery to the tissues.
- Hypothermia—massive blood transfusion can lead to hypothermia. Core body temperature <35 °C leads to increased risk of coagulopathy, and a temperature of <30 °C can cause ventricular dysrhythmias. A fluid warming device should be used for administering blood and IV fluids, plus a forced-air warming device to warm the patient.
- Hyperkalemia—stored blood has increased extracellular potassium concentration due to cell lysis, which can lead to hyperkalemia in the patient.
- Citrate toxicity and hypocalcemia—a citrate phosphate dextrose solution is added to preserve stored blood. With decreased perfusion, the liver is not able to metabolize citrate to bicarbonate, which tends to cause metabolic alkalosis. Once metabolic acidosis clears up with adequate resuscitation, metabolic alkalosis supervenes in the postoperative period. Additionally, the excess citrate binds to calcium that can lead to hypocalcemia. Calcium supplementation may be required when blood is infused at >50 ml/min and in the presence of hypothermia or liver disease. Hypocalcemia is treated by administering calcium chloride (calcium gluconate is preferably not used as the liver has to metabolize the gluconate first).

Blood Disorders

(i) Anemia

Anemia is a deficiency in the concentration of functional red blood cells in the circulation. Anemia can also be due to lack of or defective hemoglobin chains causing a decrease in oxygen carrying capacity. Anemia can be caused by either blood loss (hemorrhage), decreased RBC production (ineffective erythropoiesis), or increased RBC destruction (hemolysis). Uncommon causes of anemia are summarized in Table 8.3.

Diagnosis of Anemia

When evaluating a patient with anemia, a thorough history and physical examination should be performed. In a healthy patient, anemia is considered as a hemoglobin level below 10 g/dl; however, signs of anemia may not develop until the hemoglobin drops below 7 g/dl. Symptoms and signs of anemia include fatigue, weakness, pallor, dyspnea, and lightheadedness. A decrease in red cell mass leads to reduced viscosity and an increase in venous return and cardiac output. Sympathetic stimulation leads to an increase in cardiac contractility. Chronic anemia may also cause cardiomegaly. Tachycardia associated with acute anemia is most likely a sign of hypovolemia.

In anemia, the regional blood flow is redistributed from the nonvital organs to the vital organs (heart, brain). Anemia results in increased 2,3-DPG concentration in RBCs, which shifts the oxyhemoglobin curve to the right, favoring oxygen unloading. Oxygen delivery remains essentially unchanged until hemoglobin concentration falls below 7 g/dl.

Laboratory tests performed to diagnose anemia include a peripheral smear (for erythrocyte size and shape) and a complete blood count, which includes RBC count, hemoglobin concentration, mean corpuscular volume (MCV), red cell distribution width (RDW), and reticulocyte count. The reticulocyte count is elevated in anemias caused by RBC destruction and low in anemias caused by a failure of RBC production. Other tests that may be useful include serum iron and ferritin levels, vitamin B_{12}/folate levels, serum bilirubin, LDH and haptoglobin levels, and direct antiglobulin test.

Table 8.3 Uncommon types of anemias

Anemia type	Description	Treatment/notes
Thalassemias	Autosomal recessive inherited disorders with decreased production or failure to synthesize normal globin chains (α or β). Patients have anemia, hemolysis, and bone marrow hyperplasia	Patients are prone to iron overload and infections and have splenomegaly. Mild forms require no treatment, while severe forms require regular transfusions or bone marrow transplantation
Hereditary spherocytosis	Rare anemia caused by an inherited RBC cytoskeletal abnormality, with splenic destruction of fragile RBCs resulting in chronic hemolysis. Patients have anemia, jaundice (elevated serum bilirubin), and splenomegaly	Treated with splenectomy, blood transfusion/exchanges for anemia
Glucose-6-phosphate dehydrogenase (G6PD) deficiency	X-linked recessive disorder, characterized by chronic hemolytic anemia on exposure to infection and certain drugs, such as antimalarial drugs, nitrofurantoin, probenecid, phenacetin, vitamin K, quinidine, and nitroprusside. These trigger hemolysis by forming peroxidases	Usually asymptomatic, avoid infection and certain drugs, blood transfusion for hemolysis, or dialysis for severe renal failure
Immune hemolytic anemias	Characterized by antibody formation against one's own RBC membrane, red blood cell life span reduced from 120 to just few days. Hemolysis can be either autoimmune (warm and cold antibody, according to the optimal temperature at which the antibodies act to destroy RBCs), drug induced (acetaminophen, cephalosporins, hydralazine, or hydrochlorothiazide), or alloimmune (hemolytic disease of the newborn, where maternal antibodies against fetal RBCs, with incompatible Rh or ABO blood groups, are produced and cross the placenta)	Evidence of hemolysis (elevated serum bilirubin (jaundice), raised haptoglobin, and serum LDH, reticulocytosis); warm antibody anemia is treated with steroids and immunosuppressive agents; cold antibody anemia is treated by avoiding the cold environment

Types of Anemias

Megaloblastic anemia: This is caused by impaired DNA synthesis during red cell production and is commonly due to deficiency of folic acid and/or vitamin B_{12}. Long-term and repeated exposure to nitrous oxide can also produce a megaloblastic anemia with neurologic changes. This type of anemia is commonly seen in critically ill patients, ileal resection and gastric bypass patients, alcoholics, and parturients.

Signs, in addition to anemic symptoms, may include flow murmurs, splenomegaly, neurological disorders (ataxia, loss of deep tendon reflexes, loss of posterior column sensations), dyspnea, headache, fatigue, sore tongue (glossitis), and diarrhea. Lab tests show increased MCV and decreased hemoglobin concentration and reticulocyte count. Additionally, serum vitamin B_{12} levels and RBC folate levels are measured. Preexisting neurologic deficits should be documented and may preclude use of regional anesthetic techniques.

Iron-deficiency anemia: This results from insufficient iron intake/adsorption or from hemolysis. Symptoms include pallor, fatigue, and weakness. It is diagnosed by the presence of a microcytic (low MCV) anemia; increased RDW; hypochromic anemia, with a low serum ferritin and iron levels; and high serum transferrin and total iron-binding capacity.

Anemia of chronic disease: This occurs in patients with chronic infection, chronic immune activation, or malignancy (Hodgkin's disease, lung and breast carcinoma). Anemia is seen in diseases such as rheumatoid arthritis, SLE, and chronic renal failure. The cause is likely an increased level of hepcidin, which regulates iron metabolism and prevents the release of iron from its stores. Abnormal uptake and accumulation of iron result in impaired erythropoiesis. The diagnosis is largely one of exclusion, and laboratory evaluation reveals a mild normochromic, normocytic anemia with a low reticulocyte count and normal total body iron stores (ferritin). Treatment is correction of the underlying disease.

Sickle cell disease: Sickle cell disease (SCD) is an autosomal recessive inherited blood disorder, which results in abnormal sickle-shaped red blood cells. Individuals can have a defect in one gene or both the genes causing sickle cell trait or sickle cell disease, respectively. Patients with sickle cell trait are often asymptomatic. The genetic defect results in the formation of abnormal hemoglobin S (HbS), which results from a single amino acid substitution. Glutamic acid is substituted by valine at the sixth position of the hemoglobin β-chain. This causes the HbS molecules to associate and polymerize upon deoxygenation, resulting in distorted, sickle-shaped red blood cells.

Hemoglobin gel electrophoresis can detect the abnormal hemoglobin S. The abnormally shaped red cells undergo destruction (hemolysis) causing anemia (Hb 6–8 g/dl). The bone marrow tries to replace the cells, but production (high reticulocyte count) does not match the rate of destruction. Even when fully oxygenated, some erythrocytes still remain dehydrated and sickled. Sickle cell disease is often precipitated by infection and acidosis. The disease results in sickle cell crisis, which can be of various types, such as vaso-occlusive (obstruction of capillaries by sickle cells causing restriction of blood

Table 8.4 Complications of sickle cell disease

System	Complications
Neurological	Pain crisis, stroke, retinopathy, neuropathy
Pulmonary	Acute chest syndrome, airway hyperreactivity, restrictive lung disease, pulmonary embolism, pulmonary hypertension
Genitourinary	Chronic renal insufficiency, urinary tract infection, priapism
Gastrointestinal	Cholelithiasis, liver disease, dyspepsia
Hematological	Hemolytic anemia, acute aplastic anemia (cessation of bone marrow activity), splenic fibrosis
Orthopedic/skin	Osteonecrosis, osteomyelitis, leg ulcers
Immunological	Immune dysfunction

flow and ischemic pain), aplastic, splenic sequestration, or hemolytic crisis. Complications of SCD are listed in Table 8.4.

Treatment of SCD consists of supportive care; administration of folate, magnesium, zinc, pneumococcal vaccine, prophylactic penicillin, and hydroxyurea (increases fetal Hb levels which interfere with HbS polymerization); transfusion for aplastic crisis or sequestration; and administration of analgesics for pain. Bone marrow transplant is the only definitive cure for sickle cell disease.

Preoperative assessment should include evaluation for presence of infection, dehydration, vaso-occlusion, and end-organ damage. Intraoperatively, the aim is to avoid sickling triggers such as hypothermia, hypoxemia, acidosis, hypovolemia, and hypotension. In addition, patients should be adequately hydrated, and fluid replacement should be selected over vasoconstrictors, when possible. Tourniquets should be avoided, as they produce local stasis and acidosis. Prophylactic transfusion is frequently employed in surgical patients with SCD. Prophylactic red blood exchange has not been shown to be superior to simple RBC transfusion in the preoperative setting. Regional techniques may be employed, but epinephrine should be avoided as it causes vasoconstriction.

(ii) Polycythemia

Polycythemia is defined as elevated red cell concentration. It can be either due to increased production of red cells (erythrocytosis) called as absolute polycythemia or decreased plasma volume called as relative polycythemia. Absolute polycythemia can be primary or secondary.

Absolute Polycythemia

- Primary—polycythemia vera is a myeloproliferative disorder of the bone marrow characterized by increased production of red blood cells. The hematocrit is often >55 %, and clinical signs include vertigo, increased propensity to form blood clots (thrombosis causing MI, stroke, pulmonary embolism, or DVT), and hepatosplenomegaly. Phlebotomy is used to lower the hematocrit and prevent hyperviscosity. Myelosuppressive drugs, such as hydroxyurea, are also used.
- Secondary—caused by increased erythropoietin secretion in response to chronic tissue hypoxia (ascent to high altitude, COPD, and sleep apnea) or in renal cell tumors that secrete erythropoietin.

Relative polycythemia: This occurs due to decreased plasma volume, which can occur due to loss of body fluids due to burns or dehydration.

(iii) Coagulation abnormalities

Coagulation immediately begins when the endothelial lining of a blood vessel is breached due to an injury. Hemostasis, cessation of blood loss from a damaged blood vessel, is achieved by forming clots or thrombus. Spontaneous thrombus formation in normal endothelium is prevented by proteins such as antithrombin, protein C, prostacyclin, tissue factor pathway inhibitor, plasmin, and tissue plasminogen activator. However, when the endothelium is damaged, these anticoagulant proteins are downregulated and procoagulants are upregulated. The steps in the coagulation cascade are as follows:

- Formation of platelet plug or primary hemostasis: Once the endothelial lining is damaged, it exposes collagen to which circulating platelets bind to form a platelet plug. The adhesion of platelets is strengthened by von Willebrand factor.
- Formation of fibrin strands to strengthen the platelet plug or secondary hemostasis: Fibrin strands are formed to strengthen the platelet plug. The fibrin is formed by the action of certain plasma proteins called as clotting or coagulation factors. The coagulation cascade consists of two initial pathways: the tissue factor pathway (extrinsic pathway) and the contact activation pathway (intrinsic pathway). These two initial pathways converge into a common pathway, leading to the formation of thrombin and fibrin (Fig. 8.1).

The various coagulation factors are listed in Table 8.5. All factors, except factors III, IV, and VIII, are synthesized in the liver. Factors II, VII, IX, and X (plus proteins C and S) are vitamin K-dependent for their synthesis. Common laboratory tests of hemostasis are listed in Table 8.6.

Platelet Disorders

Thrombocytopenia

The normal platelet count is between 150,000 and 450,000/μl of blood. Thrombocytopenia is commonly defined as a platelet count less than 100,000/μl. Platelet disorders can be subdivided into disorders of platelet number and platelet function.

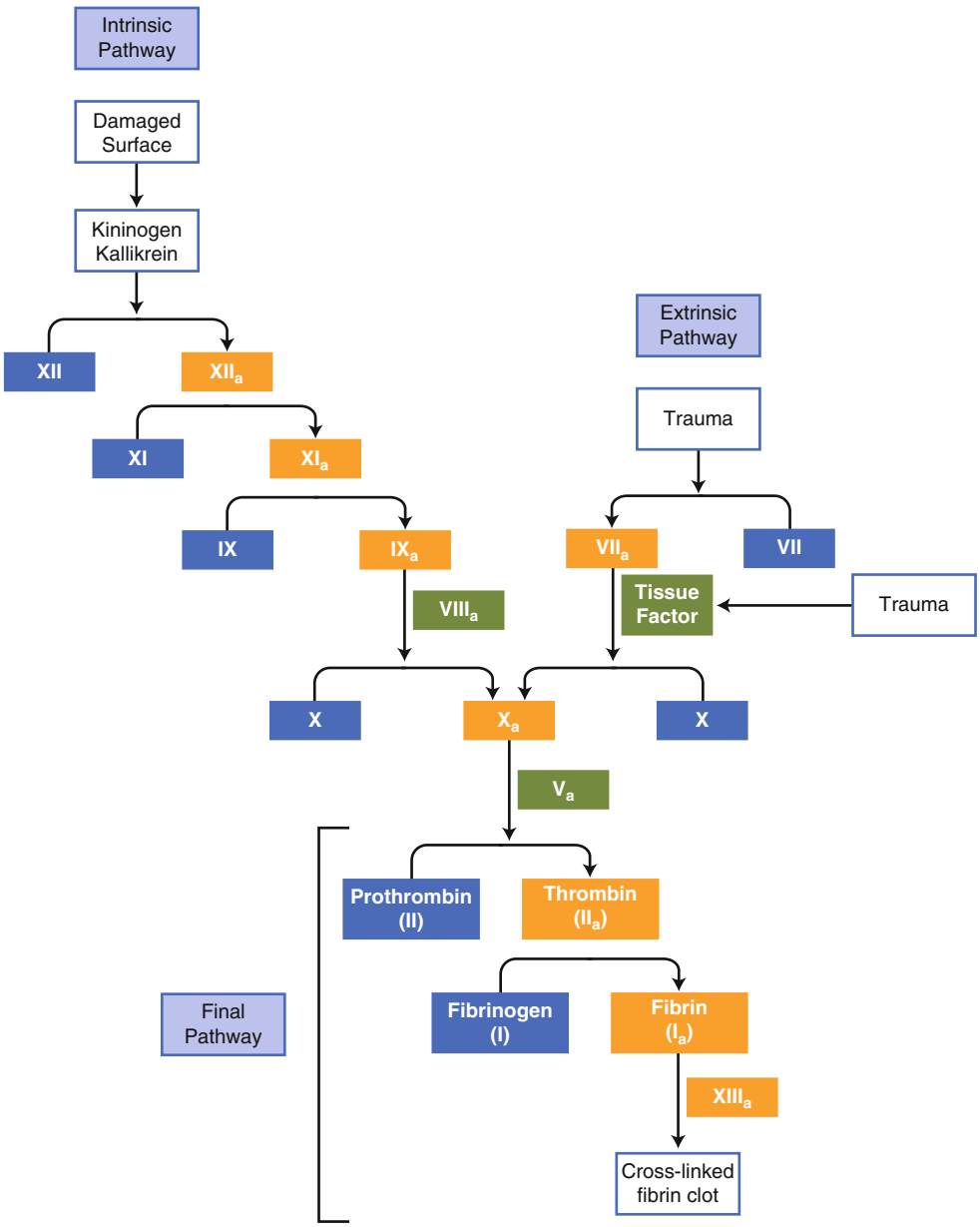

Fig. 8.1 The coagulation cascade

Quantitative platelet disorders

Causes for thrombocytopenia include decreased production, increased destruction/consumption, sequestration, and dilution. Common causes of decreased production of platelets include drug effects (valproic acid), sepsis, chemotherapy or radiation therapy, alcohol toxicity, and certain vitamin deficiencies (B_{12}/folate). Increased platelet destruction and consumption occur in conditions, such as DIC, drug exposure, autoimmune states (ITP), HELLP syndrome, and physical destruction (CPB). Dilution of platelets typically occurs after massive resuscitation/transfusion. Splenic sequestration is found in patients with hypersplenism.

Surgical bleeding due to thrombocytopenia does not typically occur until the platelet count falls below 50,000/μl, and spontaneous bleeding is not typically seen unless the platelet count falls below 5–10,000/μl. Dilutional thrombocytopenia is the most common cause of intraoperative coagulopathy.

Qualitative platelet abnormalities

The most common causes of acquired platelet dysfunction are various antiplatelet agents, such as the COX inhibitors, dipyridamole, ticlopidine, clopidogrel, and glycoprotein IIb/IIIa antagonists (abciximab, tirofiban, eptifibatide). Vitamin E and herbal supplements, such as garlic, gingko, and

ginseng, are also inhibitors of platelet function and should be discontinued at least 1 week prior to surgery. Qualitative platelet disorders can also be seen in various systemic conditions including uremia, liver disease, myelodysplastic syndromes, and DIC. Platelet transfusion may be necessary to support surgery in spite of a normal platelet count.

Von Willebrand Disease

Von Willebrand disease (vWD) is the most common inherited coagulation disorder, affecting 1–2 % of the general population. vWD occurs from a qualitative or quantitative deficiency of von Willebrand factor (vWF). vWF strengthens the platelet plug that is formed to plug the injured blood vessel. Also, vWF is a carrier for factor VIII.

Acquired forms of vWD are associated with lymphoproliferative disease, tumors, autoimmune disease, hypothyroidism, cardiac valvular defects, and medications (valproic acid). The most common symptom of vWD is mucocutaneous bleeding such as easy bruising, epistaxis, gingival bleeding, and menorrhagia. If suspected in a patient for an elective procedure, the case should be cancelled until a proper hematologic work-up is obtained. Depending on the severity, vWD can be classified as type 1, 2, or 3. Type 1 vWD is treated with desmopressin, while type 2 and 3 vWD are treated with factor VIII-vWF concentrates. Desmopressin or DDAVP is a synthetic analogue of ADH/vasopressin.

Table 8.5 Various coagulation factors

Factor	Name
I	Fibrinogen
II	Prothrombin
III	Tissue factor
IV	Calcium
V	Proaccelerin
VII	Proconvertin
VIII	Antihemophilic
IX	Thromboplastin
X	Stuart
XI	Prethromboplastin
XII	Hageman
XIII	Fibrin stabilizing

Coagulation Disorders

Inherited Coagulation Disorders

Hemophilias: These are x-linked recessive inherited disorders. Males are affected, while females are carriers. Hemophilia A (more common) is characterized by a deficiency of factor VIII, while hemophilia B is characterized by a deficiency of factor IX. Young male patients may have unexplained bruising or bleeding and should be referred to a hematologist.

Patients with hemophilia A or B usually demonstrate an isolated prolongation of aPTT, with normal PT, thrombin clotting time, fibrinogen level, and platelet count. Bleeding severity relates to the degree of factor deficiency and commonly occurs into the joints (80 %), muscles, and GI tract. Treatment is aimed toward replacement of the specific coagulation factor, either human or recombinant. Recombinant factor replacement minimizes infectious disease exposure.

Acquired Coagulation Disorders

Vitamin K deficiency: Vitamin K is necessary for the synthesis of factors II, VII, IX, and X, as well as the anticoagulant proteins C and S. Vitamin K consists of two subunits, K1 (found in green leafy vegetables), and K2 (synthesized by intestinal bacteria). Therefore, vitamin K deficiency can be acquired due to poor diet or by taking antibiotics that destroy

Table 8.6 Laboratory tests for hemostasis

Platelet function	Platelet count	150,000–450,000/μl
	Bleeding time	Normal <10 min
	Platelet function and aggregation analysis	Abnormal in patients taking antiplatelet drugs and herbal supplements
Coagulation studies	Prothrombin time (PT)—tissue coagulation pathway (extrinsic) assessment	Normal 11–14 s, prolonged with low levels of factors I, II, V, VII, and X and liver disease; INR standardizes results across laboratories
	Partial thromboplastin time (PTT)—contact activation pathway (intrinsic) assessment	Normal 24–35 s, prolonged with low levels factors I, II, V, VIII, IX, X, XI, and XII; heparin prolongs PTT
	Thrombin time (TT)	Normal 22–32 s, prolonged with low levels of factors I and II
	Activated clotting time (ACT)	Normal 80–180 s, ACT test is used to monitor heparin therapy when given in large doses
	Thromboelastography	Measures time taken to form initial clot and time taken to complete clot formation, clot strength, and clot lysis
Fibrinolysis tests	D-dimer levels	When plasmin cleaves cross-linked fibrin, fibrinolytic states, such as DIC
	Fibrin degradation products	Excessive activity of plasmin, which degrades fibrin, elevated in DIC

INR international normalized ratio

intestinal bacteria. Biliary obstruction, malabsorption, cystic fibrosis, and resection of the small intestine can additionally contribute to vitamin K deficiency. Vitamin K deficiency leads to prolongation of the PT, with factor VII typically depleted relatively early. Vitamin K is administered intramuscularly, while urgent treatment of vitamin K deficiency requires intravenous administration, which is given slowly to prevent hypotension. Improvement in coagulopathy is usually apparent in 6–8 h after administration.

Medications

Warfarin: It is a systemic anticoagulant, which is administered to prevent or treat thromboembolic complications from medical conditions, such as mechanical heart valves, atrial fibrillation, venous thromboembolism, acute MI, and stroke. Warfarin works by inhibiting vitamin K epoxide reductase, preventing vitamin K synthesis and its dependent coagulations factors (II, VII, IX, X). Since warfarin is metabolized in the liver by the cytochrome P450 system, other medications inhibiting or activating the cytochrome P450 system affect the metabolism of warfarin. Rapid reversal of warfarin can be accomplished by administration of FFP and vitamin K. Alternatively, in emergencies, such as a patient on warfarin with intracranial hemorrhage, infusion of prothrombin complex concentrate (PCC) should be considered. PCC contain factors II, VII, IX and X, and provide immediate replacement of factors that are affected by warfarin therapy.

Heparin: Unfractionated heparin acts by binding reversibly to antithrombin III, accelerating antithrombin's inhibition of coagulation factors XII, XI, X, IX, plasmin, and thrombin. Heparin's effect can be measured by monitoring the PTT. Heparin has a half-life of about 90 min, however, the action of heparin can be immediately reversed by administering protamine. Low-molecular-weight heparin (LMWH) stimulates anti-Xa factor activity, rather than antithrombin activity. Therefore, LMWH's action cannot be measured by monitoring PTT. Its half-life is longer (about 5 h) than heparin, and thus LMWH can be given once daily as a maintenance dose. Other anticoagulant medications are direct thrombin inhibitors, such as argatroban, and direct factor Xa inhibitors such as fondaparinux.

Disorders of Fibrinolysis

Disseminated intravascular coagulation (DIC): It is a pathological activation of coagulation mechanisms throughout the body, which happens in response to a variety of diseases (Table 8.7). Small and numerous blood clots are formed inside the blood vessels, which consumes the coagulation proteins and platelets, with extensive fibrinolysis. The normal process of coagulation is disrupted and abnormal bleeding occurs from skin sites, gastrointestinal tract, respiratory tract and surgical wounds. DIC is associated with thrombocytopenia, elevated fibrin split products, elevated D-dimers, hypofibrinogenemia, and prolongation of PT and PTT.

Table 8.7 Precipitating conditions for DIC

Precipitating condition	Examples
Massive tissue injury	Trauma, burns, rhabdomyolysis, extensive surgery (e.g., aortic surgery)
Cancers	Lung, pancreas, prostate, and stomach cancers and acute leukemia
Obstetric	Abruptio placentae, preeclampsia, amniotic fluid embolism, retained intrauterine fetal demise, abortion
Infections	Sepsis from bacterial, viral, protozoal, and fungal infections
Miscellaneous	Liver disease, allergic reactions, drug interactions, transplant rejection

Treatment of DIC is primarily supportive and aimed toward correcting the underlying cause. It is important that the coagulation process is interrupted in DIC. Treatment with FFP (to replace coagulation factors), cryoprecipitate (to replace fibrinogen), and platelet concentrates may be considered in the setting of diffuse bleeding. Very rarely, the use of heparin is considered for patients with extensive thromboembolism.

Disorders of Thrombosis

Heparin-induced thrombocytopenia (HIT)

This is diagnosed when heparin administration is accompanied by an otherwise unexplained fall in platelet count (usually >50 %) or by other clinical signs, such as development of new thrombosis, skin lesions, or an acute systemic reaction (fever, chills, tachycardia, dyspnea), occurring after about 5 days of initiation of heparin therapy (the 4T score). Heparin sulfate acts as a hapten, which stimulates the immune system to produce IgG antibodies against the heparin, which itself is bound to platelet factor 4. The IgG–heparin–platelet factor 4 complex activates platelets, which form clots with an increase in platelet consumption, leading to thrombocytopenia.

HIT usually persists for about 3 months. Treatment for patients with suspected or confirmed HIT is cessation of heparin and initiation of nonheparin anticoagulants (lepirudin, argatroban) to prevent thrombotic complications. LMWHs should be avoided as they cross-react with HIT antibodies. Similarly, warfarin should be avoided during HIT as it may lead to warfarin necrosis (skin gangrene). Platelet transfusions should also be avoided in HIT as they may worsen the formation of clots.

Autoimmune hypercoagulable states

Anticardiolipin antibody and lupus anticoagulant are two examples. These can result in venous or arterial thromboses, thrombocytopenia, and recurrent fetal losses. These patients are at increased risk for developing ischemic and valvular heart disease, as well as recurrent cerebral infarcts, headaches, and visual disturbances. These patients may be on chronic anticoagulation.

Blood Substitutes

Blood substitutes using hemoglobin-based oxygen carriers or inert chemicals to deliver O_2 to tissues are currently under investigation. Perfluorocarbon solutions are chemically inert, but carry O_2 in solution, and are undergoing phase II and III clinical trials. Hemoglobin-based O_2 carrier solutions (chemically modified human or bovine hemoglobin that carries O_2 in solution) are also undergoing phase III clinical trials in the United States. Both perfluorocarbons and Hb-based O_2 carriers have short plasma half-lives, and none are currently licensed for use in North America.

Clinical Review

1. Normal blood volume in an adult is approximately (ml/ kg)
   A. 50
   B. 70
   C. 80
   D. 100
2. All of the following are complications of massive blood transfusion, except
   A. Hypercalcemia
   B. Thrombocytopenia
   C. Citrate toxicity
   D. Hypothermia
3. ABO typing is mandatory for
   A. Fresh frozen plasma
   B. Platelets
   C. Packed red blood cells
   D. All of the above
4. If the recipient's blood group is not known and blood transfusion has to be started in an emergency, the following blood type should be used for transfusion:
   A. AB positive
   B. AB negative
   C. O positive
   D. O negative
5. Administration of a unit of packed red cells will raise the hematocrit by approximately (%)
   A. 1
   B. 2
   C. 3
   D. 4
6. CPDA-1 stored blood has a shelf life of about (days)
   A. 7
   B. 21
   C. 35
   D. 48
7. Compared to fresh blood, stored blood has
   A. Lower potassium
   B. Increased 2,3-diphosphoglycerate
   C. Decreased dextrose
   D. Red cell viability of 120 days
8. Warfarin inhibits the synthesis of clotting factors
   A. II, VII, IX, X
   B. II, V, VII, IX
   C. II, V, IX, X
   D. V, VII, IX, X
9. Low-molecular-weight heparin effect can be monitored by measuring
   A. PTT
   B. PT
   C. ACT
   D. None of the above
10. Desmopressin is preferably used to treat the following type of von Willebrand's disease
    A. Type I
    B. Type 2
    C. Type 3
    D. Type 4

Answers: 1. B, 2. A, 3. C, 4. D, 5. C, 6. C, 7. C, 8. A, 9. D, 10. A

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Part II

Anesthetic Pharmacology

Mechanisms of Anesthetic Action

9

Daniela Damian and Andrew Herlich

In 1846 Oliver Wendell Holmes coined the term *anesthesia* from the Greek word "anaesthesia" meaning "without sensation," after William T.G. Morton, a Boston dentist, performed the first public demonstration of an inhalational anesthetic (ether). The most accepted current definition of general anesthesia is "a drug-induced, reversible condition composed of the behavioral states of unconsciousness, amnesia, analgesia, and immobility along with physiological stability." A major challenge to defining ideal state of general anesthesia is the fact that the site and mechanism of action of general anesthetics are not entirely known.

Basic Mechanisms of Anesthetic Action

A logical approach to investigate the potential action of general anesthetics starts with consideration of the path from peripheral sensorial receptors, which follows the spinothalamic neural pathway through the spinal cord, midbrain, and thalamus to the cerebral cortex. The peripheral receptors can be excluded as the primary target due to their insensitivity to general anesthetics. Recent data suggests that anesthetic action on the spinal cord leads to *immobility* secondary to depression of excitability of spinal motor neurons as evidenced by decreased amplitude of motor-evoked potential and inhibition of excitatory synaptic transmission at the spinal level (Fig. 9.1).

The action of general anesthetics on the brain is responsible for loss of consciousness and amnesia. More specifically, the inhibition of the reticular activating system (RAS), thalamus, and cortex leads to the reversible loss of *consciousness*. The action on the hippocampus, amygdala, prefrontal cortex, and regions of the sensory and motor cortices is responsible for *amnesia. Analgesia* is achieved by blunting nociceptive impulses at the level of the spinal cord.

Minimal alveolar concentration (MAC) represents the end tidal concentration expressed in standard pressure unit of an inhalational anesthetic necessary to blunt a purposeful movement to surgical stimulation in 50 % of the subjects (measure of immobility). MAC is used to compare potency of inhalational anesthetics. When anesthetics are selectively administered to the brain versus spinal cord versus the whole body in laboratory animals, different MAC values are elicited. The highest MAC value is obtained when inhalational anesthetics are administered to the brain only and the lowest when they are administered to the spinal cord in isolation. This observation has led to the conclusion that the action of inhalational anesthetics on the brain may sensitize the spinal cord to noxious stimuli and also that there are different molecular targets for immobility and amnesia.

Molecular Mechanisms of Anesthetic Action

Lipid-Based Theory and Meyer and Overton Correlation

Regarding the molecular mechanism of action of general anesthetics, previous theories purported a common path of action for all anesthetics due to their diverse chemical structure. Meyer and Overton independently observed that anesthetic potency is directly proportional with their solubility in olive oil expressed as olive oil/gas partition coefficient. Based on this observation it was thought that the anesthetic agents act on a hydrophobic lipid target; the greater the lipid solubility, the greater the anesthetic potency.

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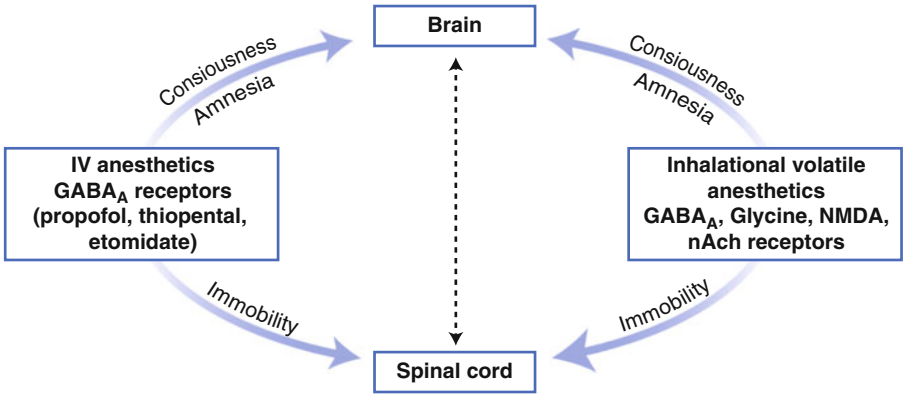

Fig. 9.1 Basic mechanisms of anesthetic action, a working hypothesis

However, one exception to this rule is the "cutoff effect," which emphasizes that the potency of an anesthetic from a homologous series increases with the chain length until it reaches a critical point. Beyond this critical point there is no anesthetic activity. Another exception refers to highly lipid-soluble molecules which are not anesthetics or produce other physiological effects such as convulsions (flurothyl, a halogenated ether family drug with opposite effects). Molecules with low lipid solubility but potent anesthetics (chloral hydrate) and molecules with equal solubility but unequal anesthetic potency (anesthetic enantiomers) are other exceptions.

Furthermore, experiments with firefly luciferase, a pure soluble protein, showed that anesthetics could inhibit this enzyme activity at concentrations identical to those required to anesthetize animals. All the anesthetics tested, including ethers, alkanes, alcohols, and ketones exerted their action by competitive blockade of a common site, preventing the photon emission secondary to interaction between the firefly luciferase and its substrate, luciferin.

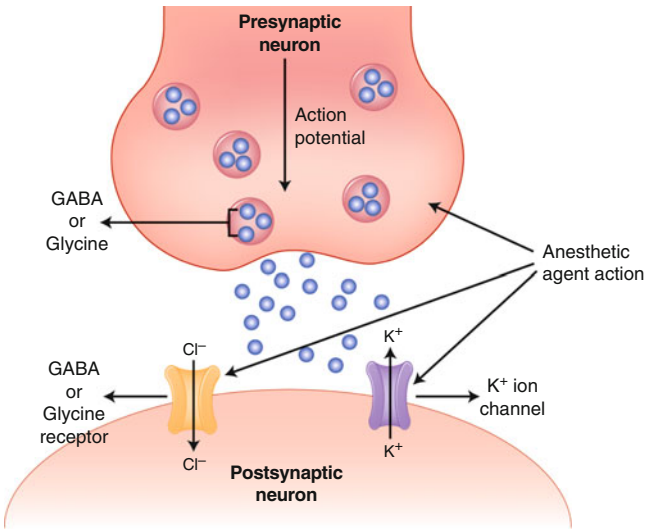

Fig. 9.2 Effects of anesthetics on inhibitory receptors and ion channels: currents passed by $GABA_A$ receptors, glycine receptors, and baseline potassium channels are potentiated by anesthetics. $GABA_A$ and glycine receptors allow primarily the influx of chloride ions leading to hyperpolarization of the cell. Baseline potassium channels also cause hyperpolarization of neuronal cells by an efflux of potassium ions (K^+ = potassium ions, Cl^- = chloride ions, GABA = gamma-aminobutyric acid)

Protein-Based Theory

Modern theories emphasize the importance of protein structures: neurotransmitters, receptors, and ion channels as targets for general anesthetics. The most studied receptor is the $GABA_A$ (gamma-aminobutyric acid type A) receptor. It is part of the superfamily of cys-loop ligand-gated receptors. Together with glycine receptors they have an inhibitory effect (Fig. 9.2). GABA stimulates $GABA_A$ receptors which increases the permeability of chloride channels and causes hyperpolarization of the cellular membrane. This results in decreased excitability. $GABA_A$ receptors represent a major target for the majority of general anesthetics (halogenated alkanes, propofol, sodium thiopental, methohexital, etomidate), being responsible for hypnosis and amnesia. GABA-mediated effects also include unconsciousness, sedation, seizures, apnea, atonia, myoclonus, and loss of corneal reflex.

Glycine receptor stimulation has similar effects as $GABA_A$ stimulation, but seems to also result in immobility (action on spinal cord and brainstem). Nicotinic *acetylcholine* and *serotonin* type 3 receptors are also members of the cys-loop ligand-gated receptor family, but with excitatory effects. Nicotinic acetylcholine receptors (neuronal and muscular) are involved in memory, autonomic function, and muscle relaxation through high permeability for monovalent cations and calcium with the resulting release of neurotransmitters. Serotonin type 3 receptors have been implicated in arousal and possible emesis through enhancing the excitability by inhibiting the resting potassium leak currents.

Glutamate receptors facilitate fast excitatory neurotransmission (Fig. 9.3). NMDA (*N*-methyl-D-aspartate) receptors and AMPA (alpha amino 3 hydroxy 5 methyl

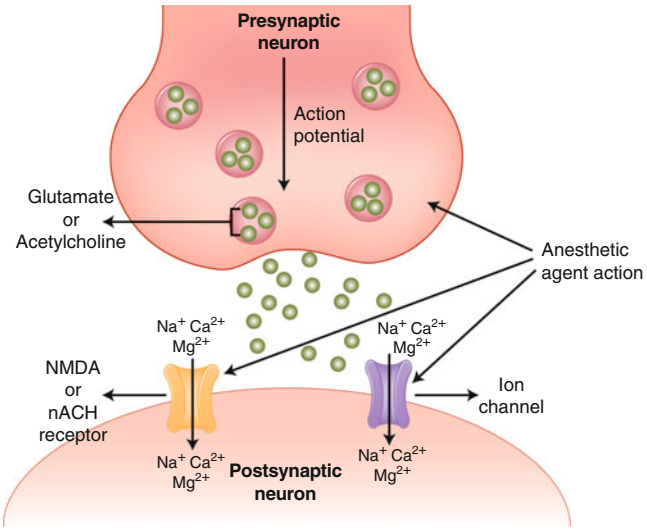

Fig. 9.3 Effects of anesthetics on excitatory ligand-gated NMDA/glutamate ion channels and neuronal nicotinic acetylcholine receptors. These receptors are cation-selective, pass sodium, calcium, and magnesium ions and are inhibited by anesthetics. Volatile anesthetics may also suppress the excitatory glutamatergic transmission via presynaptic inhibition of glutamate release (Na^+ = sodium ions, Ca^+ = calcium ions, Mg^+ = magnesium ions, Ach = acetylcholine, NMDA = *N*-methyl-D-ASPARTATE, nACh-receptor = neuronal nicotinic acetylcholine receptor)

4 isoxazolepropionic acid) receptors are the most relevant members of this class. NMDA receptors function in perception, learning and memory, and nociception by increasing conductance for calcium and magnesium. NMDA antagonists, such as ketamine, N_2O (nitrous oxide), and xenon, produce analgesia, dissociative state, hallucinations, lacrimation, salivation, papillary dilatation, bronchodilation, tachycardia, and nystagmus. The AMPA receptors are associated with perception and memory and cause increased conductance of calcium and magnesium ions.

Arousal from Anesthesia

In parallel with better understanding the general anesthetics mechanism, efforts are being made to study the arousal pathway after general anesthesia to find possible antagonists to facilitate faster recovery. The cholinergic arousal pathway has been studied most extensively. Intraventricular administration of neostigmine to rats under general anesthesia with isoflurane elicited behavioral signs of arousal. Physostigmine has been shown to reverse propofol-induced loss of consciousness in human volunteers. Recently, methylphenidate was used to actively induce emergence from isoflurane general anesthesia in rats by stimulation of the monoaminergic arousal pathway. Orexins in perifornical area of the hypothalamus, and enhanced histaminergic neurotransmission in the basal forebrain, also play roles in the emergence from general anesthesia.

Future Research

While much has been learned about general anesthesia at the molecular level, much more remains to be discovered. There are concerns related to neurotoxicity of general anesthetics on the immature brain leading to apoptosis secondary to interference with neurotransmitters glutamate and GABA on NMDA and $GABA_A$ receptors, respectively, during the synaptogenesis period. The elderly brain seems to be also vulnerable to apoptosis secondary to general anesthetic exposure, with increased production of β amyloid, postoperative cognitive dysfunction, and faster onset to Alzheimer's disease. Future research for deciphering the mechanism of action of general anesthetics potentially involving selective gene manipulation and system analysis is necessary to design more efficient and safer drugs.

Clinical Review

1. The following neurotransmitter/s is/are inhibitory:
   A. GABA
   B. Glycine
   C. Glutamate
   D. Both A and B
2. The following neurotransmitter/s is/are excitatory:
   A. GABA
   B. Glycine
   C. Glutamate
   D. Both A and B
3. Ketamine acts primarily at the following receptor:
   A. *N*-methyl-D-aspartate
   B. GABA
   C. Glycine
   D. Calcium

Answers: 1. D, 2. C, 3. A

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Inhalational Anesthetics

10

Lee Neubert and Ashish Sinha

Inhalational anesthetics are one of the most important classes of anesthetic drugs that anesthesiologists are associated with. Inhalational anesthetics are anesthetics which are administered in a gaseous form. Their use is popular because of the ease of administration, the ability to deepen or lighten the anesthesia quickly, and usually having a benign side effect profile. Since they are so commonly used, a thorough knowledge of their pharmacology is essential for anesthesia providers.

Inhalational anesthetics can be classified as nonvolatile or volatile. Nitrous oxide is the commonly used nonvolatile anesthetic and exists as a gas at room temperature. Halothane, desflurane, sevoflurane, and isoflurane are the commonly used volatile anesthetics and exist in the liquid form at room temperature. Other inhalational anesthetics, which are not commonly used, include helium and xenon.

Pharmacokinetics

The physical characteristics of inhaled anesthetics make them an excellent choice for maintenance of anesthesia. Because they have a unique "inhalation" route of administration, it provides a rapid increase in the lung concentration and access to the blood stream without necessitating intravenous access. This is particularly useful in the pediatric population where induction of anesthesia with these agents can occur prior to the placement of intravenous access. Once in the blood stream, there is minimal tissue absorption and metabolism of these agents, allowing for relative ease and rapidity in achieving a steady state of anesthesia.

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Concentration Factors

Inspired Concentration

When administering inhalational anesthetic, it is important to understand the factors determining the concentration which a patient inspires. It is important to know that this concentration is not the one leaving the vaporizer but that inspired by the patient (FI).

- The gas leaving the vaporizer mixes with the gas in the breathing circuit causing a dilutional effect.
- The breathing circuit material absorbs a small amount of vapor.
- By increasing the fresh gas flow and amount of vapor being introduced into the system, the gas within the circuit (lower concentration) becomes replaced with a higher concentration gas. Additionally, this can be augmented by using a circuit with a smaller volume.

Alveolar Concentration

The alveolar concentration of inhalational anesthetics is of specific importance. The concentration and, therefore, the partial pressure exerted by the gas on the alveolus, after equalization of the volume of distribution, is the same that is exerted on the brain. This concentration and partial pressure of the inhalational agent is the measure of anesthetic depth. The factors determining how quickly alveolar concentration (FA) reaches FI, known as the FA/FI ratio, are critical to understand. The rise in alveolar concentration is determined by several important factors.

- Blood solubility: The amount of gas taken up by the venous blood flowing through the pulmonary system depends on its solubility. Each inhalational anesthetic has a specific solubility in blood, which is referred to as the blood gas partition coefficient (Table 10.1). The higher the blood gas partition coefficient, the more anesthetic is taken up into venous blood, thereby diminishing FA. Conversely, if the agent solubility is low, then less anesthetic is absorbed into the venous blood, causing the FA to approach FI more rapidly.

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Table 10.1 Blood–gas partition coefficients of inhalational anesthetics

Agent	Blood–gas partition coefficient
Desflurane	0.42
Nitrous oxide	0.47
Sevoflurane	0.65
Isoflurane	1.46
Halothane	2.5

Table 10.2 Gas–tissue partition coefficients of inhalational anesthetics

Tissue	Desflurane	Nitrous oxide	Sevoflurane	Isoflurane	Halothane
Brain	1.22	1.07	1.69	1.57	1.88
Heart	1.22	1.02	1.69	1.57	1.7
Liver	1.49		2	1.86	2.29
Kidney	0.89		1.2	1	1.25
Muscle	1.73	1.15	2.62	2.57	2.92
Fat	29	2.39	52	50	57

- Cardiac output: The uptake of the anesthetic gas into the blood is determined by the amount of blood flowing through the lung. Increased cardiac output means presenting more pulmonary blood with a lower agent concentration needing to be saturated. Therefore, the increased uptake results in decreased alveolar concentration and consequently slowing the rise of FA/FI. In other words, the rate at which FA approaches FI is indirectly proportional to cardiac output in the absence of shunting.
- Tissue solubility: Solubility of the agent within muscle, fat, and other tissues also plays a role in determining how rapidly FA approaches FI. Compared to the alveoli, these peripheral smaller components of the volume of distribution saturate more slowly, as such the concentration in the alveoli is almost always higher than that in the brain.

Strategies to Increase the Rate of Rise of FA

In order to increase the rate at which FA reaches FI, several components can be manipulated.

- Increasing minute ventilation: By increasing minute ventilation, the amount of fresh gas entering the alveolus is increased replacing the lung volume which has had gas taken away by the pulmonary blood. Therefore, increasing minute ventilation increases FA.
- Increasing the delivered concentration: This is similar to the idea of "over-pressurization." Over-pressurization can simply be understood as the inhalational equivalent to an IV bolus. By initially administering a much higher concentration, the actual desired concentration can be more rapidly achieved. The volume of distribution of the agent is saturated quicker, and this phenomenon is known as the concentration effect.
- Second gas effect: Another gas may be added to the inhaled mixture of gases. Concomitantly administering two anesthetic gases results in a faster rise in concentration of each. This is known as the second gas effect.

Avoiding ventilation perfusion (VQ) mismatch: VQ mismatch results in shunting of blood, which exposes alveolar blood to less anesthetic gas and, therefore, lower partial pressure on the brain and slower anesthetic onset. This effect is more profound with less soluble agents.

Metabolism and Elimination

Elimination of inhalational anesthetics is primarily accomplished by exhalation, though minimal amount of elimination occurs percutaneously. Least soluble agents, that is, those with the lower blood gas partition coefficients, will have the fastest decrease of FA. These agents readily diffuse from the pulmonary venous blood into the alveoli and exhaled. Once the concentration of the agent in the venous blood drops below that of peripheral tissues, the agent stored in these tissues diffuses back into the venous blood, slowing the decline in FA (Table 10.2). Inhalational anesthetics with higher blood tissue coefficients take longer to wash out. It is generally accepted that 80–90 % of the inhalational anesthetic concentration must be eliminated for emergence to occur.

Metabolism plays a smaller role in elimination, as inhalational agents are exhaled primarily via the lungs. Halothane, isoflurane, sevoflurane, and desflurane are metabolized in the liver to fluoride compounds, which can accumulate after prolonged exposure. But these fluoride levels have not been shown to cause postoperative renal dysfunction.

Pharmacodynamics

The exact mechanism of action of inhalational anesthetics is unknown. The most common understanding is that there are multiple sites of action, which may not be uniform for all inhalational agents. Inhalational anesthetics are presumed to act on voltage-gated ion channels in cell membranes, thereby altering permeability and impairment of neurotransmitter function (see Chap. 9).

The minimum alveolar concentration (MAC) of inhalational anesthetics is defined as the concentration of gas necessary to prevent movement to surgical stimulus in 50 % of patients. The MACs of common gases are shown in Table 10.3. The MAC of nitrous oxide is 104 %. This above impossible percentage means that the MAC of nitrous oxide cannot be achieved (except in a hyperbaric chamber) and it is a weak anesthetic.

In order to achieve a level of anesthesia in which 95 % of patients do not move, it takes MAC + 25 % (1.25 MAC).

Table 10.3 MAC of inhalational anesthetics

Agent	MAC
Halothane	0.75
Isoflurane	1.17
Sevoflurane	2.05
Desflurane	6.6
Nitrous oxide	104

Table 10.4 Factors affecting MAC of inhalational anesthetics

Factor increasing MAC	Factors decreasing MAC
Hyperthermia	Hypothermia
Hypernatremia	Hyponatremia, hypercalcemia
Chronic alcoholic abuse	Acute alcoholic intoxication
Monoamine oxidase inhibitors	Chronic dextroamphetamine use
Acute cocaine intoxication	Chronic cocaine use
Acute dextroamphetamine use	Hypotension, metabolic acidosis
Ephedrine	Hypoxia, hypercarbia
	Anemia
	Pregnancy
	Local anesthetics
	Clonidine, dexmedetomidine
	Barbiturates, ketamine, propofol
	Benzodiazepines
	Opiates

In order for a patient to not recall but lose self-awareness (MAC Aware), it generally takes 0.4 to 0.5 MAC. This means for induction of anesthesia at least 0.4–0.5 MAC is needed. Emergence takes place at approximately 10–20 % MAC, which equates to 0.15–0.2 MAC, meaning that it takes more to induce anesthesia in a patient but lower levels to emerge. Yet another term is the minimum alveolar concentration which blunts the adrenergic response (MAC-BAR), which is usually 1.5 MAC. Therefore, a 1.25 MAC may stop patient movement in 95 % of patients, but it will not suppress the physical signs of pain (tachycardia, tachypnea, and hypertension).

The MAC of anesthetics is additive. Since only one volatile anesthetic can be used at a time, adding nitrous oxide as an adjunct allows the practitioner to avoid the negative side effects associated with higher concentrations of the volatile anesthetic. For example, using nitrous oxide at 0.5 MAC (52 %) combined with desflurane at 0.5 MAC (3.3 %) would result in 1 MAC and achieve a state where 50 % of patients do not react to stimulation. MAC is affected by many physiological states and pharmacologic interactions (Table 10.4). Of important note is that MAC is variable with age. From birth to one year, it is generally accepted that MAC increases to a peak. From this point on there is a decline. MAC declines at a rate of 5 % for every decade of life over 40 years of age.

Systemic Effects of Inhalational Agents

Neurologic Effects

Cerebral metabolic rate and oxygen consumption ($CMRO_2$) are depressed by all potent volatile inhalational anesthetics. These changes parallel the slowing in the electroencephalogram (EEG). For all volatile anesthetics, except for halothane, once an isoelectric EEG is achieved, it is assumed that the $CMRO_2$ has reached its nadir. Halothane concentrations above those that achieve an isoelectric EEG are usually toxic. Clinically, isoflurane causes the greatest decrease in $CMRO_2$ and causes an isoelectric EEG at 2 MAC (lower concentration), compared to desflurane or sevoflurane, which take more than 2 MAC to cause an isoelectric EEG.

Cerebral blood flow (CBF) is increased by volatile anesthetics, with halothane causing the greatest increase (avoid halothane for intracranial mass surgery). The increase in cerebral blood flow causes an increase in intracranial pressure (ICP). The rise in ICP follows the rise in CBF, meaning that halothane causes the greatest rise in ICP. Hyperventilation is commonly used before halothane (unlike other agents) preinduction or intubation in an attempt to blunt this effect. Isoflurane increases CBF and ICP above a 1 MAC concentration.

Cerebrospinal fluid (CSF) quantity is altered by volatile agents minimally but must be appreciated. Halothane has been showed to decrease CSF formation but concomitantly inhibits reabsorption, the net fluid volume being positive. Isoflurane causes no known changes, sevoflurane decreases production, while desflurane may cause a slight increase in CSF production. The resultant effects are minimal on the ICP.

Nitrous oxide increases CBF, ICP, and $CMRO_2$, but the effects are mild compared to volatile agents. Because of the mild anti-neuroprotective effect, it is used minimally in cases where increased ICP or cerebral ischemia is suspected. Nitrous oxide and xenon are the only inhalational anesthetics that have analgesic effects. The remainder of the inhalational anesthetics at high concentrations may prevent movement to painful stimulation and block adrenergic responses.

Cardiovascular Effects

Volatile anesthetics cause a dose-dependent decrease in blood pressure. Halothane is a direct myocardial depressant and causes a decrease in the cardiac contractility and the cardiac output. Isoflurane > sevoflurane > desflurane also cause a dose-dependent decrease in blood pressure, but the cardiac output is usually maintained due to an increase in heart rate. The decrease in blood pressure with these three anesthetics

occurs by decreasing the systemic vascular resistance (SVR). Halothane does not alter the SVR.

Heart rate is affected maximally by desflurane, which is seen with rapid increases in concentrations. Isoflurane also has a similar effect but to a lesser degree. Sevoflurane and halothane cause little if any difference in heart rate.

All volatile agents are coronary vasodilators. Isoflurane can be associated with a "coronary steal syndrome," where regional myocardial ischemia occurs because of blood being diverted away from fixed stenotic lesions. Halothane does not cause this syndrome as the associated hypotension decreases coronary blood flow.

The QT interval is prolonged by all volatile agents. Halothane has additionally been shown to be arrhythmogenic. This occurs because the sinoatrial discharge rate and conduction through multiple cardiac pathways is slowed leaving the heart sensitized to the effects of arrhythmogenic agents. Therefore, epinephrine is avoided with use of halothane.

Recently, it has been shown that there are cardioprotective effects provided by inhalational anesthetics. This is postulated to occur through preconditioning during induction. A brief period of ischemia starts a cascade of intracellular changes resulting in an overall state of protection from future ischemic events.

Nitrous oxide causes sympathetic stimulation, although it is a myocardial depressant. This sympathetic stimulation maintains the arterial blood pressure and cardiac output. Nitrous oxide should be used with caution in patients with coronary disease or hypovolemia. Nitrous oxide can cause pulmonary constriction, thereby causing an increase in the pulmonary vascular resistance (PVR) and right atrial pressures.

Respiratory Effects

Desflurane and, to a lesser extent, isoflurane are not pleasant to inhale and irritate the upper airway. During induction they can result in coughing, laryngospasm, and bronchospasm. Therefore, these two agents are avoided for inhalational induction. Sevoflurane, nitrous oxide, and halothane are comparatively much less irritating and are used for inhalational induction of anesthesia. It is important to know that all volatile anesthetics are bronchodilators. However, some studies have suggested desflurane to cause respiratory irritation during emergence.

Volatile anesthetics decrease the tidal volume and cause compensatory tachypnea. However, at high concentrations the tidal volume decreases significantly, and the compensatory increase in the respiratory rate is insufficient to maintain the minute ventilation. Therefore, the $PaCO_2$ rises. This increased rise in $PaCO_2$ is decreased if a change is made from using solely a volatile agent to a mixture of volatile agent with nitrous oxide. While the response to hypercarbia is blunted at high agent concentrations, the response to hypoxia is, however, blunted at lower concentrations. This becomes significant in the postoperative period where lingering low concentrations of volatile anesthetic can result in a patient's being unreactive to hypoxemia, even when seemingly awake in the recovery room. Therefore, special vigilance is required in obese patients, smokers, or those who have a history of sleep apnea. Therefore, volatile agents blunt the respiratory responses to both hypoxia and hypercarbia.

Hypoxic pulmonary vasoconstriction is inhibited by inhaled anesthetics. While normally the lung constricts blood flow to areas which are not being ventilated, under anesthesia this physiologic response is attenuated. This causes a ventilation perfusion mismatch with increased blood levels of $PaCO_2$.

Nitrous oxide also causes a decrease in tidal volume and tachypnea. However, even small amounts of nitrous oxide depress the hypoxic drive, the ventilatory response to hypoxemia. Furthermore, it is important to understand the effects of nitrous oxide on pockets of air within the body, such as in a pneumothorax, middle ear, or bowel. The 79 % nitrogen in the air filling these areas has low blood solubility and is not easily reabsorbed. If a patient is inhaling nitrous oxide, it diffuses across the membranes and causes the pockets to expand, which can have deleterious effects.

Hepatic Effects

The blood supply to the liver comes from the portal vein and the hepatic artery. Isoflurane, sevoflurane, and desflurane all cause an increase in hepatic artery flow while causing little or no decrease in portal vein flow. The total liver blood flow is maintained or decreased slightly. Halothane on the other hand decreases portal vein flow and causes hepatic artery constriction. This leads to a decrease in oxygen supply to the liver during halothane anesthesia. Nitrous oxide also decreases hepatic blood flow, but its effects are mild.

Halothane furthermore has been known to cause what is coined as "halothane hepatitis." On exposure to halothane, centrilobular necrosis occurs in the liver. Two mechanisms have been proposed for this. The first mechanism of halothane hepatitis is via the reductive metabolites of halothane, especially produced under hypoxic conditions, which causes a short-term bump in liver enzymes, fatigue, nausea, and rarely jaundice. This transient condition occurs independently of previous exposure. The second mechanism of halothane hepatitis is an immune-mediated process, where rash, fever, and eosinophilia occur after a few days following exposure to halothane. Oxidative metabolism of halothane produces trifluoroacetic acid halides (metabolites), which act as antigens. These antigens propagate an immune response, which, during a second exposure to halothane, may result in

an immune response severe enough to cause fulminant hepatic necrosis.

Halothane is generally safe to use in presence of liver dysfunction. However, if unexplained liver dysfunction (rule out other causes of hepatic dysfunction) occurred following a previous exposure to halothane, it is prudent to avoid halothane for subsequent anesthetics.

Renal Effects

Inhalation anesthetics decrease renal blood flow, glomerular filtration rate, and urine output. Volatile agents are metabolized to fluoride, which has the potential to cause nephrotoxicity. However, this has not been shown to be clinically significant.

An important concern is sevoflurane degradation by soda lime or barium hydroxide CO_2 absorbers, producing a potentially nephrotoxic metabolite called as compound A. Compound A is a vinyl ether, which in animal studies has been shown to cause nephrotoxicity and renal tubular necrosis. These findings, however, have not been substantiated in human subjects. Nonetheless, to avoid excessive formation of compound A, it is recommended that during sevoflurane anesthesia, it may be prudent to avoid low fresh gas flows (use > 2 L/min), dry CO_2 absorbents, and avoid using sevoflurane in high concentrations for anesthetics of long duration.

Musculoskeletal Effects

All volatile anesthetics relax skeletal muscle and augment neuromuscular blockade. This effect is postulated to occur at postsynaptic nicotinic acetylcholine receptors. In the pediatric population, volatile agents can be used to reach intubation conditions, using an inhalational induction technique, without using neuromuscular blocking drugs. Nitrous oxide does not cause skeletal muscle relaxation; it may cause skeletal muscle rigidity when used at high concentrations.

During cesarean section, after delivery of the baby and removal of the placenta, using greater than 1 MAC of volatile agent may cause uterine atony. Conversely, this relaxation effect can be employed beneficially in the case of uterine inversion, where atony is needed for repositioning the uterus. Malignant hyperthermia, a life-threatening condition, can be triggered by all volatile inhalational anesthetics, but not by nitrous oxide.

Hematologic Effects

Nitrous oxide has been shown to inhibit vitamin B12-dependent enzymes methionine synthetase (myelin formation) and thymidylate synthetase (DNA synthesis). With prolonged exposure, nitrous oxide can cause bone marrow suppression (megaloblastic anemia) and cause peripheral neuropathies.

When volatile agents pass through the CO_2 absorbent in the anesthesia circuit, absorbent breakdown occurs, which produces carbon monoxide. This becomes more significant if the CO_2 absorbent is dry. Carbon monoxide when inhaled by the patient produces carboxyhemoglobin, which leads to decreased oxygen delivery to the tissues. Interaction with Baralyme is known to produce more carbon monoxide than soda lime. This can be prevented by avoiding the use of dry absorbent (increased vigilance) and avoiding leaving on high fresh gas flows when the circuit is not being used. The order of carbon monoxide production at MAC concentrations from greatest to least is desflurane > isoflurane > sevoflurane = halothane.

Gastrointestinal Effects

Nitrous oxide has been proposed to increase the likelihood of postoperative nausea and vomiting, although the evidence is inconclusive. It may be prudent to avoid nitrous oxide in patients with risk factors for postoperative nausea and vomiting (previous history of N/V, GYN surgeries).

Properties of Inhalational Anesthetics

Nitrous Oxide

- Colorless, nonflammable gas, pleasant, and slightly sweet odor and taste.
- Although not flammable, it will support combustion.
- Has analgesic properties.
- MAC is 104 %, and therefore, it is frequently used in combination with other anesthetic agents.
- Can cause bone marrow suppression with prolonged use.
- Contraindicated in presence of closed air pockets (pneumothorax, middle ear) and pulmonary hypertension.

Isoflurane

- Nonflammable, halogenated ether, with a moderately high pungency that can irritate the respiratory system.
- Decreases BP (SVR) and can cause tachycardia if there is rapid increase in concentration and coronary steal syndrome.
- Bronchodilator, blunted response to hypoxemia and hypercarbia.
- Increases cerebral blood flow at concentration greater than 1 MAC.
- Skeletal muscle relaxation.

Table 10.5 Properties of inhalational anesthetics

Agent	Vapor pressure	CO_2 absorbent stability	Pungency
Isoflurane	240	CO formation when dry	++
Sevoflurane	160	Compound A formation	No
Desflurane	664	CO formation when dry	+++
Halothane	244	CO formation when dry	No
Nitrous oxide	39,000	Stable	No

CO carbon monoxide

Sevoflurane

- Sweet smelling and nonflammable.
- Used for induction and maintenance of general anesthesia and a preferred agent for mask/inhalational induction.
- Decreases BP (less than isoflurane), decreases SVR, vasodilator, and is not known to cause coronary steal syndrome.
- Bronchodilator, blunted response to hypoxemia and hypercarbia.
- Increases cerebral blood flow.
- Skeletal muscle relaxation.
- Interaction with CO_2 absorbent can produce nephrotoxic compound A. It is recommended to avoid low fresh gas flows (>2 L/min) and avoid high concentrations for long-duration anesthetic.

Desflurane

- Low blood gas coefficient (0.42), low solubility in blood and tissues, and rapid induction and emergence.

High vapor pressure (664) (Table 10.5); desflurane boils at 22.8 °C (near room temperature), which requires a special electrical vaporizer that heats the desflurane liquid at 39 °C and under 2 atmosphere pressure, to deliver desflurane as a vapor.

- Pungent smelling and an irritant to the airway.
- Decreases BP (SVR) and can cause tachycardia if there is rapid increase in concentration.
- Bronchodilator, blunted response to hypoxemia and hypercarbia.
- Increases cerebral blood flow.
- Skeletal muscle relaxation.

Xenon

There has been increasing interest in the implementation of xenon as an inhalational anesthetic. Xenon has several physical characteristics which make it a desirable maintenance anesthetic. The greatest setback to the widespread use of xenon is its expense, which to this point has prevented its implementation.

- Xenon is a nonflammable, colorless, and odorless gas that does not irritate the respiratory tract.
- Xenon has a lower blood gas partition coefficient of 0.115 than any current inhalational anesthetic, which means faster induction and emergence times.
- Xenon has strong analgesic properties, more than nitrous oxide, and causes some muscle relaxation and respiratory depression
- Unlike nitrous oxide which has a high MAC of 105, xenon's MAC is 63–71 allowing it to be combined with oxygen in inspired concentrations large enough to maintain anesthetic depth.
- Xenon has the benefit of being environmentally safer, as it is a normal microconstituent of atmospheric air.
- Xenon has been shown to provide cardiovascular stability and neuroprotection.
- Xenon is not metabolized, eliminated via exhalation, nontoxic, and stable in storage with no interaction with CO_2 absorbent.
- Xenon interacts with rubber, which causes a high loss if rubber anesthesia circuits are used.

Halothane

- Halogenated alkane compound, nonflammable, colorless, and pleasant smelling.
- Unstable in light and packaged in amber bottles with thymol preservative.
- Bronchodilator, an alternate choice for sevoflurane for inhalation induction of anesthesia in children.
- Decreases BP (decreases myocardial contractility) and does not increase heart rate.
- Bronchodilator, blunted response to hypoxemia and hypercarbia.
- Increases cerebral blood flow the greatest; avoid using for intracranial surgery.
- Skeletal muscle relaxation.
- Can cause hepatitis (greater incidence than isoflurane and desflurane).
- Arrhythmogenic, avoid using with high concentrations of epinephrine.

Inhalational Induction Technique

An inhalational induction of anesthesia technique is done mainly for pediatric patients but also for adult patients without intravenous access. Prior to sevoflurane, halothane was the most popular agent for inhalational induction. Although

halothane is pleasant smelling, it has a slow onset of action, direct cardiac depressant effects, an arrhythmogenic potential, and the ability to cause hepatic dysfunction more than any other agent. Therefore, its use has been largely replaced by newer and safer agents like sevoflurane. Sevoflurane is a sweet-smelling agent, nonirritant to the respiratory tract, with a faster onset of action, relatively better cardiovascular stability, and produces a rapid and smooth induction of general anesthesia.

Mask Inhalation Induction Techniques

- Gradual technique: With the patient on the operating table or in the parent's arms, the face mask is applied on the patient with high gas flows (for example 7 L/min nitrous oxide-66 %, and 3 L/min oxygen-33 %). Then sevoflurane is introduced gradually, increasing its concentration by 1 % every 2 breaths till the patient is asleep.
- Vital capacity single-breath technique: The anesthesia circuit is primed for at least 1 min with 8 % sevoflurane and up to 70 % nitrous oxide + 30 % oxygen at about 6 L/min fresh gas flow. In a cooperative patient, the patient exhales to residual volume and then inhales to vital capacity and attempts to hold his breath as long as tolerated or until unconsciousness. However, in an uncooperative patient, the mask is immediately applied to the patient as soon as the anesthesia circuit is primed.

Clinical Review

1. Rapid increase in concentration of the following agent can cause tachycardia:
   A. Halothane
   B. Sevoflurane
   C. Desflurane
   D. Xenon
2. Minimum alveolar concentration is affected by:
   A. Concentration of the inhalational agent
   B. Use of opiates
   C. Use of benzodiazepines
   D. All of the above
3. Coronary steal syndrome may most likely occur with:
   A. Isoflurane
   B. Sevoflurane
   C. Desflurane
   D. Nitrous oxide
4. The following inhalational agent(s) is a bronchodilator:
   A. Sevoflurane
   B. Desflurane
   C. Nitrous oxide
   D. A and B
5. Skeletal muscle relaxation is caused by:
   A. Isoflurane
   B. Desflurane
   C. Nitrous oxide
   D. A and B

Answers: 1. C, 2. D, 3. A, 4. D, 5. D

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Intravenous Induction Agents

11

Dustin J. Jackson and Patrick J. Forte

Induction of anesthesia is most often achieved using intravenous agents. Inhalational agents can also be used for induction, and this technique is commonly used in children. Propofol, thiopental, etomidate, and ketamine are the most commonly used intravenous agents. While opiates and benzodiazepines can also be used for induction, they are more often used for other purposes.

Propofol

Propofol (2,6-diisopropylphenol) is the most commonly used agent for induction of anesthesia. It is also used for the maintenance of anesthesia and for sedation in the operating room, emergency room, intensive care unit, and other procedural units. Being insoluble in aqueous solutions, propofol is manufactured as an emulsion of 10 % soybean oil, 2.25 % glycerol, and 1.2 % egg lecithin. It is milky white in appearance with a pH of about 7.0. It is commonly available for use as a 1 % (10 mg/ml) solution in 20 ml vials or 50 ml bottles.

Mechanism of Action

The mechanism of action of propofol is thought to be due to potentiation of CNS inhibitory $GABA_A$ and glycine receptors. Its sedative/hypnotic effect appears to occur via action in the brain, while its immobilizing ability seems to occur via action on the spinal cord. Propofol is highly protein bound (>96 %), and conditions associated with lower plasma protein levels, such as during cardiopulmonary bypass, have been shown to enhance the anesthetic effect of the drug by increasing the free, unbound fraction.

Initiation of action is rapid (one arm to brain circulation time). It is first taken up by the highly vascular organs, including the brain (Fig. 11.1). Initial emergence from a bolus dose of propofol occurs in 2–8 min as a result of redistribution (alpha elimination) to other organ systems (liver, kidney, muscles). The drug undergoes rapid hepatic metabolism, with the resulting inactive metabolites undergoing renal excretion (beta elimination). Despite the hepatic metabolism, liver failure has not been shown to significantly affect overall clearance. Since plasma clearance of propofol exceeds hepatic blood flow, extrahepatic metabolism is also known to exist, with the lungs playing a major role.

This rapid metabolism of propofol minimizes any residual effects after wakening. This lack of "hangover" effect makes propofol an ideal agent in ambulatory settings, where propofol induction has been associated with a more rapid recovery (Table 11.1) and earlier discharge when compared to induction with thiopental. The use of propofol for sedation for endoscopy is also associated with quicker recovery when compared to midazolam. Elderly patients have decreased clearance rates, while women have been shown to have greater clearance rates and volumes of distribution than men and therefore awaken faster from propofol anesthesia.

Cardiovascular Effects

Of all the induction agents, propofol has the most profound cardiovascular depressant effects (Table 11.2). It causes the largest reduction in mean arterial pressure (MAP) and does so via several mechanisms. The primary cause of hypotension is venous and arterial vasodilation, resulting in a reduction in cardiac preload and afterload. It also inhibits baroreceptor reflexes, thereby preventing the increase in heart rate which would typically accompany these changes, further compromising MAP. Vagally mediated reflex bradycardia,

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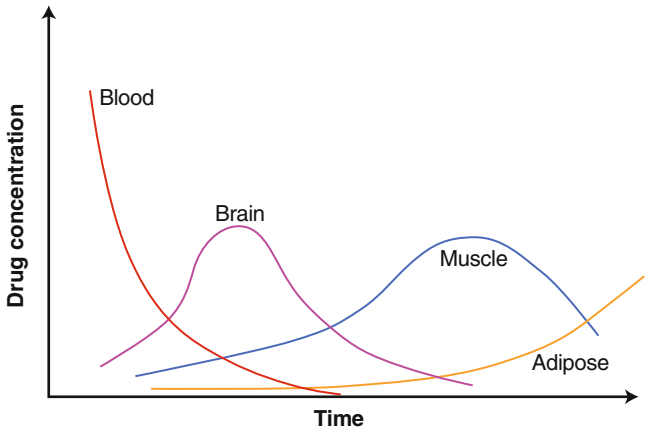

Fig. 11.1 Drug distribution in various tissues over time after an intravenous bolus dose

Table 11.1 Pharmacokinetics properties of IV anesthetic agents

Agent	Induction dose (mg/kg)	Onset of action (s)	Duration of action or awakening (min)
Propofol	1–2.5	<30	2–8
Thiopental	3–5	<30	10–15
Methohexital	1–1.5	<30	10–12
Etomidate	0.2–0.3	<30	5–10
Ketamine	1–2	45–60	12–15

Table 11.2 Cardiovascular effects of IV anesthetic agents

Agent	MAP	HR	CO	Contractility	Venodilation
Propofol	↓↓	↓	↓	↓	↓↓
Thiopental	↓	↑	↓	↓	↓↓
Etomidate	0	0	0	0	0
Ketamine	↑↑	↑↑	↑	↑/↓	0

MAP mean arterial pressure, *HR* heart rate, *CO* cardiac output

and rarely asystole, may occur due to a marked decrease in preload.

Hypotension may be exacerbated by rapid injection, large doses, old age, and impaired cardiac function. Adequate intravascular volume hydration, as well as slow and titrated dosing, can minimize the reduction in MAP in susceptible individuals, such as the elderly. However, neither the duration of fasting nor the rate of administration has been shown to make a significant difference in young, healthy patients.

Respiratory Effects

Propofol causes profound respiratory depression, consistently producing apnea at induction doses. At lower doses, such as those used for sedation, minute ventilation is reduced, with greater decreases in tidal volume than respiratory rate. The ventilatory response to hypoxia and hypercarbia is reduced as well. Propofol is generally considered the most effective agent at blocking upper airway reflexes during direct laryngoscopy or laryngeal mask airway placement. It has also been shown to decrease the incidence of bronchospasm when compared to thiopental and etomidate in healthy patients, asthmatics, and smokers. In addition, smokers anesthetized with propofol experience less coughing upon extubation than those anesthetized with sevoflurane. Propofol does not inhibit hypoxic pulmonary vasoconstriction.

Table 11.3 Central nervous system effects of IV anesthetic agents

Agent	$CMRO_2$	CBF	CPP	ICP
Propofol	↓↓	↓↓	↓	↓
Thiopental	↓↓	↓↓	↑/↓	↓↓
Etomidate	↓↓	↓↓	↑	↓
Ketamine	↑	↑↑	↑/↓	↑

CMRO2 cerebral oxygen consumption, *CBF* cerebral blood flow, *CPP* cerebral perfusion pressure, *ICP* intracranial pressure

Central Nervous System Effects

Propofol depresses the central nervous system (CNS) as well, resulting in a decreased cerebral metabolic rate of oxygen consumption ($CMRO_2$). This, along with cerebral vasoconstriction, reduces cerebral blood flow (CBF) and cerebral blood volume (CBV). The reduction in CBV reduces intracranial pressure (ICP) and effectively "shrinks" the brain to improve the neurosurgical field (Table 11.3). Despite the cerebral vasoconstriction, propofol does maintain cerebrovascular autoregulation in response to changes in MAP (within the normal range) and changes in pCO_2.

Like barbiturates, propofol affords neuroprotection from focal ischemia. All of these properties make propofol a popular choice for neuroanesthesia, though it must be realized that propofol can decrease cerebral perfusion pressure (CPP) given its depressant effects on MAP. Propofol is not an ideal choice for implantation of deep brain stimulation, as it leads to a significant decrease in the neuronal activity of the subthalamic nucleus, thereby interfering with the identification of this structure.

Propofol has anticonvulsant effects, producing burst suppression on the electroencephalogram (EEG), and can also be used to break status epilepticus when other treatments have failed. Induction with propofol sometimes produces excitatory phenomenon producing muscle twitching, spontaneous movement, or hiccupping. Propofol produces a dose-dependent decrease in the bispectral index (BIS), and this effect is additive with that of volatile anesthetics. As is the case with surgery and general anesthesia in general, propofol has been shown to disrupt circadian sleep structure by altering melatonin secretion. It has been shown to produce an equal degree of amnesia compared to midazolam when used at equal levels of sedation. When compared to midazolam,

propofol has been associated with significantly more dreaming when used for sedation. Propofol decreases intraocular pressure, and tolerance is not known to develop after long-term propofol infusions.

Dosage and Uses

A. Induction of anesthesia: 1–2.5 mg/kg. Children usually require higher doses than adults, while elderly patients require lower dosages. Women may require a higher induction dosage than men.
B. Sedation: 25–100 mcg/kg/min. Sedation with propofol is provided in the operating room, emergency room, intensive care unit, and other procedural units.
C. Maintenance of anesthesia: 50–200 mcg/kg/min. Maintenance of anesthesia can be provided with or without the addition of a volatile inhalational agent. Patients with contraindication to the use of an inhalational agent (malignant hyperthermia, muscular dystrophies) are often maintained with a propofol infusion.
D. Antiemetic effect: Propofol is known to have an antiemetic effect, which is in contrast to the pro-emetic effect of thiopental and etomidate. It can be given as a low-dose intraoperative infusion (10–20 mcg/kg/min) to prevent postoperative nausea and vomiting (PONV) and can also be used as a rescue drug with 10 mg doses followed by a 10 mcg/kg/min infusion to treat refractory PONV. Though it has been shown to decrease lower esophageal sphincter pressure during high-dose infusions, the clinical significance of this is unknown.
E. Antipruritic effect: Propofol is also unique among the induction agents, in that it has antipruritic effects.
F. Other effects: Unlike volatile agents, propofol does not seem to impair glucose tolerance, thereby potentially leading to less intraoperative hyperglycemia.

Side Effects

A. *Pain on injection*: Pain on injection is a common, undesirable effect of propofol administration, with reported incidences ranging between 30 and 90 %. Many recent studies have examined ways to eliminate or lessen this pain. Effective techniques include dilution, slow injection, injection into larger veins, pretreatment with intravenous analgesics (opiates, ketamine, dexmedetomidine, acetaminophen), or pretreatment or mixing with lidocaine (30–50 mg of 1 % lidocaine/200 mg propofol).

   Tourniquet-controlled pretreatment with lidocaine is more effective than mixing propofol with lidocaine, and combination of pretreatment with opiates and lidocaine is more effective than either technique alone. A 0.5 ml priming dose of propofol injected slowly over 30 s, 2 min prior to the main induction dose, has also been shown to decrease injection pain with the main dose. In addition, a new solvent consisting of a mix of medium- and long-chain triglycerides, as opposed to the standard long-chain formulation, has been shown to cause decreased pain on injection.
B. *Egg allergy*: Formulations of propofol contain egg lecithin, and therefore, propofol use is sometimes cited as a contraindication in egg-allergic individuals. However, the vast majority of egg-allergic individuals react to proteins found in egg white (ova albumin), and not to egg lecithin, which is found in egg yolk. Indeed, a recent review of patients with documented egg allergy who received propofol found that nearly all individuals had no reaction to the drug.
C. *Bacterial growth*: The current commonly used lipid emulsion formulation of propofol can support bacterial and fungal growth, and therefore, it is recommended that propofol should be used within 6 h of opening the vial to reduce the risk of infection from extrinsic contamination. Current formulation of propofol may contain 0.025 % of sodium metabisulfite or 0.005 % edetate to confer antimicrobial properties. Lidocaine, which possesses bacteriostatic properties, can be added to propofol to confer these properties to the mixture and potentially further reduce the risk of infection. A new bioequivalent microemulsion of the drug has been recently developed, which may be safer to use than the current formulation.
D. *Propofol infusion syndrome*: Prolonged infusions can rarely result in a condition called propofol infusion syndrome, characterized by lipemia, metabolic acidosis, rhabdomyolysis, renal failure, and cardiac failure. Children and critically ill patients, especially those receiving corticosteroids, appear to be at greatest risk.
E. *Propofol abuse*: Propofol abuse in academic anesthesiology has become a problem in recent years. Eighteen percent of all academic anesthesiology departments with training programs reported at least one incident of abuse or diversion in the past 10 years. There appears to be an association between lack of pharmacy accounting and the incidence of propofol abuse.

Thiopental

With the increasing use of propofol, thiopental is now much less frequently used than it was in the past. In fact, it is no longer available for use in the United States. Methohexital, a shorter-acting barbiturate, is still used for anesthesia for electroconvulsive therapy. Barbiturates are acidic drugs, but are manufactured as sodium salts which have a pH > 10. With this basic pH of greater than 10, thiopental precipitates when

mixed with acidic drugs, such as nondepolarizing neuromuscular blockers, which can completely occlude intravenous lines. Thiopental is available as a 2.5 % solution and the induction dose is 3–5 mg/kg in adults.

Mechanism of Action

Thiopental, being a barbiturate, shares many characteristics with other drugs of that class, including its mechanism of action: activation of GABA channels, causing increased duration of inhibitory chloride channel opening. In addition to its hypnotic actions in the brain, it also depresses the response to noxious stimuli in the dorsal horn of the spinal cord.

The onset of action of thiopental after a bolus dose has been shown to be slightly faster than that of propofol, though any clinical relevance of this is doubtful. Thiopental is highly lipid soluble and highly protein bound, but with a greater nonionized fraction, which leads to rapid initiation of action (30 s). Termination of action or awakening (10–15 min) occurs via redistribution (alpha elimination). Like propofol, thiopental also undergoes hepatic metabolism to inactive metabolites, but at a much slower rate (4–12 h beta elimination). Though emergence still occurs very rapidly after a bolus dose by redistribution, total recovery is much slower than with propofol. Indeed, a "hangover" effect from a single induction dose can last for hours, making thiopental a less attractive choice for ambulatory surgery. Compared to thiopental, methohexital is metabolized in the liver about three times faster than thiopental. Therefore, psychomotor recovery is faster with methohexital than with thiopental.

Cardiovascular Effects

Thiopental at induction doses typically results in a decrease in MAP, but to a lesser extent than that with propofol. Its hemodynamic effects are also more variable, depending largely on volume status, cardiac reserve, and preexisting sympathetic tone. Thiopental primarily causes venodilation, which reduces preload. Some degree of direct myocardial depression also occurs. In fact, thiopental possesses the strongest direct negative inotropic properties (myocardial contractility) of any IV anesthetic agent. Increases in heart rate and cardiac contractility occur as a result of a partially maintained baroreceptor response. This serves to minimize the decrease in cardiac output and MAP. However, in patients with inadequate baroreceptor response (such as in hypovolemia and congestive cardiac failure), blood pressure and cardiac output may fall dramatically. Adequate hydration, slow rate of injection, and titrated dosage help to mitigate these effects. In addition, thiopental has been shown to be less arrhythmogenic than propofol in an animal model.

Respiratory Effects

Respiratory effects of thiopental are similar to those of propofol. Apnea generally occurs with induction doses, though less consistently than with propofol. Smaller doses reduce minute ventilation from reductions in both tidal volume and respiratory rate. Thiopental is not as effective as propofol in blocking laryngeal reflexes in response to direct laryngoscopy and laryngeal mask airway placement, which may lead to laryngospasm in lightly anesthetized patients and bronchospasm in asthmatics. In addition, thiopental is associated with a greater incidence of postoperative sore throat and dysphagia after laryngeal mask airway placement when compared to propofol.

Central Nervous System Effects

Like other barbiturates, thiopental produces profound CNS depression. It is a potent cerebral vasoconstrictor, leading to reductions in CBF and ICP. Cerebral perfusion pressure is generally improved, as decreases in ICP are usually greater than decreases in MAP. Thiopental reduces $CMRO_2$ and provides protection against focal, but probably not global, cerebral ischemia. Thiopental attenuates one important cause of ischemic neuronal injury (NMDA-mediated glutamate excitotoxicity), unlike propofol, which has been found to enhance it. EEG suppression with thiopental is dose dependent, with a flatline occurring at high doses.

Like propofol, thiopental can be used to break refractory status epilepticus. Compared to propofol and midazolam, thiopental causes significantly less amnesia when used for equal levels of sedation. Thiopental has no analgesic properties, and some studies have suggested that it actually lowers the pain threshold (antianalgesic effect). Repeated administration of thiopental may cause physiologic dependency and acute tolerance.

Methohexital, in contrast to thiopental, can activate seizure foci, especially at low doses. This property of methohexital is useful in isolating seizure foci during surgical ablation. Methohexital is the drug of choice for induction of anesthesia for electroconvulsive therapy.

Other Effects

Other properties of thiopental include:

- Decreases renal blood flow and glomerular filtration rate.
- Decreases hepatic blood flow. With chronic barbiturate exposure, induction of hepatic enzymes and the cytochrome P450 system alters metabolism of certain drugs such as digoxin, tricyclic antidepressants, warfarin, and propranolol.

- An increase in the incidence of PONV, unlike propofol, which has the opposite effect.
- An unusual effect of thiopental is that patients may experience a garlic or onion taste during administration.
- Inadvertent arterial injection or infiltration into extravenous tissue causes extreme pain and potentially severe tissue injury.
- Because barbiturates stimulate the enzyme aminolevulinic acid synthase, leading to increased production of porphyrins, thiopental should not be given to patients with most types of porphyria.
- Along with etomidate, thiopental has been shown to impair eosinophil chemotaxis in vitro, though the clinical significance of this is not known.

Etomidate

Etomidate, due to its limited cardiovascular effects, is often used for induction of anesthesia in hemodynamically unstable patients and in those with significant cardiac disease. It is available as a 0.2 % solution and a typical adult induction dose is 0.2–0.3 mg/kg. The most commonly used formulation contains 35 % propylene glycol, which can cause significant pain upon injection and thrombophlebitis, similar to propofol. Similar injection techniques as those described for propofol have been used to minimize these problems. In addition, several alternative formulations have been developed which also can minimize these effects. One formulation replaces propylene glycol with 2-hydroxypropyl-β-cyclodextrin, while another uses a fat emulsion of medium- and long-chain triglycerides.

Mechanism of Action

Like propofol and thiopental, etomidate is thought to work through potentiation of $GABA_A$ receptors, though recent evidence suggests it may interact with alpha-2 adrenergic receptors as well. In addition, etomidate may have disinhibitory effects on parts of the central nervous system causing motor activity or myoclonus (30–50 % incidence with induction).

Etomidate is highly lipid soluble and protein bound, with a high nonionized fraction leading to a rapid initiation of action. Termination of action on the brain (5–10 min) is by redistribution to other organs. Etomidate is metabolized rapidly by hepatic and plasma esterases to inactive metabolites, which are excreted in the urine and bile. After the effects of a bolus dose are terminated by redistribution, this fast metabolism prevents any significant residual effects.

Cardiovascular Effects

Etomidate is most notable for its minimal cardiovascular effects. Only a very mild decrease in systemic vascular resistance (SVR) occurs with an induction dose, leading to a minimal decrease in MAP. Clinical concentrations cause no changes in myocardial contractility in vitro, and contractility and cardiac output are typically unchanged in vivo as well. Unlike propofol, etomidate seems to maintain baroreceptor reflexes. These properties make etomidate a good choice for patients in whom a decrease in MAP is particularly undesirable, such as hemodynamically unstable trauma patients or those with severe cardiovascular or cerebrovascular disease. Along with thiopental, etomidate has been shown to inhibit platelet function and prolong bleeding time, though the clinical significance of this is not known.

Respiratory Effects

Etomidate does not result in as profound respiratory depression as does propofol or thiopental, though induction doses may still result in apnea if it is co-administered with opioids. If maintaining spontaneous ventilation is desired, ketamine is probably a more reliable choice. Compared to thiopental, etomidate has been shown to lessen upper airway reflex response to direct laryngoscopy and endotracheal intubation.

Central Nervous System Effects

Like propofol and thiopental, etomidate decreases $CMRO_2$, CBF, and ICP, with the CPP well maintained. Unlike those agents however, etomidate has not been shown to provide neurologic protection from focal ischemia. It also does not raise the seizure threshold or terminate status epilepticus like the other induction agents and may actually activate seizure foci. Etomidate has no analgesic properties, and of all the IV induction agents, etomidate is most strongly associated with PONV.

Myoclonic movements, an undesirable side effect of etomidate induction, occur with a reported incidence of 30–50 %. This could prove problematic in a patient with an open globe injury, where such movements could significantly raise intraocular pressure. The incidence and intensity of these movements are dose dependent, and they are not associated with seizure-like EEG activity. The incidence can be significantly reduced in adults by pretreatment with small, subanesthetic doses of etomidate (0.03 mg/kg), but this has been shown to be ineffective in children. Other effective techniques to reduce the incidence of myoclonic movements after etomidate induction in adults include pretreatment with midazolam and opioids (fentanyl).

Other Effects

One especially unique and potentially important characteristic of etomidate is its suppression of adrenal steroid synthesis. Etomidate blocks the enzyme 11-β-hydroxylase, which is required for the production of aldosterone and cortisol. This adrenal suppression appears to be at least 100 times greater than its hypnotic potency, such that sub-hypnotic doses still result in inhibition of steroid synthesis. These effects can persist for days after discontinuation of a prolonged infusion, which has been shown to increase mortality in critically ill patients. For this reason, etomidate infusions are generally no longer used. However, the effects after a single bolus dose are less well known. Though results vary depending on the study, of which there have been many, a recent systematic review shows that adrenal suppression after an induction dose typically lasts 4–6 h in relatively healthy (ASA 1 and 2) patients. In critically ill patients, randomized controlled trials have shown the duration of adrenal suppression appears to be similar, although there is some observational data that suggests the suppression may last for up to 24 h. However, there is no evidence of any effect on mortality, and most studies show no difference in hospital or ICU length of stay or duration of ventilatory support.

Recently, two novel etomidate analogs have been developed with the goal of retaining the favorable pharmacologic properties of etomidate but effectively minimizing the adrenal suppression. The first, methoxycarbonyl-etomidate, does not appear to cause prolonged adrenal suppression following an induction dose due to its rapid metabolism by various esterases. The second, carboetomidate, has less affinity for 11-β-hydroxylase and has been shown in animal models to have dramatically less inhibitory effects on the enzyme.

Table 11.4 Properties of IV anesthetic agents

Agent	Favorable properties	Unfavorable properties
Propofol	• Rapid onset and recovery • Decreases $CMRO_2$, CBF, and ICP • Airway reflexes suppressed • Decreases nausea/vomiting	• Decrease BP, HR, and CO • Pain on injection • Decreases ventilatory drive
Thiopental	• Rapid onset and recovery • Decreases $CMRO_2$, CBF, and ICP • No pain on injection	• Decreases BP and CO and increases HR • Airway reflexes not suppressed adequately • Decreases ventilatory drive
Etomidate	• Rapid onset and recovery • Decrease $CMRO_2$, CBF, and ICP • Most stable cardiovascular profile	• Adrenal suppression • Pain on injection • Decreases ventilatory drive • Increases nausea/vomiting
Ketamine	• Analgesic properties • Bronchodilation • Minimal ventilatory suppression • Airway reflexes preserved • Increases BP, HR, and CO • Can be given by IM route also	• May increase ICP • Ischemia risk in patients with CAD • Emergence delirium

CMRO2 cerebral oxygen consumption, *CBF* cerebral blood flow, *ICP* intracranial pressure, *BP* blood pressure, *HR* heart rate, *CO* cardiac output, *CAD* coronary artery disease, *IM* intramuscular

Ketamine

Ketamine has many unique features which are distinct from the other induction agents (Table 11.4), the first being its mechanism of action. The induction dose of ketamine is 1–2 mg/kg IV, and it can also be given IM at 3–5 mg/kg for induction. Recently, the *S*-(+)-stereoisomer of ketamine has become available, which has greater anesthetic and analgesic potency than the racemic mixture and faster metabolism, affording a faster emergence and return of function.

Mechanism of Action

Unlike the other agents, which induce anesthesia by activating inhibitory GABA receptors, ketamine works by inhibiting stimulatory NMDA receptors (NMDA receptor antagonist). This is the same mechanism as the hallucinogenic drug phencyclidine, a close chemical relative of ketamine. This action of ketamine is responsible for its unique state of "dissociative" anesthesia, in which the subject is dissociated from its surroundings. In physiologic terms, ketamine suppresses sensory impulses through the thalamus, while the limbic system is excitated. This may manifest as eye opening, swallowing, and muscle stiffness.

Other mechanisms of action of ketamine include interaction with opioid receptors, with a preference for mu and kappa receptors. The affinity of ketamine for these receptors is 10 times less than that for the NMDA receptors, and naloxone does not antagonize the analgesic effects of ketamine. There is also evidence that ketamine has an antagonistic interaction with monoaminergic, muscarinic, and nicotinic receptors. Indeed, ketamine produces anticholinergic symptoms (tachycardia and bronchodilation). Ketamine at high doses has local anesthetic properties, which may occur through its ability to inhibit neuronal sodium channels.

Ketamine is highly lipid soluble but is less protein bound than other agents. Combined with the increase in cerebral

blood flow and cardiac output it produces, initiation of action is rapid. Like the other induction agents, the effects of a bolus dose of ketamine are terminated by redistribution (12–15 min) to peripheral tissues. It then undergoes rapid hepatic metabolism, with the metabolites excreted renally (elimination half-life 2 h). The primary metabolite, norketamine, is active and has one third to one fifth the potency of the parent compound.

Cardiovascular Effects

Ketamine is also the only induction agent that has stimulatory cardiovascular effects. It causes central sympathetic stimulation and blocks norepinephrine reuptake, which leads to an increase in heart rate, cardiac output, SVR, and MAP. It has been shown to exert positive inotropic (contractility) and lusitropic (myocardial relaxation) effects via β-adrenergic receptor activation. These effects can be attenuated by prior administration of benzodiazepines or opiates. In addition, ketamine has been shown to activate GABA- and glycine-mediated attenuation of cardiac parasympathetic efferent neurons, also contributing to the clinically observed tachycardia.

Despite the indirect stimulatory effects of ketamine, it has actually been shown to cause direct myocardial depression, which can be unmasked in patients with depleted catecholamine stores (critically ill patients) or in those with sympathetic blockade (spinal cord transection or spinal anesthesia). The classic teaching is that ketamine is a poor choice for induction in patients with coronary artery disease, uncontrolled hypertension, and arterial aneurysm given its hemodynamic profile. However, the drug has been shown to have no effect on postoperative troponin levels when used for induction in patients undergoing coronary artery bypass graft surgery.

Respiratory Effects

Ketamine causes little or no respiratory depression at induction doses. It is the most reliable choice of induction agent if maintenance of spontaneous ventilation is desired. It is also the only induction agent that causes bronchodilation and is therefore useful in asthmatic patients. In fact, subanesthetic doses can be used to treat persistent bronchospasm. Ketamine is also a potent stimulator of respiratory secretions, which can be prevented by prior administration of an anticholinergic agent. Unlike other hypnotics and opiates, which can have the opposite effect, ketamine has been shown to stabilize airway patency during sedation and anesthesia. Though upper airway reflexes remain largely intact, the ability to protect the airway cannot be assumed.

Central Nervous System Effects

Ketamine is also unique in its effect on the CNS. It is the only induction agent that increases $CMRO_2$, CBF, and ICP, and the traditional teaching has, therefore, been that the agent should be avoided in patients with preexisting increased ICP or decreased intracranial compliance. However, evidence now suggests that ICP does not increase when patients are mechanically ventilated, when ketamine is co-administered with a benzodiazepine, and when nitrous oxide is avoided. Ketamine may, therefore, improve CPP in patients with brain injury given its cardiovascular profile. Ketamine can produce myoclonic activity; however, it is still considered to possess anticonvulsant properties and can be used to terminate status epilepticus. It has also been used effectively in low doses to terminate Parkinsonian tremor. Ketamine as a bolus has been shown to increase bispectral index values, while slower dosing has no effect.

A particularly useful property of ketamine is its analgesic effect. Small doses can be used for analgesia and sedation without respiratory depression. Low-dose infusions (10 mg/h) can be used for additional analgesia intraoperatively or postoperatively, which is particularly useful in patients with significant opiate tolerance. In fact, intraoperative ketamine has been shown to reduce postoperative opiate usage and improve rehabilitation after spine, abdominal, hip, and knee surgery. Postoperative low-dose infusions also improve pain and decrease opiate usage. Ketamine can improve analgesia when used as an adjuvant to PCA fentanyl or morphine. After thoracotomy, the addition of ketamine to PCA morphine decreases morphine consumption and improves respiratory parameters. Intravenous ketamine has also been shown to potentiate epidural analgesia, and preoperative epidural ketamine has been shown to decrease intraoperative and postoperative analgesic requirements. Lastly, a ketamine gargle prior to induction of anesthesia has been shown to decrease the incidence and severity of postoperative sore throat.

An undesirable effect of ketamine is its association with psychomimetic emergence reactions. This can be particularly prominent after rapid wake-up from induction doses. Patients can experience nightmares, illusions, hallucinations, and delirium. The risk is lower in children and in those premedicated with benzodiazepines. The incidence has also been shown to be decreased by positive suggestion prior to induction. Despite the potential for these emergence reactions with ketamine itself, it has actually been shown to reduce the risk of emergence agitation after sevoflurane anesthesia in pediatric patients.

Other Effects

Ketamine potentiates the action of nondepolarizing neuromuscular blocking agents, a property unlike other intravenous

induction agents but shared by the volatile inhalational agents. Ketamine may also possess anti-inflammatory properties, suggested by a decrease in inflammatory cytokines during cardiopulmonary bypass when a ketamine infusion is administered. Ketamine as an intraoperative bolus has also been shown to decrease the incidence of postoperative shivering.

Clinical Review

1. The following intravenous induction agent has the slowest onset of action:
   A. Propofol
   B. Thiopental
   C. Etomidate
   D. Ketamine
2. Greatest decrease in blood pressure can occur with the following agent:
   A. Propofol
   B. Thiopental
   C. Etomidate
   D. Ketamine
3. Upper airway reflexes are best suppressed by the following agent:
   A. Propofol
   B. Thiopental
   C. Etomidate
   D. Ketamine
4. The following agent produces bronchodilation:
   A. Propofol
   B. Thiopental
   C. Etomidate
   D. Ketamine
5. Pain on intravenous injection may be greatest with:
   A. Propofol
   B. Thiopental
   C. Etomidate
   D. Ketamine
6. The following agent suppresses adrenal steroid synthesis:
   A. Propofol
   B. Thiopental
   C. Etomidate
   D. Ketamine
7. The following agent has analgesic properties:
   A. Propofol
   B. Thiopental
   C. Etomidate
   D. Ketamine
8. Psychomimetic reactions on emergence may occur with:
   A. Propofol
   B. Thiopental
   C. Etomidate
   D. Ketamine
9. Induction agent with the most stable cardiovascular profile is:
   A. Propofol
   B. Thiopental
   C. Etomidate
   D. Ketamine
10. Following agent is contraindicated in patients with porphyria:
    A. Propofol
    B. Thiopental
    C. Etomidate
    D. Ketamine

Answers: 1. D, 2. A, 3. A, 4. D, 5. C, 6. C, 7. D, 8. D, 9. C, 10. B

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Opioids and Benzodiazepines

12

James C. Krakowski and Steven L. Orebaugh

Opioids and benzodiazepines are two classes of medications often administered in conjunction with one another due to their additive and synergistic effects despite differing mechanisms of action. Although ubiquitous in the practice of medicine, perhaps no other medical specialty administers these powerful medications with such frequency and scope as that of anesthesiology. An in-depth understanding of opioids and benzodiazepines is of paramount importance to the safe and effective practice of anesthesia.

Opioids

Classification

The term *opiate* has historically been used to describe alkaloid compounds extracted from the sap of the opium poppy. In contrast, the term *opioid* reflects all compounds, both naturally occurring *and* manufactured, that produce opiate-like effects. The term *narcotic* has often been used synonymously with opioid lending to its Greek word of origin, *narkotikos* or "benumbing," although its use has fallen out of favor secondary to its legal connotations.

Opioids may be broadly classified according to their origin. The natural opium alkaloids include thebaine, codeine, and, perhaps the most recognized, morphine, which serves as the gold standard by which other opioids are compared. Semisynthetic opioids are derived as a result of direct modifications to the morphine or thebaine molecules and include compounds such as heroin (diacetylmorphine) and hydromorphone. Fully synthetic opioids are comprised of structurally distinct compounds such as methadone and the fentanyl analogues.

In addition, naturally *endogenous* opioids also exist within animals to produce physiologic opiate-like effects as hormones and neuromodulators. Several principal families of endogenous opioids have been discovered in mammalian brain to include the enkephalins, endorphins, dynorphins, and, most recently, endomorphins, which are uniquely mu-receptor-specific agonists.

Structure–Activity Relationships

Although opioid compounds possess distinct chemical structures, observed structural similarities are thought to relate to their observed clinical effects. Examining the molecular skeletal formulae of these compounds reveals discernible structural similarities such as the pentacyclic structure and accompanying phenolic hydroxyl group of morphine and its derivatives (Fig. 12.1). Furthermore, relatively minor chemical changes to the pentacyclic structure may produce significant alterations in pharmacologic effect. For example, the prototypal opioid agonist morphine differs from that of pure opioid antagonist naloxone by several functional groups. In addition to differences in agonist versus antagonist activity, alterations in opioid chemical structure may also affect lipid solubility, receptor affinity, and resilience to metabolism. One such pharmacologic distinction may be readily seen within opioid enantiomers, such that the (−)- or levo-stereoisomer configuration possesses superior potency due to greater receptor specificity. Of note, (−)-morphine is the naturally occurring isomeric form, while dextrorotatory or (+)-morphine provides no analgesic effect.

Pharmacokinetics

Pharmacokinetics includes the processes of absorption, distribution, metabolism, and excretion. With respect to opioids, these processes characterize the concentration of

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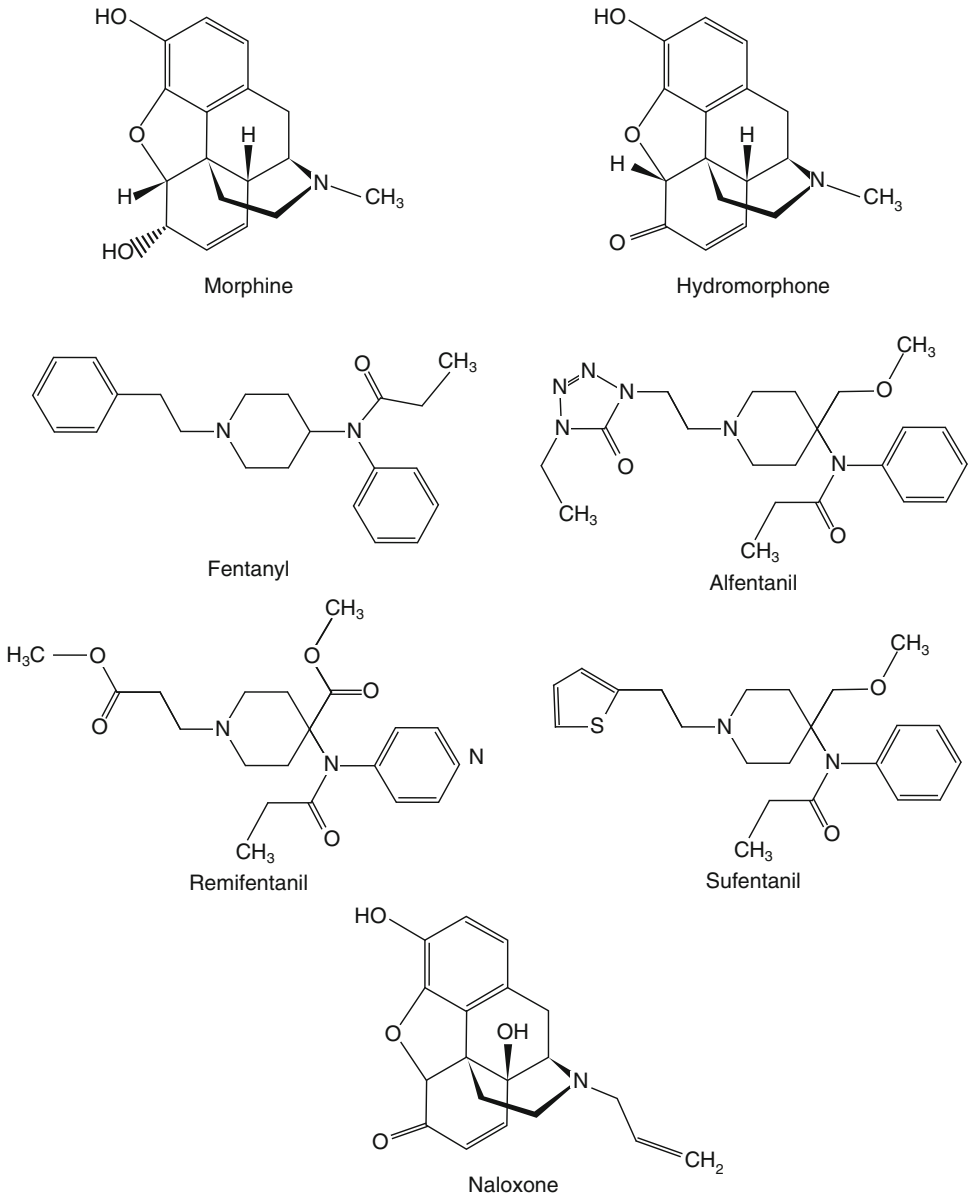

Fig. 12.1 Chemical structures of select opioid agonists and antagonist (naloxone)

administered opioid that reaches its receptor action sites with time. Opioid pharmacokinetics are primarily influenced by several variables including the route of administration, protein binding, pK_a, and lipid solubility.

Route of Administration

Opioid absorption varies with route of administration. When given orally, the majority of morphine derivatives display reduced bioavailability as a result of significant first-pass metabolism within the liver. Indeed, the bioavailability of oral morphine has been shown to vary between 35 and 75 %. To avoid the first-pass effect as well as variable gastrointestinal (GI) absorption, opioids are most often clinically administered intravenously (IV) during the perioperative period. Parenteral opioid utilization also provides a more rapid attainment of peak plasma concentration and subsequent physiologic effects.

Protein Binding

Opioids circulate as a variable fraction bound to plasma proteins, which are primarily albumin and alpha1-acid glycoprotein (AAG). The unbound or free fraction of opioid is proportional to its volume of distribution, whereby the free form is able to traverse biologic membranes into peripheral tissues. Opioid-protein binding is also pH dependent so that reduced pH results in decreased binding and greater free fraction to interact with opioid receptors. The importance of opioid-protein binding may be seen clinically with the inherently decreased AAG concentrations found in newborns and infants, with subsequent rise in opioid free fraction, resulting

Table 12.1 Characteristics of select opioid agonists

Opioid agonist	Bolus dose (IV)	Peak effect	Plasma half-life	Context-sensitive half-time (3 h infusion)
Morphine	0.02–0.05 mg/kg	30 min	3–4 h	
Hydromorphone	0.002–0.005 mg/kg	15 min	2–4 h	
Methadone	0.02–0.05 mg/kg	20 min	>24 h	
Meperidine	0.25–0.5 mg/kg	7 min	2–4 h	
Fentanyl	0.5–1 mcg/kg	3 min	1 h	2 h
Sufentanil	0.1–0.2 mcg/kg	3 min	1 h	<0.5 h
Alfentanil	5–15 mcg/kg	2 min	15 min	1 h
Remifentanil	0.1–0.3 mcg/kg	1.5 min	10 min	

in lower dosing thresholds for both anesthesia as well as respiratory depression. In contrast, elevated AAG levels occur in a variety of pathophysiologic states including burn injuries, trauma infection, the postoperative period, and other inflammatory states.

pK_a

In order to gain access to their central nervous system (CNS) receptor sites, opioids must traverse biologic lipid membranes, most notably the blood–brain barrier. This property is heavily dependent on their degree of ionization and lipid solubility. Opioids may be classified as weak bases with pK_a values typically greater than 7.4, excluding alfentanil and remifentanil, which possesses pK_a values of ~6.5 and ~7.07, respectively. Thus, the majority of opioids compounds remain in the charged or *ionized* state at physiologic pH, leaving a minority in the uncharged state with ability to penetrate the CNS.

Lipophilicity

The lipophilicity of opioids may also be quantified numerically via the octanol–buffer partition coefficient, wherein a greater value signifies greater hydrophobicity of the drug and consequently increased distribution and membrane permeability. For example, morphine possesses an octanol–buffer partition coefficient 1, while that of fentanyl is 955. These physicochemical properties are evident clinically in that morphine administration has been shown to result in a much slower time-to-peak effect (20 min) in comparison to fentanyl (3–4 min) or its analogues, alfentanil and remifentanil (within 2 min).

Elimination

The elimination of opioids primarily occurs via enzymatic metabolism within the liver. This biotransformation produces hydrophilic rather than lipophilic compounds ultimately suitable for renal excretion. The necessary metabolic reactions may be subdivided into phase 1, oxidative or hydrolytic reactions via the liver's cytochrome P450 (CYP) pathway, and phase 2, conjugation reactions, namely, glucuronidation via uridine diphosphate glucuronosyltransferase (UGT). The majority of opioids undergo CYP enzymatic metabolism with notable exceptions including the glucuronidation of morphine and hydromorphone. Because the CYP pathway is ubiquitous in drug metabolism, opioids metabolized by these means are potentially subject to changes in clearance by other coadministered medications that either induce or inhibit the CYP3A4.

Opioid plasma half-life values vary from minutes to hours (Table 12.1). In contrast to its relatively brief onset and duration of effect, an opioid such as fentanyl displays a relatively long plasma half-life due to its high lipophilicity causing significant redistribution into peripheral tissues. These tissues in turn may serve as a depot or reservoir, allowing the drug to slowly reenter the circulation. Duration of action of intravenous anesthetics has historically been related to the elimination half-life. This method does not accurately account for the effect of redistribution to the central plasma compartment during continuous anesthetic infusions. Thus, Hughes et al. defined the *context-sensitive half-time* as the time required for the plasma drug concentration to decrease by half after infusion discontinuation. The "context" therefore represents the total infusion time.

Pharmacodynamics

Opioid pharmacodynamics encompasses their mechanism of action through the binding of opioid receptors in order to produce biochemical and physiologic effects. Evidence supporting the notion of multiple opioid receptor subtypes stems from radiolabeling and physiologic studies performed during the 1970s. Four principal classes of opioid receptors have ultimately been confirmed via molecular cloning, including the MOP, or mu-opioid receptor (μ); DOP, or delta-opioid receptor (δ); KOP, or kappa-opioid receptor (κ); and, most recently, NOP, or nociceptin/orphanin FQ receptor (ORL-1).

The activation of specific opioid receptor subtypes has been shown to produce a variety of physiologic and behavioral effects (Table 12.2). Perhaps the best known effect is

Table 12.2 Physiologic effects of the opioid receptor subtypes

	Receptor			
Effect	MOP (μ)	DOP (δ)	KOP (κ)	NOP (ORL_1)
Analgesia	+++	++	++	–
Sedation	++	–	++	–
Respiratory depression	+++	++	–	–
Decreased gastrointestinal motility	++	++	+	–
Euphoria	+++	–	–	–
Dissociative and deliriant effects	–	–	+++	–
Miosis	++	–	–	–

MOP mu-opioid receptor, *DOP* delta-opioid receptor, *KOP* kappa-opioid receptor, *NOP* nociceptin-opioid receptor, ORL_1 opiate receptor-like protein (Adapted from Rang H, et al. Analgesic drugs, Rang & Dale's pharmacology, 7th ed. Churchill Livingston; 2010:503–24)

that of analgesia, which is predominantly produced by activation of opioid MOP receptors. In addition to analgesia, MOP receptor activation also may result in unwanted effects including respiratory depression and dependence (see side effects).

The mechanism by which opioids produce analgesia resides in their inhibitory influence on neuronal pain pathways. Opioid agonists bind their corresponding opioid receptors located on the presynaptic terminals of nociceptive Aδ- and C-fibers within the spinal cord. This opioid-GPCR interaction results in the characteristic inhibition of the adenylyl cyclase enzyme responsible for the conversion of adenosine triphosphate (ADP) to cAMP. Reduced intracellular cAMP concentrations subsequently lead to the inhibition of voltage-gated calcium channels, thereby preventing the release of pronociceptive neurotransmitters, including substance P, gamma-aminobutyric acid (GABA), and calcitonin gene-related peptide (CGRP). Opioid agonists also produce analgesia supraspinally by impeding the release of inhibitory neurotransmitter GABA within the brain's periaqueductal gray (PAG) matter region. This inhibition of GABA subsequently disinhibits the release of norepinephrine (NE) and serotonin (5-HT) to the spinal posterior (dorsal) horn, which in turn blunts afferent nociceptive pathways.

Pharmacogenetics

Clinical opioid dosing has been shown to vary by as much as 40 %, and a portion of this variability is thought to occur as a result of genetic differences affecting opioid pharmacokinetics and pharmacodynamics. One allelic disparity may be seen in the CYP2D6 enzyme responsible for codeine metabolism, wherein individuals with poor enzyme activity possess reduced codeine efficacy as a result of decreased codeine metabolism to morphine. Similarly, single-nucleotide polymorphisms in the OPRM1 gene responsible for the opioid mu-receptor protein have been associated with significantly increased opioid requirements as well as decreased opioid-induced miosis and respiratory depression. Pharmacogenetics provides a continued area of interest in Anesthesia-related research in hopes of providing insight into the heterogeneity of patient responsiveness and effective opioid therapy.

Indications and Usage

The anatomical distribution of opioid receptors has been localized to the brain and spinal cord of the CNS as well as throughout nerves innervating peripheral tissues. Opioid receptor activation at these sites has been shown to elucidate an array of physiologic and behavioral effects, many of which have been harnessed for patient benefit in the perioperative period.

Analgesia

Opioids are often administered to provide analgesia for both acute and chronic pain states. These effects are mediated through direct inhibition of nociceptive pathways as well as attenuation of pain perception, likely through the sense of euphoria and sedating effects. Morphine and related opioid compounds selectively block nociception while sparing the somatosensory discrimination of proprioception, light touch, and temperature change. An important feature of opioid analgesia is that opioids are more effective in relieving continuous, dull quality pain often accompanying tissue injury and inflammation, rather than sharp, intermittent, or neuropathic pain.

When administered with analgesic dosing, opioids have proven clinically relevant in conjunction with the inhalational maintenance of anesthesia by significantly reducing the minimum alveolar concentration (MAC). When combined with sevoflurane, fentanyl has also been demonstrated to reduce the MAC associated with blocking the adrenergic response to surgical incision and laryngoscopy with tracheal intubation.

Sedation and Anxiolysis

Opioids have been shown to produce drowsiness and cognitive impairment. These effects may be amplified by concomitant use of other anxiolytics such as benzodiazepines. The involved areas of the brain are thought to be similar to those affected by known sedative–hypnotic class medications such as propofol and the benzodiazepine midazolam, as brain imaging has revealed these areas show a similar decrease in signaling after morphine administration. Additionally, these

sleep-inducing and anxiolytic effects assist analgesic properties by decreasing attention to noxious stimuli.

Potent opioids such as fentanyl and its derivatives are often used as anesthetic adjuncts, reducing the required concentrations of volatile anesthetics needed for general anesthesia. However, if opioids are utilized as a primary anesthetic, the additional need for unconsciousness and amnesia must be addressed. These aspects of a complete general anesthetic may be supplied with the coadministration of a benzodiazepine or element of volatile agent.

Respiratory Depression

Equianalgesic doses of opioids cause similar respiratory depression by binding to MOP and DOP receptors within the medulla. The depressant mechanism on medulla is twofold, involving inhibition of respiratory rhythm and hence rate and reduced sensitivity of medullary chemoreceptors to carbon dioxide. Typical analgesic doses of opioids are sufficient to produce increased $PaCO_2$ levels. Although respiratory depression may be the greatest safety concern involving opioids, this effect may be employed therapeutically in certain instances. For example, opioid administration may be used to treat subjective dyspnea or "air hunger," resulting in agitation, seen in chronic pulmonary disease and congestive heart failure, or to depress the spontaneous rate in patients receiving mechanical ventilation. As with sedation, the concomitant use of anxiolytics such as benzodiazepines acts synergistically in depressing respiration.

Cardiovascular Stability

Opioids given in typical therapeutic doses generally do not compromise hemodynamic stability, which allows their use during times when cardiac demand poses a concern. High doses of opioids, such as those used for anesthetic induction, are known to cause reproducible bradycardia. Animal studies using fentanyl suggest that MOP receptor action within the nucleus ambiguous of the medulla decreases the inhibitory effect of GABA on cardiac vagal tone, thereby disinhibiting the parasympathetic reduction in heart rate. This decrease in heart rate coupled with the reduction in preload and inotropy has allowed morphine to be a well-established therapy in reducing myocardial oxygen consumption in acute myocardial infarction and providing symptom relief from angina.

Cough Reflex Suppression

Most opioids possess antitussive properties, blunting the cough reflex possibly through a mechanism of inhibition of the cough center within the medulla.

Miosis

Pupillary constriction has been long recognized as a diagnostic clinical finding of opioid exposure independent of tolerance. This phenomenon has proven clinically relevant in the diagnosis of opioid intoxication because other causes of sedation or respiratory depression typically result in mydriasis. The mechanism of opioid-induced miosis stems from the disinhibition of the Edinger–Westphal nucleus, allowing the parasympathetic ciliary ganglion to subsequently activate pupillary constriction.

Side Effects and Toxicity

Despite their many effective clinical uses, the administration of opioids may result in a number of profound side effects. Many opioid-induced side effects have been attributed to specific receptor subtypes (Table 12.2). The central and peripheral receptor distribution often corresponds with their observed toxicity, including respiratory depression and reduced GI motility, respectively. Additional caution should be implemented in patients with known hepatic or renal insufficiency, as found with advanced age, because these disease states may exacerbate opioid toxicity through impaired metabolism and clearance, respectively.

Respiratory Depression

Respiratory depression remains the leading cause of mortality in acute opioid toxicity. Therapeutic doses of opioids are sufficient to cause respiratory depression with a characteristic decrease in respiratory rate that may also exhibit irregular rhythm. In addition, higher doses may cause reduced tidal volumes and decreased pulmonary compliance by affecting neuronal input to the upper airway, chest, diaphragm, and accessory muscles.

This dose-dependent respiratory depression may be worsened by a number of clinical factors including coadministered medications such as benzodiazepines, bimodal extremes of age, decreased stimulation with sleep or analgesia, and disease states resulting in lung dysfunction or reduced responsiveness to elevated $PaCO_2$. Furthermore, because opioids reduce the sensitivity of medullary chemoreceptors to elevated $PaCO_2$, oxygen therapy during this time may lead to precipitous apnea by eliminating the hypoxia serving as the sole respiratory driving force. Obstructive sleep apnea has been shown to be a significant risk factor for respiratory depression in patients receiving opioids.

Sedation and Cognitive Impairment

Opioid-induced sedation and resultingcognitive impairment may worsen respiratory depression and may be exacerbated by coadministered depressant or anxiolytic medications. These drugs are typically avoided in cases of head trauma in order to avoid a confounding decrease in mentation or hypercapnia-induced cerebral vasodilation.

Cardiovascular Effects

In addition to bradycardia, opioids may cause several effects to warrant caution in patients with severe hypovolemia. One such effect is peripheral vasodilation and consequent reduction in preload, which is of particular concern with the histamine-releasing effect of morphine. Orthostatic hypotension may also result through the inhibition of baroreceptors.

Euphoria

Euphoria remains a prominent secondary effect of MOP receptor activation that assists in opioid analgesia, yet may increase the potential for abuse and addiction. Opioid-induced euphoria and rewarding properties are thought to entail the mesolimbic dopamine system and its connections from the ventral tegmental area (VTA) to the nucleus accumbens. The continuous exposure to beta-endorphin activity on MOP receptors during chronic pain states results in the dysfunction of MOP receptor function within the VTA, and this process may account for the reduced experience of euphoric effects despite beneficial analgesia in chronic pain sufferers. In contrast, some patients may experience dysphoria after opioid exposure that is attributed to agonist activity on KOP receptors.

Nausea and Vomiting

The incidence of nausea and vomiting is similar among opioids administered in equianalgesic doses. The mechanism of emetogenic response is mediated through opioid stimulation of the chemoreceptor trigger zone within the medullary area postrema, and this ill effect typically diminishes as tolerance develops with continued dosing.

Gastrointestinal and Urinary Effects

Opioid administration is known to cause reduced GI motility while increasing sphincter tone. As a result, constipation is a frequent, clinically significant side effect that may be observed after a single dose of morphine. Although constipation is perhaps the most common GI grievance, delayed gastric emptying and decreased absorption may also occur. The mechanism of these phenomena is thought to primarily involve MOP receptor activation within the peripheral enteric innervation of the gut. Additionally, opioid use may adversely increase GI regulatory sphincter tone, which is evident with narrowing of the sphincter of Oddi that may cause colicky, biliary-related pain.

Opioid exposure may also adversely affect urination, particularly in the postoperative period, by producing difficulty in voiding that may lead to urinary retention. These effects are thought to occur as a result of the opioid-induced inhibition of the detrusor contraction, voiding reflex, and sensation of bladder fullness.

Muscle Rigidity and Proconvulsant Activity

High-dose administration of opioids is known to cause increased incidence of muscle rigidity, convulsions, and difficulty with mask ventilation. Increased rigidity primarily involves the jaw and chest wall musculature and often occurs following anesthetic induction dosing, while seizure activity remains rare even at supratherapeutic levels. The mechanism responsible for these side effects is thought to involve a decrease in GABA neurotransmitter release, resulting in disinhibition within the brain. Although opioid metabolites are generally inactive, the metabolites M3G of morphine and H3G of hydromorphone have been shown to possess epileptiform activity in animal models. Although difficulty in patient ventilation after opioid administration was once thought secondary to chest wall muscle rigidity, it has been shown more likely a result of central MOP receptor stimulation causing laryngeal vocal cord closure.

Inhibition of Thermoregulation

Opioids are known to disrupt natural thermoregulation by significantly reducing the thresholds for both shivering and vasoconstriction and suppressing the fever response, which may mask the presence of infection or inflammation.

Immune Modulation

Opioids have also been shown to modulate both cellular and humoral immune system functioning, inhibiting the activity of phagocytes, natural killer cells, cytokine release, and antibody creation. This immune suppression is thought to occur via both central and peripheral opioid receptor activation and may explain the increased incidence of infection associated with chronic opioid use. Additionally, animal studies have shown that clinical doses of morphine result in the progression of breast tumor neovascularization.

Hormonal Effects

Opioids affect the release of many hypothalamic–pituitary–adrenal axis hormones. One prominent result is decreased levels of circulating sex hormones that may occur within hours through hypogonadotropic hypogonadism. Opioid exposure also inhibits dopamine release, resulting in elevated prolactin levels, and may also increase the release of antidiuretic hormone (ADH).

Paradoxical Response

Paradoxical responses following opioid therapy have been reported in which patients experience increased sensitivity to painful stimuli. This heightened nociceptive state is thought to stem from opioid-induced sensitization of nociceptive pathways both centrally and peripherally. Patients experiencing this opioid-induced hyperalgesia may display reduced opioid effectiveness without known disease progression or new onset pain complaints or generalized allodynia unrelated to prior pain.

Tolerance, Dependence, and Withdrawal

Tolerance is a known consequence after opioid administration, displaying reduced receptor agonist activity that subsequently

requires progressively higher doses in order to achieve a similar effect. Significant variability exists with regard to tolerance susceptibility among opioid-induced clinical effects such that decreased efficacy in analgesia may be seen rapidly, while the effects of respiratory depression, miosis, and reduced gastrointestinal motility remain relatively spared.

Opioid tolerance is thought to result from adaptive changes at multiple levels, including individual MOP receptors, cells, synapses, and their larger, interconnected neuronal networks. These adaptations attempt to maintain homeostasis in spite of opioid agonism and, when continued over extended periods, may provide the basis for dependence and opioid withdrawal syndrome following abrupt discontinuation. Opioid withdrawal signs and symptoms are often the inverse of their observed clinical effects, exhibiting such effects as agitation, hypertension, fever and chills, diaphoresis, nausea and vomiting, and diarrhea.

Opioid Agonists

Morphine

The term *morphine* stems from "Morpheus," the Greek god of dreams, and was first coined by Serturner with the isolation of this drug from opium at the start of the nineteenth century. As the archetypal MOP receptor agonist, morphine provides a gold standard by which other opioids are compared. Morphine is available in a variety of preparations for administration orally and parenterally, yet possesses relatively poor CNS penetrance due to its albumin-bound fraction, ionization at physiologic pH, low lipid solubility, and rapid glucuronidation.

Morphine remains ubiquitous due to its many therapeutic uses including analgesia, sedation, and cardiovascular benefits. As a relatively long-acting opioid analgesic averaging 1–3 h, morphine is used in treating both acute and chronic pain states. As a hydrophilic compound with greater difficulty in crossing lipid membranes, morphine is often administered via epidural route for slow onset and prolonged duration. Through vasodilatory and bradycardic effects, morphine is commonly used in relieving angina and as a standard co-therapy in myocardial infarction, reducing myocardial oxygen demand. Morphine also remains a choice therapy in treating dyspnea from pulmonary edema.

Morphine metabolism occurs at hepatic and extrahepatic sites, producing active metabolites contributing to both its therapeutic use and side effect profile. Morphine-6-glucoronide (M6G) is the predominant metabolite that holds greater analgesic effect than its parent compound. The lesser metabolite, morphine-3-glucoronide (M3G), possess proconvulsant activity and may lead to hyperalgesia with accumulation. The clearance of these metabolites may be profoundly affected by decreased renal function, leading to their accumulation and toxicity.

Many prominent side effects of morphine result from its unique stimulation of histamine release from mast cells independent of opioid receptors, causing effects ranging from pruritus and skin urticaria to hypotension and bronchospasm, hence morphine should be used with caution in asthmatics. Additionally, caution should be used in patients with sulfa allergies as parenteral morphine preparations often contain sulfites.

Methadone

Methadone is a synthetic MOP receptor agonist known for possessing both a longer plasma half-life and higher oral bioavailability in comparison to morphine. Because of a high lipid solubility and greater tissue protein binding relative to plasma, methadone possesses a large volume of distribution and, consequently, a plasma half-life that may exceed 24 h. This results in a characteristically prolonged onset and duration of opioid effect.

In comparison with morphine, methadone has been shown to have decreased incidence of withdrawal signs, observed euphoric effect, and is generally thought to be less prone to tolerance development and potential for abuse. Thus, the pharmacologic profile of methadone permits its primary use in treating opioid withdrawal. In addition to its MOP receptor-mediated analgesic properties, methadone also antagonizes *N*-methyl-D-aspartate (NMDA) receptors, which may assist in treating neuropathic pain resistant to other opioids.

Hydromorphone

Hydromorphone remains a commonly utilized semisynthetic MOP receptor agonist during the perioperative period. Like morphine, hydromorphone may be administered through a variety of routes, yet it has a more rapid onset approximately within 5 min due to greater lipid solubility. The peak effect may require up to 20 min to allow for adequate BBB penetration. With a potency roughly 8 times greater than that of morphine and concentrated formulations available, hydromorphone may prove advantageous in dosing patients with elevated opioid requirements.

Fentanyl

Fentanyl is a synthetic MOP receptor agonist with potency roughly 80–100 times that of morphine. Fentanyl has greater lipid solubility than both hydromorphone and morphine, with a quicker onset time of less than 30 s and achievement of maximum effect within minutes. Upon entering the plasma, fentanyl rapidly distributes to vascular sites including the brain, heart, and lungs and from these sites rapidly redistributes to muscle and adipose tissues. Consequently, termination of action occurs more rapidly than morphine primarily through drug redistribution rather than elimination. Adipose tissue serves as a reservoir, gradually releasing the drug back into circulation, particularly with accumulation after large or frequent dosing. Thus, much like methadone, the plasma half-life of fentanyl may extend well beyond its

observed clinical effects. Fentanyl and its analogues also circulate largely bound to the acute phase reactant, AAG.

In addition to parenteral and transbuccal delivery, the high potency of fentanyl permits administration via transdermal patch. This route displays a delayed onset and steady state level and may remain active for 24 h following removal due to delayed release from subcutaneous stores.

Sufentanil

Sufentanil is a fentanyl analogue with potency roughly 500–1,000 times that of morphine. It is the most lipophilic of the commonly used opioids. Despite similar characteristics to fentanyl, including its clinical use and toxicity, sufentanil displays less volume of distribution, greater duration of analgesia, and decreased respiratory depression.

Alfentanil

Alfentanil is a fentanyl analogue with potency roughly 20 times that of morphine. In contrast to most opioids, alfentanil possesses a lower pK_a value of 6.5, so that the majority of the drug is available in the nonionized form at physiologic pH, thereby allowing a greater portion of the drug to penetrate into the CNS. In comparison with fentanyl, alfentanil possesses decreased lipid solubility, volume of distribution, and potency, yet displays more rapid onset and overall briefer duration of effect. Reduced plasma clearance and half-life prolongation of alfentanil have been shown to occur in patients with hepatic cirrhosis and are thought to occur due to a relatively low hepatic extraction ratio.

Remifentanil

Remifentanil is a fentanyl analogue that possesses similar potency. The structure of remifentanil is unique in its hydrolytic cleavage by plasma and tissue esterases, which differ from pseudocholinesterase and are thus unaffected by its deficiency. Although not as pronounced as alfentanil, remifentanil also possesses a pK_a value less than physiologic pH, permitting rapid CNS penetration. Its context-sensitive half-time is roughly 4 min, is independent of infusion duration, and minimally affected by hepatic and renal function. Due to such pharmacologic properties, remifentanil infusion may be used for sedation and analgesia during monitored anesthesia care or general anesthesia cases. However, it can increase incidence of hypotension and bradycardia intraoperatively.

Meperidine

Meperidine is a weak MOP receptor agonist with roughly 1/5 the potency of morphine. In addition to relatively weak MOP receptor effects, meperidine also exhibits anticholinergic and local anesthetic activity. It is often utilized postoperatively as an effective anti-shivering therapy, reducing the shivering threshold twofold greater than that of vasoconstriction. Meperidine is known to have a significant side effect profile, including typical morphine-like side effects and histamine release, as well as proconvulsant activity from its metabolite, normeperidine.

Opioid Partial Agonists and Mixed Agonist–Antagonists

In contrast to pure opioid agonists, opioid partial agonists and mixed agonist–antagonists offer analgesia primarily through KOP receptor agonism, while additionally binding DOP and MOP receptors to produce a variety of desirable and side effects. The KOP receptor agonist activity aids in producing analgesia, yet this receptor also produces a variety of adverse effects that may deter abuse (Table 12.2). The ability of these medications to offer analgesia ceases at a point during continued dosing due to a ceiling effect, and their diminished effect on MOP receptors creates the potential for withdrawal symptoms.

Buprenorphine serves as an opioid partial agonist due to its low MOP receptor efficacy despite high binding affinity. Its analgesic potency is 25–50 times that of morphine with relatively high lipid solubility.

Butorphanol and nalbuphine are classified as opioid mixed agonist–antagonists, possessing KOP receptor agonist activity while antagonizing MOP receptors. Butorphanol displays analgesic potency 7 times greater than morphine and MOP receptor antagonist activity 1/40 that of naloxone. Nalbuphine displays antagonist activity much greater than its analgesic potency, which is similar to that of morphine.

Opioid Antagonists

Naloxone and naltrexone are opioid, competitive antagonists with high affinity for opioid receptors yet low efficacy. Both medications are capable of producing severe opioid withdrawal symptoms, which can include tachycardia, hypertension, arrhythmias, flushing, restlessness, sweating, nausea, and vomiting (sympathetic nervous system overactivity).

Naloxone

Naloxone is a pure, nonspecific opioid antagonist of MOP, DOP, and KOP receptors. Parenteral administration provides rapid antagonism and reversal of opioid effects within minutes. Caution must be utilized with naloxone dosing due to the brief reversal duration allowing for longer-acting opioids to reproduce their agonist effects in less than 1 h, necessitating vigilant, repeat dosing. Of note, naloxone has proven ineffective in reversing ill effects due to opioid partial agonists or the normeperidine metabolite, which may be the result of a lengthy receptor-bound state. It is available as 0.4 mg/ml and is diluted to 10 ml before use (40 mcg/ml). Dose is 40–80 mcg IV titrated to effect.

Naltrexone

Naltrexone possesses three to five times the potency of naloxone with a lengthier duration typically greater than 24 h. It is available for oral use or as a depot preparation injected monthly. It is used to treat opioid and alcohol dependence.

Peripheral Opioid Antagonists

Methylnaltrexone and alvimopan are two MOP receptor antagonists that lack the ability to cross the BBB. They have been specifically developed to treat peripheral opioid side effects such as constipation and ileus through solely antagonizing peripheral MOP receptors.

Benzodiazepines

Structure–Activity Relationships

Benzodiazepine compounds share a benzene ring paired with a seven-membered diazepine ring. All benzodiazepines contain a negatively charged substituent at position 7, which is necessary for receptor activation, and those administered perioperatively possess a 5-aryl substituent, which confers increased potency. The nature of these substituents determines the specific pharmacologic activity. For example, flumazenil displays competitive antagonist activity through a keto-residue functional group at position 5 and methyl group at position 4 rather than the 5-aryl substituent found in benzodiazepine agonists (Fig. 12.2).

Pharmacokinetics

The benzodiazepines (BZDs) commonly utilized in anesthesia include midazolam, diazepam, and lorazepam. These compounds display similar pharmacokinetics with regard to their distribution, yet their selection is often determined by significant differences in clearance and duration of action. The BZDs commonly used in anesthesia may be given orally, yet are typically administered intravenously, and all exhibit high protein plasma binding. Similar to opioids, the effects of benzodiazepines mainly occur through receptor binding within the CNS, which is generally rapid due to high lipid solubility.

BZDs also undergo primarily hepatic metabolism via phase 1 cytochrome P450 oxidation and phase 2 conjugation reactions prior to renal excretion akin to opioid metabolism. Short-acting BZDs such as midazolam and lorazepam undergo direct conjugation with glucuronic acid, whereas the oxidative metabolism of diazepam results in an active metabolite, nordazepam, whose plasma half-life of approximately 60 h significantly increases the duration of effect.

Pharmacodynamics

Benzodiazepines produce their effects through augmentation of inhibitory $GABA_A$ receptors within the CNS. BZD agonists allosterically bind the $GABA_A$ receptor between its α and γ subunits, enhancing the opening frequency of GABA-associated chloride channels, which in turn facilitate the binding of the inhibitory neurotransmitter GABA.

Indications and Usage

Through enhancement of the activity of the CNS inhibitory neurotransmitter GABA, BZDs are able to produce a variety of physiologic and behavioral effects. As dosing is incrementally increased from low to high, BZDs may produce anxiolysis and antiseizure effects followed by sedation, amnesia, and eventual unconsciousness. These effects may prove advantageous during anesthetic management throughout the perioperative period.

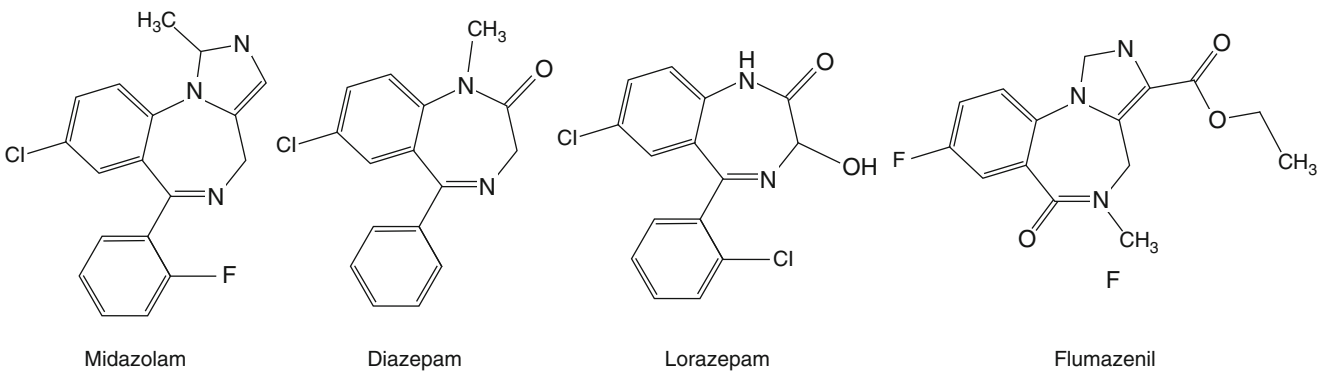

Fig. 12.2 Chemical structures of select benzodiazepine agonists and antagonist (flumazenil)

Sedation

BZDs have been shown to provide sedation likely through $GABA_A$ receptors containing the α1 subunit type. Similar to other intravenous anesthetics, the mechanism of BZD-induced sedation and sleep is thought to be multiple and complex. They may involve $GABA_A$ receptors within efferents from the ventrolateral preoptic nucleus (VLPO) of the hypothalamus ascending to the cortex and descending to the brainstem and spinal cord, thereby decreasing arousal and muscle tone. Inhibition of the thalamic and midbrain reticular formation nuclei may also be involved in providing unconsciousness. Furthermore, tonic extrasynaptic $GABA_A$ inhibition is thought to be critical in regulating synaptic conduction throughout the CNS, and midazolam has been shown to increase this tonic inhibition.

Anxiolysis

The anxiolytic effect of BZDs is thought to occur through $GABA_A$ receptors containing α2 and α3 subtypes. Small BZD doses have been shown to significantly reduce preoperative cortisol levels associated with the stress response.

Anterograde Amnesia

BZDs are known to cause anterograde amnesia that is thought to be related to the existence of $GABA_A$ receptor-mediated tonic inhibition within pyramidal neurons of the hippocampus. The combination of anterograde amnesia, sedation, and anxiolysis makes BZDs attractive and commonly implemented premedications for both diagnostic and surgical procedures. In addition, premedication with BZDs may also confer antiemetic properties postoperatively.

Anticonvulsant

BZDs are often used as first-line treatment for seizure activity and status epilepticus. The rationale behind BZD effectiveness in these conditions includes impaired inhibitory mechanisms and reduced numbers of exposed $GABA_A$ receptors within the dentate gyrus during seizure activity.

Induction and Maintenance of General Anesthesia

An infusion using a BZD such as midazolam has often been successfully administered in conjunction with boluses of opioids for induction and maintenance of both general anesthesia and monitored anesthesia care sedation. Indeed, BZDs possess less respiratory and hemodynamic effects than comparable sedative–hypnotic intravenous agents. However, propofol has largely replaced BZD infusion in such cases due to ease of titration, since midazolam possesses a context-sensitive half-time three times longer than that of propofol. BZDs remain prevalent as preoperative medications.

Alcohol Withdrawal

BZDs have also been successfully employed in the treatment of alcohol withdrawal, thought effective as a result of similar GABAergic activation.

Side Effects and Toxicity

Although generally regarded as a relatively safe class of anesthetics, BZD use may lead to a number of side effects that either surface or worsen with hepatic disease, the concomitant use of other depressant medications, and advanced age.

Respiratory Compromise

Several patient populations warrant monitoring with BZD exposure as they are particularly susceptible to respiratory compromise, including children, the elderly, patients with sleep apnea or COPD, and those taking other depressants such as opioids and alcohol. BZDs may affect spontaneous breathing by decreasing upper airway muscle tone, decreasing tidal volumes, and decreasing the ventilatory response to hypoxia. Unlike opioids, which cause a rightward shift of the CO_2 response curve, BZDs cause a flattening of the curve.

Cardiovascular Effects

With high dosing, BZDs are known to cause decreased systemic vascular resistance and elevated heart rate through increased inhibition of GABAergic receptors located within the hypothalamic paraventricular nucleus, causing decreased sympathetic outflow.

Paradoxical Effect

Paradoxical reactions involving aggression have been reported, particularly in children and elderly patients, and may result from the disinhibition of behavior regulation.

Tolerance, Dependence, and Withdrawal

Similar to opioid therapy, both tolerance and dependence are known potential complications of BZD use. BZD tolerance is often seen with chronic receptor occupancy such as in prophylactic therapy for epilepsy. In contrast to the more immediate withdrawal syndrome after opioid discontinuation, the abrupt discontinuation of BZD intake may cause delayed withdrawal symptoms with short-acting BZDs presenting sooner than longer-acting compounds. BZD withdrawal symptoms are typically opposite of agonist activity and may include nervousness, anxiety, tremor, weight loss, and possibly convulsions.

Benzodiazepine Agonists

Midazolam

Midazolam may be classified as an ultrashort-acting BZD with an effective duration of less than six hours. Of the com-

monly used anesthetic BZDs, midazolam possesses the greatest lipid solubility and pK_a value. The high lipophilicity helps to explain the rapid onset of 30–60 s, large volume of distribution, and rapid initial fall in plasma concentration after intravenous bolus due to redistribution. Although midazolam metabolism produces an active metabolite, it is rapidly cleared by conjugation and subsequently excreted. Of the aforementioned anesthetic BZDs, midazolam is most likely to be administered by infusion due to the shortest context-sensitive half-time. Pediatric oral syrup formulations are available for use.

Lorazepam

Lorazepam may be classified as a short-acting BZD with an effective duration of 12–18 h. Exclusively hepatic conjugation of lorazepam produces no active metabolites, and accordingly its metabolism is unaffected by modifiers of the cytochrome P450 system. The IV formulation may be toxic at high doses secondary to the additive propylene glycol.

Diazepam

Diazepam may be classified as a long-acting BZD with an effective duration of 24–48 h. Because of nearly 100 % bioavailability, diazepam is often administered orally. Hepatic oxidative metabolism results in an active metabolite, *N*-desmethyldiazepam, which possesses decreased elimination and with half-life of up to 200 h.

Benzodiazepine Antagonist Flumazenil

Flumazenil is a competitive $GABA_A$ receptor antagonist that provides therapeutic and diagnostic reversal of BZD-induced sedative effects. It possesses poor bioavailability and is administered intravenously in repeated doses over several minutes and titrated to effect rather than as a single, large bolus. Similar to opioid reversal with naloxone, caution should be utilized when administering flumazenil for BZD reversal as its brief duration often necessitates re-dosing within 30 min. Flumazenil administration may potentially result in BZD withdrawal symptoms or seizure activity, particularly after chronic BZD use or when inadvertently given in barbiturate and tricyclic antidepressant overdose. Of note, animal models have shown a degree of flumazenil inverse agonist activity at the $GABA_A$ receptor including anxiety and proconvulsant effects.

Clinical Review

1. Opioid analgesia primarily occurs via the following receptor:
   A. Mu
   B. Delta
   C. Kappa
   D. FQ
2. Opioid with the highest potency among the following is:
   A. Morphine
   B. Fentanyl
   C. Sufentanil
   D. Alfentanil
3. Tolerance does not occur to the following effect of opioids:
   A. Nausea
   B. Euphoria
   C. Pruritus
   D. Miosis
4. Hypotension and bradycardia may be most likely seen with use of:
   A. Alfentanil
   B. Remifentanil
   C. Sufentanil
   D. Fentanyl
5. Flumazenil is a competitive benzodiazepine antagonist at the following receptor:
   A. GABA
   B. NMDA
   C. Mu
   D. Kappa

Answers: 1. A, 2. C, 3. D, 4. B, 5. A

Further Reading

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Neuromuscular Blocking and Reversal Agents

13

Emily L. Sturgill and Neal F. Campbell

One of the primary anesthetic goals for the intraoperative management of surgical patients is akinesia. When patients are pharmacologically unable to move, surgical exposure is enhanced and the total anesthetic dose is reduced. There are a number of medications and combinations of medications that can cause akinesia. The most common medications used in the operating room are the muscle relaxants.

Physiology of Neuromuscular Transmission

Muscle relaxants, also known as neuromuscular relaxants or neuromuscular blockers, induce a state of pharmacologic paralysis by interfering with the normal processes of neurotransmitter–receptor interaction at the neuromuscular junction. A neuromuscular junction is a region of approximation of the motor neuron and the muscle cell, which are separated by a narrow synaptic cleft (Fig. 13.1). Normally, as an impulse propagates down the presynaptic motor nerve, calcium influx stimulates the release of acetylcholine by exocytosis. The acetylcholine diffuses across the synaptic cleft towards the muscle fiber.

The nicotinic acetylcholine receptor on the postsynaptic membrane requires two acetylcholine molecules to bind to each alpha site prior to its activation. Once the two molecules are bound, a conformational change ensues resulting in activation of the associated ion channel. The resultant influx of sodium causes membrane depolarization and subsequent muscle contraction. The sodium channel closes and the acetylcholine molecules dissociate. Degradation of the remaining acetylcholine molecules occurs by acetylcholinesterase. When a neuromuscular blocker is given, the normal interaction of acetylcholine with the nicotinic receptor is attenuated, and muscle contraction is inhibited.

Classification of Muscle Relaxants

There are two main types of muscle relaxants: depolarizing and nondepolarizing. Depolarizing muscle relaxants physically resemble acetylcholine and are therefore direct agonists on the acetylcholine receptor (noncompetitive antagonism of acetylcholine). They cause initial depolarization of the skeletal muscle membrane and muscle contraction, followed by flaccid paralysis. This process is due to the higher affinity of the drug for the acetylcholine receptor as compared with acetylcholine. The depolarizing muscle relaxant remains bound after muscle contraction as it is metabolized slowly and not by acetylcholinesterase (which metabolizes acetylcholine). The bound drug blocks subsequent native acetylcholine stimulation. In addition, the postsynaptic membrane must repolarize before the sodium channels will open in response to another stimulus. The classic example of a depolarizing neuromuscular blocker is succinylcholine. It is the only clinically used depolarizing agent at present.

The second type of muscle relaxants is the nondepolarizing type. Nondepolarizing agents are competitive antagonists of acetylcholine at the postsynaptic membrane. The amount of acetylcholine present in the synaptic space, as well as number of acetylcholine receptors upregulated, will affect a nondepolarizing neuromuscular blockade. There are several nondepolarizing muscle relaxants that are routinely used for pharmacologic paralysis, and each can be subclassified by its chemical structure, duration of action, or potency. For each drug, an equivalent amount of receptors (approximately 500,000) need to be blocked to induce akinesia, which is

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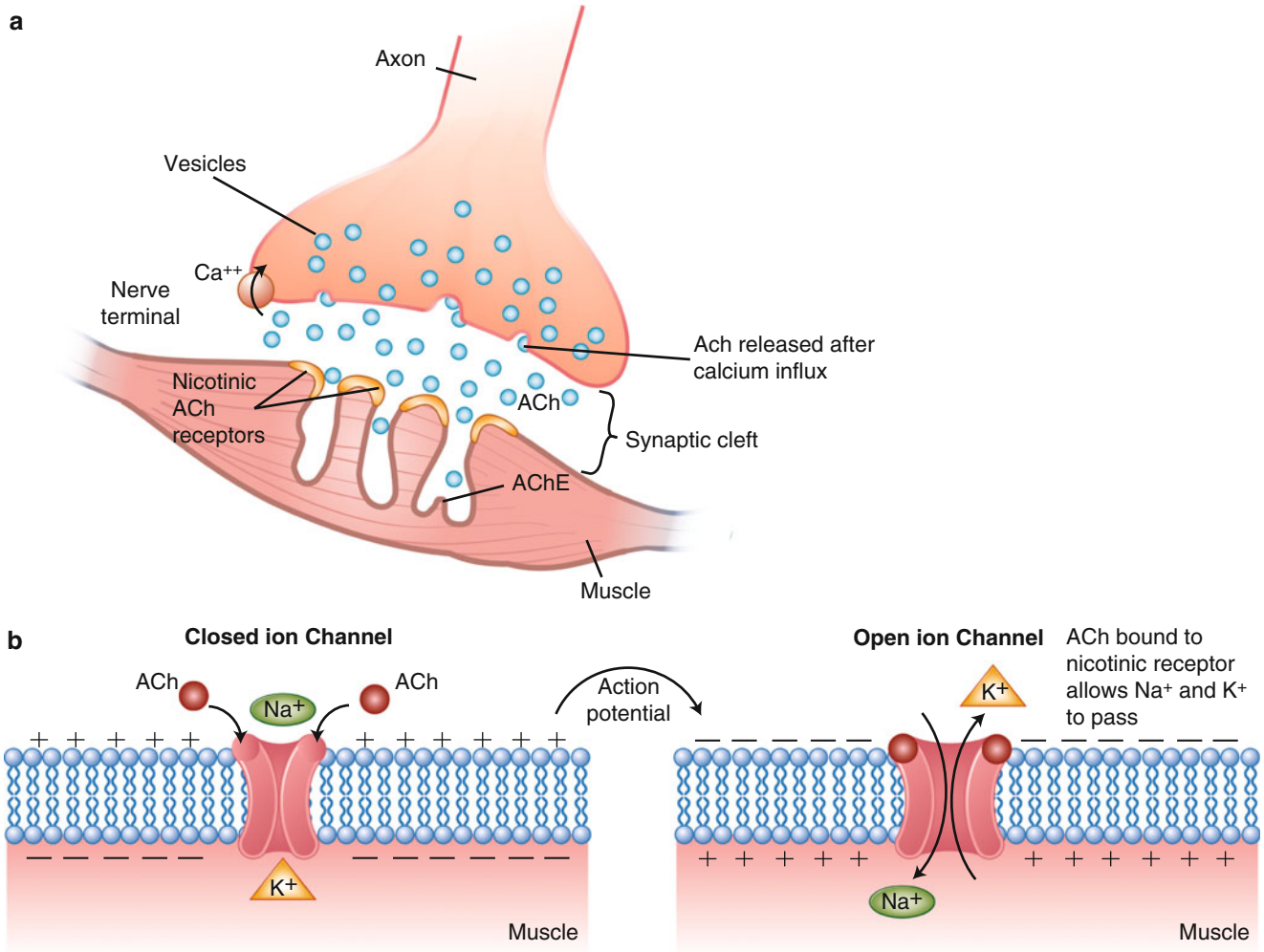

Fig. 13.1 Physiology of neuromuscular transmission. (**a**) At the neuromuscular junction, where calcium influx causes release of Ach. Ach then binds to the postsynaptic nicotinic Ach receptors at the motor endplate. (**b**) Binding of two Ach molecules opens up the ion channel leading to an action potential, which causes muscle contraction (Ach-acetylcholine)

easily obtained by doses that are routinely administered clinically. However, a less-potent drug administered in a higher relative dose produces a more rapid onset. Rocuronium, for example, is an intermediate-acting nondepolarizer that has the advantage of rapid onset.

Neuromuscular blocking agents do not cause unconsciousness, analgesia, or amnesia. Therefore, ensuring that a patient is appropriately anesthetized prior to drug administration is prudent to avoid patient awareness. In addition, all skeletal muscles throughout the body will be affected, including those involved in respiration. Therefore, the patient's airway must be maintained at the time of administration either by bag-mask ventilation, laryngeal mask airway placement, or endotracheal intubation. Furthermore, standard monitors as defined by the American Society of Anesthesiologists (nerve stimulator) must be available and employed.

Specific Muscle Relaxants

Depolarizing Muscle Relaxant: Succinylcholine

Chemical structure: Succinylcholine is the only and most widely used and readily available depolarizing neuromuscular relaxant. Its molecular structure directly explains its mechanism of action in that it consists of two acetylcholine molecules joined through the acetate methyl group. The molecule is able to activate both alpha sites on the acetylcholine receptor and does so with greater affinity than acetylcholine. As a result, succinylcholine first induces muscle contraction and then blocks any further neurotransmitter–receptor interaction leaving the skeletal muscle in a state of flaccid paralysis. Visible contractions known as fasciculations are typically present prior to total pharmacologic paralysis.

Table 13.1 Drugs that prolong duration of action of succinylcholine

Reduce plasma cholinesterase activity (prolong succinylcholine/mivacurium)	Oral contraceptives MAOIs Glucocorticoids Pancuronium
Irreversibly inhibit plasma cholinesterase activity	Echothiophate Organophosphates

Table 13.2 Dosing and administration of succinylcholine

Adult intubating dose	0.5–1.5 mg/kg
Short procedure	0.3–1.1 mg/kg over 10–30 s
Long procedure	0.3–1.1 mg/kg followed by 0.04–0.07 mg/kg maintenance dose
Pediatric intubating dose	2.0 mg/kg
Rapid sequence intubation	1.5 mg/kg
Intramuscular	3–4 mg/kg (max dose 150 mg)
Electroconvulsive therapy	0.5–1.0 mg/kg

Metabolism: Succinylcholine is rapidly cleared in the plasma by nonspecific plasma esterases. Only a small fraction of the administered dose reaches the neuromuscular junction. There are two ways in which the effects of succinylcholine can be prolonged: first, hypothermia and medications that affect plasma cholinesterase activity prolong the duration of succinylcholine (Table 13.1); second, patients who have a deficiency of butyrylcholinesterase (pseudocholinesterase), one of the nonspecific esterases, will also have prolonged paralysis after administration of succinylcholine. The butyrylcholinesterase enzyme activity can be determined clinically by calculating the dibucaine number. Dibucaine, an amide local anesthetic, selectively inhibits normal plasma cholinesterase with minimal effects on atypical cholinesterase. It causes 80 % inhibition of normal butyrylcholinesterase cholinesterase and 20 % inhibition of the abnormal enzyme. This response is predictable and can be used to determine whether a patient is homozygous for normal enzyme (80 %), heterozygous (60 %), or homozygous for abnormal enzyme (20 %). Patients with deficiency of this enzyme, who have received succinylcholine causing prolonged muscle relaxation, can be treated with mechanical ventilation (until muscle function returns to normal) and possible administration of fresh frozen plasma.

Dosage and uses (Table13.2): Muscle paresis occurs within 0.8–1.4 min following administration, which makes succinylcholine an ideal drug for rapid sequence induction (RSI). The duration of action is approximately 6–11 min. This rapid offset time is clinically useful for short case durations, potentially difficult airways, or patients who are prone to hypoxia. Other uses include electroconvulsive therapy, need for emergent intramuscular administration, and laryngospasm rescue.

Side effects: Common side effects of succinylcholine administration include elevation in plasma potassium concentration (ranging from 0.5 to 1 mEq/L), postoperative myalgias from muscle fasciculations, and transient increases in intragastric, intracranial, and intraocular pressures. With regard to intragastric and intracranial pressure, transient increases appear to be directly related to muscle fasciculations and can be reduced by pretreatment with a "defasciculating dose" of a nondepolarizing agent and intravenous lidocaine as appropriate. However, intraocular pressure and its transient increase with succinylcholine administration may occur independent of fasciculations. The significance of this minor pressure elevation is often debated, and avoiding succinylcholine in ophthalmologic trauma cases may minimize any further protrusion of vitreous humor from the eye. Less common side effects of succinylcholine include masseter muscle spasms, malignant hyperthermia, and anaphylaxis.

Contraindications to the use of succinylcholine include acute trauma, severe burns, myopathy, extensive degenerative neuropathy, hyperkalemia, prolonged paralysis with previous use, or family history of malignant hyperthermia. Succinylcholine has a black box warning due to acute hyperkalemic rhabdomyolysis leading to dysrhythmias in children with undiagnosed myopathies. It can also cause bradycardia, especially in the pediatric population.

Nondepolarizing Muscle Relaxants

Nondepolarizing muscle relaxants can be classified by their chemical structure: aminosteroids, benzylisoquinolines, and the new isoquinolines. This distinction can be used to explain their side effects. The aminosteroid agents have vagolytic properties causing an increase in heart rate, mean arterial pressure, and cardiac output upon administration. The benzylisoquinolines stimulate the release of histamine and have secondary cardiovascular effects including hypotension, tachycardia, and facial flushing. More recently, the isoquinoline compounds have also shown histamine release in early trials comparable to the benzylisoquinoliniums.

Newer nondepolarizing muscle relaxants within the aminosteroid class have been developed that have reduced side effect profiles. With the exception of cisatracurium, the benzylisoquinolines have not shown a similar improvement in side effect profiles.

Rocuronium (Aminosteroid)

Rocuronium is an intermediate acting aminosteroid nondepolarizing muscle relaxant. It is less potent than other intermediate acting agents and has a rapid onset of 0.9–1.7 min. These properties allow it to be used as an alternative to succinylcholine when RSI is desired (Table 13.3). Duration of action is 36–73 min making it more useful for cases that are of medium to long duration.

Rocuronium has few side effects, although hypersensitivity reactions and anaphylaxis have been reported. Vagolysis

Table 13.3 Dosing and administration of rocuronium

Intubating dose	0.6–1 mg/kg
RSI	0.6–1.2 mg/kg
Defasciculating dose	0.06 mg/kg or 1/10 the intubating dose
Maintenance dose	0.1–0.2 mg/kg
Continuous infusion	10–12 mcg/kg/min initially followed by 4–16 mcg/kg/min titrated to desired level of paralysis (1 twitch)

Table 13.4 Dosing and administration of vecuronium

Intubating dose	0.08–0.1 mg/kg
Maintenance dose	0.01–0.015 mg/kg
Continuous infusion	0.8–1.2 mcg/kg/min

is minimal, and hemodynamic stability is maintained at doses up to four times the ED95 (0.3 mg/kg). Rocuronium is excreted unchanged through the biliary system with a small percentage excreted unchanged in urine. The duration of action is prolonged in the presence of hepatic impairment.

Vecuronium (Aminosteroid)

Vecuronium is an intermediate acting aminosteroid nondepolarizing muscle relaxant. It has a higher potency than rocuronium with an onset time of 2–3 min. Its duration of action is 40–45 min, making it useful for cases of medium to long duration (Table 13.4). Vecuronium has a few side effects, including hypersensitivity and rare anaphylactic reactions. Similar to rocuronium, it has minimal cardiovascular effects at clinically used doses.

Vecuronium is metabolized in the liver and excreted through the biliary system. Therefore, hepatic disease will prolong its duration of action. Additionally, during metabolism, deacetylation produces a partially active metabolite. This active metabolite has less clinical impact in the operating room than with prolonged administration in the intensive care unit (ICU). Studies that examine ICU patients paralyzed long term with vecuronium suggest a higher incidence of prolonged blockade and critical illness polyneuropathy. Prolonged effects for typical use in the operating room are seen only with severe renal impairment (creatinine clearance < 10 mL/min).

Pancuronium (Aminosteroid)

Pancuronium is a long acting aminosteroid nondepolarizing muscle relaxant with high potency. Its onset time is 3–4 min and the duration of action is 85–100 min. Pancuronium exhibits the vagolytic effects characteristic of the aminosteroid class. Patients develop tachycardia and mild increases in cardiac output. It also has the potential to cause hypersensitivity reactions. It is deacetylated to a limited extent in the liver. It can be used in cases of long duration (cardiac bypass) in the absence of renal failure, but its use has been largely replaced by the intermediate acting agents. Pancuronium is excreted unchanged in the urine. Its use should be avoided for prolonged administration or in the setting of renal impairment. Dosage: 0.06–0.1 mg/kg (intubating dose), 0.01 mg/kg (maintenance).

Table 13.5 Dosing and administration of cisatracurium

Intubating dose	0.15–0.2 mg/kg
Maintenance dose	0.03 mg/kg
Continuous infusion	1–2 mcg/kg/min

Atracurium (Benzylisoquinoline)

Atracurium is a benzylisoquinoline compound that consists of 10 stereoisomers. It has an intermediate onset (3 min) and duration of action (45 min). In clinical practice, it has been replaced by cisatracurium, due to the same favorable traits and fewer side effects (Table 13.6). Atracurium is metabolized by Hoffman elimination and plasma esterases. Hoffman elimination is an enzyme-independent hydrolysis that relies on physiologic pH and temperature. Laudanosine is a byproduct of this metabolic process and can cross the blood brain barrier. In animal studies, this metabolite has been shown to induce epileptiform activity in high concentrations. Atracurium can stimulate histamine release and cause associated tachycardia, hypotension, or bronchospasm. Dosage: 0.2–0.3 mg/kg (intubating dose), 0.08–0.1 mg/kg (maintenance).

Cisatracurium (Benzylisoquinoline)

Cisatracurium is a benzylisoquinoline nondepolarizing muscle relaxant and, as the name implies, is one of the stereoisomers of atracurium. It is an intermediate acting agent with an onset of 2–8 min and duration of action of 45–90 min (Table 13.5). Hoffman elimination of cisatracurium makes it useful for cases of medium to long duration in the presence of renal and or hepatic impairment. The amount of laudanosine produced from cisatracurium is significantly less than that produced during the metabolism of atracurium. Unlike atracurium and other benzylisoquinolines, cisatracurium does not stimulate the release of histamine and therefore does not cause cardiovascular side effects or anaphylaxis.

Mivacurium (Benzylisoquinoline)

Mivacurium is a benzylisoquinoline nondepolarizing muscle relaxant of short duration. It is no longer commercially available in the United States. A unique property among its class is a lack of cumulative effect on administration. Therefore, it can be given either as multiple boluses or continuously and maintains a consistent steady state concentration. As with other members of its class, mivacurium stimulates histamine release. Like succinylcholine, it is metabolized by plasma pseudocholinesterase. The duration of action is prolonged twofold in the setting of renal failure and threefold in liver failure.

Table 13.6 Dosing and administration of gantacurium

ED95	0.19 mg/kg
RSI	0.45–0.52 mg/kg

Gantacurium (Isoquinoline)

Gantacurium is a new ultrashort acting isoquinoline nondepolarizing muscle relaxant previously known as 430A. Gantacurium was intended to replace succinylcholine and fit the profile of an ideal agent. An ideal neuromuscular blocking agent is one with a fast onset and offset, predictable effect, no prolongation with hepatic or renal disease, and devoid of side effects. In studies to date, the drug has been able to induce rapid paralysis to facilitate RSI, with duration of less than 10 min, and undergoes chemical degradation at physiologic pH. The onset of action is in 1.3–2.1 min with a typical dose, and 60–90 s with the rapid sequence dose. Duration of action is approximately 7 min (Table 13.6).

During initial human trials, histamine release was present in 25 % of patients tested at 2.8 times the ED95 (0.54 mg/kg) and 75 % of patients at 3.8 times the ED95 (0.72 mg/kg). The recorded symptoms were tachycardia, hypotension, and facial flushing. In each case these symptoms were self-limited and did not require pharmacologic intervention. Metabolism occurs by pH-sensitive hydrolysis and cysteine adduction. Endogenous cysteine combines with gantacurium in vitro resulting in rapid chemical degradation. This novel mechanism has led to the potential development of L-CYSTEINE exogenous administration as a reversal agent. This will be discussed later in the chapter.

Factors Affecting Neuromuscular Blockade

Disease states: Patients with hepatic (metabolism) or renal (excretion) disease will affect the duration of neuromuscular blockade. In addition, the effect of neuromuscular blocking agents on neuromuscular disease has significant anesthetic implications. For example, patients with myasthenia gravis have an autoimmune reduction (downregulation) in postsynaptic acetylcholine receptors. These patients are resistant to depolarizing agents but exquisitely sensitive to nondepolarizing agents. Patients with Lambert Eaton Myasthenic Syndrome have impaired/decreased release of Ach from the presynaptic terminal. These patients are more sensitive to nondepolarizing agents than to depolarizing agents. Duschenne's muscular dystrophy patients, on the other hand, have a progressive degeneration of skeletal muscle and are, therefore, at high risk for developing hyperkalemic cardiac arrest if succinylcholine were to be administered. Indeed, meticulous preoperative planning along with vigilant intraoperative and postoperative management is needed when caring for these patients, particularly if one considers the use of a neuromuscular blocking agent.

Table 13.7 Agents affecting neuromuscular blockade

Potentiation	Inhalational anesthetics Local anesthetics Antibiotics (aminoglycosides, vancomycin, tetracyclines, bacitracin, polymixins) Lithium Magnesium Procainamide Quinidine Lasix Cyclosporine Dantrolene Calcium channel blockers
Attenuation	Anticonvulsants Calcium Azathioprine

Agents: Many pharmacologic perioperative interventions can have an effect on the neuromuscular blockade. It is helpful to divide these into agents that cause the blockade to be potentiated or attenuated (Table 13.7). The mechanisms responsible for potentiation or antagonism are not well understood, but most are thought to be secondary to effects on calcium uptake, distribution, or metabolism.

Other factors: Hypothermia, by decreasing the metabolic rate, prolongs neuromuscular blockade. Electrolyte imbalance, such as hypermagnesemia, hypocalcemia, and hypokalemia, prolongs neuromuscular blockade. Respiratory acidosis also prolongs neuromuscular blockade.

Clinical Monitoring of Neuromuscular Blockade: The Peripheral Nerve Stimulator

The clinical basis of nerve stimulation involves applying an electrical stimulus directly over a motor nerve and monitoring the associated response. This motor response can be used to determine the degree of neuromuscular blockade and is important to ensure ideal intubating conditions, maintain adequate paralysis during critical operative periods, and monitor return of function so that extubation criteria can be met.

With the administration of neuromuscular blocking agents, paralysis is evident in the following sequence: diaphragm, adductor muscles of the vocal cords, orbicularis oculi, and the masseter muscle. However, the diaphragm and laryngeal muscles are relatively resistant to most neuromuscular blocking agents meaning that, although the diaphragm is the first muscle to be affected, the time to reach maximum effect is prolonged when compared to the adductor pollicus muscle. This is also true on return of function. The first evidence of return to function is in proximal muscle groups, but return of full strength is seen first in the diaphragm.

The most common monitor for neuromuscular blockade is the peripheral nerve stimulator. Two electrodes are placed on the skin over a desired nerve, typically <6 cm apart (see chapter on patient monitoring). Normothermia and clean skin help avoid impedance. With stimulation and in the face of no pharmacologic blockade, the adductor pollicis muscle will contract. Other nerve distributions to monitor include the posterior tibial with the flexor hallucis brevis contracting upon stimulation and the facial nerve with the orbicularis occuli contracting upon stimulation. Clinically, the facial nerve response is a better predictor of intubating conditions, whereas the ulnar nerve response is a better predictor of pharyngeal muscle recovery. The latter may prove useful in determining whether extubation criteria are met.

Clinical Application of the Peripheral Nerve Stimulator

Train of four (TOF): This is the most commonly used method in the operating room to titrate the administration of neuromuscular blocking drugs and reversal agents. Four twitches at 2 Hz in 2 s are administered. Loss of the fourth response is equivalent to a 75–80 % blockade, third = 85 %, second = 90 %, and first = 98–100 %. The TOF ratio is equal to the amplitude of the fourth response divided by the first. A ratio of 0.7 is equivalent to diaphragm recovery and >0.9 implies significant pharyngeal muscle function recovery.

Tetanic stimulation: This involves administering a high-frequency stimulus of 50–200 Hz for 5 s to an extremity. This stimulates the release of acetylcholine into the synaptic space. If there is a full response and lack of fade, this can be indicative of recovery from neuromuscular blockade.

Post-tetanic count: This method can be used when there is partial or no response to a TOF. A tetanic stimulus of 50 Hz is administered for 5 s, which is followed by a TOF stimulus. If post-tetanic twitches are present (increase in evoked response-potentiation), the return of TOF is imminent.

Double burst stimulation: This method was introduced in the late 1980s to monitor minor neuromuscular blockade. Two bursts of 50 Hz with a 750-ms interval are administered. If the impulses fade upon the second burst, this correlates with an incomplete recovery or a TOF < 0.6.

Single twitch: This is administered as a single pulse of 0.2 ms duration. It can be used to monitor neuromuscular blockade provided by succinylcholine during endotracheal intubation or when it is administered as an infusion. It is also used in research when evaluating the onset of action of new neuromuscular blocking agents.

Neuromuscular Blockade Reversal Agents

Nondepolarizing neuromuscular blockade is reversed by using anticholinesterase agents (neostigmine). These act indirectly by inhibiting acetylcholinesterase, the enzyme that metabolizes acetylcholine. This results in an increase in acetylcholine present in the synapse to compete with the neuromuscular blocking drug. Neuromuscular blockade by succinylcholine is not reversed with these agents because it is eliminated from the neuromuscular junction by diffusion and then rapid metabolism by nonspecific esterases. In fact, the duration of action of succinylcholine can be prolonged by inhibiting the esterase enzymes, which metabolize succinylcholine.

Reversal of neuromuscular blockade is important to prevent postoperative residual weakness and is associated with a significant reduction in postoperative morbidity and mortality at 24 h. Symptoms of muscular weakness are present even at a TOF ratio of >0.7. Reversal may be administered after at least one twitch is present on the peripheral nerve stimulator. Ideally two or more twitches should be present for the most effective reversal.

Specific Neuromuscular Blockade Reversal Agents

Neostigmine

Neostigmine forms a reversible covalent bond with the esteratic site of the acetylcholinesterase molecule. In addition to inhibiting acetylcholinesterase directly, it also stimulates the release of acetylcholine from the nerve terminal and causes minor inhibition of plasma cholinesterase. Initial effects are seen within 3–5 min with a peak effect at 10 min and duration of 30–45 min. Dosage is 0.04–0.08 mg/kg.

Neostigmine is metabolized in the liver and excretion is primarily in the urine with 50 % of the drug excreted unchanged. The associated side effects of neostigmine are secondary to the increase of acetylcholine concentration at the muscarinic receptors. These side effects include increased salivation, lacrimation, urination, defecation, GI upset, emesis, and miosis (SLUDGEM). Additional side effects include QT prolongation, bradycardia, and bronchoconstriction. Administration of anticholinergic medications, such as glycopyrrolate (0.2 mg/mg of neostigmine), help to reduce these cholinergic symptoms.

Edrophonium

Edrophonium forms a reversible ionic bond with the anionic site of the acetylcholinesterase molecule. Unlike neostigmine, edrophonium does not stimulate the release of acetylcholine from the nerve terminal nor does it inhibit plasma cholinesterase. The major difference in administration is the

onset and duration of action. It takes effect within 30–60 s and has duration of action of 10 min. Dosage 0.5–1.0 mg/kg.

The adverse effects are similar to neostigmine. Edrophonium is typically administered with the anticholinergic drug atropine (0.014 mg of atropine/mg of edrophonium) because both medications have a similar onset of action. Edrophonium is excreted primarily in the urine unchanged.

Sugammadex

Sugammadex is a new reversal agent recently approved by the FDA for use in the United States. It is a cyclic oligosaccharide, shaped like a donut, with openings on either side known as the primary and secondary face. Each face is lined with hydroxyl groups making the molecule water soluble. The interior is lined by carbon atoms creating a lipophilic core. This allows sugammadex to bind to small lipophilic molecules, while the inclusion complex as a whole remains water soluble and can be easily excreted. Once bound, the rate of dissociation of an inclusion complex is extremely low with an incidence of 1/25,000.

Sugammadex binds steroidal nondepolarizing neuromuscular blocking drugs with the highest affinity for rocuronium followed by vecuronium and pancuronium. Once in the plasma, not only does it rapidly clear the agent, it creates a concentration gradient for diffusion out of the neuromuscular junction. Native circulating steroid hormones are tightly bound to their carrier molecules, minimizing the ability of sugammadex to affect their plasma concentration. Sugammadex does not bind to the benzylisoquinoline nondepolarizing muscle relaxants (cisatracurium) or to succinylcholine. Therefore, if paralysis is needed after reversal, benzylisoquinolines are recommended. Since sugammadex does not act on acetylcholinesterase, the coadministration of anticholinergic medication is not necessary.

The clinical implications of sugammadex are profound. This agent can be used for rapid reversal of profound block or as an alternative to succinylcholine (rocuronium-sugammadex) when a short duration of neuromuscular blockade is required. Regarding the latter, rocuronium could be administered as RSI, thus avoiding the side effects associated with succinylcholine, and then reversed within minutes. In this way, rocuronium with sugammadex rescue fits the same favorable clinical profile as succinylcholine. A linear relationship exists between the dose administered and degree of block reversed. This response is not seen with neostigmine. In phase III trials the median time to recovery of TOF>0.9 was 1.4 min. Dosage 2–8 mg/kg for reversal (depending on the density of neuromuscular blockade).

Adverse effects reported during clinical trials include QT prolongation, allergic reactions, hypertension/hypotension, procedural pain, nausea, vomiting, pyrexia, headache, sore throat, cough, and constipation. Many of these effects may be due to coadministration with other anesthetic agents. QT prolongation in the presence of sugammadex was compared with that of moxifloxacin as a positive control in phase I trials. With administration up to eight times, the recommended dose, the QT prolongation was significantly less than 10 ms. With administration of 4 and 32 mg/kg doses, the mean QTc interval differences were 1.8 and 2.8 ms, respectively, in comparison to 18.6 ms induced by 400 mg of moxifloxacin.

L-Cysteine

L-Cysteine is a newer agent. It was developed in light of the new isoquinoline compound, gantacurium. It is being investigated as a possible neuromuscular blockade reversal agent. Endogenous cysteine combines with gantacurium in vitro, resulting in chemical degradation. Exogenous administration has shown promising results in animal studies to rapidly reverse neuromuscular blockade. This novel mechanism could be employed at any time during blockade, regardless of the number of twitches present. There are no known adverse effects at this time of exogenous L-cysteine.

Anticholinergics

Glycopyrrolate

Glycopyrrolate is a synthetic quaternary amine, and quaternary amines do not cross the blood brain barrier. Therefore, glycopyrrolate does not cause anticholinergic central nervous system side effects that scopolamine, atropine, and other tertiary amines do. It (and not atropine) is given in conjunction with neostigmine because its onset more closely resembles neostigmine. It is administered at a dose of 0.01–0.02 mg/kg. Common side effects are xerostoma, constipation, and dyspepsia. Contraindications to use include urinary tract obstruction, GI obstruction, and acute angle closure glaucoma.

Atropine

Atropine is a tertiary amine, which allows for CNS penetration. Its onset is more closely correlated with that of edrophonium than that of neostigmine. Severe cardiac arrhythmias have occurred when atropine was used in conjunction with neostigmine. The exact mechanism is unclear. It is administered at a dose of 0.015–0.03 mg/kg. Peripheral anticholinergic side effects resemble those of glycopyrrolate. Due to CNS penetration, patients may also exhibit central anticholinergic effects (blurred vision, cognitive impairment). The contraindications to use are the same as glycopyrolate.

Clinical Review

1. The major neurotransmitter involved in neuromuscular transmission is
   A. Gamma amino butyric acid
   B. Acetylcholine
   C. Glutamic acid
   D. Dopamine
2. The following drug can be used for RSI in a patient with a serum potassium of 5.5 meq/L
   A. Sugammadex
   B. Succinylcholine
   C. Rocuronium
   D. Cisatracurium
3. Longest acting muscle relaxant among the following is
   A. Cisatracurium
   B. Atracurium
   C. Vecuronium
   D. Pancuronium
4. Glycopyrrolate is combined with neostigmine to reverse neuromuscular blockade to reduce the following side effects of neostigmine
   A. Muscarinic
   B. Nicotinic
   C. Beta-adrenergic
   D. Alpha-adrenergic
5. Sugammadex has the highest affinity for
   A. Vecuronium
   B. Pancuronium
   C. Rocuronium
   D. Cisatracurium

Answers: 1. B, 2. C, 3. D, 4. A, 5. C

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Antiemetics

14

Wendy A. Haft and Richard McAffee

Postoperative nausea and vomiting (PONV) remains one of the most common complications of anesthesia and is estimated to occur in approximately 20–30 % of patients receiving general anesthesia. PONV is associated with multiple risk factors including certain patient characteristics, specific surgical and anesthetic techniques, and commonly used medications in the perioperative period. This anesthetic complication contributes to preoperative anxiety in patients with a history of PONV, decreased patient satisfaction, and even serious postoperative complications such as wound dehiscence and aspiration.

Risk Factors for PONV

An understanding of the risk factors for PONV can help anesthesia providers identify at-risk patients and work toward prevention with prophylactic antiemetics. Some common risk factors include female gender, history of PONV, history of motion sickness, use of volatile anesthetics, use of opioids, laparoscopic procedures, gynecologic procedures, and nonsmoking status. Risk scores have been developed to assist in identifying such patients. For example, the Apfel score used in adult patients utilizes four factors: female gender, history of PONV or history of motion sickness, postoperative use of opioids, and nonsmoking status. Zero factors correspond to 10 % risk, one factor to 20 % risk, two factors to 40 % risk, three factors to 60 % risk, and four factors to 80 % risk of PONV.

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Physiology of Nausea and Vomiting

Nausea and vomiting are physiologic processes that require coordination of multiple organ systems, extending from the brain to the gastrointestinal tract. There are many causes of nausea including medications, motion sickness, and certain diseases (i.e., malignancy and pregnancy). The chemoreceptor trigger zone (CTZ) in the area postrema at the end of the fourth ventricle contains receptors for numerous neurotransmitters involved in vomiting, including dopamine, opioid, serotonin $5HT_3$, and NK_1 receptors. The CTZ receives input from the binding of these neurotransmitters and relays signals to the nucleus tractus solitarius (NTS) in the brainstem and the vomiting center in the lateral medullary reticular formation to initiate the coordination of vomiting. Similarly, the vestibular system, which contains numerous H_1 histamine and M_1 muscarinic receptors, and the gastrointestinal tract, which is rich in $5HT_3$ receptors, also send afferent signals to the vomiting center in the medulla as a result of emetic stimuli. Stimulation of these brainstem centers results in activation of pharyngeal, thoracic, and abdominal muscles to help expel gastric contents.

Pharmacology of Antiemetics

Given the numerous factors involved in the experience of nausea and the coordination of vomiting, there exist many categories of antiemetic drugs that act at different receptors along these pathways. Some antiemetic drugs act as antagonists at histamine, dopamine, serotonin, muscarinic, or NK_1 receptors (Table 14.1). Other commonly used antiemetics act through alternate mechanisms, as discussed below. The multifactorial nature of PONV highlights the importance of multimodal antiemetic therapy. Studies have shown that the effects of antiemetics are generally additive. In addition, if a patient fails treatment with one class of antiemetics, another class should then be instituted, rather than giving multiple doses of either the same drug or other drugs within that class.

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Table 14.1 Overview of antiemetics

Drug category	Mechanism of action	Specific drugs	Typical dose
Serotonin ($5HT_3$) antagonists	Antagonism of serotonin $5HT_3$ receptors in the CTZ, the medullary vomiting center, and in the periphery	Ondansetron	4–16 mg IV
		Granisetron	1 mg IV
		Dolasetron	100 mg IV
		Palonosetron	0.25 mg IV
Dopamine antagonists	Inhibition of dopaminergic receptors in the CTZ	Droperidol	0.625–1.25 mg IV
		Haloperidol	1–2 mg IV
		Perphenazine	4–8 mg by mouth
		Prochlorperazine	5–10 mg IV
		Metoclopramide	10–20 mg IV
Corticosteroids	Unknown mechanism – possibly due to anti-inflammatory effect	Dexamethasone	4–10 mg IV
Anticholinergics	Inhibition of muscarinic receptors in the vestibular system and the vomiting center in the medulla	Scopolamine	1.5 mg transdermal patch
Histamine (H_1) blockers	Antagonism of histamine receptors in the vestibular system	Diphenhydramine	4–10 mg IV
Neurokinin (NK_1) antagonists	Inhibition of substance P in the area postrema and throughout the GI tract and blockade of signals from the CTZ to the NTS in the brainstem	Aprepitant	40 mg by mouth

CTZ chemoreceptor trigger zone, *NTS* nucleus tractus solitarius

Serotonin $5HT_3$ Receptor Antagonists

Serotonin $5HT_3$ receptors are present in the CTZ, the medullary vomiting center, and peripherally in vagal and spinal afferent nerves. $5HT_3$ receptor antagonists are common antiemetics used for both the prevention and treatment of PONV. The most commonly used $5HT_3$ receptors available in the United States are ondansetron, dolasetron, granisetron, and palonosetron. Ondansetron, dolasetron, and granisetron are available in oral and intravenous (IV) preparations, whereas palonosetron is available for administration by IV route only.

$5HT_3$ receptor antagonists have fewer side effects compared to other available antiemetics; however, they have been known to cause constipation, headache, dizziness, QTc prolongation, and cardiac arrhythmias. Palonosetron has greater $5HT_3$ receptor affinity, which results in its longer half-life of 40 h (compared to a half-life of 4–9 h for the other drugs in this class), and it is not associated with QTc prolongation. Administering a $5HT_3$ receptor antagonist with a corticosteroid at the induction of general anesthesia may provide better PONV prophylaxis than either drug class alone.

Ondansetron, the most commonly used $5HT_3$ receptor antagonist, is generally administered in doses ranging from 4 to 16 mg IV prophylactically at the induction of anesthesia or for the treatment of PONV postoperatively. Other research has demonstrated increased efficacy when ondansetron is given at the end of surgery but prior to leaving the operating room. Some studies have shown that 4 mg of ondansetron IV is effective for the prevention and treatment of PONV, whereas other studies have demonstrated 8 mg IV to be the minimum effective dose in adults.

Dopamine Antagonists

There are three classes of dopamine receptor antagonists commonly used as antiemetics: phenothiazines, butyrophenones, and benzamides. The antiemetic properties of these drugs are due to inhibition of dopaminergic receptors in the CTZ. The use of this class of medications is limited by side effects, especially sedation and extrapyramidal symptoms, and should be avoided in patients with Parkinson's disease.

The most commonly used phenothiazines are perphenazine, promethazine, and prochlorperazine. Perphenazine is available only in an oral form and it is recommended that it be given preoperatively. The typical dose is 4–8 mg, which has been shown to result in effective control of PONV while producing limited side effects. Studies have demonstrated that perphenazine given preoperatively enhances the antiemetic effects of ondansetron and dolasetron. Promethazine is used for both prophylaxis and treatment of PONV. It also has anticholinergic and antihistaminic properties, which can result in substantial sedation, thus limiting its use.

The most commonly used butyrophenone as an antiemetic is droperidol. Droperidol acts through the same mechanism as the phenothiazines and is also typically used as prophylaxis against PONV. Studies have demonstrated that droperidol is equally effective in preventing PONV as the combination of ondansetron and dexamethasone. However,

droperidol is still most effective when used in combination with other antiemetics. The recommended dose of droperidol is 0.625–1.25 mg IV. A "black box" warning on droperidol does exist for higher doses (>/=2.5 mg IV) due to cases of QTc prolongation and torsades de pointes, so discretion should be exercised when using droperidol in patients taking other medications that may prolong the QTc interval. Haloperidol, another butyrophenone, has also been shown to have antiemetic properties in low doses (1–2 mg IV), but it has a shorter duration of action than droperidol.

Metoclopramide, a benzamide used as an antiemetic, works by inhibiting dopaminergic receptors in the CTZ and by increasing gastric motility through peripheral activity as a cholinomimetic. Prophylactic and treatment doses of metoclopramide usually range 10–20 mg by mouth or IV every 6 h. Many recent studies comparing metoclopramide and other antiemetics, such as ondansetron and droperidol, have shown that metoclopramide is less effective in the prevention of PONV.

Corticosteroids

Dexamethasone and methylprednisolone are two corticosteroids used as antiemetics. As described above, dexamethasone has been shown to have enhanced antiemetic properties when combined with ondansetron. Corticosteroids are well known for their anti-inflammatory properties, but the basis behind their use as antiemetics is not well understood. Dexamethasone is generally administered in doses of 4–10 mg IV at the induction of anesthesia. It is recommended that dexamethasone not be routinely given as PONV prophylaxis in patients with diabetes mellitus. No convincing data has shown that adrenal suppression or inhibition of wound healing occurs with a single dose preoperatively.

Histamine (H_1) Blockers

H_1 receptor antagonists act through inhibition of histamine receptors in the vestibular system. Nearly all drugs in this category are also weak anticholinergics through inhibition of muscarinic M_1 receptors present in the vestibular system. The mechanism of action of this class of drugs makes them most useful in patients with a history of motion sickness, and they are generally weak antiemetics when used alone. In practice, antihistamines are used in combination with other more potent antiemetics. H_1 receptor antagonists can also decrease the risk of extrapyramidal side effects when given with dopamine antagonists used for the prevention and treatment of PONV. Commonly used H_1 blockers are diphenhydramine, dimenhydrinate, hydroxyzine, and meclizine. These medications can cause significant sedation and dry mouth secondary to their anticholinergic properties and thus should be used with caution in some patients.

Anticholinergics

The most commonly used anticholinergic in the prevention of PONV is scopolamine. Scopolamine is traditionally given as a 1.5 mg patch placed behind the ear that acts transdermally over 72 h. It is recommended that scopolamine be administered preoperatively and is most effective when initiated the day prior to surgery. However, it has also been shown to be effective if given 2–4 h before the end of surgery or even in the postoperative period. Scopolamine acts by inhibiting muscarinic receptors in the vestibular system as well as the vomiting center in the medulla. Thus, it is particularly effective in patients with a history of motion sickness. The fact that scopolamine is long acting, when given transdermally, and does not require repeated dosing is one benefit for its use in same-day surgery patients. However, the use of scopolamine in such patients can be limited by its sedating effects, and care should be exercised in elderly patients, who are most sensitive to these effects. Transdermal scopolamine has been showed to cause less sedation than oral or IV preparations.

Neurokinin 1 Receptor Antagonists

Neurokinin 1 (NK_1) receptor antagonists have been shown to decrease the incidence of PONV in high-risk patients, particularly when used with other antiemetics. NK_1 receptor antagonists function by inhibiting signals received from the chemoreceptor trigger zone (CTZ) by the nucleus tractus solitarius (NTS) in the brainstem. Another mechanism for their action is through inhibition of substance P, a neuropeptide that binds in the area postrema and throughout the GI tract to cause nausea. The most commonly used NK_1 antagonist is aprepitant. The typical dose is 40 mg orally preoperatively, most commonly given within 3 h of surgery. Research has shown that aprepitant is most effective when combined with other antiemetics, particularly corticosteroids and $5HT_3$ receptor blockers.

Aprepitant has few side effects, is nonsedating, and has been shown to be longer acting than other commonly used antiemetics. Thus, it may be particularly beneficial in patients undergoing same-day surgeries for which postdischarge nausea and vomiting is a concern. Aprepitant does have a higher cost than other antiemetics, which may limit its use in some situations. Aprepitant also affects the hepatic metabolism of many drugs. Importantly, oral contraceptive serum hormone levels may decrease, and therefore, alternative nonhormonal contraception is recommended when using this drug. This

interaction may somewhat limit the use of aprepitant in young women at risk for PONV. Another oral NK_1 receptor antagonist, rolapitant, is currently in clinical trials.

Emetogenic Trigger Avoidance

Opioids and volatile anesthetics are two drug classes that have been implicated as risk factors for PONV, and, thus, avoidance of these triggers has been shown to decrease the risk of PONV in at-risk patients. One technique in minimizing the use of volatile anesthetics is the maintenance of anesthesia with an IV infusion of agents such as propofol or dexmedetomidine. In addition to its benefit in sparing the use of volatile anesthetics, propofol by itself is an antiemetic. The mechanism of action behind propofol's antiemetic properties is likely multifactorial. Activation of gamma-aminobutyric acid (GABA) receptors by propofol directly inhibits neurons in the area postrema and decreases serotonin levels in this same region, resulting in a breakdown in the pathways causing nausea and vomiting. Studies have shown that a single induction dose of propofol alone does not result in effective prevention of PONV. However, combining a single induction dose of propofol with an intraoperative maintenance infusion does decrease the risk of PONV.

Many patients experience PONV in association with opioid use. There are numerous opioid-sparing techniques that can be utilized in such patients to decrease their risk of PONV. Certain regional anesthetic techniques can reduce a patient's need for postoperative opioids. Similarly, perioperative use of nonopioid analgesics such as ketorolac, acetaminophen, ketamine, clonidine, and dexmedetomidine can decrease opioid requirements. Many patients with a history of PONV experience significant anxiety regarding the recurrence of this complication, which itself can trigger nausea and vomiting. Benzodiazepines, such as lorazepam and midazolam, can be used for the prevention of anticipatory nausea and vomiting in the perioperative period.

Nonpharmacological Techniques

Electroacupuncture and acupressure are nonpharmacological techniques that have been extensively studied in the prevention and treatment of PONV. Electroacupuncture involves electrical stimulation with a needle that administers about 1 Hz of stimulation either as a single twitch, double burst, tetanus, or train-of-four. Recent studies have shown that tetanic stimulation is most effective in the prevention of PONV. Acupressure involves a bracelet containing a magnet or an electrical stimulator that is applied to the wrist at the P6 acupoint, which is located along the distal wrist over the median nerve. These techniques can be applied as prophylaxis either preoperatively or intraoperatively. Electroacupuncture is effective postoperatively as rescue for PONV. Evidence suggests that electroacupuncture and acupressure may decrease opioid requirements postoperatively.

Clinical Review

1. The following drug does *not* prolong the QTc interval on the electrocardiogram:
   A. Ondansetron
   B. Dolasetron
   C. Droperidol
   D. Palonosetron
2. Metoclopramide is contraindicated in patients with:
   A. Asthma
   B. Parkinsonism
   C. Depression
   D. Rheumatoid arthritis
3. Aprepitant prevents nausea and vomiting by inhibiting the following receptors:
   A. Neurokinin
   B. Bradykinin
   C. Cytokinin
   D. Kallikrein
4. Use of the following agent intraoperatively may prevent postoperative nausea and vomiting:
   A. Desflurane
   B. Etomidate
   C. Propofol
   D. Remifentanil

Answers: 1. D, 2. B, 3. A, 4. C

Further Reading

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NSAIDs and Alpha-2 Adrenergic Agonists

15

Stephen M. McHugh and David G. Metro

While narcotics remain the primary drug class for the treatment of perioperative pain, there is strong interest in utilizing alternative analgesics with the goal of reducing narcotic-related side effects such as hypoventilation, nausea, and constipation. Three categories of medication useful for this multimodal analgesia are the nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and the α2-adrenergic agonists. Since their analgesic properties show a ceiling effect, they usually cannot be used as the sole agent for postoperative pain. These classes of medication provide pain relief via non-opioid pathways and are frequently combined with narcotics for additive effect. In addition, NSAIDs, acetaminophen, and α_2-agonists have therapeutic uses distinct from pain relief, and their versatility makes them valuable tools in the perioperative period.

NSAIDs

The NSAIDs are a widely used class of drugs with different varieties available over the counter and via prescription. Intravenous (IV) and oral (PO) formulations exist as well as subclasses designed to have reduced side effects. They are used for their analgesic, antipyretic, and anti-inflammatory properties.

Pharmacology

All NSAIDs exert their effects through the inhibition of the cyclooxygenase (COX) enzymes. The COX enzymes convert arachidonic acid into prostaglandin (Fig. 15.1). The COX-1 enzyme is constitutively expressed throughout the body and is important in such processes as gastric mucous production and platelet aggregation. The COX-2 enzyme is inducible and functions at sites of inflammation where it contributes to the production of pain. Nonselective NSAIDS such as ibuprofen, ketorolac, and naproxen inhibit both the COX-1 and COX-2 enzymes. Specific COX-2 inhibitors such as celecoxib are highly selective for the COX-2 isoenzyme and were developed with the goal of reducing the side effects of COX-1 inhibition (such as gastric ulceration) while maintaining the pain relief characteristic of the nonselective NSAIDs.

Clinical Uses

In the perioperative period, NSAIDs are primarily used for their analgesic effect. They may be used alone for mild to moderate pain or in conjunction with narcotics for moderate to severe pain. They are frequently termed "opioid sparing" because their use in combination with opioids has been shown to reduce a patient's overall opioid requirement while providing an equivalent level of analgesia. Administration of NSAIDs significantly reduces postoperative narcotic requirements in both children and adults. Ketorolac 30 mg IV has been reported to provide equivalent analgesia as morphine 10 mg IV, although more recent studies suggest that morphine may be more effective. Because narcotic doses are reduced, patients receiving NSAIDs experience fewer narcotic-related side effects, including reduced nausea and vomiting and reduced postoperative sedation.

Ketorolac is a nonselective NSAID, and because it can be given IV, it is frequently used in the perioperative period when patients have restricted PO intake. Standard doses are 15–30 mg q6h (or prn); however, doses up to 60 mg and as low as 7.5 mg have been used (Table 15.1). The course of treatment should not exceed 5 days to reduce NSAID-related side effects, particularly renal injury. Recently, IV ibuprofen has become available for injection (via infusion). Standard dosage is 400–800 mg q6h as needed (maximum of 3,200 mg daily).

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Orally administered nonselective NSAIDs include ibuprofen and naproxen. These medications are used for their analgesic effects in the perioperative period as well as for long-term management of pain due to multiple causes. They are also frequently used for their antipyretic properties which derive from COX inhibition in the hypothalamus.

Side Effects

The main side effects associated with nonselective NSAIDs are due to inhibition of the COX-1 enzyme. The COX-1 enzyme is active at multiple sites in the body and plays important roles in platelet aggregation, regulation of afferent renal arteriolar tone, and production of gastric mucous. Accordingly, the major side effects of these drugs are bleeding, renal injury, and gastric ulceration. Importantly, inhibition of platelet function is a major limitation to the use of NSAIDs in the immediate postoperative period. There is also concern that the anti-inflammatory effect of NSAIDs inhibits bone healing. For this reason, some clinicians recommend against their use in orthopedic surgery or following a bone fracture.

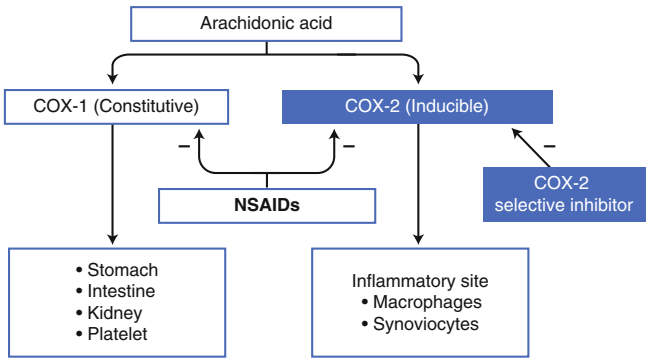

Fig. 15.1 Mechanism of action of NSAIDs

COX-2 Inhibitors

Because of the side effects characteristic of the nonselective NSAIDs, COX-2 selective inhibitors were developed to provide analgesia without the risks of COX-1 inhibition. Three COX-2 inhibitors were approved for use in the USA: rofecoxib, valdecoxib, and celecoxib. These medications were successful in reducing the risk of gastric ulceration and lacked the antiplatelet effects of traditional NSAIDs. However, rofecoxib and valdecoxib were discontinued from the market in 2004 and 2005, respectively, due to an increased risk of cardiovascular events in patients taking these drugs (coronary vasoconstriction caused by inhibition of prostacyclin production, which is a vasodilator). Celecoxib remains available in the USA, and standard doses for acute pain are 100–200 mg PO BID with the option of a one-time loading dose of 400 mg.

Acetaminophen

Acetaminophen is another non-opioid analgesic that is effective for mild to moderate pain. While its mechanism of action is not completely understood, it has no significant effect on the COX enzymes at peripheral sites. However, its centrally mediated analgesic effect is likely due to COX inhibition in the CNS in addition to interactions with NMDA receptors,

Table 15.1 Commonly used COX inhibitors

Drug	Route of administration	Dosing	Side effects/notes
Aspirin	PO, PR	325–650 mg q4h (max 4 g/day)	Nausea, risk of bleeding, hyperuricemia, should not be used in children less than 12 years of age due to the risk of Reye's syndrome (acute encephalopathy, fatty liver)
Ibuprofen	PO, IV	400–800 mg q4–6 h (max 3,200 mg/day)	Nausea, risk of bleeding, renal injury, gastric ulceration, salt and fluid retention, risk of myocardial infarction and stroke
Naproxen	PO	250–500 mg q12h (max 1,250 mg/day	Nausea, risk of bleeding, renal injury, gastric ulceration, cardiovascular effects
Ketorolac	IV, IM, PO, nasal spray	30 mg IV q6h (max 120 mg/day), 10 mg PO q4–6 h (max 40 mg/day)	Reduce dose to 15 mg IV q6h in patients older than 65 years or less than 50 kg weight, and those with renal impairment. Maximum days of continuous treatment for 5 days
Celecoxib	PO	100–200 mg QD/BID	Avoid in patients allergic to sulfa drugs, possible cardiovascular effects
Acetaminophen	PO, PR, IV	325–1,000 mg PO/PR q4–6 h, 1 g IV q6h (max 4 g/day)	Hepatotoxicity

COX cyclooxygenase enzyme, *PO* oral, *PR* rectal, *IM* intramuscular, *IV* intravenous

Table 15.2 α_2-Adrenergic agonists

Drug	Route of administration	Dosing	Side effects/notes
Clonidine	PO, IV, transdermal, epidural	• PO-0.1–0.3 mg PO bid • IV-3 mcg/kg IV bolus and 0.3 mcg/kg/h infusion • Patch-0.1–0.3 mg/24 h q7 days • Epiduraly-30 mcg/h for cancer pain	Can be given IM and as an adjunct in peripheral nerve blocks. Side effects: bradycardia, hypotension, rebound hypertension on sudden discontinuation of drug
Dexmedetomidine	IV	1 mcg/kg bolus over 10 min, then infusion 0.2–1 mcg/kg/h	Prepare as: 2 ml of drug in total 50 ml of 0.9 % saline (4 mcg/ml). Side effects: hypotension, bradycardia

PO oral, *IM* intramuscular, *IV* intravenous

serotonergic pathways, and cannabinoid receptors. Like NSAIDs, the antipyretic effects of acetaminophen are derived from COX inhibition in the hypothalamus.

Acetaminophen has long been available in oral (PO) and rectal (PR) formulations. Oral dosing prior to surgery is effective for postoperative analgesia for short procedures. For patients unable to take medications by mouth, PR formulations were the only available choice until recently. Intravenous acetaminophen was introduced to the USA in 2010 and has quickly become a valuable option for the control of perioperative pain. Like the NSAIDs, IV acetaminophen has opioid-sparing effects. Standard dosing is 1,000 mg IV q6h given as a 15 min infusion. Regardless of the route of administration, the total dose of acetaminophen should not exceed 4 g in 24 h to avoid hepatotoxicity.

α_2-Adrenergic Agonists

Like NSAIDs, α_2-agonists inhibit pain through pathways distinct from opioids and are an important option in multimodal analgesia. However, these versatile drugs have a spectrum of effects much wider than simple pain relief. The two drugs in this class, clonidine and dexmedetomidine, are utilized for such extensive indications as procedural sedation, antihypertension, treatment of alcohol and opioid withdrawal, and peripheral nerve blockade.

Pharmacology

α_2-agonists exert much of their therapeutic effect by binding to presynaptic α2-receptors in the CNS. This interaction reduces body-wide sympathetic outflow and inhibits afferent pain signals in the spinal cord. While clonidine and dexmedetomidine both act at the α_2-receptor, dexmedetomidine has more than seven times greater specificity for this receptor. This difference may explain some of the variation in therapeutic uses between the two drugs. Clonidine can be administered via multiple routes; however, an oral dose has a half-life of 6–12 h. Dexmedetomidine is given intravenously and has a half-life of 2 h. Both drugs are metabolized hepatically and excreted renally.

Clonidine

Clonidine is a very versatile drug. It is effective in the treatment of multiple conditions and can be administered via many routes, including orally, transdermally, intravenously, epidurally, and perineurally. Its most familiar use is likely as an antihypertensive medication, and many patients will present for surgery taking this drug. While IV clonidine has been used in multimodal analgesia regimens, this medication is more likely to be used with a local anesthetic and narcotic for epidural anesthesia or with a local anesthetic alone for peripheral nerve blockade. A typical starting dose for epidural clonidine infusion is 30 mcg/h (Table 15.2). In combination with a local anesthetic in a peripheral nerve block, administration of 1 mcg/kg of clonidine can increase the duration of pain relief by more than 40 %. Postoperatively, it is useful in treating the subjective symptoms of alcohol and opioid withdrawal. However, it must be remembered that clonidine does not replace benzodiazepines in the treatment of alcohol withdrawal.

Side Effects

Sedation, bradycardia, and orthostatic hypotension are major side effects of clonidine. Notably, discontinuation of clonidine requires a weaning period because abruptly stopping this drug can result in dangerous rebound hypertension.

Dexmedetomidine

Dexmedetomidine was introduced to the USA in 1999 and is used as a sedative, anxiolytic, and analgesic for multiple indications. Unlike other IV anesthetic medications, the sedation produced by dexmedetomidine is not associated with significant respiratory depression and causes less upper airway obstruction than propofol. This quality has made it especially valuable for sedation during procedures under MAC, particularly for patients at risk of upper airway obstruction. Dexmedetomidine is also very useful as a sedative during awake fiber-optic intubations due to its lack of respiratory depression.

For procedural sedation, a loading dose of 1 mcg/kg over 10 min followed by an infusion of 0.2–1 mcg/kg/h is used. However, infusions up to 1.4 mcg/kg/h have been shown to be safe. It is approved for sedation in the ICU for less than 24 h, but sedation for longer periods has been reported without incident. Because of its inherent analgesic properties, dexmedetomidine also reduces opioid requirements. For this reason, it is a valuable option for analgesia in chronic opioid users and in patients at risk for opioid-related side effects.

Dexmedetomidine possesses several qualities that make it a particularly useful anesthetic during neurosurgical procedures. Unlike volatile anesthetics, it does not cause any significant alteration in motor or somatosensory evoked potentials. Because patients are usually arousable and able to interact during sedation with dexmedetomidine, it plays a valuable role during awake craniotomies. Additionally, there is emerging research suggesting that dexmedetomidine may have neuroprotective effects when used as part of an anesthetic regimen.

Side Effects

Hypertension may develop immediately following a bolus dose of dexmedetomidine. This is often followed by variable degrees of hypotension and bradycardia during the period of infusion.

Clinical Review

1. All of the following drugs are available in the United States for intravenous administration, EXCEPT
   A. Ibuprofen
   B. Acetaminophen
   C. Ketorolac
   D. Celecoxib
2. Celecoxib inhibits the enzyme
   A. Cyclooxygenase-1
   B. Cyclooxygenase-2
   C. Both A & B
   D. Phosphodiesterase
3. Pain is mediated primarily by
   A. Cyclooxygenase-1 enzyme pathway
   B. Cyclooxygenase-2 enzyme pathway
   C. Both A & B
   D. Alpha-2 adrenergic receptor antagonism
4. The following is not an effect of dexmedetomidine
   A. Sedation
   B. Anxiolysis
   C. Tachypnea
   D. Bradycardia

Answers: 1. D, 2. B, 3. B, 4. C

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Diuretics

16

Daniel S. Cormican and Shawn T. Beaman

Diuretics are pharmacologic agents that increase urine excretion or cause diuresis. There are a multitude of clinical indications for which diuretics may be given. Although increased urine production is the end product, this may not be the primary reason for diuretic administration. For anesthesiologists, familiarity with diuretics, including their mechanism of action, side effects, clinical implications, and impact on anesthetic provision, is essential, as diuretics are very widely used. Diuretics were the ninth most prescribed class of medication in 2010 ("lipid regulators" were the most prescribed). Some patients come to the hospital for surgery having taken oral diuretics for years for treatment of chronic conditions, while other patients may require single/multiple doses of intravenous diuretic administration in the operating room or critical care unit.

Diuretics are classified either by their mechanism of action or by their site of action within the nephron of the kidney. Comprehension of diuretic mechanism of action necessitates understanding of the basic physiology of the nephron. While discussion of in-depth renal physiology is outside the scope of this chapter, review of foundational concepts will facilitate further discussion on mechanism of action of diuretics. The kidney functions to maintain fluid and solute balance, regulate acid/base status, and excrete toxins/waste. The nephron is the functional unit of the kidney; Fig. 16.1 describes some actions of the nephron components. It should be noted that all diuretics can cause hypovolemia, up to varying extents. Preoperatively, all diuretics should be held in the morning of the surgery, and electrolytes, especially potassium, should be measured before the surgery.

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Thiazide Diuretics

Hydrochlorothiazide (HCTZ) is the most common thiazide in clinical use. Other thiazides include chlorothiazide, indapamide, hydroflumethiazide, trichlormethiazide, and bendroflumethiazide. Metolazone has thiazide-like properties.

Mechanism of Action

Thiazides work primarily at the distal convoluted tubules (DCT) to inhibit Na^+ and Cl^- reabsorption, which leads to greater Na^+ and Cl^- delivery to more distal portions of the nephron. Water "follows the salt," and urine output is thus increased.

Side Effects

As with all diuretics, hypovolemia can occur. For thiazides in specific, one must be aware of possible hypokalemic–hypochloremic metabolic alkalosis, hyponatremia, hypomagnesemia, hypercalcemia (increased calcium reabsorption in the distal tubules), hyperglycemia, and hyperuricemia. Idiosyncratic acute angle glaucoma after thiazide administration has been reported.

Clinical Applications/Implications in Anesthesiology

Thiazides, given orally, are commonly used as first-line agents for treatment of hypertension. Thiazides may also be used for volume overload situations (e.g., pulmonary edema, congestive heart failure). Thiazides may be used for treatment of nephrogenic diabetes insipidus. Metolazone and loop diuretics (often bumetanide) together have a synergistic effect that may produce profound diuresis in patients resistant to diuresis with single

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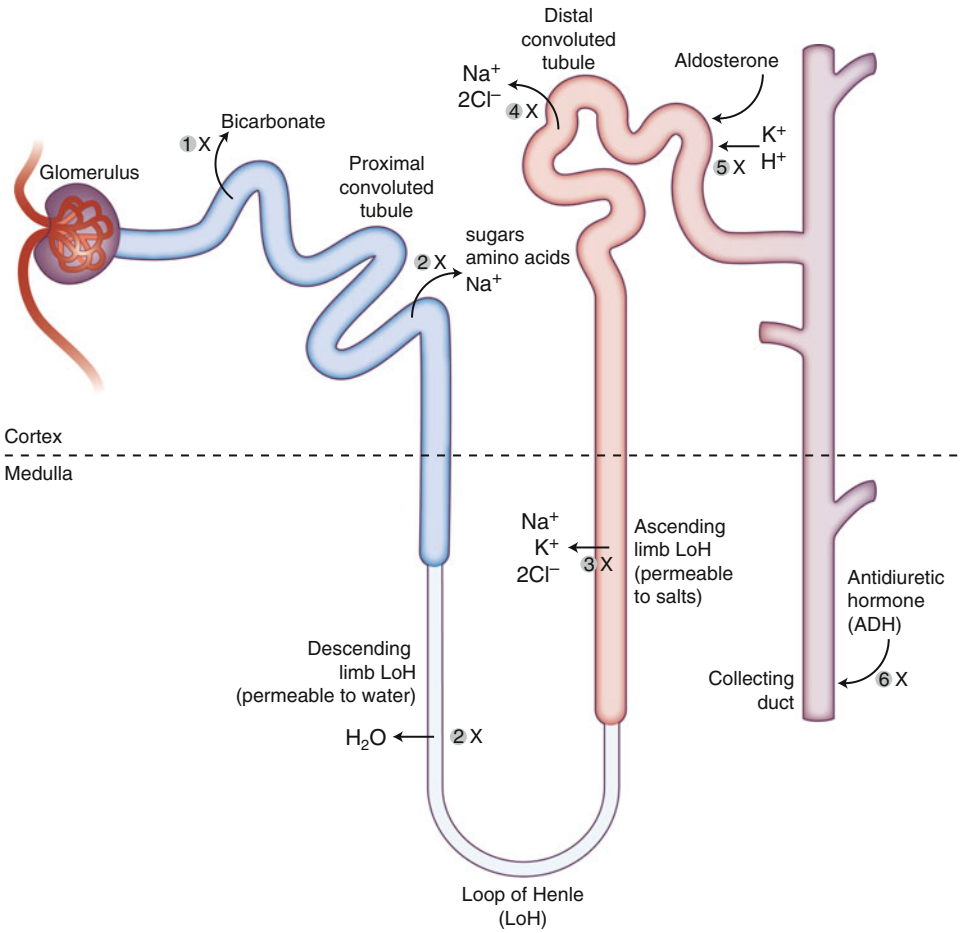

Fig. 16.1 The nephron: diuretics and their site and mechanism of action. (1.) Acetazolamide, (2.) mannitol, (3.) furosemide (loop diuretics), (4.) thiazides, (5.) spironolactone, (6.) antidiuretic hormone antagonists

agent therapy. One must be aware of implications related to thiazide side effects. Hypovolemia may complicate blood pressure management and tissue perfusion. Electrolyte imbalances (especially hypokalemia) may prolong nondepolarizing neuromuscular blockade and exacerbate skeletal muscle weakness.

Loop Diuretics

Furosemide is the most commonly used loop diuretic. Other loop diuretics include ethacrynic acid, bumetanide, and torsemide. Doses are as follows: furosemide (20–100 mg), ethacrynic acid (50–100 mg), bumetanide (0.5–1 mg), torsemide (10–100 mg).

Mechanism of Action

Loop diuretics work at the medullary portion of the ascending loop of Henle, blocking the $Na^+/K^+/2Cl^-$ transporter, limiting Na^+ reabsorption, and thus delivering more Na^+ and Cl^- to the distal portions of the nephron. Of note, furosemide has a prostaglandin-stimulating action within the kidney, which increases renal blood flow, further promoting diuresis. Loop diuretics also increase the excretion of calcium and magnesium.

Side Effects

As with all diuretics, hypovolemia can occur. For loop diuretics in specific, one must be aware of hypokalemic–hypochloremic metabolic alkalosis, hyponatremia, hypomagnesemia, and hyperuricemia (increased urate reabsorption). Reversible hearing loss is rare but has been reported, especially in patients on high doses of loop diuretics. Loop diuretics, with the exception of ethacrynic acid, contain a sulfonamide nucleus and should be used cautiously in patients with sulfa-/sulfonamide allergies.

Clinical Applications/Implications in Anesthesiology

Loop diuretics are commonly used in an oral form to help reduce volume overload in patients with renal dysfunction, CHF, or liver dysfunction. Loop diuretics can be useful for

treatment of increased intracranial pressure, rapid correction of hyponatremia, treatment of hypertension in combination with a thiazide diuretic, or as supplemental treatment of hypercalcemia or hyperkalemia. Note that furosemide can be given as an oral form or IV form; the oral to IV dose ratio is 3:1. Bumetanide may be paired with metolazone (a thiazide diuretic) to produce profound, prolonged diuresis in patients refractory to single agent diuretic therapy. One must be aware of implications related to loop side effects. Hypovolemia may complicate blood pressure management and tissue perfusion. Electrolyte imbalances (especially hypokalemia, hypocalcemia) may prolong nondepolarizing neuromuscular blockade and exacerbate skeletal muscle weakness.

Carbonic Anhydrase Inhibitors

Acetazolamide is the most commonly used carbonic anhydrase inhibitor. It is a weak diuretic and is administered in a dose of 250–500 mg intravenously.

Mechanism of Action

Carbonic anhydrase inhibitors cause noncompetitive inhibition of the carbonic anhydrase enzyme; carbonic anhydrase is used to catalyze the reactions between water, carbon dioxide, carbonic acid, and bicarbonate. In the proximal tubule (PT) of the kidney, inhibition of carbonic anhydrase causes an increase in renal bicarbonate excretion (alkalinization of urine). In the eye, acetazolamide inhibits aqueous humor production, which reduces intraocular pressure.

Side Effects

Acetazolamide may cause mild hyperchloremic metabolic acidosis, which is related to increased renal excretion of bicarbonate.

Clinical Applications/Implications in Anesthesiology

Acetazolamide is prescribed for treatment of glaucoma or altitude sickness. One must be aware of implications related to carbonic anhydrase side effects. Hypovolemia may complicate blood pressure management and tissue perfusion. When encountered, the metabolic acidosis may alter the function of other anesthetic medications or create an additive acidosis in the setting of concomitant respiratory acidosis. Perioperative normal saline administration may worsen hyperchloremic acidosis as well.

Osmotic Diuretics

Mannitol is the most commonly used osmotic diuretic. Use of urea is also described in the literature, but it is rarely administered by anesthesiologists. Mannitol is a 6-carbon sugar and undergoes almost no reabsorption in the proximal tubule. It is hypertonic and increases excretion of water, sodium, and potassium. However, excessive water loss can lead to hypernatremia.

Mechanism of Action

Osmotic diuretics work, as the name suggests, by increasing the osmolarity of plasma. After intravenous administration, the hyperosmolar plasma draws fluid along the osmotic gradient, so that fluid leaves intracellular spaces for the extracellular space. The increased extracellular fluid is carried as expanded intravascular volume. Once in the kidney, the increased osmolarity of renal tubular fluid prevents reabsorption of water, resulting in increased urine volume. Mannitol may have vasodilatory properties as well, increasing renal blood flow and enhancing free radical scavenging.

Side Effects

Vasodilation produced by mannitol can decrease blood pressure and/or transiently increase cerebral blood volume (CBV). The initial intravascular fluid expansion caused by mannitol administration may be poorly tolerated by persons with poor cardiac function (pulmonary edema).

Clinical Applications/Implications in Anesthesiology

Mannitol may be requested by neurosurgeons for the treatment of intracranial pressure elevation or for optimization of operating conditions for intracranial procedures. Gentle, judicious administration of the drug, 0.25–1 g/kg, is recommended in these situations (as an infusion over 10 min or in small, divided doses), to minimize the increase in cerebral blood volume. Moreover, mannitol administration in patients without an intact blood–brain barrier may draw fluid into the brain thus increasing CBV. The clinical effect of mannitol begins 15–30 min after administration.

Potassium-Sparing Diuretics

Triamterene and amiloride are the most commonly used potassium-sparing diuretics.

Mechanism of Action

These medications act in the collecting duct to alter transport mechanisms, which results in decreased Na^+ reabsorption and increased water excretion, resulting in increased urine output. Moreover, the normal excretion of potassium in the distal nephron is inhibited, decreasing its excretion.

Side Effects

For potassium-sparing diuretics in specific, hyperkalemia and metabolic acidosis are of obvious concern. Nausea, vomiting, diarrhea, and muscle cramping may be seen.

Clinical Applications/Implications in Anesthesiology

Potassium-sparing diuretics are most frequently prescribed to patients with hypokalemia who are in need of diuretic therapy; these patients are often taking other diuretics that cause hypokalemia (especially loop diuretics and thiazides). Hypovolemic effects of diuretic administration can cause unwanted hemodynamic issues perioperatively. Hyperkalemia may cause dysrhythmias or muscle weakness.

Aldosterone Antagonists

Spironolactone is the most commonly used agent in this class; eplerenone is a newer agent in this class.

Mechanism of Action

Aldosterone is a hormone which acts in the renal collecting tubules, causing increased Na^+ (and thus water) reabsorption and K^+ excretion. Spironolactone is structurally similar to aldosterone and binds to aldosterone receptors, resulting in diuresis as Na^+, and water reabsorption is diminished. K^+ secretion is inhibited. Spironolactone has some antiandrogenic properties.

Side Effects

Hyperkalemia and metabolic acidosis are potential risks. Due to spironolactone's hormonelike structure, gynecomastia, hirsutism, and menstrual cycle changes are not uncommon; eplerenone has fewer side effects.

Clinical Applications/Implications in Anesthesiology

Spironolactone is most commonly prescribed for treatment of chronic volume overload states, like CHF and cirrhosis. It may also be paired with other diuretic agents (like thiazides) to augment diuresis while counteracting any potassium-wasting effects. Persons with hyperaldosterone syndromes may take this medication as well. Perioperatively, hypovolemic effects of diuretic administration can cause unwanted hemodynamic issues perioperatively. Hyperkalemia may cause dysrhythmias or muscle weakness.

Antidiuretic Hormone (ADH)/Vasopressin Antagonists

Conivaptan and tolvaptan are two of the most commonly used ADH antagonists.

Mechanism of Action

ADH antagonists act in the collecting ducts in the nephron, blocking ADH effects on vasopressin-class receptors. Conivaptan acts at V1a and V2 receptors, and tolvaptan is selective for V2 receptor antagonism. V2 receptor blockade results in free water excretion (termed "aquaresis").

Side Effects

As with all diuretics, hypovolemia can occur. For ADH/vasopressin antagonists in specific, allergic reactions, muscle weakness, and liver toxicity may be seen.

Clinical Applications/Implications in Anesthesiology

This class of medication is relatively new to clinical medicine; the Food and Drug Administration approved clinical use of conivaptan in 2005. These medications are administered intravenously only and are prescribed to treat hyponatremia believed to be caused by ADH abnormalities. A large clinical trial reported improvements in heart failure patients treated with tolvaptan, including increased weight loss and subjective improvements in dyspnea, although there was no improvement in morbidity or mortality with this medication.

Clinical Review

1. The following diuretic can cause pulmonary edema on initiation of therapy:
   A. Furosemide
   B. Mannitol
   C. Acetazolamide
   D. Spironolactone
2. The following diuretic is specifically used to decrease production of aqueous humor:
   A. Furosemide
   B. Mannitol
   C. Acetazolamide
   D. Thiazide
3. This diuretic may be used in patients with advanced liver disease to spare potassium:
   A. Furosemide
   B. Mannitol
   C. Acetazolamide
   D. Spironolactone
4. This diuretic may be used in the presence of hypocalcemia:
   A. Furosemide
   B. Mannitol
   C. Acetazolamide
   D. Thiazide
5. This diuretic may cause ototoxicity:
   A. Furosemide
   B. Mannitol
   C. Acetazolamide
   D. Thiazide

Answers: 1. B, 2. C, 3. D, 4. D, 5. A

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Cardiovascular Pharmacology

17

Ali R. Abdullah and Todd M. Oravitz

Understanding the intricate pharmacodynamics and pharmacokinetics of cardiac drugs is one of the most important aspects of anesthesiology. There are literally hundreds of cardiovascular drugs and dozens of possible targets in the body for which any possible response is conceivable. It is imperative to select the most appropriate drug for a desired action while minimizing side effects. This chapter describes the pharmacology of commonly used cardiovascular and adjunct drugs in the practice of anesthesiology.

Nitrates

Nitroglycerin

Mechanism of Action

NTG acts as a smooth muscle relaxant leading to nitric oxide-mediated vascular dilation (Fig. 17.1). Nitrogen oxide containing compounds enter the smooth muscle cells and undergo a series of reactions leading to the formation of nitric oxide (NO), which stimulates guanylyl cyclase (GC). GC then produces cyclic guanosine monophosphate (cGMP), which dilates the smooth muscle. Chronic NTG use can lead to tolerance. This is due to excessive SH (sulfhydryl) metabolism, which is required for the formation of NO. SH donors (e.g., *N*-acetylcysteine) can reverse NTG tolerance.

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Clinical Effects

NTG improves myocardial oxygen delivery and reduces oxygen demand. Unlike nitroprusside, NTG is more of a venodilator than an arteriolar dilator. In fact, administrating large doses of NTG during cardiopulmonary bypass (CPB) cases can exacerbate venous sequestration of blood and impede venous return to the pump. At very low dosage, NTG dilates capacitance venous vessels, thereby, effectively reducing venous return to the heart, preload, and cardiac filling pressures. The effect of NTG on the coronary circulation is complex; however, there are a number of important physiological responses in the coronary circulation: epicardial coronary artery dilation, increased coronary collateral flow (beneficial for ischemic areas), and improved subendocardial blood flow, all leading to increased oxygen supply and decreased myocardial oxygen consumption (MVO_2).

NTG also affects pulmonary circulation by vasodilating both the pulmonary arteries and veins with a consequential reduction in right atrial pressure, pulmonary artery pressure (PAP), and pulmonary capillary wedge pressure (PCWP). NTG also produces bronchodilation. Other systemic effects of NTG include dilatation of renal, cerebral (headache), and cutaneous vessels. There is no risk of cyanide toxicity, which is a concern for nitroprusside.

Clinical Indications

NTG is used for the treatment of myocardial ischemia/angina (unstable, exertional, or Prinzmetal's) and hypertension. During treatment hypotension may be encountered, which may be reversed by slowing the infusion rate or treated with vasopressors. Furthermore, mild reflex tachycardia and increased inotropy can occur, which can be diminished by the addition of beta-blockers or calcium channel blockers. NTG is administered via an infusion, 0.25–10 mcg/kg/min, and is available in glass containers, as it may degrade when in contact with plastic. NTG can also be administered sublingually (peak effect in 3–4 min) or transdermally (nitropaste—applied every 24 h).

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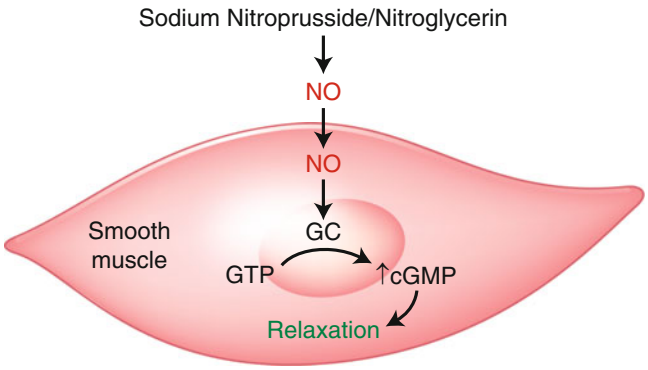

Fig. 17.1 Mechanism of action of nitrates (*NO* nitric oxide, *GC* guanylyl cyclase, *cGMP* cyclic guanosine monophosphate)

Nitroprusside

Mechanism of Action

The mechanism of action of sodium nitroprusside (SNP) is similar to NTG. It should be noted that nitric oxide is a potent vasodilator (half-life <10 s) and has its effects throughout the body. Inhaled nitric oxide is often used for treatment of pulmonary hypertension, especially in ICU patients.

Sodium nitroprusside on administration enters red blood cells and results in the formation of 5 cyanide ions and methemoglobin (an electron added to oxyhemoglobin). The cyanide ions exert their toxicity by combing with methemoglobin to form cyanmethemoglobin, combining with thiosulfate in the liver to form thiocyanate, and inhibiting the cytochrome oxidase enzyme system. All these effects can lead to cyanide toxicity (metabolic acidosis, dysrhythmias, tachyphylaxis of its hypotensive effect/acute tolerance). Treatment of cyanide toxicity includes limiting administration of sodium nitroprusside to less than 0.5 mg/kg/h and administration of 100 % oxygen. Methemoglobinemia is treated with intravenous methylene blue (1–2 mg/kg).

Clinical Effects

Sodium nitroprusside is a potent vasodilator, causing dilation of both the venous and arteriolar beds leading to a decrease in peripheral vascular resistance. It causes a reduction in mainly the preload, but also the afterload. The decrease in preload decreases myocardial oxygen requirements, but this effect is attenuated with an increase in heart rate (reflex tachycardia) and myocardial contractility, which increase oxygen demand. Sodium nitroprusside also dilates cerebral and pulmonary blood vessels, thereby, increasing blood flow. However, this increase in blood flow may be offset by reduction in arterial blood pressure. Therefore, administration of sodium nitroprusside may lead to increased intracranial pressure and ventilation-perfusion mismatch (less blood flow to ischemic areas).

Clinical Uses

Sodium nitroprusside is an extremely potent vasodilator and leads to a rapid lowering of blood pressure. An arterial line is used to monitor the blood pressure during sodium nitroprusside administration. It is administered via an infusion in a dose of 0.25–10 mcg/kg/min. Its onset of action occurs in 2 min and action lasts briefly after stopping the infusion. The solution is protected from light because of degradation by light.

Hydralazine

Mechanism of Action

Hydralazine acts as a direct arteriolar smooth muscle dilator, thus lowering peripheral vascular resistance (afterload) and the blood pressure. The exact mechanism remains unclear, but it may interfere with calcium utilization or activation of guanylyl cyclase.

Clinical Effects

Hydralazine lowers the blood pressure, which leads to an increase in heart rate and myocardial contractility. To offset these effects in cardiac compromised patients, beta-blockers may be given. Also, hydralazine leads to cerebral and renal vasodilation, and therefore, it is beneficial to use in patients with renal disease as it maintains renal blood flow. Some unwanted side effects include peripheral edema, lupus-like syndrome, pancytopenia, and peripheral neuropathy.

Clinical Indications

Hydralazine is used to treat hypertension intraoperatively. It is available in a vial, 20 mg/ml, and is diluted to 10 ml (2 mg/ml) prior to use. It is administered in 2–4 mg doses, up to 20 mg. The onset of action is in 10–15 min and lasts long for 2–4 h.

Adrenergic Agonists

Dopamine (DA), norepinephrine (NE), and epinephrine (EPI) are endogenous catecholamines. DA is primarily found in the CNS. NE is formed by the hydroxylation of DA and is predominately synthesized and stored in the postganglionic sympathetic nerve endings. Conversely, EPI is synthesized in the adrenal medulla by chromaffin cells; in fact, over 80 % of catecholamines produced in the adrenal medulla is EPI, and the rest is NE (Fig. 17.2). Catecholamines exert their effect on alpha, beta, and/or DA receptors.

The neurotransmitter that is mainly responsible for adrenergic activity of the sympathetic nervous system is NE. The release of NE into the synaptic gap is solely based on the depolarization of the nerve and the subsequent increase in calcium. The action potential permits calcium ion to enter the nerve ending and release of NE into the synaptic gap.

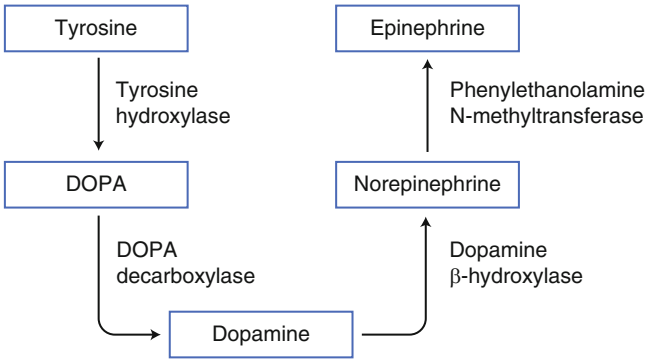

Fig. 17.2 Synthesis of norepinephrine and epinephrine

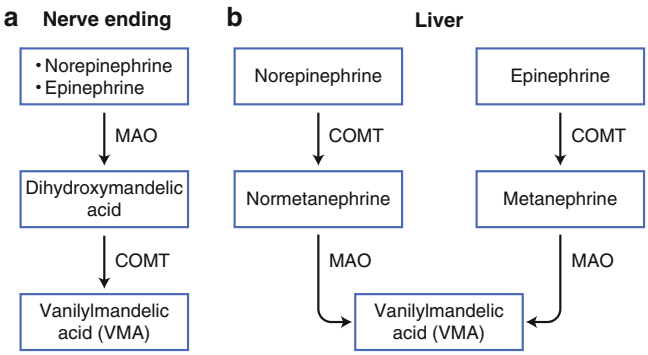

Fig. 17.3 Metabolism of norepinephrine and epinephrine in (**a**) nerve endings, (**b**) liver (*MAO* monoamine oxidase, *COMT* catechol-O-methyltransferase)

Sympathetic stimulation also causes the release of glucocorticoids from the adrenal cortex, which in turn stimulates the conversion of NE to EPI. Increased sympathetic activity is seen among patients with CHF and chronic stress, and during surgical stimulus. Almost 75 % of catecholamines released into the synaptic gap are removed by an energy-requiring reuptake into the neuron. The remainder of catecholamines are reabsorbed systemically (diffusion) and/or metabolized by monoamine oxidase (MAO) and catechol-O-methyltransferase (COMT). VMA (vanillylmandelic acid), the final metabolic product of catecholamine degradation, is excreted in the urine (Fig. 17.3).

There are two subtypes of alpha-receptors: alpha-1 and alpha-2. Historically, this classification is based on the response to the alpha antagonists yohimbine (alpha-2 sensitive) and prazosin (alpha-1 sensitive). Alpha-1 receptors (Table 17.1) are found in the smooth muscle in the body: the coronaries, skin, uterus, intestinal, and splanchnic beds. The response to alpha-1 stimulation is primarily vasoconstriction, bronchoconstriction, uterine contractions, and contraction of sphincters (gastrointestinal and genitourinary). Postsynaptic myocardial alpha-1 receptor stimulation causes mild positive inotropy with subsequent augmentation in LV function and stroke volume. It is believed that during episodes of cardiac insults (ischemia, reperfusion) alpha-1 receptors, due to enhanced responsiveness, play a role in malignant arrhythmias.

Alpha-2 receptors are found both on the presynaptic (predominate) and postsynaptic nerve terminals. Stimulation of presynaptic alpha-2 receptors results in inhibition of NE release. Stimulation of postsynaptic alpha-2 receptors causes sedation (CNS), peripheral vasodilation, and lowering of blood pressure.

Epinephrine

Epinephrine (EPI) is an endogenous adrenergic agonist, which is synthesized, stored, and released from the adrenal medulla. It has a variety of clinical indications including treatment of status asthmaticus, cardiac arrest, shock, anaphylaxis, and also prolongation of regional anesthesia (when mixed with local anesthetics). It has a dose-dependent effect on *alpha- and beta*-receptors. At low dosages (<0.03 mcg/kg/min), beta effects predominate, which include increases in heart rate, myocardial contractility, and cardiac output. Beta-2 stimulation causes bronchodilation and lowering of diastolic blood pressure due to skeletal muscle vasodilation (Tables 17.2 and 17.3).

At higher dosages (>0.15 mcg/kg/min) of EPI, the alpha effects are pronounced. This leads to increases in blood pressure (systolic) and coronary and cerebral perfusion pressures. Therefore, the physiological response on alpha- and beta-receptors by EPI demonstrates considerable variations (i.e., EPI can stimulate beta-receptors on some beds while stimulating alpha-receptors in others). EPI also possess strong pro-arrhythmogenic properties, especially in times of high sympathetic states (surgery, ischemia, hypoxia, sepsis). Excessive doses can lead to myocardial ischemia, cerebral bleeding, and arrhythmias. Classically described in literature is the administration of halothane with EPI leading to increased sensitization of the myocardium to the arrhythmogenic effects of epinephrine.

Epinephrine is available in vials of 1 mg/ml (1:1,000) or in prefilled syringes of 0.1 mg/ml (1:10,000). It is also commonly added to local anesthetic solutions at a concentration of 1:200,000 (5 mcg/ml). EPI is administered in boluses of 0.05–1 mg depending on the indication. It can also be given via an infusion of 0.01–0.3 mcg/kg/min or 2–20 mcg/min (prepared as 1 mg in 250 ml of $D_5W = 4$ mcg/ml).

Norepinephrine

A precursor to EPI, NE serves as an endogenous mediator of the sympathetic nervous system. It has direct alpha-1 stimulation with no beta-2 activity. Stimulation of alpha-1 receptors by NE leads to intense vasoconstriction, an

Table 17.1 Alpha- and beta-receptor effects in various parts of the body

Organ	Alpha-1 receptor effects	Beta-receptor effects
Eyes	Radial muscle contraction (mydriasis)	Ciliary muscle relaxation
Lungs	Bronchoconstriction	Bronchodilation (β2)
Heart		Increase heart rate, contractility, conduction (β1)
Blood vessels	Constriction	Dilation (β2)
GI tract	Sphincter contraction	Decreased tone, motility (β2)
Pancreas	Decrease insulin secretion	Increase insulin secretion (β2)
Bladder	Sphincter contraction	Relaxation (β2)

Table 17.2 Adrenergic agonist effects on alpha- and beta-receptors

Drug	Alpha-1	Alpha-2	Beta-1	Beta-2
Epinephrine	++	++	+++	++
Norepinephrine	++	++	++	0
Phenylephrine	+++	+	+	0
Ephedrine	++	0	++	+
Dopamine	++	++	++	+
Dobutamine	0	0	+++	+

Table 17.3 Physiological effects of adrenergic agonists

Drug	Heart rate	Mean arterial pressure	Cardiac output	Systemic vascular resistance
Epinephrine	↑↑	↑	↑↑	↓/↑
Norepinephrine	↓	↑↑↑	↓/↑	↑↑↑
Phenylephrine	↓	↑↑↑	↓	↑↑↑
Ephedrine	↑↑	↑↑	↑↑	↑
Dopamine	↑	↑	↑↑↑	↑
Dobutamine	↑	↑	↑↑↑	↓

increase in afterload, and reflex bradycardia. Stimulation of beta-1 receptors increases myocardial contractility, which may increase cardiac output. However, this increase in cardiac output is offset by the alpha-1 effects of NE. Therefore, NE is usually reserved for the treatment of refractory shock.

Since NE lacks chronotropic effects, it can improve coronary perfusion pressure without causing ischemia. However, the increase in ventricular filling pressures that NE causes can be attenuated by administrating a vasodilator. While end-organ ischemia is a concern with NE, maintaining MAP greater than 70 mmHg and an adequate cardiac output will minimize this effect. NE is available in 4 ml ampoules (4 mg/4 ml). It is administered as an infusion (4 mg in 250 ml of $D_5W = 16$ mcg/ml) in a dose of 0.01–1 mcg/kg/min or 2–20 mcg/min.

Ephedrine

Ephedrine has both direct and indirect (predominate) actions on alpha- and beta-receptors. Its actions are similar to EPI, but it is less potent than EPI. Ephedrine causes an increase venous return (preload), blood pressure, heart rate, and myocardial contractility, with subsequent increase in cardiac output. Ephedrine is used to treat intraoperative hypotension, though temporarily as the cause is determined. Other effects of ephedrine include its antiemetic properties and treatment of hypotension with spinal anesthesia in obstetrics. Ephedrine does not cause a decrease in uterine blood flow and is, therefore, the vasopressor of choice for obstetrics anesthesia. Administration of ephedrine in patients taking monoamine oxidase inhibitors (for depression) can lead to a hypertensive crisis due to sudden and massive release of adrenergic neurotransmitters. Ephedrine is available as 50 mg/ml 1 ml vials. It is commonly diluted to 5 or 10 mg/ml (with normal saline) and is administered in dosages of 5–10 mg boluses (0.1 mg/kg). Repeated doses of ephedrine may lead to tachyphylaxis (decreased stores of NE).

Phenylephrine

Phenylephrine is a potent alpha-1 agonist. When used in high doses, it has effects via alpha-2 and beta-receptors. Alpha-1 effects of phenylephrine include peripheral vasoconstriction, increase in systemic vascular resistance and blood pressure. Because it can cause reflex bradycardia, a drop in cardiac output can occur. It also causes a decrease in renal blood blow. It is available as 10 mg/ml 1 ml vials, and is diluted before use in 100 (100 mcg/ml) or 250 ml (40 mcg/ml) of

D_5W. It is administered to treat intraoperative hypotension in boluses of 40–80 mcg or via an infusion in a dose of 0.15–1 mcg/kg/min.

Dopamine

Dopamine is an adrenergic agonist with its activity being dose dependent:

- At doses of 0.5–2 mcg/kg/min, *dopamine* receptors are stimulated which cause vasodilation, especially in the renal vasculature, which promotes diuresis. This dose of dopamine is commonly referred to as renal-dose dopamine.
- At doses of 2–10 mcg/kg/min, dopamine stimulates *beta-1* receptors, which leads to increase in heart rate, myocardial contractility, cardiac output, and blood pressure.
- At doses of 10–20 mcg/kg/min, dopamine stimulates *alpha-1* receptors, which increases systemic vascular resistance and blood pressure but decreases renal blood flow.

Dopamine is used to support cardiac output and maintain blood pressure. Controversy exists whether dopamine actually preserves renal function. Some studies have demonstrated that renal-dose dopamine improves renal blood flow, glomerular filtration rate, and natriuresis in healthy humans; however, in high-risk patients with acute renal failure or oliguria, no such improvements may be seen. Dopamine administration can cause profound tachycardia and dysrhythmias. Dopamine plus nitroglycerin or nitroprusside (inodilator effect-inotropic and vasodilator effects) are often combined to further improve cardiac output by reducing afterload. Dopamine is prepared by adding 200 mg to 250 ml D_5W (800 mcg/ml).

Dobutamine

As a synthetic sympathomimetic drug, dobutamine is a highly beta-1 selective drug. It is a potent inotropic drug (increases myocardial contractility) used in cardiogenic shock to support cardiac output. Its mild beta-2 effects cause peripheral vasodilation. Dobutamine decreases left ventricular filling pressures and improves coronary blood flow, with minimal increase in heart rate, thus maintaining a positive oxygen balance. Dobutamine is prepared by adding 1 g/250 ml (4 mg/ml) and given in doses of 2–20 mcg/kg/min.

Beta-Adrenergic Blockers

Beta-blockers antagonize effects at the beta-receptors. They are commonly used to treat hypertension, supraventricular arrhythmias, and myocardial ischemia and infarction. Beta-blockers also reduce mortality after myocardial infarction. They reduce myocardial oxygen consumption, improve coronary blood flow, and prolong diastolic perfusion period by way of:

- Slowing the heart rate and increasing flow to ischemia areas
- Decreasing myocardial contractility
- Decreasing AV node conduction
- Decreasing the blood pressure and cardiac output

Stimulation of beta-receptors (adrenergic receptors) leads to increased release of norepinephrine (NE) in the synaptic cleft, which is the neurotransmitter responsible for most of the effects. There are two subtypes of beta-receptors: beta-1 and beta-2. Beta-1 is predominately found in the myocardium, SA node, and the ventricular conduction system. Stimulation of these receptors (increased cAMP) leads to increased heart rate, myocardial conduction, and contractility. In heart failure increased circulating catecholamine levels lead to a downregulation of the beta-1 receptors with relative sparing of the beta-2 type.

Beta-2 receptors are also found in the myocardium but to a lower extent and are mostly concentrated in the blood vessels of the skin, muscles, bronchi, and mesentery. Also, beta-2 receptors are concentrated on the presynaptic membrane (as opposed to postsynaptic beta-1 receptors). Stimulation of beta-2 receptors leads to vasodilation, bronchodilation (smooth muscle relaxation), and relaxation of the bladder and the bowel. Other effects include stimulation of gluconeogenesis and hypokalemia (drive potassium intracellularly). In general, beta-blockers can be nonselective (i.e., block both beta-1 and beta-2 receptors) or selective (block either beta-1 or beta-2 receptors, preferably).

Propranolol

Propranolol is a nonselective beta-blocker, that is, it blocks both beta-1 and beta-2 receptors. Due to its high lipid solubility and high first-pass metabolism, propranolol is not the preferred drug for the treatment of perioperative hypertension, tachycardia, or ischemia. Furthermore, it readily crosses the blood–brain barrier and can cause adverse CNS effects (depression, sleep disturbances, fatigue). It has an equal affinity for both subsets of beta-receptors while lacking intrinsic sympathomimetic activity (i.e., agonist and antagonist properties). Consideration should be taken in patients with reduced cardiac output states and liver disease due to decrease flow (potentiated by propranolol). Other adverse effects include bronchospasm (beta-2 receptor antagonism), bradycardia and heart block, and congestive heart failure. It is important to remember that abrupt discontinuation of propranolol may lead to rebound effects (hypertension, tachycardia). Propranolol is given in increments of 0.5 mg intravenously, up to 0.1 mg/kg, with doses titrated to the desired effect.

Metoprolol

Metoprolol is more beta-1 selective and less lipid soluble compared to propranolol, which makes it the ideal drug for treatment of perioperative hypertension, tachycardia, or ischemia. Similar to propranolol, it lacks intrinsic sympathomimetic activity and membrane-stabilizing activity. In clinical practice today, it is considered safe to use in patients with reactive airway disease (minimal beta-2 antagonism). It is available in vials of 5 mg (1 mg/ml) and is administered in doses of 1–5 mg, with a maximum dose of 15 mg.

Esmolol

Esmolol is a short-acting selective beta-1 blocker with minimal beta-2 antagonism. What makes esmolol unique among beta-blocking agents is its ester group. This property makes it liable to hydrolysis by red blood cell esterases (half-life 7–9 min). Its brief duration of action makes it ideal for blunting the stimulatory response to intubation or intense surgical stimulation. Esmolol causes a dose-dependent decrease in heart rate mainly, with its blood pressure lowering effects not as much. Esmolol has little effect on the bronchial tone and is, therefore, safer to use in patients with reactive airway disease. Dose: 0.2–0.5 mg/kg, followed by an infusion of 50–300 mcg/kg/min. 10 ml vials are available in a concentration of 10 mg/ml for boluses, and 2.5 g/10 ml concentration is available for preparing infusions.

Labetalol

Labetalol consists of a mixture of four stereoisomers with both selective alpha-1 and nonselective beta (1 and 2) receptor-blocking properties. The ratio of alpha-beta effectiveness is 1:3 after oral administration and 1:7 after intravenous administration. These alpha and beta effects decrease peripheral vascular resistance and the blood pressure. Labetalol has intrinsic sympathomimetic activity (partial beta-2 agonist leading to vasodilation). As a result, it causes peripheral vasodilation with no reflex tachycardia (heart rate, stroke volume, and cardiac output usually remain unchanged). Labetalol is available as 5 mg/ml and is given in doses of 0.1–0.2 mg/kg intravenously.

Calcium Channel Blockers

Calcium plays a crucial role as a quintessential cellular messenger involved in blood coagulation, enzyme reactions, bone metabolism, neuromuscular transmission, endocrine secretion, and muscle contraction. Calcium channel blockers (CCB) are commonly used to treat hypertension, supraventricular arrhythmias (verapamil, diltiazem), and arterial and coronary vasospasms. CCBs have a similar effect as beta-blockers in that they reduce myocardial oxygen demand by the following mechanisms:

- Decrease myocardial contractility (verapamil > diltiazem, but not nicardipine)
- Prolong AV nodal refractory period (verapamil > diltiazem)
- Decrease heart rate by affecting the SA node (verapamil > diltiazem, but possible reflex increase with nicardipine/nifedipine)
- Vasodilation (including coronary), decrease peripheral vascular resistance (SVR)
- Decrease blood pressure
- Decrease cardiac output (by verapamil, diltiazem, but possible increase with nicardipine/nifedipine)
- Depression of myocardial contractility

Calcium channels are found throughout the body (e.g., cardiac muscle, smooth muscle, sarcoplasmic reticulum, mitochondria). CCBs work by blocking voltage-gated calcium channels, thereby slowing calcium intake into the cell. As a result, there is a decrease in dromotropy, inotropy, and chronotropy. There are numerous types of calcium channels in the body. The L-type calcium channels are often referred to as "slow" channels and predominately found in cardiac tissue. L-type channels are responsible for phase 2 cardiac action potential and these channels are antagonized by CCBs. The T-type calcium channels, which are also found in cardiac tissue, are responsible for phase 0 cardiac depolarization. T-type channels are not antagonized by CCBs.

CCBs are categorized into two major groups: dihydropyridine and non-dihydropyridine. The difference between the two types of CCBs, besides their chemical structure, is based on their selectivity toward cardiac and peripheral L-type calcium channels. Dihydropyridines (nifedipine, nicardipine, nimodipine) tend to be more peripheral vascular selective (vasodilation, tachycardia) and are, therefore, primarily used to treat hypertension. Non-dihydropyridines (verapamil, diltiazem) are selective for the myocardium and are used mainly to treat arrhythmias and angina. It is important to select (Table 17.4) the right CCB when treating for HTN, angina/ischemia. Selecting a dihydropyridine to treat angina, for example, may lead to tachycardia and increased inotropy, therefore exacerbating the underlying cause.

Nifedipine

Nifedipine causes vasodilation that is accompanied by afterload reduction, leading to tachycardia and an increase in cardiac output. Its antianginal effect occurs by reducing afterload and LV volume, thereby reducing myocardial oxygen demand. Nifedipine is also one of the most potent coronary vasodilator.

Table 17.4 Properties of calcium channel blockers

Physiologic action	Verapamil	Diltiazem	Nifedipine
Heart rate	↓	↓	↑
Sinoatrial node conduction	↓	↓↓	0
Atrioventricular node conduction	↓	↓	0
Myocardial contractility	↓↓	↓	0
Vascular dilatation	↑	↑	↑↑
Coronary flow	↑	↑	↑

Nicardipine

Nicardipine produces both peripheral vasodilation and coronary dilatation. Because if its rapid onset and short duration of action, it can easily be used to titrate BP (IV route). It possesses little cardio-depressant effects and reflex tachycardia is uncommon, unlike nifedipine. It also produces cerebrovascular vasodilation but to a lesser extent than nimodipine. It is administered as an infusion 1–4 mcg/kg/min.

Nimodipine

Nimodipine is a highly lipophilic molecule that produces more cerebrovascular vasodilation than any other CCB. Nimodipine is rarely used for cardiovascular indications. It is used for the prevention of vasospasm produced by subarachnoid hemorrhage improving neurological outcomes.

Verapamil

Besides sharing a similar structure to papaverine, verapamil undergoes extensive first-pass metabolism and has an active metabolite (norverapamil) that has 20 % the potency of the parent compound. Due to extensive metabolism in the liver, a decreased dose should be used in patients with liver disease. The degree of myocardial depression (decrease contractility and heart rate) is more than it produces peripheral vasodilation. Verapamil is commonly used to treat supraventricular tachydysrhythmias as it decreases nodal conductivity. It is extremely effective in converting atrial fibrillation/flutter to sinus rhythm or slowing ventricular response. Caution should be used when it is combined with beta-blockers as this can result in complete AV block. Dose: 1–2 mg IV prn.

Diltiazem

Similar to verapamil, diltiazem serves as a better coronary than peripheral vasodilator. Also, diltiazem causes less myocardial depression than verapamil. It decreases contractility and heart rate. It is used for treatment of supraventricular tachydysrhythmias (including WPW syndrome) and rate control for atrial fibrillation. Dose: 20 mg IV bolus and infusion of 3–15 mg/h.

Phosphodiesterase Inhibitors

Phosphodiesterase inhibitors (PDIs) exert their inotropic and vasodilating effects without alpha- or beta-adrenergic stimulation. As a result, PDIs are useful agents in patients who are beta-blocked or have beta-blocker receptor down-regulation. PDIs specifically inhibit PDE III, which leads to an increase in cAMP and calcium influx as well as activation of protein kinases. In cardiac tissue, it is this increase in phosphorylation that promotes an increase in intracellular calcium stores leading to positive inotropy. Conversely, in vascular smooth muscle, phosphorylation and increased calcium stores leads to vasodilatation and a decrease in peripheral vascular resistance. As a result, PDIs are often referred to as "inodilators." There are two common PDIs used in practice today: amrinone and milrinone.

Amrinone

Amrinone has strong vasodilating properties and mild inotropic properties. Amrinone causes a dose-related improvement in cardiac output (increase), LVEDP (decrease), pulmonary artery pressure (decrease), LVEF (increase), and systemic vascular resistance (decrease). The heart rate and mean arterial pressure are not significantly affected. Because of its hemodynamic effects, it is not uncommon to use amrinone with a beta-agonist (e.g., dobutamine) to improve cardiac output. A number of studies demonstrate the effectiveness of amrinone over dobutamine for weaning from CPB as assessed by SV, CO, SVR, and PVR. Side effects of oral forms of amrinone include a dose-dependent thrombocytopenia and centrilobular hepatic necrosis (caution when using halothane) with chronic use. However, thrombocytopenia has not been seen with acute IV administration of amrinone. Amrinone is administered as a loading dose of 0.75 mg/kg followed by an infusion of 5–10 mcg/kg/min, with a total daily maximum dosage of 10 mg/kg/day.

Milrinone

Milrinone, a second generation PDI and a derivative of amrinone, has similar effects to that of amrinone. However, its inotropic effect is 20 times (more potent) than that of amrinone. Furthermore, no significant thrombocytopenia has been reported with use of milrinone. Because of its short-term hemodynamic effects, milrinone is easier to titrate than amrinone. Milrinone has been approved for the short-term therapy of congestive heart failure. It is administered as a loading dose of 50 mcg/kg followed by an infusion of 0.375–0.75 mcg/kg/min, with a total daily maximum dosage of 1.13 mg/kg/day.

Arginine Vasopressin

Arginine vasopressin (AVP) along with desmopressin are synthetic preparations that have similar effects to antidiuretic hormone (ADH) released from the posterior pituitary. AVP, historically, was used for the treatment and diagnosis of diabetes insipidus. AVP targets the vasopressin V-receptors (V1 and V2). V1 receptors are found in vascular smooth muscles and cardiac tissue, while V2 receptors are exclusively found in renal tissue and regulate renal function (increasing water reabsorption). Non-renal effects of AVP include vasoconstriction and inotropy. Clinical indications for AVP include septic shock and cardiac arrest (VFib, pulseless VT, or CHF). AVP has a modest effect on pulmonary circulation; therefore, AVP can be used for treatment of hypotension associated with right ventricular failure. The lowest infusion dose of AVP should be used due to the risk of ischemic skin lesions and organ ischemia.

Drugs Used During Cardiovascular Procedures

Heparin

Heparin is a sulfated glycosaminoglycan with a molecular weight range of 10–30 kDa. It is found in the lungs, liver, and the intestines. The exact physiological purpose of in vivo heparin remains unclear; however, it may serve a role in immunological response as it is found in high concentration within mast cells. In fact, anticoagulation in the body is done by heparan sulfate proteoglycans derived from endothelial cells.

Mechanism of Action

The anticoagulation effect of heparin occurs by the binding of heparin to antithrombin III (ATIII), an enzyme inhibitor, which causes a conformational change that results in the activation of ATIII. Subsequently, activated ATIII inactivates thrombin and factors Xa, IXa, XIa, and XIIa. Conversely, low molecular weight heparin (LMWH) inhibits factor Xa only. Numerous factors influence the pharmacokinetics and pharmacodynamics of heparin. For example, male smokers demonstrate rapid clearance of heparin. While liver disease does not affect the metabolism of heparin, renal failure prolongs its elimination. More importantly, hypothermia also prolongs the effect of heparin. The half-life of heparin is about 90 min, and that of low molecular weight heparin is about 4–6 h.

Clinical Uses

Heparin is used for treatment of acute thrombotic events (myocardial infarction), atrial fibrillation, to prevent deep vein thrombosis and pulmonary embolism, and for anticoagulation during surgical procedures, such as vascular surgeries and cardiopulmonary bypass. The anticoagulant effect of heparin is measured by serial estimations of activated partial thromboplastin time (aPTT) or the activated clotting time (ACT). Typical loading dose of heparin on-CPB and off-CPB are 300 U/Kg and 200 U/Kg, respectively. ACT goal for on-CPB is greater than 400, while off-CPB ACT goal is greater than 300.

Side Effects

Adverse effects of heparin use include bleeding, heparin resistance, and thrombocytopenia. Heparin has a narrow therapeutic index and an adequate level of anticoagulation is achieved by serial measurements of aPTT or ACT. What is often referred to as heparin resistance or altered heparin responsiveness occurs in up to 21 % of patients. Interestingly enough, 65 % of these patients responded to added ATIII.

There are two types of HIT: type I and type II. Type I occurs almost instantaneously during heparin administration, where heparin binds to platelet membranes leading to their inactivation. Type I HIT is transient, usually asymptomatic, and rarely requires treatment. Type II HIT, which is more severe than type I, is characterized by platelet counts dropping below 100,000/mm^3 or decline by up to 50 % over several days. In type II HIT, the underlying mechanism is believed to be IgG antibodies binding to complexes of heparin and platelet factor-4. Type II HIT should be diagnosed and treated promptly as it carries a significant mortality risk. Depending on the platelet count and clinical manifestation, heparin should be stopped immediately, and, if needed, alternative anticoagulation drugs should be considered such as lepirudin, bivalirudin, argatroban, or danaparoid, which are direct thrombin inhibitors. Warfarin should not be considered as an alternative in patients who develop HIT due to the risk of warfarin-induced skin necrosis.

Heparin rebound is a phenomenon where the reappearance of heparin into the circulation leads to clinically apparent

bleeding. The etiology is believed to be a result of release of heparin sequestered in tissues or lymphatics, delayed clearance, and/or protamine having a faster clearance compared to heparin.

Protamine

Protamine is used to reverse the anticoagulation effects of heparin. It is a polycationic compound derived from salmon sperm. Protamine, a highly basic peptide, forms ionic bonds with the negatively charged heparin to form a complex that is devoid of any activity, thereby preventing the activation of ATIII. The elimination of heparin-protamine complexes occurs in the reticuloendothelial system and possibly by macrophages in the lung.

Side effects of protamine administration include systemic hypotension, pulmonary hypertension, and allergic reactions. Protamine can cause hypotension due to neurogenic reflex, histamine release causing a decrease in SVR, or direct myocardial depressant action. Allergic reactions to protamine (anaphylactoid reactions) can occur in patients who have previously received protamine (insulin preparations containing protamine-diabetic patients). These reactions can cause hypotension, bronchospasm, flushing, and pulmonary edema. Protamine is not used to reverse heparin in such patients. Heparinase and recombinant PF-4 are alternative medications under research to reverse the effects of heparin.

Protamine is dosed at 1 mg/100 U of heparin. It is diluted in 100 ml of normal saline and, after a test dose of 2 ml, is given as a slow infusion over 10–15 min. If hypotension develops, it can be treated with phenylephrine (40–80 mcg bolus). Severe allergic reaction may require the administration of epinephrine.

Antifibrinolytics

Aminocaproic acid is a lysine analogue and competitive inhibitor of lysine-binding sites located on plasminogen and fibrinogen, thereby leading to inhibition of plasmin formation and inhibition of fibrinolysis. It is commonly administrated during CPB cases once the desired ACT is achieved to minimize bleeding. Because of its antifibrinolytic properties, there is an inherent risk for thrombosis. Dosage may have to be reduced in patients with renal disease. Transient hypotension may occur if it is administered rapidly. Dose: loading dose 5 g over an hour, then 1 g/h for up to 8 h.

Aprotinin is another medication, which has antifibrinolytic properties. It is a serine protease inhibitor derived from bovine lung tissue. It is used in cardiac surgery in patients who are at increased risk for bleeding. Because it can produce allergic reactions (anaphylaxis), it is given after a test dose (1 ml). Standard dosage varies from 1 to 2 million kallikrein inhibiting units (KIU) administered over 30 min, followed by 0.25–0.5 million KIU/h for the remainder of the surgery. Aprotinin has been implicated in developing renal failure; hence, its use is limited.

Clinical Review

1. The most strongest arteriolar dilator among the following is
   A. Nitroglycerin
   B. Nitroprusside
   C. Hydralazine
   D. Verapamil
2. The following is involved primarily in causing the effects of nitroglycerin
   A. Nitrogen oxide
   B. Adenylyl cyclase
   C. Nitric oxide
   D. Cytochrome oxidase
3. The neurotransmitter that is mainly responsible for function of the sympathetic nervous system is
   A. Dopamine
   B. Serotonin
   C. Epinephrine
   D. Norepinephrine
4. Bronchodilation occurs by stimulation of the following receptor
   A. Alpha-1
   B. Alpha-2
   C. Beta-1
   D. Beta-2
5. Calcium channel blocker with the most cardiac depressant effects is
   A. Verapamil
   B. Diltiazem
   C. Nifedipine
   D. Nicardipine
6. The adrenergic agonist commonly associated with the fight/flight response is
   A. Epinephrine
   B. Norepinephrine
   C. Dopamine
   D. Serotonin
7. Heparin binds to the following to cause anticoagulation
   A. Factor VIII
   B. Plasmin
   C. Thrombin
   D. Antithrombin

Answers: 1. B, 2. C, 3. D, 4. D, 5. A, 6. A, 7. D

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Local Anesthetics

18

John E. Tetzlaff

Local anesthetics are organic molecules used in clinical medicine to achieve reversible interruption of electrical activity in excitable cells, thereby producing transient loss of sensory, motor, and autonomic function (Table 18.1). To understand why local anesthetic molecules achieve their intended action, it is necessary to understand the anatomy and physiology of the nerve cell fiber, which allows transmission of electrical signals, and the organic chemistry of the molecules that interrupt these signals. It is then possible to use these basic concepts to understand the properties of the commercially available local anesthetics in clinical use, and how the individual agents differ in their actions.

Anatomy and Physiology of Nerve Conduction

The fundamental unit of excitable tissue is the nerve cell (Fig. 18.1). The major parts of the nerve cell include the cell body, the nucleus, dendrites, and the axon. The lipoprotein nerve cell membranes of the axon and to a lesser degree the dendrites are involved in electrical activity. Most of the axons in the body are covered with a discontinuous insulating substance, called myelin (Fig. 18.2), with gaps determined by the size and function of the nerve (nodes of Ranvier).

The physiological basis for nerve conduction is the movement of sodium and potassium ions across the axonal membrane through ion channels (Fig. 18.3). Sodium channels exist in three states: resting, activated (open), or inactivated. The sodium channels allow movement of sodium only in the open state, while potassium moves freely, achieving electrical neutrality and determining the electrical charge intracellularly, with sodium restricted to the extracellular side when the sodium channels are closed. The result is that sodium is the predominant extracellular cation and potassium the predominant intracellular cation. Following chemical, mechanical, or electrical stimuli, movement of sodium occurs into the cell via open sodium channels causing depolarization. At a given threshold (−55 mV) an action potential occurs and this segment of the axon causes depolarization of adjacent axonal membrane (neural conduction). The electrical neutrality is rapidly restored by egress of potassium outside the cell, inactivation of voltage-gated sodium channels, and the balance restored by energy-dependent sodium/potassium ATPase (transports three sodium ions out of the cell for every two potassium ions it transports inside the cell). In axons covered with myelin (myelinated nerves), the depolarization occurs at the nodes of Ranvier, with sodium movement at one node causing opening of the sodium channels at the adjacent node.

Conduction block occurs when this process is interrupted by sodium channel blockade, which can be reversible or nonreversible. Clinical conduction block with local anesthetics occurs exclusively in the reversible group, with irreversible block occurring with pesticides and animal venom. All reversible sodium channel block occurs on the intracellular side of the sodium channel (Fig. 18.4). For physiologic reasons, local anesthetics are delivered on the extracellular side, because intraneural injection into the axon would cause damage to the nerve cell membrane. This means that the molecule chosen must be capable of diffusing across the axonal membrane (lipid solubility), and occupy the open face of the sodium channel on the intracellular side (ionic bonding). The crossing of the neural membrane occurs at the Nodes of Ranvier in myelinated axons, and blockage of consecutive nodes increases the probability of conduction block. This is the reason why conduction block occurs quickly in smaller, unmyelinated (C) nerve fibers and slowest in the larger myelinated (A) nerve fibers (Table 18.2).

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Table 18.1 Dosages and duration of action of **commonly** used local anesthetics

Agent	Spinal	Epidural	Nerve block	Duration[a]
Lidocaine	Can be used	2 %, 15–30 ml	2 %, 30–50 ml	1–1.5 h
Ropivacaine	Can be used	0.2 %, 10–20 ml	0.5 %, 30–50 ml	3–4 h
Bupivacaine	0.75 %, 1–2 ml	0.25 %, 10–20 ml	0.25 %, 30–50 ml	3–4 h
Mepivacaine	Can be used	Can be used	1.5 %, 30–50 ml	2–3 h
Chloroprocaine	Not used currently	3 %, 15–30 ml	Can be used	0.5–1 h

[a]Addition of epinephrine 5 mcg/ml (1:200,000) prolongs the duration of the block

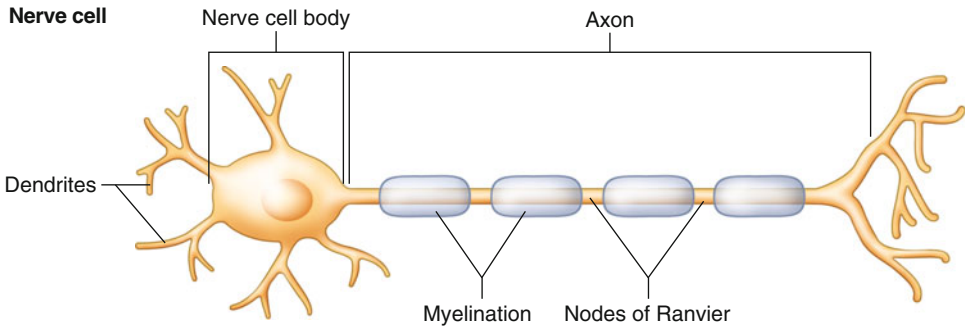


Fig. 18.1 Anatomy of a nerve cell

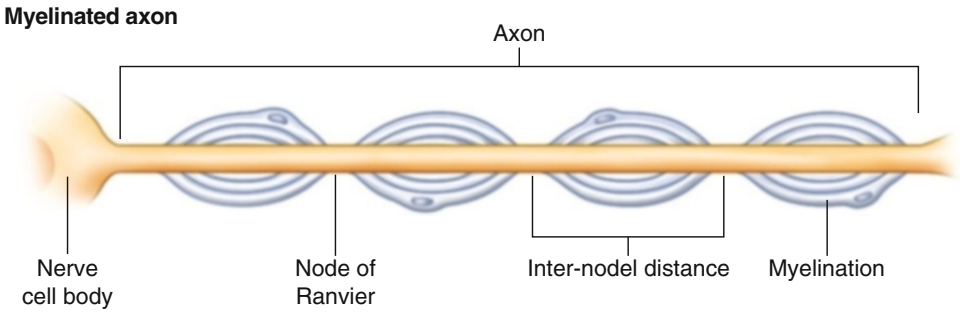


Fig. 18.2 The myelinated axon

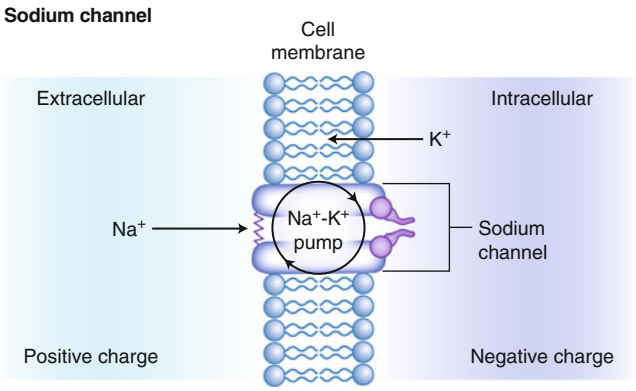


Fig. 18.3 Sodium channel, potassium movement, and the sodium–potassium ATPase pump

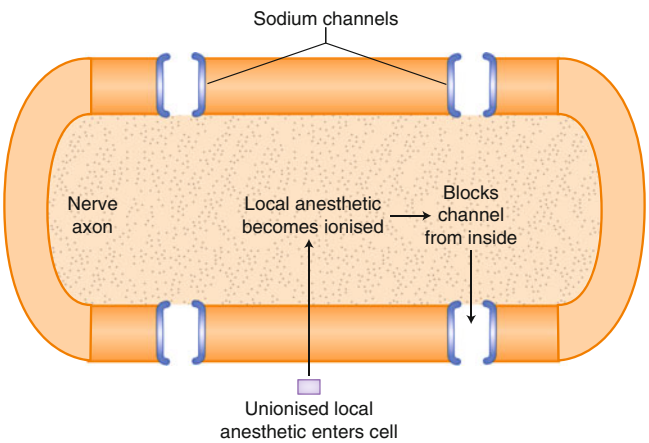


Fig. 18.4 Mechanism of action of local anesthetics

Table 18.2 Peripheral nerve fiber types

Fiber type	A-alpha	A-beta	A-gamma	A-delta	B	C
Mode of conduction	Motor, proprioception	Light touch, pressure, proprioception	Motor	Pain, cold temperature, touch	Autonomic	Pain, temperature, touch
Size	4+	3+	2+	2+	1+	1+
Myelination	Yes	Yes	Yes	Yes	Yes	No

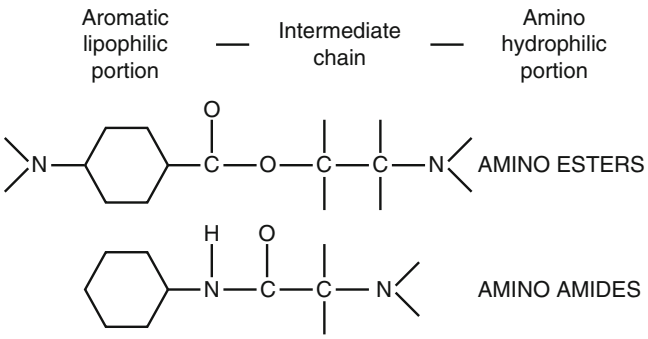


Fig. 18.5 Chemical structure of local anesthetics

Organic Chemistry of Local Anesthetic Molecules

The prototype local anesthetic agent has four structural elements that contribute to function (Fig. 18.5). They are all amphipathic molecules, which means that within the molecule there are elements with different purposes. All local anesthetics are weak bases, manufactured and stored at acid pH as sodium (or carbonate) salts. The largest element is the hydrophobic side of the molecule which creates lipid solubility. On the opposite side of the molecule is the hydrophilic element, allowing for ionic activity. The hydrophilic side is a tertiary amine for all commercially available local anesthetics except benzocaine (a secondary amine). The hydrophobic and the hydrophilic elements are linked via an intermediate chain of between 3 and 7 carbon equivalents in size. Within the intermediate chain is a bond (either amide or ester) that determines the type of molecule and its metabolism in the body. The amino amides originate from and are metabolized to anilines whereas the amino esters are related to para-aminobenzoic acid (PABA).

Lipid solubility is determined by the size of the hydrophobic element of the molecule, but also by aliphatic substitutions on the intermediate chain and the hydrophilic element. Lipid solubility determines the potential for the molecule to cross the axonal membrane, and hence determines the potency and toxicity. More lipid solubility means more potency and potential for central nervous system (CNS) toxicity.

Protein binding is an indirect measure of the potential for the molecule to remain embedded in the substance of the axonal membrane. The greater the protein binding affinity of a given local anesthetic, the longer the duration of conduction block with that agent. Because lipid solubility is an important determinant of protein binding, potency and duration of local anesthetics are usually similar, that is, highly potent agents also have a long duration of conduction block.

The pK_a of the molecule is determined by the tertiary amine, the ionic signature. The pK_a is the pH for a given molecule at which the cationic (ionic) and base (unionized) forms are in equal concentrations. Commercial local anesthetics have pK_a between 7.6 and 9.3 and are manufactured as sodium salts at an acid pH (5.0–5.5, unless manufactured with epinephrine which requires storage at a pH less than 3.0 to prevent spontaneous hydrolysis of the epinephrine). In the bottle/vial, the majority of the molecules are cationic (>1,000:1).

Properties of Local Anesthetics

The properties of local anesthetics that describe their unique clinical characteristics include speed of onset of action, potency, duration of action, and toxicity.

Onset of action of a local anesthetic can be enhanced by using a higher dose, higher concentration, and a pK_a which is close to the physiologic pH (more availability of the unionized form). Speed of onset of conduction block is the time from injection of the solution to interruption of neural activity. This is determined by the need for the solution to be injected extracellularly, the time for a substantial number of molecules to cross the axonal membrane and occupy the sodium channels. The solution injected is predominately cationic, and the cation has very limited potential to cross the lipid membrane. Extracellular buffering (mostly bicarbonate) raises the pH from 5.0 to physiologic, where the cation/base ratio increases to about 70:30. Some of the base then begins to cross the cell membrane to the intracellular side. Once on the intracellular side, the base rapidly converts to the cationic state because of the more acidic intracellular pH, which rapidly occupies the sodium channels. The latency to onset is determined first by the distance of injection to the nerve cell membrane (accuracy of the person performing the

block, and the hydrophilic properties of the agent), and secondly by the cation/base ratio. The higher the concentration of the base, the faster the onset of conduction block. Since the base concentration at acid pH is less as the pK_a increases, the speed of onset of action is inversely proportionate to pK_a. For example, the pK_a of lidocaine is 7.6 and bupivacaine is 8.3, with lidocaine having a substantially increased speed of onset of action. This is also the physiologic basis for preblock alkalinization of a local anesthetic solution with bicarbonate to increase the speed of onset of action.

Potency of a local anesthetic is directly related to the amount of the base that ultimately crosses the axonal membrane, and to the lipid solubility of the base form of the agent. The potency increases in direct proportion to lipid solubility. The local anesthetic with the least lipid solubility is procaine and it has the lowest potency. Conversely, bupivacaine has the highest lipid solubility and is the most potent local anesthetic available commercially.

The duration of action of a local anesthetic is determined by the affinity of the agent to remain embedded in the axonal membrane. The axonal membrane is a hydrophobic, lipoprotein environment. The duration of a given agent is best estimated by the protein binding of the agent, although it is also influenced by lipid solubility. As protein binding increases, so does the duration of action. In general, as the lipid solubility increases, so does protein binding and hence duration of action of the local anesthetic. For example, the least protein bound agent is 2-chloroprocaine, which also has the shortest duration of action. Conversely, etidocaine and bupivacaine have the highest protein binding potential and also the longest duration of action.

System Effects and Toxicity of Local Anesthetics

Local anesthetics besides being available as injectable solutions are also available for topical application of eyes (absorbed via the mucous membranes), and for dermal anesthesia (EMLA cream). Systemic absorption of local anesthetics is determined by site of injection, dose, addition of vasoconstrictor, and pharmacologic profile of the local anesthetic. The uptake of local anesthetic into the blood from greatest to least is IV > tracheal > intercostal > caudal > paracervical > epidural > brachial > sciatic > subcutaneous. Toxicity of local anesthetics is directly related to the potency and lipid solubility of the drug. More highly toxic drugs have a smaller gap between the therapeutic and the toxic dose (therapeutic index).

Cellular Effects

Cytotoxicity of local anesthetic solutions is related to the pH injected and the direct cellular impact after injection. At some concentration, all local anesthetics are cytotoxic, and this limits the upper concentration available for clinic use. 2-chloroprocaine has the highest potential for cytotoxicity, because of low pH, use of preservatives, and other unknown mechanisms.

Neurological Effects

Neurotoxicity of local anesthetics occurs when local anesthetic accumulates in the central nervous system (CNS), particularly the limbic brain, where inhibitory neurons are blocked at a lower concentration than excitatory, with the result being excitation, agitation, uncontrolled motor activity, and at some concentration, seizure activity. The most potent agents, bupivacaine and etidocaine, are agents with the greatest potential for neurotoxicity. CNS impact occurs from the free form of the local anesthetic (non-protein bound), which does not accumulate until protein binding capacity is exceeded, and then does so rapidly. This means that the same agent will be more neurotoxic with faster accumulation in the blood, as in intravascular injection or when the agent is injected into a highly vascular area, such as the intercostal or the caudal epidural space. It also means that there will be less toxicity when vasoconstrictors (epinephrine) are mixed with the solution, reducing vascular uptake. In general, the toxicity of the esters is less than the amides because of the rapid metabolism of the ester bond by cholinesterase. The amides are metabolized in the liver prior to elimination and have much longer half-lives.

With the unbound form of local anesthetic increasing in the CNS, the first manifestation is excitation, originating within the limbic system, including agitation, tremor, and uncontrolled motor activity. Because of the proximity of the cell bodies of the cranial nerves in the brainstem, paresthesia (tingling of the face, numbness on the tongue), spots before the eyes, or ringing in the ears is also reported. Tremor and involuntary motor activity (muscle twitching) can follow, and if progression continues, seizure activity can occur. Toxicity is potentiated by hypoxia, hypercarbia, and acidosis, and as a result, early effective resuscitation is important. Raising the seizure threshold with barbiturates or benzodiazepines is also an option to prevent or treat seizure activity. It is important to limit the motor activity associated with seizures as it greatly increases oxygen demand while reducing the potential for oxygen delivery.

Transient neurological symptoms (TNS) are defined as symmetrical bilateral pain in the back or buttocks or pain radiating to the lower extremities after recovery from spinal anesthesia. TNS is thought to occur with using highly concentrated solutions of the local anesthesia for spinal anesthesia. The concentrated solution causes localized inflammation and irritation of the nerve roots. Pain can be treated with opioids and or NSAIDS, and muscle spasms treated with a muscle relaxant, with resolution of symptoms usually in 1–2 weeks. Incidence of TNS is greatest with lidocaine > mepivacaine > ropivacaine > bupivacaine. Other

risk factors for TNS include multiple attempts for spinal anesthesia, use of a cutting-edge needle (Quinke), obesity, and lithotomy position for surgery.

Continuous spinal anesthesia, especially using small bore micro-catheters, may cause cauda-equina syndrome (irritation and damage of spinal nerve roots by localized highly concentrated local anesthetic solution). These micro-catheters are no longer used; however, caution still should be used while administering local anesthetics via continuous spinal anesthesia. Bupivacaine appears to be more safer, in this respect, than lidocaine for continuous spinal anesthesia.

Cardiac Effects

All local anesthetics have effects on the heart at some concentration. These effects include a decrease in myocardial contractility, conduction velocity, myocardial automacity, and the duration of the refractory period. Blockage of cardiac sodium channels by the local anesthetic produces these effects. This leads to bradycardia, hypotension, heart block, and even cardiac arrest. About two or three times the blood levels of local anesthetic that produce seizures are required to produce major cardiac toxicity.

While lidocaine in low doses is used to treat ventricular arrhythmias, highly lipid-soluble agents, such as bupivacaine and etidocaine, more commonly cause cardiac toxicity. Unlike lidocaine, which enters and exits the cardiac sodium channels rapidly, bupivacaine and etidocaine enter rapidly and exit more slowly, predisposing to accumulation and selective cardiac toxicity. This occurs when the primary conduction system is blocked and reentrant pathways activated, with the potential for non-perfusing reentrant arrhythmia, such as ventricular tachycardia and ventricular fibrillation. In addition, the more rapid the heart rate, the greater is the accumulation of bupivacaine. Cardiac toxicity is undoubtedly a lipid solubility property, because mepivacaine, which has significant lesser toxicity, only differs in the substitution of a butyl (4-carbon) for a methyl (1-carbon) on the tertiary amine. This may also explain the mechanism of intralipid rescue from bupivacaine cardiac toxicity.

Treatment of local anesthetic toxicity includes stopping the injection of the local anesthetic, airway management, treatment of seizures (diazepam 5–10 mg, midazolam 2–4 mg, propofol 50 mg)), cardiopulmonary resuscitation (treatment of hypotension or arrhythmias—do not use lidocaine), and administration of 20 % intralipid for severe or refractory toxicity (1.5 ml/kg bolus and then 0.25–0.5 ml/kg/min).

Methemoglobinemia

Some local anesthetics, such as prilocaine and benzocaine, can cause the oxidation of the iron in hemoglobin from ferrous (FE^{2+}) to ferric (FE^{3+}) causing methemoglobinemia. When the amount exceeds a threshold (about 4 g/dl), cyanosis becomes visible. This is clinically innocuous in healthy patients, but the cyanosis and lower saturation readings are not easily distinguished from hypoxemia. In patients with diminished pulmonary reserves, the reduced oxygen carrying capacity can be symptomatic, and can be treated with methylene blue (1 mg/kg), with rapid reversal.

Allergic Reactions

Immune-mediated allergy to local anesthetics is very uncommon. Within the amide/ester families, true allergy is substantially more common in the ester group of local anesthetics, which are related to PABA. Allergy to amides, particularly lidocaine, has been mistakenly identified, when the true allergy was to additives, such as methylparaben, which is used as a preservative in multi-dose vials. Allergy testing is an option, but the sensitivity and specificity are limited.

Miscellaneous Effects

Some studies have demonstrated that amide local anesthetics decrease platelet aggregation and prevent thrombosis, which lower the incidence of thromboembolic events, in patients receiving epidural anesthesia. Local anesthetics are also known to potentiate nondepolarizing muscle relaxant blockade. Opioids, such as morphine and fentanyl, potentiate the action of local anesthetics for pain relief. Drugs such as propranolol and cimetidine decrease hepatic blood flow and the metabolism of amide local anesthetics, thereby increasing their blood levels and potential for toxicity.

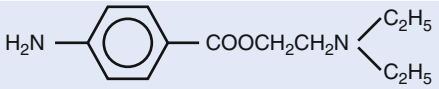
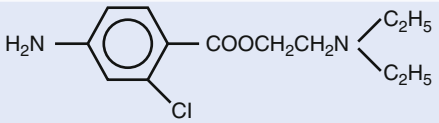
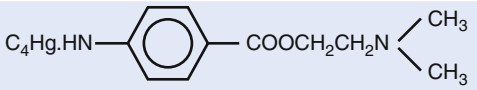
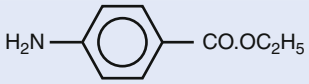
Classification of Local Anesthetics

The most basic classification of local anesthetic is based on the molecular origin of the hydrophobic group. The amino ester agents are derived from PABA, and the amino amides are derived from the aniline family. It is appropriate to describe each agent in both families by the pK_a, speed of onset of action (fast, intermediate, slow), and the duration of action (short, intermediate, long).

Ester Local Anesthetic Agents

The ester agents (Table 18.3) all have in common a brief plasma half-life (0.5–4.0 min) and as a result, a relatively low potential for toxicity. None of the agents with selective cardiac toxicity are found in the ester family. Ester local anesthetics, except cocaine, are metabolized (hydrolyzed) in the plasma by pseudocholinesterase (plasma cholinesterase) to water-soluble

Table 18.3 Ester local anesthetics

Agent	Structure	Molecular weight	% Protein binding and Duration of action	pK_a	Lipid solubility and potency
Procaine		236	6 +	9.0	+
Chloro-procaine		271	<1 +	9.0	+
Tetracaine		264	75 ++++	8.5	+++
Benzocaine		165	<1 +	2.5	+

metabolites, which are excreted by the kidneys. Deficiency of pseudocholinesterase leads to increased blood levels. The action of intrathecally injected ester local anesthetics is terminated by absorption into the bloodstream as the CSF lacks the enzyme pseudocholinesterase. Cocaine is primarily metabolized in the liver by N-methylation and hydrolysis.

Procaine

The pK_a of procaine is 9.0 with low lipid solubility and very low protein binding potential, resulting in a local anesthetic with low potency, slow onset, and short duration of action. The toxicity potential is limited as a result of the extremely short plasma half-life (<20 s) because of rapid plasma hydrolysis by cholinesterase. The short duration of action is predicted by the lowest protein binding potential of all the commercially available local anesthetics. The maximum dose is about 1,000 mg with infiltration in the average sized adult. Clinical use of procaine at the present time is very limited. Examples include cases requiring extensive skin infiltration (awake craniotomy) and for subarachnoid block combined with tetracaine.

Chloroprocaine

The pK_a of chloroprocaine is 9.0, and it must be prepared in an acid medium (pH 2.5–4.0) for chemical stability. Its toxicity is extremely low, related to the brief plasma half-life (<30 s), which allows the agent to be used in relatively high concentrations (2–3 %). The result is a local anesthetic with a rapid onset and brief duration of action, with very limited toxicity potential. It is difficult to create a toxicity situation because the prodrome of parenteral chloroprocaine is so profound that it is difficult to accumulate enough chloroprocaine in the CNS to create toxicity. The maximum dose is 800–1,000 mg in the average sized adult and higher with added epinephrine. The most typical clinical use is for epidural anesthesia, especially in obstetrics. Brief peripheral block (30–60 min) can be achieved, and recently there has been renewed interest in chloroprocaine for subarachnoid block in the outpatient setting.

There has been controversy with the use of chloroprocaine historically. In the early use of chloroprocaine there were reports of spinal cord injury (transverse myelitis, chemical meningitis) that resulted from unintended massive intrathecal injection during planned epidural anesthesia. Initially attributed to chloroprocaine, these events were ultimately attributed to a preservative (sodium metabisulfite). Another controversy evolved from the next preservative, ethylenediamine tetraacetic acid (EDTA) which causes sustained paravertebral muscle spasms after outpatient epidural anesthesia. This too has been resolved with the elimination of preservatives from chloroprocaine solutions.

Tetracaine

Tetracaine has a pK_a of 8.5 with very high lipid solubility and protein binding potential, resulting in a local anesthetic with high potency, slow onset, and long duration of action. The high lipid solubility predicts CNS toxicity, which is higher than for procaine and 2-chloroprocaine, although events should be relatively uncommon due to the short plasma half-life (2.5–3.0 min). The maximum dose is about 2 mg/kg or 120 mg. Tetracaine is prepared as a liquid or as a lyophilized power. The most common application is spinal anesthesia. Less frequently, tetracaine is mixed with shorter acting local anesthetic solutions (lidocaine, mepivacaine, or chloroprocaine) to greatly increase the duration of peripheral or plexus block to 6–8 h. Tetracaine is also an excellent choice for topical anesthesia for ophthalmology, or endoscopy as long as toxic doses are avoided.

Cocaine

Although cocaine is an ester local anesthetic, it has limited use for conduction block. It has a pK_a of 8.5 and high lipid solubility and intermediate protein binding potential, which predicts high potency as well as toxicity. Cocaine is prepared for clinical use as a liquid alkaloid (to reduce diversion) for topical application at variable pH. The concern with cocaine, aside from diversion for illicit use, is its potential to block re-uptake of catecholamines, resulting in vasoconstriction, tachycardia, hypertension, and the potential to induce myocardial ischemia. The ability of cocaine to produce intense vasoconstriction makes it ideal for topical anesthesia of mucous membranes for surgery (e.g., nasal surgery). However, this intense vasoconstriction can cause neural toxicity (neuritis) with direct application. In addition, cocaine use has the potential to induce coronary vasospasm even in normal coronary arteries, which has resulted in myocardial infarction in young otherwise healthy adults.

Benzocaine

Benzocaine is the only local anesthetic that is not a tertiary amine, being a 2-carbon (secondary amine). The pK_a of 2.5 and the low lipid solubility and protein binding potential create a local anesthetic with a limited application profile, being used almost exclusively for topical anesthesia of mucous membranes. The estimated maximum dose is 200–300 mg for the average sized adult. Excessive topical application of benzocaine, especially in pediatric cases, has been reported to cause methemoglobinemia.

Amide Local Anesthetic Agents

All of the agents in the amide family (Table 18.4) are metabolized in the liver prior to elimination, and their termination of action is by redistribution. As a result, their plasma half-lives are much longer than the ester agents, and the potential for toxicity is higher. Amide local anesthetics are metabolized in the liver (N-dealkylation and hydroxylation) by p450 enzymes. Rate of metabolism is greater for lidocaine > mepivacaine > ropivacaine > bupivacaine. Liver disease or a reduction in hepatic blood flow leads to decreased metabolism of amide local anesthetics.

Lidocaine

Lidocaine has a pK_a of 7.9 with intermediate lipid solubility and protein binding potential. As a result, lidocaine has an intermediate speed of onset of action, intermediate potency, duration of action, and toxicity. When prepared plain, the pH of the solution is 5.0–5.5, and when prepared with epinephrine commercially, the pH is adjusted to below 2.5 to prevent spontaneous hydrolysis of the epinephrine. Clinically, lidocaine is the most versatile local anesthetic, with a use profile for virtually every option for conduction block. The dose limit is 5 mg/kg or a total dose of 500 mg, and somewhat higher (7 mg/kg) depending on the application when epinephrine is added. It is a safe topical anesthetic and can be used for epidural and conduction block with duration of action of 90–120 min, or 20–30 % longer with added epinephrine.

Lidocaine has a long history of use for spinal anesthesia, although more recently, the hyperbaric (5 % lidocaine in 8.25 % dextrose) application has been associated with transient neurological symptoms (TNS) that persist from days to weeks. Lidocaine is the only local anesthetic which is extensively used parenterally as an antiarrhythmic, to suppress noxious airway reflexes (coughing), for treatment of chronic pain, or to prevent increases in intracranial pressure associated with endotracheal intubation or suctioning.

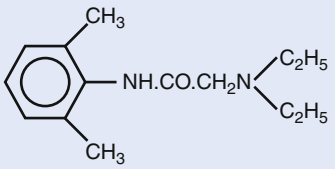
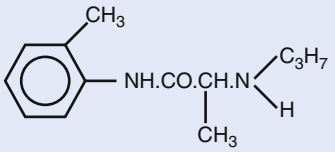
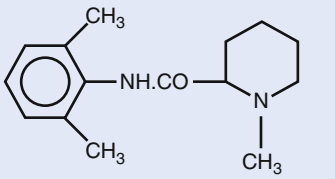
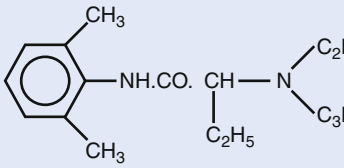
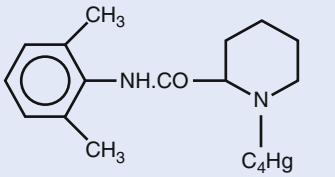
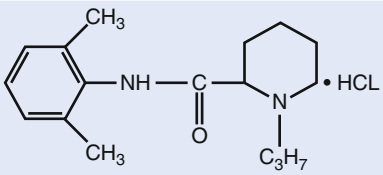
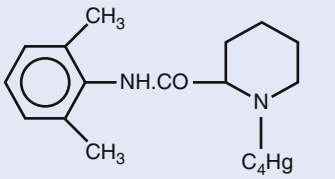
Prilocaine

Prilocaine was created as a modification of lidocaine with a simplified tertiary amine designed to increase the speed of metabolism and, therefore, reduce toxicity. It has a pK_a of 7.5 and intermediate lipid solubility and protein binding potential, resulting in intermediate potency and toxicity. The plasma half-life is shorter than lidocaine; however, metabolism to o-toluene is associated with causing methemoglobinemia. Although this is clinically insignificant in healthy patients, it is not easily distinguished from hypoxemia and can have clinical implications for patients with diminished pulmonary reserves. Even though the methemoglobinemia is short-lived and easily treated with methylene blue (1 mg/kg), this has limited the clinical use of prilocaine to topical application as part of the mixture with lidocaine (eutectic mixture of local anesthetics—EMLA). When used for peripheral block, it has a duration of 1–2 h. It may be the ideal agent for intravenous regional anesthesia, although the potential for methemoglobinemia makes lidocaine a more common choice by far. Epidural prilocaine would have a duration of 60–90 min.

Mepivacaine

Mepivacaine was created as an amide which incorporated a simplification of the double ring structure, which would increase potency compared to lidocaine. It has a pK_a of 7.8, and intermediate lipid solubility (slightly greater than

Table 18.4 Amide local anesthetics

Agent	Structure	Molecular weight	% Protein binding and duration of action	pK_a	Lipid solubility and potency
Lidocaine		234	64 ++	7.9	++
Prilocaine		220	55 ++	7.9	++
Mepivacaine		246	77 ++	7.8	++
Etidocaine		276	94 ++++	7.7	++++
Bupivacaine		288	96 ++++	8.2	++++
Ropivacaine		262	95 +++	8.2	+++
Levobupivacaine		288	96 ++++	8.2	++++

lidocaine) and protein binding potential, resulting in an agent with intermediate onset, duration, potency, and toxicity. The maximum dose is reported at 400 mg without epinephrine in the average adult, although higher doses have been frequently reported to be safe, especially when epinephrine is added. Clinical uses for mepivacaine include infiltration, peripheral block, and epidural anesthesia with duration about 20 % longer than lidocaine, also extended by epinephrine. Spinal anesthesia has duration of 60–90 min. Controversy with TNS and lidocaine spinal anesthesia has increased the choice of mepivacaine for spinal anesthesia, with an excellent block and slightly longer duration.

Dibucaine

Dibucaine has a pK_a of 8.4, pH of 4.5–5.0, high lipid solubility, and protein binding potential, resulting in intermediate onset, very long duration, considerable potency, and high toxicity. There is limited use of dibucaine for clinical appli-

cations. Dibucaine is also used in vitro for assessment of the activity of cholinesterase in the serum. When normal cholinesterase is mixed with dibucaine, enzyme activity is inhibited. Genetically abnormal cholinesterase is much less inhibited for unknown reasons. When inhibition is more than 80 % the enzyme is normal, if less than 20 % inhibited the patient is homozygous abnormal, and if 40–50 % inhibited, the patient is confirmed as heterozygous abnormal.

Etidocaine

Etidocaine was also designed as a modification of lidocaine with an alkyl substitution on the intermediate ring resulting in a more lipid-soluble molecule. It has a $p\mathrm{K}_a$ of 7.7 and high lipid solubility, potency, and protein binding potential. This results in an agent that has an intermediate speed of onset with long duration and high toxicity potential. The maximum dose is 300–400 mg in an average sized adult, higher with added epinephrine. The block created is characterized by dense motor block with more limited sensory block, a unique element of etidocaine which has limited its use because of sensory sparring. It is also characterized by an increased probability of selective cardiac toxicity similar to bupivacaine. When used clinically for peripheral or epidural block, it has a long (3–12 h) duration of action. Its use is very limited in the United States.

Bupivacaine

Bupivacaine was created as a modification of mepivacaine, with the lengthening of one of the aliphatic substitution of the tertiary amine from one to four carbons, greatly increasing the lipid solubility, potency, and toxicity of the agent. The $p\mathrm{K}_a$ is 8.2 and the lipid solubility and protein binding potential are the highest of available agents. The result is a slow onset, high potency, very long duration, highly toxic agent, limiting the total dose to 2–3 mg/kg. Because of the lipid solubility, it has selective cardiac toxicity, related to the fast-in, slow-out kinetics of bupivacaine with cardiac sodium channels. Entry and accumulation causes blockade of the primary cardiac conducting system, predisposing the patient to non-perfusing reentrant arrhythmia, such as ventricular tachycardia or fibrillation, which is resistant to treatment. This limits the use of the most concentrated bupivacaine (0.75 %), which is contraindicated for obstetric applications. The reports that lipid solutions can attenuate bupivacaine cardiac toxicity have led to the availability of intralipid (rescue dose 1.5 ml/kg to start, followed by 0.25–0.5 ml/kg/min) for treatment of refractory cardiac toxicity.

A unique property of bupivacaine is selective preference for sensory block at lower concentrations with minimal motor block, and ideal combination for obstetric epidural analgesia or postoperative pain control at concentrations below 0.25 %. Bupivacaine is also an excellent choice for spinal anesthesia either plain or in a hyperbaric mixture with dextrose. When used for surgical epidural anesthesia, the sensory block is more routinely complete than the motor block. Toxicity limits the enthusiasm for topical application of bupivacaine.

Ropivacaine

Ropivacaine was designed as a modification of bupivacaine to achieve the same clinical properties, but with reduced selective cardiac toxicity. This resulted from the comparison of bupivacaine to mepivacaine, with the only structural difference being the aliphatic substitution on the tertiary amine (methyl for mepivacaine and butyl for bupivacaine). The increase from 1 to 4 carbon substitution created the favorable properties of bupivacaine, but also its cardiac toxicity profile. Further, the reduction from four carbons to three carbons (propyl) was thought to combine the conduction blocking properties of bupivacaine with the low cardiac toxicity of mepivacaine. The result was ropivacaine with a $p\mathrm{K}_a$ of 8.2 and very similar lipid solubility and protein binding potential as bupivacaine, that is, a slow onset, long duration agent with high potency and toxicity.

Clinical studies confirm the substantial reduction of selective cardiac toxicity that was predicted. One unique property is that ropivacaine is a weak vasoconstrictor, with some potential issues with end-organ vascular supply. Clinical experience suggests that ropivacaine produces almost a similar conduction block to bupivacaine (equal sensory, but less dense motor block), making it a good safety choice for high concentration, large total dose application, such as plexus block for surgery or surgical epidural anesthesia.

Levobupivacaine

Levobupivacaine was created from bupivacaine because of the observations made during the production of ropivacaine. Ropivacaine was created as an isomer (the levorotatory form) as opposed to bupivacaine, which is a racemic mixture. The observation of reduced cardiac toxicity with the levo form of ropivacaine led to speculation that there might be a difference between dextro and levo forms of bupivacaine, and indeed it was found that the dextro form of bupivacaine was substantially slower in exiting cardiac sodium channels. This led to studies of the levo form, or levobupivacaine, as a potential agent with all the favorable properties of bupivacaine with reduced selective cardiac

toxicity. Levobupivacaine has the same pK_a, lipid solubility, and protein binding potential as bupivacaine, and has the same profile of slow onset, long duration, and high potency. Clinical investigation confirms reduced cardiac toxicity compared to bupivacaine but not as much as the reduction with ropivacaine.

Options for Topical Anesthesia

Tetracaine–Adrenaline–Cocaine

Tetracaine, adrenaline, and cocaine (TAC) were mixed in the attempt to achieve topical anesthesia for repair of lacerations in children. When TAC is applied directly to open wounds or mucous membranes, topical anesthesia with intense vasoconstriction results. Young children better tolerate repair of laceration with topical TAC in contrast to infiltration. The toxicity, when occurs, is related to the absorbance of cocaine and tetracaine from the mucous membrane. Overdoses in children have resulted in seizures and death. High absorbance makes use of TAC on mucous membrane in small children relatively contraindicated. Alternative options for topical anesthesia have been identified, which have resulted in the decreased use of TAC due to its toxicity and the abuse potential (cocaine).

When TAC is compared to cocaine alone, improved analgesia was found with the TAC. A lidocaine–epinephrine–tetracaine mixture also creates comparable topical anesthesia to TAC, but with a reduced toxicity potential. A bupivacaine–epinephrine–cocaine mixture also achieves good topical anesthesia, but carries the concern of bupivacaine-associated cardiac toxicity, and abuse potential of with cocaine. Topical tetracaine (excellent absorbance of tetracaine via intact mucous membranes) has excellent results for ophthalmology and endoscopy procedures as long as toxic dose limits are avoided.

EMLA

The search for agents capable of creating cutaneous anesthesia (penetration of intact dermis) without injection led to development of eutectic mixture of local anesthetic (EMLA). EMLA was developed from the 1:1 oil/water emulsion base forms of 5 % lidocaine and 5 % prilocaine, which is capable of penetrating intact dermis. The action of EMLA on the skin is characterized by a biphasic action, starting with vasoconstriction which evolves to vasodilatation and erythema. When applied under an occlusive dressing (1–2 g/10 cm^2), blanching of the skin is evident after 20 min. After resolution of vasoconstriction, topical anesthesia can be anticipated between 45 and 60 min after application, with its effect lasting for another 60 min. There is minimal plasma absorbance that follows the normal metabolic pathways for the components, with a side effect profile of erythema, edema, skin blanching, and methemoglobinemia (prilocaine).

EMLA should not be used on broken skin, mucous membranes, and newborns (up to 1 month of age). All cutaneous procedure may be possible pain-free, including blood drawing, intravenous placement, immunization, arterial line placement, and elective epidural catheter placement. Minor suturing, cannulation for hemodialysis, and central line placement can be made less painful. Various minor urologic, ENT, gynecology, plastic surgery, and acute pain procedures can be facilitated with EMLA.

Compounding of Local Anesthetics

Mixtures have been designed to increase the speed of onset, to prolong duration of action, or to achieve a lower toxicity profile, by compounding a fast onset agent with one of longer duration. The acid base characteristics of the solution achieved can influence the outcome. When the acid solution of chloroprocaine is added to other agents, there can be decreases in the potency and duration of subsequent conduction block. Although evidence is scarce, there is a general belief that the toxicity of local anesthetic mixture is additive. A solution containing 50 % of the toxic dose of local anesthetic X, and 50 % of the toxic dose of local anesthetic Y, will have the same implications as 100 % of the toxic dose of either local anesthetic alone.

Additives to Local Anesthetic Solutions

Epinephrine

Use of epinephrine in local anesthetic solutions results in vasoconstriction and lower plasma levels of the agent. Reduced vascular uptake can also result in a longer duration conduction block, or one with more density because the local anesthetic remains in contact with the neural structure longer prior to uptake. In some applications (e.g., spinal anesthesia) epinephrine increases the quality of the block, particularly the density of the motor block. Addition of epinephrine (5 mcg/ml or 1:200,000) prolongs the duration of action in the order tetracaine > lidocaine > bupivacaine.

Clonidine

Limited reports suggest that clonidine adds to the density and/or duration of peripheral or plexus block, perhaps by direct action on receptors. When used in the neuraxis, cloni-

dine potentiates local anesthetic solutions by direct CNS effects, with a side effect profile characterized by orthostasis and potential hemodynamic instability.

Phenylephrine

Phenylephrine has been used in peripheral and neuraxial blocks in a manner similar to epinephrine to achieve reduced plasma uptake and prolonged duration of action of the local anesthetics achieved. Reports confirm that the vasoconstrictive effect occurs to a lesser degree when compared to epinephrine. In addition, bradycardia can occur with the use of phenylepherine.

Bicarbonate

The goal of alkalinization is to add enough sodium bicarbonate to the local anesthetic immediately prior to injection to increase the pH from acid to near physiologic so as to increase the speed of onset of action. The chemical stability of the agent determines the pH that can be achieved without precipitation, as adding sodium bicarbonate to local anesthetics decreases the stability of the solution. The more lipid-soluble agents will precipitate at lower pH, limiting clinical efficacy of this technique for bupivacaine compared to lidocaine and mepivacaine which can be alkalinized above pH 7.0. After adding bicarbonate to lidocaine or mepivacaine, the mixture remains stable for 20–30 min, after which precipitation will eventually begin to occur. About 1 ml of sodium bicarbonate (8.4 %) is added to 10 ml of 1 % lidocaine, while only 0.1 ml is added to 10 ml of 0.25 % bupivacaine.

Rationale for Development of New Local Anesthetics

Among the pipecolyl xylide agents, mepivacaine (methyl substitution on the tertiary amine) has low cardiac toxicity, and bupivacaine (butyl substitution) has a higher potential of cardiac toxicity, despite their structural similarity. This led to the creation of ropivacaine (propyl substitution) with the objective of creating a molecule with the favorable properties of bupivacaine and the lower cardiac toxicity of mepivacaine. Further work has demonstrated that in the racemic mixture of dextro and levorotatory bupivacaine, the dextrorotatory form has much more cardiac toxicity. This led to the synthesis of levobupivacaine, again with the objective of retaining the favorable properties of bupivacaine, but with reduced cardiac toxicity.

Clinical Review

1. Nerve conduction is quickest in the following nerve fiber:
   A. A-alpha
   B. A-gamma
   C. B
   D. C
2. Potency of a local anesthetic is most closely related to
   A. pK_a
   B. Protein binding
   C. Lipid solubility
   D. Structure
3. Duration of action of a local anesthetic is most closely related to
   A. pK_a
   B. Protein binding
   C. Lipid solubility
   D. Structure
4. For epidural anesthesia, the fastest acting local anesthetic is
   A. Lidocaine
   B. Prilocaine
   C. Procaine
   D. Chloroprocaine
5. The most lipid-soluble local anesthetic among the following is:
   A. Lidocaine
   B. Mepivacaine
   C. Bupivacaine
   D. Ropivacaine
6. EMLA cream is a mixture of
   A. Procaine and lidocaine
   B. Procaine and bupivacaine
   C. Prilocaine and lidocaine
   D. Prilocaine and bupivacaine
7. All are true statements regarding addition of epinephrine to a local anesthetic, except
   A. Increases the duration of the block
   B. Makes the block more dense
   C. Increases toxicity of the local anesthetic
   D. Epinephrine has a local anesthetic effect by itself
8. Transient neurologic symptoms can occur with
   A. Lidocaine
   B. Ropivacaine
   C. Bupivacaine
   D. All of the above
9. Local anesthetic with the highest potential for toxicity is
   A. Ropivacaine
   B. Levobupivacaine

C. Bupivacaine
D. Tetracaine

10. Intralipid is used for treatment of local anesthetic toxicity because it
    A. Inhibits the generation of action potential
    B. Increases clearance of local anesthetic
    C. Decreases absorption of local anesthetic into the blood stream
    D. Raises the pH/pK_a of the local anesthetic

Answers: 1. A, 2. C, 3. B, 4. D, 5. C, 6. C, 7. C, 8. D, 9. C, 10. B

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Allergic Reactions

19

Scott M. Ross and Mario I. Montoya

Allergic reaction or hypersensitivity is the term used to describe an immune response resulting in an exaggerated or inappropriate reaction, which is harmful to the host. So why do we care about this exaggerated response? Why do healthcare providers place so much emphasis on patient allergies, including but not limited to placing stickers on the front of patient's chart, patient wristbands, and timeouts stating a patient's allergies prior to incision in the operating room? True hypersensitive reactions to medications, when they occur, can range from a mild rash to severe conditions, such as bronchospasm, cardiovascular collapse, and even death. It is for these reasons that emphasis is placed on knowing the patient's allergies and taking appropriate steps to avoid these events. It is also important to know that allergic reactions can sometimes be confused with typical side effects of medications, which are labeled as allergies. For example, the histamine blocker diphenhydramine can cross the blood–brain barrier and cause sedation, or opioids can stimulate histamine release and cause flushing or pruritus, which are mislabeled as allergies.

Incidence

The risk of an allergic drug reaction occurring is approximately 1–3 % for most drugs, and about 5 % of adults in the United States may be allergic to one or more drugs. The overall incidence of perioperative anaphylaxis is estimated at 1 in 10,000–20,000 anesthetic procedures, whereas it is estimated at 1 in 6,500 administrations of neuromuscular blocking agents (NMBAs). Females are three times more likely than males to have perioperative anaphylaxis. Perioperative incidence of allergic reactions to common medications is depicted in Fig. 19.1.

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Pathophysiology

Hypersensitivity is an excessive and undesirable reaction produced by a normal immune system. This reaction can be damaging, discomfort producing, and sometimes fatal. Hypersensitivity reactions require a pre-sensitized (immune) state of the host. Based on the mechanisms involved and the time taken for the reaction, hypersensitivity reactions can be divided into four types (Table 19.1).

Type I Hypersensitivity

The first step in type I hypersensitivity reactions involves an antigen binding to an antibody, IgE, on the surface of mast cells and basophils, which is known as sensitization (Fig. 19.2). This results in very little if any type of reaction upon initial exposure. It is the subsequent exposure to the same or similar antigen that results in an allergic reaction. After being sensitized to a specific antigen, the host recognizes the offending antigen and forms a cross-linking of two IgE antibodies, which results in degranulation and release of mediators from both mast cells and basophils. These mediators include histamine, arachidonic acid metabolites (leukotrienes and prostaglandins), kinins, eosinophil chemotactic factor of anaphylaxis (ECF-A), and platelet-activating factor (PAF). For unknown reasons, nonallergic individuals exposed to antigens result in IgG antibody formation and lack the cross-linking of IgE antibodies.

Histamine activates receptors directly by binding H_1, H_2, and H_3 receptors. The receptors of primary concern in type I reactions are mainly the H_1 and H_2 receptors. H_1 receptor activation results in flushing, tachycardia, and increase in mucous production, whereas H_2 receptor activation increases gastric secretion and vascular permeability. Arachidonic acid metabolites, both leukotrienes and prostaglandins, are responsible for creating physiological changes in the host resulting in unwanted side effects. Leukotrienes are involved

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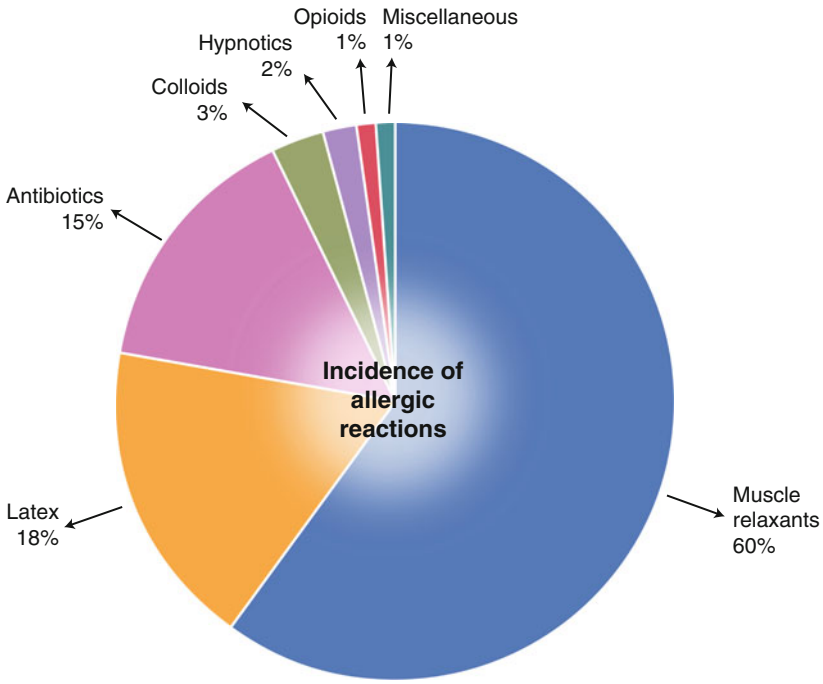

Fig. 19.1 Incidence of allergic reactions to agents used in the perioperative period

Table 19.1 Types of hypersensitivity reactions

	Type I	Type II	Type III	Type IV
Mechanism	Immediate	Cytotoxic	Immune complex mediated	Delayed cell mediated
Response time	15–30 min	Minutes to hours	3–10 h	48–72 h
Antibody	IgE	IgM, IgG	Mainly IgG, IgM,	None
Antigens	Exogenous	Surface of cells	Soluble (not attached), exogenous or endogenous	Organs and tissues

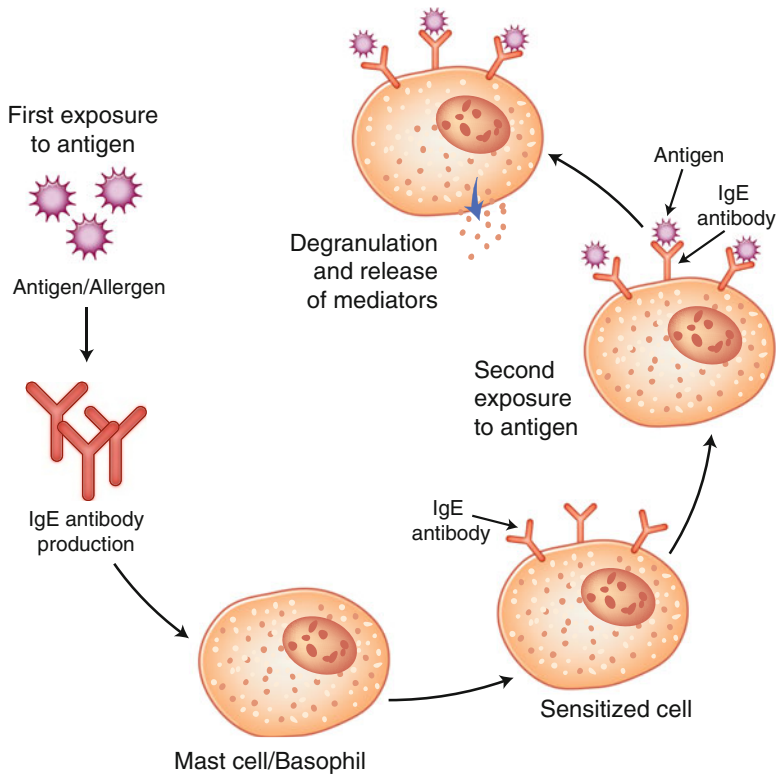

Fig. 19.2 Mechanism of type I hypersensitivity reactions

in bronchoconstriction via smooth muscle contraction, increased vascular permeability, and myocardial depression. Prostaglandins produce vasodilatation, bronchospasm, increased vascular permeability, and pulmonary hypertension.

Kinins are small peptides that produce vasodilatation, increase vascular permeability, and bronchoconstriction. They are also involved in stimulating the release of nitric oxide and prostacyclin. ECF-A is a small-molecular-weight peptide mediator involved in chemotaxis of eosinophils at the site of the allergic reaction and inflammation. PAF is involved in stimulating both platelets and leukocytes to release inflammatory products and is responsible for local and systemic anticoagulation.

Anaphylaxis is one example of a type I allergic reaction along with allergic rhinitis, extrinsic asthma, urticaria, and angioedema (lisinopril). Anaphylaxis is an exaggerated form of type I hypersensitivity and can be caused by food (peanuts), drugs (penicillin), latex, contrast dye, and shellfish. This reaction, as stated above, requires prior exposure to the specific offending antigen or a similar structured molecule to form cross-linked IgE antibodies. If not recognized early, anaphylaxis can become life threatening.

Type II Hypersensitivity

Type II hypersensitivity is cytotoxic, involving complement activation. An antigen is introduced into the host, which is attached to an antibody, IgG or IgM. This combination of antigen–antibody activates complement, which results in the lysis of the antigen. After lysis of the antigen, phagocytosis is initiated. Examples of type II hypersensitivity reactions include hemolytic transfusion reactions, autoimmune hemolytic anemia, drug-induced hemolytic anemia (quinine, penicillin, hydralazine), and heparin-induced thrombocytopenia.

Type III Hypersensitivity

Type III hypersensitivity reactions involve the formation of antigen–antibody complexes, which are then deposited in various tissues. This deposition initiates an inflammatory response involving complement and neutrophil activation, resulting in damage to the tissue for that given organ system. The antigen may be exogenous (bacterial, viral, parasitic) or endogenous (non-organ-specific autoimmunity such as systemic lupus erythematosus (SLE)). The antigen is soluble and not attached to the organ involved. Examples of type III hypersensitivity reactions include serum sickness, skin reactions (SLE, Arthus reaction), SLE (kidneys), polyarteritis (arteries), and rheumatoid arthritis (joints).

Type IV Hypersensitivity

Type IV hypersensitivity is also known as delayed type hypersensitivity due to the absence of immediate signs and symptoms. This reaction involves sensitized T-cell lymphocytes (helper T cells), which releases lymphokines. Lymphokines are involved in inflammation and activation of T lymphocytes (cytotoxic T cells). Cytotoxic T cells specifically attack and kill these antigens on subsequent exposure. This reaction results in tissue damage. Examples of type IV hypersensitivity reactions include graft-versus-host reactions, tuberculin immunity, and contact dermatitis (poison ivy, chemicals, heavy metals).

Nonimmunologic Release of Histamine

These reactions are similar to type I hypersensitivity reactions, in that they produce the same symptoms. However, they are *not* considered hypersensitivity reactions because they are mediated by agents without IgE–allergen interaction. Many pharmacologic agents (thiobarbiturates, hydralazine, carbamazepine, phenytoin, sulfonamides, vancomycin, atracurium, mivacurium, morphine, meperidine, codeine) and other stimuli (exercise, emotional stress, anaphylatoxins C4a, C3a, C5a) are capable of nonimmunologic histamine release.

Prevention of Allergic Reactions

Though not 100 % preventable, many steps can be taken to eliminate the chance of allergic reactions. These include red flags in a patient's chart, patient wristbands, and a thorough history from the patient to differentiate true allergies from common side effects of certain medications. Knowing the most common pharmacologic and nonpharmacologic antigens that elicit allergic reactions can help the physician be more vigilant when administering such agents. Commonly used agents that can cause an allergic reaction during anesthesia are listed in Table 19.2. Pharmacological prophylaxis to prevent allergic reactions (histamine receptor blockers, corticosteroids) before a surgical procedure is not supported by current data.

NMBDs (succinylcholine, rocuronium, vecuronium) are the most common drugs that cause intraoperative anaphylaxis and are responsible for about 60 % of the total number of intraoperative allergic reactions. Antibiotics, especially the beta-lactams, are the most common drugs causing anaphylaxis in the general population. It is important to know that patients who are allergic to penicillin have 5–10 % cross-reactivity to cephalosporins. Too rapid administration of vancomycin may cause red man syndrome (flushing,

Table 19.2 Agents commonly implicated in allergic reactions during anesthesia

• *Anesthetic agents*
Induction agents (barbiturates, etomidate, propofol)
Ester local anesthetics
Muscle relaxants (succinylcholine, nondepolarizing muscle relaxants)
Opioids (meperidine, morphine, fentanyl)
• *Other agents*
Blood products (whole blood, packed cells, fresh-frozen plasma, platelets, cryoprecipitate)
Bone cement (methyl methacrylate)
Colloid volume expanders (dextrans, protein fractions, albumin, hetastarch)
Latex
Vascular graft material
• *Drugs*
Antibiotics (cephalosporins, penicillin, sulfonamides, vancomycin)
Aprotinin
Cyclosporin
Drug preservatives
Insulin
Nonsteroidal anti-inflammatory drugs
Protamine
Radiocontrast dye

pruritus, hypotension), which is due to nonimmunologic histamine release (chemically mediated), and not a true allergic reaction.

Patients may be allergic to ester local anesthetics and to drug additives/preservatives such as methylparaben, which are both metabolized to para-aminobenzoic acid (PABA), which causes the allergic reaction. Allergic reactions to amide local anesthetics are extremely rare. Morphine, an opioid, causes release of histamine, which can lead to urticaria, itching, and vasodilation. This is more correctly labeled as a pseudoallergy (nonimmunologic reaction), as true immunologic reactions to opioids are extremely rare. Colloids, such as albumin, dextran, and hetastarch, are commonly used for volume resuscitation. Among the colloids, hetastarch is least likely to cause an allergic reaction.

Patients allergic to eggs are usually allergic to ovalbumin (egg white), which is different from human serum albumin. Similarly, patients allergic to eggs are not likely to have an allergy to propofol. Propofol is formulated as a lipid emulsion which contains 10 % soybean oil, 2.25 % glycerol, and 1.2 % egg lecithin (purified egg yolk). Protamine, which is used to reverse the effects of heparin, may cause an IgE/IgG mediated hypersensitivity reaction, and also nonimmunologic histamine release. These reactions may lead to urticaria, systemic hypotension, and elevated pulmonary artery pressure. Diabetic patients taking NPH insulin or protamine zinc insulin have an increased risk to a protamine reaction as these insulin preparations contain protamine.

Aside from medications, the use of latex-containing products is a concern for allergic reactions. The most common reaction to latex is irritant contact dermatitis, but urticaria, rhinitis, and even anaphylaxis can occur. Individuals at increased risk for latex allergy include healthcare workers and children with spina bifida, urogenital abnormalities requiring frequent catheterization, and certain food allergies (patients with allergies to bananas, kiwi, and avocados have been reported to have antibodies that cross-react with latex). Many hospitals have taken actions to eliminate use of latex-containing products. Pharmacological prophylaxis to prevent latex allergy before a surgical procedure is not supported by current data.

Often, prevention refers to a thorough workup of a patient who experienced a perioperative allergic/anaphylactic reaction as to identify the causative agent. Initially, after an anticipated anaphylactic reaction, the anesthesiologist may obtain blood samples within 30 min for histamine levels and within 15 and 60 min for tryptase levels. An increase in total tryptase concentrations is highly suggestive of mast cell degranulation as seen in anaphylaxis, but its absence does not preclude the diagnosis. Repeat tryptase levels may be obtained after 24 h for comparison to baseline levels. The skin allergy test remains the gold standard for the detection of IgE-mediated reactions and should be performed by a dermatologist or allergist.

Anaphylaxis

Anaphylaxis is a potentially life-threatening type I hypersensitivity reaction. It is a medical emergency. It is important to recognize anaphylaxis early, as it may progress in severity within minutes to conditions, such as bronchospasm and cardiac arrest, and cause death. One has to be very diligent in diagnosing an anaphylactic reaction perioperatively because many of the signs are mistaken for other causes. Also, it may be difficult to diagnose an anaphylactic reaction under anesthesia as the symptoms and signs may be masked.

The commonly involved target systems include the skin, the respiratory, and the cardiovascular (Table 19.3). Ring and Messmer created a Clinical Severity Scale (Grade I to IV) of Immediate Hypersensitivity Reactions. Grade I includes cutaneous signs (erythema, urticaria with or without angioedema), Grade II includes cutaneous signs plus moderate multivisceral signs (hypotension, tachycardia, dyspnea), Grade III includes the previous plus severe multivisceral signs (shock, arrhythmias, bronchospasm, laryngeal edema), while Grade IV progresses to respiratory and cardiac arrest.

Table 19.3 Clinical manifestations of anaphylaxis

System	Symptoms and signs
Respiratory	Dyspnea, coughing, wheezing, sneezing, tightness of throat (laryngeal edema), stridor, hoarseness of voice, acute respiratory failure
Cardiovascular	Retrosternal oppression, hypotension, tachycardia, dysrhythmias, pulmonary hypertension, cardiac arrest
Skin	Itching, flushing, urticaria (hives), periorbital redness and edema, perioral edema
Gastrointestinal	Nausea and vomiting, abdominal pain, diarrhea

Table 19.4 Management of anaphylaxis

Immediate/initial therapy
1. Stop administration of the antigen
2. Maintain airway and administer 100 % O_2
3. Discontinue all anesthetic agents and notify surgeon
4. Start intravascular volume expansion
5. Give epinephrine (5–10 mcg IV bolus with hypotension, titrate as needed; 0.1–1.0 mg IV with cardiovascular collapse)
6. Call for help
Supportive/secondary therapy
1. Diphenhydramine (antihistaminic)—0.5–1 mg/kg
2. Corticosteroids (0.25–1 g hydrocortisone, 1–2 g methylprednisolone)
3. Epinephrine infusion—4–8 mcg/min
4. Vasopressors for treatment of hypotension (norepinephrine)
5. Vasopressin for refractory shock, starting infusion of 0.01 units/min, IV boluses of 40 units for cardiovascular collapse

Treatment of Anaphylaxis

A treatment plan is critical in combating the physiological effects that take place during an allergic reaction, most notably anaphylaxis. This must be initiated as soon as the reaction is recognized. Things to consider after the treatment of anaphylaxis in the perioperative period are the need for continued intubation and admission to the intensive care unit. Treatment of anaphylaxis should be prioritized according to initial and secondary therapy (Table 19.4).

Initial therapy: Administering intravenous epinephrine and intravascular volume expansion are key aspects of perioperative management for anaphylaxis. Epinephrine is an alpha and beta agonist, which acts to alleviate many of the symptoms of anaphylaxis, including hypotension, bronchospasm, and cardiac arrest. Poor outcomes, including death, are associated with either late or absent administration or inadequate dosing of epinephrine.

Volume resuscitation (via a large bore IV) is as important because many of the mediators released during anaphylaxis lead to increased vascular permeability and leakage of fluid into the interstitial space. Up to 40 % of intravascular volume can be lost through this process, which results in volume depletion and adds to the hypotension. Initially 2–4 l of lactated Ringer solution, normal saline, or a colloid should be administered, with an additional 25–50 ml/kg if hypotension persists. Resuscitation with colloids has not proven to be any more beneficial than using crystalloid alone.

Secondary therapy: In secondary therapy, adjuncts to the above treatments are administered to alleviate the mediator-induced response. Bronchospasm can make ventilation difficult leading to high airway pressures, which could result in barotrauma. In addition to epinephrine, bronchodilators, such as albuterol or terbutaline, and anticholinergics may be administered. Histamine release accounts for many of the unwanted effects during anaphylaxis. These effects can be treated with an H_1 antagonist such as diphenhydramine, 0.5–1 mg/kg. Corticosteroids have anti-inflammatory properties that may help with preventing the activation and migration of inflammatory cells. Persistent hypotension or cardiovascular collapse can be treated with a catecholamine infusion such as epinephrine (4–8 mcg/min) or norepinephrine (4–8 mcg/min).

Anaphylactic shock refractory to catecholamines is sometimes seen due to desensitization of the adrenergic receptors or secondary to nitric oxide (NO) production. NO plays a pivotal role during anaphylaxis by contributing to hypotension and resistance to vasopressors. Vasopressin (ADH) directly decreases intracellular concentrations of nitric oxide by decreasing the second messenger guanosine 3′,5′-cyclic monophosphate (cGMP). Vasopressin actions are different from that of epinephrine, as it does not increase cardiac contractility, thus decreasing myocardial oxygen demand.

Clinical Review

1. In the general population, allergic reactions most commonly occur due to
   A. Antibiotics
   B. Muscle relaxants
   C. Latex
   D. Opioids
2. The most common cause/causes of intraoperative anaphylaxis is/are
   A. Antibiotics
   B. Muscle relaxants
   C. Latex
   D. Opioids

3. Allergic reactions are least likely to the following colloid:
   A. Albumin
   B. Dextran
   C. Hetastarch
   D. Gelatin
4. A protamine reaction most likely causes
   A. Systemic hypertension
   B. Pulmonary hypotension
   C. Systemic and pulmonary hypotension
   D. Systemic hypotension and pulmonary hypertension
5. Mainstay treatment for an anaphylactic reaction is
   A. Intravascular volume expansion
   B. Administration of epinephrine
   C. Administration of H_1 receptor blockers
   D. Correction of hypotension by using norepinephrine infusion

Answers: 1. A, 2. B, 3. C, 4. D, 5. B

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Drug Interactions

20

Ana Maria Manrique-Espinel and Erin A. Sullivan

Drug interactions occur when one drug alters the pharmacological effect of another drug. The pharmacological effect of one or both drugs may be increased or decreased, or a new and unanticipated adverse effect may be produced. The practice of anesthesiology involves administering multiple drugs. In addition, patients may be on several medications for their underlying medical conditions. Therefore, it is of prime importance to understand these interactions so as to produce the best therapeutic effects with least adverse effects.

Mechanisms of Drug Interaction

Drug interactions can be one of three types: pharmaceutical, pharmacokinetic, or pharmacodynamic as described below.

(a) *Pharmaceutical*: A pharmaceutical interaction is said to occur when drugs interact chemically or physically before they are administered or absorbed systemically. Examples of pharmaceutical interactions include precipitation of thiopental when mixed with neuromuscular blockers (succinylcholine, vecuronium) in a syringe or intravenous tubing, precipitation of bupivacaine with addition of sodium bicarbonate, and production of carbon monoxide when desflurane interacts with dry sodalime or baralyme.

(b) *Pharmacokinetic*: Pharmacokinetic interactions occur when the combination of drugs results in the modification of absorption, distribution, metabolism, or elimination of either drug. Examples include the following:

- Absorption: Decrease in rate of absorption of local anesthetics with addition of epinephrine which causes vasoconstriction, the "second gas effect" when rapid uptake of nitrous oxide increases the alveolar concentration of inhalational anesthetic agent.
- Distribution: Hypoproteinemia leading to decreased protein binding and increased free drug concentration in the plasma, a decrease in cardiac output causing increased end-tidal concentration of inhalational anesthetic agents.
- Metabolism: prolongation of action of succinylcholine by neostigmine (which inhibits the enzyme pseudocholinesterase responsible for metabolizing succinylcholine), potentiation of action of indirect-acting sympathomimetics like ephedrine by monoamine oxidase enzyme inhibitors (MAOIs). The monoamine oxidase enzyme metabolizes neurotransmitters, and therefore, MAOIs increase the amount of neurotransmitter available to be released, and concomitant administration of ephedrine may lead to a hypertensive crisis. Another example is the metabolism of many anesthetic drugs by the cytochrome P450 (CP450) enzyme system. Since the CP450 enzyme system is also stimulated/inhibited by several other drugs, these drugs indirectly affect the metabolism of anesthetic drugs. Drugs that stimulate the CP450 enzyme include phenobarbital, phenytoin, carbamazepine, and ethanol, whereas drugs that inhibit the CP450 enzyme include cimetidine, erythromycin, fluconazole, verapamil, and grapefruit juice.
- Elimination: Inhalational anesthetic agents are mainly eliminated via the lungs. If alveolar ventilation is depressed by opioids, elimination of inhalational anesthetic agents is delayed and anesthesia is prolonged. Quinidine decreases the excretion of digoxin by the kidneys, thus increasing its plasma concentration.

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Furosemide decreases the excretion of gentamicin, increasing its potential for nephrotoxicity and ototoxicity.

(c) *Pharmacodynamic*: this interaction occurs when one drug alters the sensitivity of the biological site or receptor of the drug to the effect of another drug. These interactions can be synergistic, additive, or antagonistic.
- Synergistic: This interaction occurs when the pharmacologic effect of a drug is increased by the other drug, the final effect being greater than that produced by the individual drugs (the effect produced is greater than the additive effects). The two drugs usually have different mechanisms or sites of action. Examples include potentiation of nondepolarizing muscle relaxants by inhalational volatile anesthetic agents (vecuronium-isoflurane), increased ventilatory depressant effects when opioids are concurrently administered with benzodiazepines, and a decrease in minimum alveolar concentration (MAC) of an inhalational agent when opioids are administered.
- Additive: In this interaction the pharmacologic effect of a drug is equal to the sum of the effects of both drugs. The two drugs usually have the same mechanism or site of action. Examples include additive muscle relaxant effects of vecuronium and rocuronium (two nondepolarizing muscle relaxants) or CNS toxicity with lidocaine and bupivacaine (two amide local anesthetics).
- Antagonist: This interaction occurs when the pharmacologic effect of a drug is decreased or inhibited by the other drug. Antagonism may be partial or complete. Examples include inhibition of the effect of benzodiazepines with flumazenil, or reversal of neuromuscular blockade produced with vecuronium antagonized by neostigmine.

Anesthetic Drug Interactions

Drug interactions between anesthetic medications (used to induce and maintain anesthesia) and other medications that the patients is taking to treat their medical conditions are very frequent, especially in the elderly population. In the perioperative setting, severe undesired effects may occur that may be potentially life threatening. Drug interactions may affect several systems; however, there are four major areas where drug interactions may cause an adverse perioperative event.

1. Effect on state of consciousness and anesthesia induction drugs (propofol, etomidate, ketamine), opioids, benzodiazepines, antidepressants, alcohol, lithium
2. Effect on muscle relaxation (Table 20.1)
3. Effect on coagulation (anticoagulants, antiplatelet drugs, herbal medications)
4. Effect on cardiovascular or hemodynamic changes (Table 20.2)

Anesthetics may have synergic or additive interactions between them allowing desired effects such as improvement in hypnosis and muscle relaxation. Propofol, ketamine, thiopental, etomidate, opioids, benzodiazepines, and alpha-2 agonists have synergistic interaction with the volatile anesthetic agents, leading to a decrease in MAC. An example of additive interaction is the theoretical use of two inhalational agents, which will not decrease MAC for any of the two agents. Common medications that interact with neuromuscular blocking drugs and volatile anesthetic agents are shown in Tables 20.1 and 20.2, respectively. Some specific drug interactions are listed in Table 20.3.

Table 20.1 Drugs that prolong or shorten neuromuscular blockade

Prolong	Shorten
Antibiotics: aminoglycosides (gentamicin, tobramycin), tetracycline	Carbamazepine
Calcium channel blockers	Methylxanthines
Lithium	Phenytoin (chronic exposure)
Local anesthetics	Ranitidine
Magnesium	Theophylline
Quinidine	
Volatile inhalational anesthetics	

Table 20.2 Drugs affecting minimum alveolar concentration of inhalational anesthetics

Decrease MAC	Increase MAC
Propofol	Cyclosporine
Ketamine	MAOIs
Nitrous oxide	Chronic alcohol exposure
Opioids	
Benzodiazepines	
Local anesthetics	
Clonidine	
Dexmedetomidine	
Acute alcohol exposure	

Table 20.3 Specific drug interactions

Drug	Mechanism of interaction	Notes
Central nervous system		
Selective serotonin reuptake inhibitors (SSRIs): fluoxetine, paroxetine,sertraline, citalopram	Inhibition of cytochrome P450 (CP450), increase in serotonin transmission	Serotonin syndrome (cognitive-headache, agitation, confusion, autonomic-hypertension, tachycardia, diaphoresis, hyperthermia, somatic-myoclonus, hyperreflexia)
Tricyclic antidepressants: amitriptyline, imipramine, doxepin, protriptyline	Metabolized by CP450 system, increase in serotoninergic and noradrenergic transmission, decrease in cholinergic, histaminergic and alpha-adrenergic transmission	Orthostatic hypotension, cardiac arrhythmias, antimuscarinic actions (dry mouth, blurred vision), prolonged action by cimetidine, fluoxetine, calcium channel blockers
Monoamine oxidase inhibitors: phenelzine, tranylcypromine	Increase in serotoninergic, noradrenergic and other amine transmission	Hypertensive crisis-ephedrine, meperidine, foods (tyramine-aged cheese, alcohol), serotonin syndrome-tryptophan
Levodopa	Increases dopaminergic transmission, used to treat parkinsonism	Avoid metoclopramide and phenothaizines (block dopamine), arrhythmias
Bromocriptine, lisuride	Direct acting dopamine agonist	Vomiting, hypotension, worsening psychotic symptoms
Lithium	Increase in glutaminergic and serotonin transmission, may affect acetylcholine activity at nerve terminal, narrow therapeutic/toxic dose ratio	Prolongs neuromuscular blockade, use with haloperidol-toxic encephalopathy, inhibits ADH-nephrogenic diabetes insipidus
Carbamazepine	Induces CP450 enzymes, competition for acetylcholine receptors at the neuromuscular junction	Accelerates metabolism or elimination of warfarin, phenytoin, benzodiazepines, decreased duration of neuromuscular blockade
Phenytoin	Anticonvulsant, up-regulation of acetylcholine receptors	Warfarin and trimethoprim increase phenytoin levels, acute exposure prolongs NMB, chronic exposure shortens NMB
Cardiovascular system		
Vasodilators: nitroprusside, nitroglycerin	Release nitric oxide and increase cGMP, potentiation of vasodilatation caused by volatile inhalational agents	Increased vascular smooth muscle relaxation, hypotension, not to be used with sildenafil
Beta-blockers: metoprolol, propranolol	Decreased beta-adrenergic transmission, decrease cardiac muscle contractility	Hypotension, bradycardia, hypoglycemia, must not be used as first line treatment in cocaine overdose (unopposed alpha-adrenergic effects)
Calcium channel blockers: diltiazem, verapamil	Coronary and peripheral vasodilator, decrease muscle contractility, inhibit cytochrome enzymes	Hypotension, prolonged NMB, may increase levels of digoxin and theophylline, avoid verapamil in WPW syndrome and when dantrolene is used as the combination may cause severe hyperkalemia and myocardial depression
Clonidine	alpha-2 adrenergic receptor agonist	Potentiation of hypotension and sedation produce by intravenous and inhalation agents
Amiodarone	Inhibits CP450, increases levels of digoxin, phenytoin, warfarin	Arrhythmias, bleeding, pulmonary fibrosis, hyper or hypothyroidism
Angiotensin converting enzyme inhibitors: lisinopril, enalapril	Inhibit conversion of angiotensin I to II	May cause hypotension if administered preoperatively, dry cough, hyperkalemia
Procainamide and quinidine	Inhibit CP450 system, decreased presynaptic acetylcholine release	Prolong NMB, thrombocytopenia
Statins: simvastatin, lovastatin	Inhibit cholesterol synthesis by inhibiting enzyme HMG-CoA reductase	Raised liver enzymes, myopathy
Antiemetics		
Ondansetron, granisetron, dolasetron	5-HT_3 receptor antagonists, adjunct for treatment of opioid withdrawal symptoms	Prolong QT interval, headache
Droperidol, metoclopramide	Dopamine antagonist, do not use in parkinsonism	Prolong QT interval (droperidol), extrapyramidal effects
Corticosteroids	Membrane stabilizing effects	hyperglycemia, peptic ulceration, impaired wound healing
Herbal medications		
Echinacea	Promote wound healing, treat respiratory and urinary infections	Hepatotoxicity
Ephedra	Sympathomimetic, used for energy building, weight loss	Increases risk for hypertension, arrhythmias, stroke, myocardial infarction, effects potentiated with MAOIs
Garlic	Used for hypertension, hyperlipidemia, decreases platelet aggregation	Increases risk of bleeding

(continued)

Table 20.3 (continued)

Drug	Mechanism of interaction	Notes
Ginger	Inhibits serotonergic pathways, used for nausea and motion sickness	Interferes with warfarin, increases risk of bleeding
Ginseng	Sympathomimetic, energy building	Risk of bleeding, hypoglycemia, exaggerated sympathomimetic response, avoid MAOIs
Kava	Potentiate GABA system, used for anxiolysis	Hepatotoxicity, excessive sedative effects from anesthetics
St. John's Wort	Inhibit MAOI, induce CP450, used for depression, anxiety	Excessive sedative effects from anesthetics, may cause serotoninergic syndrome
Valerian	Potentiate GABA system, sedative, anxiolytic	Risk of hepatic dysfunction, cardiac and electrolyte disturbances
Antibiotics		
Aminoglycosides (gentamicin, tobramycin), tetracycline, polymixins	Decrease presynaptic acetylcholine release, blockade of Ach receptors	Prolong neuromuscular blockade, increase actions of trimethaphan and verapamil
Chemotherapeutic agents		
Azathioprine: May shorten effects of warfarin and non-depolarizing NMB, prolongs action of succinylcholine		
Bleomycin: High perioperative oxygen concentrations usage are associated with postoperative respiratory failure in patients with previous pulmonary fibrosis		
Doxorubicin: Increased risk of arrhythmias, CHF, myocardial depression		
Methotrexate: Cytotoxic effects may be potentiated by nitrous oxide		
Cyclosporine: May increase MAC requirements for isofluorane		

Clinical Review

1. Respiratory depressant effects of opioids and benzodiazepines, when administered concurrently are
   A. Additive
   B. Synergistic
   C. Antagonistic
   D. Competitive
2. The following drug most likely prolongs neuromuscular blockade produced by succinylcholine
   A. Vecuronium
   B. Cisatracurium
   C. Midazolam
   D. Neostigmine
3. Minimum alveolar concentration (MAC) of volatile inhalational agents is increased by
   A. Acute exposure to alcohol
   B. Chronic exposure to alcohol
   C. Hyperthyroidism
   D. Aminoglycoside antibiotics
4. Neuromuscular blockade is prolonged by
   A. Local anesthetics
   B. Chronic exposure to phenytoin
   C. Carbamazepine
   D. Calcium
5. In critically ill patients, the QT interval may be prolonged by
   A. Dexamethasone
   B. Metoclopramide
   C. Ondansetron
   D. Gentamicin

Answers: 1. B, 2. D, 3. B, 4. A, 5. C

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Part III

Regional Anesthesia & Pain Management

Spinal and Epidural Anesthesia

21

John H. Turnbull and Pedram Aleshi

Spinal and epidural anesthesia are the commonest central neuraxial anesthesia techniques used in the operating room and for labor and delivery. These techniques are employed for almost all age groups, for both intraoperative and postoperative pain, and therefore, a thorough understanding of the techniques, various types of equipment available, and the associated side effects and complications is essential for anesthesiologists.

Anatomy of the Vertebral Column and Spinal Cord

A fundamental knowledge of vertebral anatomy and its relationship to associated neurological and vascular structures is essential to the successful and safe placement of a neuraxial blockade.

The Bony Anatomy

The spinal column consists of 24 true vertebrae and two sets of fused vertebrae (total of 33 vertebrae) stacked upon one another from the cranium to the tip of the coccyx (Fig. 21.1). This column forms the bony enclosure of the spinal cord and supports the weight of the body while allowing mobility in multiple spatial planes. The vertebrae are classified according to their location and structure. The first 7 extend from the base of the cranium through the neck and are called cervical vertebrae. Of these, the first and second vertebrae, referred to as the atlas and axis, respectively, are atypical. Their unique articulations allow for a wider range of movement than can occur in other areas of the axial skeleton. Attached to the ribs, the thoracic vertebrae comprise the next 12 segments followed inferiorly by 5 lumbar vertebrae. The most caudal portion of the vertebral column consists of 5 fused sacral vertebrae and four small rudimentary coccygeal vertebrae.

Although vertebrae differ in their structure and function depending on their location, most of the articulating vertebrae are comprised of a body, an arch, and seven processes (Fig. 21.2). The vertebral body is the largest and most anterior structure, providing strength to the vertebral column. The intervertebral discs, which function as shock absorbers to the axial skeleton, separate the vertebral bodies. Pedicles arise from the vertebral body and project posterior to join paired, adjoining laminae. Together, these form the vertebral arch that provides the bony protection of the spinal column.

Seven processes arise from the vertebral arch. At the junction of the right and left laminae, the spinous process projects posteriorly. A spinous process overlaps the process below it with progressively steeper projections from the lumbar to the thoracic regions. This often makes placement of an epidural via the midline approach challenging in the mid- to upper thoracic region. Transverse processes arise from the vertebral arch at the junction of the lamina and pedicle and project posterolaterally. Superior and inferior articular processes project from the junction of the lamina and pedicle. Each articular process has an associated articular facet, enabling extension and flexion of the spine. The spinous and transverse processes allow for the attachment of the deep back muscles, while the articular process restricts movement in particular directions.

The vertebral column has four normal curvatures—cervical, thoracic, lumbar, and sacral. The thoracic and sacral curvatures are concave anteriorly, while the cervical and lumbar are concave posteriorly. This importance becomes apparent

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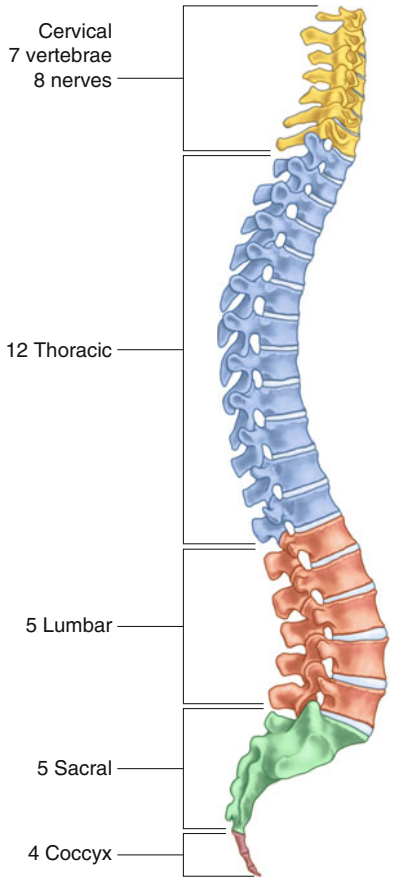


Fig. 21.1 The vertebral column

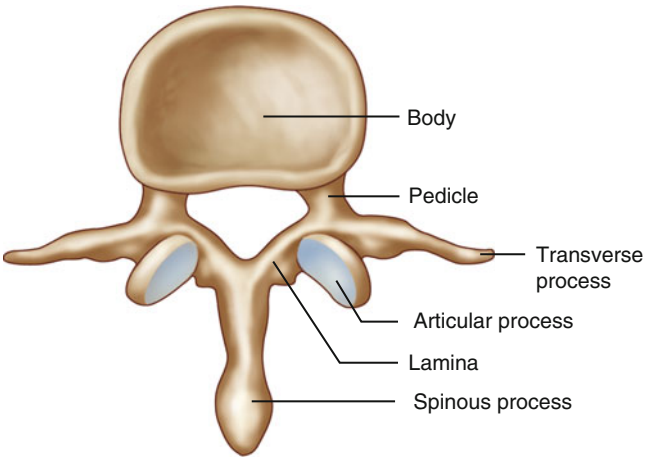


Fig. 21.2 Structure of a vertebra

when considering the baricity of anesthetic solutions and their distribution in the intrathecal space depending on the position of the patient immediately following intrathecal injection of an anesthetic.

Ligaments

Multiple ligaments link the bony components of the spinal column. They provide a path through which the epidural or intrathecal space may be accessed by a traversing needle. The most posterior of these ligaments and, therefore, the first encountered is the strong supraspinous ligament. The weaker interspinous ligament immediately follows. Together, these ligaments unite adjacent spinous processes in a vertical fashion. Encountered next, the ligamentum flavum (Fig. 21.3) links adjacent lamina and is the final ligament encountered prior to entering the epidural space. It is the strongest and most elastic of the ligaments, often described as having a hard, rubber-like feel as the needle transverses its strong fibers. The posterior longitudinal ligament is anterior to the epidural space and the dural sac, but posterior to the vertebral bodies, so it is not traversed in placement of neuraxial anesthesia. Finally, the anterior longitudinal ligament is anterior to the vertebral bodies.

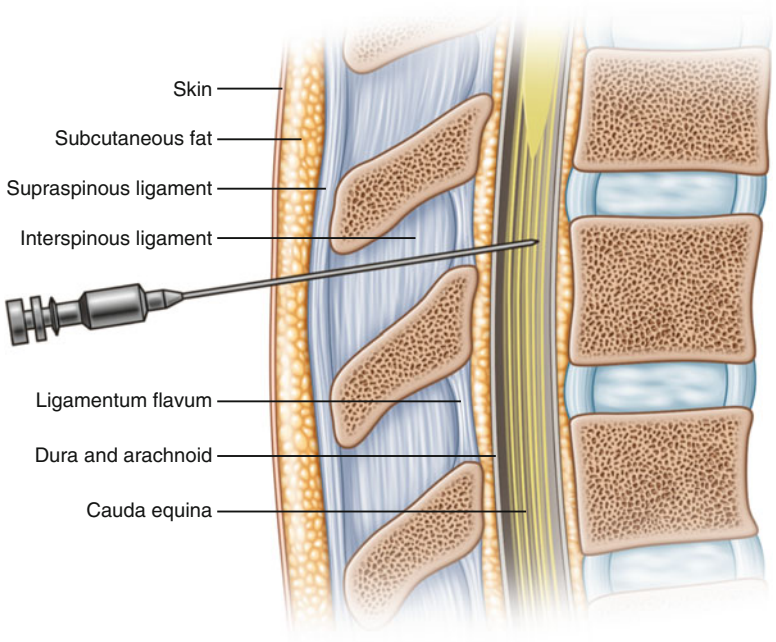
Spinal Cord

The spinal cord originates from the medulla oblongata in the brainstem and extends to the lumbar region of the spinal canal. It serves as a major neural conduction pathway between the body and the brain, as well as a major reflexive center. In newborns, the cord terminates between the L2 and L3 vertebrae, while in adults it usually extends only to the disc space between L1 and L2. However, as evidenced by MRI scans, the spinal cord extends to L3 in approximately 2 % of adults.

Spinal Nerves

Thirty one (31) pairs of spinal nerves (C1–8, T1–12, L1–5, S1–5, and one coccygeal nerve) emerge from the spinal cord and exit the spinal canal via the intervertebral foramina, except for the coccygeal nerve that exits through the sacral hiatus. Each spinal nerve is comprised of an anterior and posterior nerve root. These are formed by the convergence of anterior and posterior rootlets that arise from the surface of the spinal cord. The part of the spinal cord from which rootlets emerge to form nerve roots comprises a segment of the spinal cord and forms the basis of dermatomal distribution of sensation. Although the spinal cord terminates at L2 in most adults, vertebral discs below this level have corresponding spinal nerves. These nerves emerge as the cauda equina from the inferior aspect of the spinal cord, called the lumbosacral enlargement. The fibers of the cauda equina travel in the lumbar cistern (subarachnoid space), bathed in CSF, until they emerge from the spinal canal at the corresponding vertebral level.

Fig. 21.3 Spinal ligaments



Blood Supply

Not surprisingly, the spinal cord is dependent on a rich blood supply. One anterior and two posterior longitudinal spinal arteries feed the anterior and posterior aspects of the spinal column, respectively. Rather than forming a continuous longitudinal blood supply to the spinal cord, interruption of the anterior spinal artery occurs with segmental blood supply provided by penetrating medullary arteries that arise from the aorta and transit through the intervertebral foramina. In general, three large and discrete areas of distribution along the anterior spinal cord exist, the cervicothoracic area, the mid-thoracic area, and the thoracolumbar area. In addition, these arteries provide blood supply to the posterior and anterior roots of the spinal nerves and their coverings. The largest anterior radicular artery, also known as the artery of Adamkiewicz or anterior radicularis magna, arises from T9 to T12 in 75 % of individuals but may originate as high as T5 or as low as L2. Spinal veins form plexuses that run longitudinally inside and outside the vertebral canal and can often be engorged during pregnancy.

Meninges

The spinal meninges, which consist of the dura mater, arachnoid mater, and pia mater, encase and support the spinal cord and spinal nerve roots. Tough, fibrous tissues comprise the dura mater, the outer most layering of the meninges. The spinal dura arises from and is continuous with the cranial dura mater and extends to the coccyx to form the dural sac. The caudal end of the dural sac is tethered to the coccyx by the filum terminale. The dura extends into the intervertebral foramina enclosing the anterior and posterior nerve roots to form the dural root sleeves.

The arachnoid mater is a lacelike matrix of avascular, fibrous, and elastic tissue that encloses the subarachnoid space. The arachnoid is not attached to the dura but is held against the outer meningeal layer by the pressure of the CSF. Under normal conditions, a spinal needle transverses both the dura and the arachnoid, simultaneously. The subdural space is therefore a potential space in which bleeding may occur (subdural hematoma) or accidental deposition of anesthetic. The pia mater, the innermost meningeal layer, is a thin, delicate yet impermeable layer of fibrous tissue that closely adheres to the surface of the spinal cord. The pia continues to the filum terminale.

The subarachnoid space, filled with cerebral spinal fluid, resides between the arachnoid and the pia maters. Denticulate ligaments, approximately 20 lateral extensions of the pia mater, suspend the spinal cord in the dural sac by adhering to the internal surface of the dura.

Spinal Versus Epidural Blockade

Both spinal and epidural anesthesia occur as a result of inhibition of sensory, motor, and autonomic fibers at the level of the nerve root. However, the two techniques differ in the location of anesthetic deposition and in a number of attributes that may make one technique preferred over the other.

Spinal (also referred to as intrathecal or subarachnoid) anesthesia occurs with the injection of an anesthetic solution

into the cerebrospinal fluid. Given the spinal cord does not extend beyond the level of L2 in most adults, injections are limited to interspaces below this level to reduce the risk of spinal cord damage. The technique essentially provides an "anesthetic transection" of the spinal cord with loss of neurologic function below a certain segmental distribution. In contrast, epidural anesthesia occurs with injection of anesthetic into the epidural space, the potential space just outside of the dura through which the spinal nerves traverse. Rather than producing a transection of neural transmission, epidural anesthesia allows for segmental anesthesia with the possibility of continued neurologic function caudal to a band of neural interruption.

Spinal anesthetics are often easier to perform, require less time, and are less dependent on optimal patient positioning during placement. Moreover, aspiration of cerebrospinal fluid at the time of placement provides a quick, real-time assessment of accurate needle position necessary for a successful block. As the anesthetic is delivered within the dural sac, less anesthetic solution is required compared with epidural injection, while producing a more rapid and profound motor and sensory blockade.

Epidural anesthesia has several advantages compared to spinal anesthesia. Epidural anesthesia is more easily titrated, in terms of both the segmental location of the block and the block's intensity. Epidural anesthesia is often accompanied by less profound hypotension than would be seen with spinal anesthesia. Finally, the routine placement of catheters with epidural techniques allows for easy re-dosing of the block and its transition into the postoperative period as a means of acute, postoperative pain management. Although intrathecal catheter placement is an option, the FDA ordered the withdrawal of all intrathecal microcatheters (27–32 gauge) in 1992. Large bore epidural catheters (19–20 gauge) may be used for intrathecal infusion and newer spinal catheters are now just entering practice.

Physiologic Effects of Neuraxial Blockade

Depending on the technique and agents administered, neuraxial blockade can produce profound systemic homeostatic changes. Both spinal and epidural techniques produce similar physiologic consequences although the incidence and severity vary between the techniques.

Cardiovascular

Hypotension, the most common side effect associated with a subarachnoid block, occurs with an observed incidence of 33 % in a non-obstetric population. Decreased venous and arterial vascular tone leads to the pooling of venous blood, a diminished cardiac output, and decreased systemic vascular resistance. Significant hypotension more often occurs with sensory blocks above T5. This phenomenon likely results from the blockade of sympathetic fibers to the upper extremities that otherwise reflexively constrict to mitigate the vasodilatory effects of the block in the lower extremities. In addition, a sensory block above T1 inhibits the sympathetic cardioaccelerator fibers, thus blunting the reflexive tachycardia that accompanies acute drops in blood pressure.

Hypovolemia exaggerates this response, while other risk factors for significant hypotension during spinal anesthesia include advanced age and the combination of general and spinal anesthesia. Epidural blockade may also induce systemic hypotension with the level blockade likely contributing to the significance of the hemodynamic changes. However, the changes are generally less profound as the onset of sympathetic blockade is more gradual than with spinal anesthesia.

Bradycardia, with an incidence of 13 %, and rarely asystole may occur as a result of spinal anesthesia. Again, the blockade of cardioaccelerator fibers may contribute to this occurrence, although decreased preload seems to be the most significant contributor to bradycardia. Risk factors for bradycardia include a baseline low heart rate, the use of beta-blockers, and ASA physical status I. The latter occurrence is likely due to the rather high vagal tone of young, healthy patients. Other dysrhythmias may occur during spinal anesthesia but with much less frequency.

Respiratory

Neuraxial anesthesia minimally alters respiratory physiology in healthy patients. Given that the phrenic nerve with fibers originating from C3–C5 innervates the diaphragm, high thoracic sensory blocks only minimally affect respiratory mechanics. Tidal volume is largely preserved with small decreases in vital capacity, likely reflecting blockade of accessory muscles of respiration (intercostal and abdominal muscles) and thus decreasing the expiratory reserve volume. Elderly patients undergoing lumbar and thoracic epidural anesthesia experience similarly limited alterations in respiratory mechanics.

Patients with preexisting pulmonary disease and limited respiratory reserve, such as those with severe chronic obstructive pulmonary disease, may be more dependent on accessory muscles to maintain adequate ventilation. Therefore, they may be more susceptible to significant alterations in ventilatory mechanics during neuraxial anesthesia. Mild decreases in forced expiratory volume at one second (FEV_1) and vital capacity (VC) are noted in patients with moderate to severe COPD undergoing thoracic epidural or spinal anesthesia. However, the mechanics of quiet breathing

appear to be little changed compared to healthy patients and neuraxial anesthesia is often well tolerated.

Gastrointestinal

Neuraxial blockade between T5 and L1 effectively eliminates sympathetic outflow to the abdominal organs producing intestinal hyperperistalsis and thus a small, contracted gut. Nausea and vomiting occur frequently with neuraxial techniques, with an incidence of 18 % and 8 %, respectively, during spinal anesthesia in a non-obstetric population. Etiology of this occurrence likely reflects unopposed parasympathetic activity as atropine appears to be a more effective treatment compared to blood pressure elevation alone. A high sensory blockade, the use of procaine, a history of motion sickness, and hypotension during subarachnoid block appear to be associated with an increased risk for the development of nausea and vomiting.

Renal and Urinary tract

Decreases in blood pressure produce little change in the glomerular filtration rate due to autoregulation of renal blood flow. Delay in micturition and urinary retention are common occurrences during neuraxial blockade for both spinal anesthetics and lumbar epidurals. The potency and dose of anesthetic solution and the addition of opioids, especially long-acting variants, appear to increase the time for return to normal bladder function.

Retention may lead to bladder distension and even rupture in extreme cases. Therefore, careful consideration should be given to intermittent or continuous catheter drainage especially in the setting of intravascular expansion necessary to maintain preload during a neuraxial anesthetic. However, a common misconception is that an epidural catheter requires the retention of a Foley catheter throughout the epidural's use in the postoperative period. Thoracic epidurals normally have little effect on innervation of the bladder and therefore will not contribute to postoperative urinary retention. A trial to discontinue a Foley catheter early in the postoperative period during an epidural's continued use should be considered with careful monitoring of the patient's fluid status.

Spinal Anesthesia

Spinal anesthesia often proves an ideal anesthetic technique for surgeries involving the lower extremities, pelvis, perineum, and lower abdominal area, while a reduced dose of anesthetic produces a block ideal for labor analgesia. Most often, a single injection via a spinal needle delivers anesthetic into the subarachnoid space. Additionally, a catheter may be placed to allow for intermittent or continuous delivery of anesthetic. This technique allows for tighter control in the titration of anesthetic and the ability for re-dosing.

Mechanism

Delivery of local anesthetic into the subarachnoid space induces a rapid and dense blockade of sensory, motor, and autonomic neural transmission. Compared to epidural anesthesia, only small doses of local anesthetic are required to abolish neural transmission due to the lack of dural and arachnoid coverings of nerves within the intrathecal space. Studies revealing the intrathecal distribution of local anesthetic implicate a number of potential sites of action. Not surprisingly, high concentrations of local anesthetics can be found in the posterior nerve roots as they exit the dura. Local anesthetics also diffuse through the pia mater and into the spinal cord, with higher concentrations noted in the posterior and lateral columns, as well as the gray matter of the spinal cord.

Anatomic differences among nerve fibers, including size and myelination, account for their differing sensitivities to blockade by local anesthetics. Blockade of unmyelinated, small diameter sympathetic fibers precedes blockade of the larger, myelinated sensory and motor fibers. The sympathetic block usually exceeds the somatic and motor block by two dermatomal levels, but sometimes by as many as six. This may help to explain the hypotension that accompanies even low sensory blockades. As for the sensory nerve fibers, the C-fibers, which are sensitive to temperature, are blocked first and remain blocked the longest (Fig. 21.4). A-delta fibers, which are responsible for pinprick sensation, are blocked next but are faster to recover than the C-fibers. The fibers that give sensation to touch, the A-beta fibers, are blocked last and recover the fastest. The length of blockade

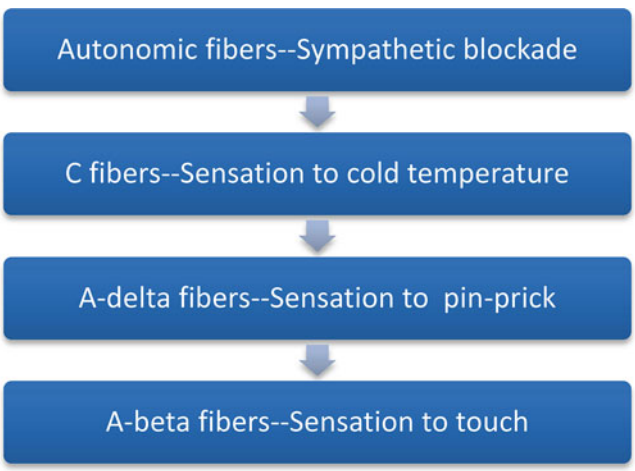


Fig. 21.4 Progression of blockade during spinal anesthesia

of the A-beta fibers correlates with the length of surgical anesthesia. Finally, the motor fibers are the least sensitive to blockade and typically are blocked two to four levels below the sensory blockade.

Besides the dose of local anesthetic injected, several other factors influence the extent of spread of an anesthetic in the subarachnoid space, including the curvature of the spinal canal, the patient's position for and following injection, and the baricity of the anesthetic solution. An individual's volume of cerebrospinal fluid as determined by MRI estimation appears to be the most important factor in determining extent of anesthetic dermatomal distribution. This proves to have little clinical utility as a patient's volume of CSF is neither routinely measured nor easily predicted based on a patient's characteristics. However, it may help to explain why higher peak sensory levels often occur in patients who are older, obese, or pregnant. In these patients CSF volume is often, although not always, diminished compared to younger, leaner patients.

Intrinsic characteristics of cerebrospinal fluid may play a role in the effects of a subarachnoid block, as the CSF serves as the solvent in which the anesthetic must act. The density of CSF is not constant among patients and varies with characteristics commonly encountered in patients during spinal anesthesia, including age, pregnancy, and illness. Even small changes in the density of CSF affect the baricity of the anesthetic solution—defined as the relative density of the anesthetic solution in relation to its solvent. This may help to explain the observed clinical differences among these patient populations in the extent of anesthetic spread.

Elimination of local anesthetic from the intrathecal space depends on vascular absorption of the anesthetic solution. Intrathecal metabolism does not occur. Blocks covering wider dermatomal areas regress faster than blocks covering fewer dermatomes when the same anesthetic dose is used. The increased surface area allows for faster absorption of the anesthetic by the blood vessels of the pia mater. Toxic blood levels of local anesthetics do not occur because of the relatively small doses required for spinal anesthesia.

Preoperative Evaluation and Consent

As with all anesthetics, a thorough preoperative history and physical exam should identify absolute and relative contraindications for spinal anesthesia (Table 21.1). Particular attention should be focused on a history of cardiovascular, neurologic, and hematologic conditions that may preclude the placement of a neuraxial block. Routine testing of platelet concentration and coagulation studies are not recommended in the absence of clinical suspicion of a bleeding abnormality. The anesthetist should consult with the surgical team regarding the appropriateness of a spinal technique.

Table 21.1 Contraindications for Neuraxial anesthesia

Absolute
1. Patient refusal
2. Abnormal coagulation
3. Thrombocytopenia
4. Localized infection over needle insertion site
5. Significant elevation of ICP
Relative
1. Severe aortic stenosis
2. Severe hypovolemia
3. Idiopathic hypertrophic cardiomyopathy
4. Mitral stenosis
5. Bacteremia
6. Preexisting neurologic disease

As part of the preoperative visit, a discussion regarding the benefits and potential complications associated with a subarachnoid anesthetic should be undertaken. It may be helpful to stratify risks according to their relative risk of occurrence. That is, it may be more helpful to first describe relatively common occurrences such as treatable hypotension, nausea and vomiting, backache, and post-dural puncture headache. This can be followed by a discussion of the more serious, yet uncommon complications such as nerve damage and infection. Providing rough data on the relative occurrence may help to allay the fears of patients who come to surgery or labor and delivery with misconceptions regarding the risks of spinal anesthesia.

Preparation

As with induction of general anesthesia, monitors are applied prior to the placement of a spinal block. These should include standard ASA monitors, including noninvasive blood pressure cuff and pulse oximetry. When ECG and capnography are not applied they always should be immediately available. With the administration of anxiolytics or opioids, supplemental oxygen is often desirable. Emergency equipment including suction, advanced airway equipment, induction agents, and vasoactive medications should be immediately available. Intravenous access should be established and readily accessible for administration of premedication or emergency vasoactive medications and fluids.

Single-use, disposable spinal trays are commercially available. One should note the agent, concentration, and baricity of the local anesthetic available in the tray, as the formulation may not be appropriate for all situations. Adjunct agents, such as opioids or epinephrine, may be added to local anesthetic solutions as clinically indicated and may require an assistant to pass the drug off in a sterile fashion.

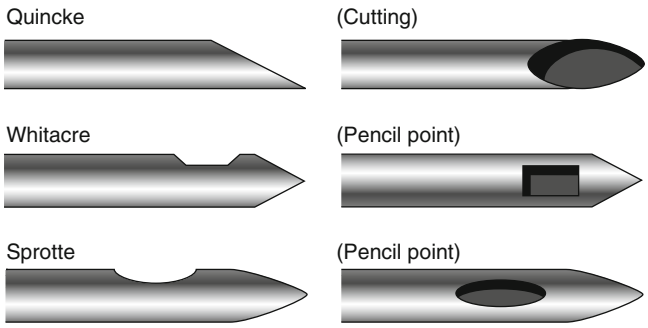


Fig. 21.5 Tip designs of common spinal needles. Note: the Whitacre and Sprotte are both pencil-point needles, but the Sprotte needle has a more proximal opening than the Whitacre needle

Sterile technique with hand washing, hat, mask, and sterile gloves is universally required. The insertion site should be broadly prepped with antiseptic solution. Currently, most prepared kits are prepackaged with betadine. Care should be taken not to contaminate gloves, work surfaces, or equipment with the solution due to its potential neurotoxicity. Time for drying must be adequate to ensure proper skin sterilization. Chlorhexidine may also be used as a skin prep agent, as it has several advantages over betadine including faster onset of action, extended duration of action, and rare bacterial resistance. Although it lacks FDA approval for use prior to lumbar puncture due to lack of clinical safety regarding its potential for neurotoxicity, a retrospective analysis of more than 12,000 spinal anesthetics did not reveal an increased risk of neurologic complications associated with its use.

Spinal Needles

Spinal needles are classified on how they transverse the dura—those that cut the dura (Quincke) and those that spread the dural fibers (Sprotte or Whitacre). Cutting needles have a bevel tip, while non-cutting needles have a pencil point with the opening on the side of the needle rather than at its tip (Fig. 21.5). Post-dural puncture headache occurs less frequently with smaller-gauged non-cutting needles. All of the needles are designed with stylets to avoid coring out a track of tissue and the potential contamination of the intrathecal space.

Technique

Patient Positioning and Anatomic Landmarks

Patient positioning and appreciation of anatomy through palpation of landmarks are essential to the successful, safe placement of a subarachnoid block. Blocks may be performed in the seated, lateral, or prone position. Patient position should be chosen to optimize successful placement, patient comfort and safety, and spread of anesthetic to cover appropriate surgical targets. Consideration may also be given to the eventual surgical position required.

Spinals are generally performed at an interspace level below the conus medullaris to prevent traumatic damage to the spinal cord. Below this level, once the spinal needle enters the subarachnoid space, it is able to push aside fibers of the cauda equina although direct trauma is still possible. The choice of interspace generally does not affect the maximum height of the block, but it may play a role in other characteristics of the block. With hyperbaric bupivacaine, injection of anesthetic at the L2–3 interspace compared to L4–5 produces no higher peak dermatomal levels, but the speed of onset to the peak is faster. However, spread with isobaric bupivacaine is more unpredictable and the choice of interspace likely influences the maximum height of the block.

The midline should be identified with palpation of spinous processes with specific focus at the levels surrounding the site of proposed injection. Drawing a line from the iliac crest to midline may help to identify the L3–L4 intervertebral space, although anatomic landmarks accurately identify the correct interspace only 30 % of the time. A tendency occurs to indentify the L3–4 interspace higher than its actual location. This implies that at least one-third of subarachnoid blocks could unknowingly be placed at the L2–L3 interspace or above. This may place the spinal cord at risk of traumatic damage in a small but significant proportion of patients. Thus, it is not recommended to knowingly attempt a subarachnoid block above the level of L3. Ultrasonography, a quick, noninvasive technique, improves the identification of the correct interspace with a reliability of approximately 70 % and may improve patient safety.

Sitting Position

The seated position facilitates placement of a subarachnoid block by increasing flexion of the spine and thus increasing the size of the lumbar interspinous spaces. Patients should be encouraged to relax their shoulders, slouch forward, and push their lower backs toward the practitioner. This position may also aid in the identification of midline in obese patients. Gravity favors distension of the dural sac, thus making the target for the spinal needle larger, while the increased intradural CSF pressure facilitates the identification of free-flowing CSF.

The seated position may not be the most appropriate position for all patients undergoing a spinal block. Patients who require heavy sedation or those with fractures that preclude easy movement to the seated position are poor candidates. Vasovagal syncope may complicate the placement of the block and put the patient at risk for a traumatic fall. In addition, sitting favors the caudal distribution of a hyperbaric anesthetic solution, thus producing a "saddle block" of the perineum if the patient remains in a seated position for a prolonged period. To avoid this, as in the case of a cesarean section, use of an isobaric solution or the timely transition of the patient to the supine position may be necessary.

Lateral Decubitus

The lateral decubitus positioning provides the most patient comfort and is most appropriate for heavily sedated or frail patients. Landmarks are often more difficult to discern, specifically the identification of midline and interspinous spaces. Flexion of the spine by positioning the patient in the fetal position with legs and head tucked toward the body may help to increase the interspinous space and facilitate success.

Prone Position

The prone position, also known as the jackknife position, is primarily used for patients undergoing perineal procedures. This position poses several challenges for the practitioner, including limited flexion of the spine and decreased dural sac pressure sometimes requiring aspiration of CSF to confirm needle placement. In addition, access to the airway is limited should emergent airway management be required. However, once the block is complete little additional maneuvering is required for surgical positioning.

Approach

Prior to insertion of the spinal needle, the skin and soft tissue overlying the intended entry point are anesthetized with a local anesthetic, typically lidocaine. The intrathecal space may be accessed either by a midline or paramedian approach (Fig. 21.6).

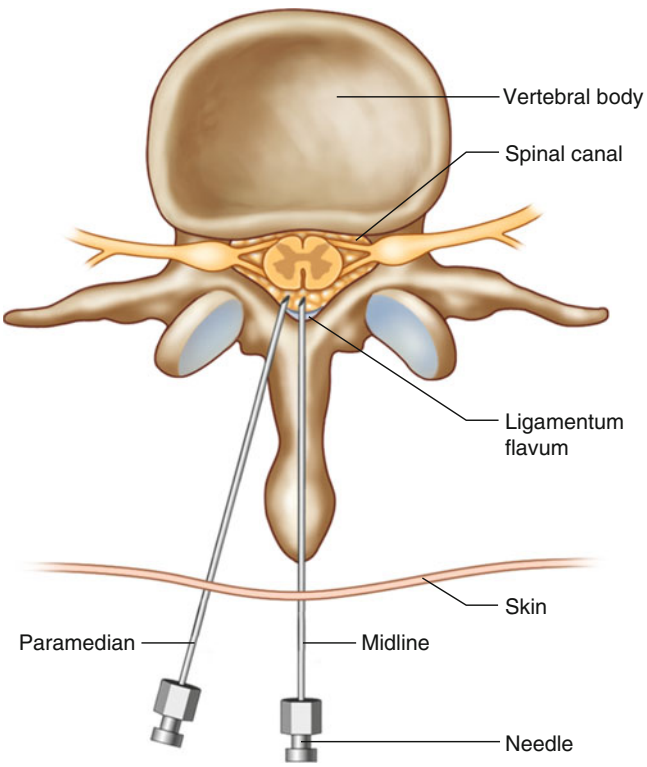


Fig. 21.6 Spinal anesthesia: midline and paramedian approach

Midline Approach

The midline approach is generally easier as it passes through less sensitive tissue and requires less angulation of the needle in three dimensions. In this approach, the local anesthetic needle can be used has a "finder" needle, although deep infiltration of local anesthetic is unnecessary and should be avoided especially in thin individuals whose intrathecal space may be as shallow as 3 cm below the surface of the skin. With the paramedian approach, deeper local anesthetic infiltration improves patient comfort. It may be helpful to contact lamina with the local anesthetic needle to anesthetize the periosteum that will be contacted by the spinal needle.

In most patients, the midline approach is the most popular technique for accessing the intrathecal space. With the patient prepped and draped, reestablishment of landmarks is often helpful. Obesity may obscure the identification of midline. In this case, it may be helpful to ask the patient if the intended site feels midline or off to one side. Insertion of the spinal needle through the skin should occur either midway between two adjacent spinous processes or just cephalad to the superior aspect of the inferior spinous process of the interspace being traversed.

Many techniques involve the initial placement of an introducer needle into the spinous ligament through which a smaller-caliber spinal needle is inserted. This helps to stabilize the spinal needle through the skin and soft tissue to prevent deviation from midline that can occur with beveled needles. As the needle is advanced, the practitioner often appreciates a characteristic change in resistance as the spinal needle traverses the ligamentum flavum. This normally is followed by a classic "pop" sensation as the needle pierces the dura and enters the subarachnoid space. Removal of the stylet should allow the free flow of clear CSF. If CSF does not flow freely, reorientation of the needle by 90° increments may improve flow. Aspiration of CSF by a syringe attached to the spinal needle may be required with very small gauge spinal needles or with patients in the prone position.

Paramedian Approach

The paramedian approach is the ideal technique for patients in whom traversing the interspinous space proves difficult, such as those with degenerative disease of the spine or patients in whom ideal positioning may be difficult. Rather than entering midline, entry of the spinal needle occurs 1.5 cm lateral to midline of the spinous process below the intended interspace. Entering skin and contacting the lamina with the spinal needle help to establish landmarks. The needle is then withdrawn slightly and redirected midline by 10–15° and slightly cephalad. If periosteum is contacted, redirection of the needle cephalad often allows the needle to "walk off" the lamina and into ligamentum flavum. Thus, in this technique the supraspinous and interspinous ligaments are bypassed. In cases where the intrathecal space cannot

easily be entered, it is best to reestablish landmarks or move to another interspace.

The Taylor technique involves a paramedian approach at the level of L5–S1. Midline approach at this level is often difficult due to the acute downward angulation of the L5 spinous process. The insertion site is 1 cm medial and caudal to the posterior superior iliac spine. The needle is then directed in a medial and cephalad orientation. Again, if periosteum is contacted, the needle is walked off the sacrum into the subarachnoid space.

Anesthetic Administration

Once placement of the needle in the intrathecal space is confirmed, the practitioner's nondominant thumb and index finger should stabilize the spinal needle against the patient's back to prevent dislodgement of the needle from the intrathecal space during anesthetic injection. Firm attachment of the anesthetic syringe is key to avoid accidental spillage of anesthetic. Prior to injection, visualization of a "swirl" is confirmation of CSF aspiration. Half of the anesthetic solution is injected followed by a second aspiration to confirm continued placement of the needle within the subarachnoid space. Following injection of anesthetic, the needle and introducer are removed from the patient's back and the patient is repositioned, if necessary, to the appropriate position for ideal distribution of anesthetic to achieve a specific anesthetic level. Important considerations of anesthetic administration are discussed below.

Baricity

Local anesthetic solutions may be classified based on their density compared to the density of CSF, which is termed as their *baricity*. Anesthetics may be hyperbaric, hypobaric, or isobaric. Baricity affects the direction in which an anesthetic distributes in the CSF and thus the eventual distribution and extent of anesthesia. Temperature plays a role in the baricity of anesthetics as a solution's density decreases with its increasing temperature. Anesthetics are generally stored at room temperature (23 °C), but once injected into the CSF the temperatures of the two quickly equilibrate to that of body temperature (37 °C). This temperature change may alter the performance of synthetically hyperbaric anesthetic solutions as more physiologically hypobaric.

Hyperbaric Solutions

Hyperbaric solutions are the most commonly chosen solutions as they achieve greater cephalad spread of anesthetic with the patient in the supine position following injection. Solutions are made hyperbaric by the addition of glucose, such as the commonly used 0.75 % bupivacaine with 8.25 % glucose. 1 % tetracaine may be diluted with an equal volume of solution of 10 % glucose. Lidocaine was once available as a 5 % solution; however, this concentration is no longer advisable given the considerable evidence as to its association with transient neurologic syndrome. Plain 2 % lidocaine may be made hyperbaric with the addition of 10 % glucose in a 3–1 ratio (lidocaine:glucose), producing 1.5 % lidocaine with 7.5 % glucose.

The contour of the lumbar and thoracic spine plays a crucial role in the anesthetic distribution when hyperbaric solutions are used. In the supine position, the injection of a hyperbaric anesthetic administered cephalad to the lumbar lordosis will follow gravity toward the thoracic kyphosis. Placing the patient in a Trendelenburg position may accentuate this effect and produce a higher block. The cervical lordosis helps to prevent the solution from traveling more cephalad and protects against the development of a total spinal. Patient position immediately following injection may be exploited in other ways. For example, leaving the patient in a seated position will produce a saddle block, while leaving a patient in a lateral position may produce a unilateral block.

Isobaric Solutions

Isobaric solutions are employed when limited spread of the anesthetic from the injection site is desired. However, isobaric solutions offer less predictability in the range of segmental blockade. Because the anesthetic does not distribute throughout the intrathecal space, it often provides a denser motor blockade and prolonged duration. Isobaric solutions can be particularly helpful when quick patient repositioning is not possible after the administration of the intrathecal anesthetic, such as with a combined spinal epidural when time is required for catheter placement in the epidural space. Commercially available epidural solutions are often substituted for intrathecal use when isobaric solutions are desired.

Hypobaric Solutions

Hypobaric solutions are typically used for rectal and perineal surgery when administered in the jackknife position, as well as spinal surgery when the desired affect is to have the anesthetic "float" to the dorsal aspect of dural sac while the patient is prone. It may also be helpful for a patient undergoing unilateral hip surgery who is unable to lie on the operative side during block placement. A unilateral block can be achieved with hypobaric anesthetic with the patient lying on the nonoperative side. Such a block performed with a hypobaric anesthetic exhibits a slower time to regression than when the same block is performed with an isobaric solution. Hypobaric solutions are not commercially available and must be mixed by the practitioner with distilled water.

Choice of Local Anesthetic

Local anesthetics reversibly interrupt neural transmission by blocking sodium channels and thus prevent depolarization

Table 21.2 Local anesthetics used for spinal anesthesia

Drug	Concentration (mg/ml)	Dose (mg)	Onset (min)	Duration (h)
Lidocaine[a]	20	50–100	3–5	1
2-Chloroprocaine[a]	20–30	40	5–10	1
Bupivacaine	5–7.5	4–15	5–10	1–3
Ropivacaine	5–10	7.5–15	5–10	1–2.5
Tetracaine	5–10	6–16	5–10	1–4

[a]Lidocaine and chloroprocaine are not commonly used. Addition of epinephrine prolongs duration of action (especially to tetracaine)

and repolarization of the nerve fiber. The receptor site for all local anesthetics is within the cell and thus an agent's lipophilicity affects potency and speed of onset. Local anesthetics are reviewed in detail in another chapter. Here, we review properties of local anesthetics that are specific to spinal anesthesia (Table 21.2).

Lidocaine

Lidocaine, a fast- and short-acting anesthetic, produces an intense blockade. It was once a widely used intrathecal anesthetic; however, its use has been tempered by its association with neurologic injury when injected intrathecally. This was first identified in the 1990s following several reports of cauda equina syndrome when overdoses of lidocaine were given during continuous spinal anesthesia. Soon thereafter, reports of permanent neurologic damage following single-injection spinal of lidocaine appeared in the literature and the phenomenon was termed transient neurologic symptoms (TNS). A recent Cochrane review found a strong association of intrathecal lidocaine injection with TNS with an odds ratio of 7.31 (95 % CI 4.16–12.86). Similar rates of injuries were seen with mepivacaine as well.

2-Chloroprocaine

Initially associated with possible cases of neurotoxicity reported in the 1980s, chloroprocaine is gaining renewed interest as a spinal anesthetic especially in the ambulatory setting. Chloroprocaine has a mean effective duration of 60 min for surgical anesthesia. Its onset is comparable to bupivacaine, while its regression has proven to be better with faster recovery of motor function and earlier discharge from post-anesthesia care units. As for its safety concerns, the previous formulation of the anesthetic with a low pH and the addition of the antioxidant sodium bisulfite may have been responsible for the neurologic injuries seen following the injection of rather large doses. Although a new formulation lacking preservative evaluated in numerous patients found no evidence for its neurotoxicity, animal studies demonstrate functional impairment and histological damage even with the preservative-free formulation. For this reason, the widespread use of chloroprocaine has not been widely adopted.

Bupivacaine

Bupivacaine, the most widely used intrathecal anesthetic, is most commonly used as a longer-acting agent. It comes in a number of hyperbaric and plain formulations with concentration from 2.5 to 7.5 mg/ml. Onset occurs within 5–10 min. Duration of action (60–120+ min) is dose dependent and also affected by the solution's baricity.

Ropivacaine

Ropivacaine is a less potent and shorter-acting intrathecal anesthetic compared to bupivacaine. When compared in patients undergoing elective lower abdominal, ropivacaine's time of onset and extent of spread are equal to bupivacaine. However, the time to sensory block regression, time to motor block recovery, and time to independent mobilization is shortened. This may prove most beneficial in ambulatory surgery centers as home discharge criteria may be achieved faster with ropivacaine. Currently, hyperbaric ropivacaine is not commercially available and must be mixed at the bedside, thus increasing the risk for potential medication administration errors.

Tetracaine

Prior to the introduction of bupivaxcaine, tetracaine, an ester anesthetic, was a widely used spinal anesthetic. It is commercially available as crystals that must be reconstituted immediately prior to injection. The crystals, susceptible to changes by heat, cold, and light, must be stored carefully and thus limit the drug's suitability for inclusion in single-use spinal kits.

Tetracaine's time to regression of sensory blockade is considered comparable, if not slightly prolonged to that of bupivacaine. However, tetracaine may produce less reliable anesthesia in certain clinical scenarios, including pain associated with tourniquet use. Given these findings and the need to reconstitute the crystal form of the drug at the bedside, tetracaine is used less frequently as a spinal anesthetic.

Adjuncts

Several classes of adjunctive medications have been evaluated for use with local anesthetics during spinal anesthesia. The adjuncts often accentuate the intensity or length of the

surgical block. Adjuncts may also provide a longer-term postoperative effect separate from the surgical blockade.

Vasoconstrictors

Vasoconstrictors, such as epinephrine or phenylephrine, are added to local anesthetic solutions to increase the length of the blockade. The vasoconstrictive effect leads to decreased absorption of the anesthetic from the intrathecal space. Since anesthetics are not metabolized in the CSF, this decreased rate of elimination prolongs their effect. The recommend dose is 0.1–0.3 mg of epinephrine and 2–5 mg of phenylephrine. No clinical difference in time to regression is noted between equipotent doses of these two agents.

Vasoconstrictors do not produce equal results among all local anesthetics. Tetracaine appears to be most sensitive to the prolonging effects of vasoconstrictors. Epinephrine prolongs bupivacaine's duration more modestly with increasing time to regression more significantly seen in the lumbosacral region compared to the thoracic dermatomes. Epinephrine added to chloroprocaine can produce flu-like symptoms likely a result of chemical meningitis. Therefore, epinephrine's use with chloroprocaine is not recommended.

Opioids

Opioids play a synergistic role to enhance surgical anesthesia and also provide longer-lasting postoperative analgesia beyond the extent of the surgical anesthesia. The agents bind *mu* receptors and modulate neurotransmission of afferent A and C fibers in the dorsal horn of the spinal cord. Opioids do not enhance the motor blockade of a local anesthetic. Side effects can include nausea, intense pruritus, and respiratory depression.

Intrathecal morphine is administered at a dose of 0.1–0.4 mg. Its hydrophilic structure allows for a long duration of action, while facilitating its spread throughout the intrathecal space. Its onset occurs 2–4 h following injection, but may provide pain relief as long as 24 h postinjection. For this reason, patients must be monitored for 24 h following injection as it travels cranially to the brainstem contributing to possible respiratory depression.

Synthetic opioids, such as fentanyl and sufentanil, are administered in doses of 10–25 mcg and 2.5–10 mcg, respectively. As these opioids are lipophilic they quickly diffuse into the spinal cord and thus generally only affect dermatomes near their injection site. Their administration leads to a prolonged and often intensified block. Their use may allow for the reduction in the dose of local anesthetic. Pruritus is common and its intensity and incidence may be influenced by the choice of local anesthetic with procaine being the most severe. Respiratory depression can occur soon after injection, approximately in 20–30 min, while delayed respiratory depression is not a concern. Therefore, unlike morphine, patients may be discharged the day of surgery when short-acting synthetic opioids are administered.

α-2 Agonists

Clonidine may be used intrathecally to augment a subarachnoid block. Doses of 15–150 mcg have been most often studied with a dose-dependent increase in the time to regression of blockade noted. Motor blockade and the time to first analgesic request following surgery are also increased but without dose responsiveness. Clonidine may potentiate the depth of the subarachnoid block as evidenced by fewer episodes of intraoperative pain. As expected, episodes of hypotension are more common than when local anesthetic is used alone.

Neostigmine

Intrathecal neostigmine significantly prolongs the effects of local anesthetics. However, its high incidence of significant nausea and vomiting, which approaches 75 %, precludes its routine use as an intrathecal adjunct.

Continuous Spinal Anesthesia

Insertion of a catheter into the intrathecal space allows for repeated administration of anesthetic to maintain a subarachnoid block through a long surgical procedure or when a slow titration of an anesthetic is required. The latter may be particularly helpful in patients with cardiac lesions to avoid the rapid hemodynamic changes that often accompany single-injection subarachnoid blocks.

Generally, an 18-gauge Tuohy needle from an epidural kit is used to access the intrathecal space in a manner similar to a single-injection spinal. Once the free flow of CSF is confirmed, an epidural catheter is threaded into the intrathecal space. Care should be taken to not advance the catheter more than 2–4 cm into the subarachnoid space in order to avoid traumatic damage to the spinal cord. When threading of the catheter is difficult, it can be helpful to rotate the Tuohy needle in 90° increments and advancing the catheter again. During this maneuver the catheter should be completely removed from the needle to prevent shearing and to confirm the continued flow of CSF.

Continuous spinals have similar risks to single-injection spinals with a few caveats. The risk of post-dural puncture headache is increased and may be as high as 78 % in young, healthy parturients. However, non-obstetrical continuous spinals are often most appropriate for elderly patients with cardiovascular disease who are at low risk for post-dural puncture headaches.

Microcatheters (25 and 27G) were developed to reduce the risk of headache, but their use was associated with permanent neurological injury, including cauda equina syndrome. A slower rate of injection of anesthetic through the smaller-caliber catheter may have contributed to maldistribution of anesthetic within the intrathecal space, while repeated dosing may have exacerbated this phenomenon

leading to toxic intrathecal levels. As a result, the FDA has prohibited their use and they have been withdrawn from the market. Larger catheters and more dilute local anesthetic solutions fail to demonstrate this neurotoxicity.

Complications of Spinal Anesthesia

Post-Dural Puncture Headache

Post-dural puncture headache (PDPH) is the most common complication of a spinal anesthetic although the incidence has decreased with the development of new, smaller-gauge spinal needles. The incidence is highest among young adults and obstetrical patients with a decreasing risk associated with advancing age. Smaller, non-cutting needles decrease the incidence from as high as 5 % to less than 1 %. The headache occurs as a result of leakage of cerebral spinal fluid through a dural puncture site. This leads to decreased intradural pressure, and tension on the meninges and nerves resulting in an intense headache often relieved with recumbency. Cranial nerve palsies may also occur as a result of traction on cranial nerves. Although the headache is not dangerous, the symptoms can be quite debilitating and for a recent parturient may hinder mother–newborn bonding. Conservative management includes bed rest, hydration, and caffeine. When these fail to improve symptoms, an epidural blood patch may be considered.

Neurologic Complications

Although serious neurologic injury is a rare complication of a spinal anesthetic, many patients will refuse neuraxial anesthesia due to a fear of neurologic injury. Transient radiculopathies occur with an incidence of 6 per 10,000 spinals and generally resolve within 3 months. Cauda equina syndrome, characterized by a sensory deficit in the perianal region, bowel and bladder incontinence, and various motor deficits, may present following regression of the block. It often resolves over weeks to months but may produce lasting neurologic deficits. Incidence of this complication has been reported as 1.2 per 10,000 blocks.

Adhesive arachnoiditis is the most devastating neurologic injury. This insidious process occurs several weeks to months following a spinal block with the gradual progression of sensory and motor deficits of the lower extremities. It is pathologically characterized by proliferation and scarring of the meninges and vasoconstriction of the spinal cord vasculature.

Pain radiating to the buttocks or legs following the intrathecal injection of local anesthetic is referred to as transient neurologic symptoms (TNS). Neither sensory nor motor deficits should be present to make this diagnosis. The administration of lidocaine appears to be a significant risk factor for the development of this syndrome with an incidence of 12 % compared to 1.4 % for bupivacaine or tetracaine administration. Lithotomy position and outpatient surgery appear to increase the risk for developing symptoms when lidocaine is administered but are not risk factors with bupivacaine administration. Although neurologic deficits are not present, this syndrome should not be disregarded as an annoyance, as one-third of patients report pain symptoms as severe and may be quite debilitating. Most symptoms resolve within 72 h though some may last for months. In a minority of cases symptoms may persist for greater than 1 month, but in 118 confirmed cases of TNS prospectively evaluated all patients were symptom free by 6 months.

Infection

Bacterial or aseptic meningitis may develop following a spinal block with patients presenting with fever, nuchal rigidity, and photophobia. A low index of suspicion should exist for this as bacterial meningitis requires prompt evaluation and treatment while aseptic meningitis resolves spontaneously. Microscopic examination of the cerebral spinal fluid reveals leukocytosis. In aseptic meningitis, gram stain and culture are negative. When clinical suspicion is present, antibiotics should be started while studies are pending.

Hemodynamic Collapse

Spinal anesthesia has been associated with cardiac arrest in otherwise healthy patients with an observed incidence as high as 6.4 per 10,000 blocks. Premonitory symptoms often do not precede many of these events. It is believed the sudden sympathectomy causes a sudden decrease in the afterload without a compensatory tachycardiac response due to inhibition of the cardioaccelerator fibers. Although unexplained cardiac arrest is more common in younger, healthy patients, survivability following the event appears to be inversely proportional to age and ASA classification.

Failed Blocks

A failed, patchy, or incomplete block that yields inadequate anesthesia for a surgical procedure can have significant implications on a patient's perioperative management. Failure can be characterized by an inadequacy in the extent, density, and duration of the block. It may be evident at the time of the procedure or may progress during the surgical case. Supplementation with infiltration of local anesthetic into the surgical field, administration of intravenous sedation or analgesia, or conversion to general anesthesia may be required.

Failure rate for spinal block is estimated to be between 1 and 4 % but may be less than 1 %. Causes of failed spinal blocks include the obvious inability to successfully access the intrathecal space, poor agent selection, and inappropriate patient positioning following the block. Orifices of non-cutting needles may not completely enter the subarachnoid space allowing loss of anesthetic agent into the epidural

space despite adequate flow of CSF. The dura and arachnoid may also act as a flap valve over the opening of the pencil-point needle.

Epidural Anesthesia

The epidural space provides a second neuraxial target for the deposition of local anesthetic to induce a sensory blockade. Anesthetic may be delivered as a single injection or more commonly via an indwelling catheter as a continuous infusion or intermittent boluses. Indications for epidural blockade include surgical anesthesia, postoperative and labor analgesia, and chronic pain management. Unlike the on–off clinical characteristic of spinal anesthesia, epidural anesthesia can more finely be tailored to the needs of the clinical situation, such as the creation of a segmental blockade. The choices of local anesthetic, dosage, volume of infusion, and level of injection easily alter the intensity and extent of the blockade. As such, the often-unwanted effects of neuraxial anesthesia, such as hypotension and motor blockade, may be more easily balanced with desired clinical affects.

Mechanism

Although incompletely understood, local anesthetics deposited within the epidural space likely act in multiple locations, including the spinal nerve roots, dorsal root ganglia, extradural nerves, and the spinal cord. Evidence suggests the transition point at which the spinal nerve root exits the subarachnoid space and enters the nerve sheath to be the most important site of action. The dura and arachnoid are substantially thinner at this point. Presumably, this allows for easier penetration of anesthetic into the nerve tissue, as evidenced by a significantly higher level of local anesthetic found within nerve roots compared to other structures.

Diffusion of local anesthetic from the epidural space into the subarachnoid space also likely contributes to the blockade. Once within the subarachnoid space, local anesthetic may penetrate the spinal cord, with highest concentrations found in the lateral and posterior columns. However, the dilution of anesthetic by the CSF limits its potency.

The segmental extent of an epidural blockade is dependent on the longitudinal spread of anesthetic within the epidural space. From a lumbar injection site, spread usually occurs in a cephalad rather than caudal direction likely due to pressure gradients within the epidural space. More symmetrical distribution occurs from thoracic injection sites. The volume of anesthetic infused over a period of time influences the amount of spread within the epidural space, although it can be difficult to predict volume required to cover a particular number of vertebral segments. Intrinsic factors of the epidural space, such as scarring and areas of stenosis, also affect anesthetic spread.

Several clinical factors may influence the extent of spread within the epidural space and thus the sensory level achieved during epidural anesthesia. Increasing age likely leads to decreasing compliance of the epidural space, which reduces the volume by as much as 40 % required to achieve a sensory level. Body weight does not affect the spread of anesthetic, while height may contribute slightly to the extent of spread. The influence is likely more significant at extremes, as a very short person requires less volume to be infused than a much taller person to achieve a similar level. Position contributes slightly to the spread of anesthetic and thus patients should be positioned appropriately and repositioned if necessary to achieve a particular segmental level. Finally, additives, especially opioids, can affect the spread of an epidural anesthetic.

The intensity and quality of the block can be titrated by changing the concentration of local anesthetic. A more concentrated formulation of local anesthetic generally induces a stronger sensory blockade. With that comes an increased incidence and severity of unwanted side effects, including hypotension and motor blockade. Additives may also improve the quality of a blockade with combinations of additives and local anesthetics producing synergistic effects while minimizing unwanted side effects.

Preoperative Evaluation and Consent

As with a spinal anesthetic, a thorough preoperative history and physical exam should precede the placement of an epidural block. Care should be taken to identify absolute and relative contraindications. Routine testing of platelet concentration and coagulation studies are not recommended in the absence of clinical suspicion. Communication with the surgeons regarding the planned operative and postoperative course to determine the appropriateness of neuraxial anesthesia or postoperative epidural analgesia is paramount. Given the segmental nature of an epidural block, understanding the surgical plan, with particular attention to the incision location and extent, is critical to the placement of a successful epidural.

Patients must be informed of the risks associated with epidural anesthesia. Dichotomizing risks according to common and rare events may help to frame the discussion. A patient's refusal of epidural anesthesia is an absolute contraindication. In addition to the discussing risks, discussing the procedural steps and reasonable expectations for pain control will help to build rapport with a patient and family. It is important that postoperative and laboring patients be aware that well-functioning epidural anesthesia reduces somatic pain rather than eliminating it completely. Finally, informing patients

that patchy or inadequate epidurals may be improved upon by multiple techniques will further help to establish the anesthetist as an ally for the patient in their postoperative or peripartum course.

Preparation

Standard ASA monitors, including pulse oximetry, and an automatic noninvasive blood pressure cuff, are applied to the patient prior to the initiation of an epidural block. ECG should be immediately available. Oxygen is often supplied via nasal cannula while sedation is administered as needed via an intravenous line. Suction, airway equipment, and emergency medications should be immediately available in the room where the block is being performed. As with spinal anesthetics, sterile technique is required for placement of an epidural block. The skin site must be sterilized with an antiseptic solution, such as betadine or chlorhexidine.

Single-use, disposable epidural kits are packaged with standard epidural needles. In general, epidural needles are larger in size than spinal needles. The larger caliber facilitates the placement of a catheter through the needle into the epidural space. The type of epidural catheter differs among brands of kit.

The most commonly used epidural needle is a 17- or an 18-gauge Tuohy with a curved tip. A stylet should always be securely in place when advancing the needle to prevent coring of tissue and plugging of the needle, which may interfere with identification of the epidural space. Most providers prefer a Tuohy with a short point at the tip although blunted tips are available and may be most appropriate for novices (Fig. 21.7). Alternatively, a Crawford needle has a no curved tip. This may be particularly useful for a paraspinous approach as the 45–60° angle required for placement may make catheterization of the space difficult with a curved tip needle. However, the Crawford needle is more likely to core tissue and become plugged or traverse the dura and produce a wet tap.

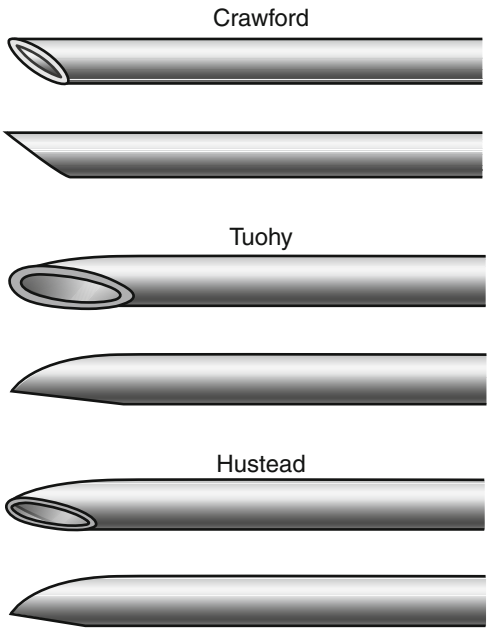


Fig. 21.7 Tip designs of epidural needles

Technique

Patient Positioning and Anatomic Landmarks

Patients may be positioned in a similar manner to spinal blocks—sitting, lateral decubitus, or prone. The seated position provides the practitioner with the best anatomy for successful placement, yet may not be appropriate for all patients. Patients who require general anesthesia or deep sedation for placement may be more safely positioned on their side. Prone positioning is generally limited to fluoroscopic placement of single-injection epidurals for chronic pain indications.

Knowledge of the planned surgical incision is key to choosing the correct interspace for epidural placement. The umbilicus receives innervation from T10 and serves as a helpful landmark when choosing an interspace. For abdominal procedures above or involving the umbilicus, a T7–9 epidural is often chosen. Thoracic procedures generally require a T4–6 epidural placement, which correlates to an interspace just above the level of the inferior angle of the scapula. For procedures of the lower abdomen, pelvis, and lower extremities, an epidural is often placed at L3–4 as with spinal anesthetics. This interspace roughly correlates to the superior aspect of the iliac crest (Fig. 21.8).

Approach and Identification of Epidural Space

As with spinal anesthesia, the epidural space may be approached from the posterior by a midline or paramedian approach. The vertebral level often dictates which approach is chosen for placement. In the lumbar and lower thoracic regions, the spinous processes are stacked upon each other a more parallel manner, allowing for the easy passage of a needle anteriorly through the interspinous space. The projections of the spinous processes become progressively steeper in the higher thoracic and cervical regions. This makes the midline placement of an epidural through the interspinous space more difficult if not impossible. Therefore, with epidurals placed at the mid-thoracic level and above, the paramedian approach may improve success rates. With all techniques, the skin and soft tissue is anesthetized with plain lidocaine, usually 1 or 2 %. With the paramedian approach, injection of local anesthetic near the sensitive periosteum improves patient comfort.

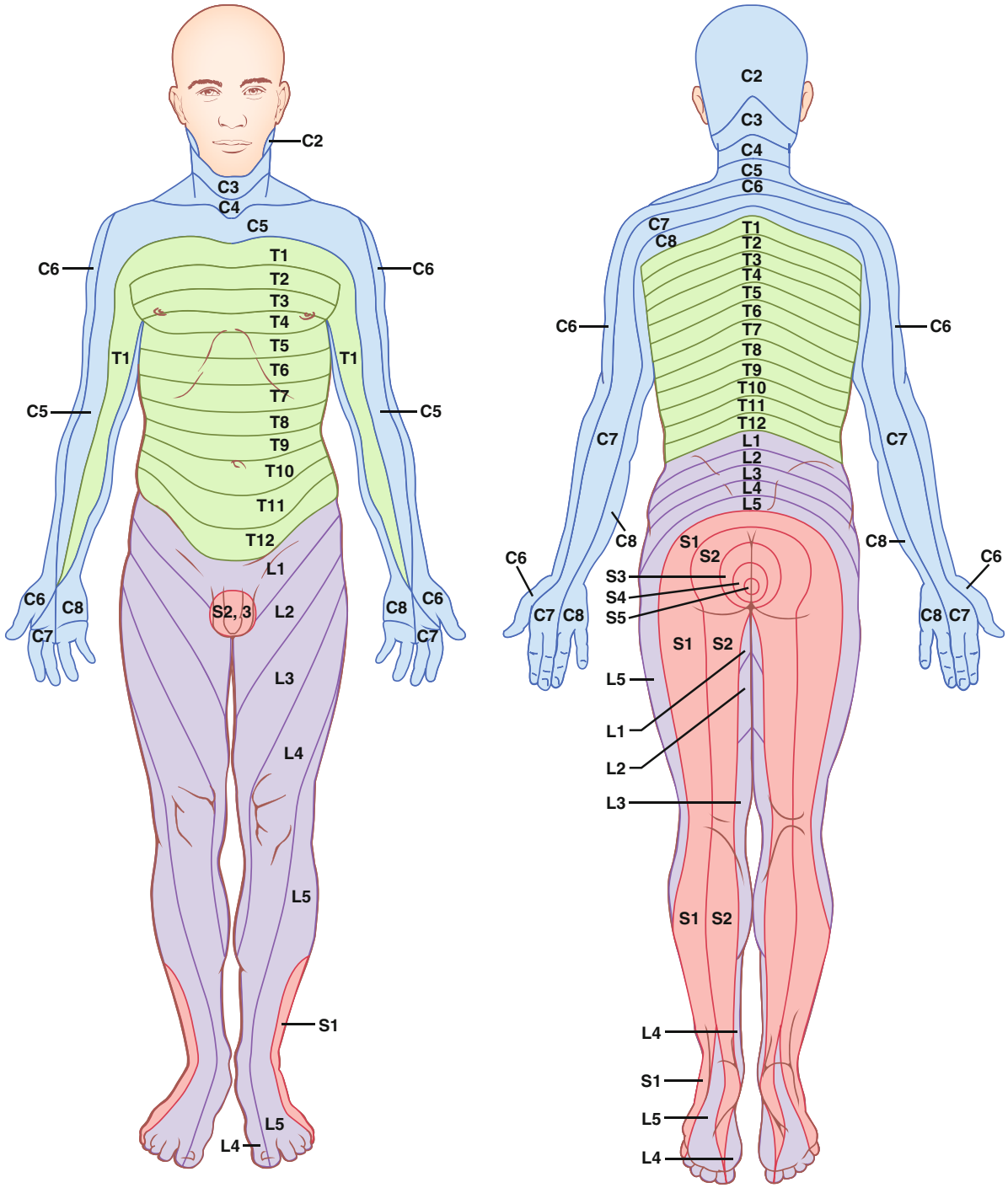


Fig. 21.8 The dermatomes

For the midline approach, palpation helps to identify the spinous processes with a specific focus on midline. The patient should be encouraged to slouch forward to make the interspinous spaces as large as possible. The epidural needle with the stylet in place is inserted through the skin between the two spinous processes. From there, the needle is directed straight or slightly cephalad at an angle of 10–25° in the lower thoracic region with more acute angles (30–50°) in the mid- and upper thoracic regions. The needle is advanced until a change of resistance is noted, usually indicating (if midline) that the needle has entered the interspinous ligament. At this point, the stylet is removed.

Alternatively, the paramedian approach is particularly helpful with mid- to high thoracic epidurals where a spinous process projects at a steep angle over the process below it. This leaves little room for the advancement of a needle

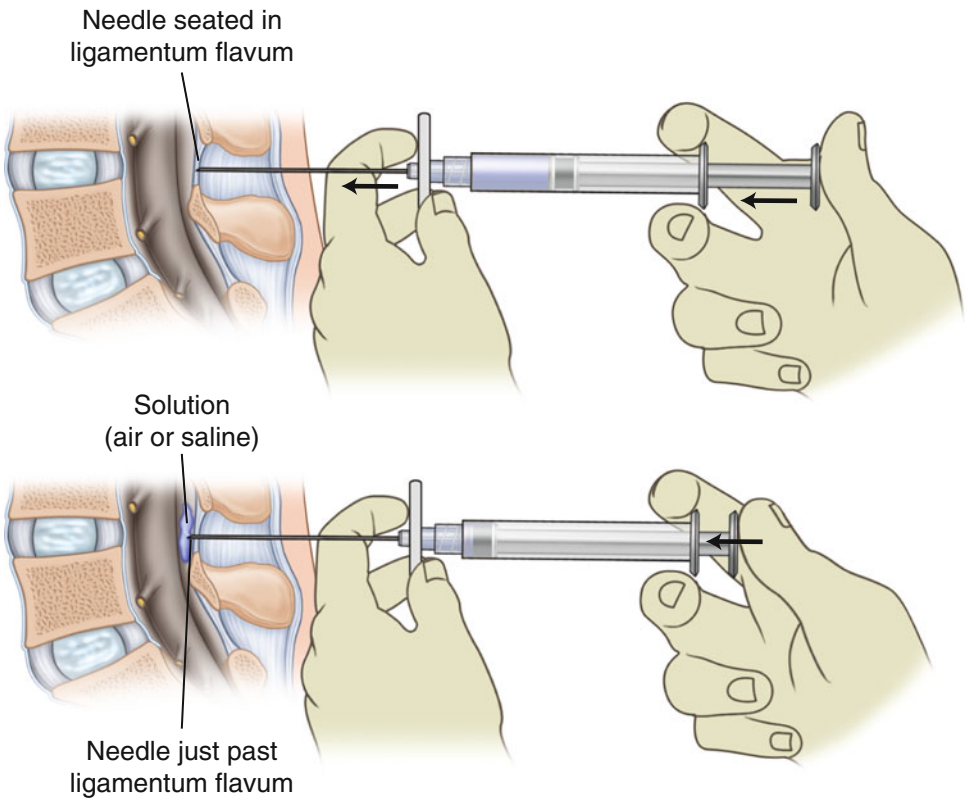


Fig. 21.9 Loss of resistance epidural technique. Once the epidural needle is positioned in the ligamentum flavum, the stylet is removed, and a syringe with air (or saline with an air bubble) is attached to the syringe. Maintaining pressure on the plunger, the epidural needle is advanced further, slowly and carefully. As soon as the epidural space is entered, there is a loss of resistance, and the air (or saline) in the syringe enters the space

through the interspinous space. In this approach, the entry site occurs 1.5 cm lateral to either side of midline just below the chosen interspace. The needle with its stylet in place is directed anteriorly until contact with bony lamina is made. The needle is withdrawn slightly and angled at a 10–25° toward midline and advanced in a slightly cephalad orientation. Should bone be encountered, redirect the needle progressively more cephalad and perhaps less medially until it "walks off" the lamina into the ligamentum flavum. Again, a change in consistency of the tissue is often noted when the needle enters ligament. At this point, the stylet is removed.

After removal of the stylet, a loss of resistance syringe (glass or plastic) filled with either normal saline or air is firmly attached to the hub of the epidural needle (Fig. 21.9). The needle and syringe are slowly advanced while applying continuous pressure to end of the syringe's plunger. When applying pressure, the plunger should have a tough, elastic feel to the practitioner's hands. Rapid tapping of the plunger also may be used as an alternative to continuous pressure, though care should be taken that only small movements are made between taps to avoid unknowingly passing through the epidural space into the intrathecal space. Once the tip of the needle enters the epidural space, a loss of resistance should be noted with the easy injection of the syringe's contents, although care should be taken to limit the amount of air injected.

Sometimes a loss of resistance is subtle and the question arises as to whether epidural space has been accessed. When this occurs, IV tubing primed with NS with one end attached to the hub of the epidural needle and the other held up to create a column confirms epidural placement if the fluid in the IV tubing flows freely into the epidural space. If the patient is asked to take slow deep breaths, respiratory variation of the dropping fluid can be appreciated.

An alternative to the loss of resistance technique involves filling the epidural needle hub with saline once the needle is seated in ligament. The drop of fluid hangs from the opening of the hub as the needle is slowly advanced. Once the needle passes into the epidural space, the negative pressure within the space draws the drop of fluid into the needle. Plugging of the epidural needle with tissue cored out during advancement may prevent the negative pressure being transmitted to the hub of the needle. This would hinder identification of the epidural space and result in inadvertent dural puncture.

Catheter Placement

Once identified, the epidural space may be cannulated to allow for repeated dosing of anesthetic or continuous infusion. With curved needle tips, it is recommended to orient the tip in the direction in which you wish the catheter to thread although this does not guarantee advancement in that direction. Catheters should be advanced 3–5 cm beyond the tip of the epidural needle (Fig. 21.10). The deeper the catheter is placed the less likely it is to become dislodged, but the more likely it is to produce a unilateral or patchy

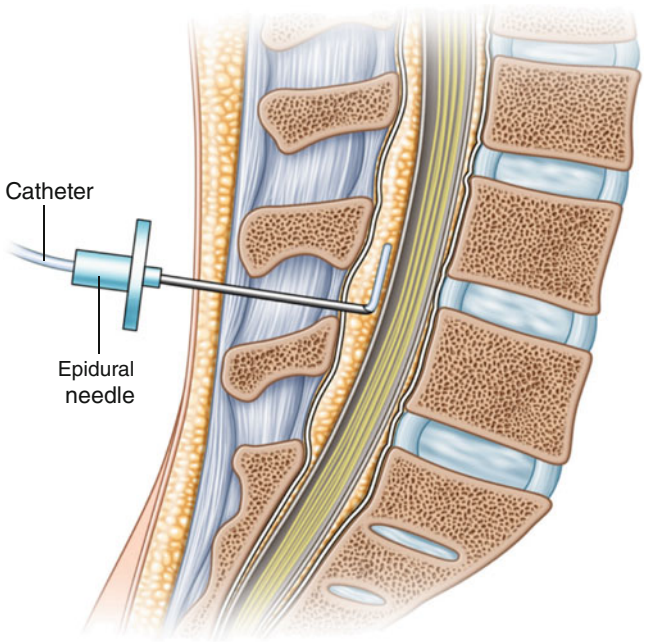


Fig. 21.10 Epidural catheter insertion

block. When threading beyond the needle tip is not possible, repeated dilation of the epidural space with normal saline and rotation of the epidural needle may be helpful.

Test Dose and Epidural Activation

When performed as a blind technique (without fluoroscopy), the correct placement of the catheter within the epidural space must be confirmed. The doses required for epidural anesthesia are significantly higher than those required for spinal anesthesia. As such, a misplaced intravenous catheter may lead to significant local anesthetic systemic toxicity, including seizures and cardiac arrest. Unidentified subarachnoid catheters may induce total spinals as a result of an intrathecal overdose of anesthetic.

Negative aspiration of blood or CSF does not rule out the misplacement of a catheter. Most commonly, a 3 ml solution containing 1.5 % lidocaine and 5 mcg/ml (1:200,000) epinephrine is administered as a test dose. Rapid sensory or motor changes suggest a subarachnoid injection, while an intravenous injection may be indicated by a metallic taste in the mouth, perioral numbness, ringing of the ears, or an increase in the heart rate of at least 20. False positive and negative results may occur. Increases in heart rate may accompany painful stimuli, such as contractions, despite the correct location of the catheter. Conversely, patients taking beta-blockers may not respond as expected to an intravenous injection of low-dose epinephrine.

Although a test dose may be administered via the epidural needle prior to insertion of the catheter, this would fail to recognize a catheter that migrates intravascularly during placement. For this reason, testing should be done through the catheter and not the needle. Intravenous catheters should immediately be removed, while intrathecal catheters may be left in place in appropriate clinical situations. Clear labeling of the catheter and communication among all healthcare workers who may access or manage an intrathecal catheter are essential to its safe retention within the subarachnoid space.

Once a catheter's location is confirmed, anesthetic administration may begin. Activation of an epidural occurs more slowly than with spinal anesthetics. Incremental bolus dosing of anesthetic provides an efficient and effective method to quickly induce a sensory blockade while limiting the toxicity associated with an inadvertent intravascular injection. Similarly, incremental dosing helps to attenuate the cardiovascular side effects of a larger bolus dose at the initiation of an anesthetic. As compared to a continuous infusion, bolus dosing by manual injection helps to spread anesthetic within the epidural space to induce wider levels of blockade.

Anesthetic Administration

Choice of Local Anesthetic

Local anesthetics differ in their speed of onset, duration, density of sensory and motor blockade, and side effect profile. The choice of local anesthetic is influenced by the desired clinical effect. Commonly chosen agents for surgical anesthesia include lidocaine 2 %, chloroprocaine 3 %, and mepivacaine 2 %, while commonly prescribed anesthetics for postoperative and laboring analgesia include ropivacaine and bupivacaine (Table 21.3). The concentrations used for postoperative and labor analgesia may be altered to balance analgesia with motor block and hypotension.

Adjuncts

Opioids

Similar to intrathecal modality, epidural administration of morphine and hydromorphone adds analgesic potency without increasing the incidence or severity of hypotension and motor blockade. Their hydrophilic structure allows more up/down diffusion in the epidural space. These drugs can be used as an infusion or single injection. More lipophilic synthetic opiates, such as fentanyl and sufentanil, create a more segmental analgesia and cover fewer dermatomes with rapid uptake into the CNS. Similar to epidural administration of opiates, the side effects include pruritus, sedation, and respiratory depression. At low doses, opiates' side effects are minimized while maintaining some local anesthetic sparing properties. This allows the use of more dilute local anesthetic solutions to minimize hypotension and motor blockade.

A single dose of 2–5 mg of morphine can provide postoperative analgesia for up to 24 h. This is recommended just prior to the discontinuation of the epidural catheter.

Table 21.3 Local anesthetics commonly used for epidural anesthesia

Drug	Concentration (%)	Onset (min)	Duration (h)
Lidocaine	2	10	1–1.5
Ropivacaine	0.1–0.25	15	2–2.5
Bupivacaine	0.0625–0.125	20	2.5–3
Chloroprocaine	3	5	45 min^{-1}

If the epidural is used postoperatively, 1–2 mcg/ml of fentanyl adds significant potency to the analgesic property of the epidural. If the epidural is not covering the entire surgical/painful area, addition of hydromorphone instead of fentanyl allows for wider spread of analgesia.

Vasoconstrictors

Epinephrine adds to the potency of the epidural solution. Analgesic potency of epinephrine in the epidural space is not through vasoconstriction. Bupivacaine alone causes a decrease in spinal and dural blood flow and addition of epinephrine does not further decrease the blood flow. There is strong evidence for direct epinephrine analgesic property, most likely for its alpha-2 mechanism.

Clonidine

Despite its FDA black box warning, epidural clonidine is used with some frequency in the United States. The risk of hemodynamic instability, hypotension, and bradycardia may be unacceptable in some patients, but in others, the benefits may outweigh the risks. A single injection of 30–100 mcg or an infusion of 1–2 mcg/ml are reasonable doses. Patients should be watched carefully for hemodynamic instability and routine use of epidural clonidine is not recommended.

Neostigmine

As mentioned above, intrathecal neostigmine (10 mcg) produces unacceptable nausea and vomiting in patients, but epidural neostigmine is much better tolerated. It is not currently indicated for epidural use, but multiple ongoing studies are under way to evaluate its use for postoperative analgesia and labor analgesia.

Troubleshooting

Patchy epidural blocks are a common occurrence and may decrease patient satisfaction with the anesthetic block. In general, areas of decreased analgesia occur when anesthetic fails to reach corresponding nerve roots or when the concentration of anesthetic is too low. A sensory exam may reveal distinct areas of increased sensation associated with a dermatomal distribution or a more diffuse process, such as a unilateral or failed block. Care should be taken to discriminate between somatic, temperature, and visceral sensation during the history taking and examination.

When encountering a patchy block, a practitioner may increase the rate of anesthetic infusion or allow a patient-directed bolus. However, a high-pressure, manual bolus of anesthetic by the anesthesiologist more consistently improves the quality and extent of the blockade. Presumably, this helps to distribute anesthetic around nerve roots that were previously poorly exposed. If these steps fail to correct a patchy block, consideration should be given to manipulating the catheter. A small withdrawal of the catheter may help facilitate bilateral distribution of anesthetic in the epidural space, especially if the catheter had been advanced more than 4–5 cm within the epidural space. Care should be taken to ensure one does not pull the catheter out during this step.

Alternatively, replacement of the epidural catheter may help to re-dilate the epidural space and allow for more even spread of anesthetic and improved block conditions. In the case of epidural catheters required for surgical anesthesia, removal of the catheter with the subsequent placement of a subarachnoid block may be undertaken. Care should be taken to consider reducing the dosage of subarachnoid anesthetic as total or unpredictably high spinal blocks have been reported when preceded by the unsuccessful bolus of an epidural catheter.

Hypotension is a common occurrence during epidural anesthesia, especially with the use of thoracic epidurals. Quite often an activated epidural may unmask previously compensated hypovolemia. In addition to recommending intravascular fluid expansion, reducing the local anesthetic concentration in the epidural solution may improve the patient's hemodynamics. A pure narcotic solution will also eliminate the vasodilatory effects of the local anesthetic although this will likely lessen the analgesic quality of the block.

Combined Spinal–Epidural Technique

Although epidurals may be used as the sole surgical anesthetic, the time required to achieve adequate surgical anesthesia often limits its use in the operating room. To overcome this limitation, a combined spinal–epidural (CSE) technique may be chosen to achieve a rapid onset, dense surgical block with the ability for re-dosing for long surgical procedures. Such a technique limits the risks associated with an intrathecal catheter and allows for the continuation of the catheter for postoperative analgesia should that be desirable.

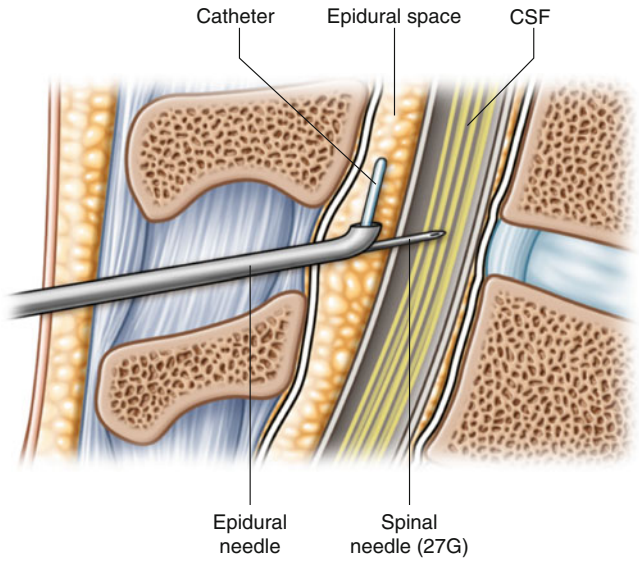


Fig. 21.11 Combined epidural spinal technique. Note the spinal needle exiting the Tuohy needle via the back-eye of the needle

CSEs may be performed with a through-needle technique or as two sequential procedures. In the former technique, the epidural space is identified via a Tuohy needle as with any standard epidural placement (Fig. 21.11). Once the space is identified, a spinal needle is advanced through the Tuohy needle. Often the characteristic pop of the spinal needle traversing the dura mater can be appreciated. Once the free flow of CSF is confirmed, an intrathecal dose of anesthetic is given through the spinal needle. The spinal needle is subsequently removed followed by the catheterization of the epidural space in the usual fashion through the Tuohy needle. The Tuohy needle is withdrawn and the catheter secured. In the sequential technique, the spinal anesthetic is placed in a typical fashion followed by a second puncture at the same or different level for epidural catheter placement.

For both techniques consideration should be given to the density of the local anesthetic chosen for the spinal, as the patient will be unable to quickly change position following administration of the intrathecal dose. Intraoperative activation of the epidural occurs prior to the expected length of the duration of the intrathecal anesthetic. Testing of the epidural should occur at this time even if it occurred at initial placement. Identifying an intrathecal catheter will be subtler given the existing intrathecal anesthetic. However, a larger than expected hemodynamic change may indicate a misplaced catheter.

Complications of Epidural Anesthesia

Complications from epidural anesthesia are similar to spinal anesthesia. Major neurologic complications are rare with epidural anesthetics, occurring at a rate of <1–7.6 per 10,000 anesthetics. The variation in the rate of complication reported in the literature likely occurs as a result of varying definitions of "serious" complications. Patients with preexisting neurologic disease, such as those with diabetic neuropathy, may be at increased risk for neurologic complications though the absolute incidence of complications still remains low.

Inadvertent puncture of the dura may produce a "wet tap" evident by the free flow of warm CSF from the epidural needle. The stylet may be replaced and the needle withdrawn with a new attempt to identify the epidural space to follow. Conversely, a catheter may be threaded through the epidural needle and placed within the intrathecal space. Dosage of anesthetic should be changed accordingly and the catheter should be clearly labeled as "intrathecal" to avoid medication dosage errors.

The decision to convert to spinal catheter analgesia rather than reattempting an epidural is dependent on practitioner preference, the catheter's clinical indication, and the location or eventual location of the patient. Such decisions may be influenced by comfort of the nursing staff on managing intrathecal catheters and the monitoring and oversight of an individual nursing unit. Prospective studies do not support the conversion to a continuous spinal as a means to reduce the incidence of post-dural puncture headache, while retrospective data show mixed results. However, conversion to continuous spinal in the event of an inadvertent dural puncture improves the establishment of the neuraxial blockade.

Inadvertent dural puncture and intrathecal catheterization are most often easily recognizable complications of epidural catheterization. Conversely, unintentional subdural catheterization often presents with more subtle findings and may be an under recognized phenomenon though the reported incidence is 0.82 %. Subdural catheterization and injection likely occur as a result of a dissection between the otherwise approximated dural and the arachnoid membranes. Proposed risk factors include procedures complicated by a technically difficult identification of the epidural space or when catheterization is preceded by accidental dural puncture, planned subarachnoid injection, or epidural needle rotation to facilitate catheter placement.

A high index of suspicion for subdural injection should be given to epidurals behaving in an unusual fashion. Subdural injection may present as a fast onset and excessive sensory blockade with motor sparing. Typically, the cephalad spread of the block is much more than intrathecal or epidural injection as the subdural space is very small and a small dose can travel far cephalad. Conversely, an unexplained unilateral, patchy, or failed block may indicate subdural catheter. Hypotension, bradycardia and respiratory depression may also more often accompany a subdural injection of anesthetic even with small doses of local anesthetic injection.

Epidural Blood Patch

Post-dural puncture headache is a rather common and potentially debilitating occurrence following neuraxial anesthesia with an incidence of approximately 1 % following epidural anesthesia. Although PDPH itself is not dangerous, the symptoms may be quite debilitating, especially in the postpartum period when it may interfere with maternal–infant bonding. An expectant approach to management includes opioid and non-opioid analgesics, caffeine, recumbency, and intravenous fluid loading. However, conservative management quite often proves ineffective.

Epidural blood patch is a safe and effective treatment for PDPH. The procedure involves advancing a Tuohy needle into the epidural space with a loss of resistance technique as performed for the placement of any epidural. In the case of a previous lumbar epidural, an interspace within one or two levels of the original site is preferable as skin and soft tissue tenderness over the previous site may preclude comfortable placement, although there is no data on success rates. When a blood patch is performed for a PDPH following a thoracic epidural, a blood patch performed in the lumbar region may still prove effective.

Once the epidural space is identified, blood from the patient is aspirated under sterile conditions into a plain syringe. This may be performed either by the practitioner or an assistant. Blood drawn prior to accessing the epidural space may clot and be unusable. Some advocate for the placement of a new intravenous line prior to accessing the epidural space to allow for easier availability of blood. If this technique is chosen, care should be taken to place the intravenous line under sterile conditions and retain the line within the sterile field. Approximately 20 ml of blood is then slowly injected into the epidural space. Injection should be halted or slowed with significant back pain or any radicular symptoms.

The blood patch initially increases the pressure within the epidural space and thus relieves the traction placed on the meninges. Long-term relief necessitates the resolution of the dural leak. In the case of an epidural blood patch, coagulated blood may help to seal the dural tear and eliminate CSF leakage. Short-term partial or complete relief of symptoms occurs in approximately 90 % of cases. Patients often appreciate a significant improvement in symptoms immediately following placement. However, recurrence is a common phenomenon and a repeat blood patch may be required in 15 % of cases. Should a third blood patch be required, the exclusion of other, less common causes of postpartum headache is warranted followed by a referral to an interventional pain specialist with the ability to place a blood patch under fluoroscopy.

Special Considerations

Patients with Spine Pathology and Prior Spine Surgery

Patients with prior spine surgery may present a challenge in placement of neuraxial anesthesia. Depending on the location, number of levels involved, and the specific spine procedure performed, identification of midline landmarks for a neuraxial approach may be difficult. Additionally, scar tissue formation may obliterate the epidural space. Despite these concerns, successful placement of spinals, epidurals, combined spinal-epidurals, and spinal catheters have all been reported.

Hebl et al. reviewed 937 patients with preexisting spinal stenosis, lumbar disc disease, or prior spine surgery who got neuraxial anesthesia for surgery. The overall success rate was over 97 % and history of spine surgery did not affect the success rates or technical complications. In a prospective evaluation of 42 parturients with a history of lumbar discectomy, no differences in bupivacaine consumption, time to placement of the block, and mode of delivery were noted compared to control groups. However, attempts at more than one interspace occurred more frequently in the patients with a history of discectomy (17 vs. 2 %).

Neuraxial techniques may be safe and effective in patients with more extensive surgical histories, as well. Crosby and Halpern report uncomplicated placement of epidural catheters in five of nine attempts in a series of patients with history of Harrington spine instrumentation. Difficulties encountered included multiple attempts prior to successful insertion, blood aspirated from the catheter, ineffective blockade, inadvertent dural puncture, and the inability to define the epidural space despite attempts at multiple levels. Similarly, 63 % of patients with corrected and uncorrected scoliosis underwent successful placement of continuous spinal catheterization.

In evaluating the evidence, there are no contraindications in placement of neuraxial block in patients with spine pathology and prior spine surgery. Risks and benefits of each technique must be weighed for each patient and the higher incidence of technical difficulty and failure must be discussed with patients prior to attempts at neuraxial blockade.

Anticoagulants and Neuraxial Anesthesia

Guidelines from ASRA provide information regarding neuraxial blockade in the setting of anticoagulants and other drugs affecting clot formation. These guidelines are regularly updated with newer drugs. In general NSAIDS and aspirin alone are not contraindications for neuraxial anesthesia.

Prophylactic subcutaneous injection of unfractionated heparin is also not a contraindication based on the most recent guidelines. The recommendation for low molecular weight heparin is to wait 12 h after a prophylactic dose and 24 h after a treatment (full anticoagulation) dose. Practitioners must review the most up-to-date guidelines published by ASRA (see also chapter on orthopedic anesthesia).

Clinical Review

1. The most common side effect of spinal anesthesia is
   A. Nausea
   B. Hypotension
   C. Bradycardia
   D. Urinary retention
2. While performing spinal anesthesia, the first ligament that is encountered is
   A. Supraspinous
   B. Ligamentum flavum
   C. Anterior longitudinal ligament
   D. Posterior longitudinal ligament
3. Highest incidence of post-dural puncture headache occurs with the following similar gauge needles:
   A. Quincke
   B. Sprotte
   C. Whitacre
   D. Pencil point
4. The most important factor in the spread of spinal local anesthetic solution is
   A. Addition of epinephrine
   B. Vertebral level of injection
   C. Height of the patient
   D. Baricity
5. A 34-year-old patient receives a bupivacaine spinal anesthesia. After placement of the spinal the heart rate drops to 20 bpm and the blood pressure to 50/42 mmHg. Initial step in management is administration of
   A. Ephedrine
   B. Phenylephrine
   C. Epinephrine
   D. Oxygen and Trendelenburg position

Answers: 1. B, 2. A, 3. A, 4. D, 5. C

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Peripheral Nerve Blocks

22

Michael Tom and Thomas M. Halaszynski

Despite improvements over the last decade and better understanding of acute postoperative pain pathophysiology, there remains a continuous demonstration that perioperative pain management needs to be more optimized. Therefore, regional anesthesia (RA) techniques, especially peripheral nerve blockade (PNB) procedures, have gained widespread popularity as part of a multimodal approach to perioperative pain management. Perioperative use of RA and analgesia may attenuate adverse perioperative pathophysiology from inadequately treated pain and improve patient outcomes (Table 22.1). In addition, PNB has been identified with many distinct advantages over general anesthesia and central neuraxial anesthesia. Relevant indications, contraindications, possible complications, and suggestions for PNB utilized in the perioperative setting are summarized in Tables 22.2, 22.3, and 22.4. This chapter will describe the following PNBs.

- Upper extremity nerve blocks
  - Interscalene brachial plexus block (bpb)
  - Supraclavicular bpb
  - Suprascapular bpb
  - Infraclavicular bpb
  - Axillary bpb
  - Brachial plexus nerve *branch* blocks
  - Digital and Metacarpal nerve blocks
  - Intravenous regional anesthesia
- Cervical plexus block
- Lower extremity nerve blocks
  - Femoral
  - Lumbar plexus
  - Sciatic
  - Popliteal
  - Ankle

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Upper Extremity Nerve Blockade

Anatomy of the Brachial Plexus

The brachial plexus consists of anterior rami of roots $C_{5–8}$ and T_1 (there also may be contributions from C_4 and/or T_2) and supplies both sensory and motor innervation to the upper extremities. The C_5–T_1 nerve roots divide to form three trunks (inferior, middle, and superior), which then divides into three anterior and three posterior divisions as they pass over the first rib and dive below the clavicle. The six divisions further develop into lateral, medial, and posterior cords as they pass through the axilla. Five primary terminal nerve branches form and include musculocutaneous, radial, axillary, median, and ulnar nerves (Fig. 22.1). The brachial plexus travels (typically) with a vascular supply that is contained within a neural vascular bundle along a large portion of its path from its origin to terminal nerve branches. Innervation of the upper extremity is shown in Fig. 22.2.

Preparation Technique

Equipment preparation: sterile towels, gloves and gauze pads, marking pen, antiseptic solution, peripheral nerve stimulator, syringes, and needles for local infiltration and nerve block placement.

Patient preparation: Signed anesthesia and surgical consent, Monitors "on" and appropriate sedation (midazolam, fentanyl).

Needles: 25 G 1.5 in. needle for skin infiltration, and 22G 2–4 in. short bevel insulated stimulation needle.

Commonly used agents: 3 % chloroprocaine, 2 % lidocaine, 0.5 % ropivacaine, 0.5 % bupivacaine (Table 22.5).

Approximate dose: 20–40 ml of local anesthetic.

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Table 22.1 Benefits of peripheral nerve blockade

Opioid-sparing effect
Improved acute pain relief
Promote mobilization and physical rehabilitation therapy
Reduced requirement for sedatives/hypnotics/general anesthetic needs (decrease MAC)
Reduced postoperative nausea/vomiting, cognitive dysfunction as associated with GA
Decreased surgical stress response in patients with significant comorbidities (cardiovascular disease, respiratory disease)
Economic benefits associated with "Fast Track" surgery (early PACU discharge)

Table 22.2 Peripheral nerve blocks matched to appropriate surgical procedure

Nerve block	Indications	Special problems and contraindications
Interscalene brachial plexus block	Shoulder, arm, elbow surgery	Phrenic and/or recurrent laryngeal nerve block, dyspnea, Horner's syndrome
Supraclavicular brachial plexus block	Arm, elbow, forearm, hand surgery	Pneumothorax, missed ulnar nerve
Infraclavicular brachial plexus block	Elbow, forearm, hand surgery	Pneumothorax
Axillary brachial plexus block	Forearm, hand surgery	Intravascular injection can cause seizures, missed musculocutaneous nerve
Femoral nerve block	Anterior thigh, knee surgery	Relative contraindication with femoral vascular grafts
Sciatic nerve block (posterior approach)	Surgery on the knee, tibia, ankle, foot	Patient positioning may be difficult
Popliteal block (intertendinous)	Corrective foot surgery, achilles tendon repair	Prone position may be difficult
Lumbar plexus block	Hip, anterior thigh, knee surgery	Hemodynamic effects, patient anticoagulation, dural puncture
Ankle block	Surgery on foot, toes	Not performed in presence of inflammation
Intravenous regional block (Bier block)	Hand, foot surgery	Local anesthetic not to be mixed with epinephrine, duration of surgery should range from 20 min to about an hour

Table 22.3 Contraindications to peripheral nerve blockade

Infection at site
Patient refusal
Pre-block neurologic compromise to intended site
Patient positioning (severe painful extremity)
Allergic reactions (to local anesthetic)
Coagulopathy

Table 22.4 Complications of peripheral nerve blockade

Infection
Hematoma
Bleeding
Nerve injury
Patient discomfort (failed or partial block)
Persistent paresthesias
Intravascular injection
Dural puncture (with some blocks)

Interscalene Block

Interscalene blockade targets the brachial plexus at the level of nerve roots or trunks. It is used routinely for surgeries/postoperative pain management of the shoulder and lateral aspect of the upper arm.

- Rotator cuff repair, arthrolysis, and acromioplasty of the shoulder
- Arthroscopic shoulder surgery and arthroplasty of the shoulder
- Proximal humerus surgery, humerus open reduction, and internal fixation (ORIF)

An interscalene block often does not provide adequate blockade for hand, arm, and forearm surgeries as the ulnar nerve may not be blocked. Blockade of the ulnar nerve may happen by using larger local anesthetic volumes or supplemental blockade of the ulnar nerve at a more distal location.

Surface Anatomy, Landmarks, and Procedure

Landmarks include lateral and posterior borders of sternal and clavicular heads of sternocleidomastoid (SCM) muscle, C_6 tubercle, interscalene groove (formed by the anterior and middle scalene muscles), upper border of cricoid cartilage, and the clavicle (Fig. 22.3).

The patient is positioned supine with the head turned away from side to be blocked and arms relaxed at the side. A line is drawn laterally from the top portion of cricoid cartilage in a direction toward and past the posterior border of (SCM) muscle (coincides with C_6 transverse process). This line will serve as the path along which to take when searching for appropriate muscle twitch. The bony tubercle of the

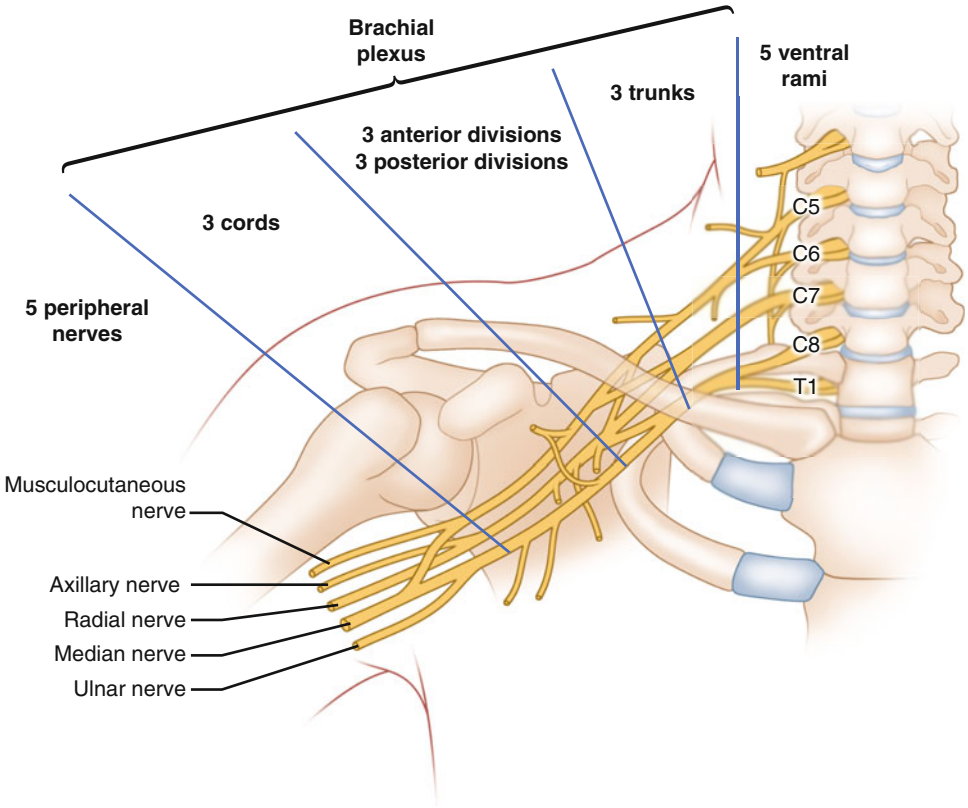

Fig. 22.1 Anatomy of the brachial plexus

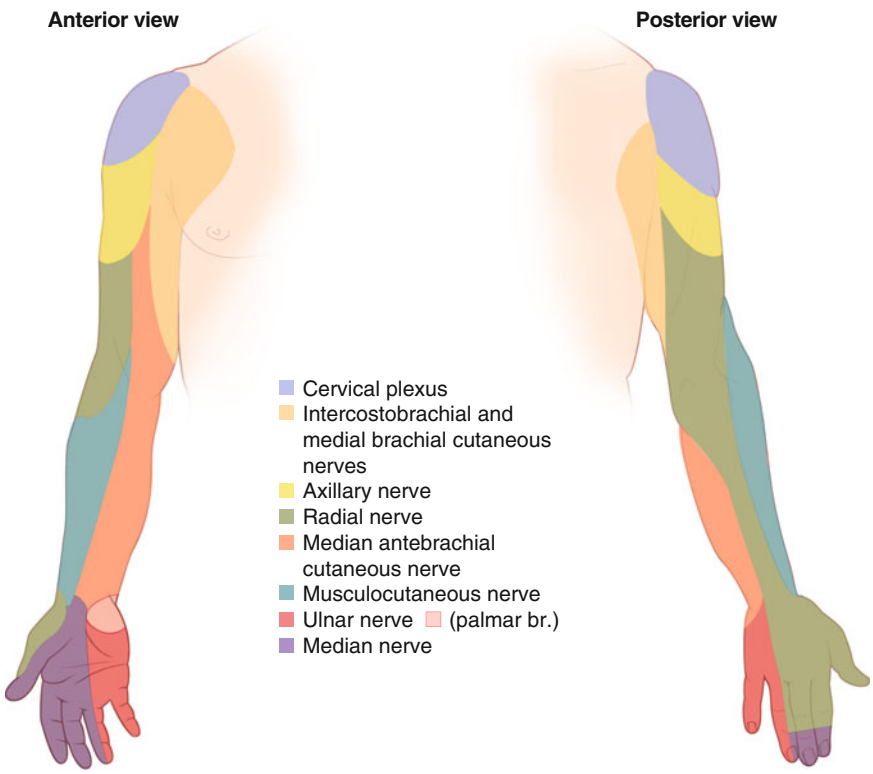

Fig. 22.2 Innervation of the upper extremity

Table 22.5 Commonly used local anesthetics for peripheral nerve blockade

Local anesthetic(s)	Onset (min)	Anesthesia duration (h)	Analgesia duration (h)
3 % 2-Chloroprocaine (+HCO_3 + epinephrine)	5–10	1.5	2.0
1.5 % Mepivacaine (+HCO_3)	10–20	2–3	2–4
1.5 % Mepivacaine (+HCO_3 + epinephrine)	5–15	2.5–4	3–6
2 % Lidocaine (+HCO_3)	10–20	2.5–3	2–5
2 % Lidocaine (+HCO_3 + epinephrine)	5–15	3–6	5–8
0.5 % Ropivacaine	15–20	6–8	8–12
0.75 % Ropivacaine	5–15	8–10	12–18
0.5 % Bupivacaine (+epinephrine)	20–30	8–10	16–18

Epinephrine concentration: 1:200,000, HCO_3–sodium bicarbonate addition

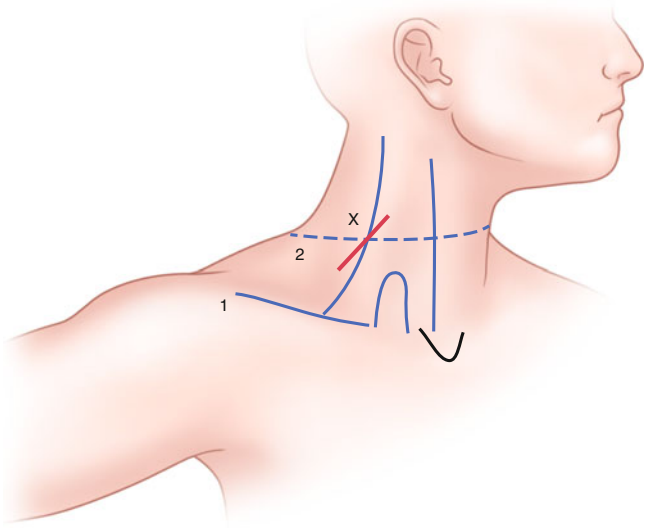

Fig. 22.3 Surface landmarks for an interscalene approach to the Brachial Plexus. The external jugular vein is shown in red and the sternocleidomastoid muscle identified in blue. Line 1 is the clavicle and the dashed line 2 at the C_6 vertebral process represents the line/path along which to follow in search of the appropriate muscle response. Point "X" marks the initial needle entry site

C_6 transverse process can often be palpated along this line. The posterior border of the SCM muscle is marked which bisects the previously drawn line. The posterior border of the SCM muscle can easily be palpated by instructing the patient to raise their head off the table and/or flex the neck. The interscalene groove is marked by palpating for the groove immediately behind and deep to the posterior border of the SCM muscle (point along the C_6 transverse process line).

A 22G 2 in. b-bevel needle connected to a nerve stimulator set at 1.0 mA (activate nerve stimulator subsequent to subcutaneous needle placement) is inserted at the mark of the interscalene groove and directed perpendicular to the skin. The block needle is inserted until an appropriate motor twitch of the deltoid or biceps muscle is obtained at a stimulation between 0.2 and 0.5 mA or paresthesia to the arm or thumb is elicited. Muscle twitch typically occurs superficially at a depth of 1–2 cm (up to 3 cm in obese patients). About 20–40 ml of local anesthetic is injected following frequent negative aspiration of blood/CSF. A single orifice catheter may be inserted (provides continuous infusion of local anesthetic) although securing and maintaining such a catheter in the interscalene groove may be difficult.

Pearls and Pitfalls

Pearls

Twitches of the following muscles provide similar block success: pectoralis, deltoid, triceps, biceps, and any twitch of hand or forearm. The external jugular vein crosses close to the insertion site for this classical interscalene block approach. Since shoulder surgery may entail massive nociceptive input, an interscalene block will typically provide relief of reflex muscle spasm and deep somatic pain.

Pitfalls

Possible side effects from an interscalene block include blockade of phrenic nerve and the sympathetic chain (located in region of the cervical nerve roots). The phrenic nerve is affected in 90–100 % of interscalene blocks, which could result in an ipsilateral diaphragmatic paralysis. Therefore, in patients with respiratory compromise (such as severe COPD), creating a hemidiaphragm may not be tolerable. Blockade of the stellate ganglion sympathetic chain can cause Horner's syndrome, which is characterized by ipsilateral myosis, ptosis, and anhidrosis. Nasal stuffiness and blockade of the recurrent laryngeal nerve can occur causing hoarseness.

Additional complications include infection, hematoma, and pneumothorax (as the cupola of the lung may be located in the vicinity of C_6 tubercle). A pneumothorax must be considered if the patient develops chest pain or cough, even hours following the block. Severe complications from an inadvertent intravascular injection (external jugular vein—which transverses the interscalene groove, and the vertebral artery—which is anterior to the cervical nerve roots) with as little as 1–3 ml of local anesthetic (especially into the vertebral artery)—may result in seizures. An additional complication is injection of the local anesthetic solution into the intervertebral foramina that could result in a high spinal or epidural block.

Supraclavicular Block

The supraclavicular blockade targets divisions of the brachial plexus for upper extremity surgeries and covers the axillary, radial, medial, and musculocutaneous nerves distribution,

but with possible sparing of the ulnar nerve. When used for shoulder surgery, the addition of a superficial cervical nerve block is often required. Indications include primary anesthesia and postoperative pain management for humerus (distal), elbow, forearm, hand, or wrist surgeries (with or without a continuous catheter), and upper extremity proximal arteriovenous (AV) fistula surgery.

Surface Anatomy, Landmarks, and Procedure

Landmarks include the sternocleidomastoid muscle, anterior and middle scalene muscles, clavicle, 1st rib, and the subclavian artery. The patient is positioned supine or semi-sitting with the head turned away from side to be blocked and arms remaining relaxed at the side. The brachial plexus is targeted at the midpoint of the clavicle (Fig. 22.4a). A 22G 2 in. b-bevel needle is connected to a nerve stimulator set at 1.0 mA (activate nerve stimulator subsequent to subcutaneous needle placement), and inserted 1 finger width cephalad to the mid-clavicular point and directed caudally (2.5 cm lateral to the SCM muscle attachment of the clavicle, Fig. 22.4b).

The first rib is contacted with the needle at a depth of 2–4 cm and then "walked off" the first rib until a corresponding muscle twitch is obtained at a threshold of 0.2–0.5 mA or a paresthesia to the arm or thumb is elicited. NOTE: Use caution and avoid directing the block needle medially toward the cupola of the lung. Following desired nerve stimulation (flexion or extension of wrist or digits), 20–40 ml of local anesthetic is injected in incremental doses with frequent negative aspiration. A single orifice catheter may be inserted and used for continuous infusion of local anesthetic solution.

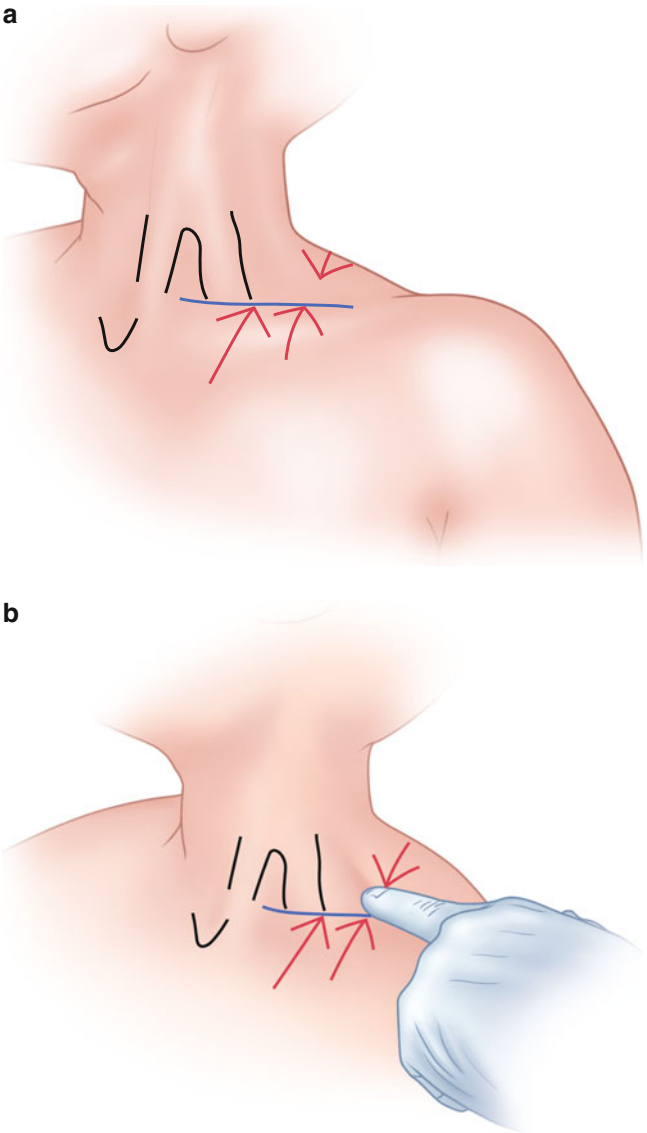

Fig. 22.4 Landmarks for the supraclavicular approach to brachial plexus. (**a**) Sternal notch and the sternocleidomastoid (SCM) muscle are identified in black and the clavicle in blue. The medial *red arrow* (pointing cephalad) indicates the lateral portion of the SCM muscle attachment to the clavicle. The lateral *red arrow* (pointing cephalad) is approximately 1 thumb width (2.5 cm) lateral to the medial *red arrow* and provides a margin of safety (away from the pleural dome). (**b**) Sternal notch and the sternocleidomastoid (SCM) muscle are identified in *black* and the clavicle is marked in *blue*. The single *red arrow* pointing caudad is the point of needle entry. This point is located cephalad to the palpating finger positioned above the *blue line* marking the clavicle. *Red arrows* on each side of the palpating finger identify the direction of the advancing needle that is aligned parallel to the body midline

Pearls and Pitfalls

Pearls

Brachial plexus block at this level (cephaloposterior and lateral to the subclavian artery) may show muscle stimulation or paresthesia before the needle contacts the first rib. The middle trunk of the brachial plexus (median nerve) is more posterior to the artery and spread of local anesthetic to this area can be slow. If a tourniquet is used for surgery and placed on the upper arm, blockade of the intercostobrachial nerve in the axilla is necessary.

Pitfalls

Puncturing the lung cupola can cause a pneumothorax (0.5–6 % incidence). Such a complication should be considered if a patient coughs or develops chest pain (even hours after block placement). The risk of pneumothorax is increased if the block needle is directed medially. Patients with lung disease may not be candidates for this block. Phrenic nerve or sympathetic chain blockade is possible although less common than after an interscalene block. Bleeding, infection, hematoma, nerve injury, and intravascular injection (subclavian vessels are in the region) are potential problems. A supplemental ulnar nerve block may be necessary if the ulnar nerve distribution is missed. A superficial cervical plexus block should be added for shoulder surgery as this approach often misses the skin overlying the shoulder.

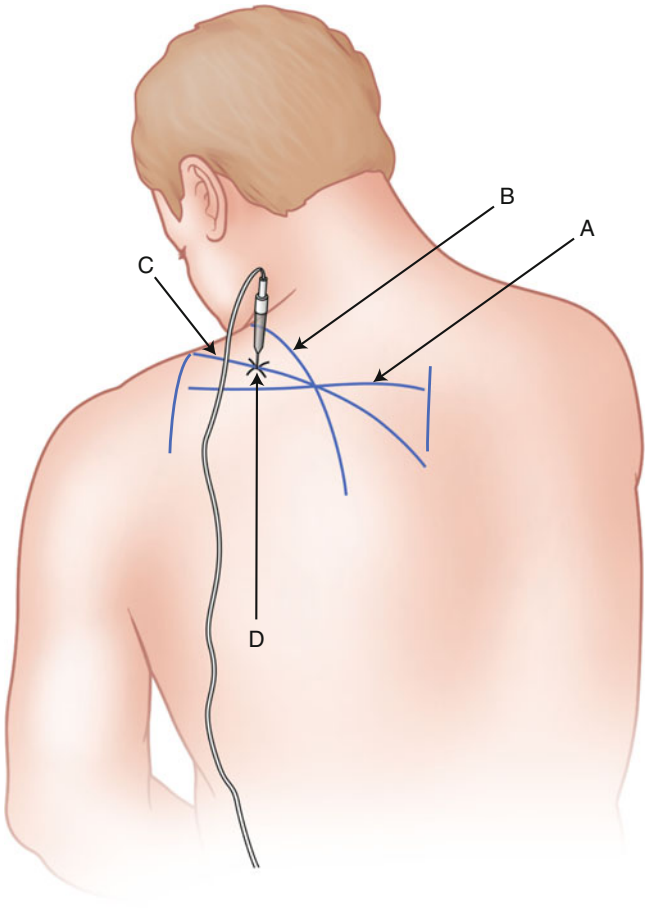

Fig. 22.5 Suprascapular nerve injection. Spine of the scapula (**A**) is identified. A perpendicular line (**B**) is drawn from the angle of the scapula upward to bisect the spine of the scapula. About 2 cm lateral to the intersecting point (**D**), in the upper outer quadrant of the scapula (**C**), the needle is inserted

Suprascapular Block

The suprascapular nerve is formed from the fibers of C_5 and C_6 nerve roots (some contribution from C_4), and passes through the suprascapular notch under the coracoclavicular ligament. The suprascapular block is useful for the diagnosis, treatment, pain management, and surgery involving the shoulder girdle. It can also be used specifically for the treatment of "frozen shoulder" adhesive capsulitis, complex regional pain syndrome type I, and shoulder joint pain.

Surface Anatomy, Landmarks, and Procedure

Landmarks include the spine of the scapula which is palpated laterally to identify the acromion (Fig. 22.5). With the patient seated, the spine of the scapula is identified and a perpendicular line is drawn from the angle of the scapula upward to bisect the spine of the scapula.

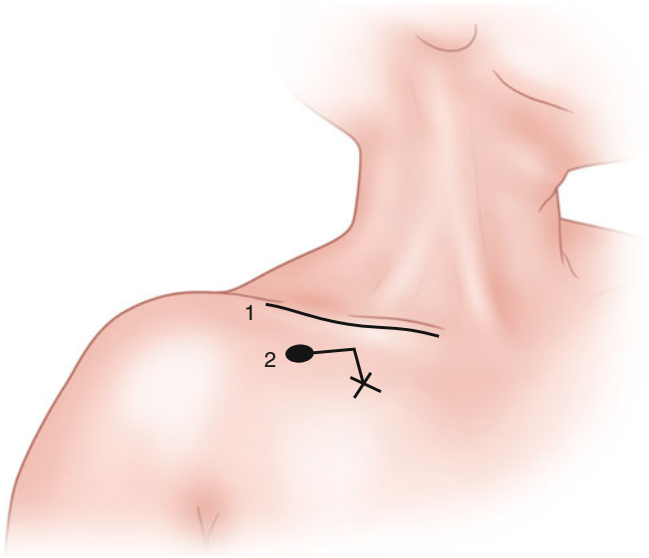

Fig. 22.6 Coracoid approach (landmark) for infraclavicular brachial plexus block. Line #1: clavicle, and filled circle #2: coracoid process. Point "X" is the needle insertion site positioned 2 cm inferior and medial to the coracoid process

A 25 G 2 in. needle is inserted about 2 cm lateral to the intersecting point, in the upper outer quadrant of the scapula (at the junction of spine of the scapula and acromion). The needle is directed inferiorly toward the scapula, and upon encountering the body of the scapula it is walked off superiorly and laterally until the needle enters the suprascapular notch. Once a paresthesia is elicited, the block needle should not be advanced any further. However, if paresthesia is not elicited, the needle is advanced half an inch further until it crosses the coracoclavicular ligament, after which 10 ml of local anesthetic is slowly injected after negative aspiration.

Infraclavicular Block

Infraclavicular blockade of brachial plexus occurs at level of the brachial plexus cords below the clavicle. Indications include anesthesia and/or postoperative analgesia with or without a continuous catheter for elbow, forearm, wrist, hand, and surgeries distal to mid humerus, including distal AV fistula surgery.

Surface Anatomy, Landmarks, and Procedure

Landmarks include the pectoralis major and minor muscles, subscapularis and teres major muscles, serratus anterior muscle, humerus, scapula, clavicle, and the coracoid process (Fig. 22.6). The patient is positioned supine, with the head turned toward the contralateral side and the arm to be blocked at the side or flexed at the elbow and resting on the abdomen. Following local skin infiltration and sterile preparation, a 2 in. 22G b-bevel needle is connected to

a nerve stimulator set at 1.0 mA and inserted perpendicularly to the skin 2 cm caudad and 2 cm medial to the coracoid process.

The block needle is directed in a vertical and parasagittal plane aimed toward the axilla while searching for a paresthesia to the distal upper extremity or an appropriate muscle twitch (stimulation between 0.2 and 0.5 mA). NOTE: Muscle twitch/stimulation at wrist or hand, and NOT the musculocutaneous nerve, is considered appropriate. After negative aspiration of blood, 30–40 ml of local anesthetic is injected (with frequent negative aspiration). The brachial plexus depth during infraclavicular block can vary from 2 to 8 cm depending on body habitus (average 4 cm). Continuous infusion of local anesthetic can be provided with a single orifice catheter.

Pearls and Pitfalls

Pearls

Supine positioning and maintaining the arm in a neutral or comfortable position is a benefit. The infraclavicular block placement site is useful for securing a catheter as catheter position is easily maintained for prolonged postoperative analgesia.

Pitfalls

An infraclavicular block may cause discomfort as the pectoral muscles are pierced (ensure subcutaneous local infiltration and patient sedation) and twitches elicited (after which the needle is further advanced until a distal upper extremity twitch response is obtained). Motor stimulation of the deltoid (axillary nerve) or biceps (musculocutaneous nerve) muscles may not provide reliable plexus blockade as these nerves often branch from the brachial plexus earlier. Phrenic nerve or sympathetic chain effect from the infraclavicular approach is possible, but less common than an interscalene or supraclavicular approach to the plexus. Hematoma formation, intravascular injection, infection, nerve injury, and pneumothorax are possible.

Axillary Block

Axillary blockade of brachial plexus targets the terminal nerve branches. There are several techniques for performing an axillary block including a transarterial, paresthesia-seeking, and nerve stimulation method. It is commonly performed for surgeries of the distal upper extremity. Indications include postoperative pain management and/or primary anesthesia for forearm, hand, and wrist surgeries with/without a continuous catheter. Examples of surgeries include Dupuytren's contracture release, carpal tunnel release, Colles' fracture repair, and distal AV fistula surgery.

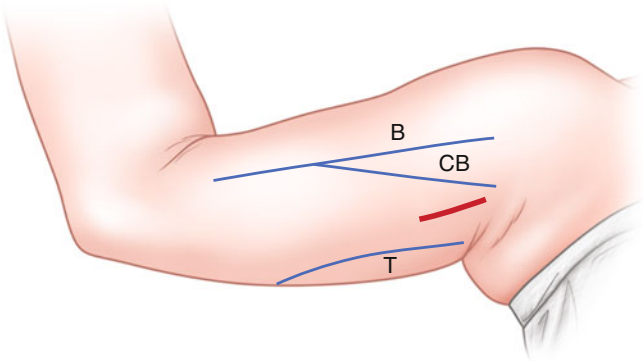

Fig. 22.7 Landmarks for the axillary brachial plexus block. *B* biceps muscle, *T* triceps muscle, *CB* coracobrachialis muscle. The axillary artery is shown in *red*

Surface Anatomy, Landmarks, and Procedure

Landmarks include the axilla, axillary artery, and the humerus (Fig. 22.7). Figure 22.8 shows the axillary nerve map. Distal to the axillary hair pad, imagine the upper arm in a cross-sectional view with the musculocutaneous nerve found outside the neural vascular bundle in the 9–12 O'clock position and embedded in the coracobrachialis muscle, the median nerve typically located in the 12–3 O'clock position above the pulse of the axillary artery and within the neural vascular bundle, the ulnar nerve usually located in the 3–6 O'clock position, and the radial nerve located in the 6–9 O'clock position (variable) below the pulse of the axillary artery (both branches within the neural vascular bundle).

The patient is positioned supine with the head neutral or away from the side to be blocked, while the arm to be blocked is abducted 90° at the shoulder and flexed 90° at the elbow. The axillary artery is then palpated and marked. Following skin preparation and local infiltration, a 22G 2 in. b-bevel needle is connected to a nerve stimulator set at 1.0 mA (activate nerve stimulator subsequent to subcutaneous needle placement). While palpating the axillary artery, the block needle is inserted at 30–45° to the skin and directed toward the axilla overlying the palpable artery in the distal axilla. The block needle is inserted searching for paresthesia or appropriate motor response at the wrist, hand, or thumb (at 0.2–0.5 mA). Consistent muscle twitch of the wrist and hand indicates ulnar, radial, and/or median nerve stimulation. About 30–40 ml of local anesthetic is injected following frequent negative aspiration.

Cognizant of the clockwise arrangement of nerves within the neural vascular bundle (ulnar, median, and radial), each quadrant should have local anesthetic injected to insure blockade of each terminal nerve. For the transarterial method, the local anesthetic should be injected in at least two locations around the artery (superficial and deep) within the neural vascular bundle (increases block success). A single orifice

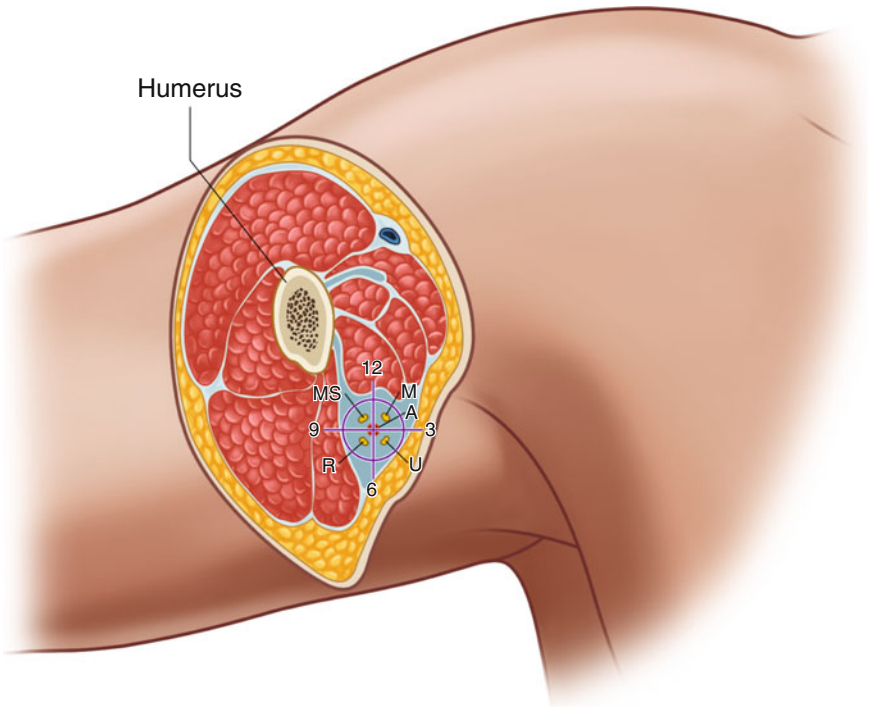

Fig. 22.8 Axillary nerve map (*A* axillary artery, *Ms* musculocutaneous, *M* median, *U* ulnar, R-radial nerves)

catheter can be inserted to provide continuous local anesthetic infusion. The musculocutaneous nerve branches higher in the axilla and passes into the coracobrachialis muscle; therefore, the musculocutaneous nerve is typically blocked outside the neurovascular bundle within the belly of this muscle. Inserting the needle into and through the coracobrachialis muscle until contacting the humerus and then pulling back a few mm off the periosteum prior to injection will cause musculocutaneous nerve blockade.

Pitfalls and Pearls

Pearls

There is a reduced incidence of pneumothorax with axillary blockade compared to other approaches of the brachial plexus. Intercostobrachial and medial brachial cutaneous nerves should be blocked (skin/sensory of medial part of upper arm), as described below, if a tourniquet of the proximal upper extremity is planned.

Pitfalls

Partial nerve blockade, intravascular injection (possible local anesthetic toxicity), hematoma formation, nerve injury, and infection are potential complications. Extremity positioning for this block (abducting the arm) may prove difficult especially in conjunction with a shoulder injury.

Radial Nerve Block

The radial nerve is formed by the fibers of C_5–T_1 spinal nerve roots and passes between the medial and long heads of the triceps muscle, giving off a motor branch to the triceps, and then progressing inferiorly giving off sensory branches to the upper arm. At the level of the lateral epicondyle (between lateral epicondyle and musculospiral groove) the radial nerve divides into superficial and deep branches. The superficial branch gives sensory innervation to the dorsum of the wrist, dorsal portion of index and middle fingers, and dorsal aspect of a portion to the thumb. Extensors of the forearm obtain most motor innervations from the deep branch of the radial nerve. Radial nerve blockade can be performed for surgeries in the distribution of the distal radial nerve or when a proximal brachial plexus block may have spared the radial nerve distribution.

Surface Anatomy, Landmarks, and Procedure

Radial Nerve Block at the Humerus

The radial nerve is identified at about 3 in. above the lateral epicondyle of humerus. The radial nerve traverses along the musculospiral groove between heads of the triceps muscle. A 25G 1.5 in. needle is inserted eliciting a paresthesia in the distribution of innervation of the radial nerve. About 7–10 ml of local anesthetic is injected following negative aspiration and no evidence of persistent paresthesia.

Radial Nerve Block at the Elbow

The lateral margin of biceps tendon is identified at the crease of the elbow. In sterile fashion, a 25G 1.5 in. needle is inserted lateral to the biceps tendon at the crease and directed superior-medially. Upon eliciting a paresthesia and subsequent to negative aspiration, 7–10 ml of local anesthetic is slowly injected.

Radial Nerve Block at the Wrist

The patient is positioned supine with the operative arm adducted. The flexor carpi radialis tendon is identified by asking the patient to flex the wrist. Following aseptic preparation of the wrist, a 25G 1.5 in. needle is inserted perpendicular and lateral to the flexor carpi radialis tendon, medial to the radial artery at the level of the distal radial prominence. Subsequent to a paresthesia, 3–4 ml of local anesthetic is injected when there is no persistent paresthesia and negative blood aspiration.

Intercostobrachial and Median Cutaneous Nerve Block

These blocks are typically performed to decrease tourniquet discomfort and augment a brachial plexus block. Fibers from C_8 and T_1 nerve roots form the medial cutaneous nerve. Fibers of the second intercostal (T_2) nerve form the intercostobrachial nerve that has communication with the median cutaneous nerve. Both nerves exit the axilla parallel to the triceps muscle and outside the brachial plexus sheath.

Surface Anatomy, Landmarks, and Procedure

The patient is positioned supine with the operative arm abducted 90°. The anterior axillary line and the superior margin of the biceps muscle are identified in the area of the distal axillary hair pad. Following aseptic preparation, a 25G 2 in. needle is inserted to its full length (placed subcutaneously) and directed from the biceps to the triceps muscles. Subsequent to negative aspiration, a subcutaneous skin wheal is created as 5–10 ml of local anesthetic is injected while the needle is being withdrawn.

Median Nerve Block

The median nerve is composed of fibers from C_5–T_1 spinal roots and passes anterior-superior to the axillary artery before exiting the axilla along with the brachial artery. At the level of the elbow, the median nerve lies medial to brachial artery and gives off a number of motor branches to the flexor muscles of the forearm. At the level of the wrist, the median nerve lies between the tendons of palmaris longus muscle and flexor carpi radialis. The median nerve provides sensory innervation to palmar surface of the hand (part), palmar surface of the thumb-index-middle fingers, radial surface of the ring finger, and the distal dorsal surfaces of the index and middle fingers. Median nerve blockade is performed for surgeries in the distribution of median nerve or when a brachial plexus block may have spared the median nerve.

Surface Anatomy, Landmarks, and Procedure

Median Nerve Block at the Elbow

The patient is placed supine with the arm adducted to the side and the elbow placed in a slightly flexed position. The brachial artery pulsations at level of the elbow are palpated. A 25G 1.5 in. needle is inserted at a point medial to brachial artery and advanced in a superior-medial direction. Paresthesia is elicited at about half to three-quarters inch depth and about 5–7 ml of local anesthetic is injected after confirmation of no persistent paresthesia.

Median Nerve Block at the Wrist

The patient is placed supine with the arm adducted completely to the side of patient and the elbow maintained in a slightly flexed position. The palmaris longus tendon is identified after the patient makes a fist and flexes the wrist. A 25G 1.5 in. needle is inserted in a sterile fashion medial to the tendon with a slight superior trajectory (just below the crease of wrist) to elicit a paresthesia. Subsequent to paresthesia (usually occurs at a depth of ½ inch) and after negative aspiration, 3–5 ml of local anesthetic is injected following absence of persistent paresthesia.

Ulnar Nerve Block

The spinal roots C_6–T_1 form the ulnar nerve, which is positioned inferior and anterior to the axillary artery above the axilla. The ulnar nerve exits the axilla along with the brachial artery. At the elbow, the ulnar nerve lies between the medial epicondyle of the humerus and the olecranon process. The nerve continues distal between the heads of flexor carpi ulnaris and further downward along with the ulnar artery. It divides into dorsal and palmar branches approximately 1 in. proximal to the wrist crease. The dorsal branch provides sensation to the dorsum of the hand, and the dorsal half of the little and ring finger, while the palmar branch provides sensation to the palmar aspect of the palm, and the palmar half of the little and the ring finger. Ulnar nerve blockade is performed for surgeries in the distribution of ulnar nerve or when a brachial plexus block may have spared the ulnar nerve distribution (rescue block).

Surface Anatomy, Landmarks, and Procedure

Ulnar Nerve Block at the Elbow

The patient is positioned supine and the arm is abducted 85–90°. Landmarks identified are the medial epicondyle of humerus and the olecranon process, between which lies the ulnar nerve sulcus. In aseptic fashion, a 25G 1 in. needle is inserted in a slightly cephalad direction to elicit paresthesia (observed at a depth of about ½ inch). Following negative

aspiration, 5–7 ml of local anesthetic is injected in the absence of persistent paresthesia.

Ulnar Nerve Block at the Wrist

With the patient supine, the ulnar block is performed with the arm fully adducted and the wrist slightly flexed. The flexi carpi ulnaris tendon is identified and a 25 G 1 in. needle is inserted at the level of the styloid process on the radial side of tendon in a cephalad direction. Paresthesia is elicited at a depth of about ½ inch, and in the absence of persistent paresthesia and after negative aspiration, 3–5 ml of local anesthetic is injected.

Digital and Metacarpal Nerve Block

The median and ulnar nerve fibers give rise to common digital nerves that divide as they reach the distal palm after passing along the metacarpal bones. Volar digital nerves run along the ventro-lateral aspect of the fingers alongside the digital vein and artery providing sensation to the fingers. Fibers from the ulnar and radial nerves form smaller dorsal digital nerves and supply the dorsum of fingers up to the proximal joints.

Surface Anatomy, Landmarks, and Procedure

Digital Nerve Block

The patient is positioned supine and the arm is abducted with the elbow slightly flexed. After sterile preparation, a 25G 1.5 in. needle is inserted on each side of the digit base to be blocked from the dorsal to the palmar aspect of the finger. About 1–2 ml of local anesthetic is injected following negative aspiration.

Metacarpal Nerve Block

In aseptic fashion, a 25G 1.5 in. needle is inserted on both sides of the metacarpal bone proximal to the metacarpal head from the dorsal all the way to the palmar surface of the hand. Subsequent to negative aspiration, 1–2 ml of local is injected and pressure is applied at the injection site after removal of the needle to prevent formation of hematoma.

Intravenous Regional Anesthesia (Bier Block)

Principle

Local anesthetic injected into a distal vein diffuses from blood vessels to the surrounding soft tissues and nerves to provide anesthesia to the extremity, while circulation to the extremity is occluded with a tourniquet. This block is performed for surgeries involving the hand, forearm, or elbow (examples include excision of wrist ganglia, manipulation of forearm fractures, palmar fasciotomy). Bier block is often performed for surgery of the upper extremity, but may also be used for lower extremity surgery.

Surface Anatomy, Landmarks, and Procedure

A 22G intravenous catheter is placed as distally as possible (this intravenous catheter is later used for injection of local anesthetic). A double bladder tourniquet is applied on the arm over cotton padding (as far proximal as possible). The extremity to be anesthetized is then elevated to drain the blood (gravity effect). An Esmarch bandage is used to exsanguinate the extremity by circumferentially wrapping around the entire extremity beginning from the most distal portion to the previously placed double bladder tourniquet. The proximal bladder of the double tourniquet is inflated to 100 mmHg above the patient's systolic blood pressure. The Esmarch bandage is then removed and preservative-free lidocaine (0.5 %, 30–50 ml) is injected into the previously placed intravenous catheter. After injection, the intravenous catheter is removed (please see Fig. 25.2, Chap. 25).

In chronic pain conditions, bretylium, reserpine, and methylprednisolone with lower concentrations of lidocaine may also be injected for pain relief. After 45–60 min, or to reduce tourniquet discomfort, the distal cuff can be inflated over the anesthetized area and the proximal cuff then deflated (after confirmation of inflation of the distal bladder). At least 20 min should elapse following initial injection of the local anesthetic drug prior to slowly and intermittently releasing the double bladder tourniquet. Release of the tourniquet may be performed safely by deflating to just below the systolic pressure for a few seconds followed by quick reinflation. This is conducted repeatedly to permit slow washout of local anesthetic and observing the patient for any signs of local anesthetic toxicity.

Cervical Plexus Block

Cervical plexus block provides anesthesia/analgesia of the head and neck regions. Depending on the type of surgery, the cervical plexus can be blocked at a superficial and/or deep level. Superficial branches of the cervical plexus innervate the skin and superficial structures of the head, neck, and shoulder area. Deep branches of the plexus innervate muscles of the deep anterior neck and diaphragm. Therefore, a superficial cervical plexus block is used for superficial cutaneous surgeries of the head and neck, while the deep cervical plexus block is used for deeper surgeries of the neck, such as carotid artery or thyroid surgery. These blocks are also useful to supplement other regional techniques on the upper torso.

Preparation Technique

Equipment preparation: sterile towels, gloves and gauze pads, marking pen, antiseptic solution, syringes, and needles for local infiltration and nerve block placement.

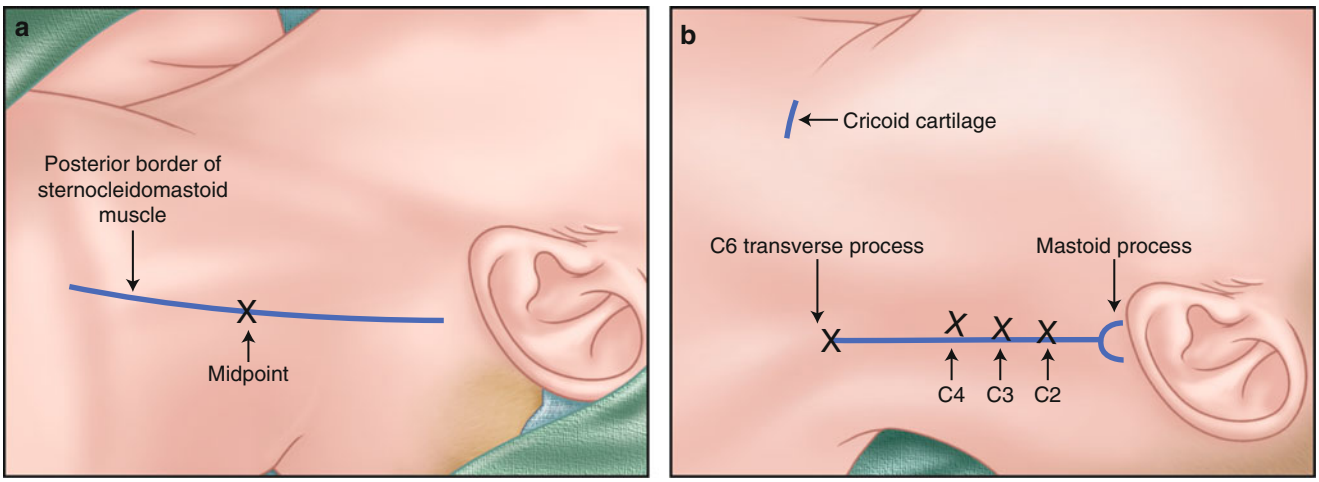

Fig. 22.9 Landmarks for superficial (**a**) and deep (**b**) cervical plexus blocks

Patient preparation: Monitors "on" and appropriate sedation (midazolam, fentanyl).

Needles: 25 g 1.5 in. needle for skin infiltration, and 22G 2 in. short bevel block needle.

Commonly used agents: 3 % chloroprocaine, 2 % lidocaine, 0.5 % ropivacaine, 0.5 % bupivacaine.

Dose: Superficial cervical plexus—5–10 ml, Deep cervical plexus—3–5 ml at each level (C_2, C_3, C_4), or 15 ml at C_3 only.

Surface Anatomy, Landmarks, and Procedure

The cervical plexus is formed from anterior rami of C_1 through C_4 nerve roots and lies anterior to the cervical vertebrae and posterior to the sternocleidomastoid muscle. There are five components of the cervical plexus: (a) cutaneous branches (supply the lesser occipital, greater auricular, transverse cervical, and supraclavicular nerves); (b) ansa cervicalis (innervates the infrahyoid and geniohyoid muscles); (c) phrenic nerve (the only motor nerve to innervate the diaphragm); (d) contributions to the accessory nerve (Cranial nerve XI; innervates the sternocleidomastoid and trapezius muscles); and (e) direct muscular branches (supply prevertebral muscles of the neck).

To perform a superficial cervical plexus block the patient is positioned supine with the head turned away from the side to be blocked and arms relaxed at the side. The posterior border of the sternocleidomastoid muscle is palpated and marked. Next the midpoint of the muscle is identified (Fig. 22.9a). The block needle is then inserted at the midpoint of the posterior border of the sternocleidomastoid to approximately half the depth of the muscle, and 3–4 ml of local anesthetic is injected. Also a subcutaneous injection of additional local anesthetic is performed cephalad and caudad along the length of the posterior border of the sternocleidomastoid muscle.

To perform a deep cervical plexus block the transverse process of C_6 (Chassaignac's) tubercle is palpated at the level of the cricoid cartilage. Then the mastoid process behind the ear is palpated. A lined is drawn between the mastoid process and Chassaignac's tubercle (Fig. 22.9b). The transverse processes of the other cervical vertebrae lie on or near this line. First, the transverse process palpated below the mastoid process will be C_2. Subsequently the transverse processes of C_2 to C_4 (C_4 transverse process lies at about the level of the mandible) are palpated and marked. The block needle is inserted with the tip directed medially and caudally until it rests on the transverse process. Once the transverse process is contacted, the needle is withdrawn 1–2 mm and local anesthetic is slowly injected with frequent negative aspirations. After completing the injection, the needle is removed and the block repeated at the next cervical level.

Pearls and Pitfalls

Pearls

Many institutions perform only a superficial cervical plexus block, and the surgeon then infiltrates the deeper structures as required. In addition, the surgeon will place local anesthetic around the carotid body for hemodynamic control.

Pitfalls

Possible side effects include blockade of phrenic nerve and the sympathetic chain (located in region of the cervical nerve roots). Bilateral deep cervical plexus blocks, which would result in total diaphragmatic paresis, should not be performed. Phrenic nerve blockade could result in an ipsilateral diaphragmatic paralysis. In patients with respiratory compromise (such as severe COPD), creating a hemidiaphragm may not be tolerable. Caution should be exercised in patients receiving a deep cervical plexus block for carotid endarterectomy surgery. These patients could have atheromatous plaques that may be dislodged with head hyperextension or cause cerebral ischemia with head rotation.

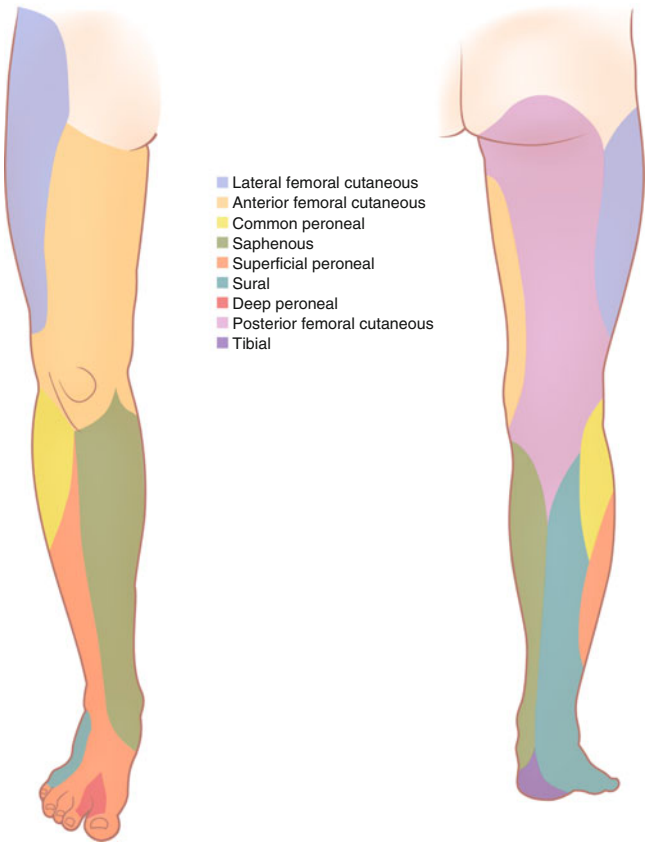

Fig. 22.10 Innervation of the lower extremity

For carotid endarterectomies, the surgeon must infiltrate the carotid body with local anesthetic because the cervical plexus does not innervate the carotid body. Additional complications include infection, hematoma and possible pneumothorax (cupola of the lung may be located at the C_6 tubercle), inadvertent intravascular injection resulting in seizures (vertebral artery which lies anterior to the cervical nerve roots), and injection of local anesthetic solution into the intervertebral foramina that could result in a high spinal or epidural block.

Lower Extremity Nerve Blockade

Peripheral nerves of the lower extremity originate from the lumbar and lumbosacral plexi. The lumbar plexus consists of L_1–L_5 nerve roots, whereas the lumbosacral plexus contains contributions from L_4–S_3. The four major nerves of the lower extremity include femoral, obturator, lateral femoral cutaneous, and sciatic nerves. Sciatic nerve is the only nerve not originating from the lumbar plexus. Assessment of anesthesia after peripheral nerve blockade can be difficult without the understanding of lower extremity innervations, in addition to a slower onset of blockade compared to upper extremity brachial plexus blockade. Innervation of the lower extremity is shown in Fig. 22.10.

Preparation Technique

Equipment preparation: sterile towels, gloves and gauze pads, marking pen, antiseptic solution, peripheral nerve stimulator, syringes, and needles for local infiltration and nerve block placement.

Patient preparation: Monitors "on" and appropriate sedation (midazolam, fentanyl).

Needles: 25 G 1.5 in. needle for skin infiltration, and 22G 2–6 in. short bevel insulated stimulation needle.

Commonly used agents: 3 % chloroprocaine, 2 % lidocaine, 0.5 % ropivacaine, 0.5 % bupivacaine (Table 22.5).

Approximate dose: 20–40 ml of local anesthetic.

Femoral Nerve Block

Femoral nerve is the largest nerve originating from the lumbar plexus. It innervates the anterior thigh, medial side of the calf, as well as the anterior quadriceps muscle. The femoral nerve block is one of the basic nerve blocks because it is easy to perform along with a low risk of complications. A femoral nerve block can be used as a primary anesthetic for surgery on the anterior thigh or for superficial surgery on the medial side of the calf, and for postoperative pain management for knee (total knee replacement) and distal femur surgeries.

Surface Anatomy, Landmarks, and Procedure

Landmarks include the inguinal ligament, inguinal crease, and the femoral artery (Fig. 22.11). The patient is positioned supine, and for obese patients the lower abdomen may be retracted back (with tape) to permit access to the inguinal area. The point of needle insertion is located 1 cm lateral to the femoral artery pulse and 1–2 cm below the inguinal crease. A 22G 2 in. short bevel needle is connected to a nerve stimulator set at 1.0 mA. After skin disinfection and subcutaneous infiltration with local anesthetic, the needle is inserted at a 45° angle to the skin in a slightly cephalad direction. As the needle is advanced, it is possible to feel two "pops" as it transverses the fascia lata and fascia iliaca. The needle is advanced further until a patellar twitch is achieved with a current output between 0.2 and 0.5 mA. After negative aspiration, 20–40 ml of local anesthetic is injected (volume block). A continuous catheter may be inserted for postoperative pain control.

Pearls and Pitfalls

Pearls

The needle tip should be positioned below the fascia lata and fascia iliaca, but the "pop" may be harder to feel through the fascia iliaca. To ensure that the needle is below the fascia iliaca, once a patellar twitch is obtained, the needle can be advanced further until the twitch is lost. The needle is then

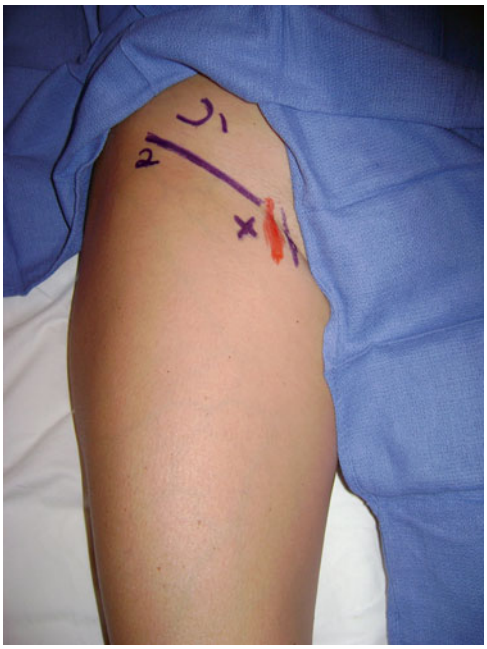

Fig. 22.11 Landmarks for the femoral nerve block. The anterior superior iliac spine (attachment of inguinal ligament) is identified as #1, the inguinal crease is identified as line #2 (marked in *blue*), and the femoral artery is drawn in *red*. The needle insertion site (blue X) is located below the inguinal crease 1–2 cm lateral to the artery

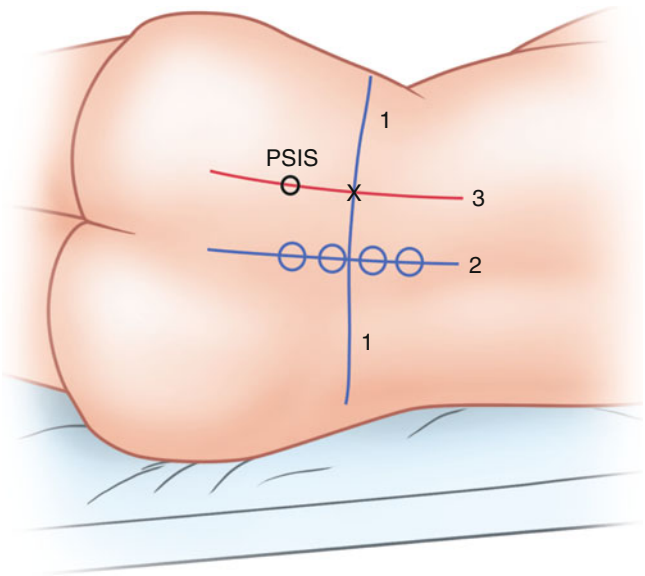

Fig. 22.12 Landmarks for approach to the lumbar plexus block. PSIS—posterior superior iliac spine, vertical line#1 is the bicrestal line (connects right and left iliac crests), line#2 is the midline, and *circles* on line# 2 are palpable spinous processes, line# 3 is the parasagittal line (parallel to line# 2 and 4–5 cm lateral) and should be perpendicular to line# 1. Point "X" is the needle insertion site

withdrawn until the twitch is regained between 0.2 and 0.5 mA. Local anesthetic is deposited at this position.

Pitfalls

Although femoral nerve blocks have a low risk for complications, complications that can occur include vascular puncture, femoral nerve compression by hematoma formation, infection, and nerve injury.

Lumbar Plexus Block

Lumbar plexus block targets nerves ($L_{2–4}$) as they exit the intervertebral foramen and are embedded in the psoas major muscle. The body of the psoas major muscle is where the lumbar plexus nerve roots reorganize into branches of the plexus. Local anesthetics are injected into the body of the psoas major muscle around the $L_{2–4}$ nerve branches, which then spread to the lumbar nerve roots. Major nerves of the lumbar plexus include the genitofemoral, lateral femoral cutaneous, femoral, and obturator nerves. Indications include anesthesia and postoperative analgesia for surgeries involving the femoral shaft and femoral neck, knee surgery, and surgery on the anterior thigh.

Surface Anatomy, Landmarks, and Procedure

Landmarks include the spinous processes, iliac crest, and the posterior superior iliac spine (Fig. 22.12). The patient is placed in the lateral decubitus position with the surgical side nondependent (operative side up). A line is drawn between the iliac crest and the midline marked by the spinous processes. A second line, parallel to the midline, is drawn from the posterior superior iliac spine perpendicular to the first line. Needle insertion point is at the intersection of the two lines (4–5 cm lateral to midline). After skin disinfection and subcutaneous infiltration with local anesthetic, a 4 in. stimulating needle connected to a nerve stimulator (set at 1.5 mA) is inserted perpendicular to the skin. The first twitches elicited should be local twitches from the paravertebral muscles. The needle is then slowly advanced until twitches of the anterior quadriceps muscles are elicited at an average depth of 6–8 cm. Once these twitches are present at stimulation between 0.5 and 1.0 mA, 25–35 ml of local anesthetic is slowly and incrementally injected with frequent intermittent negative aspiration.

Pearls and Pitfalls

Pearls

Average onset time for lumbar plexus blockade is 15–25 min. The first sign of onset is usually the loss of sensation in the

saphenous nerve distribution, followed by the anterior thigh and knee. If the desired quadriceps twitches are not obtained, needle direction and depth can be adjusted slightly either laterally (use caution with medial adjustment) or cephalad and caudad until appropriate twitches are obtained. For example, needle twitches of the hamstrings at a depth of 6–8 cm indicate that the needle was inserted too far caudally and the needle needs to be redirected cranially. If needle contacts bone at a depth of 4–6 cm with no twitches seen, then the needle is most likely contacting the transverse process and needs to be redirected slightly caudally or cranially to get past the transverse process. If no twitches are elicited and the needle is deep (about 10 cm), the needle is likely too far lateral and needs to be redirected medially. Flexion of the thigh (with needle depth >6–8 cm) indicates direct stimulation of the psoas muscle. At this depth, further advancement could place the needle intraperitoneally. If this situation should occur, the needle is withdrawn and again redirected.

Pitfalls

Complications of lumbar plexus block procedure include infection, renal or iliopsoas hematoma, epidural spread, hypotension from a unilateral sympathectomy, and local anesthetic toxicity. Patients receiving lumbar plexus blockade may be at a higher risk of local anesthetic toxicity compared to other peripheral nerve blocks. This is secondary to larger volumes of local anesthetic needed for a lumbar plexus block as well as the intramuscular location of the injection. Unlike other peripheral nerve blocks, the goal of nerve stimulation should *not* be less than 0.5 mA (strive for 0.5–1.0 mA). This is because dural sleeves surround the nerve roots of the lumbar plexus. Stimulation at less than 0.5 mA could indicate that the needle is placed inside the dural sleeve, which could result in the injected local anesthetic track retrograde to the epidural or subarachnoid space. Lumbar plexus block should be avoided in patients who are anticoagulated because of the higher risk of hematoma and the uncompressible nature of the area if bleeding were to occur.

Sciatic Nerve Block

The sciatic nerve is the largest peripheral nerve in the body measuring more than 1 cm proximally. The sciatic nerve provides sensory innervation to the posterior thigh and the entire lower leg and foot, except for the medial aspect of the leg to the medial malleolus, which is supplied by the saphenous nerve. The sciatic nerve block can be used as a primary anesthetic and/or for postoperative analgesia for surgeries involving posterior aspect of the thigh, hamstrings, biceps femoris muscle, lateral ankle, foot, and digits. Sciatic nerve block can be used in conjunction with a femoral nerve block for anesthesia/ analgesia for knee surgeries.

Surface Anatomy, Landmarks, and Procedure

(a) *Classic (Labat) technique*: Landmarks include the greater trochanter, sacral hiatus, and the posterior superior iliac spine (Fig. 22.13a). The patient is placed in a lateral decubitus position with the extremity to be blocked nondependent, with the hip and knee flexed, and with the knee resting on the dependent extremity (Sim's position). Lines are drawn between the greater trochanter and the posterior superior iliac spine and between the greater trochanter and sacral hiatus. From the midpoint of the line between the greater trochanter and posterior superior iliac spine a perpendicular line is drawn down to intersect the line between the greater trochanter and sacral hiatus. This intersection is the needle insertion point. A 4 in. short bevel needle is connected to a nerve stimulator with an initial setting of 1.5 mA. After skin disinfection and subcutaneous infiltration with local anesthesia, the needle is inserted perpendicular to the skin. The first twitches seen are from the gluteal muscles. As the needle is advanced further, the gluteal twitches disappear and twitches of the hamstrings, calf muscles, foot, or toes are seen indicating stimulation of the sciatic nerve. The goal is to obtain these twitches between 0.2 and 0.5 mA. Once this is achieved, 20–40 ml of local anesthetic solution is injected. A continuous catheter can also be placed for postoperative pain control.

(b) *Anterior approach:* Landmarks include the femoral crease, femoral artery pulse, anterior superior iliac spine, greater trochanter, and the pubic tubercle (Fig. 22.13b). The patient is positioned supine and a line is drawn from the anterior superior iliac spine to the pubic tubercle, and this line is then divided into three parts. A second line is drawn parallel to the first, medial from the cephalad aspect of the greater trochanter. Then, a third line is drawn perpendicular from medial third of the first line to intersect the second line. This intersection (located over the lesser trochanter of the femur) represents the point of initial needle insertion. With the leg and foot in the neutral position, the lesser trochanter may obstruct the route to the sciatic nerve. External rotation of the leg by about 45° exposes the nerve and allows the needle to pass through unobstructed. A 15 cm long, short bevel insulated stimulation needle is connected to a nerve stimulator set at 1.5 mA. After skin disinfection and subcutaneous infiltration with local anesthetic, the needle is inserted perpendicular to the skin. Typically, quadriceps twitches are seen during needle advancement, but as the needle is advanced deeper, these twitches disappear. Stimulation of the sciatic nerve, seen as twitches of the calf muscles, foot, or toes, is typically seen at a depth of 8–12 cm. Once stimulation is achieved at 0.2–0.5 mA and after negative aspiration, 20–40 ml of local anesthetic is slowly injected.

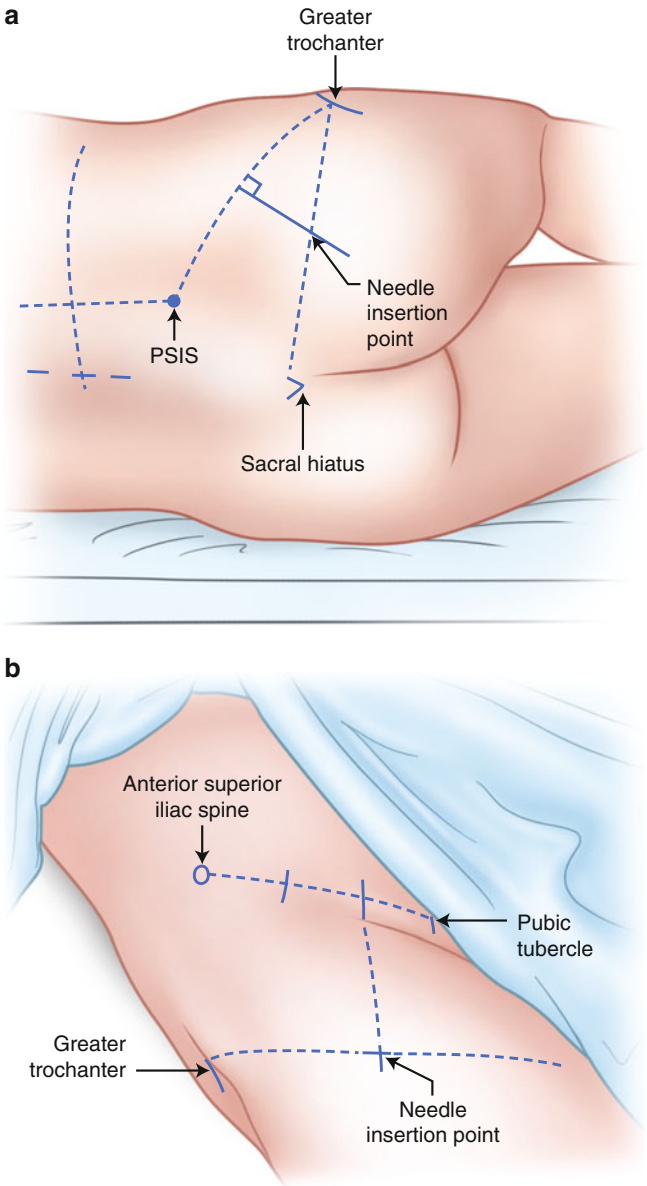

Fig. 22.13 (**a**) Classical approach (Labat's) to the sciatic nerve block. The greater trochanter (GT) is identified and a straight line is drawn from midpoint of GT to the posterior-superior iliac spine (PSIS). Another line is drawn connecting the midpoint of GT to the sacral hiatus. A 4–5 cm long third line is drawn caudo-medially perpendicular to the midpoint of the first line and serves as the needle insertion site. The *solid blue line* represents a furrow formed between long head of the biceps femoris and medial edge of the gluteus maximus muscles (represents course of the sciatic nerve toward the leg). (**b**) Landmarks for anterior approach to sciatic nerve block. Draw a line from the anterior superior iliac spine to pubic tubercle, and divide the line into thirds. Draw a second line, parallel to the first, medial from the cephalad aspect of the greater trochanter. Then, draw a third line perpendicular from medial third of the first line to intersect the second line. This intersection (located over the lesser trochanter of the femur) represents the point of initial needle insertion. With the leg and foot in the neutral position, the lesser trochanter may obstruct the route to the sciatic nerve. External rotation of the leg by about 45° exposes the nerve and allows the needle to pass through unobstructed

Pearls and Pitfalls

Pearls

In the classic approach, if sciatic nerve stimulation is not achieved in the first pass, the needle can be redirected medially or laterally 5–10°. If these maneuvers do not elicit nerve stimulation, reassessment of the patient's position and landmarks should be undertaken. The sciatic nerve block at this level is above the area where the nerves supplying the hamstring muscle branch out. Therefore, twitches of any of the hamstring muscles are acceptable for sciatic nerve localization during the classical approach.

In the anterior approach, hamstring muscle stimulation is not a reliable sign because at this level the branches to the hamstring muscles may have already left the sciatic nerve. An elicited hamstring muscle twitch could be the result of direct muscle stimulation. If bone is contacted with the anterior approach, it is usually contacting the lesser trochanter of the femur. This can be avoided by rotating the foot laterally to shift the lesser trochanter out of the needle path. If this does not work, the needle can be redirected or reinserted medially.

Pitfalls

Infection, hematoma, nerve injury, and vascular puncture are potential complications. Complications seen with the anterior approach include the above as well as possible femoral nerve injury, though rare. The anterior approach is not amenable to catheter insertion because of its deep location and perpendicular needle insertion angle. The long needle path and the tendency of the short bevel needle to bend during insertion make this an advanced nerve block technique. Therefore, this approach is typically reserved for patients who cannot be positioned for the classic approach.

Popliteal (Approach) Sciatic Nerve Block

Popliteal sciatic nerve block is a relatively simple block to perform that provides surgical anesthesia for the calf, tibia, fibula, foot, and the ankle. Analgesia after a popliteal block usually lasts longer than an ankle block. Neural blockade of the lower extremity with a long-acting local anesthetic such as bupivacaine or ropivacaine can provide analgesia after foot surgery for 12–24 h. Indications include primary anesthesia and postoperative analgesia for foot surgery, achilles tendon repair, and ankle surgery.

Surface Anatomy, Landmarks, and Procedure

(a) *Prone approach*: Landmarks include the popliteal crease, tendon of the biceps femoris (lateral), and

tendons of the semitendinosus and semimembranosus (medial), Fig. 22.14a. The patient is positioned prone with the operative side/ft over the edge of the bed/stretcher. The landmarks indicated above are identified and marked. The needle insertion point is marked about 7 cm above the popliteal fossa at the midpoint between the biceps femoris tendon and the semitendinosus and semimembranosus tendons. A 22G 4 in. needle is connected to a nerve stimulator initially set at 1.5 mA. After skin disinfection and subcutaneous infiltration with local anesthetic, the needle is inserted caudad to cephalad at a 45° angle. An ideal response should be from sciatic nerve stimulation and not local twitches. Acceptable muscle twitches from sciatic nerve stimulation are dorsiflexion and eversion (common peroneal nerve) or plantar flexion and inversion (tibial nerve). Once appropriate stimulation is obtained, the nerve stimulation is decreased until twitches remain at 0.2–0.5 mA, usually seen at a depth of 3–5 cm. After negative aspiration, 30–40 ml of local anesthetic is injected. A single orifice catheter may be inserted to provide continuous local anesthetic infusion for a more prolonged analgesic effect.

(b) *Lateral approach*: Landmarks include the popliteal crease, tendon/muscle of the biceps femoris (lateral), and vastus lateralis muscle (Fig. 22.14b). The patient is positioned supine (or lateral decubitus) with the operative side/leg and foot supported or lifted from the bed/stretcher, so that movements of the foot or toes can be easily observed. The landmarks are identified and marked with plans for needle insertion at least 7 cm superior to the popliteal crease in the groove between vastus lateralis and biceps femoris (the groove between vastus lateralis and biceps femoris is identified by pressing the fingers in the lateral groove). The block needle is then connected to a nerve stimulator set at 1.5 mA. After skin disinfection and subcutaneous infiltration with local anesthetic, the block needle is inserted in a horizontal plane between the vastus lateralis and biceps femoris muscles and advanced to contact the femur. Contacting the femur is key because it shows information on depth of the nerve (about 1–2 cm beyond the skin–femur distance) as well as on the angle that the needle will need to be redirected posterior to the bone in order to stimulate the nerve. The needle is then withdrawn to the subcutaneous tissue and redirected 30° posterior to the angle at which the femur was contacted, and advanced toward the nerve. The goal of nerve stimulation is to obtain visible twitch of the foot or toes while current is decreased and twitches remain at 0.2–0.5 mA (at a depth of about 5–7 cm).

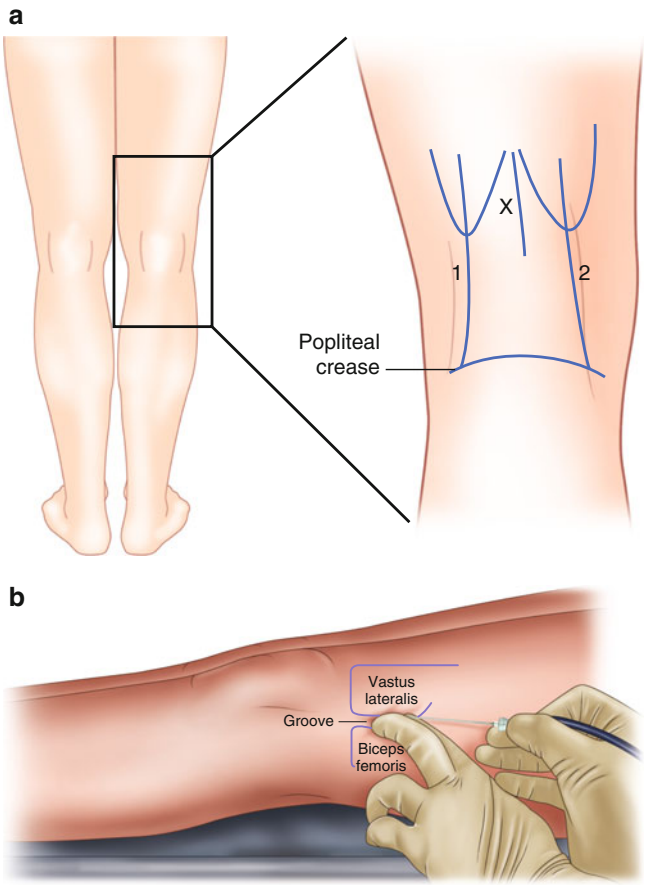

Fig. 22.14 (**a**) Landmarks for intertendinous popliteal approach (prone) of the sciatic nerve block. Sciatic nerve is positioned between tendons of the biceps femoris muscle (BF) laterally (*blue* Line#1) and the semitendinosus/semimembranosus (ST/SM) muscle medially (*blue* Line#2). Needle insertion site (X) is marked lateral to the midline between BF and ST/SM muscle tendons approximately 7–10 cm cephalad to the popliteal crease. (**b**) Landmarks for popliteal approach (lateral) of the sciatic nerve block. Landmarks include the popliteal crease, tendon/muscle of the biceps femoris (lateral), and vastus lateralis muscle. The landmarks are identified and marked with plans for needle insertion at least 7 cm superior to the popliteal crease in the groove between vastus lateralis and biceps femoris (the groove between vastus lateralis and biceps femoris is identified by pressing the fingers in the lateral groove)

[Note: When the sciatic nerve is not localized, the needle is withdrawn to the subcutaneous level and the following approach implemented. (1) Visualize a mental image of the plane of initial needle insertion and redirect the needle in a 5–10° posterior angulation. (2) If the above maneuver fails, withdraw needle and reinsert with another 5–10° posterior redirection. (3) If maneuvers 1 or 2 fail, withdraw the needle to the skin and reinsert 1 cm inferior to the initial insertion site and repeat the above steps.] Following appropriate foot/ankle stimulation, the needle is stabilized, and following negative aspiration, 35–40 ml of local anesthetic is injected. A single orifice catheter may be inserted to provide continuous local anesthetic infusion for a more prolonged analgesic effect.

Pearls and Pitfalls

Pearls

When a small change in needle position results in a characteristic change of the foot twitch (from common peroneal to tibial), this indicates that the stimulating needle is cephalad to the level of splitting of the sciatic nerve into the common peroneal and tibial nerve branches. A muscle twitch less than 0.5 mA may not be possible in patients with diabetes, peripheral neuropathy, or severe peripheral vascular disease. In patients with such comorbidities, a twitch response 0.5–1.0 mA is acceptable. Blocking the sciatic nerve at the popliteal fossa allows sparing of the hamstring muscles that may permit the patient to continue to flex the knee and, therefore, more safely ambulate with assistance.

Pitfalls

Complications include infection, vascular puncture and hematoma, nerve injury, and local anesthetic toxicity. Local twitches of the biceps femoris muscle indicate lateral placement of the needle, which should be then withdrawn and redirected medially (about 5–10°). A local twitch from the semitendinosus or semimembranosus muscles indicates medial placement of the needle (needle should be withdrawn and redirected laterally 5–10°). Vascular puncture is usually due to placement of needle into the popliteal artery or vein (medial needle placement), and therefore, the needle should be withdrawn and redirected laterally. If bone is contacted, the needle is placed too deep and should be withdrawn slowly watching for a foot twitch. If gastrocnemius muscle twitches are seen, it indicates stimulation of muscular branches of the sciatic nerve, which are usually outside the sciatic nerve sheath (this twitch should not be accepted as proper sciatic nerve stimulation) and the needle should be further advanced until foot twitches are seen.

Ankle Block

An ankle block involves anesthetizing five peripheral nerves that innervate the foot and the ankle. The nerves blocked are the sural, posterior tibial, superficial peroneal, deep peroneal, and the saphenous nerves. This block is easy to perform and does not require nerve stimulation, special positioning, or awake patient cooperation. Indications include primary anesthesia and postoperative analgesia for all types of foot surgery, including hallux valgus repair, foot osteotomy, arthroplasty, and amputations.

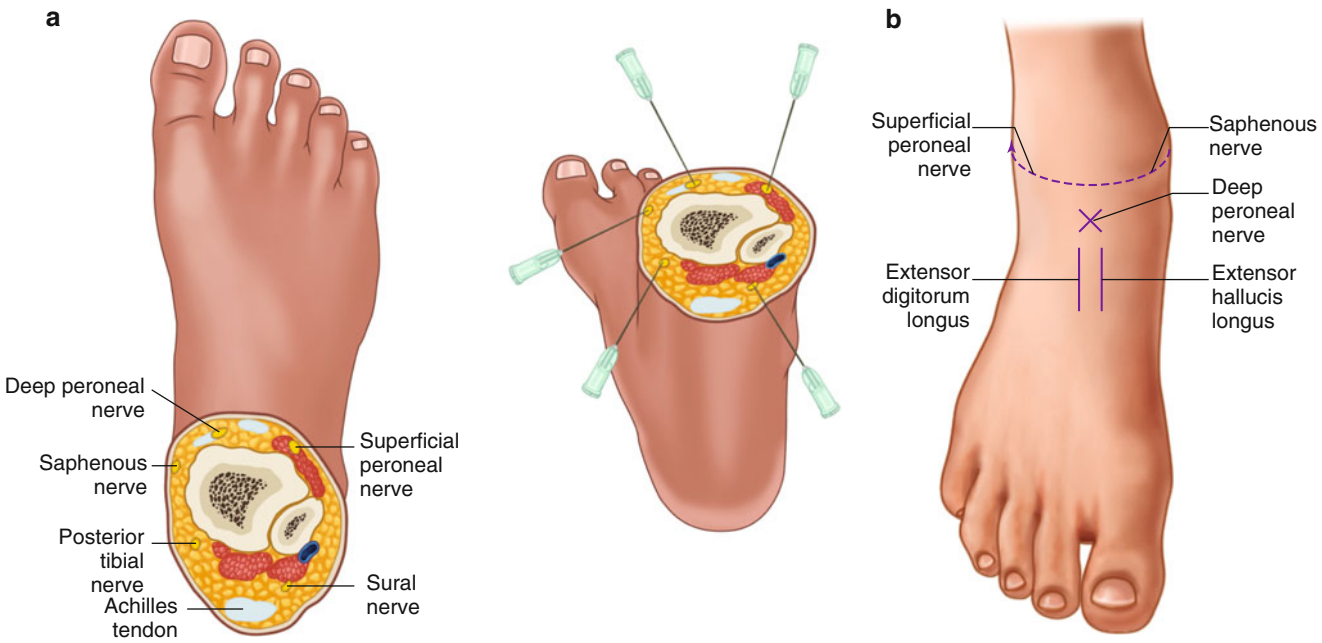

Fig. 22.15 (**a**, **b**) Landmarks for an ankle block. Extension of the great toe will accentuate extensor hallucis longus tendon (medially) and extensor digitorum longus tendon (laterally) indicated by parallel *blue lines. Blue dashed line* connects lateral and medial malleolus. Needle insertion site (X), lateral to extensor hallucis longus tendon and deep to the retinaculum (distal to the *blue dashed line*), will block deep peroneal nerve. Injecting subcutaneously toward the medial malleolus will block the saphenous nerve, and injecting subcutaneously along a path to the lateral malleolus will block the superficial peroneal nerve blockade (this partial circumferential injection should occur along the blue dashed line connecting the lateral and medial malleolus). NOT pictured: Midway between the achilles tendon and the medial malleolus is the insertion site to block the posterior tibial nerve (deep to the retinaculum and posterior to posterior tibial artery). The sural nerve is blocked just lateral to the achilles tendon and pointing toward the lateral malleolus

Surface Anatomy, Landmarks, and Procedure

Landmarks include the medial and lateral malleoli, achilles tendon, extensor hallucis longus tendon, posterior tibial artery, and the dorsalis pedis artery (Fig. 22.15a, b). The ankle block is performed with the patient supine, foot elevated (placing a bump under the mid portion of calf). After skin disinfection, the saphenous, superficial peroneal, and sural nerves are blocked with a subcutaneous infiltration of 10–15 ml of local anesthetic along a circumferential line just proximal to the malleoli and anterior from the achilles tendon from the medial malleoli to the lateral malleoli. The deep peroneal nerve is blocked with 5–8 ml of local anesthetic injected just lateral to the extensor hallucis longus tendon (medial to extensor digitorum longus tendon) along the same circumferential line drawn above. The posterior tibial nerve is blocked by injection of 5–8 ml of local anesthetic placed posterior to the posterior tibial artery pulse, which is located posterior to the medial malleolus.

Pearls and Pitfalls

Pearls

By extending the great toe, the extensor hallucis longus tendon is easily identified. Local anesthetic containing epinephrine should be avoided in distal extremity nerve blockade for risk of vascular compromise. An ankle block differs from other peripheral nerve blocks because it requires multiple subcutaneous injections. Awake patients can benefit from anxiolysis and analgesia with midazolam and fentanyl.

Pitfalls

An ankle block should be avoided in patients with foot edema, infection, or vascular compromise and in patients with a risk of compartment syndrome.

Clinical Review

1. The following nerve may not be blocked while performing an interscalene block:
   A. Musculocutaneous
   B. Ulnar
   C. Radial
   D. Medial
2. Highest incidence of pneumothorax is seen with the following block:
   A. Interscalene
   B. Supraclavicular
   C. Infraclavicular
   D. Axillary
3. The following nerve may not be blocked while performing an axillary nerve block:
   A. Musculocutaneous
   B. Ulnar
   C. Radial
   D. Medial
4. The following local anesthetic solution is most commonly used to perform an intravenous regional block:
   A. Lidocaine 2 %
   B. Ropivacaine 0.25 %
   C. Lidocaine 2 % with 1:200,000 epinephrine
   D. Lidocaine 0.5 %
5. Anatomical location of femoral artery, vein, and nerve from the medial to lateral is in the following order
   A. Vein, nerve, artery
   B. Artery, vein, nerve
   C. Vein, artery, nerve
   D. Nerve, vein, artery
6. Epidural spread of local anesthetic can most commonly occur with the following nerve block:
   A. Sciatic
   B. Femoral
   C. Popliteal
   D. Lumbar plexus
7. Landmarks to perform a sciatic nerve block via the classic approach include
   A. Lesser trochanter, posterior superior iliac spine, and greater trochanter
   B. Iliac crest, posterior superior iliac spine, and greater trochanter
   C. Iliac crest, greater trochanter, and sacral hiatus
   D. Greater trochanter, posterior superior iliac spine, and sacral hiatus
8. The deep peroneal nerve supplies sensation to the
   A. Anterior aspect of the foot
   B. Web space between the great toe and the second toe
   C. Anterior and medial aspect of the foot
   D. Web space between the second and the third toe

Answers: 1. B, 2. B, 3. A, 4. D, 5. C, 6. D, 7. D, 8. B

Further Reading

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Ultrasound-Guided Peripheral Nerve Blocks

23

Thomas M. Halaszynski and Michael Tom

First described in 1978, ultrasound-guided peripheral nerve blockade continues as a new and rapidly growing field in anesthesiology, due in part to the advent of more advanced ultrasound technology developed in the 1990s. This chapter describes commonly performed ultrasound-guided techniques in an easy to follow step-by-step manner. The chapter goals are to impart a recognition and appreciation of how ultrasound use in peripheral nerve block procedures may enhance the application of understanding of human anatomy by anesthesia practitioners and clinicians. Additional references are needed to better understand ultrasound terminology, physics of ultrasound, ultrasound probe selection and equipment, ultrasound knobology, and how to optimize image quality.

Conventionally, peripheral nerve block procedures are performed by eliciting a paresthesia or by nerve stimulation techniques without visual guidance. Such approaches to nerve blockade are highly dependent upon knowledge of surface anatomical landmarks for localization of neural structures. It is, therefore, theorized that regional anesthesia techniques may have an increased success rate, have lower incidence of negative consequences, require smaller local anesthetic volumes, and induce a faster onset of effect when an ultrasound is used in conjunction with anatomical understanding of peripheral nerve anatomy.

Ultrasound-assisted peripheral nerve blockade can:

- Identify nerve location, especially in patients with difficult anatomical landmarks
- Image nerves in short axis (cross-sectional views)
- Provide real-time block needle guidance and direction (allowing needle adjustments in depth and direction)
- Real-time imaging of local anesthetic spread upon injection
- Identify and appreciate surrounding vital structures (vessels, pleura, etc.)
- Reduce the number of needle passes/attempts
- Identify aberrant anatomy
- May reduce the risk and incidence of inadvertent nerve injury

This chapter describes the following ultrasound-guided nerve blocks:

- Upper Extremity Brachial Plexus Nerve Blocks
  - Interscalene
  - Supraclavicular
  - Infraclavicular
  - Axillary
- Lower Extremity Nerve Blocks
  - Femoral
  - Sciatic
  - Popliteal

Upper Extremity Nerve Blockade

Preparation Technique

Equipment preparation: sterile towels, gloves and gauze pads, antiseptic solution, syringes, 13 MHz linear array transducer, sterile ultrasound sheath, and needles for both local infiltration and nerve block placement

Patient preparation: Monitors "on" and appropriate sedation (midazolam, fentanyl).

Needles: 25G 1.5 in. needle for skin infiltration, and 22G 2–4 in. short bevel needle.

Commonly used agents: 3 % chloroprocaine, 2 % lidocaine, 0.5 % ropivacaine, 0.5 % bupivacaine

Approximate dose: 10–30 ml of local anesthetic.

Interscalene Block

Interscalene blockade targets the brachial plexus at level of nerve trunks or roots, and is used for primary anesthesia and/or postoperative pain management for surgeries on the

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shoulder/shoulder joint, lateral 2/3rds of clavicle, and proximal humerus surgeries (with or without a continuous catheter). These surgeries include rotator cuff repair, acromioplasty of the shoulder, arthroscopic shoulder surgery, and open reduction and internal fixation (ORIF) of the humerus. NOTE: Interscalene block for wrist, forearm, and hand surgeries often will not provide adequate coverage of the ulnar nerve distribution. However, blockade of ulnar nerve distribution may be achieved by using larger local anesthetic volumes or supplemental blockade of the ulnar nerve at a more distal location.

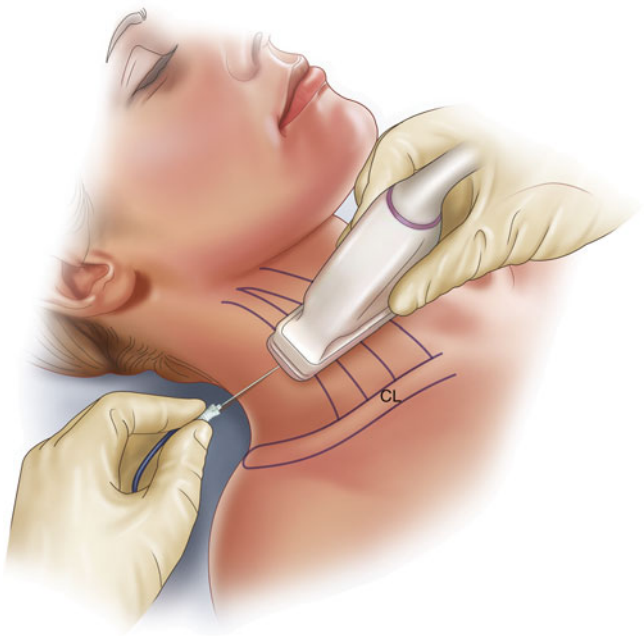

Fig. 23.1 Suggested initial ultrasound probe position for ultrasound-guided interscalene block

Ultrasound Anatomy and Needling: The patient is positioned supine or lateral decubitus with the face turned away from the operative side. The skin is disinfected and the ultrasound probe is covered by a sterile sheath. The ultrasound probe is then placed in the supraclavicular fossa where the brachial plexus is identified next to and posterior-lateral to the subclavian artery. Ultrasound probe is then moved proximally in a cephalad direction and held with a transverse orientation (Fig. 23.1). As the ultrasound probe is moved cephalad, typical divisions of the brachial plexus as seen in the supraclavicular fossa will organize into three nerve roots (C_5, C_6, and C_7).

The nerve roots are seen as three round hypoechoic circles usually stacked on top of one another and positioned between the anterior and middle scalene muscles (Fig. 23.2). The carotid artery and the internal jugular vein can be seen anterior and medial to the anterior scalene muscle. The skin at the posterior-lateral end of the probe is anesthetized by subcutaneous infiltration of local anesthetic. The block needle is advanced in-plane with a posterior to anterior direction and advanced until the needle tip is positioned just posterior-lateral to the C_5 and C_6 nerve roots. After negative aspiration, 10–25 ml of local anesthetic is slowly injected in small 3–5 ml aliquots. A continuous single orifice catheter may be inserted to provide continuous infusion of local anesthetic.

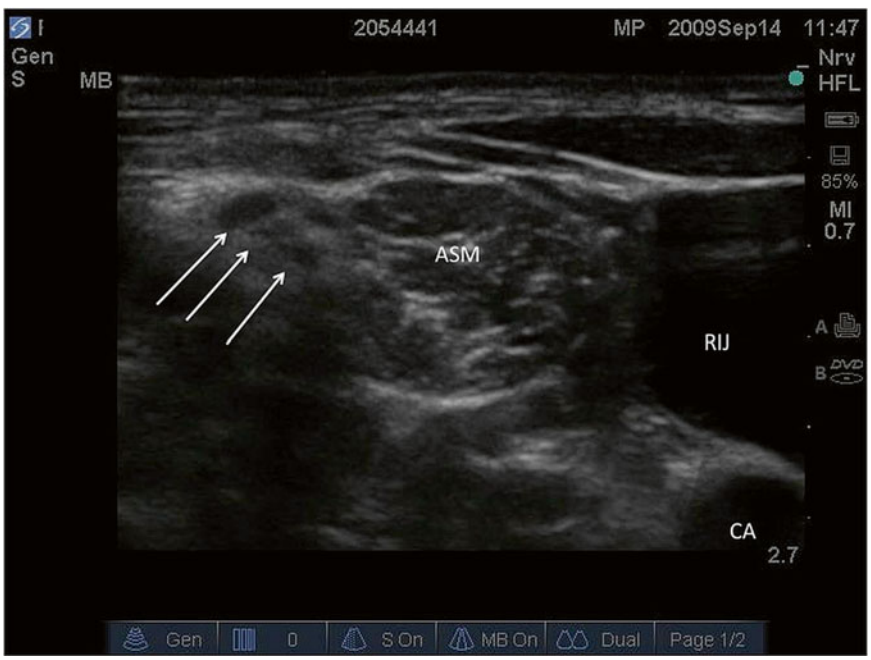

Fig. 23.2 Interscalene brachial plexus and anatomical relations with the ultrasound probe in the transverse plane. *ASM* anterior scalene muscle, *CA* carotid artery, *RIJ* right internal jugular vein, *arrows* identify roots/trunks of the brachial plexus and target for injection of local anesthetic

Pearls and Pitfalls

Pearls: Although it has been described that phrenic nerve involvement occurs in 90–100 % of interscalene blockade procedures, this complication may be prevented or minimized by reducing/eliminating spread of local anesthetic to the anterior and medial nerve roots. Techniques such as depositing the local anesthetic posterior to the brachial plexus, and observing that the injection is not spreading anterior to the nerve roots/trunks, along with minimizing the amount of local anesthetic used to just surround the nerve roots, will decrease the incidence of phrenic nerve blockade.

Pitfalls: Side effects from an interscalene block include infection, blockade of phrenic nerve (resulting in a hemidiaphram) and the sympathetic chain (located in region of the cervical nerve roots), intravascular injection, local anesthetic toxicity, neuraxial spread/injection (resulting in a "high" spinal), nerve injury, and hematoma formation. Patients may complain of dyspnea if the phrenic nerve is blocked, as it causes ipsilateral diaphragmatic paralysis. For patients with respiratory compromise (severe COPD), blocking one side of the diaphragm may not be a tolerable side effect. In addition, a Horner's syndrome commonly occurs if the stellate ganglion (sympathetic chain) is blocked, resulting in ipsilateral myosis, ptosis, and anhidrosis. Blockade of the recurrent laryngeal nerve may occur, which causes hoarseness of voice. Severe complications of an intravascular injection (external jugular vein transverses the interscalene groove and vertebral artery is anterior to the cervical nerve roots) from an inadvertent injection (as little as 1–3 ml) of local anesthetic into the vertebral artery may result in seizures.

Supraclavicular Block

Ultrasound-guided supraclavicular blockade typically targets the brachial plexus at the level of nerve divisions. It is used as primary anesthesia and/or postoperative pain management for surgeries on the humerus (distal), elbow, forearm, hand, or wrist (with or without a continuous catheter), and also upper extremity AV fistula surgery. There may be a delay in onset of ulnar nerve blockade or complete sparing of the ulnar nerve. When this block is performed for shoulder surgery, the addition of a superficial cervical nerve block may be required.

Ultrasound Anatomy and Needling: The patient is placed supine with the head turned away from the side to be blocked. The skin is disinfected and ultrasound probe protected by a sterile sheath. The ultrasound probe is placed in the supraclavicular fossa, parallel to the clavicle (Fig. 23.3), and then the subclavian artery is identified by directing the probe in a lateral to medial direction until an arterial pulsation is detected. The ultrasound probe is usually held in an oblique coronal orientation to achieve a cross-sectional view of the artery. The subclavian artery lies on top of the first rib, which is hyperechoic. The hypoechoic area seen below the rib is the lung. Moderately hyperechoic and shimmering appearance of the pleura can be seen below the first rib in some patients.

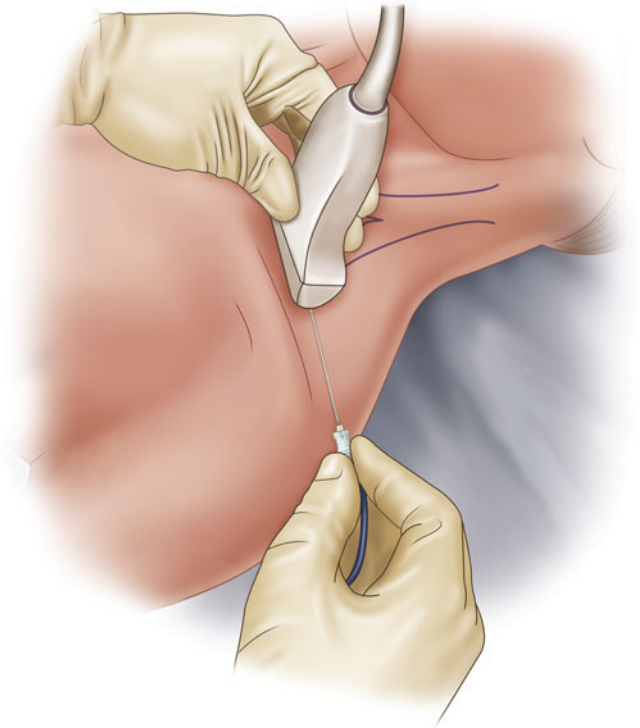

Fig. 23.3 Suggested ultrasound probe position for ultrasound-guided supraclavicular block. *Blue* markings identify the sternocleidomastoid muscle with the clavicular portion most lateral. The needle is inserted in-plane

The brachial plexus (divisions) is posterior and lateral to the subclavian artery arranged as a group of hypoechoic circles, sometimes described as a "cluster of grapes" (Fig. 23.4). The inferior trunk or division of the brachial plexus located in the corner defined by the subclavian artery and the first rib ("corner pocket") may be difficult to image in some patients. After subcutaneous infiltration of local anesthetic, posterior and lateral to the ultrasound probe, the block needle is inserted in-plane and advanced to the "corner pocket" under constant needle tip visualization in order to avoid a pneumothorax. After negative aspiration, a small aliquot of 3–5 ml of local anesthetic is slowly injected. Injection of local anesthetic in this area allows the brachial plexus to become more superficial and also better ensures blockade of the inferior trunk/division (ulnar nerve). The needle can then be redirected to inject local anesthetic around

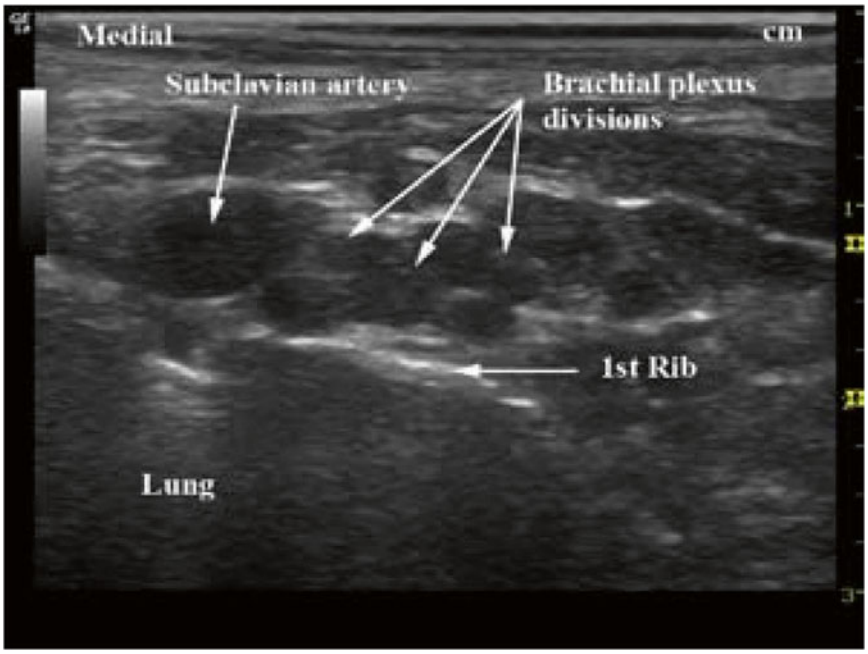

Fig. 23.4 Supraclavicular ultrasound anatomy. The brachial plexus at this level (divisions/trunks) appears as hypoechoic circles/ovals in a cluster just lateral to the subclavian artery. Immediately caudad to the 1st rib is the pleura

the rest of the brachial plexus using a total of 15–25 ml of local anesthetic. A continuous single orifice catheter may be inserted to provide continuous infusion of local anesthetic.

Pearls and Pitfalls

Pearls: Blockade of the intercostobrachial nerve in the axilla is necessary if a tourniquet will be used and placed on the upper arm. This approach to the brachial plexus provides a fast onset of effect as well as more complete anesthesia/analgesia of the upper extremity from a single injection.

Pitfalls: The cupola of the lung may be located in the block placement area, therefore, a pneumothorax is possible. Such a complication should be considered if a patient develops cough or chest pain (even hours after block placement). A phrenic nerve or sympathetic chain blockade is possible, although less common than with an interscalene block. Risk of phrenic nerve or sympathetic chain blockade can be decreased by avoiding local anesthetic spread anterior and medial to the subclavian artery. Bleeding, infection, hematoma formation, nerve injury, and intravascular injection (subclavian vessels are in the region) are potential problems. A supplemental ulnar nerve block may be necessary if the ulnar nerve distribution is missed. A superficial cervical plexus block should be added for shoulder surgery as this approach often misses the skin overlying the shoulder.

Infraclavicular Block

Infraclavicular blockade of the brachial plexus occurs at the cord level of the plexus below the clavicle. The cords are named according to their relation to the axillary artery: lateral, medial, and posterior. Lateral cord is formed from the anterior divisions of superior and middle trunks, medial cord is formed from anterior division of the inferior trunk, and posterior cord is formed from posterior divisions of all three trunks. The brachial plexus, spread around the axillary artery at this level, is not as compact as the more proximal trunks. Therefore, this block may have a longer latency, and may not be as dense, as a supraclavicular nerve block. This block can be performed as a primary anesthesia and/or postoperative pain management, with or without a continuous catheter for surgeries on the distal/mid humerus, elbow, forearm, wrist, or hand, and also distal AV fistula surgery.

Ultrasound Anatomy and Needling: The patient is supine with the arm to be blocked in a neutral position and the elbow flexed. The skin is disinfected and the ultrasound probe is protected with a sterile sheath. The ultrasound probe is placed with a parasagittal orientation in the infraclavicular fossa (area between the pectoralis major and deltoid muscles), aiming to identify the axillary artery (Fig. 23.5). The cords of the brachial plexus (medial, lateral, posterior) are arranged around the axillary artery according to their names. The cords typically have a hyperechoic appearance in the infraclavicular area (Fig. 23.6), while a hypoechoic area posterior and medial to the nerves and vasculature represents the lung. Superficial to the brachial cords is the pectoralis major and minor muscles.

The skin is anesthetized with subcutaneous infiltration of local anesthetic at the cephalad end of an ultrasound transducer positioned in the infraclavicular fossa. A short bevel needle is advanced in-plane toward each of the cords, while maintaining needle visualization to avoid causing a

pneumothorax. About 5–10 ml of local anesthetic is deposited next to each of the three cords with the first target being the posterior cord. If a continuous catheter is to be placed, it is usually placed next to the posterior cord since local anesthetic deposited in this area usually spreads to all the cords.

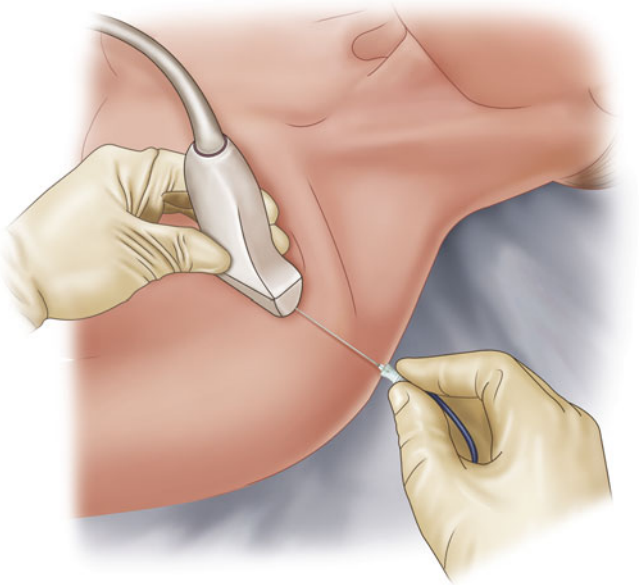

Fig. 23.5 Suggested ultrasound probe and needle orientation for an infraclavicular brachial plexus block

Pearls and Pitfalls

Pearls: Infraclavicular block placement site is useful for securing a catheter as this position is easily maintained for prolonged postoperative analgesia.

Pitfalls: An infraclavicular block procedure may cause patient discomfort as the pectoral muscles are pierced by the needle (ensure adequate subcutaneous local infiltration and patient sedation). Phrenic nerve or sympathetic chain blockade from an infraclavicular block approach is possible, but less common than an interscalene or supraclavicular approach. Hematoma formation, intravascular injection, infection, nerve injury, and pneumothorax are possible complications.

Axillary Block

Axillary blockade of brachial plexus at level of the terminal nerve branches is appropriate for providing primary anesthesia and/or postoperative pain management for elbow, forearm, hand, and wrist surgeries, with or without a continuous catheter. This block can be used for surgeries of the distal upper extremity, such as hand surgery (Dupuytren's contracture release), wrist surgery (posterior synovial cyst removal, carpal tunnel release, Colle's fracture repair), forearm surgery (distal AV fistula surgery), and elbow surgery (treatment of epicondylitis).

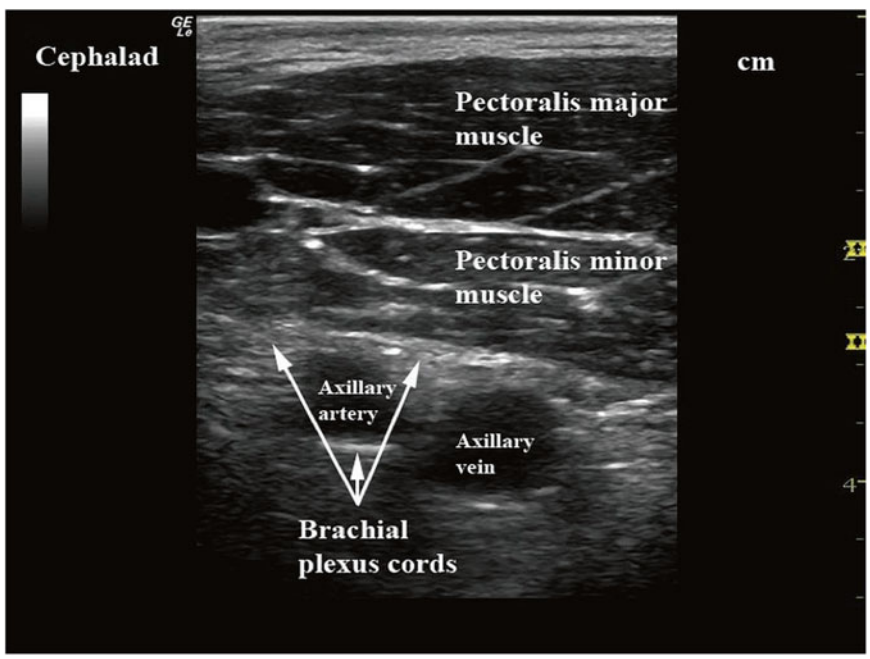

Fig. 23.6 Ultrasound anatomy of the infraclavicular (cords) brachial plexus. There may be increased difficulty to image the block needle and clearly identify the cords due to the increased depth of the brachial plexus from the skin surface [more hyperechoic nerve structures at the 3 (medial cord), 6:30 (posterior cord), and 8 (lateral cord) o'clock positions around the axillary artery]

Ultrasound Anatomy and Needling: The patient is placed supine with the extremity to be blocked abducted (90°), externally rotated, and flexed at the elbow (90°). After skin disinfection and placing a sterile ultrasound cover around the transducer, the probe is placed transversely across the axilla at the border between pectoralis and biceps muscles (Fig. 23.7). On the ultrasound image, the neurovascular bundle is located inferior to the coracobrachialis and biceps muscles and superior to the triceps muscle and humerus. The neurovascular bundle consists of the brachial artery and vein(s) along with the radial, median, and ulnar nerves. On ultrasound image, the nerves appear as hyperechoic structures with the median nerve usually superficial and anterior to the axillary artery, the ulnar nerve typically lateral to the artery, and the radial most commonly posterior to the artery (Fig. 23.8). The musculocutaneous nerve is typically seen in the fascia between the biceps and coracobrachialis muscles.

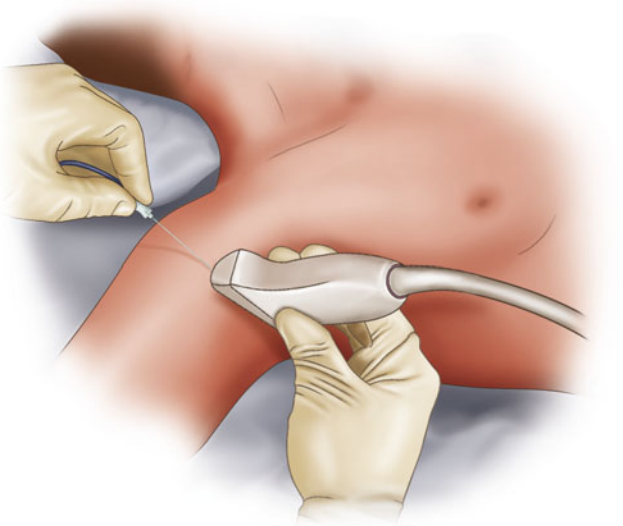

Fig. 23.7 Ultrasound probe is positioned high in the axilla (intersection of pectoralis major with the biceps muscle). At this level, the axillary artery and all the three main nerves to be blocked (median, ulnar, radial) should be in view on the ultrasound image

After skin preparation and subcutaneous infiltration of local anesthetic, a 5 cm short bevel needle is advanced in-plane from the superior side of the transducer. The needle is advanced to the musculocutaneous nerve between the biceps and coracobrachialis muscles, and after negative aspiration, 5 ml of local anesthetic is slowly injected. The needle is then redirected to the posterior region of the artery toward the radial nerve and 5 ml of local anesthetic is deposited in this location after negative aspiration. Then the needle is directed toward the ulnar and median nerves where 5 ml of local anesthetic is deposited around each nerve.

Pearls and Pitfalls

Pearls: There is a smaller potential for pneumothorax with an axillary block compared to other approaches of the brachial plexus. Multiple needle insertion points are usually needed to block all four nerves.

Pitfalls: Partial nerve blockade, intravascular injection (concern for local anesthetic toxicity), hematoma formation, nerve injury and infection are possible. Extremity positioning

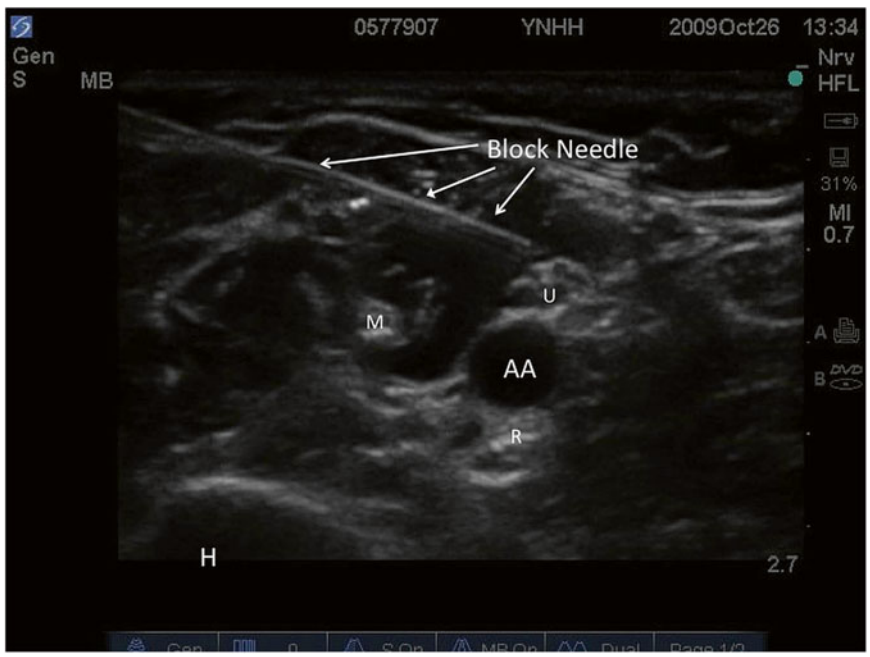

Fig. 23.8 Ultrasound view (transverse plane) demonstrating anatomical relations of the axillary brachial plexus, *H* humerus, *AA* axillary artery. In-plane block needle position for ultrasound-guided axillary block, *M* median nerve, *R* radial nerve, *U* ulnar nerve. Note location of local anesthetic (hypoechoic) spread within the axillary sheath

for this block (abducting the arm) may prove difficult, especially if there is a shoulder injury. If a tourniquet of the upper extremity is to be used, additional blockade of the medial brachial cutaneous and intercostobrachial nerves within the axilla must be performed to provide anesthesia of skin overlying the medial upper arm.

Lower Extremity Nerve Blockade

Preparation Technique

Equipment preparation: sterile towels, gloves and gauze pads, antiseptic solution, syringes, 13 MHz linear array transducer, sterile ultrasound sheath, and needles for both local infiltration and nerve block placement

Patient preparation: Monitors "on" and appropriate sedation (midazolam, fentanyl).

Needles: 25G 1.5 in. needle for skin infiltration, and 22G 2–6 in. short bevel needle.

Commonly used agents: 3 % chloroprocaine, 2 % lidocaine, 0.5 % ropivacaine, 0.5 % bupivacaine

Approximate dose: 10–40 ml of local anesthetic.

Femoral Nerve Block

Femoral nerve is the largest branch originating from the lumbar plexus. It innervates the anterior thigh, medial side of the calf, as well as the quadriceps muscle. Femoral nerve blockade is a commonly performed basic nerve block with a relatively low risk of complication. It is used as a primary anesthetic for surgery on the anterior thigh (quadriceps surgery), or for superficial surgery on the medial side of the calf. It is used for postoperative pain management for knee or distal femur surgeries, such as total knee replacement.

Ultrasound Anatomy and Needling: Patients are placed supine for this block. The skin is disinfected and the ultrasound transducer is covered with a sterile sheath. With a transverse orientation, the probe is placed on the patient between the inguinal crease and inguinal ligament (Fig. 23.9). The transducer is toggled until the circular/oval femoral artery is in view. If the common femoral artery has already split into deep and superficial femoral arteries, the probe should be moved proximally until a single common femoral artery is seen. The femoral nerve is located in a hyperechoic triangular area formed by the femoral artery medially (triangle base), iliopsoas muscle infero-laterally, and the fascia iliaca lateral and superficial (Fig. 23.10). The oval or flat femoral nerve is not usually seen in the triangular area until it becomes surrounded by local anesthetic.

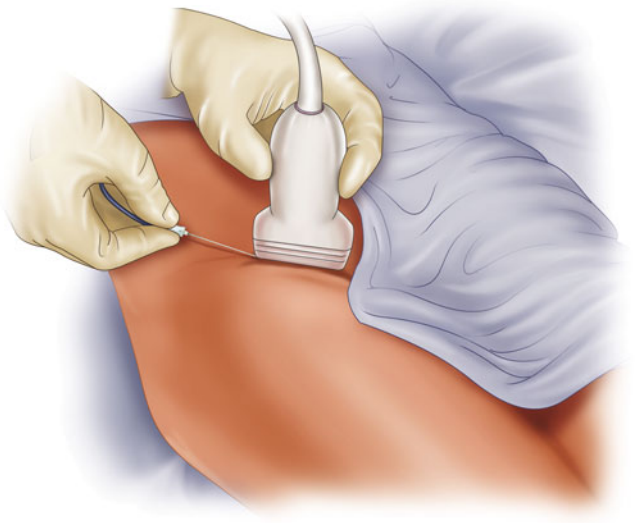

Fig. 23.9 Ultrasound probe orientation for femoral nerve blockade. Note medial-lateral orientation of the probe, which is placed just caudad to the inguinal ligament to optimize cross-section imaging of the femoral anatomy. The needle orientation is shown in an in-plane technique with the needle parallel to the ultrasound probe in a lateral-medial orientation (alternative would be an out-of-plane technique)

After subcutaneous infiltration of local anesthetic on the lateral side of the transducer following skin cleansing, a short bevel needle is advanced in-plane toward the apex of the triangle. Two "pops" can be felt as the needle is advanced through the fascia lata and then the fascia iliaca. Once the needle tip has entered the triangle and after negative aspiration, the local anesthetic is slowly injected within the triangle. At this point, the femoral nerve becomes usually more clearly delineated from the surrounding fascia. A continuous single orifice catheter may be inserted to provide continuous infusion of local anesthetic.

Pearls and Pitfalls

Pearls: The needle tip must be positioned below both fascia lata and fascia iliaca, but the "pop" may be less obvious through the fascia iliaca.

Pitfalls: Femoral nerve blocks have a low risk for complications, but may include vascular puncture and femoral nerve compression by hematoma formation, infection, and nerve injury.

Sciatic Nerve Block (Subgluteal Approach)

The sciatic nerve is the largest peripheral nerve in the body, measuring more than 1 cm proximally. Sciatic nerve block is usually combined with a femoral nerve block for lower

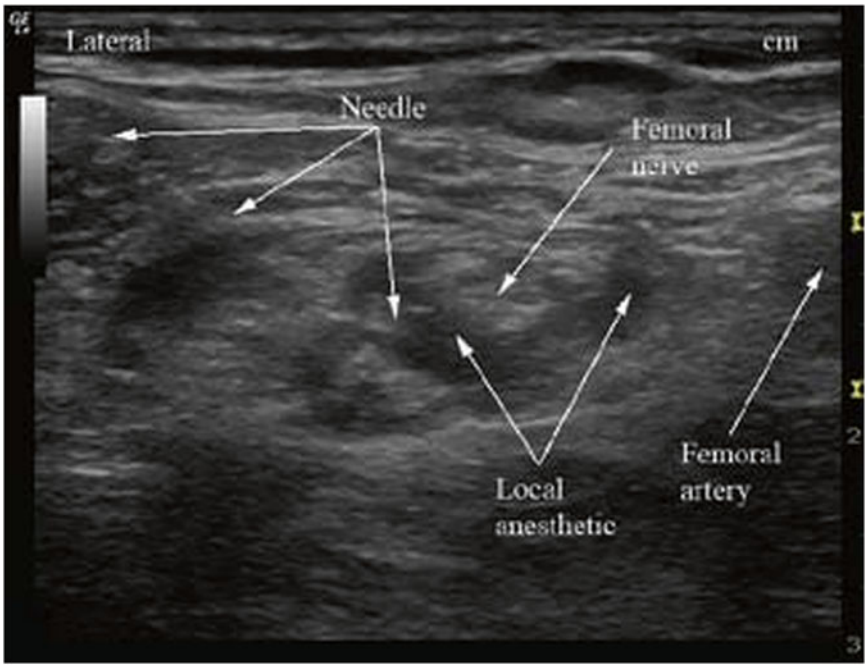

Fig. 23.10 Spread of local anesthetic (hypoechoic) around the femoral nerve. Lateral *arrows* identify the block needle. Note the mixed natured appearance (*white-gray-black*) of the femoral nerve lateral to the femoral artery

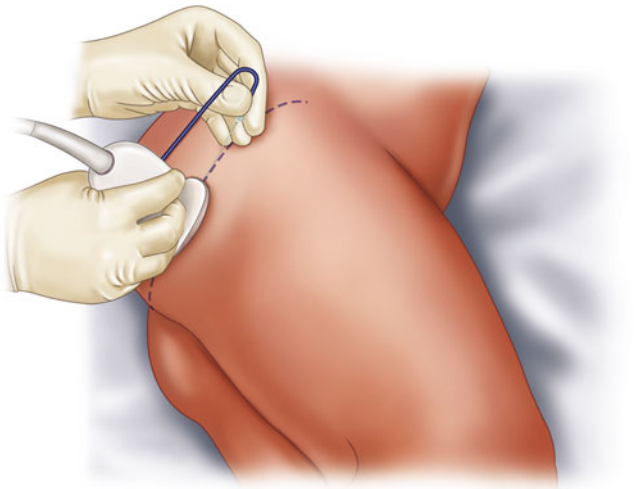

Fig. 23.11 Ultrasound probe position for subgluteal approach to the sciatic nerve. A stimulating nerve block needle is positioned in-plane in relation to the ultrasound probe. Ischial tuberosity is located on the medial end and greater trochanter on the lateral end (upper most) of the *dashed blue line*

extremity surgery. The sciatic nerve provides sensory innervation to the posterior thigh and the entire lower leg and foot, *except* for medial aspect of the leg to the medial malleolus, which is supplied by the saphenous nerve. The subgluteal approach to sciatic nerve blockade provides less patient discomfort during needle insertion compared to the infragluteal technique.

Sciatic nerve block is used as a primary anesthetic and/or postoperative analgesia for surgeries involving the posterior aspect of the thigh, hamstrings, biceps femoris muscle, lateral ankle (ORIF), foot, and the digits. It is used in conjunction with a femoral nerve block for anesthesia/ analgesia of the knee (total knee replacement).

Ultrasound Anatomy and Needling: The patient is placed lateral decubitus with the operative side in a nondependant position. A line is drawn connecting the ischial tuberosity and the greater trochanter, which serves as a reference point for ultrasound transducer placement, as the sciatic nerve usually lies midway along this line (Fig. 23.11). The skin is disinfected and the ultrasound transducer is covered with a sterile sheath. The transducer is placed over (parallel) the previously drawn line and an ultrasound image will reveal the above landmarks, with the ischial tuberosity medial and the greater trochanter lateral. The sciatic nerve will lie midway between the bony (hyperechoic) landmarks, deep to the gluteus maximus and superficial to the quadratus femoris muscle at a depth of 3–12 cm (Fig. 23.12). The sciatic nerve also appears hyperechoic, and oval or flattened wedge-shaped structure, surrounded by hypoechoic tissues.

After cleansing the skin, it is anesthetized at the lateral end of a properly positioned ultrasound probe with a deep subcutaneous injection of local anesthetic. The needle is advanced in-plane from the lateral side of the transducer toward the sciatic nerve. When a nerve stimulator is used, the needle is advanced until twitches are obtained between 0.2

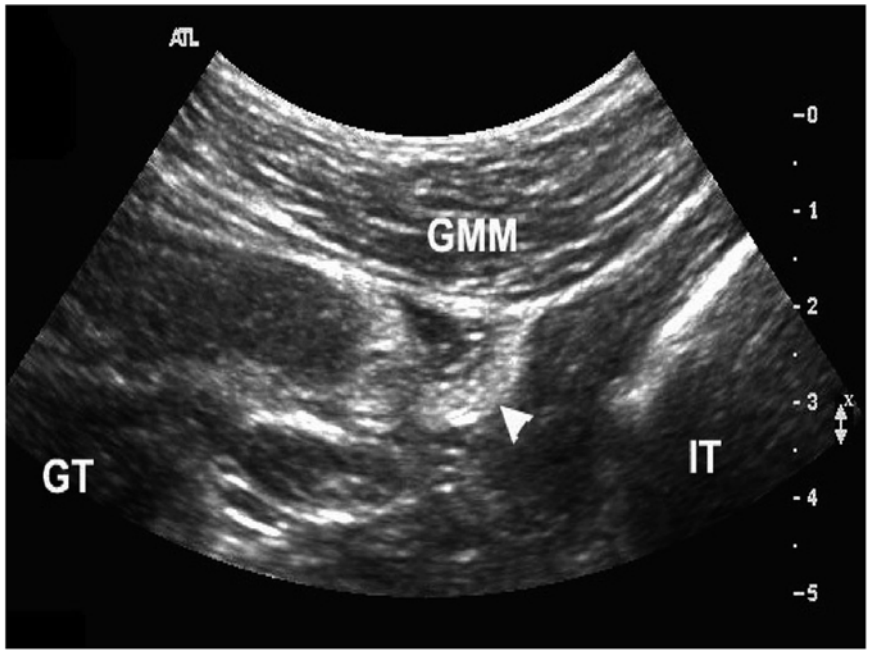

Fig. 23.12 Ultrasound image of the subgluteal approach to the sciatic nerve. *GMM* gluteus maximus muscle, *GT* greater trochanter, *IT* ischial tuberosity, *arrow* identify the sciatic nerve about midway between GT and IT

and 0.5 mA. After negative aspiration, 20–25 ml of local anesthetic is injected as the needle is redirected to ensure that the local anesthetic surrounds the nerve. A continuous single orifice catheter may be inserted to provide continuous infusion of local anesthetic.

Pearls and Pitfalls

Pearls: Due to the deeper location of the sciatic nerve and the use of a lower resolution, curved transducer, a peripheral nerve stimulator can be used to assist in confirming the target as the sciatic nerve. Injecting small amounts of dextrose can help locate the tip of the block needle.

Pitfalls: Infection, vascular puncture and hematoma formation, and nerve injury are possible complications. Needle visualization may be difficult with this approach depending upon patient body habitus, as the nerve can be 10 cm deep to skin surface. If a nerve stimulator is used, it may be observed that the needle tip is adjacent to the nerve, and yet there is no evidence of muscle twitch. If this is observed, injecting local anesthetic surrounding the sciatic nerve is usually sufficient for complete blockade.

Popliteal Sciatic Nerve Block

A popliteal approach to the sciatic nerve is a versatile block to perform and provides surgical anesthesia of the calf, tibia, fibula, foot, and the ankle. In addition, postoperative analgesia after such a block will last longer than an ankle block for foot surgery. Neural blockade of the lower extremity with a long-acting local anesthetic, such as bupivacaine or ropivacaine, may provide analgesia after foot and ankle surgery for 12–24 h. Blockade of the sciatic nerve in the area of the popliteal fossa permits sparing of hamstring muscles, which allows patients to continue to flex the knee. This block is used as a primary anesthetic and/or postoperative analgesia for foot surgery, Achilles tendon repair, and ankle surgery (ORIF).

Ultrasound Anatomy and Needling: The patient is placed lateral decubitus, prone, or supine with the area of the operative lower leg permitting access to the popliteal fossa. The skin is disinfected and the ultrasound transducer is covered with a sterile sheath. The transducer is then placed in the popliteal fossa with a transverse orientation (Fig. 23.13). The popliteal artery is easily identified and the tibial nerve is usually seen superficial to the artery. The biceps femoris muscle lies lateral, and the semimembranosus and semitendinosus lie medial to the nerve. The ultrasound transducer is deliberately moved proximally within the fossa area, and while keeping the tibial nerve in view during the advancement, the common peroneal nerve can be seen coming in from the lateral side. The common peroneal and tibial nerves will typically converge to form the sciatic nerve between 5 and 10 cm above the knee flexor crease (Fig. 23.14). The vasculature is considerably deeper than the hyperechoic sciatic nerve at this location and the sciatic nerve is imaged as being surrounded by a thick mesoneurial sheath. Within the sciatic nerve sheath, both the tibial and common peroneal nerves are covered by their own epineurium.

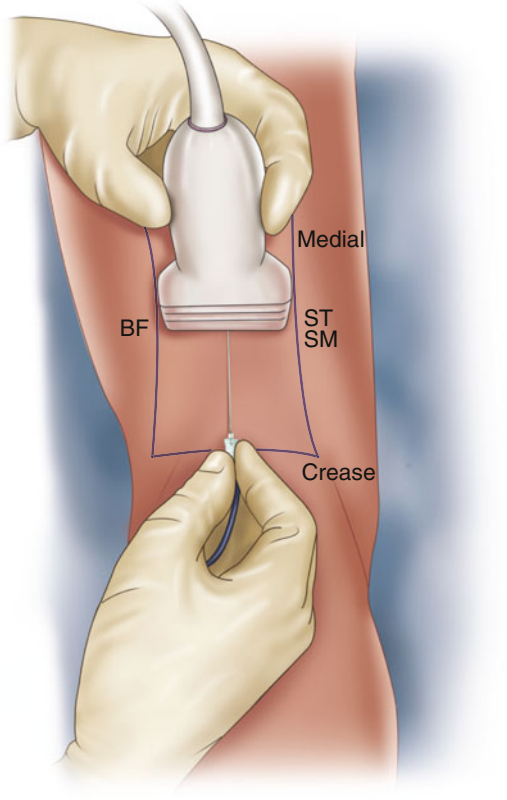

Fig. 23.13 Suggested ultrasound probe placement and needle insertion for sciatic nerve block in the popliteal fossa. *ST & SM* semimembranosus and semitendinosus muscle tendons (medial), *BF* biceps femoris muscle tendons (lateral). NOTE: Nerve block needle in this image depicts an out-of-plane orientation

The skin is cleaned, then anesthetized by subcutaneous infiltration of local anesthetic from the lateral side of the transducer, and a block needle is advanced in-plane toward the sciatic nerve. A "pop" sensation can be felt and seen on ultrasound image as the needle punctures through the mesoneurial sheath. After negative aspiration, 20–30 ml of local anesthetic is slowly injected, while the needle is redirected to ensure that the nerve is surrounded by local anesthetic. A continuous single orifice catheter may be inserted to provide continuous infusion of local anesthetic.

Pearls and Pitfalls

Pearls: Effective blockade of the sciatic nerve can take several minutes given both the size and thickness of its sheath. Pressure with the ultrasound probe may help to optimize nerve imaging.

Pitfalls: Infection, vascular puncture and hematoma formation, and nerve injury are possible complications.

Further Reading

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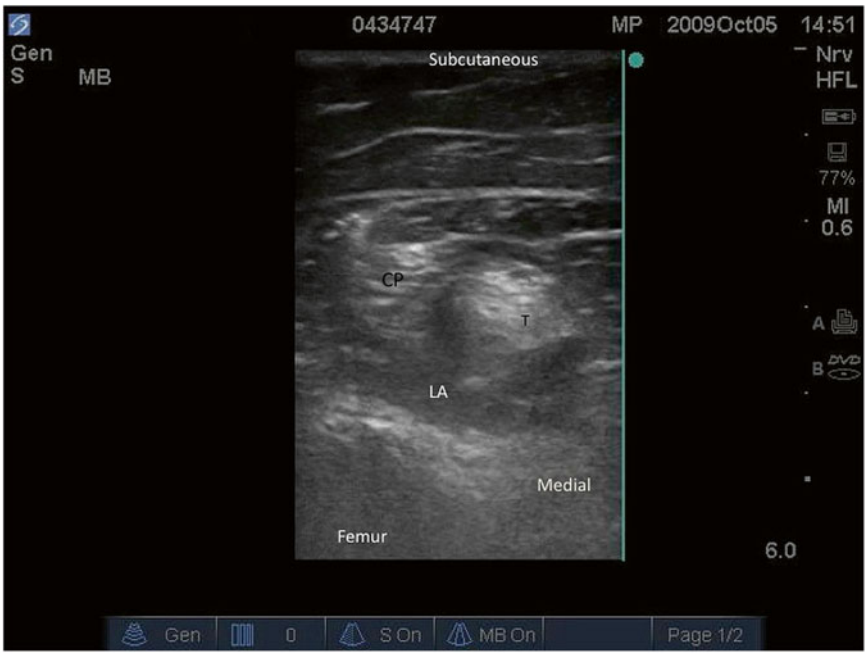
Fig. 23.14 Ultrasound image of sciatic nerve components in the popliteal fossa. Common peroneal (CP) and tibial (T) nerve components of the sciatic nerve become more defined subsequent to injection of local anesthetic (LA)



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Pain Management

24

Ramana K. Naidu and Thoha M. Pham

First attested in English in 1297, the word *pain* comes from the Latin word *poena*, for "punishment, penalty." Pain is an adaptive response to protect us from our environment. The International Association for the Study of Pain defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. This definition was penned by Harold Merskey in his 1964 Oxford thesis and was first published in the journal *Pain* in 1979.

The specialty of pain medicine seeks not only to relieve pain, but to restore function, and prevent or eliminate disability. John Bonica has been ascribed as the creator of a multidisciplinary approach to pain management. He, an anesthesiologist, brought together several fields including psychiatry, neurology, and physiatry, to collaborate in the care of individual chronic pain patients. This multidisciplinary approach seeks to provide patients with an improved quality of life by treating the whole person, not just the symptom; it is now the foundation of pain management.

Designations: Acute/Chronic/Cancer Pain

The definition for acute versus chronic pain should not be defined by a finite period of time, as has been done historically. Previous definitions looked at acute pain as that which just occurred, and chronic pain as that lasting more than 1, 3, or 6 months. Aside from time, there is a physiologic difference as well. Acute pain tends to be an adaptive and healing process versus chronic pain, which seemingly carries no purpose; it becomes a disease. Therefore, an all-encompassing definition for chronic pain is pain that persists beyond the expected period of healing. Admittedly, it still leaves much to be desired.

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There were an estimated 12.7 million cancer cases in 2008; it is expected to grow to 21 million by the year 2030 (World Cancer Research Fund International). Cancer patients experience a unique pattern of pain that can be manifested by the cancer, as well as by iatrogenic treatments such as surgery, chemotherapy, and radiation. Often, their pain is more debilitating than the prospect of death; the risks and benefits of pain management in these patients carry a different set of rules that is unique to the individual. For this reason, cancer pain receives distinct attention in pain management.

Pain Pathways

The sensation of pain involves complex mechanisms. We have gained significant understanding of many of the processes and the balance of how pain can be both adaptive and detrimental. The neural process of encoding and processing noxious stimuli is termed *nociception*. Consider the Cartesian model of pain that shows a simple linear pathway from injury to the brain. Although a novice model of pain, it serves as a starting point in understanding the process of nociception from the periphery to the central nervous system.

Peripheral Sensation

Sensation is described as either *epicritic* (non-noxious) or *protopathic* (noxious). There are nociceptors that are specific for qualia including mechanical, thermal, and chemical stimuli. The peripheral sensory nervous system is comprised of two distinct classes: larger rapid conducting myelinated A-fibers and slower smaller unmyelinated C-fibers (Table 24.1). It is the difference in these action potential velocities that explains the two-wave model of pain. Initially, there is an immediate sharp localized pain at the site of injury (A-delta), followed by a wave of non-localizable burning or tingling pain (C-fiber).

P.K. Sikka et al. (eds.), *Basic Clinical Anesthesia*,
DOI 10.1007/978-1-4939-1737-2_24,

Table 24.1 Neural blockade with local anesthetics

Fiber	Primary function	Order of susceptibility	Signs of blockade
A-alpha	Motor—skeletal muscle	5th—last	Loss of motor function
A-beta	Sensory—touch, pressure	4th	Loss of sensation to touch, pressure
A-gamma	Proprioception	3rd	Loss of proprioception
A-delta	Fast pain, temperature	2nd	Pain relief, loss of temperature sensation
B	Preganglionic sympathetic	1st	Increased skin temperature
C	Slow pain, postganglionic sympathetic	2nd	Pain relief, loss of temperature sensation

Ascending Pathway

From the periphery, nociceptor activation initiates an action potential that then must ascend the nervous system to reach the brain (Fig. 24.1). This ascending pathway uses a 3-neuron model. A *first-order* neuron, or nociceptor, reaches the dorsal horn of the spinal cord, in the Rexed laminae, where it synapses with a *second-order* neuron. The cell body of this first-order neuron is in the dorsal root ganglion (DRG). The signal is then passed on to the second-order neuron, which then ascends the spinal cord to reach the thalamus, primarily via the spinothalamic tract. From there, a *third-order* neuron finally delivers this peripheral sensory information to the cortex of the brain, where pain is perceived.

The ascending process involves transduction, conduction, and transmission. Specifically, transduction is the process by which mechanical, thermal, or chemical energy is transformed into electrical energy. Conduction is the process by which this action potential travels through the nociceptor. This energy, via the process of transmission, will transfer information from the first-order to the second-order neuron and then further to arrive at the cortex. Finally, perception is the conscious experience of pain nociception, including sensory and emotional processes.

Descending Pathway

The descending pathway provides modulation of the perception of pain from higher centers. There is no discrete "pain center" in the brain. Descending pathways originate at the level of the cortex, the thalamus, and the brainstem. Activation of these descending inhibitory fibers can modulate or "block" the activity of laminae I, II, V, and VII dorsal horn neurons. Modulation is a complex phenomenon that changes the quality, severity, and duration of pain perception. The main neurotransmitters implicated are norepinephrine, serotonin, and the endogenous opioids. These impulses can work in an inhibitory or sometimes facilitative manner. Impairments in descending modulation may be responsible for the transition from acute to chronic pain.

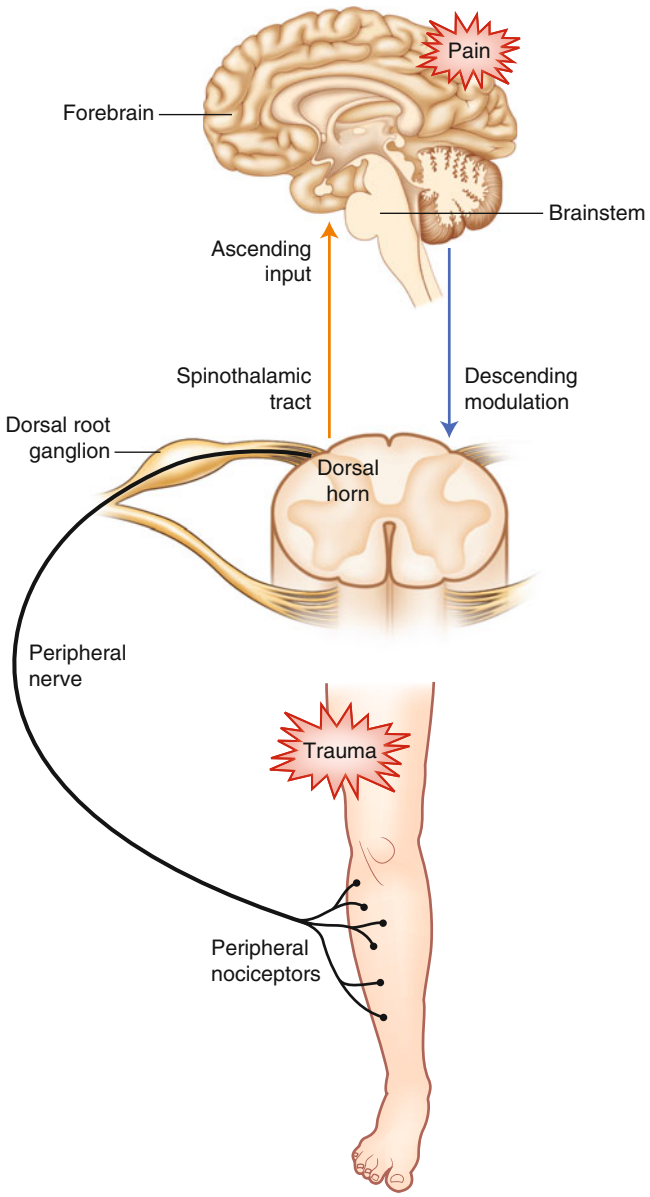

Fig. 24.1 The pain pathway

These inhibitory systems can be activated by brain stimulation, peripheral nerve stimulation, and intra-cerebral microinjection of opioids. Centrally acting analgesic drugs

can also cross the blood–brain barrier to activate these inhibitory control systems. However, it's generally not this simple. Pain is a complex perception that is influenced by prior experience. This sensation is also influenced by emotional states. Hence, the response to pain management therapies varies from patient to patient.

Peripheral Modulation

A myriad of chemicals are released by injured cells, including hydrogen, potassium, prostaglandins, bradykinin, histamine, and cytokines such as interleukins and TNF-alpha. Substance P, glutamate, aspartate, and ATP have excitatory effects on nociception, while beta-endorphins, somatostatin, acetylcholine, enkephalins, glycine, GABA, norepinephrine, and serotonin have inhibitory effects on nociception. These chemicals serve several physiologic purposes, one of which is to sensitize peripheral nociceptors. The process, called *peripheral sensitization*, results in allodynia and hyperalgesia:

Hyperalgesia—increased response to what is usually a painful stimulus

Allodynia—painful response to what is ordinarily a non-pain stimulus

Peripheral sensitization in the acute stage can be protective, forcing organisms to learn behaviors that avoid further damage and protect the affected area. Persistant peripheral sensitization, however, contributes to the disease of pain.

Central Modulation

It was once believed that the brain had a finite number of neurons and degeneration with aging was an incessant process. However, subsequent research has shown how dynamic the adult human brain can be. In particular, pain can be a nidus of neural plasticity, thereby altering perceptions and thresholds over time.

The descending pathway can have both facilitative and inhibitory effects. Alterations in this pathway can lead to hyperalgesia, and in few cases insensitivity. Therefore, this is a source of interest as therapeutic changes to these systems may have profound consequences on pain perception as well as transition from acute to chronic pain.

Within the dorsal horn of the spinal cord, there are two subsets of neurons: nociceptive-specific (NS) and wide-dynamic range (WDR). WDR neurons lie in Rexed lamina III to V and respond in a graded fashion depending on the intensity of stimulus. Repeated stimulation of unmyelinated C-fibers at intervals of 0.5–1 Hz leads to not only increased discharges but expansion in receptor field size as well. This phenomenon, known as *wind-up*, is primarily attributed to C-fibers and the WDR neurons.

Clinically, pain wind-up is the perceived increase in pain intensity over time when a given painful stimulus is delivered repeatedly above a critical rate. Glutamate released by these pathologically sensitized fibers underlies this wind-up phenomena. Glutamate will interact with postsynaptic NMDA receptors, to further support the sensitization of the dorsal horn. Therefore, NMDA antagonism can be helpful in chronic pain patients who demonstrate this pain wind-up.

Similarly, chronic exposure to exogenous opioids can induce nociceptive sensitization leading to a state of *opioid-induced hyperalgesia*. This condition is characterized by a paradoxical response to opioid therapy, such that patients experience increased levels of pain with increasing doses. This should be suspected in patients with continued and progressing pain complaints despite escalating doses of opioids in the context of no further disease progression. Treatment strategies involve reduction of opioid therapy, and/or supplementation with NMDA receptor modulators.

The Gate Control Theory of Pain

As discussed above, the transmission of sensory inputs from primary first-order to secondary neurons is subject to modulation, or gating, in the substantia gelatinosa of the dorsal horn. Gating can provide anti-nociception via local segmental and/or widespread supraspinal pathways. Wall and Melzack's *Gate Control Theory* (Fig. 24.2) proposes that pain is a functional balance between the ascending information traveling into the spinal cord via large and small nerve fibers, such that increasing activity of the large fibers can limit the transmission of information from smaller fibers. Thus, ascending non-painful sensory inputs (via large A-beta fibers) help gate the painful (activated smaller C-fibers) stimulus. Large fibers carry non-nociceptive information, whereas the small fibers carry nociceptive information. With a non-painful stimulus the large fibers are activated, which stimulate the inhibitory neuron. However, with a painful stimulus the small fibers are activated, which inhibit the inhibitory neuron causing the gate to open, which leads to pain.

Types of Pain

There are different ways to describe pain. We have thus far discussed the ambiguity in describing pain by temporal relationships: acute versus chronic. Pain can also be described based on context such as related to iatrogenic treatment such as surgery, syndrome (post-herpetic neuralgia or trigeminal neuralgia), or cancer. Below are the commonly described

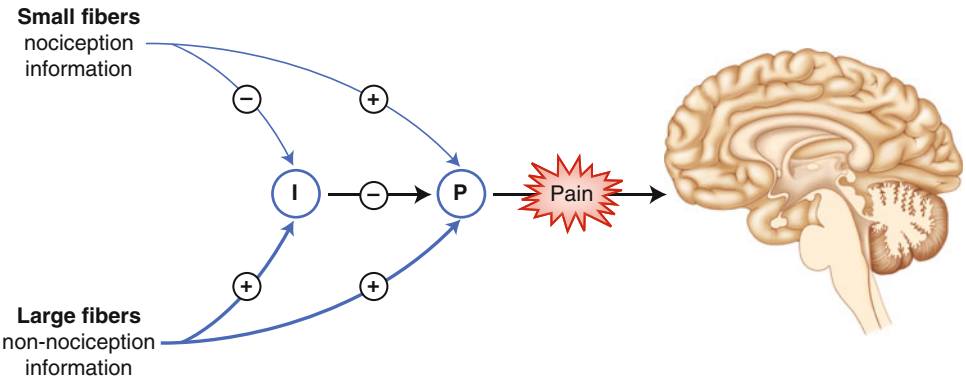

Fig. 24.2 Gate control theory of pain (*I* inhibitory neuron, *P* projection neuron)

Table 24.2 Differences between nociceptive and neuropathic pain

	Nociceptive	Neuropathic
Causes	Signaling from normal nerves detecting stimuli from damaged tissue, or potential damage to tissue if insult prolonged	Abnormal process of sensory input from damaged neural structures
Types	Somatic versus Visceral	Peripheral versus Central
Descriptors	*Somatic*: squeezing and sharp, dull and achy, easily located *Visceral*: pressure-like, diffuse, squeezing, poorly localized	Burning, shooting, tingling, lancinating
Treatment	Responsive to opioids and non-opioids	Generally unresponsive to opioids, requiring use of adjuvants

types of pain based on mechanism. In an effort to standardize nosology, these are terms that should be utilized to improve communication among healthcare providers.

- ***Nociceptive*** pain is physiological pain produced by noxious stimuli that occurs without tissue damage or sensitization (Table 24.2). In this model, a noxious stimulus is detected, but no physiologic change occurs to affect the nervous system. Nociceptive pain is further divided into somatic and visceral pain. Somatic pain is generally localizable and described as sharp. Visceral pain is non-localizable, diffuse, and aching pain. Structures that produce somatic pain include bones, tendons, and muscles. Visceral pain is associated with organs.
- ***Neuropathic*** pain is initiated or caused by a primary lesion or dysfunction in the central and/or peripheral nervous system. Neuropathic pain is commonly not reversible and often considered to be much more severe and resistant to treatment.
- ***Functional*** pain is amplification of nociceptive signaling in the absence of either inflammation or neural lesions. Essentially it is pain that does not have any known organic cause, and is most often used to describe abdominal pain of unclear etiology.
- ***Inflammatory*** pain is a result of tissue damage leading to inflammation which in turn leads to sensitization of the system. This leads to a physiologic change, which decreases the discriminatory ability of peripheral nociceptors as well as heightens sensitivity to all stimuli including spontaneous pain. These changes are usually temporary and part of the healing process. In small numbers of patients these changes are permanent and lead to chronic pain.

There are other types of pain that do not neatly fit into a category but deserve discussion.

- ***Referred*** pain is pain that occurs in a non-damaged part of the body as a result of damage to another structure with shared neuronal pathways. A common example is Kehr's sign. When a diaphragmatic injury occurs as a result of splenic injury, renal calculi, surgery, etc, patients can experience pain in their shoulders. This is because the phrenic nerve shares its cervical origin (C_{3-4}) with the supraclavicular nerve.
- ***Psychogenic*** pain is a psychiatric disorder that is manifested as pain. The DSM-IV attempts to group some of these disorders. Pain disorder is chronic pain that is a result of psychological stress. Somatoform disorder is symptoms that cannot be explained fully by a general medical condition, direct effect of a substance, or attributable to another mental disorder.

Acute Pain

The Joint Commission mandates that all patients have the right to adequate assessment and management of their pain. Better pain control, depending on the agents and modalities

used, leads to benefits in terms of decreased cardiovascular and respiratory complications. Endocrine, immunologic, gastrointestinal, and hematological outcomes can be improved as well. Most importantly, quality of recovery is improved, as we are becoming aware that acute pain may in fact become persistent if not treated properly.

Hospitals have started employing Acute Pain Services to provide the best pain management for their patients. Complex large systems can compromise patient safety, requiring relentless communication and coordination with almost every specialty in medicine. Anesthesiologists board certified in Pain Management are in a unique position to lead a pain service, as they are intimately involved with surgical services in the operating room, understand that acute pain can become chronic, and have the skills to intervene. An acute pain service may also be linked to a chronic and/or palliative cancer pain service and, therefore, knowledge in dealing with these patients is equally important.

Pain Evaluation

The evaluation of pain requires a comprehensive and systematic approach to obtain a thorough history and physical examination to establish a differential diagnosis. Physicians must be meticulous diagnosticians to ensure treatable etiologies have not been overlooked. Secondary data including imaging, laboratory values and tests can aid in diagnosis. Additional assessment of the patient's understanding of their pain, their goals, their psychosocial behavior, and their cultural beliefs is paramount for optimal pain management. There are several measures of pain which all attempt to objectify the subjective experience of pain. The Numerical Rating Scale (NRS), Faces Pain Scale (FPS), Visual Analog Scale (VAS), and the McGill Pain Questionnaire (MPQ) are the most commonly used in the United States.

When asking patients to rate the intensity of their pain, the appropriate scale for the appropriate patient and the appropriate situation should be utilized. The most frequently used is the NRS, which is a quick means to extract a morsel of information. Pediatric, elderly, or cognitively impaired patients may benefit from the Wong-Baker Faces Pain scale. Intubated patients may point on the VAS chart when able to follow commands.

Patient's pain should be systematically assessed on a consistent basis. It is now commonly considered "the fifth vital sign." The location and intensity of all the painful areas should be evaluated, while recognizing that perioperative pain may be related to factors other than post-incisional pain. Improper positioning and preexisting pain conditions commonly complicate the postoperative course.

The underlying mechanism or pain generator needs to be determined in order to provide the most focused therapy. Oftentimes, a specific cause cannot be determined. One of the best ways to define the etiology of pain is to have the patient use adjectives to describe the character of the pain (aching, burning, dull, electric-like, sharp, shooting, stabbing, tender, throbbing). Matching these descriptors to the likely type of pain can then tailor treatment.

In the postoperative period it is important to additionally determine the functional ability of the patient. Specifically does the pain affect the patient's ability to deep breathe, cough, get out of bed, and ambulate while in the hospital? These functional benchmarks can prevent postoperative pulmonary complications such as atelectasis and pneumonia and hematological complications such as deep venous thrombosis and pulmonary embolism. Inadequate pain control is a common denominator.

Some providers use the PQRST (Provocation, Quality, Radiation, Severity, Timing) mnemonic that is used in first aid and will make variations for application to pain management. Additionally, electronic medical records can provide templates that practitioners can follow. Either way, a systematic approach to the pain assessment in each patient should be carried out regularly to ensure adequate pain management.

Analgesic Modalities Via Phases of Care

Understanding the phases of care in preventing and treating pain is important and challenging. The pre-anesthesia clinic plays a paramount role in understanding and stratifying patients who would be candidates for regional anesthesia and those that may require a higher level of acute pain management. Patients on opioids should understand that their tolerance to, and dependence on, opioids makes their postoperative care challenging. Often, fulfilling their chronic opioid requirements, not to mention providing additional analgesia for their acute pains, is a difficult task perioperatively. In some, the use of opioids is just not sufficient and may be counterproductive in those who develop opioid-induced hyperalgesia. These patients, in particular, will require a multimodal approach emphasizing non-opioid therapies.

Adjunctive medications such as gabapentin or acetaminophen can decrease pain and opioid requirements. Neuronal sodium-channel blockade with regional anesthetic techniques is one of the best ways to prevent and treat pain. Therefore, consider neuraxial as well as peripheral ways to employ regional anesthesia while appreciating the time and quality, the surgery, the contraindications, and the overall postoperative course.

During the intraoperative period, anesthesiologists are accustomed to identifying and treating pain. The goal is to ensure safe emergence with appropriate pain control using cardiovascular and ventilator measures to do so. It is in the post-anesthesia care unit or on the floor or intensive care unit that the Acute Pain Service first makes contact with the patient. Several things have or have not occurred to give the patient the proper pain management course up to that point.

Pain is subjective and the provider must accept the patient's report of pain. Even when a patient states they have

Table 24.3 Commonly used non-opioid analgesics in adults

Drug	Usual dose (mg)	Maximum dose (mg)
Acetaminophen	650–1,000 q 6 h	4,000
Ibuprofen	400–800 q 4–6 h	3,200
Diclofenac	50, q 6–8 h	200
Ketorolac	15–30 q 6 h—IV	120—IV
Naproxen	250–500 q 6–8 h	1,500
Celecoxib	100–200, q 12–24 h	400

13 out of 10 pain, recognize that it provides useful information. The patient's level of pain and degree of pain relief should be assessed on a regular basis. It is important to follow trends and utilize whatever objective data are available. Of equal importance, the analgesic plan should be discussed with the patient and their family members—the hardest thing for family members is to see their loved one in pain, and to believe no one is doing anything about it. Therefore, it is important to understand the patient's expectations for their pain management in order to offer reasonable goals of therapy while not compromising patient safety.

Preemptive Analgesia

Initiating an analgesic regimen before the onset of a noxious stimulus to limit the pain experience and prevent central sensitization is the concept of preemptive analgesia. The perioperative setting is where preemptive analgesic techniques are utilized most often as the exact timing and onset of the noxious stimulus are known and thus can be preempted. Allowing a barrage of nociceptive information to reach the spinal cord can be detrimental to the patient by altering both peripheral and central sensory processing. Thus, providing systemic mu-opioid agonists or local anesthetics via peripheral nerve or epidural catheters throughout the perioperative period are clinically effective ways of providing analgesia, blunting the pain response and avoiding central sensitization. Preemptive analgesia should be utilized for any activity, therapy, or procedure with the potential to activate A-delta and C-fibers.

Non-pharmacologic Measures

Extremes of temperature, whether hot or cold, can help to reduce muscle tension, or reduce inflammation. Acupuncture and electro-acupuncture have been shown to be of benefit in the acute setting both to improve pain and to reduce common side effects of opioid analgesics; however they require specific training and time to administer. Similarly, hypnosis has been shown to reduce pain associated with medical procedures but again is specialized and time-consuming. Transcutaneous Electrical Nerve Stimulation (TENS) has shown conflicting results in terms of an analgesic benefit in the acute setting, but it has been shown to reduce the need for pharmacologic therapies. Similarly, there is limited evidence of benefit in the acute setting for guided imagery. Nonetheless, these simple interventions should not be overlooked. Though the evidence to support their use is mixed, the risks are low and application of use is easy. For some patients, the benefits are significant.

Pharmacologic Measures

Acetaminophen

Acetaminophen, also known as paracetamol or APAP (**acetyl-para-a**mino**p**henol), was synthesized in the late nineteenth century (Table 24.3). Its mechanism of action is speculated to be inhibition of a cyclooxygenase isotype, COX-3. It exerts its effect as both an analgesic and antipyretic. Although IV formulations have existed in the UK, Australia, New Zealand, Japan, and India for many years, the United States did not have FDA approval for IV acetaminophen until 2010.

The major concern is hepatotoxicity, acute liver failure, and death. It is the number one reason for acute liver toxicity in the Western world. In adults, the limit is 4 g/day; however still, individuals are susceptible to liver damage. Other insults such as alcohol use and hepatitis contribute to the risk of liver damage when taken with APAP. Because APAP is an antipyretic, one must be aware that there are situations where the addition of APAP may prevent fevers from occurring, which are an early sign of an inflammatory response or infection.

COX Inhibitors/NSAIDs

These drugs have been ubiquitously called Nonsteroidal Anti-Inflammatory Drugs (NSAIDs). Drug nomenclature is evolving to describe drugs based on the mechanism of action if known; therefore, this author describes them as COX inhibitors. Understanding the arachidonic acid metabolism pathway and the relative COX-1 to COX-2 inhibition of drugs in this class can help direct therapy. These drugs have anti-inflammatory, antipyretic, and analgesic effects.

The COX-1 inhibitors are associated with renal, gastrointestinal, and hematologic toxicity. COX-2 inhibitors produce less GI toxicity; however they can increase cardiovascular risk over time. Therefore, if patient is without serious GI contraindications, dual COX agents (ibuprofen) are recommended with concomitant use of GI prophylaxis.

Despite the ubiquitous use of NSAIDs, adverse clinical syndromes (hypertension, salt and water retention, edema, hyperkalemia) are infrequent. Nevertheless, patient populations at risk for renal adverse effects, including those with

age-related declines in glomerular filtration, hypovolemia, congestive heart failure, cirrhosis or nephrosis, and known preexisting renal insufficiency, should use other modalities.

Antiepileptic Drugs (AEDs)/Anticonvulsant Drugs (ACDs)/Membrane Stabilizers

Originally developed for seizure prophylaxis and treatment, neuronal channel blockers have a role in pain management. Medications from this class are most effective for neuropathic pain conditions (e.g., post-herpetic neuralgia, trigeminal neuralgia, phantom limb pain) or diseases that are known to cause neuropathy (e.g., diabetes, HIV, cancer, and its treatments). The most commonly used agents are gabapentin, pregabalin, lamotrigine, levetiracetam, carbamazepine, oxcarbazepine, tiagabine, topiramate, and zonisamide.

While these drugs are mostly utilized in chronic and cancer pain, there is growing interest in these medications in the acute pain setting. For example, gabapentin is being used preoperatively to help with postoperative analgesia. Interestingly, studies have shown that the anesthetic requirements are decreased with this premedication; however optimal dosing is still being investigated.

Benzodiazepines and Antispasmodic Drugs

In patients with unremitting pain, the descending inhibitory actions of GABA may be compromised such that pain signals are conducted unfiltered to the brain. Benzodiazepines, such as diazepam, have been shown to enhance the action of GABA to alleviate chronic pain when delivered into the spinal canal. In practice, however, such injections are done in a few selected cases. More often, benzodiazepines are administered orally or parentally for systemic uptake to act on $GABA_A$ receptors in the spinal cord. However, undesired consequences stem from additional actions on the brain—sedation, delirium, and memory impairments.

Baclofen is a derivative of GABA and is an agonist for the $GABA_B$ receptors. Beneficial antispasmodic effects result from actions at spinal and supraspinal levels. A beneficial property of baclofen is in the possible treatment of alcohol dependence by inhibiting withdrawal symptoms and cravings.

Other antispasmodics commonly used are carisoprodol, cyclobenzaprine, tizanidine, methocarbamol, and metaxalone. These drugs have the effect of causing muscle relaxation via disparate mechanisms. Each drug in this class behaves somewhat differently with different side effects. While typically muscle relaxant medications are not used in the acute setting, there are situations when they might be useful. Short-term use of cyclobenzaprine has been shown to be effective for acute pain symptoms.

Intravenous Local Anesthetics

Most studies of intravenous (IV) lidocaine have been conducted on patients with neuropathic pain syndromes. Cell membranes of injured peripheral nerves can exhibit an increased density of sodium channels which contribute to persistent non-evoked discharges that produce a central hyperexcitable state. Therefore, inhibition of sodium channels by lidocaine can inhibit neuronal ectopic discharges. Studies have shown that IV lidocaine infusions (1–6 mg/kg over 30–60 min) are clearly superior to placebo only in the first day of therapy, probably superior to placebo after 5 days, and no better than placebo after 1 week. There have been other studies demonstrating the benefit of lidocaine IV infusions in post-laparotomy analgesia.

Topical Agents

Topical ointments, gels, salves, and patches have been developed to provide analgesia. They are the oldest method of drug delivery. The general principle is that they work at the site of action without significant systemic absorption. Caution should be employed to avoid placing these patches over open wounds or areas of skin compromise. Additionally, patients with increased BMI may not have good tissue penetrability for the drug to provide benefit. Nearly every class or analgesic agent can be prepared by compounding pharmacies for directed topical use.

Lidocaine (5 %) can provide adequate sodium-channel blockade to the nerves that it contacts. It can be helpful for superficial neuropathic and musculoskeletal pain complaints. Capsaicin cream is derived from the extract of hot chili peppers. It works at the vanilloid receptor TRPV1 and its use depletes substance P and other neuropeptides causing analgesia; it is most widely used in neuropathic pain. Topical diclofenac can provide COX inhibition, which can be useful to attenuate inflammatory pain.

NMDA Antagonists

Compounds which antagonize the NMDA receptor include ketamine, dextromethorphan, nitrous oxide, and memantine. Thus far the one that is used most often in acute postsurgical pain is ketamine, although active research is under way on memantine. Ketamine, a dissociative hypnotic, can be used at low doses (high doses may produce hypersalivation, sympathomimetic, and psychogenic effects), while providing analgesia. It is clinically useful in patients with opioid tolerance because it mitigates opioid use and improves VAS scores. At low doses it has anti-hyperalgesic properties. Methadone and levorphanol are mu agonists with additional NMDA-antagonistic properties so should be considered for those on chronic opioid therapy with signs of wind-up or hyperalgesia.

Opioids

Opioids are the most ubiquitous and arguably most effective pharmacologic agents to provide analgesia (Table 24.4). The most accurate nomenclature states that all compounds that work at opioid receptors should be called opioids. The term narcotic is a legal term and should be reserved for those in law. Additionally, the term opiate should be reserved for

Table 24.4 Commonly used opioids in adults

Opioid	Oral dose (mg)	IV dose (mg)
Morphine	10–30 q 4 h	4–10 q 2–4 h
Morphine controlled release (MS Contin)	15–30 q 8 h	–
Hydromorphone (Dilaudid)	2–4 q 4 h	0.2–1 q 4 h
Oxycodone[a]	5–10 q 4 h	–
Oxycontin (extended release oxycodone)	10–20 q 12 h	–
Tramadol	50–100 q 4–6 h	–
Codeine	15–60 q 4 h	–
Hydrocodone[b]	5–10 q 4 h	–
Transdermal fentanyl (25 mcg/h)[c]	Every 3 days	–

Named [a]Percocet, [b]Vicodin with addition of acetaminophen. [c]Transdermal fentanyl is mainly used in the treatment of chronic pain, and not acute pain

naturally occurring alkaloids such as morphine, thebaine, or codeine. Some of the principles relevant to acute pain management include:

1. Routes of administration
2. Patient-controlled analgesia
3. Managing side effects
4. Opioid conversion

Routes of Administration

Opioids can be administered via almost any route of administration. Generally, the postoperative period is a time when patients must remain NPO and the preferred route of administration is intravenous. Intramuscular injection has fallen out of favor due to variability in kinetics and adverse reactions, but still has use in select situations.

Opioids that have *(a) a short time of onset, (b) steady maintenance state, and (c) non-active metabolites* are preferred in acute pain management. The naturally occurring alkaloid, morphine, is the father drug for opioid management. It is one of the essential drugs per the World Health Organization (WHO). However, it has its deficiencies: its onset of action can take 30 min, it can be histaminergic, and its metabolites, particularly morphine-3-glucuronide, can be neurotoxic. Hydromorphone, on the other hand, has a shorter onset of action, is less histaminergic, and its metabolites seem to be less active than morphine—therefore, is better tolerated in patients in renal failure. Fentanyl is a lipophilic medication that is often misnomered as a "short-acting drug." True, its duration of action is related to its large volume of distribution, and therefore, it is redistributed quickly. However, the half-life of fentanyl is similar to morphine and hydromorphone, but only when it approaches its volume of distribution.

Sustained release formulations should generally only be initiated in the acute setting if pain is present most of the time, and it is assumed that the pain generator will last for an extended period of time (>2 weeks). Additionally, these long-acting formulations should be reserved for opioid-tolerant patients once it is clear that around-the-clock therapy is necessary. Opioid-naïve patients should be initially treated with immediate release versions to ensure tolerability, prior to transition to sustained release agents.

Although formulations of transdermal, transmucosal, transbuccal, and intranasal opioids have been created, there are inherent issues with safety that prevent their use in the acute postoperative setting. However, there are select cases when such routes can be utilized. Technologies are being developed to take advantage of this route while maintaining patient autonomy and safety.

Patient-Controlled Analgesia

Patient-controlled intravenous analgesia (PCA) is a means of enabling a patient to control their pain management. It is a machine that can be filled with a syringe or tubing that is set to give doses of medication no sooner than a set period of time. Hitting the button before the allotted period results in no medication administration. It is a requirement that patients are competent to use the equipment and are alert, aware, and oriented. Additionally, only the patient has the right to push the button.

The principle of PCA relies on the therapeutic window. A proper loading dose is required to reach and surpass the Minimum Effective Analgesic Concentration (MEAC). It is at this point that patients note pain relief. If more opioid is given, the side effects of the medication become apparent. This is the toxic threshold, and there can be several toxic thresholds depending on the type of side effect. For example, nausea may occur at a certain concentration, while pruritus occurs at a different concentration, altered mental status, etc. Each individual has different thresholds based on their genotype and phenotype. It is possible to have patients with a toxic threshold below the MEAC; for example, one could have a patient who is nauseous but also needing more opioid for pain control. This is a patient who would benefit from analgesia from another receptor.

PCA machines allow for the setting of the following parameters:

Table 24.5 Patient-controlled analgesia—common agents and suggested management

Drug	Demand dose	Lock out (min)	1 h limit	Continuous/basal rate (if indicated)
Morphine (1 mg/ml)	0.5–1 mg	6–10	10 mg	0.5–1 mg/h
Hydromorphone (0.2 mg/ml)	0.1–0.2 mg	6–15	2 mg	0.1–0.5 mg/h
Fentanyl (50 mcg/ml)	10–50 mcg	6–10	100 mcg	10–50 mcg/h

- Demand (bolus) dose
- Lockout interval
- Hourly limit
- Continuous (basal) infusion

Nurses can additionally apply:

- Rescue (loading) dose

Demand (Bolus) Dose

The demand dose is the amount of opioid the patient receives each time they activate the machine by pushing the button. The appropriate demand dose is small enough to minimize side effects, but large enough to provide effective analgesia.

Lockout Interval

The lockout interval is the amount of time set between the demand doses. During this time the patient cannot administer the opioid even if the system is activated. Lockout intervals between 5 and 10 min are commonly used.

Hourly Limit

To ensure further safety, an hourly limit is set for the maximum amount of opioid received by the patient. Hourly limits can be set for 1 h or more. An hourly limit is determined by the settings of demand doses and lockout interval.

Continuous (Basal) Infusion

Continuous infusions are not commonly used in acute pain, and only should be considered in select situations, such as opioid-tolerant patients who cannot achieve nocturnal pain control with other modalities. However studies have shown that nighttime basal infusions do not improve sleep or analgesia. Continuous infusions are avoided in high-risk patients, elderly patients, patient with sleep apnea, or the morbidly obese, as they are prone to developing respiratory depression.

Rescue Dose

While on a PCA, patients may require additional doses in times of intense nociception (dressing change, ambulation after surgery), or when the level of analgesia from a PCA is inadequate. These doses of opioids are termed as rescue doses, and are delivered by a healthcare provider.

Opioid Choices for PCA

Several opioids can be used in PCA (Table 24.5). The typical opioids include morphine and hydromorphone. The phenylpiperidines fentanyl, sufentanil, alfentanil, and remifentanil can only provide analgesic benefit for a short duration. When the volume of distribution of fentanyl is approached, however, the duration of relief can be similar to hydromorphone. Meperidine (pethidine in the UK) has fallen out of favor because of the neurotoxicity (lowered seizure threshold) of its metabolite normeperidine. The onset of action of methadone is so prolonged that its use in a PCA is questionable, although it has been used.

In the opioid-tolerant patient these doses will need to be individualized based on the amount of opioid the patient takes per day leading to higher initial demand doses and possibly the initial use of continuous infusions. High-risk patients, identified as elderly (age 70 or above), morbidly obese, or those with a history of obstructive sleep apnea, should have lower initial demand doses (e.g., one-half the usual demand dose) and opioid-sparing strategies are of utmost importance.

Monitoring and Management of PCA

Respiratory depression events can lead to anoxic brain injury or death. These are serious consequences and, therefore, safety measures and vigilance must be applied. The Anesthesia Patient Safety Foundation (APSF) has recommended the use of continuous monitoring of oxygenation (pulse oximetry) and ventilation in patients receiving PCA. Continuous monitoring should be used in all patients, especially for high-risk patients (elderly, obstructive sleep apnea, morbidly obese).

If the patient does not receive adequate pain relief with a given demand dose, one can increase the demand dose or decrease the lockout interval. In addition to talking to patients about their pain experience, one can collect objective data from PCA machines. One should have access to PCA usage, and some PCA pump manufacturers provide graphical data on opioid use, demand dosing, and allocation of doses when permitted. This data can be helpful to determine when patients experience pain, whether they are being undertreated, or whether there are behaviors that need to be examined.

Table 24.6 Equianalgesic dose of opioids

Drug	PO (mg)	IV (mg)
Morphine (MS Contin)	30–60	10
Codeine	200	–
Fentanyl	–	0.1
Meperidine (Demerol)	300	75
Oxycodone (Percocet, Oxycontin))	20	–
Hydrocodone (Vicodin)	20	–
Hydromorphone (Dilaudid)	8	1.5

Safety and Efficacy of PCA

While continuous infusions of opioids can lead to over medication and respiratory depression, patient-controlled analgesia has an inherent safety mechanism built in. That is, if the patient is getting sedated by the demand doses of the PCA, then he/she will not further activate the PCA machine. One of the major benefits of PCA is that it allows each patient to titrate the amount of opioid they receive. Furthermore, some degree of placebo effect may be imparted by the use of a PCA, thereby enhancing overall pain control. Other benefits of PCA over nurse-administered opioids include improved patient satisfaction, similar rates of side effects (except a higher incidence of pruritus), slight reduction in length of hospital stay, and a lower incidence of pulmonary complications.

Managing Side Effects of Opioids

Respiratory depression events are sentinel events and given their potentially life-threatening nature, mu-receptor antagonism is necessary to reverse this side effect. Since the half-life of naloxone is shorter than that of the opioid being reversed, a single dose of naloxone may not be sufficient; repeat doses or even a continuous infusion may be necessary. Reversal events result in a return of pain, and sometimes managing this pain is far more difficult than ever before in the patient's course. Intensive monitoring of the patient should be initiated in these situations to ensure that the life-threatening event does not recur after the effects of naloxone have dissipated.

Constipation is a side effect of opioid therapy that does not gain tolerance with use. In fact, one such opioid, loperamide (imodium), is indicated for this purpose as an antidiarrheal. Prevention is paramount in all patients who require opioids, especially those on chronic therapy. Stool softeners, pro-motility agents, and osmotic agents are first-line options. Oral naloxone has limited systemic bioavailability due to first-pass glucuronidation and can antagonize the enteric mu-opioid receptors. Methylnaltrexone, a quaternary ion, is unable to pass across the blood–brain barrier. Thus, it causes peripheral mu antagonism to reverse opioid effects on the enteric system with preservation of central agonism and analgesic benefit. Another medication, alvimopan, has a high affinity for peripheral mu receptors and also does not significantly reverse analgesia.

Opioid-Induced Itch (OII) has historically been treated with diphenhydramine. Unfortunately, this has led to some dire consequences given the many ways that the drug works—antihistamine, anticholinergic, sedative, and hypnotic. It is on the Beers Criteria of drugs not to be used in patients greater than 65 years of age. The effect in children is often paradoxical, leading to hyperactivity, and some patients enjoy the hypnotic effects of IV formulation, and demand its use. If a patient develops urticaria, a hypersensitivity reaction, which can happen with drugs such as morphine or codeine, then diphenhydramine is appropriate. However, regarding opioid-induced itch, the leading theory currently is that there is a central mechanism in the medulla oblongata. While IV Benadryl should be specifically used for anaphylactic/anaphylactoid reactions, nalbuphine, a partial mu antagonist and kappa agonist, may be a useful option in that it partially antagonizes the mu receptor without clinically producing abstinence syndrome or a recrudescence in pain relief in the opioid tolerant. Butorphanol, a mixed mu agonist/antagonist and kappa agonist, has also been used in opioid- and non-opioid-induced itch. There has been mixed evidence with 5-HT_3 antagonists. Some have also advocated a low-concentration propofol infusion, but clearly there are potential safety issues with this approach.

Opioid Conversion: Equianalgesic Potency

Opioid conversion is an important concept allowing healthcare providers to discuss the opioid tolerance of patients in a unified manner. This can be important in transferring care from one provider to another, or in opioid rotation. Below is a method to opioid conversion in acute and chronic pain settings. One must be mindful of the pitfalls in conversion. Historically, oral morphine has been the parent drug in which all other conversions can be made (Table 24.6).

STEP 1: Calculate the daily opioid requirement. Include ALL of the opioids (oral, epidural, prn) administered.

STEP 2: Convert to ORAL MORPHINE. Use a table or an application, which can roughly provide good estimates.

STEP 3: ALWAYS CONSIDER INCOMPLETE CROSS-TOLERANCE. Cross-tolerance is the extension of physiologic resistance for a substance to others of the same

type or class, even those to which the body has not been exposed. In most instances, cross-tolerance is incomplete and can range from 20 to 30 %.

STEP 4: THE PRICE IS RIGHT. Similar to the popular daytime game show, bidding/guessing a dose closest to the patient's requirements wins. If one over bids, the game is automatically lost as going over when it comes to opioids can have disastrous consequences. When in doubt, start at a low dose and tailor as the patient's pain dictates.

Acute Pain in the Opioid Tolerant

One should expect that opioid requirements for these patients will be significantly higher than in the opioid-naïve patient. The pain thresholds are lower with more pain complaints and higher pain scores are endorsed. It is important to know that this can be likely a result of not opioid tolerance, but of opioid-induced hyperalgesia. In addition to replacement of chronic baseline requirements, increased doses are required to provide any noticeable relief. Thus, discussion of reasonable goals and expectations of analgesic therapy with the patient is crucial. An Acute Pain Service can provide care for these patients as they can be challenging. These patients often know what agents have either worked or not worked for them in the past. The use of multimodal therapy in this patient population is especially important as opioid therapy alone will leave much to be desired.

Regional Anesthesia

The importance of regional anesthesia cannot be understated in acute pain management. Some of the pitfalls with regional anesthesia at this time include the time it takes to perform, the lack of quality in planning and performing blocks, and poor management of catheters once they are placed. For this reason, surgeons may have negative views of regional anesthesia. When done correctly, regional anesthetics are the best analgesics; in these situations, there are surgeons who demand regional anesthesia for their patients. The current trend in academic programs creating and developing regional anesthesia and acute pain fellowships demonstrates the growing awareness of the importance of regional anesthesia and the need for specialization. Currently, there are studies being done on long-acting local anesthetics, for example, depo local anesthetics and biologic sodium-channel blockers, such as saxitoxin. Providing days of relief rather than hours might be a significant leap in postoperative pain management possibly reducing the incidence of chronic pain after surgery.

Patient-Controlled Epidural Analgesia

From a physiologic standpoint, epidurals block action potentials of nerves. The concentration of the local anesthetic, in general, determines which nerves are affected. Small diameter nerves are more susceptible than larger diameter nerves. Therefore, at appropriate concentrations, epidurals will block A-delta and C-fiber transmission while sparing motor A-alpha nerve transmission. The C-fiber blockade leads to sympatholysis with the potential to increase renal, mesenteric, hepatic, and coronary blood flow, depending on the level blocked.

Patient-Controlled Epidural Analgesia (PCEA) serves the same principles as PCA in that the patient has control of their pain management. Despite numerous attempts, the ideal PCEA solution (commonly local anesthetics, opioids, and/or clonidine) and even the ideal delivery variables (similar to PCA—bolus volume, lockout time, hourly limit, basal rate) remain controversial. Commonly used local anesthetics include bupivacaine (0.0625–0.2 %) or ropivacaine (0.1–0.2 %), while commonly used opioids include fentanyl (1–4 mcg/ml) or hydromorphone (10–50 mcg/ml).

In distinct contrast to IV PCA where basal infusions are not commonly used, a continuous infusion is routinely used for PCEA (6–14 ml/h). By self-administering a bolus volume the patient may supplement, or "top off" their epidural during periods of increased pain. If multiple boluses are initiated each hour, patient will likely benefit from an increased basal infusion rate. However, should hypotension or dense motor blockade result, a more dilute local anesthetic solution may facilitate maintenance of this higher rate. If hypotension persists, the epidural infusion may need to be stopped, and alternate methods for pain control (IV PCA) may have to be used.

Patients with nausea and vomiting are treated with antiemetics or discontinuation of the opioid from the epidural solution. Pruritus is treated with nalbuphine (2.5–5 mg every 4 h prn). Persistent pruritus can be treated with a naloxone infusion (0.4 mg/l of IV fluid, about 250 ml/h). Generally, PCA therapy has a higher incidence of nausea and vomiting, while epidurals have a higher incidence of pruritus, urinary retention, and varying degree of motor block. Persistent motor block and back pain may indicate the development of epidural hematoma. The patient should have an immediate MRI to rule out the hematoma, and if diagnosed, should have an urgent decompression laminectomy.

The evidence thus far favors epidural analgesia for acute pain management in improving postoperative pain control, reducing postoperative pulmonary complications, reducing postoperative ileus, improving lower extremity graft survival, reducing incidence of deep vein thrombosis and pulmonary embolism, and decreasing time to mobilization and length of ICU and hospital stay. Further studies need to be conducted on whether epidurals can help ameliorate renal dysfunction. Other theoretical advantages, although not statistically proven at this time, include improved wound healing and decreased infection risk. The use of PCEA can lead to improved patient satisfaction.

Chronic Pain

Chronic pain is a disease. It is pain that persists beyond the expected period of healing. Historic definitions base it on duration: pain that lasts longer than 1, 3, or 6 months. Unlike acute pain syndromes, chronic pain is a more complex issue

Table 24.7 Assessment of chronic pain

Complete pain history 1. Pain location 2. Intensity/severity of the pain 3. Type of pain – burning, throbbing, shooting, stabbing, aching 4. Initiating factors 5. Aggravating and relieving factors 6. Duration of pain
Effect of pain on 1. Physical functions 2. Sleep 3. Work and economy 4. Mood 5. Family and social life 6. Sex life
Physical examination—General, pain site evaluation, neurological and musculoskeletal
Associated psychological factors and depression, cognitive impairment
Diagnostic tests—sensory testing, diagnostic nerve blocks, pharmacological tests, radiography, CT scan, MRI
Treatments received—its benefits and any adverse effects

given the bio-psycho-social-genetic influences. While chronic pain is not a normal part of aging, it is widely accepted as so, which leads to under-treatment with resultant reduced quality of life, decreased socialization, depression, sleep disturbances, cognitive impairment, and malnutrition. As such, a multi-modality approach addressing these complex interrelated factors is necessary to achieve successful chronic pain management. The multi-modality approach to addressing chronic pain syndromes should utilize pharmacological, interventional, psychological, rehabilitation approaches, along with complementary and alternative medicine.

According to the recent 2010 census, there are 40 million residents aged 65 and over, representing 13 % of the US population. It is estimated that chronic pain currently affects more than 50 % of older persons living in a community setting and greater than 80 % of nursing home residents. Further estimates suggest that by 2030, 1 out of every 5 Americans will be in this geriatric population. Therefore, as the average age of the population continues to rise, there will be a concomitant dramatic increase in the numbers of persons living with chronic pain.

Assessing Chronic Pain

Assessing the patient's pain presents the initial challenge, as the pain is often complex and multifactorial. The chronic pain patient's health status is frequently complicated by multiple medical problems with many potential sources of pain. Skeletal pain related to osteoarthritis, osteoporosis, fractures, contractures, and spinal spondylosis may exist. Neuropathic pain due to previous stroke, spinal stenosis, and peripheral neuropathies related to diabetes, herpes zoster, and cancer treatment, along with myofascial pain due to deconditioning, poor posture, and skin ulcers, also occur with high frequency in the aging population. Depression, disability, and impaired cognitive function are additional confounding factors that may hinder the evaluation. Nonetheless, the initial assessment of a patient's chronic pain should always begin with a thorough history and physical exam.

The gold standard for the assessment of pain is the patient's self-report. A thorough history should include location, distribution, and severity, along with identification of associated events or activities that precipitate or alleviate the pain (Table 24.7). Descriptors relating to the quality of the pain (burning, stabbing, spasms, dull, aching, throbbing) are also useful. A complete medication history, including medications prescribed, trialed, or used (prescription, over-the-counter drugs, and home remedies), noting those that have and have not provided relief, is also essential to this initial assessment. Laboratory and diagnostic tests, other associated conditions (i.e., insomnia, anxiety, depression, agitation, frustration, and anger), and behavioral assessments should be reviewed if available.

Physical Examination

The physical examination should generally focus on the musculoskeletal and neurological system, although evaluation of other systems may aid in diagnosis of certain pain syndromes. For musculoskeletal pain complaints, one should inspect the muscle bulk and assess range of motion, strength, tenderness to palpation, and spasticity or presence of contractures. Special tests with various eponyms may aid in specific syndromes.

Neurologically, assessing for motor strength, sensory (tactile, pin prick) changes, and deep tendon reflexes, along with recognizing other neurological symptoms or deficits, should be noted. Brief assessment of the cranial nerves and

gait are useful as well. The physical exam may reveal trigger points, bony deformities, or local inflammation at certain sites that may suggest certain treatable pathologies. Additionally, when combined with the pain history, a determination of nociceptive (somatic or visceral) versus neuropathic etiologies for the patient's pain may be elucidated.

Imaging and Diagnostic Testing

Imaging is most appropriately used to rule out serious pathology in cases involving orthopedic injury, new-onset back pain, back pain that is worse at night or when supine, pain in those with a history of cancer, or those with worrisome constitutional symptoms (fever, anorexia, weight loss). Most patients will not need imaging for a definitive diagnosis of underlying pathology. Red flag symptoms such as neurologic deficits, new dysfunction of bowel or bladder, severe abdominal pain, or signs of shock or peritonitis will also warrant further diagnostic work-up and imaging.

Magnetic Resonance Imaging uses a magnetic field to create resonant frequency in the atomic nuclei of the body. This property allows several tissues to be contrasted, in large part due to their water content. This mode of imaging is useful for soft tissue detail. It is generally contraindicated in patients with magnetic hardware and can be costly in comparison to other imaging modalities.

Computerized Tomography (CT) uses ionizing radiation in multiple planes for examination of various structures. It is useful to detect small fractures and abdominal neoplasms. Plain radiographs take a single frame of a structure using ionizing radiation. This can be an appropriate study for fractures, and may be used for postoperative spine film studies. Ultrasound differentiates tissues based on the reflection to longitudinal ultrasonic waves. It is easily applied for dynamic situations in pain management such as where a needle is being placed. Ultrasound can also use the *Doppler effect* to locate vascular flow and estimate stenotic lesions and velocity of flow.

Neurophysiologic testing includes several studies including but not limited to Electromyography/Nerve Conduction Study (EMG/NCS) and Qualitative Sensory Testing (QST). EMG/NCS examines the velocity and amplitude of action potentials. Patterns of testing can help differentiate the type of neuromuscular disease that is occurring. QST examines the small and large fiber function by assessing thermal, mechanical, vibration, and electrical stimuli. Autonomic testing can be done examining the sympathetic responses.

A physician must be able to understand what data is useful from the history, physical examination, imaging, diagnostic tests, and laboratory values to derive a conclusion as far as diagnosis and treatment plan. Furthermore, such a physician must have good understanding of the resources available to ensure that the patient maximizes their potential for functional and analgesic outcomes.

Treatment Model

We have described a multidisciplinary approach to acute pain management, and it is of utmost importance in chronic pain. Consider a five-finger model to pain management: (a) Pharmacologic management, (b) Interventions, (c) Psychology, (d) Rehabilitation, and (e) Complementary and Alternative Medicine (CAM) to help ensure that multiple different therapies are being utilized.

Pharmacologic Management

Many different classes of medications have been used as in the treatment of pain. Given the varying pain physiologies, rarely one single medication can be completely effective in all types of pain. The most common approach is to try various different classes of medications both individually and in combination until optimal pain relief is obtained. Polypharmacy can lead to both synergistic analgesic effects as well as a reduction in individual medication side effects due to dose reduction. Good knowledge of the pharmacodynamics, pharmacokinetics, interactions, and adverse effects of these medications is essential in the treatment of these conditions.

Non-Opioid Analgesics

Many of the non-opioid analgesic agents have been discussed in the acute pain section of this chapter. Acetaminophen, COX inhibitors, anticonvulsants, antispasmodics, and topical agents play an even larger role when it comes to addressing chronic pain states. Additionally, the antidepressant class of medications can enhance the descending inhibitory systems.

COX Inhibitors/NSAIDs

COX inhibitors are the most commonly prescribed medications for pain, and with chronic use carry increased risk of GI bleeding and renal dysfunction. If patients are taking OTC or prescribed COX-1 inhibitors, they must be aware of the potential side effects. Gastrointestinal protection with proton pump inhibitors or H_2-blockers may mitigate the risk of GI bleeding.

COX-2 inhibitors can be very useful in chronic pain, but it comes at the expense of increased cardiovascular risk. While these medications can be very useful in an acute setting, their constitutive use can lead to adverse cardiovascular events. Therefore, the risks of these medications must be weighed with the patient. Some individuals, such as those with rheumatoid arthritis, may be willing to take on the risk in order to improve the quality of their lives.

Antidepressants

Antidepressants can be used to manage not only the depression associated with the chronicity of their disease, but can also address the pain itself (Table 24.8). Extensive data

Table 24.8 Antidepressants used in pain management

Drug	Daily dose (mg/day)
Selective norepinephrine reuptake inhibitors (SNRIs)	
Venlafaxine (Effexor)	37.5–225
Duloxetine (Cymbalta)	30–120
Milnacipran (Savella)	12.5–200
Selective serotonin reuptake inhibitors (SSRIs)	
Fluoxetine (Prozac)	10–80
Sertraline (Zoloft)	50–200
Paroxetine (Paxil)	10–50
Citalopram (Celexa)	20–40
Escitalopram (Lexapro)	10–20
Tricyclic antidepressants (TCAs)	
Amitriptyline (Elavil®)	50–150
Nortriptyline (Aventyl®, Pamelor®)	50–150
Desipramine (Norpramin®, Pertofrane®)	50–200
Imipramine (Tofranil)	50–200
Doxepin (Sinequan)	50–200

Table 24.9 Anticonvulsants used in pain management

Drug	Daily dose (mg/day)
Carbamazepine (Tegretol®)	200–1,200
Oxcarbazepine (Trileptal®)	600–1,800
Lamotrigine (Lamictal®)	25–500
Phenytoin (Dilantin®)	300
Topiramate (Topamax®)	25–300
Gabapentin (Neurontin®)	300–1,800
Pregabalin (Lyrica)	150–600
Levitiracetam (Keppra)	1,000–1,500

support a role for the monoamine neurotransmitters, serotonin and norepinephrine, in the descending modulation of pain. Norepinephrine appears to play a more significant role as Serotonin Norepinephrine Reuptake Inhibitors (SNRIs) and Tricyclic Antidepressants (TCAs) provide more meaningful analgesic benefit when compared to pure Selective Serotonin Reuptake Inhibition (SSRIs).

Tricyclic agents exert their analgesic effect by restoring inhibitory controls through blockade of noradrenalin and serotonin reuptake. Unfortunately the tricyclics are limited by significant anticholinergic side effects that many patients find intolerable. This includes orthostatic hypotension, arrhythmia, impotence, and sedation.

As prolonged pain states can impact a person's psychological health, often manifesting as depression, antidepressants can enhance mood while simultaneously mitigating their perception of pain. Newer antidepressants have fewer side effects and have variable reuptake inhibition of serotonin and norepinephrine. The SNRIs seem to be more effective as analgesics than the SSRI medications, as animal models indicate that noradrenergic effects, and to a lesser degree serotonergic effects, reduce pain-related behaviors.

Anticonvulsant Drugs (ACDs)/Antiepileptic Drugs (AEDs)/ Membrane Stabilizers

Anticonvulsant drugs are neuronal membrane stabilizers. Although originally produced to treat seizures, their effect on pain was seen early in their development. Medications from this class are most effective for neuropathic pain conditions or diseases that are known to cause neuropathy (Table 24.9). An additional accepted indication is chronic radiculopathy confirmed by patient report of dermatomal pain with objective physical examination findings corroborated with abnormal imaging or EMG/NCV abnormalities.

Carbamazepine is an effective sodium-channel membrane stabilizer, but it may produce bone marrow depression, while phenytoin causes undesirable cosmetic effects (gum hyperplasia, hirsutism) and ataxia at high doses. Carbamazepine is the drug of choice in trigeminal neuralgia. Other sodium-channel membrane stabilizers include topiramate, which has beneficial side effects: (1) It is a rare analgesic to cause weight loss, (2) It is sedating. Caution must be used in patients with kidney stones. Lamotrigine is also used, but it has the rare and dreaded potential to cause Stevens-Johnson syndrome, and therefore, patients must be wary of any rash.

Table 24.10 Benzodiazepines used in pain management

Drug	Typical oral prescribing dose (mg)
Alprazolam (Xanax®)	0.25–0.5 qd-tid
Chlordiazepoxide (Librium®)	10–25 qd-tid
Clonazepam (Klonopin®)	0.25–0.5 tid
Diazepam (Valium®)	5–10 qd-bid
Lorazepam (Ativan®)	0.5–2 qd-tid
Oxazepam (Serax®)	10–15 qd-tid
Flurazepam (Dalmane®)	15–30 hs
Midazolam (Versed®)	Doses vary depending on individual patient needs
Temazepam (Restoril®)	15–30 hs
Triazolam (Halcion®)	0.125–0.25 hs

The calcium-channel membrane stabilizers include gabapentin, pregabalin, and levetiracetam. Gabapentin causes weight gain and sedation. Nonetheless, among neuropathics it seems to have the most tolerable side effect profile. Pregabalin, the pro-drug to gabapentin, utilizes a gastric transport mechanism which can allow for better systemic absorption.

In general, newer anticonvulsants have fewer side effects and differences in their activity are reflected on whether they are calcium- or sodium-channel membrane stabilizers. One from each class of membrane stabilizer can be used in a multimodal approach to difficult neuropathic pain states.

Sodium-Channel Blockers

Mexiletine, a sodium-channel blocker that is often times considered an oral lidocaine, reduces pain by adhering to peripheral nerves to reduce conduction of pain signals from the peripheral nerves en route to the central nervous system and the brain. Over time, the feeling of pain is diminished. It is theoretically advantageous in sodium-channel neuropathic states and is being used experimentally to treat pain associated with different kinds of peripheral neuropathy. It is also a Class 1B antiarrhythmic and caution should be used in those with sinus node depression.

NMDA Antagonists

Glutamate, an excitatory neurotransmitter, works at the AMPA and NMDA receptor. Effects at the NMDA receptor play a role in descending modulation. NMDA antagonists have demonstrated analgesic effects. The various medications in this class include ketamine, memantine, dextromethorphan, and methadone. Ketamine has shown considerable efficacy in treating neuropathic pain and can be administered PO/IM/IV and the intranasal route.

NMDA antagonists are used as co-analgesics together with opiates to manage otherwise intractable pain, particularly if the pain is neuropathic in nature. It has the additional benefit of countering the spinal sensitization or wind-up phenomena experienced in some with chronic pain. At low doses, the psychotropic side effects are less apparent and well addressed with benzodiazepines. Ketamine is a co-analgesic, and so is most effective when used alongside a low-dose opioid. While it does have analgesic effects by itself, higher doses can cause disorienting side effects, including hallucinations.

Memantine is an oral NMDA antagonist currently used in management of Alzheimer's disease. Its use is under study in the management of chronic pain. There have been case reports of its use in reducing opioid consumption and decreasing pain scores in the acute postoperative period.

Benzodiazepines/Muscle Relaxants

Muscle relaxants are a varied group of medications which involve depression of the central nervous system. The mechanism of action is thought to be through the depression of the descending reticular activation system and not via peripheral inhibition. In patients with chronic pain syndromes, the descending inhibitory actions of GABA become severely compromised such that pain signals are conducted to the brain nearly unfiltered.

Benzodiazepines, such as diazepam, have been shown to enhance the action of GABA to alleviate chronic pain when delivered into the spinal canal (Table 24.10). In practice, however, such injections are done in few selected cases. More often, benzodiazepines are administered orally for systemic uptake to act on $GABA_A$ receptors in the spinal cord. However, undesired consequences stem from additional actions on the brain–sedation, memory impairments, and addiction. Therefore chronic use is generally ill-advised.

Baclofen is a derivative of GABA and is an agonist for the $GABA_B$ receptors. Beneficial antispasmodic effects result from actions at spinal and supraspinal levels. Appreciated for its retention of therapeutic benefits even after many years of chronic use, recent studies indicate that tolerance may develop in some receiving intrathecal delivery of baclofen. A secondary beneficial property of baclofen is in the possible treatment of alcohol dependence by inhibiting withdrawal symptoms and cravings. However, discontinuation of baclofen in chronic users can be associated with an abstinence

syndrome which resembles benzodiazepine and alcohol withdrawal. Patients receiving baclofen intrathecally have the greatest risk of life-threatening withdrawal.

Sedation is a common side effect with most of the muscle relaxants. Carisoprodol has long-term dependency liability, while cyclobenzaprine is related to tricyclic antidepressants. Unlike carisoprodol, methocarbamol has greatly reduced abuse potential. Metaxalone is generally considered to have the least incidences of side effects.

Topical Medications

Topical medications have advantage of providing effective therapy without severe side effects of systemic absorption. However, limitations for topical agents include the ability to treat only relative small areas and systemic absorption. Capsaicin, a vanilloid agonist, causes conduction analgesia without associated suppression of motor or sensory function unrelated to pain. As part of a cream, gel, or liquid for topical application, the most common mixture is 10 % ketoprofen, 5 % lidocaine, and 10 % ketamine. Other ingredients found useful by pain specialists, their patients and compounding pharmacists include diclofenac, gabapentin, amitriptyline, cyclobenzaprine, clonidine, tramadol, and longer acting local anesthetics.

Opioid Analgesics

The use of opioids in non-cancer chronic pain is controversial and deserves debate. Opioids are ubiquitous, effective, and their history stretches to the oldest medical texts. They can be a blessing for a person suffering from nonmalignant chronic pain. However, the receptors for opioids (mu, kappa, delta, and ORL-1) exist in several tissue types besides the nervous system that the pain targets, and for this reason, these medications have a host of side effects. While many focus on the acute side effects associated with opioid administration, there are long-term consequences to opioid use, which can negatively impact one's life, and actually make their chronic pain worse. It is determining the benefits versus the risks in long-term use that must be weighed in each individual case.

Multiple routes of administration include oral, intravenous, epidural, intrathecal, topical, buccal, rectal, and inhalational. Given the inherent risk of abuse and dependence, these are classified as Schedule II drugs. Tolerance and dependence are common amongst all opioid medications. The development of tolerance and dependence is more significant in patients of ages 20–60 years. Reducing analgesia due to tolerance can be aided by opioid rotation.

Short-acting Opioids

These are medications that last anywhere from a few seconds to a few hours. There are myriad medications to address various situations. For example, burn patients may need an extremely short-acting drug for dressing changes. In chronic pain, short-acting opioids are generally used for what is called "breakthrough" pain. Typically, patients that have chronic pain will have a particular activity or time when they need optimal relief, and these are periods where short-acting opioids can be useful.

Combination acetaminophen-opioid medications are ubiquitous in the United States, and the reasons for this include the synergism of acetaminophen with opioids and the fact that these were Schedule III drugs, meaning they were not as highly regulated as their pure mu-opioid counterparts. In October 2014, the DEA rescheduled all hydrocodone products as Schedule II, recognizing their abuse potential.

It is estimated that 15 % of Caucasians have attenuated cytochrome p450 2D6 deficiency and as such have decreased metabolism of codeine into its effective drug, morphine. Patients who have allergies to codeine, hydrocodone, or oxycodone may benefit from switching to a non-codeine opioid such as hydromorphone or morphine.

Long-acting Opioids

Sustained release formulations of morphine, oxycodone, hydromorphone, and oxymorphone are available and should be utilized in the opioid-tolerant chronic pain patient. Once a patient's opioid requirements are realized, every effort should be made to maximize the use of long-acting agents to provide less fluctuation in analgesic blood levels, fewer adverse side effects, and less frequent dosing.

The synthetic opioids in the morphinan (levorphanol and butorphanol) and diphenylpropylamine (methadone) series are long-acting opioids that have other analgesics mechanisms. Although having been around for several decades, these drugs have historically been used in addiction medicine as an opioid replacement to curb withdrawals from the cessation of illicit opioid use.

Methadone's use requires an understanding of the unique pharmacology of the drug, especially its extended duration of action and its dose-dependent potency. Also, as it takes a few days to reach a stable plasma concentration, patients will need to be followed closely to monitor its effectiveness and side effects. It must also be realized that methadone is a racemic mixture of a mu agonist and an NMDA antagonist which makes patients have a lesser degree of analgesic-tolerance development with more robust analgesic benefit. Additionally, it has norepinephrine and serotonin reuptake inhibition to contribute to descending modulation. As methadone does not follow a linear conversion to other opioids, it should be considered uniquely. Methadone does not require a sustained release polymer coating in order to provide continuous systemic uptake. As such, methadone is ideally suited for chronic pain patients. However, patients should be monitored for dose-dependent QT prolongation during chronic therapy.

Levorphanol is the levorotatory stereoisomer of the synthetic morphinan (dextrorotary isomer is the common cough suppressant dextromethorphan) and as such is an active morphine-like analgesic. It has the same properties as morphine with respect to the potential for habituation, tolerance, physical dependence, and abstinence syndrome. Its advantage in chronic pain is that it is 4–8 times more potent than morphine with a longer half-life. Its additional NMDA-antagonistic effects, similar to methadone, make it more effective for neuropathic pains.

Butorphanol is most closely structurally related to levorphanol with similar mu agonism, NMDA-antagonism effect. As such, it has favorable use in chronic pain and is available in injectable, tablet, and intranasal spray formulations. Transdermal fentanyl is not appropriate for acute pain, especially in the opioid naïve. There is a black box warning against its use in the acute setting due to the risk of severe respiratory depression from the delayed peak effect of the drug as the pain level decreases. It is intended for use in patients who are already tolerant to opioids of comparable potency.

Partial Opioid Agonists

There is a subset of opioid medications that are partial agonists and have SNRI activity. These drugs are tramadol and tapentadol. Sustained release formulations of these medications have been developed. These medications can be used in neuropathic pain, and also are useful in the elderly population where full mu agonism may not be tolerable.

Mixed Agonist/Antagonists

In the 1940s and 1950s there was an explosion of drug development in opioid medications. Hundreds of compounds were produced via either altering the parent molecule of morphine or creating de novo synthetic molecules. These compounds were then studied and it was found that some molecules had partial or full agonism at one receptor, while partial or full antagonsim at another receptor. These compounds were grouped into the mixed agonist/antagonist category. Use of the compounds requires a great understanding of opioid pharmacology. Their use can be particularly useful for managing side effects, pain management, and addiction medicine.

Buprenorphine is a partial mu agonist and kappa antagonist. The potential advantages are due to its partial mu agonism, partial or full agonism at ORL-1, and kappa antagonism. Therefore, theoretically, the risk of tolerance and dependence is decreased. Because this medication has a long half-life, it has been used in addiction medicine as well as pain management. Recently, a transdermal preparation gained FDA approval for use in chronic pain management up to 80 MEQs (morphine equivalents).

Nalbuphine is a kappa agonist and partial mu antagonist. It can be useful to treat opioid-induced itch. Many institutions rely on diphenhydramine to deal with pruritus, but because diphenhydramine has many receptor sites, it is not the ideal medication for the elderly—it is on the Beers Criteria list of drugs that should not be used in the elderly (age >65 years). Therefore, a more appropriate solution for these may be treatment with nalbuphine. This medication is also an analgesic, and interestingly has been seen to be more effective as an analgesic in women as compared to men.

Opioid-Related Side Effects

Many of the common side effects related to opioid use are well known. Respiratory depression, nausea, pruritus, constipation, urinary retention, altered mental status, and bradycardia can all be encountered with therapy. ‘As patients continue to take opioids, tolerance to these adverse acute side effects (except constipation and miosis) develops. The issues of tolerance, dependence, and addiction are the stages of physiologic and psychologic hijacking that occurs with prolonged opioid use.

- **Tolerance**: A state of adaptation in which in time more of the drug is required to achieve the same effect.
- **Dependence:** A state of adaptation demonstrated by withdrawals that occur with abrupt diminution of the concentration of the drug or administration of an antagonist.
- **Addiction:**
  1. Loss of control to the drug
  2. Compulsive use
  3. Continued use despite consequences/harm
  4. Craving
- **Pseudo-Addiction**: An iatrogenic condition in which the behaviors witnessed are consistent with addiction yet are caused by under-treated pain.

Although the effect of opioids on a plethora of tissues has been known, the long-term consequences of opioids are beginning to be realized. Exogenous opioid peptides suppress the hypothalamic–pituitary–adrenal (HPA) axis by influencing the release of hypothalamic corticotropin-releasing factors, contributing to hypocortisolism, hypothyroidism, and hypogonadism. The potential consequences of hypogonadism include decreased energy, mood, libido, and erectile dysfunction in men, oligomenorrhea or amenorrhea in women, and bone density loss or infertility in both sexes. One should thus monitor for hypogonadism in all chronic opioid patients.

Opioid-induced hyperalgesia is the phenomenon in which patients who are taking opioids for an extended period of time (of unknown duration) develop hyperalgesia. That is to say those events that were minimally painful before they were taking opioids now feel significantly more painful. It is a phenomenon that exists, but the degree to which it exists varies among individuals. Nonetheless, the notion that the very drugs we are using to attenuate pain are actually augmenting pain is provocative.

Table 24.11 Steroids used in pain management

Drug	Duration	Eqivalent dose (mg)	Half-life (h)	Relative anti-inflammatory potency	Relative mineralocorticoid activity
Cortisone	Short	25	8–12	+	++
Hydrocortisone		20	8–12	+	++
Prednisone	Intermediate	5	18–36	++	+
Prednisolone		5	18–36	++	+
Triamcinolone		4	18–36	++	0
Methylprednisolone		4	18–36	++	+
Dexamethasone	Long	0.75	36–72	++++	0
Betamethasone		0.75	36–72	++++	0

All steroids listed above can be used as injectables, except prednisone (oral only)

Interventional Pain Management

Interventional pain modalities may aid both the diagnosis and treatment of certain pain syndromes. If successful, interventions can alleviate the need for high-dose medication use and provide opioid-sparing effects, thereby sparing the patient from unwanted side effects. Common procedures to consider include epidural steroid injections, nerve blocks, and major joint injections.

Neural blockade as a diagnostic tool for painful disorders is particularly useful in chronic pain due to several characteristic features. By IASP definition, pain can be purely subjective with uncertain, or even nonexistent, pathophysiology. This particularly rings true with chronic pain. Emotional, financial, social, and even legal factors compound this complex and multifaceted condition. To clarify these perplexing clinical situations, diagnostic blocks can be attempted. The information gained may then provide guidance for medications, injections, ablative or even surgical options.

A differential neural block refers to the clinical phenomena that nerve fibers with different functions have different sensitivities to local anesthetics. In particular, fiber size is an important characteristic that governs its susceptibility. Graduated neuraxial (spinal or epidural) blockade using increasing concentrations of local anesthetics to selectively produce sympathetic, sensory, and motor blockade is the most commonly used differential nerve block. If pain relief occurs with a dilute local anesthetic concentration, sympathetically mediated pain is assumed. However, if pain persists despite a very concentrated solution with evidence of motor blockade, a more central or supratentorial origin of pain is considered. Likewise, should pain subside with placebo, psychogenic etiologies can be surmised. Alternatively, assessing a patient's response to pain after a concentrated block regresses, whether peripheral or neuraxial, can provide similar information. As such, differential neural blockade may provide distinction between sympathetic, somatic and psychogenic sources of pain.

Pharmacology

Two types of injectates are commonly used for pain procedures, local anesthetic and adrenocortical steroid (glucocorticoids). Local anesthetics produce varying degrees of neural blockade. Commonly used local anesthetics are lidocaine (1–2 %) and bupivacaine (0.25–0.5 %) in these concentrations as higher concentrations can be associated with neurotoxicity. To enhance speed of onset of action, lidocaine can be mixed with 0.9 % sodium bicarbonate (9:1 ml), while bupivacaine is not mixed with bicarbonate because of resulting precipitate formation. Epinephrine is generally not used in chronic pain procedures, as it could exacerbate sympathetic-mediated pain.

Glucocorticoids, triamcinolone or methylprednisolone (long-acting depot preparations), are commonly used in interventional pain medicine (Table 24.11). They reduce inflammation by stabilizing leukocyte membranes, decreasing activity of irritating nerves, decreasing edema, and reducing scar formation. Our practice is to limit interlaminar epidural steroid injections of 80 mg of MPA or equivalent to four times per year on average. It is important to know that steroids can suppress the hypothalamic–pituitary–adrenal axis for 2–4 weeks. In addition, all glucocorticoids have systemic effects, but the degree of systemic effects in neuraxial pain procedures is quite variable. Patients with diabetes or hypertension should be informed of increased values in their diseases and take appropriate measures to manage this. Rare but serious complications such as open angle glaucoma or avascular necrosis can and have occurred.

Neurolytics are commonly used in patients with cancer pain, and produce long-lasting neurolysis. The commonly used neurolytics are alcohol (50–95 %) and phenol (6–10 %). Phenol acts as an anesthetic at lower concentrations, is more viscous, is less painful upon injection than alcohol, and is hyperbaric to cerebrospinal fluid (sinks down). It causes demyelination and protein coagulation. Alcohol is hypobaric in cerebrospinal fluid (floats on top), and is more painful

upon injection. It extracts phospholipids and cerebrosides from neural tissue resulting in neural damage. Neurolysis of peripheral nerves with cutaneous sensory distribution can result in neuropathic pain, and is hence avoided.

Imaging

There are several means to image the progress of needle insertion or medication administration. Fluoroscopy is widely used for office-based and surgical procedures. Ultrasound use in pain management has increased in the last few years and will have a stronghold in pain management because of its ease of use and lack of radiation exposure. Certainly it is a useful tool that can decrease the time it takes to perform blocks; however, whether ultrasound use adds safety is under current review. In some procedures, it can provide an extra margin of safety showing soft tissue structures such as vasculature and nerves, where fluoroscopy cannot, and may turn out to be a superior means of performing regional anesthesia over landmark or nerve stimulation techniques. Other advanced imaging techniques include CT scan and MRI.

Procedures

The following is a list of common procedures that pain management physicians can perform. There are variations to all of these procedures, and this list is by no means comprehensive. Patients should be informed of the risks, benefits, and alternatives to these procedures and informed consent must be retained.

Epidural Steroid Injections

The anatomy of the epidural space and spinal cord is described in previous chapters. Epidural steroid injections (ESIs) are performed under fluoroscopic guidance. A steroid, and may be a local anesthetic, is placed in the epidural space near the nerve roots. The local anesthetic relieves pain immediately, while the steroid reduces inflammation in 12–48 h. Local anesthetics are not used for cervical epidurals. An epidural steroid injection may provide relief for up to 3 months. If the pain is not relieved, or partially relieved, the epidural steroid injection may be repeated in 2–4 weeks.

Indications of epidural steroid injections include treatment of pain radiating in the distribution of spinal nerves, spinal stenosis, neurogenic claudication, and discogenic back pain. Varieties of ESI include:

- Interlaminar approach: This is performed under fluoroscopy for cervical, thoracic, and lumbar spine using the loss of resistance technique (Fig. 24.3). If a prior laminectomy has been performed at that vertebral level, this approach should not be used because of lack of reliable landmarks. For these instances, a transforaminal or caudal approach should be used to limit the risk of dural puncture.
- Transforaminal approach: This is performed most commonly for the lumbar spine (Fig. 24.4). The transforaminal approach has a greater chance of delivering injectate to the anterior epidural space, which is the site of presumed pathology in disc herniations. Cervical and thoracic transforaminal injections are not commonly used as they have high complication rates.

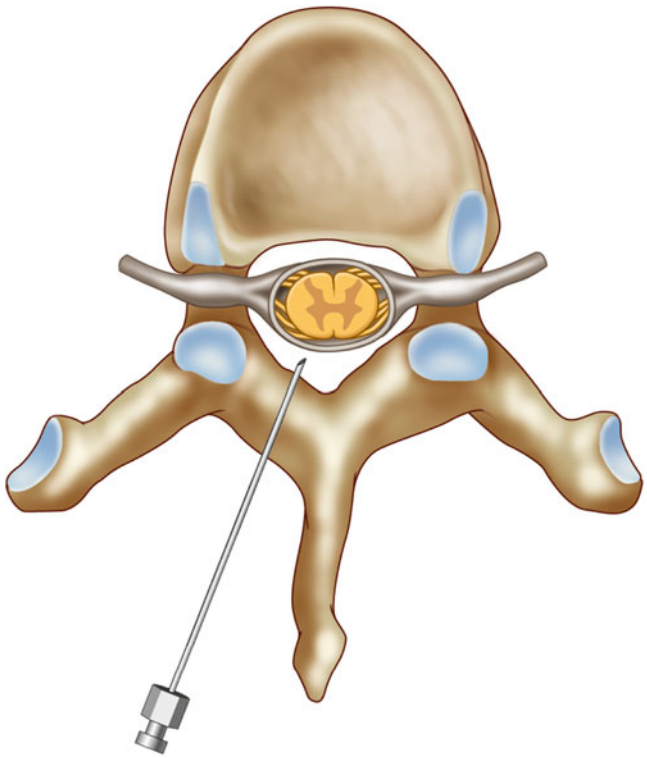

Fig. 24.3 Interlaminar epidural steroid injection

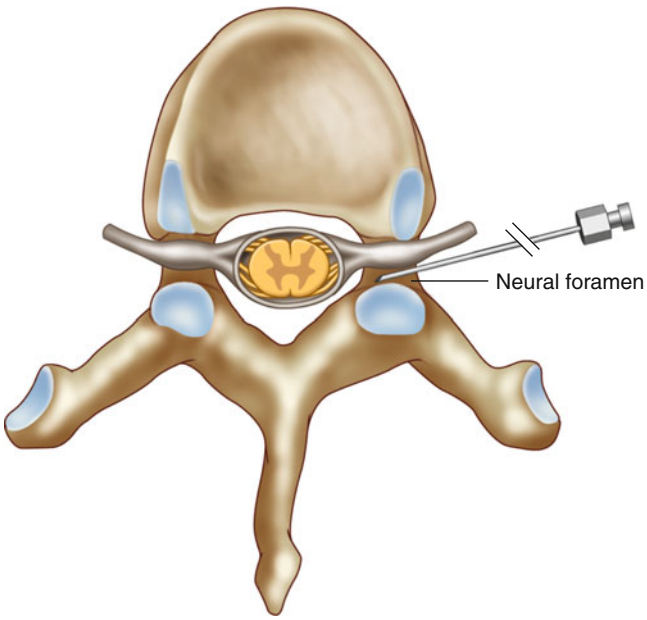

Fig. 24.4 Transforaminal epidural steroid injection

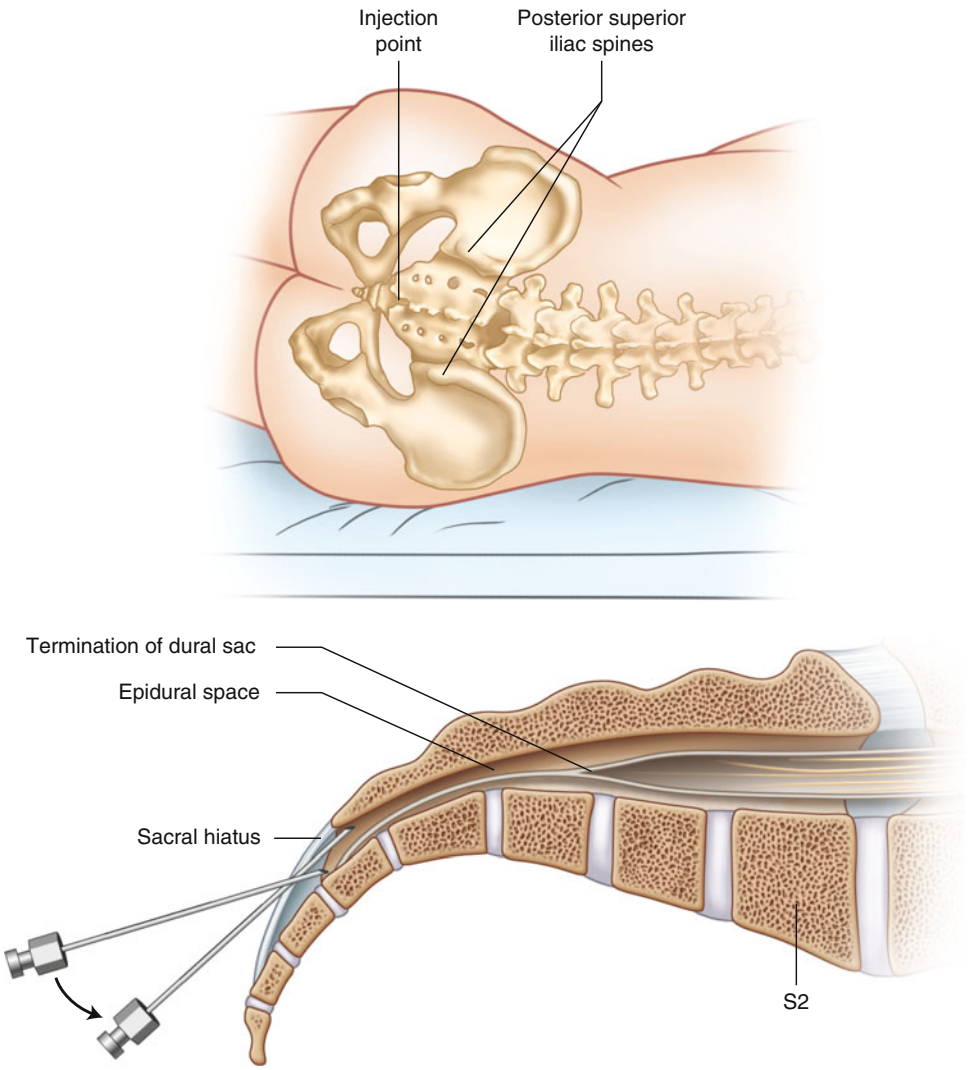

Fig. 24.5 Landmarks for caudal epidural injection

- Selective spinal nerve blocks: or selective nerve root blocks are used as a diagnostic procedure to determine if a specific root level is the source of pain.
- Caudal approach: This is performed for injecting the local anesthetic/steroids via the caudal approach (Fig. 24.5). This approach is generally considered safe.

Facet Joint Blocks

Medial Branch Nerve Blocks

Degenerative changes occur in the spine with age, which lead to loss of cushioning effect provided by the intervertebral disc. As a result the facet joints bear more weight and become hypertrophied and painful. Medial branch nerve blocks (MBB) are diagnostic blocks (local anesthetic, or with a steroid), and if they provide relief, are followed by radiofrequency lesioning (destruction) of the medial branch nerves.

Intra-articular Facet Blocks

Facet injections involve injection of a local anesthetic and/or steroid inside the diarthrodial facet joint (Fig. 24.6). With the patient in the prone position the facet joint is localized using fluoroscopy. A 4–5 in. 22/25G spinal needle is inserted into the desired facet joint in the spine. The position of the needle is confirmed by fluoroscopy, and by injection of contrast medium. This is followed by injection of the drugs.

Sacroiliac Joints

Sacroiliac Joint Injections

Degenerative changes of the sacroiliac joint are a common cause of axial back pain, especially in the elderly population. Imaging of the joint is not accurate in determining these changes, and tenderness to palpation over the sacroiliac joint may be the single most accurate exam. For severe pain, a diagnostic or therapeutic block can be performed as necessary or

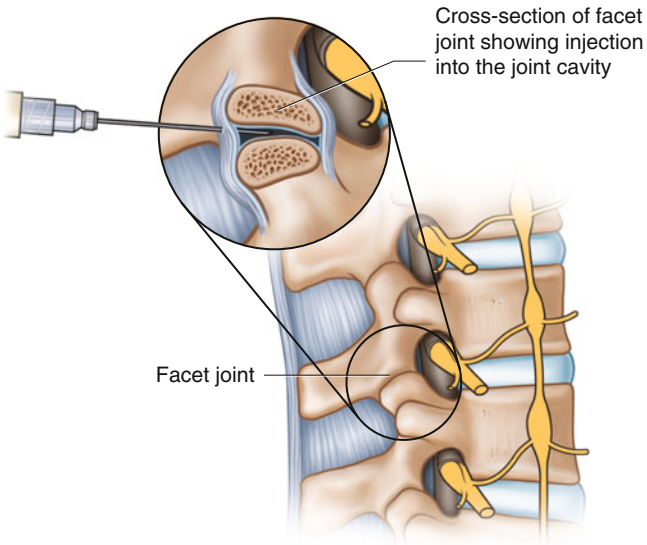

Fig. 24.6 Facet joint injection

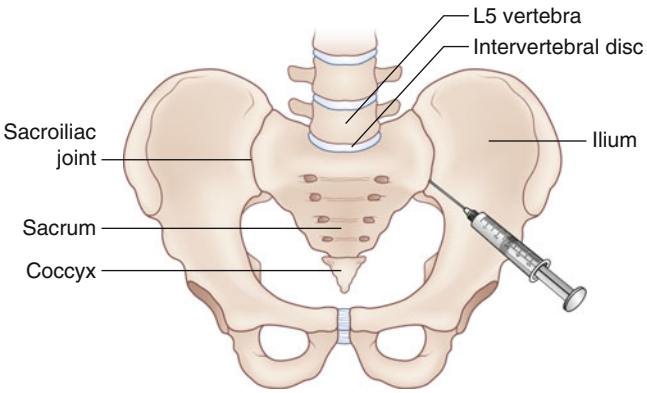

Fig. 24.7 Sacroiliac joint injection

alternatively radiofrequency lesioning of the joint can be performed. To perform the block, the patient is placed in the Sims position with the pelvis rotated (Fig. 24.7). A syringe is filled with contrast medium, and is then attached to a 22G spinal needle with an extension tubing. The spinal needle is inserted and advanced through the skin, capsule, and ligaments until it is introduced into the joint. The needle location is confirmed by injection of 1 ml of contrast (the joint is outlined as viewed under fluoroscopy). The drugs are then injected (lidocaine or bupivacaine with/out corticosteroid).

Radiofrequency Lesioning

Conventional radiofrequency lesioning (RFL) is mostly used for the treatment of axial back pain produced by facet arthropathy and sacroiliac joint arthropathy. Prior to RFL a diagnostic block is performed (pain relief of greater than 50–75 %). RFL consists of causing permanent damage to the nerve. The tissue is exposed to a current from an active electrode, which generates heat. Thermal injury occurs by exposing the nerve to a temperature of 80°C (cessation of neural functions occurs at 42.5–44 °C). The therapeutic effect of RFL lasts for about 6 months, after which the destroyed nerve tissue tends to regenerate.

Alternatively pulsed RFL can be used, which does not involve heating and hence avoids tissue damage. Pulsed RFL can be used on peripheral nerves, ganglions (dorsal root, Stellate ganglion, Gasserian), and intervertebral discs. The exact mechanism of how pulsed RFL works is not known. Pulsed RFL causes voltage fluctuations and generates low temperatures that do not damage cells, causing possible inhibition of the synaptic activation of C-fibers in the dorsal horn neurons.

Cryoablation

Cryoablation (or cryoneurolysis) is a process in which extreme cold is used to produce analgesia, by freezing or disrupting conduction through a peripheral nerve. A diagnostic injection with a local anesthetic must be performed first to ensure that neurolysis of the nerve can successfully address a patient's pain complaint. If an adequate response is obtained, a cryoprobe is inserted near the nerve in question to provide focused cryogenic freezing at the tip and the surrounding tissues. As such, meticulous placement of the cryoprobe near the nerve is essential, and is often times aided by imagery or nerve stimulation. This targeted nerve disruption may provide an analgesic effect for weeks to months without true damage (cell body death) to the frozen structures. Wallerian nerve degeneration is induced but without disruption of the endoneurium, perineurium, and epineurium such that nerve regeneration readily occurs. As such, cryoablation is typically deemed safer than RFL in that it is less likely to produce subsequent neuroma formation, hyperalgesia syndrome, or deafferentation pain. Common neuropathies that respond well to cryoablation include ilioinguinal, iliohypogastric, intercostal, and occipital neuralgias.

Sympathetic Ganglion Blocks

Sympathetic Nervous System Anatomy

The cell bodies of the preganglionic nerve fibers of the sympathetic nervous system arise from T_1–L_2. The sympathetic chain is comprised of ganglia containing the cell bodies of sympathetic postganglionic fibers, which are located on both sides of the vertebral column. The cervical sympathetic ganglia include the superior, middle, and inferior cervical ganglia. The stellate ganglion is formed by fusion of the inferior cervical ganglion with the first thoracic ganglion, and provides sympathetic innervation of the head, neck, and upper limbs. Eleven sympathetic ganglia lie in the thoracic region juxtaposed to the necks of the ribs. Sympathetic innervation of the abdominal viscera is supplied by the celiac plexus. Sympathetic blocks are used in the diagnosis and

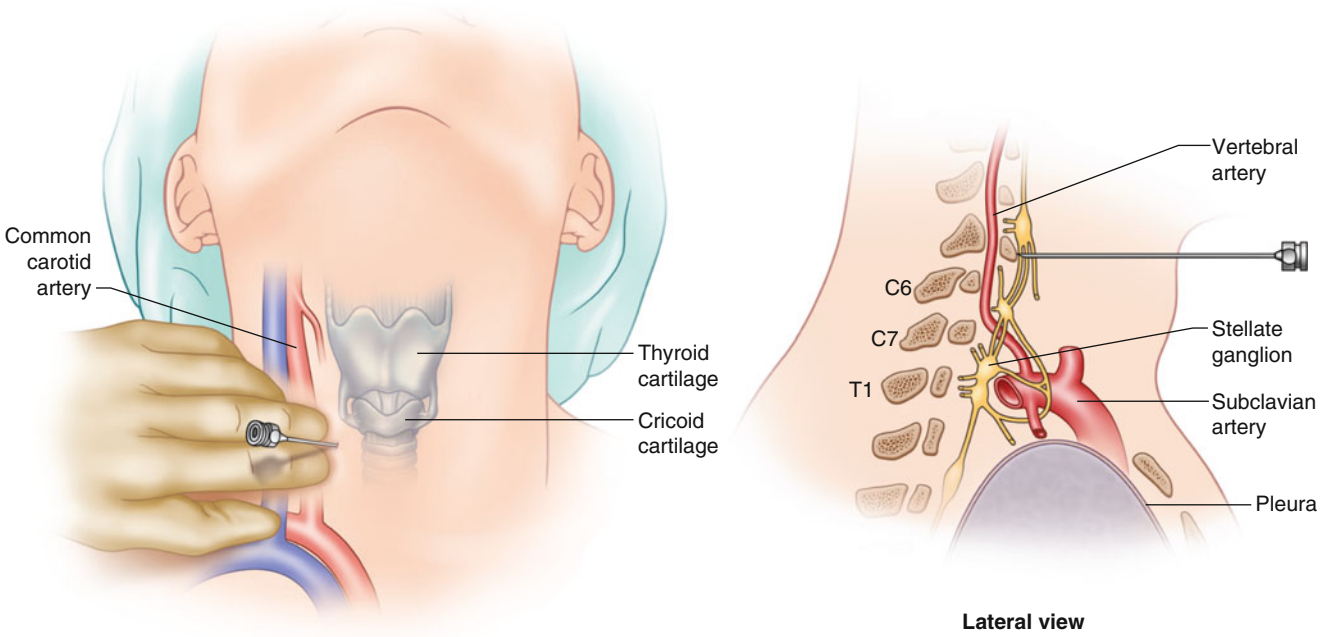

Fig. 24.8 Stellate ganglion nerve block

treatment of pain that is mediated by the sympathetic nervous system. A successful sympathetic block will lead to an increase in temperature of the limb by at least 1–2 °C or loss of sweating.

Cervical Sympathetic Block/Stellate Ganglion Block

Stellate ganglion blocks (Fig. 24.8) are performed under fluoroscopy for intractable pain, vascular spasm (Raynaud's phenomenon), and hyperhidrosis of the head, neck, and upper extremity. The stellate ganglion lies at the level of C_7 in front of the neck of the first rib, with the vertebral artery passing over it. Complications of stellate ganglion block include Horner's syndrome with nasal congestion, intravascular injection, difficulty swallowing, vocal cord paralysis, epidural spread of local anesthetic, and pneumothorax.

The patient is positioned supine with a roll under the shoulder for extension of the head and neck. At the level of the cricoid cartilage, the sternocleidomastoid muscle is retracted laterally and the transverse process of the C_6 is palpated (Chassaignac's tubercle). A 22–25G 1.5 in. needle is directed caudally and medially toward the junction of the lateral portion of C_7-T_1. Once bone is encountered, the needle is withdrawn by 1 mm and 1 ml of contrast dye is injected under fluoroscopy. Following this, 3–5 ml of local anesthetic is injected.

Celiac Plexus Blocks

Celiac plexus is a network of ganglia, which includes the celiac ganglia, superior mesenteric ganglia, and the aorticorenal ganglia. This plexus is located at the T_{12}–L_1 level, anterior to the aorta, epigastrium, and crus of the diaphragm, and supplies the sympathetic innervation to the abdominal viscera. Celiac plexus blocks are indicated for diagnosis and treatment of pain from visceral structures innervated by the celiac plexus. These viscera include pancreas, liver, gallbladder, omentum, mesentery, and alimentary tract from the stomach to the transverse colon. Neurolytic celiac plexus blocks (phenol, alcohol, or radiofrequency ablation) are indicated as a palliative measures for intractable pain from upper abdominal malignancies, such as pancreatic carcinoma. Complications of celiac plexus block include hypotension (most common), pneumothorax, puncturing of the kidneys, bleeding (puncturing of the aorta or vena cava), and damage of the artery of Adamkiewicz causing paraplegia.

With the patient in the prone, lines are drawn connecting the spine of T_{12} with points 8 cm lateral at the edges of the 12th ribs. A 5 in. 22G needle is first placed on the left side, as the aorta is a helpful landmark to assist with correct placement (Fig. 24.9). The needle is advanced on the previously drawn line at an angle of 45° toward the body of T_{12} or L_1. Once the bone is contacted (7–9 cm depth), the needle is withdrawn slightly, and reinserted at an increased angle of 5–10° so that the tip slides off the vertebral body anterolaterally. The needle is further advanced another 2 cm past the original insertion depth. Aortic pulsations can be felt as they are transmitted along the needle when it is correctly placed. The procedure is repeated on the right side. After injection of contrast dye to confirm the needle position, and negative aspiration (blood, urine, CSF), a diagnostic block (10–20 ml of local anesthetic), or a neurolytic block (phenol, alcohol), can be performed.

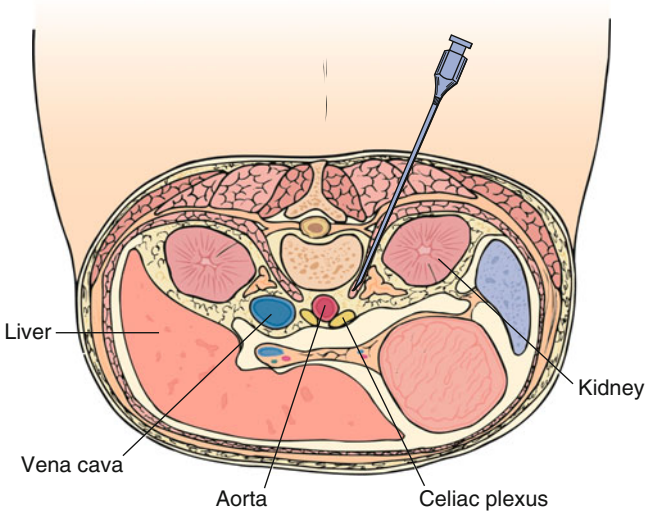

Fig. 24.9 Celiac plexus block

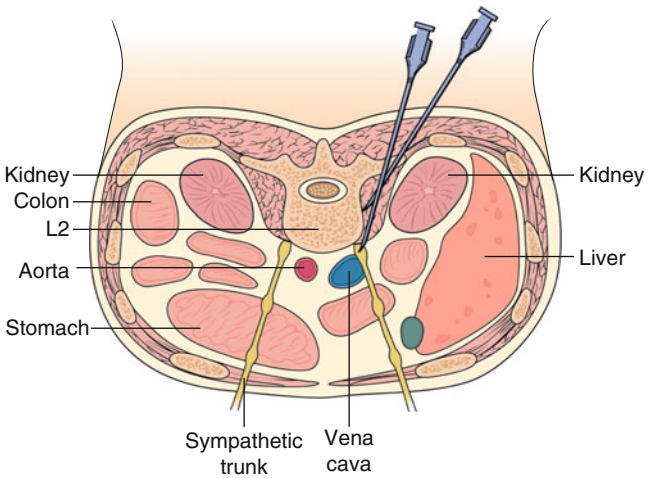

Fig. 24.10 Lumbar sympathetic block

Lumbar Sympathetic Blocks

Lumbar sympathetic blocks are performed for sympathetic mediated and neuropathic pain conditions. The lumbar sympathetic chain is located along the anterolateral border of the lumbar vertebral bodies. Blockade of the second and third ganglia results in close to complete sympathectomy of the lower limb. The patient is positioned prone and the spinous process of L_2 and L_3 is identified and marked (Fig. 24.10). A horizontal line is drawn through the midpoint of the L_2 interspace and extended 5 cm to the right and left of midline. Fluoroscopy is also used to identify the L_2 transverse process and vertebral body. A 20G 5 in. needle is inserted at an angle of 30–45° on each side (bilaterally), 5 cm lateral to L_2 spinous process, and advanced until it is 1–2 mm posterior to the vertebral body. After contrast media is injected to confirm the needle position, about 15–20 ml of local anesthetic is injected. Successful block is indicated by vasodilation and temperature rise in the involved lower limb.

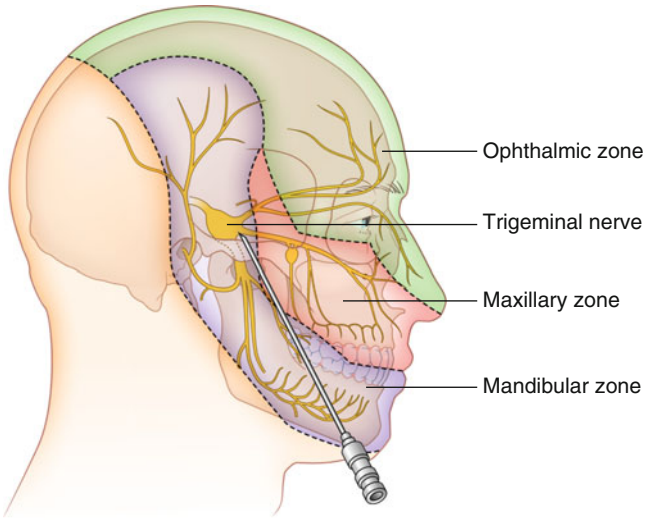

Fig. 24.11 Trigeminal nerve block

Complications of this block include blockade of L_2 somatic nerve root (most common), inadvertent injection into the subarachnoid space, epidural space, or intravascular (vena cava, aorta, lumbar vessels), infection, retroperitoneal hematoma, sympathectomy-mediated hypotension, and failure of ejaculation after a bilateral block.

Hypogastric Plexus Block

Hypogastric plexus blocks are performed for diagnosis and treatment of pain from pelvic viscera and pelvic malignancies. The superior hypogastric plexus, which lies over the aortic bifurcation and anterior to the L_5 vertebral body, is targeted. Bilateral or unilateral, diagnostic, or neurolytic blocks can be performed.

Ganglion Impar Block

The Ganglion Impar represents the termination of the sympathetic chain and rests anterior to the sacrococcygeal junction. This block is done for coccydynia (tail bone pain), perirectal pain, or neurolytic pain from malignancy. Advantage of performing the Ganglion Impar block over other neurolytic procedures for rectal pain is that the bowel and bladder functions are generally spared.

Peripheral Nerve Blocks

Single injections, with local anesthetics and/or steroids), can be used to block peripheral nerves. They can be used both for diagnosis and treatment of chronic pain conditions. Examples for peripheral nerve blocks include:

- Trigeminal nerve block: for trigeminal neuralgia (Fig. 24.11)
- Greater and Lesser occipital nerve blocks: for occipital headache or neuralgia (Fig. 24.12)
- Cervical plexus block (superficial and deep plexus blocks): to providing analgesia to the head and neck

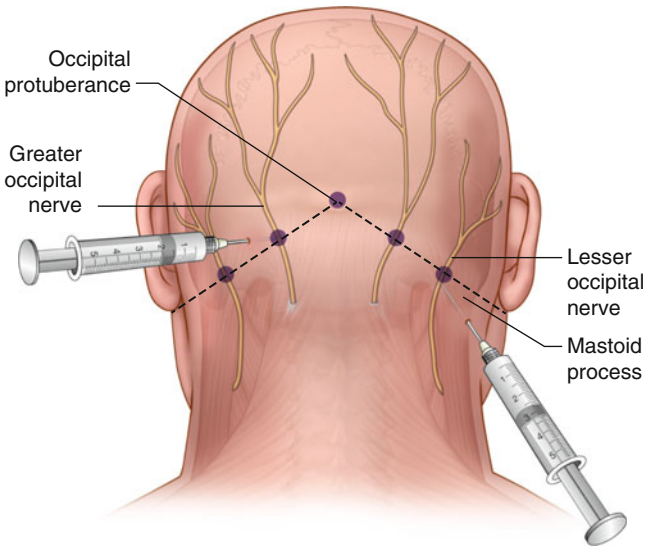

Fig. 24.12 Occipital nerve block

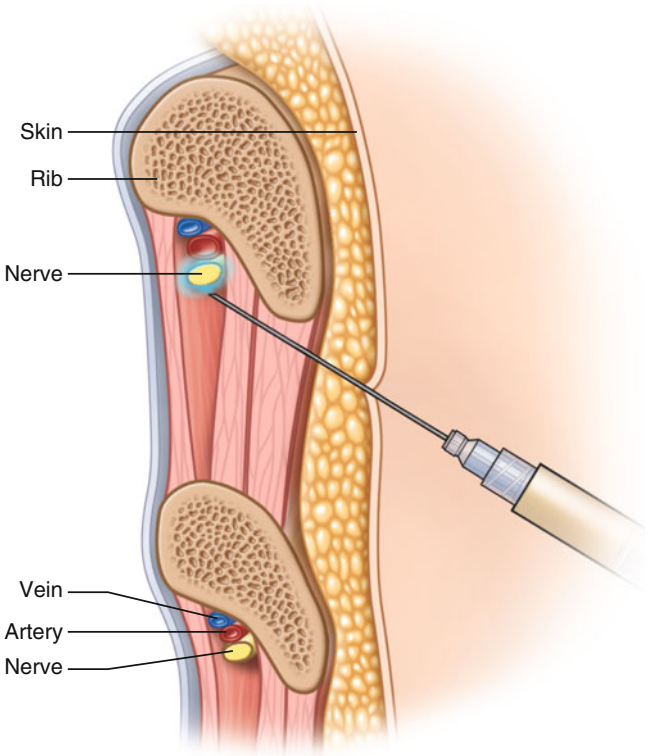

Fig. 24.13 Intercostal nerve block

region, for surgeries such as carotid endarterectomy and thyroid surgeries, and for pain from trauma, CRPS, and neuropathic pain

- Suprascapular nerve block: for shoulder pain from arthritis or adhesive capsulitis
- Intercostal nerve blocks: for neuropathic chest pain secondary to post-thoracotomy syndrome, post-herpetic neuralgia (Fig. 24.13)

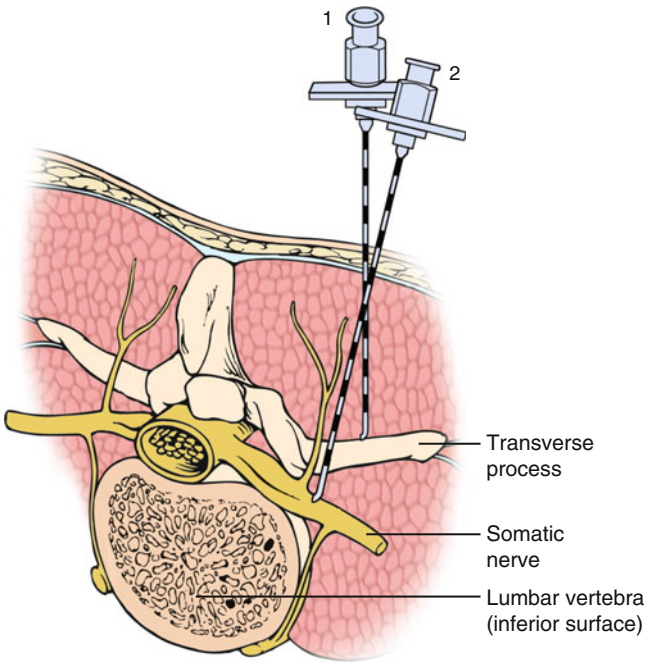

Fig. 24.14 Paravertebral nerve block

- Paravertebral nerve block: for postoperative and surgical analgesia for breast, thoracic, renal and abdominal surgeries, fractured ribs, and post-herpetic neuralgia. Advantages include avoidance of thoracic epidural injection, low risk of pneumothorax, and multiple level of analgesia with a single injection. A 10 cm 22 G Tuohy spinal needle is inserted perpendicular to the skin, 2.5–3 cm from the spinous process. Care should be paid to avoid medial needle direction (risk of epidural or spinal injection). Once the transverse process is contacted, the needle is withdrawn to the skin and redirected superior or inferior to walk off the transverse process. The aim is to insert the needle to a depth of 1 cm past the transverse process (Fig. 24.14)
- Lateral femoral cutaneous nerve block: for treating meralgia paresthetica (field block with the local anesthetic injected 1 in. medial and 1 in. inferior to the anterior superior iliac supine, deep to the fascia—Fig. 24.15)
- Ilioinguinal and Iliohypogastric nerve blocks: for treating ilioinguinal neuropathy secondary to post-herniorrhaphy or post-laparoscopic trocar pain. For ilioinguinal nerve block (Fig. 24.16), the 25G 1.5 in. needle is inserted 2 in. medial and inferior to the anterior superior iliac spine, directed toward the symphysis pubis to enter the external oblique fascia. For the iliohypogastric block the needle entry point is 1 in. medial and below the anterior superior iliac spine.
- Genito-femoral nerve block: for post-hernia or scrotal pain.
- Pudendal nerve (S_{2-4}) block: (transvaginally or transperineally) for chronic pelvic or perineal pain secondary to pudendal nerve entrapment or compression by sacrospinous ligament.

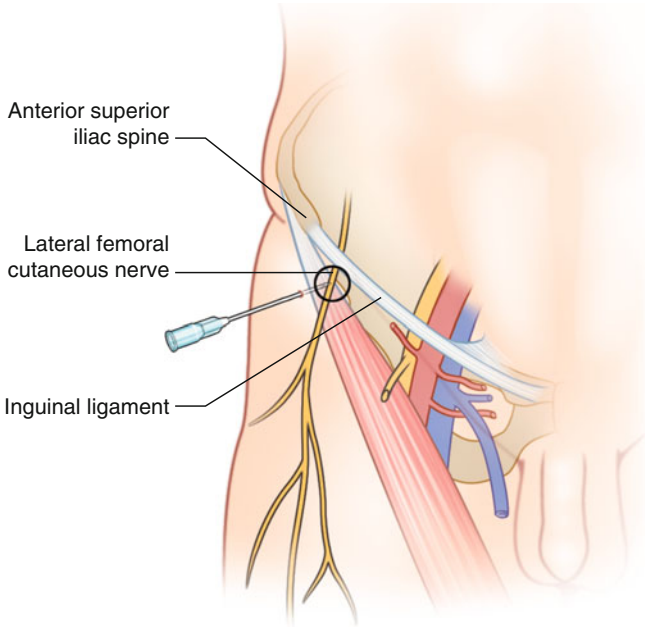

Fig. 24.15 Lateral femoral cutaneous nerve block

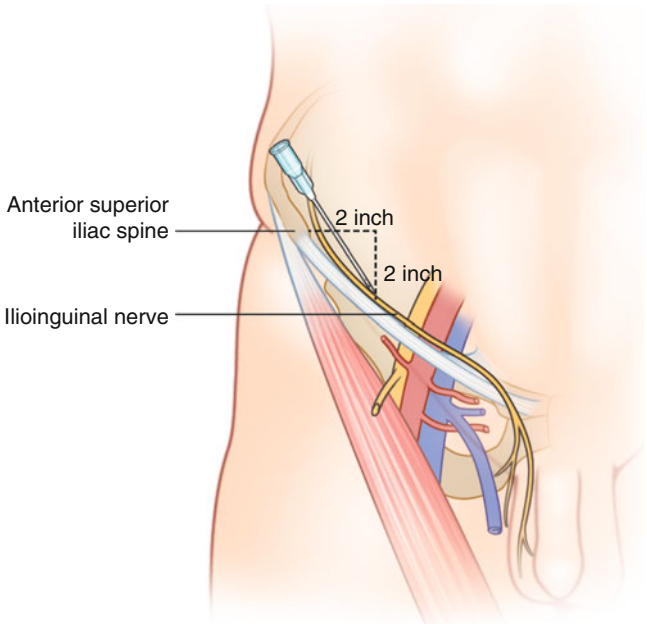

Fig. 24.16 Ilioinguinal nerve block

Implantable Therapies

If the therapies described above do not provide adequate pain relief, then indwelling and implantable devices can be inserted, which provide a longer duration of pain relief. These devices are inserted in patients with refractory pain (malignant or nonmalignant pain) who are not candidates for surgical approach, have not responded to oral medications, or are intolerant of certain side effects of the medications. However, it is important to know that these devices have associated risks of infection, bleeding, and malfunction. Therefore, before proceeding with these therapies a thorough evaluation and discussion with the patient is absolutely necessary.

Kyphoplasty

In the United States, about 700,000 osteoporosis-related vertebral compression fractures occur annually. Pathologic fractures can also occur as the spine is a common site for tumor metastasis. The two common treatment options for painful compression fractures include vertebroplasty and vertebral body augmentation (or balloon kyphoplasty-additional benefit of height restoration). Both therapies involve percutaneous placement of polymethylmethacrylate cement via cannulas into the vertebral body, so as to fill and stabilize the fracture. Vertebral body augmentation involves an additional step of inflating a balloon prior to cementing, and as such this reduces the fracture and restores body height (increases the distance between end plates). When the balloon is deflated, it leaves a bone void for the cement (Fig. 24.17). The procedure provides immediate pain relief, and is usually performed under general anesthesia. It takes about 1 h/fracture with little or no postoperative rehabilitation necessary.

Indwelling Epidural Catheters

Epidural catheters are inserted and then tunneled subcutaneously for stability. A port-a-cath can be inserted subcutaneously, which is attached to the epidural catheter. Epidural catheters are usually used in patients who are too frail (cancer patients) to withstand invasive procedures and have a limited amount of time to live. Risk of infection increases with time. Intrathecal catheters are not currently FDA approved, as complications from spinal microcatheters occurred in the 1990s.

Intrathecal Infusion Pump Implantation

A spinal catheter is inserted and then tunneled subcutaneously. It is then attached to a programmable pump, which is inserted in a pocket created, commonly, on the anterior abdominal wall. Since these pumps are programmable, dosing changes can easily be done. Implanted intrathecal pumps require significant maintenance and coordination with patients. They can be refilled every 2–4 months depending on the flow rate. Complications of these pumps include mechanical problems with the pump, infection, bleeding, and human dosing errors that can lead to overdose or withdrawals.

Dorsal Column and Deep Brain Stimulation

Spinal cord stimulation may be a treatment option for patients who suffer from chronic extremity or back pain. It involves electrical stimulation of the CNS or peripheral nerves. Electrodes are implanted epidurally, along peripheral nerves (median, radial, sciatic, tibial, peroneal, ilioinguinal, occipital nerves), or along the sacrum for pelvic/bladder

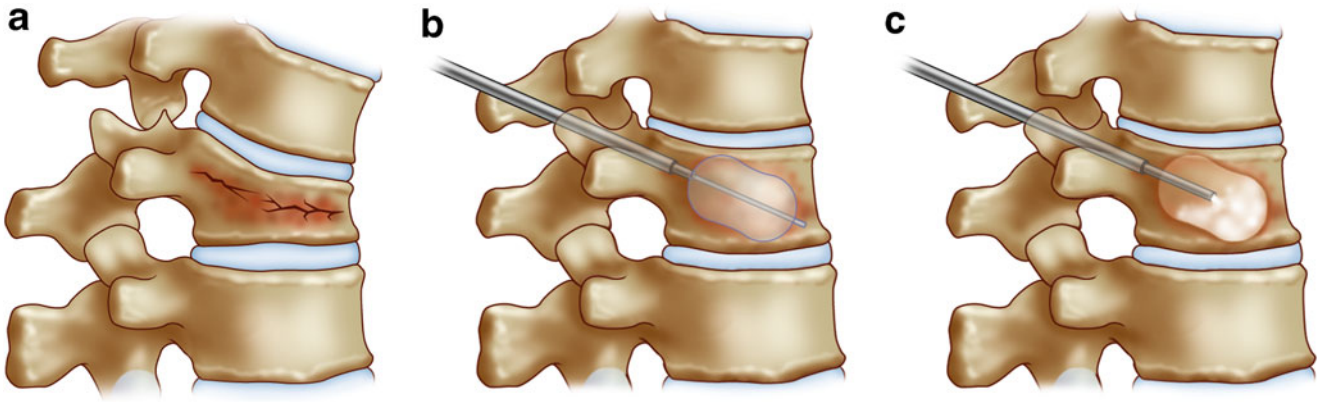

Fig. 24.17 Kyphoplasty. (**a**) Fractured vertebra, (**b**) insertion of a balloon, (**c**) injection of cement

pain. Deep brain stimulation is sometimes used by neurosurgeons for central pain syndromes.

Psychological Approach

Coexisting psychological problems including depression, anxiety, mood disorders, personality disorders, and history of abuse are commonly associated with chronic pain. Substance abuse is particularly high in chronic pain patients and can interfere with pain management strategies. The psychological assessment and treatment includes hypnosis and visualization, guided imagery, biofeedback, cognitive behavior therapy, group therapies, and family therapy.

Rehabilitation

Rehabilitation strategies are an important tool for the successful management of chronic pain. Focused therapies are directed at the injured part of the body. These therapies include the use of modalities such as application of heat/cold compresses, stretching, exercising, work conditioning, and strength training. Patients may have individual and group therapies so as to improve compliance.

Complementary/Alternative Medicine (CAM)

Patients take more non-prescribed therapeutics than prescribed therapeutics. Many patients advocate for the use of naturopathic and homeopathic treatments and this should not be condemned by allopathic medicine. There may be benefit to these remedies; however the evidence often is lacking. Sometimes, there are risks with these therapies, and these must be considered when creating a pain management plan.

Common and Unique Complaints and Syndromes

In the following sections, we will highlight some of the most common and unique complaints and syndromes in pain management. By no means is this list comprehensive as pain physicians see a wide gamut of pain conditions and complaints.

Myofascial Pain

Myofascial pain syndrome (MPS) is a common cause of chronic somatic pain involving a single muscle or a muscle group seen after injury, strain, or repetitive use. It is characterized by regional pain (aching, deep, steady pain) associated with focal point tenderness, "trigger points" with reproduction of a referred pain pattern, and limited range of motion of the affected muscle. This is distinct from fibromyalgia in which there is widespread, generalized pain with its associated tender points. Imaging, though helpful to rule out other causes of pain, does not play a role in chronic myofascial pain syndromes. Diagnosis is confirmed on physical examination with the presence of "trigger points" within tight, ropy bands in affected skeletal muscles. A positive "jump sign" is often elicited whereby the patient jumps away during palpation of a trigger point.

The first-line treatment for myofascial pain is physical therapy emphasizing restoration of muscle strength and elasticity. Massage therapy, ultrasound therapy, TENS, and acupuncture may provide additional myofascial benefits as can occupational workstation assessments focusing on proper ergonomics. Trigger point injections with local anesthetics (and usually corticosteroids) can provide analgesia, while at the same time confirming the diagnosis and assisting with functional rehabilitation. Some experts believe that "dry-needling" is equally important as infiltration during trigger point injections to release the muscle contraction knots. Furthermore, "dry-needling" that elicits a local twitch response (LTR) indicates proper needle placement into the trigger point and thus should improve treatment outcome. Drugs that can be used to mitigate the pain include antidepressants (SNRIs), pregabalin, or baclofen.

Low Back Pain

The most common chronic pain complaint in the pain clinic is low back pain. It is second most common neurological complaint, headache being the most common. Back pain accounts for millions of primary care physician visits annually, and is a leading factor in disability and lost productivity.

Table 24.12 Causes of back pain

• Back muscle sprain or strain
• Injured or torn ligament in the back
• Degenerative changes in intervertebral discs due to aging
• Spondylolisthesis (anterior or posterior displacement of a vertebra or the vertebral column in relation to the vertebrae below)
• Lumbar spinal stenosis, sciatica and scoliosis
• Coccydynia or tailbone pain
• Sacroiliac joint dysfunction (the joint where the spinal column attaches to the pelvis)
• Osteoarthritis, rheumatoid arthritis
• Vertebral fracture from osteoporosis
• Spondylitis (inflammation or infection)
• Tumor
• Trauma
• Poor posture
• Excessive weight

People between the ages of 30–50 years are commonly affected, with the incidence equal in men and women. Up to 80 % of adults will experience at least one significant episode of low back pain in their lifetime. Back pain can be acute or chronic (pain lasting more than 3 months). Acute back pain is usually due to trauma or arthritis, while chronic pain is progressive and the etiology is difficult to determine. Causes of back pain are listed in Table 24.12.

Assessment and Diagnosis

Every attempt should be made to correctly diagnose back pain. If the cause of the back pain is known, such as a tumor, infection, or a radiculopathy, it should be treated. Radiculopathy is a condition where a set of nerves roots has a neuropathy and results in pain, weakness, numbness, or difficulty controlling specific muscles. Back pain is labeled as nonspecific when all red flag or serious conditions have been ruled out. Patients with chronic back pain are about six times more likely to have depression, and patients with depression are twice as likely to develop back pain.

Evaluation of patient with back pain begins with a thorough medical history and physical examination. The patient is inquired about any history of previous episodes or any health conditions that might be related to the pain. The characteristics of the pain are inquired, its onset, site, severity, duration, and any limitations in movement. Patients with lumobosacral radiculopathy can be tested with the straight-leg test (Lasegue's test). The test consists of passive hip flexion with knee extended, with passive ankle dorsiflexion. This maneuver causes traction of L_4, L_5, and S_1 nerve roots, and provokes radicular pain extending past the knee in the elevated leg. Another test, the crossed straight-leg, is a more specific test, where lifting the asymptomatic leg provokes radicular pain in the symptomatic leg. Other tests include the lumbar quadrant test for diagnosing facet arthropathy, and the FABER or Gaenslen's tests for diagnosing sacroiliitis.

There are several imaging techniques that can diagnose low back pain. These include lumbosacral *radiography* (good for diagnosing fractures, but not for intervertebral disc herniation), *discography* (injected dye into the spinal disc outlines the damaged areas), *myelograms* (injected contrast dye into the spinal canal, allowing visualization of spinal cord and nerve compression caused by herniated discs or fractures), *CT scans* (disc rupture, spinal stenosis), and *MRI* (bone degeneration, injury, or disease in tissues and nerves, muscles, or ligaments). Other tests include *electromyography* (assesses electrical activity in a nerve and can detect if that results in muscle weakness results), nerve conduction studies, evoked potential (EP) studies, *bone scans* (disorders of the bone), and *ultrasound imaging* (tears in ligaments, muscles, tendons, soft tissue masses in the back).

Treatment

Acute low back pain is usually self-limiting and resolves with medical therapy, without intervention. Chronic pain is usually progressive and the etiology for nonspecific back pain is difficult to determine. Weight loss, proper posture, avoiding straining, or lifting heavy weights can prevent back pain. Back pain can be treated as follows:

- Medications: opioids/non-opioids: ibuprofen, antidepressants (SNRIs), anticonvulsants, and topical agents
- Interventional therapies: (1) epidural local anesthetic (with steroids) blocks, or injection of agents into soft tissues, joints, or nerve roots, (2) spinal cord stimulation, (3) transcutaneous electrical nerve stimulation (TENS), where a battery-powered device sends mild electric pulses along nerve fibers to block pain signals to the brain
- Psychological: biofeedback, stress reduction, yoga. In biofeedback the patient is trained to gain control over certain bodily functions, including muscle tension, heart rate, and skin.
- Rehabilitative: (1) physiotherapy, cold (initially) and then warm compresses, bed rest for 1–2 days, and then exer-

cises to build back muscle strength, if tolerated, (2) s*pinal manipulation* to restore back mobility
- Alternative therapies: acupuncture
- Minimally invasive treatments to seal fractures: (1) Vertebroplasty: a glue-like epoxy is injected into the vertebral body, which quickly hardens to stabilize and strengthen the bone and provide immediate pain relief, (2) Kyphoplasty: prior to injecting the epoxy, a special balloon is inserted and gently inflated to restore height to the bone and reduce spinal deformity.

If the above procedures do not provide relief, then surgery may have to be undertaken. Following is a list of surgical procedures that can be performed: *Discectomy* to remove pressure on a nerve root from a bulging disc or bone spur; *Foraminotomy* to enlarge the *foramen* where the nerve root exits the spinal canal; *IntraDiscal Electrothermal Therapy* to use thermal energy (heat) via a needle inserted into the disc to treat pain resulting from a cracked or bulging spinal disc; *Nucleoplasty (*or plasma disc decompression), to use radiofrequency energy to create a plasma field in the disc that removes tissues and decompresses the nerve; *Radiofrequency lesioning* to cause destruction of nerves by using electrical impulses; *Spinal fusion* to strengthen the spine and prevent painful movements, where the disc(s) between two or more vertebrae are removed and the adjacent vertebrae are "fused" by bone grafts or metal devices; *Spinal laminectomy* (spinal decompression), where the lamina is removed to increase the size of the spinal canal and relieve pressure on the spinal cord and nerve roots; *Rhizotomy* to cut the nerve root to block nerve transmission; *Cordotomy* to cut *the* bundles of nerve fibers on one or both sides of the spinal cord to stop transmission of pain signals to the brain, and *Dorsal root entry zone operation* to destroy the pain transmitting spinal neurons.

Complex Regional Pain Syndrome

Complex Regional Pain Syndrome (CRPS) is a unique syndrome of unclear etiology, characterized by neurogenic inflammation, nociceptive sensitization, vasomotor dysfunction, and maladaptive neuroplasticity. CRPS usually begins in the arm or leg and then spreads to other parts of the body; it is an aberrant response to tissue injury. It is characterized by swelling, skin changes of color (redness progressing to pale) and temperature (warm progressing to cold), and continuous, intense burning or stabbing neuropathic pain out of proportion to the severity of the injury. These changes are accompanied by allodynia (perception of pain from a nonpainful stimulus), hyperesthesia (an exaggerated sense of pain), hyperhidrosis (increased sweating), and edema. The joints in the affected extremity become stiff, with softening of the bones. This leads to the movement being painful. In effect, in CRPS there is dysregulation of the sympathetic and the autonomic nervous system.

CRPS is classified into two types based on the "definite" presence of nerve damage:
- CRPS Type I: This was formerly referred to as Reflex Sympathetic Dystrophy (RSD), and is the more common type, where the nerve injury cannot be immediately identified.
- CRPS Type II: This was formerly referred to as Causalgia in which a distinct "major" nerve injury has occurred. CRPS type II patients have evidence of disease due to neurological changes, numbness, weakness, and severe pain.

Disease Progression

- Stage I: Burning pain, vasospasm, muscle spasm, and joint stiffness at the site of injury. Vasospasm causes skin color and temperature changes (warmth and redness). Patients recover spontaneously or with treatment.
- Stage II: Worsening pain, swelling and edema, brittle and cracked nails, osteopenia, muscles begin to atrophy, and joints stiffen further.
- Stage III: More severe and spreading pain, dry glossy skin, muscle atrophy, decreased mobility, joint contractures, severe osteopenia.

Diagnosis and Treatment of CRPS

CRPS is a diagnosis of exclusion, that is, no other disease is present that can explain the signs and symptoms. Several criteria have been proposed for the diagnosis of CRPS, such as the Budapest criteria, Bruehl's criteria, and Veldman's criteria: generally, the presence of an initiating noxious event or a cause of immobilization-CRPS-I, while a definite presence of nerve injury-CRPS-II. Associated criteria are pain (with allodynia or hyperalgesia), and presence of edema, changes in skin blood flow (color, temperature), and abnormal motor activity in the area of pain. Tests that can aid in the diagnosis include thermography, quantitative sweat testing, radiography (osteopenia), electromyography and nerve conduction studies, and sympathetic blocks.

Patients early in the disease can be effectively treated or in some cases the symptoms resolve spontaneously. However, delay in treatment can result in severe pain, physical deformity, and psychological problems.
- Medications: corticosteroids (pulse doses for 2 weeks), ibuprofen (inflammation), tramadol, antidepressants (SNRIs), gabapentin, clonidine patches (sympathetic mediated pain), bisphosphonates, oral lidocaine (mexiletine), baclofen/clonazepam (muscle relaxants), topical dimethyl sulfoxide (50 %)–DMSO cream.
- Interventional therapies: (1) sympathetic blockade (stellate ganglion for upper extremity and lumbar sympathetic blockade for lower extremity), (2) IV regional blocks with guanethidine or lidocaine, (3) spinal cord stimulation, 4) graded motor imagery

- Sympathectomy: surgical, chemical, or radiofrequency
- Amputation
- Psychological: biofeedback, stress reduction
- Rehabilitative: physiotherapy
- Alternative therapies: acupuncture, hypnosis

Phantom Limb

Phantom limb pain is pain that is perceived in the absent limb or body part. It is disconcerting because the pain is quiet intense, and occurs in an area that does not exist. The pain is based on perception. Phantom limb pain is often described as crushing or burning in quality. It occurs in almost all amputees and subsides with time in many patients. About 50–80 % of patients are still affected 1 year after amputation. The cause of phantom limb has profound neuropathophysiological implications and has confronted scientists for almost two centuries. Perhaps phantom limb can be explained by a multifactorial theory, which involves the plasticity of the somatosensory system, and epigenetics to maintain phantom limb pain.

The somatosensory cortex requires remapping in order to alleviate the burden of pain in these individuals; this can be accomplished with mirror box therapy. Phantom limb pain needs to be differentiated from stump pain in which neuromas form at the distal end of amputation that carry somatic and neuropathic pain. One can apply the five-finger model of treatment for this condition, with an emphasis on central remapping via mirror box therapy. The patient places, in a mirror box, the good limb into one side, and the stump into the other, and then looks into the mirror. The patient makes "mirror symmetric" movements, seeing the reflected image of the good limb moving, and it appears as if the phantom limb is also moving. Through the use of this artificial visual feedback the patient can move the phantom limb, and unclench it from painful positions.

- Medications: Opioids/non-opioids and neuropathic medications—antidepressants, anticonvulsants, and topical agents
- Interventional therapies: Local, regional blockade of neuroma or stump, spinal cord stimulation
- Psychological: Biofeedback, stress reduction
- Rehabilitative: Mirror box therapy, physiotherapy, graded motor imagery, sensory discrimination
- Alternative therapies: Acupuncture, hypnosis

Post-Herpetic Neuralgia

Post-herpetic neuralgia is a complication of a varicella zoster virus reactivation, commonly referred to as shingles. After staying dormant in the nervous system (specifically in the dorsal root ganglia of spinal nerves) for many decades, the virus can resurface under certain circumstances, most often due to depressed immune states associated with aging, stress, cancer, or chemotherapy. Shingles is manifested as a dermatomally distributed herpetic skin rash along the path of individual nerves. Antecedent to the rash, many will describe a prodromal period with intense burning pain in the same area. Generally speaking, only one nerve is involved, and in rare cases multiple nerves. If a cranial nerve is affected and a facial rash appears, worrisome complications include herpes zoster ophthalmicus leading to loss of vision (rash typically seen on the tip of the nose) and Ramsey Hunt syndrome with deafness and facial nerve palsy (rash typically seen around the ear and ear canal). For most, however, the blister lesions will ooze, crust, and heal and the pain will resolve with minimal long-term complications.

Unfortunately for some, the pain will persist despite complete resolution of the rash representing a separate entity, post-herpetic neuralgia (PHN). This is the most common complication following shingles. Pain associated with PHN is variable and can be described as a burning, sudden, sharp, or stabbing pain, with associated mechanical or thermal allodynia. This neuropathic painful condition can be quite severe and debilitating and oftentimes relentlessly impacts one's quality of life. There is evidence that early treatment with antiviral agents (famciclovir) can reduce the duration and occurrence of PHN. In May 2006 the Advisory Committee on Immunization Practices approved a new vaccine by Merck, Zostavax, against shingles. This vaccine is a more potent version of the chickenpox vaccine, and evidence shows that it reduces the incidence of post-herpetic neuralgia. The CDC recommends use of this vaccine in all persons over 60 years old. Additionally, for treatment of this condition, one can apply topical analgesics (aspirin, gallium maltolate, lidoderm patch), administer antidepressants/anticonvulsants, relaxation techniques, heat/cold packs, or spinal cord stimulator.

Trigeminal Neuralgia

Trigeminal neuralgia, historically known as *tic douloureux*, is a neuropathic pain condition affecting one or more branches of the trigeminal nerve. Although most cases do not have a defined etiology, some of the causes include vascular compression, multiple sclerosis, and tumors. The pattern of pain is paroxysmal and is often triggered by epicritic stimuli including chewing, talking, or swallowing. In 90 % of patients the pain is unilateral, affecting one side of the face, and is described as electric shock like shooting, burning, or crushing. Pain lasts for few seconds, to minutes to hours, may occur frequently, and is cyclic with periods of remission lasting months to years. Treatment includes administration of carbamazepine (first line of treatment) and other neuropathic medications baclofen, lamotrigine, oxcarbazepine, phenytoin, gabapentin, pregabalin, valproate), interventional therapies such as Gasserian ganglion blocks, neurosurgical decompression, gamma knife therapy, and other therapies described above.

Cancer Pain

According to the ASA Task Force, cancer pain is defined as "pain that is attributable to cancer or its therapy." Pain may also arise by the body's immune response to the cancer. Cancer is the cause of approximately 12 % of deaths globally (WHO 2012). Cancer pain diminishes the quality of life for the patients by affecting daily activities, sleep, and social life. Patients commonly experience cognitive difficulties, depression, and anxiety. Although cancer pain can be relieved or well controlled, about 50 % of patients receive suboptimal treatment. Common reasons for inadequate treatment of cancer pain include underreporting of pain, treatment noncompliance, and inadequate assessment of the patient by healthcare providers.

Classification of Cancer Pain

Cancer pain, like non-cancer pain, can be classified by what parts of the body are affected: somatic, visceral, and neuropathic pain. *Somatic pain* can be cutaneous or deep tissue pain, and is usually sharp and localized. *Visceral pain* is caused by tumor infiltration or compression of abdominal and thoracic viscera, and is usually pressure-like and not well localized. *Neuropathic pain* occurs when the tumor infiltrates or compresses the nerves or the spinal cord, and is usually severe with burning or tingling. In addition, treatment modalities, such as chemotherapy, radiation, or surgery, may cause neuropathic pain. Cancer pain can also be classified as acute or chronic (lasting more than 3 months). Acute cancer pain is usually caused by treatment of the cancer. Chronic cancer pain may be intermittent or continuous, with periods of increase in intensity or flares.

Assessment and Evaluation of Cancer Pain Patients

Pain assessment and evaluation in cancer patients should include a detailed history of the pain, physical examination including a complete neurologic examination, diagnostic testing, and finally development of a management plan. History should include information about the pain (duration, intensity, and quality), medications (opioids and non-opioids), associated depression, drug, or alcohol use, and information about the cancer (staging of the tumor, and specific treatments). Physical examination should include determination of nutritional status (weight), thorough examination of the site of pain and referring sites, and complete musculoskeletal and neurological examination. Since the cancer is already diagnosed, diagnostic testing should only be used when it will contribute to the treatment of the patient's pain. A treatment plan is then formulated after thorough discussion with the patient.

Management of Cancer Pain

Patients with cancer pain should have treatment goals of relieving or decreasing pain and maintaining function. Treatment modalities for cancer pain include pharmacologic measures (opioids, non-opioids), invasive interventions, palliative therapy, and psychological counseling. Palliative therapy includes radiation therapy and chemotherapy. Palliative therapy can reduce the size of the targeted tumors and can be helpful with cancer pain. Improving psychological effects of pain can be very important in patients with cancer pain. Cancer pain can lead to depression. Pain affects almost every aspect of a patient's life: sleep, social function, sexual function, or financial situation. Therefore, patients should be educated about handling their pain, and gain control of emotional reactions. Families of patients also need to be involved in therapy sessions as these issues affect families as a whole.

Pharmacologic Measures

Pharmacologic medications to treat cancer pain include opioids, and non-opioid adjuvant medications, as described previously in the chapter. Cancer pain patients are usually prescribed long-acting medications, once the appropriate dosage and plan are formulated. Some patients may need breakthrough pain medications during flare-ups. As such, these breakthrough pain medications should be fast acting to help control the pain. Patients with late stage cancer, who are at the end of their life, benefit from opioids that can be administered as infusions (for example, morphine drip). There are a number of suggested algorithms for pharmacologic treatment of cancer pain, and the best known of these are the WHO three-step "analgesic ladder" and the four-step "modified analgesic ladder."

- Step one—mild pain: Non-opioids +/– adjuvant therapy
- Step two—mild to moderate pain: Opioids +/– non-opioids and adjuvant therapy
- Step three—moderate to severe pain: strong and long-acting opioids +/– non-opioids and adjuvant therapy
- Step four—severe to intractable pain**:** interventional therapies

Cancer pain medications may cause a number of side effects which can cause great discomfort and affect the quality of life in these patients. The most common side effect is nausea, which may not only be caused by the pain medications, but also by chemotherapy and radiation. Treatment of nausea includes 5-HT_3 antagonists, phenothiazines, intestinal motility agents (metoclopramide), antivertiginous agents, and oral dexamethasone.

The second most common side effect of opioid therapy is constipation. Treatment of constipation should be started prophylactically with the initiation of the opioid therapy, and includes stool softeners, laxatives, and dietary adjustments. Other side effects include confusion, dysphoria, depression of the hypothalamic–pituitary–adrenal axis (hypogonadism), urinary retention, pruritus, miosis, and respiratory depression.

It should be noted that there is minimal development of tolerance to constipation and miosis. Chronic administration of opioids leads to tolerance to the analgesic effect, which may need to increase the dosage or switch to another opioid. Physical dependence usually occurs with chronic opioid administration, and abrupt discontinuation of opioids may lead to withdrawal syndrome. Opioid-induced hyperalgesia is a known side effect of opioid therapy, where patients complain of pain that is out of proportion to physical findings. Opioid-induced hyperalgesia can be difficult to distinguish from tolerance. Increasing the dose of opioid further increases the sensitivity to pain, which may be severe enough to warrant discontinuation of opioid treatment.

Interventional Therapies

Interventional therapies are used in patients who continue to experience pain, or in patients experiencing significant side effects, despite the use of appropriate opioid and non-opioid medications. These therapies include regional anesthesia techniques, neurolytic blocks, spinally/epidurally administered opioids, electrical stimulation, or surgery.

- Regional analgesia techniques: where a local anesthetic and corticosteroid is injected into specific areas such as intercostal or brachial plexus. Local anesthetic blocks can be diagnostic (to identify the anatomical structure responsible for the pain), prognostic, or therapeutic. Therapeutic blocks are administered to decrease pain from tumor compression of the spinal cord or peripheral nerve structures, trigger points, reflex sympathetic dystrophy, post-herpetic neuralgia, and phantom limb pain.
- Neurolytic blocks techniques: where phenol, alcohol, and radiofrequency lesioning techniques (electric current applied under fluoroscopic guidance) are used to intentionally damage neural pathways to disrupt the pain pathways. Examples include celiac plexus block and ganglion blocks. Phenol injections are better tolerated as alcohol injections are painful.
- Spinal/epidural analgesia techniques: where opioids and other drugs, such as local anesthetics and baclofen, are administered alone or in combination for optimal pain relief. The drugs can be administered via epidural catheter (tunneled or non-tunneled), or via intrathecally implanted pumps. Intrathecally route has advantages of using less dosage, faster action, and fewer side effects as the drugs are absorbed systemically to a limited extent.
- Surgical techniques: appropriate neurosurgical destructive procedures are performed, for example, anterolateral cordotomy, stereotactic mesencephalotomy, and midline myelotomy.

Clinical Review

1. Allodynia is
   A. Painful response to a non-painful stimulus
   B. Decreased response to a painful stimulus
   C. Increased response to a painful stimulus
   D. Pain in an area that lacks sensation
2. Physiologic pain produced by a noxious stimuli that occurs without tissue damage is defined as
   A. Neuropathic pain
   B. Functional pain
   C. Referred pain
   D. Nociceptive pain
3. Tolerance does *not* occur due to the following effect of opioids:
   A. Nausea
   B. Pruritus
   C. Analgesia
   D. Constipation
4. Opioid-induced itching can be best treated with
   A. Buprenorphine
   B. Diphenhydramine
   C. Nalbuphine
   D. Butorphanol
5. Radiofrequency lesioning
   A. Involves destruction of the nerve tissue
   B. Involves passage of current to the tissue
   C. Is performed after a positive diagnostic nerve block
   D. All of the above
6. Signs of a successful Stellate ganglion block include
   A. Hypertension
   B. Vasoconstriction
   C. Nasal congestion
   D. Decrease in limb temperature
7. Mirror box therapy can be employed for
   A. Trigeminal neuralgia
   B. Phantom limb pain
   C. Pancreatic cancer pain
   D. Facet joint pain
8. After an initial injection, if the pain is not relieved, epidural steroid injections can be repeated in
   A. 2–4 weeks
   B. 8–12 weeks
   C. 3 months
   D. 6 months

Answers: 1. A, 2. D, 3. D, 4. C, 5. D, 6. C, 7. B, 8. A

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Orthopedic Anesthesia

25

Tiffany Sun Moon and Pedram Aleshi

Orthopedic surgery is unique in its depth of practice and variety of patients. From the healthy child with a broken ankle to the fragile octogenarian with a hip fracture, the spectrum of patients seen with orthopedic injuries is wide. Furthermore, procedures are vast and varied, ranging from surgery on the wrist to reoperation total hip arthroplasty, which may be associated with significant blood loss and hemodynamic perturbations. Orthopedic surgery is frequently performed on an emergent basis, requiring that practitioners be prepared to deal with patients with multiple injuries, full stomachs, and coexisting medical conditions. Besides these issues, anesthesia providers should also be knowledgeable about issues specific to, or of increased importance in, orthopedic surgery, including regional anesthesia, tourniquet use, fat embolism syndrome, infection prevention, thromboprophylaxis, and pain management.

Upper Extremity Surgery

Surgery on the Shoulder

Surgeries performed on the shoulder include rotator cuff repair, subacromial decompression, shoulder stabilization, total shoulder arthroplasty, and therapeutic arthroscopy of the shoulder joint (thermal capsular shrinkage, debridement, or release of frozen shoulder). The development of arthroscopic techniques has allowed many of these surgeries to be performed on an outpatient basis. Patients undergoing open procedures sometimes require an overnight stay. Shoulder surgery can be performed under regional or general anesthesia based on the specific surgery, patient factors, and surgeon preference.

Positioning

Shoulder surgery can be performed in the sitting or "beach chair" position (Fig. 25.1) or a lateral position. The beach chair position is preferred by many orthopedic surgeons due to advantages such as decreased bleeding, having the anatomy in the standard upright position, and the ability to use the weight of the arm for traction. In addition, should the surgeon need to convert from an arthroscopic technique to an open procedure, the beach chair position allows for greater flexibility, and minimal repositioning and redraping. Disadvantages of the beach chair position include plausible errors in blood pressure measurement, which can lead to the occurrence of adverse events such as stroke and death. Since the intravenous line is usually inserted in the nonoperative extremity, the blood pressure cuff may be placed on the calf of one of the lower extremities. Due to hydrostatic gradients from the calf to the head, the systolic blood pressure at the level of the brain may be 50 mmHg lower than the systolic blood pressure that the monitor displays when the blood pressure cuff is on the calf. Employment of deliberate hypotension, as is frequently requested by surgeons to decrease intra-articular bleeding in shoulder surgery, can further decrease blood pressure below the critical threshold for adequate brain perfusion. Furthermore, one must remember that patients with poorly controlled hypertension may have autoregulatory curves shifted to the right so that cerebral ischemia can occur at "normal" blood pressures. Placing the blood pressure cuff at the level of the heart minimizes the measurement error caused by hydrostatic gradients.

Surgery in the lateral decubitus position is not associated with a large hydrostatic gradient. Thus, the risk of iatrogenic lowering of blood pressure below critical thresholds is much lower. However, patients undergoing surgery in the lateral position may need a general anesthetic as regional anesthesia and sedation may not be sufficient for some patients to tolerate this position for prolonged periods. If the need to convert

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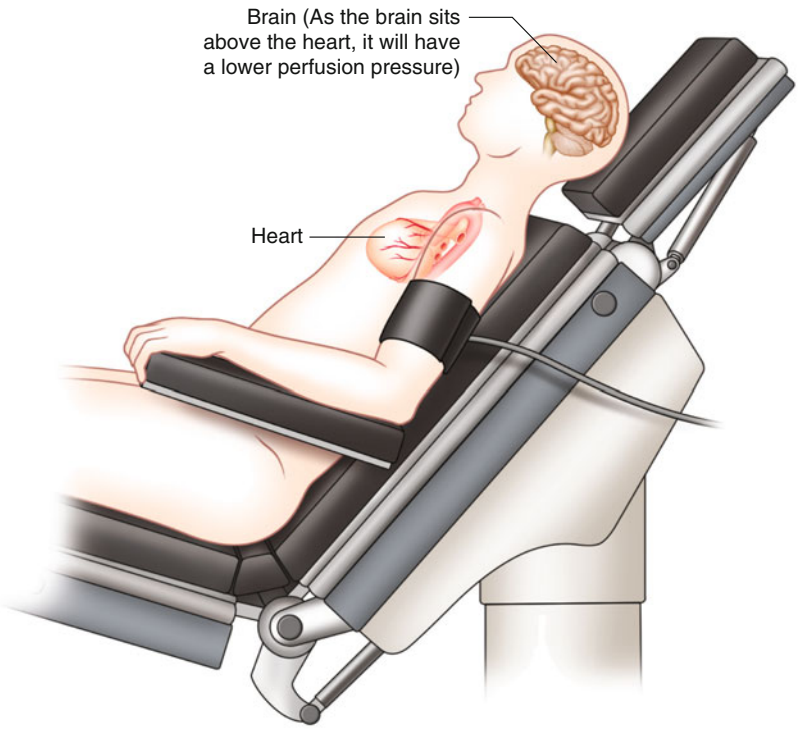

Fig. 25.1 The beach chair position for shoulder surgery

to general anesthesia arises, it can be difficult to secure the airway with the patient in the lateral position or even the beach chair position. The traction needed for surgery in the lateral decubitus position has been associated with injury to the brachial plexus, resulting in paresthesias and palsies. Ultimately, there is no objective, empirical evidence to support that one position is clearly superior to the other. It is the responsibility of the anesthesiologist to understand the risks and benefits associated with each position, and together with the surgeon, select the position safest for each patient.

Anesthetic Considerations

General anesthesia in addition to an interscalene block is the preferred anesthetic choice for most surgeons and anesthesiologists since the drapes often cover, or are near the patient's face and airway. However, surgical anesthesia can be obtained with an interscalene block and intraoperative sedation in many cases. Selection of the local anesthetic used will determine onset time and duration of block and will differ for patients in which the block is performed for surgery itself versus postoperative analgesia. Other patients may require general anesthesia for poor cardiopulmonary reserve or other reasons (e.g., refusal of interscalene block). The decision to use a laryngeal mask airway (LMA) versus endotracheal tube (ETT) should be based on patient factors (e.g., presence of gastroesophageal reflux) as well as surgical factors (e.g., duration of surgery).

Postoperative Pain Management

After shoulder surgery, a number of different analgesic modalities are available. Traditionally, opioids and NSAIDs were used for postoperative pain, but caused a multitude of side effects. Infiltration techniques including subacromial (bursal) and suprascapular injections have been used, but a review of postoperative analgesia after shoulder surgery found that subacromial and intra-articular local anesthetic infiltration was only slightly better than placebo and intra-articular infusion has been linked to cases of catastrophic chondrolysis, thereby limiting its use. In patients undergoing shoulder arthroplasty, patients receiving regional analgesia (when compared to intravenous morphine PCA), had improved analgesia, earlier functional recovery on the first three postoperative days, less nausea and vomiting, and better sleep quality postoperatively. Additionally, patients undergoing rotator cuff repair with an interscalene block had less pain, were more likely to bypass the recovery room, and meet discharge criteria sooner than patients who underwent general anesthesia without the interscalene block. Although single-injection nerve blocks are adequate for short procedures and short-term postoperative analgesia, they are inadequate for prolonged postoperative analgesia. Continuous interscalene blocks may be performed when more than 24 h of analgesia is desired. Patients could then be discharged home with specific instructions to manage and discontinue the catheter.

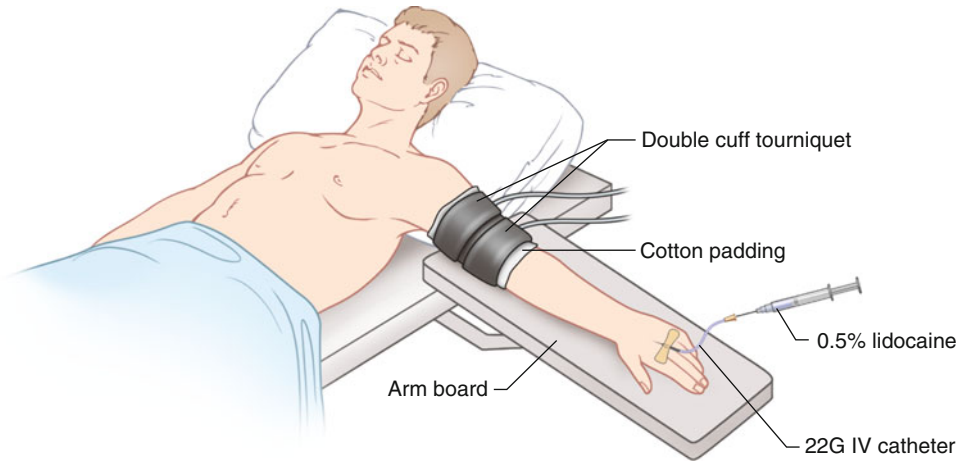

Fig. 25.2 Intravenous regional block

Surgery on the Hand, Wrist, Arm, and Elbow

Orthopedic surgery of the upper extremity ranges from carpal tunnel release and trigger finger release to humerus fracture fixation. Many patients undergoing surgery of the upper extremity are good candidates for ambulatory surgery. Patients undergoing trigger finger release and carpal tunnel release can undergo local or regional anesthesia with minimal intraoperative sedation and be discharged home soon after surgery. For short procedures with minimal postoperative pain, local infiltration with intraoperative sedation may be an appropriate choice. The dogma that epinephrine should not be injected into the digits has been recently challenged. Most of the case reports of digital ischemia with local anesthetics occurred with cocaine or prilocaine, which have been known to cause digital ischemia even without epinephrine additives. There have been no case reports of digital ischemia with commercial preparations of lidocaine with epinephrine. Thus, small amounts of local anesthetics with diluted epinephrine (1:20,000 or less) are probably safe for digital infiltration or blocks.

More extensive surgery of the upper extremity involving bones and tendons may necessitate a regional and/or general anesthetic but can be accomplished in the ambulatory setting. Peripheral nerve blocks of the brachial plexus for upper extremity surgery include interscalene, supraclavicular, infraclavicular, and axillary blocks. Comparing the relative merits of regional techniques over general anesthesia alone, patients receiving a block had a faster recovery and discharge, fewer adverse events, and better postoperative analgesia. Improvements in ultrasound technology have greatly facilitated placement of upper extremity blocks. Given the close proximity of structures such as adjacent nerves (the phrenic nerve), major vasculature (carotid, subclavian, and axillary artery), and lung apex, ultrasound can be of great utility when performing blocks. Advantages of ultrasound guidance include direct visualization of anatomic structures, detection of anatomic variants, decreased incidence of vascular puncture, and usage of smaller volumes of local anesthetic. Furthermore, ultrasound-guided peripheral nerve blocks have been shown to have shorter performance times, faster onset time, and greater block success rates when compared to other methods of nerve localization.

An anesthetic technique frequently used for hand and forearm surgery is the intravenous regional block (IVRB) or Bier block (Fig. 25.2), named after August Karl Gustav Bier, who first described the block in 1908 (see chapter on peripheral nerve blocks). Advantages of Bier block include ease of administration, rapid onset (usually within 5 min), muscular relaxation, and rapidity of recovery. Disadvantages require need for special equipment (Esmarch bandages, double cuff tourniquet) and finite duration of anesthesia and lack of postoperative analgesia. Procedures that last more than 1 h should not be performed under Bier block. Serious complications including seizures, cardiac arrest, and compartment syndrome have been reported with use of Bier blocks.

Lower Extremity Surgery

Patients who come in for lower extremity procedures span a wide spectrum, from healthy athletes necessitating ACL repairs to elderly patients with multiple comorbidities necessitating emergent hip fracture surgery. Total knee and hip arthroplasties comprise a large percentage of surgeries performed on the lower extremities. As the population ages, more procedures will be performed on patients who have significant cardiac, pulmonary, renal, and hepatic diseases. In a prospective study of over 10,000 patients undergoing elective primary total hip or knee arthroplasty, the incidence of serious adverse events including myocardial infarction, pulmonary embolism, deep venous thrombosis, and death was 2.2 %. Most of the events increased in frequency with older age, especially in patients 70 and older. These risks, in

addition to other anesthetic risks, must be discussed with patients preoperatively and all comorbid conditions should be optimized prior to elective procedures.

Surgery on the Knee

Knee Arthroscopy

Knee arthroscopy is commonly used to perform minor procedures on the patella, ligaments, or meniscus or to investigate for pathology that may be amenable to surgery at a later time. Preoperative discussion with the surgeon will enable the anesthesiologist to judge what degree of intraoperative and postoperative pain management will be necessary. For many patients undergoing simple arthroscopy, general anesthesia is the anesthetic of choice. In these patients, postoperative pain can be adequately managed with oral pain medications. For other patients who undergo knee arthroscopy combined with more extensive procedures, femoral and/or sciatic nerve blocks with long-acting local anesthetics may be necessary for adequate postoperative pain control.

Knee ACL Repair

Injury to the anterior cruciate ligament (ACL) is the most common ligamentous injury of the knee, which frequently occurs in young adults as a result of sports-related injuries. ACL repairs are generally performed arthroscopically as outpatient procedures, which have been associated with lower complication rates, lower costs, and higher patient satisfaction. The ideal anesthetic for outpatient ACL repair should be highly effective, relatively inexpensive, and have few side effects, enabling patients to return home shortly after surgery. ACL reconstruction can be performed under general or spinal anesthesia, with postoperative analgesia provided with a single shot or continuous femoral nerve block (which are usually performed preoperatively). Often, patients who have a successful femoral block may complain of posterior knee pain in the recovery room and may need a "rescue" sciatic block. This is more likely when hamstring autografts are used. Ideally, a preoperative femoral and a sciatic block will yield a prolonged pain-free postoperative course.

Total Knee Arthroplasty

Total knee arthroplasty (TKA) is one of the most commonly performed procedures in orthopedic surgery. Most patients have osteoarthritis or rheumatoid arthritis of one or both knees. Pain after TKA is substantial and can last many days following surgery. Therefore, adequate pain control postoperatively is paramount to facilitation of early ambulation, which decreases the incidence of thromboembolic disease. Furthermore, improved pain control allows for earlier commencement of physiotherapy, which has been shown to improve recovery. Anesthetic techniques for surgery include neuraxial blockade (e.g., spinal or epidural) and general anesthesia. Postoperative analgesia can be managed with intravenous, intrathecal/oral opioids, neuraxial blockade, peripheral nerve blockade, and local infiltration analgesia.

Choice of Anesthesia

Total knee arthroplasty is frequently performed under neuraxial anesthesia with intraoperative sedation. Spinals are commonly used and are advantageous because they do not involve an indwelling (epidural) catheter, but only last for a finite time period and thus may not be suitable for redo operations. Epidurals can be used for surgery, but are contraindicated in patients receiving high-dose low molecular weight heparin (risk of epidural hematoma). Therefore, use of epidurals for postoperative analgesia is somewhat limited in this population of patients who are at high risk of postoperative thromboembolic disease and are anticoagulated postoperatively. However, hemodynamic effects with epidurals are generally more gradual and thus easier to treat than with spinal anesthesia. In addition, the duration of an epidural is not limited as it is with a spinal and thus may be useful for reoperation or bilateral TKAs or if surgery becomes longer than anticipated. The epidural catheter can be removed immediately after surgery or prior to the commencement of anticoagulation. Recommendations for withholding anticoagulation prior to removal of the epidural are discussed in the section on thromboprophylaxis.

New microsomal technology now allows the delivery of a single dose of extended-release morphine into the epidural space to be released over 48 h. In one study, patients who underwent TKA who received extended-release epidural morphine versus a sham epidural had significantly lower pain scores and opioid consumption. Thus, this technique allows for prolonged analgesia while circumventing the increased risk of postoperative epidural hematoma associated with indwelling catheters. Patient selection is important, however, as an increased risk of delayed respiratory depression can be seen with extended-release epidural morphine.

Postoperative Pain Management

Management of postoperative pain following TKA is important as adequate pain control allows for faster rehabilitation and reduces the risk of postoperative complications such as joint adhesions. Conventional pain management after TKA relied on administering intravenous and oral opioids postoperatively. Patient-controlled analgesia (PCA) proved to be superior when compared to traditional nurse-administered analgesia in terms of quality of pain control and patient satisfaction, but many patients still experienced a significant amount of pain. More recently, newer approaches to pain management have focused on a *multimodal approach* and *preemptive analgesia.* The goal in preemptive analgesia is to limit the sensitization of the nervous system to painful stim-

uli, thus decreasing the amount of noxious stimuli that reaches the spinal cord and brain from the peripheral nervous system. Multimodal approaches to analgesia focus on using multiple agents to decrease the side effects of each while maximizing synergism amongst different classes of medications. Local infiltration analgesia (LIA) has increased in popularity over the past 5–10 years. LIA usually consists of injection of a long-acting local anesthetic (e.g., ropivacaine), a nonsteroidal anti-inflammatory drug (e.g., ketorolac), and epinephrine through a catheter placed in the knee.

Femoral nerve blocks are frequently utilized for management of postoperative pain in patients undergoing TKA. Placement can be guided by nerve stimulation and/or ultrasound. Both single-shot techniques and continuous techniques utilizing indwelling catheters are used. With continuous techniques, dilute solutions of local anesthetic can be infused using traditional pumps. Unlike epidurals, femoral nerve catheters are not contraindicated when thromboprophylaxis with high-dose low molecular weight heparin is started postoperatively. Femoral nerve blocks reduce PCA morphine consumption, pain scores with activity, and incidence of nausea when compared to intravenous PCA only. Traditionally, patients could only receive continuous perineural infusions as inpatients. However, with the advent of portable infusion pumps, *ambulatory* continuous peripheral infusions became possible, allowing patients the advantage of prolonged analgesia without increasing the length of hospitalization.

Despite the numerous advantages that femoral nerve catheters offer, there is ongoing concern about associated quadriceps weakness. It has been estimated that prolonged quadriceps weakness occurs in 2 % of patients with femoral nerve blocks. Patients with quadriceps femoris weakness are predisposed to falls, fractures, and decreased ability to participate in physiotherapy, which could increase the length of hospitalization. The goal in selecting a local anesthetic and concentration is to maximize the sensory block while minimizing the degree of motor block. One study comparing continuous femoral nerve blocks with equal local anesthetic mass of ropivacaine 0.1 % versus 0.4 % found the same incidence of weakness in both groups and concluded that total local anesthetic dose (mass) is the primary determinant of perineural infusion effects, rather than concentration and volume.

As more studies are done to improve the intraoperative and postoperative management of TKA patients, anesthesiologists will have more tools in their armamentarium. Nowadays, it is not uncommon for a patient undergoing TKA to have a femoral nerve catheter inserted preoperatively, undergo a spinal (or epidural) anesthetic with sedation for the surgery itself, and have postoperative pain control with a dilute infusion of local anesthetic through the femoral nerve catheter. Femoral nerve catheters can then be weaned and discontinued on postoperative day 2 or 3 as the patient is transitioned to systemic medications. Alternatively, ambulatory continuous femoral nerve infusions may be continued after discharge from the hospital with instructions for self-removal at a later time, thus allowing continued benefit from the femoral nerve catheter and avoidance of systemic medications and side effects. Determination of the optimal local anesthetic, concentration, and dose may improve the safety of continuous femoral nerve block in the future.

Surgery on the Hip

Arthroscopy

Arthroscopy of the hip is being performed more frequently, both as a diagnostic and therapeutic tool. It is used to treat many conditions including loose bodies, labral tears, synovial disorders, articular injuries, adhesive capsulitis, and femoroacetabular impingement. Many patients are athletes who are otherwise healthy, while others may be elderly with multiple comorbidities and a history of previous hip surgeries. In many circumstance, hip arthroscopy is an ambulatory procedure. For patients who have more extensive surgical manipulation or comorbidities, an overnight stay may be required. Some of these patients may have chronic hip pain and be opioid dependent, making postoperative analgesia more challenging. Neuraxial and peripheral nerve blocks may be especially advantageous in these patients with varying degrees of opioid tolerance.

General anesthesia is commonly used for the procedure as neuromuscular relaxation allows for optimal joint distraction. In addition, the airway may be difficult to secure if an untoward event occurs in the lateral decubitus position. Pain after hip arthroscopy can range from mild to severe depending on the amount of surgical manipulation intraoperatively. Despite the use of intraarticular bupivacaine at the conclusion of surgery, many patients have considerable postoperative pain and require rescue analgesics in the recovery room. However, increasing amounts of opioids can lead to significant adverse effects such as nausea and vomiting, urinary retention, and respiratory depression which may necessitate overnight admission. Paravertebral L_1 and L_2 blocks may provide sufficient postoperative analgesia following arthroscopy while sparing quadriceps strength, thus facilitating earlier postoperative ambulation. A femoral nerve block may also provide analgesia in some patients.

Hip Fracture Surgery

Hip fractures commonly affect the elderly and are a major cause of morbidity and mortality in the aging population. One-year mortality rates after hip fractures range from 14 to 36 %, increasing with patient age and comorbidities. Patients with hip fractures frequently have multiple medical comorbidities

that can significantly increase perioperative risk. Conditions such as infection, anemia, dehydration, electrolyte imbalance, and altered mental status are frequently seen in patients with hip fractures. The need for further workup and optimization of medical status must be balanced with minimizing the time before surgery, which can decrease morbidity. Anesthetic management must be thoughtfully tailored to each patient to ensure adequate analgesia while minimizing the risk for cardiac and pulmonary complications, as well as postoperative cognitive dysfunction.

For femoral neck fractures, fracture displacement is a major consideration in deciding which type of surgical fixation is appropriate. In patients under 65 years of age, nondisplaced intracapsular fractures are stabilized with percutaneous screws or pins, whereas displaced intracapsular fractures are typically treated by open reduction and internal fixation (ORIF). In patients over 65 years of age with femoral neck fractures, hemiarthroplasty and total hip arthroplasty are usually performed. Intertrochanteric and subtrochanteric fractures are usually stabilized using an intramedullary nail or sliding hip screw and a plate device.

Anesthesia for hip fracture surgery can be achieved through neuraxial techniques (e.g., spinal or epidural) or general anesthesia. There is lack of scientific data demonstrating that one anesthetic technique is clearly superior. However, regional anesthesia may offer a slight benefit over general anesthesia in reducing acute postoperative confusion in patients undergoing hip fracture surgery. Positioning patients with hip fractures for epidural or spinal placement can be challenging. Patients with dementia or delirium may have difficulty with positioning and remaining still. Many patients will not be able to tolerate the sitting position. Furthermore, these patients usually cannot bear weight on the broken hip but may be able to be positioned in the lateral decubitus position with the operative hip up.

Blood loss in hip fractures can be significant as surgical techniques for ORIF and arthroplasty often involve bleeding from transection of veins and arteries in the femoral head and neck. In addition, many patients with hip fractures may be chronically anemic due to iron-deficiency anemia, anemia of chronic disease, or anemia associated with renal disease. In patients with moderate to severe anemia, preoperative transfusion should be considered and blood should be available intraoperatively. Many elderly patients are on antiplatelet agents (e.g., aspirin, clopidogrel) or anticoagulation (e.g., warfarin) and may need platelet transfusions or reversal of anticoagulation prior to surgery. Neuraxial techniques are contraindicated in patients who have taken clopidogrel within the last 7 days or who are therapeutically anticoagulated. Patients should have preoperative labs to determine the degree of hematologic and electrolyte abnormalities present, and every effort should be made to optimize patients prior to surgery.

Total Hip Arthroplasty

In 2004, over 230,000 total hip arthroplasties were performed in the United States. Spinal and epidural techniques are frequently used for total hip arthroplasty (THA). Patients undergoing THA require less postoperative blood transfusion, less operative time, and superior postoperative analgesia with neuraxial versus general anesthesia. With spinal anesthesia, intrathecal opioids can be added to the local anesthetic to provide postoperative analgesia for up to 24 h. However, intrathecal opioids can be associated with side effects such as nausea and vomiting, pruritus, and respiratory depression. Thus, patients who receive intrathecal opioids must be properly identified to surgical and pain management teams so that additional monitoring (e.g., continuous pulse oximetry) is available.

A recent randomized trial concluded that continuous lumbar plexus block provides improved analgesia with fewer side effects compared with systemic opioids after hip arthroplasty. THA can also be performed with an indwelling lumbar plexus catheter and single-shot sciatic nerve block with intraoperative sedation. Postoperatively, the lumbar plexus catheter can be kept overnight for continued analgesia.

Total hip arthroplasty can be associated with hypotension, hypoxemia, pulmonary hypertension, cardiac arrest, and even death. These effects may be especially pronounced in patients who undergo *cemented* THAs, leading to the "bone cement implantation syndrome." The leading hypothesis suggests that pulmonary microemboli are the main culprit. The degree of embolism is determined by the intramedullary pressure generated at the time of insertion of the prosthesis, during which fat, bone marrow, and air are extruded into the femoral venous channels and subsequently embolize to the lungs. The right ventricle is subject to more stress in bilateral procedures and may predispose certain patients with preexisting RV dysfunction or pulmonary disease to pulmonary complications. Thus, patients with significant cardiac or pulmonary disease may not be good candidates for bilateral procedures.

A modified surgical technique using vacuum drainage of the proximal femur to reduce high intramedullary pressures during prosthesis insertion has been shown to significantly decrease the burden of microemboli to patients (from 93.4 to 13.4 %). This is clinically significant as patients with moderate to severe systemic diseases (ASA III-IV) undergoing THA suffer sustained increased pulmonary shunt fractions, even into the postoperative period. Despite the advantages of cementless hip arthroplasty, many orthopedic surgeons continue to use cemented techniques as the literature supports superior results of cement fixation in certain subsets of patient populations. Thus, anesthesia providers should be cognizant of the method of THA being performed.

THA can be associated with significant blood loss, especially in reoperations due to significant scar tissue that forms

after each operation. In revision hip arthroplasties involving cemented prostheses, cement and implant removal can be time-consuming and challenging and lead to significant blood loss. The incidence of blood transfusion in reoperation total hip arthroplasty ranges from 39 to 56 %. Additional intravascular access (i.e., central line) and hemodynamic monitoring (i.e., arterial line) are frequently necessary.

Intraoperative blood transfusion has been associated with an increased risk of death as well as pulmonary, septic, wound, and thromboembolic complications. Preoperative autologous donation is possible, but patients should be allowed adequate time for the hemoglobin to reach predonation levels before surgery. Many surgeons discourage the use of routine autologous donation, as 44 % of predonated autologous units are discarded and about 14 % of patients who pre-donate necessitate further allogenic transfusion. Intraoperative use of cell saver has been shown to decrease the need for transfusion by 31 %, but may be contraindicated in patients with malignancy or systemic infection. Antifibrinolytic (aprotinin or tranexamic acid) therapy may also reduce allogenic blood transfusion.

Nerve injury following THA is infrequent, ranging from 0.09 to 3.7 % in primary THA and up to 7.6 % in revision THA. Most commonly, the sciatic nerve is involved, usually the peroneal component, which can become stretched. The femoral nerve can also be injured during hip surgery, which results in quadriceps weakness and may impair patients' ability to ambulate. Electromyograms and nerve conduction studies may be helpful but may not be sensitive until weeks after the injury. Reoperation is rarely necessary and conservative treatment is followed in most circumstances.

Surgery on the Foot and Ankle

Currently, most foot and ankle surgery is performed in the outpatient setting. Pain and postoperative nausea and vomiting (PONV) are the most common reasons for hospital admission from ambulatory surgery. For inpatient procedures, postoperative analgesia is equally important as it may aid in an early discharge from the hospital. General and neuraxial anesthesia as well as peripheral nerve blocks are valid options. For surgery on the foot, a sciatic nerve block or an ankle block can provide surgical anesthesia. Surgical anesthesia has been reported to be more reliable in patients receiving ankle blocks. However, an ankle block requires multiple injections, yields a shorter duration of postoperative analgesia, and will not provide analgesia for a calf tourniquet. For the ease of performance and reliability, most anesthesiologists deliver a general anesthetic in addition to a nerve block for postoperative analgesia. Neuraxial techniques are also acceptable; however they often lead to delayed discharge times in the ambulatory setting due to persistent block and urinary retention.

For ankle surgery involving the medial aspect of the ankle or leg, a sciatic block is not sufficient because it does not cover the saphenous nerve distribution. A saphenous or a femoral nerve block in addition to a sciatic block can provide complete surgical anesthesia to the entire foot and ankle. A saphenous nerve block is advantageous over a femoral nerve block, since it does not cause quadriceps muscle weakness, which may cause difficulty with ambulation postoperatively, especially if combined with a sciatic block. However, a femoral nerve block is easier to perform for most anesthesiologists and will provide at least partial anesthesia for a thigh tourniquet.

Various methods of postoperative analgesia regimens have been studied. Postoperative pain is an important issue in patient satisfaction, mobilization, and recovery. Various techniques have been described for blocking the sciatic, saphenous, and femoral nerves for these patients. Sciatic nerve catheters placed at the popliteal fossa have gained popularity with the availability of outpatient pumps for local anesthetic infusions. These catheters have been shown to extend the duration of postoperative analgesia and improve patient satisfaction in foot and ankle surgery. For major ankle surgery, the addition of a femoral nerve catheter to a sciatic catheter has been shown to be beneficial with postoperative analgesia with movement but not at rest.

Selected Topics in Orthopedic Surgery

Regional Anesthesia

Regional anesthesia offers a number of advantages over general anesthesia including avoidance of airway manipulation, superior postoperative pain control, less postoperative nausea and vomiting, and greater patient satisfaction. Single-injection nerve blocks can provide surgical anesthesia as well as postoperative analgesia lasting 12 h or more with long-acting local anesthetics such as ropivacaine and bupivacaine. Patients who receive nerve blocks arrive to the recovery area more alert as a result of not undergoing general anesthesia. They also have less pain and nausea and vomiting, likely attributable to the decreased need for rescue opioid analgesia. Thus, the time spent in the recovery room can be much shorter for patients undergoing surgery with a regional technique than general anesthesia. This has many implications for decreasing costs and increasing patient satisfaction.

Using the same techniques utilized for single-injection blocks (e.g., ultrasound guidance and/or nerve stimulation), continuous blocks are performed by threading catheters into the perineural space. Importantly, patients with continuous

nerve catheters had better pain control and significant decrease in side effects associated with opioid use (e.g., nausea/vomiting, pruritus, sedation). The use of disposable elastomeric infusion pumps is advantageous as they require minimal instruction for use, do not require patients to interact with the unit, and can be used in ambulatory patients. Many authors have advocated for continuous regional anesthesia in the ambulatory setting. A number of commercially available pumps and catheters are available that are intended for ambulatory use and removal by the patient 48–96 h postoperatively. Careful selection of patients and substantial preoperative education and close postoperative supervision are necessary for successful implementation of ambulatory continuous blocks.

Despite its many advantages, regional anesthesia is not without risks. Complications associated with peripheral nerve blockade include bleeding, infection, and neurologic injury. Guidelines for peripheral nerve blockade in patients on anticoagulation are outlined in the section on thromboprophylaxis. Outpatient rates of infection are reported as less than 1 %, while neurologic injury ranges from 0.3 to 2.0 %. Another frequently cited "disadvantage" of regional anesthesia is the additional time required to perform blocks. This bias may lead surgeons to request general techniques in order to "avoid delaying surgery." Furthermore, emergence times may be significantly lower in patients who receive nerve blocks, potentially decreasing total OR time. At many institutions, blocks are performed in a preoperative holding area by a specialized regional team, further decreasing the turnover time between cases. However, this may not be possible in all patient care settings.

Tourniquets

Since Harvey Cushing's introduction of the first pneumatic tourniquet in 1904, the tourniquet has become universally adopted by orthopedic surgeons for its ability to create a bloodless surgical field. The tourniquet has a record of safety, efficacy, and reliability and is used in approximately 15,000 surgical procedures daily. Simply put, the goal of tourniquet application is to stop the flow of arterial blood into the limb distal to the cuff. Tourniquets are generally inflated to 100 mmHg over systolic pressure, or a preset value of 250 mmHg. Wider contoured cuffs require lower tourniquet pressures to prevent blood flow than narrow cylindrical cuffs, perhaps due to superior transmission of pressure to the underlying tissue.

Tourniquet pain occurs at the site of tourniquet application and may not be addressed by peripheral nerve blocks. Even under general anesthesia, patients often show a hemodynamic response to tourniquet after about 1 h with increase in heart rate and blood pressure. It is important to keep in mind that these hemodynamic changes from the tourniquet often quickly fade away after deflation, so the use of long-acting opiates and antihypertensive agents is not recommended. For surgery on the hand, a tourniquet may be applied to the upper arm, which can cause a severe amount of pain that would not be covered by an axillary nerve block. Knowledge of tourniquet application may allow anesthesia providers to use a different block, which would cover the site of tourniquet application. Alternatively, tourniquet pain may be treated with short acting intravenous opioids.

Despite their safety, numerous reports of neurological complications due to tourniquet use have been reported. The pathophysiology of these injuries seems to be due to compressive neurapraxia involving displacement of the node of Ranvier. Physiologically, interruption of blood supply to tissues causes cellular hypoxia, tissue acidosis, and potassium release. On tourniquet release and reperfusion, hypotension and varying degrees of systemic acidosis and hypercarbia may be seen as washout of accumulated metabolic waste occurs. Tourniquet application to lower extremities may result in a greater degree of tissue acidosis than upper extremity tourniquets due to the increased amount of tissue rendered hypoxic in the lower extremities. Similarly, tourniquets applied more proximally may generate more tissue acidosis than tourniquets applied more distally. It is recommended that tourniquet times be no longer than 2 h. Anesthesia providers should be cognizant of tourniquet inflation times and anticipate and be ready to treat potential cardiovascular perturbations upon tourniquet release.

Fat Embolism Syndrome

Fat emboli can occur in orthopedic surgery, sometimes with significant clinical consequences. Fat embolism refers to fat droplets that are extruded into venous channels and enter the peripheral and pulmonary microcirculation. Most commonly this is the result of unstable bone fragments (e.g., traumatic fractures) and reaming of medullary cavities, which increases medullary cavity pressure and allows embolization of fat, marrow, and bone into the open venous channels. Many of these events may be clinically silent. However, fat embolism syndrome (FES) can be a catastrophic complication, usually manifested by a petechial rash, deteriorating mental status, and progressive respiratory insufficiency. Due to the nonspecific nature of the manifestations, the diagnosis of FES can be difficult to make and often is a diagnosis of exclusion. Furthermore, there are no confirmatory diagnostic or radiologic tests. The varied clinical manifestations of FES are listed in Table 25.1.

Management of patients with suspected FES centers on supportive care, as there is no definitive therapy. Thus, many advocate *prevention* of FES. The single most important

Table 25.1 Clinical manifestations of fat embolism syndrome

Respiratory	Tachypnea, dyspnea, cyanosis, rales, hypoxemia (PaO_2 < 80 mmHg), elevated A-a gradient (>20 mmHg)
Central nervous system	Drowsiness, anxiety, restlessness, seizures, confusion, stupor, coma
Cardiovascular	Increased pulmonary artery pressure, hypotension, arrhythmias, decreased cardiac output
Skin	Transient petechial rash located on upper anterior torso, oral membranes, conjunctiva, which may disappear within 24 h
Hematologic	Thrombocytopenia (platelet count <150,000/ml)

preventative effort is early stabilization of fractures, especially those involving the pelvis or long bones. To this end, some centers elect to stabilize fractures with external fixation (when possible) until the patient is stable enough to undergo definitive fixation. Patients who are more severely injured and predisposed to acute lung injury (ALI) or adult respiratory distress syndrome (ARDS) may benefit from delaying definitive treatment.

Surgical procedures most commonly associated with FES are total knee arthroplasty, total hip arthroplasty, and intramedullary reaming of the femur. Fat embolism should always be suspected in the orthopedic surgery patient who has acute cardiorespiratory distress. A search for other causes should be undertaken, and appropriate laboratory and radiographic studies should be ordered as clinically indicated. Supportive care of these patients is of utmost importance, as associated mortality can be high, ranging from 5 to 33 %.

Infection Prevention

Infectious complications in orthopedic surgery can have devastating consequences and cause a significant amount of morbidity. If hardware becomes infected, subsequent operations are necessary for removal and reimplantation of hardware, as well as long-term systemic antimicrobial therapy. Recent Medicare data revealed that total hip arthroplasty is associated with a 90-day deep infection rate of 0.24 % and total knee arthroplasty is associated with a 90-day deep infection rate of 0.4 %. Risk factors for postoperative infection include diabetes mellitus, advanced age, malnutrition, obesity, concurrent urinary tract infection, steroid use, and the administration of blood products. Prophylactic antibiotic administration is usually the responsibility of the anesthesiologist and is a frequently included measure in programs designed to ensure safer surgery, such as the Centers for Medicare and Medicaid Services (CMS) and Surgical Care Improvement Project (SCIP).

Table 25.2 Recommendations for prophylactic antibiotic administration

Recommendation 1
• Prophylactic antibiotics should be carefully selected and consistent with current recommendations • Cefazolin and cefuroxime are the preferred antibiotics for patients undergoing orthopedic procedures • Clindamycin and vancomycin may be used for patients with a confirmed beta-lactam allergy • Vancomycin may be use in patients with known colonization with MRSA or in facilities with recent MRSA outbreaks
Recommendation 2
• Prophylactic antibiotics should be administered within 1 h before skin incision • Due to an extended infusion time, vancomycin should be started within 2 h before incision • When a proximal tourniquet is used, the antibiotic must be completely infused before inflation of the tourniquet
Recommendation 3
• Prophylactic antibiotics should be discontinued within 24 h of the end of surgery • There is no evidence to support continuation of antibiotics beyond 24 h

Recommendations from the American Academy of Orthopedic Surgery (AAOP) for prophylactic antibiotic administration are as outlined in Table 25.2.

As neuraxial and peripheral nerve blocks are increasingly being performed for orthopedic surgery patients, meticulous attention to prevention of infection is critical when performing these procedures. Strict aseptic technique with mask, sterile gloves, and sterile drapes as well as chlorhexidine gluconate in an alcohol base should be standard for all regional techniques. Recent evidence demonstrates that the odds of surgical site infection for patients receiving total hip or knee replacement under general anesthesia were 2.21 times higher than those who had the same procedure under epidural or spinal anesthesia. Although this data is retrospective, it suggests that neuraxial techniques impart some beneficial effect to patients in terms of infection prevention. One possible mechanism may be improved tissue perfusion and oxygenation as a result of the sympathectomy associated with neuraxial blocks.

Thromboprophylaxis

Thromboembolic complications, such as deep venous thrombosis (DVT) and pulmonary embolus (PE), remain a leading cause of mortality and morbidity after orthopedic surgery. In contrast to general surgery patients who have a 25 % rate of DVT without thromboprophylaxis, orthopedic patients have a 50–60 % rate of DVT. Orthopedic injuries associated with trauma such as hip, pelvic, and long bone fractures have the highest incidence of thromboembolic complications. Risk factors for thromboembolic events that are not associated with the

Table 25.3 Perioperative anticoagulation considerations

A. Preoperative considerations
• Full anticoagulation is a contraindication to regional techniques. These patients will need a general anesthetic
• Patients on aspirin and NSAIDs may undergo neuraxial anesthesia, as the risk of epidural hematoma is not increased
• Discontinuation of thienopyridine therapy is necessary for neuraxial blockade. Ticlopidine should be discontinued for 14 days and clopidogrel should be discontinued for 7 days prior to neuraxial blockade
• Patients on long-term warfarin therapy who are to undergo neuraxial techniques should discontinue their warfarin 4–5 days before the planned procedure, under the direction of their managing physician. The INR should be normalized before initiation of neuraxial blockade
• Patients on preoperative low molecular weight heparin (LMWH) thromboprophylaxis can be assumed to have altered coagulation. Needle placement should occur at least 10–12 h after the last LMWH dose
• In patients receiving higher (treatment) doses of LMWH, such as enoxaparin 1 mg/kg every 12 h or 1.5 mg/kg daily, it is recommended to wait at least 24 h to ensure normal hemostasis at the time of needle insertion
B. Postoperative considerations
1. Single-daily dosing of LMWH can be safely administered to patients with an indwelling catheter. The first dose should be administered 6–8 h postoperatively and the second postoperative dose should occur no sooner than 24 h after the first dose. Timing of catheter removal should ensure that catheters are removed a minimum of 10–12 h after the last dose of LMWH and subsequent doses should be delayed a minimum of 2 h after catheter removal. No additional hemostasis-altering medications should be administered due to the additive effects
2. Twice-daily dosing of LMWH is associated with an increased risk of spinal hematoma. The first dose of LMWH should not be administered until 24 h postoperatively. If an indwelling epidural catheter is used, it may be used overnight but must be removed before the first dose of LMWH. Administration of LMWH should be delayed for 2 h after catheter removal
3. If warfarin is used for postoperative thromboprophylaxis in patients with indwelling catheters, the catheters should be removed when the INR is less than 1.5. Neurologic assessment should be continued for at least 24 h after catheter removal

surgery itself include increasing age, cancer, obesity, and previous history of DVT or PE. All patients undergoing routine orthopedic procedures, especially total knee and hip arthroplasty, should have postoperative thromboprophylaxis. The American College of Chest Physicians (ACCP) Conference on Antithrombotic and Thrombolytic Therapy (8th edition) offers evidence-based guidelines for thromboprophylaxis in orthopedic surgery. Options for prophylaxis include low molecular weight heparin, fondaparinux, and adjusted-dose Coumadin. Recommendations are that treatment should be for at least 10 days and extended to 35 days in some cases.

The balance between anticoagulation and hemostasis is a delicate one that deserves thoughtful attention and planning. Hemorrhagic complications such as epidural hematomas must be recognized and treated immediately to avoid permanent paralysis. The prevalence of epidural hematoma due to neuraxial catheter placement is estimated to be 1 in 150,000 epidurals and 1 in 220,000 spinals. Since neuraxial blockade is commonly utilized in orthopedic patients who also need systemic anticoagulation, practice guidelines have been developed to encourage safe and effective use of neuraxial anesthesia. The American Society of Regional Anesthesia and Pain Medicine (ASRA) addresses the issues associated with regional anesthesia in patients receiving antithrombotic therapy in a practice advisory. Recommendations for perioperative anticoagulation in association with neuraxial and peripheral nerve blockade are described in Tables 25.3 and 25.4.

Table 25.4 Stopping newer anticoagulants before surgery[a]

Anticoagulant	Procedures with low bleeding risk (days)	Procedures with high bleeding risk (days)
Dabigatran (Pradaxa)	1	2
Rivaroxaban (Xarelto)	1	2
Apixaban (Eliquis)	1	2

[a]Stoppage times are approximately doubled in the presence of renal dysfunction (creatinine clearance <50 ml/min)

Clinical Review

1. Beach chair position can be associated with the following:
   A. Errors in blood pressure monitoring
   B. Increased bleeding
   C. Easy access to the airway
   D. Hypertension
2. An intravenous regional block is recommended for procedures lasting about
   A. 30 min
   B. 1 h
   C. 2 h
   D. 3 h

3. For surgery on the medial aspect of the leg, the following nerve block is usually performed in addition to other nerve blocks:
   A. Sciatic
   B. Femoral
   C. Saphenous
   D. Deep peroneal
4. Best treatment/prevention of tourniquet pain is
   A. Spinal anesthesia
   B. Intravenous opioids
   C. Peripheral nerve block
   D. Release of tourniquet
5. A 62-year-old patient is undergoing total knee arthroplasty under spinal anesthesia. About 30 min intraoperatively, the patient becomes tachypneic and restless and the blood pressure drops from 154/88 mmHg to 90/42 mmHg. The most likely diagnosis is
   A. Air embolism
   B. Hypotension due to excessive blood loss
   C. Pain
   D. Fat embolism

Answers: 1. A, 2. B, 3. C, 4. D, 5. D

Further Reading

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Part IV

Specialty Anesthesia

Cardiac Anesthesia

26

Mahesh Sardesai

Cardiac anesthesiology encompasses the perioperative management of patients undergoing surgery on the heart and great vessels, as well as an increasing variety of transcatheter and other nonsurgical procedures. Cardiovascular disease is the leading cause of death in the United States and other industrialized nations, and it comprises an increasing share of the disease burden in the developing world. Accordingly, the fundamental principles of cardiac anesthesiology are essential not only for cardiac surgery itself, but also for the care of patients with various degrees of cardiovascular compromise undergoing noncardiac procedures. Therefore, optimum anesthetic care of these patients requires familiarity with cardiovascular physiology, diagnostic evaluation, transesophageal echocardiography (TEE), cardiopulmonary bypass (CPB), cardiac surgical techniques, and cardiac perioperative care.

Cardiovascular Physiology

The underlying principle of perioperative management in any patient is to maintain adequate oxygen delivery to sustain the metabolic requirements of vital organs and peripheral tissues. The ultimate goal of any cardiac surgical intervention is to provide conditions that promote adequate tissue perfusion with as little cardiopulmonary burden as possible.

Blood Pressure

Tissue perfusion depends on systemic blood pressure and local vascular resistance. Local vascular resistance is determined by local vasomotor tone. Systemic blood pressure, clinically measured with a noninvasive blood pressure cuff or an indwelling arterial catheter, is expressed as mean arterial pressure (MAP), normally between 70 and 100 mmHg. normally between 70 and 100 mmHg. Pulsatile flow from cyclic cardiac contractions generates a pulse pressure, the difference between systolic blood pressure (SBP) and diastolic blood pressure (DBP). The five main physiologic parameters that contribute to blood pressure are heart rate, rhythm, contractility, preload, and afterload. Understanding these five parameters is essential to developing a clinical framework for hemodynamic management (Table 26.1). At normal resting heart rates, MAP can be estimated from measurements of SBP and DBP:

$$\text{MAP} \approx \tfrac{1}{3}\,\text{SBP} + \tfrac{2}{3}\,\text{DBP}$$

However, at high heart rates, changes in the shape of the arterial pulse pressure curve cause MAP to approach the mean of SBP and DBP. Systemic blood pressure depends on a contribution from the heart, cardiac output (CO), and a contribution from the systemic vasculature, systemic vascular resistance (SVR):

$$\text{MAP} = \text{CO} \times \text{SVR}$$

Cardiac Output

Cardiac output is the volume of blood pumped by the heart into the peripheral circulation every minute. Normal CO is approximately 5–6 L/min in a 70 kg adult male. Cardiac index (CI), equal to CO divided by body surface area (BSA), is a normalized value that allows comparison of CO among people of differing body habitus (normal CI = 2.5–4.2 L/min/m^2). CO is normally identical between the right and left sides of the heart, but certain congenital abnormalities and traumatic injuries can cause the two sides of the heart to eject different amounts of blood per cardiac cycle. CO is equal to the product of heart rate (HR) and stroke volume (SV):

$$\text{CO} = \text{HR} \times \text{SV}$$

$$\text{CI} = \text{CO} / \text{BSA}$$

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Table 26.1 Overview of physiologic determinants of systemic blood pressure

Heart rate	
Colloquial	Pulse rate, heartbeats per minute
Clinical	Periodicity or frequency of contraction
Fundamental	Intactness of nodal function and innervation
Monitoring methods	ECG, pulse waveforms
Rhythm	
Colloquial	Beat pattern, ECG tracing
Clinical	Regularity of contraction
Fundamental	Intactness of cardiac conduction system
Monitoring methods	Peripheral pulse, ECG, pulse waveforms
Contractility	
Colloquial	Heart function, ejection fraction
Clinical	Magnitude of contraction, change in pressure
Fundamental	Increase in intraventricular pressure during contraction, change in myocyte length
Monitoring methods	TEE, pulse pressure, cardiac contractions on surgical field
Preload	
Colloquial	Ventricular volume, dilation, volume status
Clinical	Chamber volume at end diastole
Fundamental	Maximum myocyte stretch
Monitoring methods	TEE, venous distension, distension of heart on surgical field
Afterload	
Colloquial	Arterial squeeze, vascular tightness
Clinical	Resistance faced by myocardium
Fundamental	Work performed by myocyte
Monitoring methods	PA catheter, TEE (by excluding other causes of hypotension)

Heart Rate

Heart rate represents the periodic impulses from the native pacemaker function of the heart's conduction system. Spontaneous, rhythmic depolarization of cells in the sinoatrial (SA) node generates impulses that are conducted through the atrioventricular (AV), the bundle of His, and the network of Purkinje fibers in the ventricles, thus spurring a coordinated cardiac contraction (Fig. 26.1). The spontaneous nodal function of the heart is modulated by the autonomic nervous system. Sympathetic stimulation (β-receptors) from upper thoracic spinal nerves increases HR, while parasympathetic stimulation (cholinergic receptors) from the vagus nerve (cranial nerve X) decreases HR. A mild reduction in HR can improve CO by providing more diastolic time for greater ventricular filling, but more significant decreases in HR will lead to a decrease in CO.

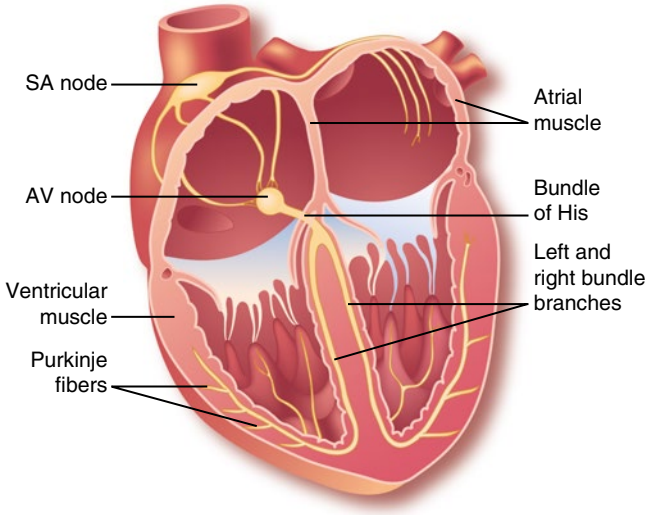

Fig. 26.1 Conduction system of the heart

Heart Rhythm

While heart rate measures the periodicity or frequency of cardiac contraction, rhythm measures the regularity or pattern of contraction. Abnormal conduction leads to irregular heart rhythms, or arrhythmias. Irregular rhythms can decrease CO by reducing diastolic filling time or by impeding the ability of the heart to contract in an efficient, coordinated fashion. Overall, then, HR represents the intactness of nodal function and autonomic innervation of the heart, while rhythm represents the intactness of the cardiac conduction system.

Stroke Volume

Stroke volume is the net amount of blood ejected by the heart per cardiac cycle, equal to the difference between end-diastolic volume (EDV) and end-systolic volume (ESV). During systolic contraction, shortening of cardiac myocytes generates a force that increases pressure inside the left ventricle. Once this pressure exceeds DBP, the aortic valve opens, allowing ejection of blood from the left ventricle into the aorta. The force of this myocardial contraction is called contractility. The percentage of ventricular blood volume that is ejected during a single contraction, an indirect yet clinically useful measure of contractility, is called the ejection fraction (EF). Unlike SV, EF does not change with body habitus. Healthy individuals typically have an EF of 55–70 %. Stroke volume is affected by preload, afterload, contractility, valvular dysfunction, and wall-motion abnormalities.

$$EF = (EDV - ESV) / EDV = SV / EDV$$

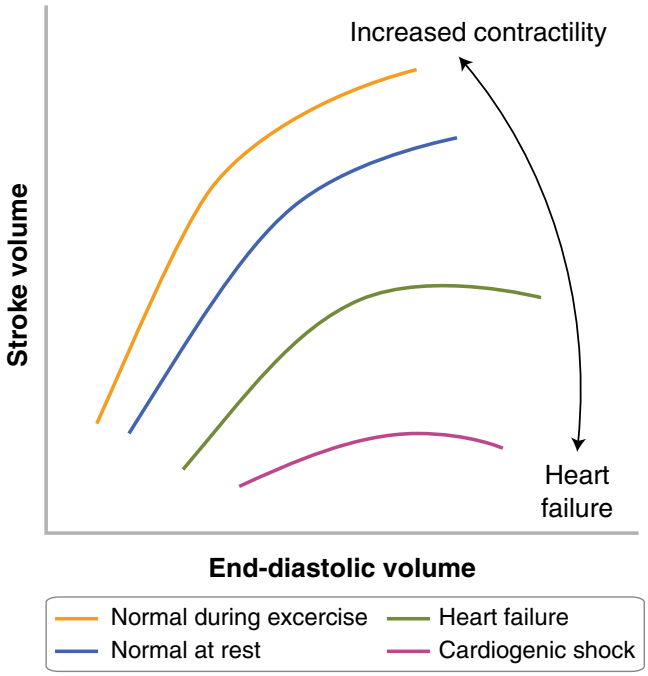

Fig. 26.2 Relationship between stroke volume and end-diastolic volume (Frank–Starling law)

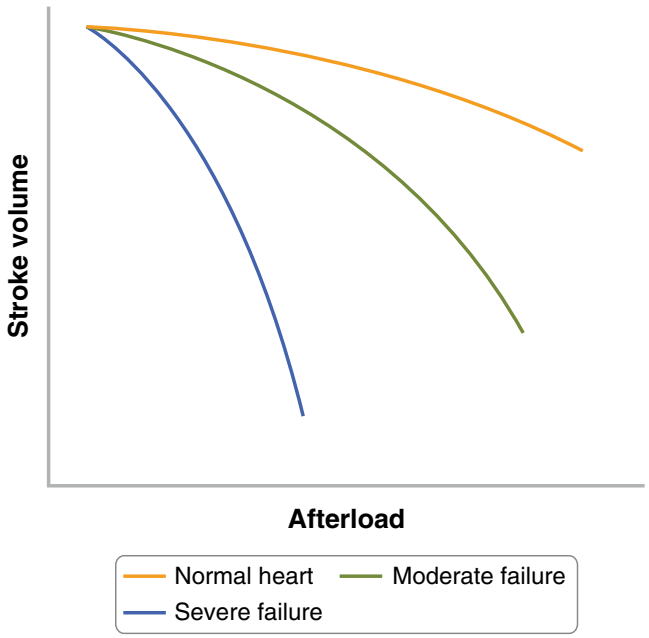

Fig. 26.3 Relationship between stroke volume and afterload

Preload

EDV (or preload) is the maximum volume of the heart during the cardiac cycle. It is the point at which the myocardium is maximally stretched prior to contraction and sarcomeres in the cardiac myocytes are the longest. The amount of muscle stretch in the myocardium at EDV is called preload. Surrogate measures of preload include central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP), and left atrial pressure (LAP). According to the Frank–Starling mechanism, small increases in preload can improve the contractile function of the heart, resulting in increased SV with relatively little change in EF (Fig. 26.2). Preload is dependent upon venous return, the blood volume, and the distribution of blood volume (posture, intrathoracic pressure).

This is appreciated clinically as a "volume responsive" heart, a situation in which volume administration improves forward blood flow and systemic blood pressure. As intraventricular volume increases further, additional increases in preload cause smaller increases in stroke volume. Changes in ventricular compliance affect the end-diastolic pressure (EDP). A poorly compliant ("stiff") ventricle will not expand easily with increased preload, leading to increased EDP and potentially detrimental venous congestion. On the other hand, in a very compliant ventricle, as in a patient with dilated cardiomyopathy, increases in preload do not lead to appreciable increases in EDP and may fail to improve SV adequately.

Afterload

The resistance that must be overcome by the ventricle with each contraction is called afterload. On a fundamental level, afterload is the work performed by the myocardium, or the force the myocardium must generate to propel blood a certain distance. CO is inversely related to afterload. Clinically, SVR is the principal determinant of afterload (Fig. 26.3). SVR (normal 900–1,500 dyn/s/cm^5) can be calculated from other hemodynamic measurements:

$$\mathrm{SVR}\left(\mathrm{dynes/s/cm^5}\right)=\frac{80\times\left(\mathrm{MAP\,mmHg}-\mathrm{CVP\,mmHg}\right)}{\mathrm{CO}\left(\mathrm{L/min}\right)}$$

According to the Hagen–Poiseuille law, laminar blood flow through vessels is inversely proportional to the fourth power of vessel radius. Although capillaries are the narrowest vessels in the entire circulation, the presence of millions of capillaries in parallel minimizes their aggregate contribution to SVR. Instead, the compliance of large arterioles plays the largest role in determining ventricular afterload.

Coronary Circulation

The heart is supplied by two coronary arteries, left and right, arising from the aorta (Figs. 26.4 and 26.5). They run on the surface of the heart and are, therefore, called epicardial arteries. The right coronary artery (RCA) branches into the right marginal artery and the posterior descending artery and supplies the right atrium, right ventricle, bottom portion of

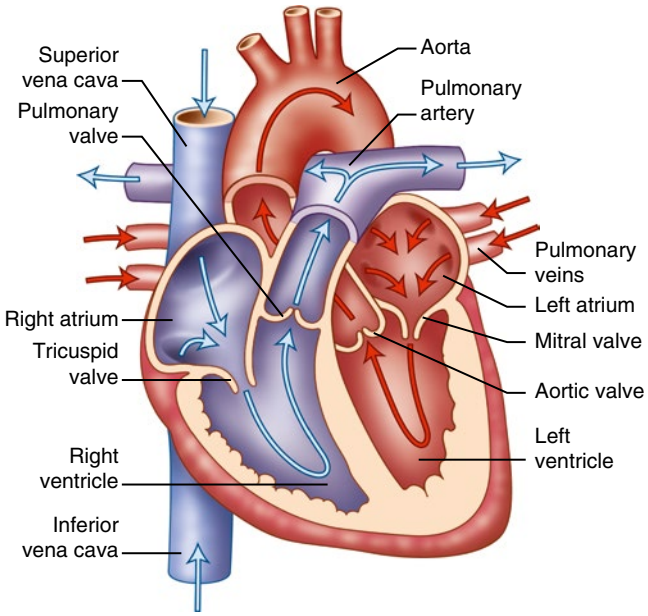

Fig. 26.4 Blood flow through the heart

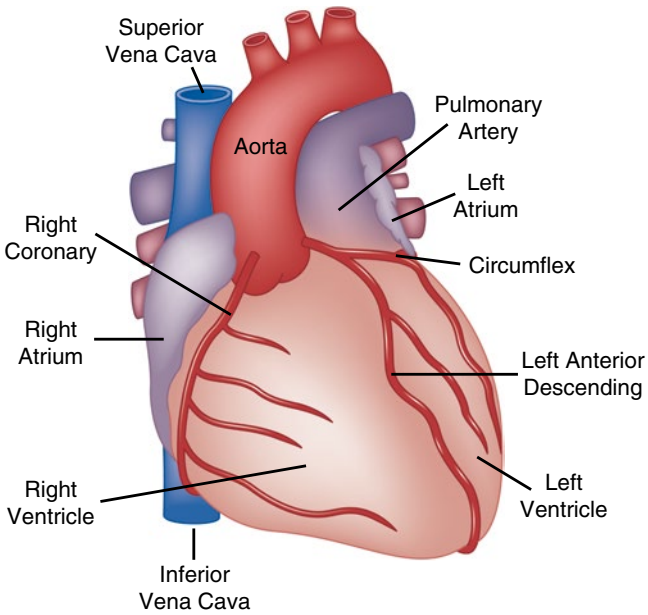

Fig. 26.5 Coronary circulation

both ventricles, and back of the septum. The left main coronary artery (LCA) branches into the circumflex artery and the left anterior descending artery (LAD) and supplies:

- Circumflex artery (CA)—supplies blood to the left atrium and side and back of the left ventricle
- Left anterior descending artery (LAD)—supplies the front and bottom of the left ventricle and the front of the septum

In people in whom the posterior descending artery arises from the RCA are right dominant (65 %), from the CA are left dominant (25 %), and both from the RCA and CA are codominant (10 %). Deoxygenated blood is returned to the chambers of the heart via coronary veins. These veins converge to form the coronary venous sinus, which in turn drains into the right ventricle. The anatomic region of heart most likely associated with the specific coronary arterial supply is:

- Inferior-Right coronary artery
- Anteroseptal-Left anterior descending artery
- Anteroapical-Left anterior descending (distal) artery
- Anterolateral-Circumflex artery
- Posterior-Right coronary artery

The two coronary arteries are end arteries, and because they are narrow are prone to atherosclerosis. Average coronary blood flow is 250 ml/min. Myocardial blood flow is closely linked with oxygen demand, which is about 8–10 ml of O_2/min/100 g. The myocardium extracts about 65 % of oxygen in the arterial blood compared with other tissues (25 %). The coronary arteries autoregulate coronary blood flow between perfusion pressures of 50–120 mmHg.

Increases in heart rate cause decreased coronary perfusion. This is because the heart gets its blood supply during diastole, and any increase in heart rate decreases diastolic time. Coronary perfusion pressure (CPP) is a balance between the diastolic blood pressure and the left ventricular end-diastolic pressure and can be calculated as:

$$\text{CPP} = \text{Diastolic blood pressure} - \text{LVEnd diastolic pressure}$$

Preoperative Management

Patient Assessment

Typically in elective cardiac surgery, and even in many emergency cases, the surgical diagnosis and operative plan have been established in advance by history, physical examination, and diagnostic testing. The patient presenting for heart surgery, by definition, has compromised cardiopulmonary function and has probably already suffered some degree of damage to other organs. The fundamental paradox of cardiac surgery is that the planned operation increases the risk of further damage to other organ systems, yet the operation itself presumably represents the best chance to "optimize" the patient's overall condition. The substantial logistical and economic resources called upon by a cardiac operation impose additional pressure to develop a perioperative risk management strategy without postponing or canceling surgery.

Therefore, the goal of preoperative evaluation should be to clarify any preexisting conditions known to be associated

with an increased risk of perioperative morbidity and mortality. Among these are:

- Age greater than 60 years
- Previous cardiac surgery
- Significant obesity (body mass index greater than 35 kg/m^2)
- Systemic or pulmonary arterial hypertension
- Acute coronary syndrome (ACS)
- Congestive heart failure (CHF)
- Diabetes mellitus
- Peripheral vascular disease
- Acute or chronic renal insufficiency
- Chronic pulmonary disease
- Neurological disease

History and Physical Examination

As with any other procedure, preoperative assessment for cardiac surgery begins with a careful history and physical examination. The patient should be asked about any past or current symptoms of chest pain, fatigue, shortness of breath, orthopnea, nocturnal angina or dyspnea, light-headedness, syncope, or palpitations. The time course and progression of symptoms should be determined, with particular emphasis on whether symptoms occur at rest or with exertion. It can be especially illuminating to identify symptoms in the context of the patient's baseline lifestyle and level of activity. For example, a patient may struggle to identify symptoms in unambiguous clinical terms but may easily describe related lifestyle changes, such as a reduced capacity to perform required job duties or abandonment of a favorite recreational activity.

Physical examination should obviously include auscultation of the heart for rhythm and the presence of any murmurs. Consultation with the primary physician or cardiologist can help delineate the progression of valvular lesions and decide if further evaluation is needed. Softer midsystolic murmurs (grade 2 or lower) that are asymptomatic and are not associated with other findings are generally thought to reflect increased flow velocity and require no further workup. However, echocardiography is recommended in patients with louder or symptomatic midsystolic murmurs. Other systolic murmurs, diastolic murmurs, and continuous murmurs reflect pathology and require echocardiography.

The degree of CHF should be assessed in terms of both American Heart Association (AHA) objective criteria as well as New York Heart Association (NYHA) functional capacity (Table 26.2). The patient's tolerated level of exertion, measured in metabolic equivalents (MET), can provide a relative measure of perioperative risk (Table 26.3).

Having cardiac surgery is a major life event by any measure, and caregivers need to be sensitive to the immense emotional burden faced by patients and their loved ones. In the preoperative period, the anesthesiologist must balance the desire for a thorough assessment and honest discussion of perioperative risks with the need to avoid placing undue psychological (and, in turn, physiologic) stress on the patient. A candid explanation of the anesthesia team's active role in the operating room—monitoring the patient continuously and providing the diagnostic and physiologic support necessary to allow the surgeon the freedom to concentrate on the technical aspects of the operation itself—can be both informative and reassuring. At the same time, many patients view the prospect of heart surgery as a signal to reconsider their

Table 26.2 New York Heart Association (NYHA) functional classification, and American Heart Association (AHA) objective assessment of heart function

NYHA class	Functional capacity in patients with cardiac disease
I	No symptoms and no limitation of physical activity (ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or angina)
II	Mild symptoms and slight limitation of physical activity (comfortable at rest, ordinary physical activity results in fatigue, palpitation, dyspnea, or angina)
III	Moderate symptoms and marked limitation of physical activity (comfortable at rest, less-than-ordinary activity causes fatigue, palpitation, dyspnea, or angina)
IV	Severe symptoms and severe limitation of physical activity (inability to carry on any physical activity without discomfort, symptoms of heart failure or angina may be present even at rest, bed-bound patients)
AHA class	**Objective assessment**
A	No objective evidence of cardiovascular disease
B	Objective evidence of minimal cardiovascular disease
C	Objective evidence of moderately severe cardiovascular disease
D	Objective evidence of severe cardiovascular disease

Examples

A patient with minimal or no symptoms but a large pressure gradient across the aortic valve or severe left main coronary artery exclusion is classified as NYHA class I, AHA class D

A patient with severe angina but normal coronary arteries on angiography is classified as NYHA class IV, AHA class A

Table 26.3 Approximate metabolic equivalents of task (MET) for various activities. One MET represents metabolic oxygen consumption of 3.5 ml kg^{-1} min^{-1}

MET	Functional status	Activity
<4	Poor	Sleeping or sitting stationary Activities of daily living: eating, dressing, bathing, using the toilet Writing, desk work Walking indoors or around the house Light housework: changing bed sheets, dusting, washing dishes
4–7	Intermediate	Brisk walking 1–2 blocks on level ground Climbing 1–2 flights of stairs or walking uphill Gardening and lawn work: raking leaves, weeding, pushing a mower Sexual relations Moderate housework: vacuuming, sweeping floors, carrying groceries
>7	Good	Heavy housework: scrubbing floors, lifting and moving heavy furniture Jogging or running Swimming, cycling, vigorous sports

own health-related behaviors and commit to improving them afterwards. The preoperative discussion offers a valuable opportunity for the anesthesiologist to reinforce this process by encouraging healthy lifestyle changes that will also reduce future anesthetic risk, such as smoking cessation and weight management.

Concomitant Diseases

Patients scheduled for cardiac surgery frequently present with multiple comorbid conditions, which may arise either independently or as a result of their compromised cardiac status. Reviewing the patient's list of prescription and over-the-counter medications can quickly reveal coexisting conditions that should be considered when developing a perioperative management plan.

Cardiovascular

Coronary artery disease often occurs in concert with cerebrovascular and peripheral vascular disease. Any history of previous stroke or transient ischemic attack, along with any residual neurologic defects, should be ascertained. Auscultation of the carotid arteries for bruits and review of any carotid Doppler studies can reveal the severity of occlusive disease, which increases the risk of perioperative cerebrovascular complications. Claudication, paresthesias, and venostasis changes suggest the presence of significant peripheral vascular disease. Peripheral pulses should be palpated, particularly in locations where arterial line placement is anticipated.

Pulmonary

The thoracotomy incision incumbent with cardiac surgery, as well as CPB itself, increases the risk of postsurgical pulmonary complications. Thoroughly assessing the patient's baseline pulmonary status can help predict the need for prolonged postoperative ventilation. Important considerations in patients with asthma or other chronic obstructive pulmonary disease (COPD) include the frequency of symptoms, time since the last attack, compliance with medications, and any previous need for intubation. Preoperative oxygen saturations, blood gases, pulmonary function tests, and chest imaging can be useful. Any history of smoking, current or remote, should be elicited. Even if undiagnosed, some degree of obstructive sleep apnea can be presumed in morbidly obese patients or those who present with snoring or daytime somnolence. Any use of supplemental oxygen or positive airway pressure therapy should be determined to help guide intraoperative and postoperative ventilation strategies.

Airway

If the physical examination suggests a difficult airway, and especially if an awake intubation is anticipated, preparations should be made for adequate topicalization, sedation, and antihypertensive therapy during intubation. If there is evidence of poor dentition or abscesses in a patient scheduled for valve surgery, preoperative dental consultation and tooth extraction may be indicated to prevent the development of prosthetic valve endocarditis.

Diabetes Mellitus

Diabetes mellitus is a major risk factor for coronary artery disease and an independent predictor of perioperative morbidity and mortality. Because of accompanying autonomic neuropathy, diabetics have an increased risk of hemodynamic lability and asymptomatic (silent) myocardial ischemia, thereby increasing overall cardiovascular risk. Delayed gastric emptying, also associated with autonomic neuropathy, can also complicate airway management. A preoperative serum glycosylated hemoglobin (HbA_{1c}) level can help characterize the quality of glycemic control in the months preceding surgery and identify those patients in

need of more aggressive perioperative and postoperative glycemic control.

Renal

Patients with even early stages of renal dysfunction experience increased morbidity from cardiac surgery. Many factors incumbent to cardiac surgery, such as large crystalloid fluid loads from CPB, hyperkalemic cardioplegia solutions, and variable or prolonged periods of systemic hypoperfusion, can adversely affect renal function. Severe renal impairment, especially when combined with anemia and metabolic acidosis, can compromise myocardial function when weaning the patient from CPB. Baseline urine production in patients with renal dysfunction should be assessed, as urine output is often used in cardiac surgery as an indicator of renal function.

Liver

Severe liver dysfunction increases the risk of severe bleeding complications from surgery. Any clinical signs of impaired clotting, such as delayed wound healing, epistaxis, or gum bleeding, should raise concern about severely reduced production of clotting factors. Preoperative administration of vitamin K or fresh frozen plasma may be warranted, keeping in mind that the added fluid load can worsen CHF and left ventricular dysfunction. Elective surgery should be delayed in patients with acute hepatitis until serum liver function tests normalize.

Laboratory Tests

Reviewing the cardiac surgical assessment and previous diagnostic tests is essential, both to assess the patient's overall medical condition and to understand more fully the planned operation. Previous surgical records may provide evidence of potential complicating factors, such as unanticipated difficult airway management or adverse events. Past surgical records are particularly important for repeat cardiac surgery. A chest radiograph can show the distance between the cardiac silhouette and the sternum, which can help judge the likely difficulty of sternotomy and intrathoracic surgical dissection. Other imaging modalities, such as computer tomography (CT) or cardiac magnetic resonance imaging (MRI), can delineate intrathoracic anatomy and highlight potential dangers for sternotomy, such as a dilated aortic root or previous coronary bypass grafts in close proximity or adherent to the sternum.

Important preoperative laboratory tests include serum hemoglobin and hematocrit, platelet count, blood urea nitrogen and creatinine levels, coagulation profiles, and liver function tests. The preoperative electrocardiogram (ECG) should be examined for signs of myocardial ischemia, prior myocardial infarction, and abnormal conduction. Stress echocardiography, myocardial perfusion studies, and cardiac catheterization can provide valuable information about valvular abnormalities, global and segmental left ventricular function, areas of induced ischemia, pulmonary hypertension, and right ventricular dysfunction (cor pulmonale). For patients scheduled for coronary artery bypass grafting (CABG), cardiac catheterization can define coronary anatomy and help determine the number and location of planned bypass grafts.

Preoperative Medications

Antihypertensives

Primary or essential hypertension is common in patients having cardiac surgery and is a major concern for risk assessment and stratification. Chronic hypertension can lead to left ventricular hypertrophy, decreased ventricular compliance, renal insufficiency or failure, and neurologic symptoms progressing to infarction. After excluding secondary causes of increased blood pressure (e.g., renal disease, pheochromocytoma, or certain drugs), one should assess the typical range of blood pressures within the patient normally lives without symptoms. Patients are typically advised to delay elective surgery until blood pressure is controlled to a normal range, but altered cerebral autoregulation may make normotension undesirable. Untreated primary hypertension that appears to resolve spontaneously ("pseudonormotension") may actually represent myocardial compromise or progression of valvular stenosis and pose a risk of cardiovascular collapse with minimal anesthetic exposure or surgical stress.

In general, patients on antihypertensive medications should continue such medications throughout the perioperative period to maintain blood pressure homeostasis at the time of surgery, though diuretics should not be given the day of surgery to minimize hypovolemia. In particular, withdrawal of β-blockers and clonidine can lead to rebound hypertension. Preoperative nitrates and digoxin should also be continued. Calcium channel blockers may have renal protective effects in patients undergoing surgery involving aortic crossclamping, but their myocardial depressant and vasodilator effects can accentuate hypotension during anesthetic induction. Refractory hypotension during and after CPB can also occur with ACE inhibitors and angiotensin II receptor antagonists. Nonetheless, the apparent renal protective benefit of these agents warrants their continuation perioperatively while treating intraoperative hypotension with appropriate vasoconstrictor therapy

Antidiabetics

Diabetics undergoing cardiac surgery require serial monitoring of serum glucose levels. Patients should be instructed to withhold their usual nutritional insulin on the day of surgery. Similarly, oral diabetes medication should be held in the morning of the surgery. Inpatients awaiting surgery may

require scheduled insulin therapy to achieve preoperative glycemic control.

The intraoperative humoral stress response can cause increased cortisol levels and decreased production of insulin, both of which can lead to hyperglycemia. Intraoperative glycemic control is achieved most efficiently with a continuous intravenous infusion protocol rather than intermittent intravenous boluses or subcutaneous injections. An insulin protocol should be started perioperatively for diabetic patients undergoing cardiac surgery, as well as for nondiabetics who have repeated serum glucose values ≥180 mg/dL. Maintaining glycemic control (120–180 mg/dL) prior to and during cardiac surgery is associated with reduced mortality, decreased neurologic injury, lower incidence of wound infections, and decreased length of hospital stay. Tighter glucose control strategies (such as 90–120 mg/dL) have not been demonstrated to lead to superior outcomes. While mild hyperglycemia appears to be well tolerated in most patients, hypoglycemia is an unambiguously undesirable complication of intensive insulin infusion therapy. Accordingly, overly aggressive intraoperative glucose control may be counterproductive, especially if it distracts from other patient care responsibilities.

Anticoagulants

Patients on chronic anticoagulant therapy (e.g., aspirin, heparin, or warfarin) or who have been recently exposed to thrombolytic agents pose a particular challenge. The preoperative evaluation should pay particular attention to the usage, dosage regimen, indications, and cessation intervals of these drugs. Ideally, such medications should be stopped several days prior to surgery to minimize postoperative bleeding complications, but these benefits should be weighed against the patient-specific risks of stopping ongoing anticoagulant therapy, such as in-stent restenosis or thromboembolism. Warfarin (Coumadin) should be stopped 5 days prior to surgery or until a normal or near-normal INR is reached. Similarly, PTT or thrombin clotting time can help verify adequate blood clotting function after discontinuing dabigatran (Pradaxa, a direct thrombin inhibitor) or rivaroxaban (Xarelto, a direct factor Xa inhibitor). Patients at high risk of thrombosis may need to be admitted to the hospital preoperatively for bridging therapy. More urgent surgery may require administration of some combination of vitamin K and fresh frozen plasma, depending on the patient's level of anticoagulation and the urgency of surgery.

Aspirin irreversibly inhibits platelet cyclooxygenase, rendering platelets inactive. Thienopyridines such as clopidogrel (Plavix) and prasugrel (Effient) also irreversibly inhibit platelet response for the life of the platelet. A newer ADP receptor/$P2Y_{12}$ inhibitor, ticagrelor (Brilinta), is an allosteric antagonist that provides reversible platelet blockade. Patients with newly diagnosed ACS may be started on dual antiplatelet therapy (aspirin and clopidogrel) to prevent further disease progression. One may suspect that discontinuing antiplatelet therapy would predispose the patient to thrombotic complications, particularly in patients with drug-eluting stents. However, studies suggest that discontinuing antiplatelet therapy a few days before surgery is actually associated with reductions in bleeding, transfusion requirements, and rates of reoperation, with no significant increase in rates of myocardial infarction, stroke, or postoperative death. Preoperative discontinuation of aspirin is also reasonable in high-risk patients, such as those who refuse blood transfusion (Jehovah's Witnesses) and those with limited sources of allogeneic blood products due to antibodies.

Patients presenting for urgent or emergent cardiac surgery may have received doses of glycoprotein IIb/IIIa receptor antagonists during cardiac catheterization. Antiplatelet effects last approximately 24–48 h for abciximab (ReoPro), 4–8 h for tirofiban (Aggrastat), and 2–4 h for eptifibatide (Integrilin). Even in nonelective surgery, a delay of 1 or 2 days can help reduce intraoperative bleeding risk while minimizing thrombotic risk. Laboratory tests of platelet inhibition, such as PFA-100 or thromboelastography (TEG), can be helpful in deciding whether to delay surgery. If surgery cannot be postponed, the increased intraoperative bleeding may necessitate acute reversal of therapy, alterations in heparin dosing for CPB, large transfusions of blood products (including platelets), or administration of procoagulant agents (such as activated factor VII).

Herbals

The preoperative review of medications should not neglect over-the-counter medications, herbal remedies, nutritional supplements, and other nontraditional therapies, as they can have important implications for anesthetic care. For example, ephedra (*ma huang*) is a sympathomimetic compound that can complicate hemodynamic management, while ginseng and gingko biloba can inhibit platelet aggregation. Patients may be reluctant to mention taking these substances unless specifically asked about them. Because complementary therapies are not consistently regulated for origin, content, and purity, all such drugs should preferably be stopped at least 7 days prior to surgery.

Cardiac Implantable Electronic Devices

Cardiac implantable electronic devices consist of permanent pacemakers, which supplement or replace the heart's native conduction system, and implantable cardioverter defibrillators (ICDs), which provide tachycardia therapy. Approximately three million people worldwide currently live with a pacemaker. In the United States alone, roughly one million people have a pacemaker, and nearly 200,000 new pacemakers are implanted annually. Pacemakers and

ICDs are implanted for a wide variety of conduction disorders and ischemic conditions (Table 26.4). The increasingly widespread use of these devices presents special challenges for perioperative management.

In addition to evaluating and optimizing coexisting conditions, preoperative evaluation of a patient with an implanted device should include determining the type of device, indication for placement, and currently programmed settings (Table 26.5). This information can frequently be obtained from the patient (wallet card) or the physician managing the device. A chest radiograph can help determine the device type by showing the number and location of pacing electrodes and shock coils. Also, the generator may also be identified by a radiopaque manufacturer logo and serial number. Locating the coronary sinus lead on a biventricular pacemaker or ICD can help avoid dislodgment during central line placement.

Nonetheless, interrogation with a programming console remains the only reliable means of evaluating assessing device settings and predicted battery life. Under ideal circumstances, all patients with a pacemaker or ICD should undergo preoperative device interrogation, not only to determine proper function but also to facilitate proper intraoperative management by the anesthesia team. However, this may not be possible in all situations, such as in emergency surgery.

Electromagnetic interference (EMI) from surgical electrocautery can be detected by the device and interfere with its normal function. Monopolar electrocautery (Bovie) creates an arc of electrical current from the single handheld electrode to the adhesive return pad; this current can threaten any electrical device or metallic implant in its path. In contrast, bipolar electrocautery confines the current between the two handheld electrodes and is preferable in these patients. If monopolar electrocautery is required for the operation, then the return pad should be placed in a location that prevents the electrical arc from crossing the device generator and leads. All patients with ICDs should have antitachycardia therapy disabled prior to surgery with monopolar electrocautery.

The sheer variety of devices and programming modes currently available makes formulaic preoperative management difficult. For example, it is commonly assumed that a magnet will convert a pacemaker to asynchronous pacing and disable antitachycardia therapy when applied to an ICD. However, magnet effects vary significantly depending on the manufacturer, model, and even specific device settings. Even when indicated, magnet placement is an unreliable technique for changing device therapy. Obesity, perspiration, patient movement, surgical positioning, and other implanted devices can interfere with proper magnet contact; loss of contact may not be readily apparent to the clinician, as the pacing function of the device would not be changed. The anesthesia team should test the magnet's effect prior to the start of surgery, paying close attention to whether the preprogrammed asynchronous pacing rate is sufficient, particularly in patients with compromised myocardial function.

Postoperatively, any device that was reprogrammed prior to surgery should be interrogated and reset appropriately.

Table 26.4 Indications for cardiac implantable electronic device implantation

Permanent pacemaker	Implantable cardioverter defibrillator (ICD)
Sinus node disease Atrioventricular node disease Long QT syndrome Hypertrophic cardiomyopathy Dilated cardiomyopathy	Ventricular tachycardia, fibrillation Post-myocardial infarction with EF ≤30 % Cardiomyopathy with EF ≤35 % Long QT syndrome Hypertrophic cardiomyopathy Awaiting ventricular assist device or heart transplant

Table 26.5 Generic codes for cardiac implantable electronic devices

Pacemaker				
Position I	Position II	Position III	Position IV	Position V
Chambers paced	Chambers sensed	Response to sensing	Programmability	Multisite pacing
O = None	O = None	O = None	O = None	O = None
A = Atrium	A = Atrium	I = Inhibited	R = Rate modulation	A = Atrium
V = Ventricle	V = Ventricle	T = Triggered		V = Ventricle
D = Dual (A + V)	D = Dual (A + V)	D = Dual (T + I)		D = Dual (A + V)
Implantable cardioverter defibrillator (ICD)				
Position I	Position II	Position III	Position IV (or Pacemaker Code)	
Shock chambers	Antitachycardia pacing chambers	Tachycardia detection	Antibradycardia pacing chambers	
O = None	O = None	E = Electrocardiogram	O = None	
A = Atrium	A = Atrium	H = Hemodynamic	A = Atrium	
V = Ventricle	V = Ventricle		V = Ventricle	
D = Dual (A + V)	D = Dual (A + V)		D = Dual (A + V)	

Most manufacturers also recommend a postoperative interrogation to confirm proper device function and adequate battery life after exposure to electrocautery or other EMI. In addition, changes in the patient's functional status after surgery may warrant new device settings to maintain adequate cardiac output and tissue oxygen delivery.

In many centers, anesthesiologists provide perioperative care for patients undergoing pacemaker and ICD placement and other electrophysiology procedures (e.g., catheter ablation of supraventricular arrhythmias). These procedures typically involve superficial tissue dissection with local anesthetic infiltration for pocket formation or catheter placement. The majority of these cases can be performed under deep sedation with spontaneous ventilation, rather than general endotracheal anesthesia. However, specific events during the procedure, such as cryoablation or ICD test shocks, are quite painful, so adequate analgesia and amnesia should be ensured. Because these procedures can be very lengthy, providers should be vigilant for ischemia of dependent body parts, atelectasis, excessive sedation, and airway obstruction. Intravenous lidocaine, often used to reduce the burning associated with propofol administration, has antiarrhythmic effects that may interfere with planned electrophysiologic studies and should probably be avoided. An acute fall in blood pressure may indicate pericardial tamponade resulting from cardiac perforation with a catheter or device lead, a situation that may require emergent surgical intervention.

Transesophageal Echocardiography

Transesophageal echocardiography (TEE) has become an integral tool in the anesthetic management of cardiac surgical patients. Perioperative TEE allows the echocardiographer to diagnose intracardiac pathology (Table 26.6), direct the surgical procedure, and assess results and complications. In addition, TEE allows continuous intraoperative monitoring of cardiac function during cardiac and noncardiac operations. It is particularly useful for intrathoracic surgeries, during which transthoracic echocardiography would not be feasible.

TEE employs a long probe inserted into the patient's esophagus (Fig. 26.6). A piezoelectric crystal at the tip of the probe emits a plane of ultrasound waves that reflect off different structures in relation to their tissue densities. The probe detects and processes these reflected waves to acquire an image. The imaging plane can be rotated up to 180° without moving the probe (multiplaning), thus allowing a structure to be imaged from multiple angles. The probe tip can be flexed in different directions, and the probe itself can be rotated or moved to different positions in the esophagus (mid-esophageal and upper esophageal windows) or stomach (transgastric and deep transgastric windows). Manipulating the probe in these ways can produce a comprehensive examination

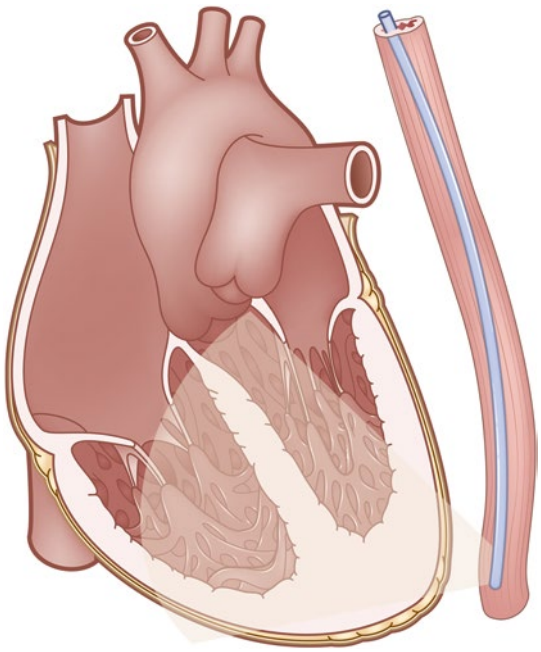

Fig. 26.6 Transesophageal echocardiography with the probe in the esophagus

Table 26.6 General indications for transesophageal echocardiography

General indication	Specific examples
1. Evaluation of cardiac and aortic structure and function	(a) Evaluation of prosthetic heart valves (b) Evaluation of paravalvular abscesses (c) Intubated patients (d) Patients with chest wall injuries (e) Patients with body habitus preventing adequate TTE examination
2. Intraoperative TEE	(a) All open-heart and thoracic aortic surgical procedures (b) Major vascular procedures (c) Noncardiac surgery in patients with known cardiovascular pathology
3. Guidance of transcatheter procedures	• Septal defect closure • Atrial appendage obliteration • Percutaneous valve replacement
4. Critically ill patients	• TEE information is expected to alter management

TEE transesophageal echocardiography, *TTE* transthoracic echocardiography

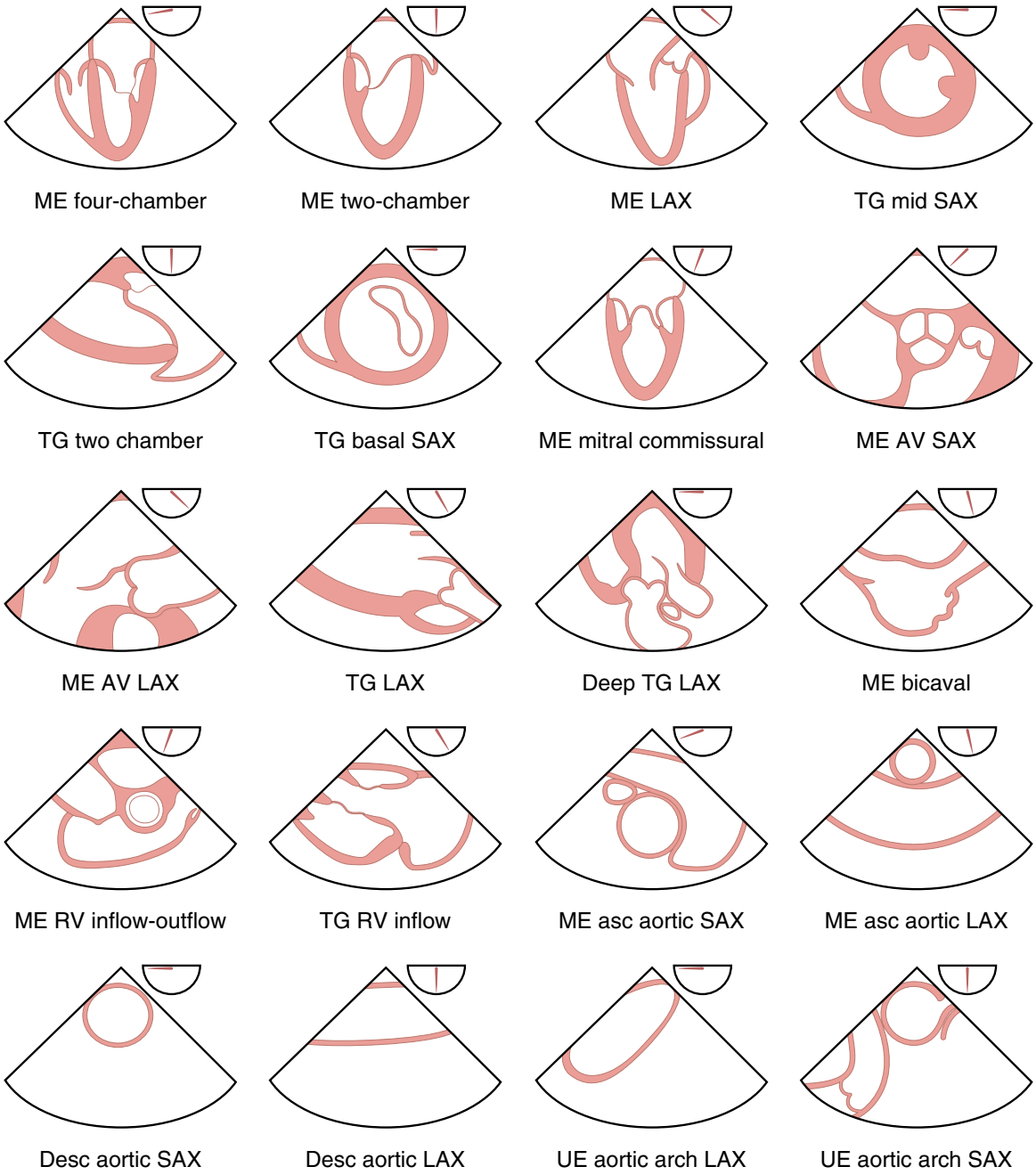

Fig. 26.7 Comprehensive TEE examination: various views (20)

of the entire heart and many other intrathoracic structures (Fig. 26.7). The ascending aorta and transverse arch are not well visualized by TEE because the left mainstem bronchus passes between the esophagus and ascending aorta, impeding penetration of ultrasound waves. Recent technological advances have produced TEE probes capable of real-time three-dimensional imaging.

Absolute contraindications to TEE include perforations, stricture, or masses that can interfere with or be exacerbated by probe manipulation (Table 26.7). A TEE exam can be performed in a patient with relative contraindications provided the anticipated benefits of TEE monitoring outweigh the risks. For example, in a patient with esophageal varices and bacterial endocarditis, the risk of esophageal bleeding associated with TEE probe placement may be outweighed by the anticipated benefit of assessing the patient for intracardiac vegetations or prosthetic valve dehiscence. Alternatively, in the setting of relative contraindications, TEE can be performed with appropriate modifications (e.g., avoiding transgastric windows in a patient with a subtotal gastrectomy). An

Table 26.7 Contraindications to transesophageal echocardiography

Absolute contraindications	Relative contraindications
Perforated viscus	History of radiation to neck or mediastinum
Esophageal stricture	History of GI surgery
Esophageal tumor	Recent upper GI bleeding
Esophageal perforation or laceration	Restricted neck mobility (severe cervical arthritis, atlantoaxial joint instability)
Esophageal diverticulum	Esophageal varices
Tracheoesophageal fistula	Coagulopathy or thrombocytopenia
Active upper GI bleeding	Active esophagitis/peptic ulcer disease

Table 26.8 Complications reported with transesophageal echocardiography

Esophageal bleeding
Esophageal perforation
Lip/Dental injury
Tracheal probe placement or laceration
Pharyngeal trauma or bleeding
Endotracheal tube malposition
Laryngospasm/Bronchospasm
Dysphagia
Hoarseness of voice
Arrhythmias

epicardial or epiaortic probe can also be handed off onto the sterile surgical field to obtain supplementary images. Epiaortic echocardiography remains the most sensitive and specific modality for visualizing calcifications in the ascending aorta that may preclude cannulation.

The overall complication rate of intraoperative TEE is very low (approximately 0.2 %) and can be minimized by careful patient preparation and probe manipulation (Table 26.8). Prior to inserting the TEE probe, an orogastric tube can be passed into the esophagus to determine if there are any strictures or other obstructions that would preclude safe passage of the larger TEE probe. Suctioning the orogastric tube before removing it will also evacuate stomach contents that can interfere with obtaining high-quality TEE images in the transgastric windows. To reduce the risk of esophageal rupture, all other esophageal instruments (e.g., esophageal temperature probes) should be removed before placing the TEE probe. The probe should never be forced blindly against resistance. If necessary, direct laryngoscopy and careful deflation of the endotracheal tube cuff can help facilitate probe placement. A bite block should be used to help protect the teeth and oral soft tissues from damage. The probe should be inspected and moved periodically during the operation to prevent pressure injury to the lips and gums. Inadequate rinsing of cleaning solutions from the probe can lead to chemical burns on oral soft tissues.

Stimulation from inserting and manipulating the TEE probe can produce adverse hypertension and tachycardia. Sufficient depth of anesthesia, analgesia, and vasoactive therapy should be ensured to avoid myocardial ischemia or heart failure from probe manipulation. Because the thoracic aorta passes close to the esophagus, large thoracic aneurysms can compress the esophagus, causing dysphagia. Probe insertion in this situation increases the risk of aortic rupture. The preoperative CT scan should be examined in advance for signs of esophageal impingement or deviation.

Perhaps the most underappreciated and dangerous consequence of intraoperative TEE is provider distraction. The eagerness to obtain optimal views and elucidate complex structures on the TEE exam can cause the operator to neglect important changes on patient monitors or the surgical field. The provider should never forget that performing a comprehensive TEE exam is only one aspect of complete anesthetic management for cardiac surgery. For this reason, it is desirable to have one anesthesia provider concentrate on monitoring and tending to the patient while another performs and interprets the TEE exam.

The National Board of Echocardiography (NBE) has developed processes by which anesthesiologists, depending on their level of training and case experience, can work toward certification in perioperative TEE. The recent introduction of basic certification affirms the value of TEE as a useful hemodynamic monitor in the noncardiac operative setting. Basic certification is intended to prepare providers, including those without specialized training in cardiac anesthesiology, to use TEE primarily for intraoperative monitoring of hemodynamic instability and guidance of inotropic and vasoactive support. Global and regional left ventricular function, right ventricular function, hypovolemia, qualitative valvular function, pulmonary embolism, air embolism, pericardial effusions, thoracic trauma, and basic septal defects can be assessed within the scope of the basic TEE examination. Advanced certification expands the scope of training to encompass complex valvular lesions, prosthetic devices, congenital defects, and other complex intrathoracic pathology. Advanced certification also prepares the provider to provide diagnostic guidance for cardiac surgical and transcatheter procedures.

Intraoperative Management

Goals and Preparation

More than in any other intraoperative settings, patients undergoing cardiac surgery have disease conditions that put them at risk of decompensating with very little warning. The overarching philosophy of cardiac perioperative care, then, is to be ready to respond to a sudden decline in the patient's condition at any time. Anesthesia providers should always be prepared to support any necessary resuscitative

Table 26.9 Sample anesthesia setup for cardiac surgery

A. **Medications:** At least one medication from each category should be readily available. Syringes and infusions do not need to be prepared in advance unless noted below or indicated by the specific physiologic requirements of the patient or planned surgery. It is highly desirable to have bolus and infusion preparations of at least one inotrope, one vasopressor, and one vasodilator ready to deliver		
Anticholinergics	Atropine	0.1 mg/ml syringe ready
	Glycopyrrolate	0.2 mg/ml syringe ready
Inotropes	Epinephrine	1 mg in 250 ml (4 mcg/ml), 0.01 mg/ml syringe ready
	Dopamine or Dobutamine	Prepare infusion as Dopamine—400 mg in 250 ml, Dobutamine—500 mg in 250 ml
	Calcium chloride	10 ml syringe ready
Vasopressors	Phenylephrine	Prepare infusion as 10 mg in 250 ml (40 mcg/ml)
	Norepinephrine	Prepare infusion as 8 mg in 250 ml (32 mcg/ml)
	Vasopressin	Prepare infusion as 100 U in 100 ml
Inotrope/vasopressor	Ephedrine	Bolus 5–10 mg syringe ready
Inotrope/vasodilator	Milrinone	Prepare infusion as 50 ml or mg of drug plus 200 ml = total 250 ml (200 mcg/ml), ready prepacks available
Vasodilators	Nitroglycerin	Glass bottles available as 200 or 400 mcg/ml
	Nitroprusside	Prepare infusion as 50 mg in 250 ml (200 mcg/ml), protect from light-put opaque cover
	Nicardipine	Prepare infusion as 10 ml of drug (25 mg) plus 240 ml = total 250 ml (0.1 mg/ml)
Anticoagulation for CPB	Heparin	Sufficient extra supply should be available in case patient needs to return to CPB, 300 U/kg for initiation of CPB
	Protamine	Syringe or infusion should be either stowed away until needed or prepared after weaning from CPB to prevent premature administration to patient, 1 mg for every 100 U of heparin
Antiarrhythmics	Lidocaine, adenosine, amiodarone, magnesium sulfate	
Sedatives/induction agents	Midazolam, thiopental, propofol, etomidate, and/or ketamine	
	Inhaled agent (e.g., isoflurane)	
Analgesics/opioids	Fentanyl, sufentanil, remifentanil	
Muscle relaxants	Succinylcholine and a nondepolarizing agent (e.g., pancuronium)	
B. **Equipment:** All equipment should be checked for proper function and adequate battery power prior to surgery		
Anesthesia machine, monitors, and invasive pressure monitor transducers		
Airway equipment: standard equipment and any specialized devices (e.g., double-lumen tubes)		
Infusion pump(s) with multiple channels		
Defibrillator with external pads		
External pacemaker generator		
TEE machine and probe		
Patient transport equipment: portable monitor, full oxygen cylinder, and bag valve mask		

maneuvers, including emergency sternotomy and CPB. It is prudent to have bolus and infusion preparations of an inotrope, a vasoconstrictor, and a vasodilator ready to use for every case, plus sufficient heparin to commence bypass (Table 26.9).

Preventing adverse hemodynamic responses to anesthetic and surgical interventions, an important goal in any operation, is especially critical in cardiac surgery (Table 26.10). Preoperative sedation and induction of general anesthesia can lead to decreases in myocardial function and peripheral vascular resistance that may be poorly tolerated in cardiac patients. Pain and increased sympathetic stimulation from incision, sternotomy, and aortic cannulation can precipitate tachycardia, hypertension, or dysrhythmias, all of which can lead to ischemia and heart failure in patients with compromised cardiac function. One useful technique is to assess preoperatively the range of vital signs within which the patient is asymptomatic, comfortable, and free of ischemia (e.g., during physical activity or stress testing), and then use this range as a goal for maintaining blood pressure and heart rate in the operating room.

Premedication

Patients about to undergo heart surgery are likely to be very anxious, but what may be an appropriate intravenous dose of midazolam or fentanyl for another patient may be excessive for a patient with compromised cardiac function. As with any surgery, clinical judgment rather than just routine practice should be used to decide upon the need for premedication prior to surgery.

Table 26.10 Common cardiovascular agents and doses

Antihypertensive agents	
Nitroglycerine	0.25–10 mcg/kg/min, 1–2 ml of 20–40 mcg/ml as bolus
Nitroprusside	0.25–10 mcg/kg/min
Esmolol	0.5 mg/kg bolus over 1 min, 50–300 mcg/kg/min infusion
Labetalol	5–20 mg
Metoprolol	2–10 mg
Hydralazine	4–20 mg
Phentolamine	1–5 mg
Nicardipine	0.25–0.5 mg bolus, 2.5–15 mg/h infusion
Vasopressors	
Epinephrine	0.001–0.1 mcg/kg/min, 2–10 mcg bolus
Norepinephrine	0.01–0.1 mcg/kg/min or 1–16 mcg/min
Dobutamine	2–20 mcg/kg/min
Dopamine	2–20+ mcg/kg/min
Ephedrine	5–25 mg bolus
Phenylephrine	20–60 mcg/min, 40–200 mcg bolus
Milrinone	0.375–0.75 mcg/kg/min, 50 mcg/kg bolus over 10 min
Vasopressin	0.01–0.04 U/min
Vasodilators	
Nitroglycerine	0.25–10 mcg/kg/min
Nitroprusside	0.25–10 mcg/kg/min
Nicardipine	2.5–15 mg/h
Fenoldopam	0.03–1.0 mcg/kg/min
Nitric oxide	10–60 ppm (inhaled)
Antiarrhythmic agents	
Lidocaine	1–2 mg/kg
Esmolol	0.5 mg/kg
Metoprolol	2–10 mg
Amiodarone	150 mg over 10 min, 0.5 mg/min
Verapamil	2.5–10 mg
Diltiazem	0.25–0.35 mg/kg, 3–15 mg/h
Digoxin	0.5–0.75 mg
Adenosine	6–12 mg

Ideally, patients should not be premedicated until they arrive in a location, such as the operating room or a preoperative holding area, where trained anesthesia personnel can monitor them continuously. Slow titration is desirable to prevent large swings in blood pressure and heart rate. Judicious premedication to sedate the patient can reduce the dosage of induction drugs required to achieve general anesthesia. Special care should be taken in patients with severe heart failure or with severe or symptomatic aortic stenosis, as they may be unable to compensate adequately for even small decreases in systemic vascular resistance. Medications that can be used for premedication include midazolam, diazepam (5–10 mg PO, the night before), morphine (0.15 mg/kg) plus scopolamine 0.2–0.3 mg intramuscularly (IM), or hydromorphone 1–2 mg IM. It should be remembered that scopolamine can cause confusion in the elderly, while the combination of a benzodiazepine and an opioid can have synergistic effects, which warrant reduction in dosage.

Intraoperative Monitoring

Standard noninvasive monitors and supplemental oxygen should be applied to the patient both in the preoperative holding area and upon arrival in the operating room. Induction of general anesthesia can cause rapid, detrimental changes in blood pressure. Therefore, continuous blood pressure monitoring is highly desirable, and an arterial line should be placed prior to induction. Before attempting a radial or brachial arterial line in a patient undergoing CABG, the anesthesia provider should confirm that it will not be in the same arm as any planned radial artery graft harvest. Patients undergoing aortic surgery may require multiple arterial lines in different locations (e.g., femoral and right radial arteries) depending on where the crossclamp will be placed during surgical repair.

Central venous access is also useful prior to induction to facilitate fluid management and vasoactive infusions. In the absence of intervening pathology, CVP is equivalent to right atrial pressure and can be affected by circulating blood volume, peripheral venous tone, and right ventricular function. Placing a central line can be deferred until after induction if the patient has an existing large-bore intravenous line or is unlikely to tolerate being conscious and stationary for the procedure. However, for patients in emergency situations with adequate large-bore access, central line placement and monitoring should not delay anesthetic induction, prompt opening of the chest, surgical control of bleeding, or initiation of bypass.

Traditionally, cardiac surgery was considered an indication in itself for the placement of a pulmonary artery (PA, or Swan-Ganz) catheter. The PA catheter allows measurement of pressures in the right ventricle and pulmonary artery, transvalvular pressure gradients across the tricuspid and pulmonic valves, and calculation of systemic and pulmonary vascular resistance. These values can help assess filling pressures throughout the heart and assist in the diagnosis and treatment of right heart failure and pulmonary hypertension. Thermodilution catheters also allow measurement of cardiac output, either intermittently or continuously, and sampling of mixed venous blood to assess total body oxygen extraction.

Several recent studies have questioned the utility of routine PA catheterization, suggesting an association with worse outcomes and even increased mortality. PA catheter data can greatly assist in hemodynamic management, especially in the postoperative setting without ready access to TEE equipment or trained operators, but this data should be evaluated in the context of the patient's overall clinical status. TEE and other less invasive methods of cardiac output monitoring can

be valuable adjuncts or, in many cases, alternatives to the PA catheter. In low-risk patients with well-preserved left ventricular function undergoing CABG, the PA catheter is unlikely to provide sufficient benefit to outweigh the risks of insertion. Placing a PA catheter is likely to yield more benefit in patients with known or anticipated right heart failure, pulmonary hypertension, severe valvular abnormalities, or contraindications to TEE.

Induction and Maintenance of Anesthesia

Anesthetic induction in cardiac patients requires navigating a careful balance between avoiding hypotension and attenuating responses to laryngoscopy, TEE probe insertion, and surgical incision. Over the past several years, a variety of anesthetic techniques have been used successfully. As with premedication, choosing among different anesthetic regimens should not be a rote practice but rather a thoughtful consideration of their individual benefits and disadvantages in the context of the patient's own physiologic profile.

Induction with high doses of opioids became popular in the 1970s and 1980s because of their hemodynamic stability and excellent attenuation of stress response when compared to the inhaled agents of the time (e.g., halothane). Induction can be achieved with large doses of morphine (1–2 mg/kg), fentanyl (50–100 mcg/kg), or sufentanil (10–25 mcg/kg). The accompanying vagotonic effects and chest wall rigidity can be counteracted to some extent with timely administration of pancuronium. However, pure high-dose opioid induction without an accompanying amnestic agent (such as midazolam or scopolamine) is associated with an unacceptably high occurrence of intraoperative awareness and postoperative recall. Also, prolonged postoperative respiratory depression lasting up to 12–24 h delays weaning from mechanical ventilation. Although high-dose opioid induction has been mostly supplanted by other techniques, it is still a useful option in high-risk patients who are expected to require prolonged postoperative ventilation.

The impetus to reduce the duration of postoperative ventilation has increased interest in combined intravenous-inhaled anesthesia techniques. Anesthesia for cardiac surgery can be induced with nearly any intravenous amnestic agent, such as etomidate (0.1–0.3 mg/kg), propofol (0.5–2 mg/kg), thiopental (1–2 mg/kg—no longer available), or ketamine (1–2 mg/kg). Etomidate is commonly used for cardiac inductions because myocardial contractility and preload remain relatively well preserved compared to other agents. Propofol can significantly reduce cardiac output and systemic vascular resistance, while thiopental can reduce cardiac preload via increased venous pooling. Nonetheless, propofol and thiopental are useful induction agents in hemodynamically robust patients, provided they are titrated slowly to achieve the desired effect with less medication. Ketamine stimulates the sympathetic nervous system, increasing heart rate and blood pressure. This makes ketamine the favored induction agent in patients with cardiac tamponade or severe hypovolemia, but the increase in heart rate can worsen myocardial ischemia. Ketamine can also depress myocardial function in patients with depleted catecholamine levels.

Anesthesia can be maintained with an inhalational agent, continuous opioid or sedative infusions, or a combination of these techniques, depending on hemodynamic stability and expected time to extubation postoperatively. If total intravenous anesthesia is used, the infusions should be delivered through a line that will not be obstructed by cannulation snares; alternatively, infusions can be given directly through the CPB machine during bypass. The inspired oxygen concentration can be titrated to oxygen saturation readings from the pulse oximeter or arterial blood gases. Many providers choose to use 100 % oxygen to maximize inspired oxygen tension, particularly in patients with known or evolving ischemic disease. An air–oxygen mixture can help prevent absorption atelectasis and reduce the risk of oxygen free radical toxicity from prolonged ventilation. Nitrous oxide is typically avoided because it decreases the maximum inspired oxygen concentration, stimulates catecholamine release, increases pulmonary vascular resistance, and enlarges air emboli.

Preparation for Surgical Incision

After induction and intubation, the operating room team may take time to complete other tasks prior to surgical incision. These may include placing a Foley catheter, positioning the patient, reviewing the baseline TEE findings, prepping and draping the legs for saphenous vein harvest, and prepping and draping the surgical field. Provided the patient remains stable, the anesthesia provider can use this period of low surgical stimulation to complete several other preparatory tasks. If not done previously, baseline arterial blood gas and activated clotting time (ACT) samples should be drawn. All intravenous lines should flow freely, infusions should be attached in line, and injection ports should be labeled and easily accessible. Pressure transducers should be leveled and zeroed properly. If a PA catheter has been placed, baseline cardiac index, vascular resistance, and mixed venous oxygen saturation values should be obtained. Any required preoperative antibiotic should be given while observing the patient for signs of an allergic response.

Careful patient positioning is essential in order to avoid soft tissue damage or peripheral neuropathy. These risks increase with hypothermia and variable perfusion while on bypass. Even though the arms are usually tucked alongside the body during cardiac surgery, excessive chest retraction can injure the brachial plexus in a manner akin to hyperextension of the

shoulder joint. The arms should be padded and not allowed to rest against the edge of the operating table to prevent radial and ulnar nerve injuries. Surgical personnel leaning against the table can cause pressure injury to fingers, particularly in obese patients. Dependent areas of the body, such as the occiput and heels, are also at risk of tissue necrosis during prolonged operations without proper padding. Lifting the legs during surgical prepping and draping increases venous return to the heart; patients with impaired ventricular reserve may not easily tolerate this increase in myocardial preload.

Adequate muscle relaxation and depth of anesthesia should be ensured prior to incision. Opioids should be titrated well in advance of incision to maintain adequate analgesia. Short-acting vasodilators, such as nitroglycerin and nicardipine, are recommended for managing transient increases in blood pressure and heart rate with incision. Anesthetic agents should be adjusted in response to signs of inadequate anesthetic depth, such as tachycardia, hypertension, or significant changes on a bispectral index (BIS) monitor. However, as a means of pure hemodynamic management, changing the inhaled agent concentration is less desirable than infusions of short-acting vasoactive agents. Changes in inhaled agent concentrations take longer to affect blood pressure than intravenous infusions, and delivering a low concentration of anesthetic agent in a hypotensive patient increases the risk of awareness and postoperative recall.

Bleeding Prophylaxis

Many clinicians use antifibrinolytic therapy during cardiac cases to decrease overall bleeding and reduce transfusion requirements. Antifibrinolytic therapy may be especially beneficial for patients who refuse blood transfusion (Jehovah's Witnesses), and for situations in which extensive blood loss is anticipated (repeat or extensive operations, coagulopathy, recent exposure to antiplatelet agents). Lysine analogs such as ε-aminocaproic acid (Amicar) and tranexamic acid (Cyklokapron, Transamin) inhibit the activation of plasminogen to plasmin, preventing the degradation of fibrin and thus promoting clot integrity. The kallikrein inhibitor aprotinin (Trasylol) was formerly used widely as a perioperative antifibrinolytic agent, but sales were suspended in 2008 after multiple studies showed increased mortality from renal and cardiovascular side effects.

Multiple clinical trials support initiating therapy prior to sternotomy to prevent the fibrinolysis that accompanies surgical trauma, inflammation, and the initiation of CPB. However, in patients with severe occlusive coronary disease or cardiogenic shock, administration of antifibrinolytics should probably be delayed until the patient is fully heparinized for CPB. Though dosing protocols vary across institutions, a usual regimen for ε-aminocaproic acid is a loading dose of 5–10 g, another 5–10 g dose in the CPB priming fluid, followed by a continuous infusion of 1–2 g/h. The infusion rate may be reduced or eliminated in patients with renal impairment. Antifibrinolytic therapy should be withheld in patients with known hypercoagulable conditions.

Some clinicians use platelet-rich plasma as a means of reducing bleeding from the surgical site. Blood is collected from the patient prior to sternotomy, then anticoagulated with citrate dextrose, and spun in a centrifuge to separate the platelet-rich plasma from the remaining plasma and red blood cells. The platelet-rich plasma can then be reinfused into the patient intravenously or applied directly to areas of surgical bleeding, such as the sternal cut edges prior to closure.

Sternotomy and Cardiac Exposure

Sternotomy is a routine event in cardiac surgery, yet one fraught with potential complications. The intense stimulation that accompanies sternotomy not only produces profound hypertension and tachycardia, but also makes this the most common period for intraoperative awareness and recall. Prior to any sternotomy, the anesthesia provider must confirm adequate hemodynamic stability, anesthetic depth, and muscle relaxation, especially if the patient already showed a response to skin incision. The anesthesia provider must stop the surgeon from performing sternotomy until these conditions are ensured. Vagal stimulation can occur during sternal retraction or pericardiotomy and can produce transient bradycardia and hypotension. Severing of coronary grafts can cause myocardial ischemia severe enough to necessitate emergency CPB. If the patient attempts to breathe during sternotomy, air can be entrained into a perforated cardiac structure. Even if sternotomy itself is uneventful, aggressive sternal retraction can cause sympathetic stimulation, brachial plexus injury, kinking of the PA catheter or introducer, and even rupture of the innominate vein.

During a first-time sternotomy, a reciprocating saw is used to cut through the midline of the sternum. Ventilation is typically stopped during a primary sternotomy to allow the heart and lungs to fall away from the sternum. After prior cardiac surgery, though, the heart, lungs, coronary grafts, or aortic grafts can adhere to the underside of the sternum, making repeat sternotomy much more hazardous. Blood products should be brought to the operating room and checked before any repeat sternotomy. To decrease the chance of damaging soft tissue, the surgeon will employ an oscillating saw from the outside to the internal table of the sternum. This process takes longer than primary sternotomy, so the patient may continue to be ventilated until the sternal table is breached. After sternotomy, further blood loss and dysrhythmias can

occur during dissection of adherent structures. External defibrillator pads may be applied to the patient in advance, as the prolonged sternotomy and surgical dissection will delay adequate exposure to use internal paddles.

After the chest is opened, the anesthesia provider should visually confirm inflation of both lungs on the surgical field. Changes in peak airway pressures, inability to deliver programmed tidal volumes, and bubbling of blood on the surgical field can signify lung injury. Depending on the extent of the injury and the patient's oxygenation status, options include continuing as planned with appropriate ventilator adjustments, clamping or suturing the injured lung tissue, isolating the injured lung with a bronchial blocker or by mainstem intubation, or commencing CPB. The provider should also ensure that all central lines are patent and the PA catheter is not anchored.

If CABG is planned, then sternotomy is often followed by surgical dissection of arterial and venous grafts: the internal mammary arteries, radial arteries, and saphenous veins. An initial intravenous dose of heparin (5,000 units) may be administered during this period. The left internal mammary artery (LIMA) is conveniently located for grafting to the left anterior descending (LAD) artery and is therefore frequently dissected ("taken down"). In some cases, the right internal mammary artery (RIMA) may also be dissected. To facilitate surgical exposure, the chest wall is lifted with a retractor, and the table is raised and tilted away from the surgeon. Before adjusting the table to this position, the anesthesia provider should ensure lines and tubing have adequate slack to prevent inadvertent extubation or line removal. Blood loss from surgical dissection of the mammary bed can be extensive and hidden, especially in coagulopathic patients, leading to hypovolemia and hypotension.

Cardiopumonary Bypass

Overview

Cardiopulmonary bypass (CPB, or "bypass") is an extracorporeal mechanical circulatory support system that mechanically diverts circulating blood volume away from the heart and pulmonary circulation. The bypass machine (colloquially, "the pump") provides systemic perfusion and gas exchange in lieu of the patient's heart and lungs, respectively. Surgery can thus be performed on a heart that is evacuated of blood, arrested, and hypothermic. CPB is required for procedures within the cardiac chambers, such as valvular surgery and mass excisions, as well as most operations on the thoracic aorta. It can also facilitate extracardiac surgeries, such as CABG and lung transplantation, as well as provide circulatory support in certain self-limited arrest conditions (e.g., intravenous local anesthetic toxicity).

A perfusionist, a highly trained technician specializing in extracorporeal cardiopulmonary support, prepares and operates the bypass machine. Depending on the institution and operative case, the perfusion team's responsibilities may also include managing cell salvage, intra-aortic balloon pumps (IABP), and extracorporeal membrane oxygenation (ECMO) equipment. Successful care of the patient before, during, and after bypass requires continual communication among the perfusionist, surgeon, and anesthesiologist throughout the operation. The CPB machine itself runs on electrical power with battery backup and, as a last resort, manual cranking of the pump itself. (The latter circumstance is one reason many centers require two-member perfusion teams, allowing one person to crank the pump in an electrical outage while the other performs other tasks.)

Components

Despite the apparent complexity of the contemporary bypass apparatus, all circuits are based on the following four mandatory components (Fig. 26.8):

1. The **venous reservoir** collects the blood drained from the patient via the venous cannula. The reservoir empties the patient's circulation passively via gravity (siphon effect). Therefore, it must be positioned lower to the ground than the patient to facilitate drainage. If emptying of the heart is inadequate for surgical exposure (as can happen in right heart failure), gravity drainage can be augmented with vacuum suction. The drawbacks of vacuum-assisted venous drainage include increased cost, mechanical complexity, and entrainment of air emboli through surgical incisions or uncapped infusion ports. While the patient is on bypass, the reservoir holds any blood in excess of the amount required to maintain the patient's circulating volume at the designated flow rate. The venous reservoir is graduated by volume. A low volume sensor automatically alarms and slows pump flow to prevent air entrainment. An in-line bubble detector positioned directly after the reservoir also protects against harmful air emboli.
2. The **pump** itself provides the driving force to propel blood through the system. Nonpulsatile flow through the circuit is generated by either a roller or centrifugal pump. Roller pumps compress the blood tubing against a backing plate, pushing blood forward in the circuit. Centrifugal pumps send blood through a series of rapidly spinning rotor cones, creating a vortex that advances blood through the circuit. In either case, the flow rate through the pump is the mechanical equivalent of cardiac output and is adjusted based on the patient's body temperature and metabolic oxygen consumption. While higher flow rates can increase systemic blood pressure and end-organ perfusion, low flow is less traumatic to blood cells and may

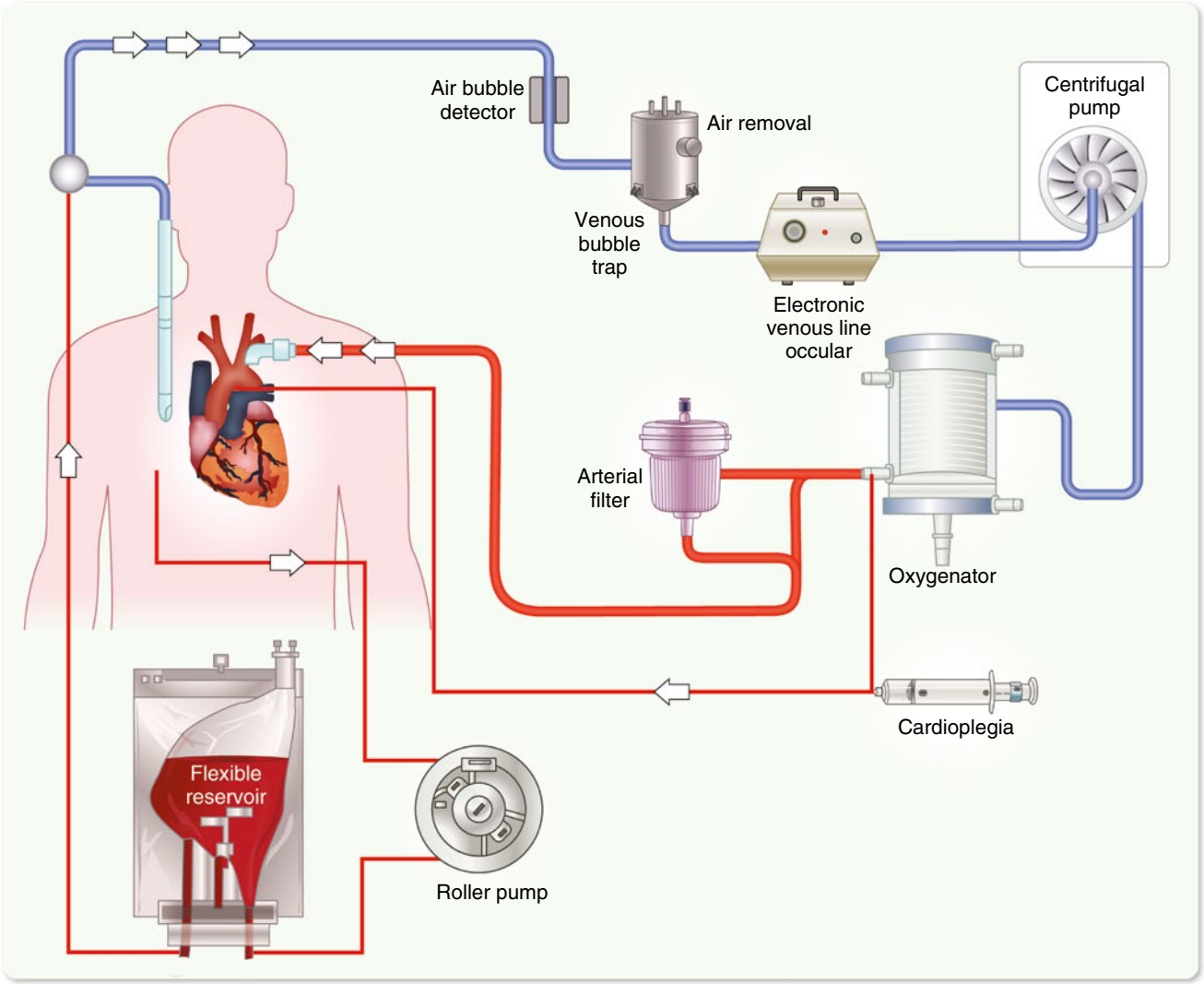

Fig. 26.8 Components of cardiopulmonary bypass system

improve myocardial protection. Recent studies suggest that creating a pulsatile flow pattern during bypass may preserve microcirculatory perfusion (thus improving end-organ oxygenation) and reduce systemic inflammatory and neuroendocrine stress responses to prolonged bypass. The clinical significance of these findings remains unclear. Pulsatile flow systems remain expensive and technically more complex than nonpulsatile systems.

3. The **oxygenator** provides an environment for gas exchange in lieu of the pulmonary alveolar-capillary unit. Bubble oxygenators, common in the past, worked by passing oxygen bubbles through a column of venous blood. Though efficient and inexpensive, they were prone to microembolus formation and did not allow independent control of oxygen and carbon dioxide concentration. As a result, they have been almost universally supplanted by membrane oxygenators, which mimic alveolar architecture by using a thin permeable membrane as an interface between blood and gas phases. An air–oxygen blender combines line oxygen and air in a designated ratio to control the P_aO_2 of the blood leaving the oxygenator. The P_aCO_2 can be controlled independently by changing the fresh gas flow rate (sweep rate) through the oxygenator.
4. A **line filter**, located at the last point of the circuit to trap any remaining particulate matter or air bubbles (up to approximately 40 μm) before blood enters the arterial cannula. This represents the final protective mechanism in the CPB circuit to guard against a potentially devastating embolus being introduced into the patient circulation.

All other components of the CPB apparatus are theoretically optional to the core function of the system. Nevertheless, over time they have become routine features in modern cardiac surgery.

- The **cardioplegia pump**, separate from the main CPB pump, delivers cardioplegia, a hyperkalemic crystalloid or mixed blood-crystalloid solution through separate cannulas placed in the aortic root or coronary ostia (antegrade cardioplegia) or coronary sinus (retrograde cardioplegia). Retrograde cardioplegia helps ensure delivery of cardioplegia solution to regions of myocardium distal to coronary blockages. The initial delivery of cardioplegia, after initiation of bypass and aortic crossclamping, arrests and cools the heart, markedly decreasing myocardial oxygen demand and providing an immobile surgical field. Repeated delivery of cardioplegia at regular intervals while on bypass (approximately every 15–20 min) helps maintain myocardial arrest and hypothermia while also washing away metabolic by-products.
- A **heat exchanger**, an integral component of the membrane oxygenator, circulates a mixture of hot and cold water to provide a temperature gradient to cool or warm the blood in the bypass circuit. This mechanism is used to control the patient's temperature during bypass. Separate heat exchangers are used to control the temperature of cardioplegia solution and blood for coronary perfusion.
- The **cardiotomy reservoir** recovers blood from various vents and suction cannulas on the surgical field. Various filters and a defoaming apparatus help remove emboli and reduce hemolysis before returning the blood to the venous reservoir. Vents may be placed in the aortic root or left ventricle to prevent ventricular distension by collecting blood passing through septal defects or transpulmonary shunts (e.g., bronchial and thebesian veins), as well as to collect entrained air to prevent embolization. Suction cardiotomy ("pump sucker") collects blood from suction cannulas on the field to conserve blood and improve surgical exposure.
- An **anesthetic vaporizer**, generally isoflurane, is placed in the fresh gas supply line to the oxygenator, allowing continued delivery of volatile anesthetic agent to the patient, as the lungs are neither perfused nor ventilated while on bypass. The ability to deliver anesthetic vapor through the circuit has significantly reduced the incidence of postoperative recall during cardiac surgery.
- A **hemoconcentrator (ultrafilter)** is sometimes added to the circuit to remove excess water and electrolytes from the circulating volume, thus concentrating the blood in a patient with an undesirably low hematocrit.

Anticoagulation for CPB

The bypass circuit comprises several meters of tubing with various filters and pumps, all of which constitutes a nidus for potential thrombus formation. Thrombotic complications of bypass can range from development of microemboli that return to the patient circulation to solidification of the entire circulating bloodstream, resulting in sudden fatal circulatory arrest. Therefore, ensuring adequate anticoagulation prior to commencing bypass and throughout the pump run is absolutely mandatory. This is usually accomplished with unfractionated heparin, a strong acid that binds to and catalyzes antithrombin III (AT III), a serine protease inhibitor that irreversibly binds and inhibits thrombin and several activated clotting factors. The end result is anticoagulation (but not thrombolysis) via decreased activation of fibrinogen and decreased fibrin clot formation.

When the surgeon is ready to begin preparing for cannulation, a large dose of heparin (typically 300 units/kg) is given intravenously. The anesthesia provider should inject the heparin through a central or large peripheral line, drawing back venous blood before and after giving the heparin to ensure reliable intravenous administration. The provider should also announce to the surgical and perfusion teams the time the heparin dose is given. A blood sample for measuring activated clotting time (ACT) is drawn 3–5 min after heparin administration. The surgeon uses this period to expose and place pursestring sutures in the eventual cannulation sites. At the same time, the perfusionist may start cardiotomy suction to recover blood lost on the surgical field during cannulation.

Normal ACT ranges from 100 to 160 s and is affected by preoperative heparin exposure. An ACT of 400–480 s is considered adequate for CPB in most centers. If ACT is inadequate after the first heparin dose, the patency of the intravenous line and the viability of the heparin vials used should be confirmed before additional heparin is given. Continued resistance to heparin may indicate congenital or acquired AT III deficiency. These patients may require administration of recombinant AT III, AT III concentrate, or fresh frozen plasma (FFP) to reestablish adequate levels of circulating AT III for sufficient heparin activity. Patients with a recent history of heparin-induced thrombocytopenia (HIT) produce circulating heparin-dependent antibodies that lead to platelet agglutination and possible thromboembolism. Patients with HIT undergoing surgery on CPB may require hematology consultation regarding alternative anticoagulants, such as bivalirudin (Angiomax) or argatroban.

Cannulation for CPB

Placing a patient on bypass begins with cannulation of the arterial and venous sides of the circulation. In most cases, the aortic cannula is placed in the aortic root, and the venous cannula is placed in the right atrium. Alternate cannulation sites may be used depending on the planned surgery or patient-specific factors. For example, intracardiac operations involving a surgical approach through the right atrium require bicaval venous cannulation (i.e., dual cannulation of the superior and inferior venae cavae). Alternatively, a

dual-stage venous cannula, with orifices for the right atrium and inferior venae cavae, can be inserted directly on the field or through a femoral vein and positioned under TEE guidance. Alternate arterial cannulation sites, such as the ascending aorta or a side graft off a subclavian artery, may be used if ascending aortic surgery is planned or if the ascending aorta is severely calcified (to prevent embolic stroke from plaque disruption with an aortic cannula). Finally, a femoral artery can be used either as a planned cannulation site in case of severe aortic disease or intrathoracic scarring, or for rapid emergency institution of bypass in acutely unstable patients. Including the groins in the sterile field when prepping and draping the patient for cardiac surgery expedites emergency femoral bypass.

In nearly all cases, arterial cannulation precedes venous cannulation. A properly positioned arterial cannula serves as an ideal volume delivery line. Therefore, cannulating the arterial limb of the circuit first can facilitate rapid resuscitation of a patient who becomes hemodynamically unstable. Even if the venous cannula has not yet been secured, bypass can be initiated with the arterial cannula alone; circulating volume can be supplemented with recovered blood from cardiotomy suction ("sucker bypass"), or with crystalloid or allogeneic blood products added directly to the venous reservoir.

Prior to insertion of the aortic cannula, systolic blood pressure should be maintained no higher than 90–100 mmHg. Higher blood pressures increase the risk of aortic dissection during cannulation. Once the cannula is inserted into the aorta and connected to the arterial line from the circuit, both the surgical and anesthesia teams should inspect the arterial cannulation tubing for air bubbles before the cannula is unclamped and opened to the patient. A test transfusion of 100 mL is performed to verify proper cannula placement and function. A rapid increase in line pressure with the test transfusion indicates the aortic cannula is either still clamped (risking circuit rupture) or malpositioned (risking aortic dissection). To ensure proper cannula position, the arterial waveform on the cannula should be pulsatile, and the mean pressure should correlate with the patient's existing arterial lines.

Venous cannulation often requires lifting or pressing the heart for surgical exposure. These maneuvers can cause hypotension or precipitate dysrhythmias. Hypotension is often transient and resolves with the end of surgical manipulation and reestablishment of adequate ventricular filling. In some cases, volume may need to be transfused through the aortic cannula to maintain adequate preload. Depending on the length and severity of any dysrhythmias, the patient may require antiarrhythmic medications, defibrillation, or immediate institution of CPB. Malpositioned venous cannulas can impede venous return, causing hypotension, or obstruct venous drainage from the head and neck, causing superior vena cava syndrome (head and neck engorgement).

The CPB circuit is primed with a crystalloid fluid that includes balanced electrolyte solutions (e.g., lactated Ringer's solution, PlasmaLyte A) and variable amounts of colloid, mannitol, heparin, calcium, and other additives. The total priming volume of the adult extracorporeal circuit is about 1,500–2,000 mL, or 25–35 % of the circulating blood volume in a typical adult. Cannulation for bypass adds this volume to the total circulation, causing significant hemodilution and impairing tissue oxygen delivery. Many centers seek to minimize this effect by replacing part of the priming volume with blood withdrawn from the patient after each cannula is inserted, a process called retrograde autologous priming (RAP, or "rapping"). By reducing the overall volume of crystalloid added to the patient's circulating volume when CPB is started, RAP limits hemodilution and reduces transfusion requirements. Small doses of vasoconstrictors may be needed to mitigate the drop in blood pressure during RAP. Anesthesia providers should also be careful not to administer large amounts of intravenous crystalloid fluids during the pre-bypass period, as these will also worsen hemodilution on bypass and increase transfusion requirements. In patients at high risk for severe hemodilution or adverse consequences from dilutional anemia (e.g., children, adults of small stature, sickle cell disease), part or all of the priming volume may be replaced with blood prior to cannulation.

Initiation of CPB

CPB is initiated after the ACT reaches an acceptable level, the arterial and venous cannulas are properly positioned and secured, and RAP is completed. The anesthesia provider should ensure adequate depth of anesthesia prior to the start of CPB. The patient should be sufficiently paralyzed to prevent movement (which can interfere with surgery and entrain air through open vessels) and shivering (which increases total oxygen demand). The Foley catheter urometer should be emptied so urine output during bypass can be measured. Invasive pressure transducers should be recalibrated and zeroed. If a PA catheter is in place, it should be withdrawn 3–5 cm to reduce the chance of pulmonary artery rupture.

To initiate bypass, the perfusionist will slowly increase the pump flow rate and assess the adequacy of venous return into the pump reservoir. There should be a visible difference in the color of blood between the arterial and venous cannulas. Inadequate venous return or failure of the heart to empty can indicate obstruction, malpositioning, or kinking of the cannulas. Previously unrecognized severe aortic insufficiency can also cause distension of the heart with CPB; immediate aortic crossclamping may be required to ensure adequate forward flow and peripheral perfusion.

As the flow rate increases, arterial blood flow will become less pulsatile until aortic ejection by the heart ceases. At this

time, systemic blood pressure is monitored as a mean pressure only. Once full flow is reached, the ventilator should be stopped, the lungs deflated, and the vaporizer on the anesthesia machine turned off. The head and neck should be examined for acute color changes, edema, and plethora. The pupils should be equal and symmetric, and conjunctival chemosis (edema) should be absent.

Soon after commencing CPB, the surgeon may place a crossclamp across the aorta proximal to the aortic cannula. This isolates the cardiopulmonary circulation from the rest of the body. The pump flow rate and MAP are momentarily lowered during crossclamp application to prevent aortic injury. Once the crossclamp is applied, cardioplegia solution is administered through cannulas placed in the aortic root or coronary ostia (antegrade cardioplegia) and coronary sinus (retrograde cardioplegia). The combination of antegrade and retrograde cardioplegia arrests the heart, perfuses the coronary circulation, and washes out myocardial metabolic byproducts. The ECG should be monitored during cardioplegia for prompt and complete arrest. The appearance of electrical activity on the ECG during arrest should be communicated to the surgeon, as additional cardioplegia may be required to prevent excessive myocardial oxygen consumption.

Hemodynamic Management on CPB

While on bypass, MAP is generally maintained between 50 and 80 mmHg, while the pump flow rate is kept at 50–65 ml/kg/min. Prior to aortic crossclamping, a higher MAP may be desirable in patients with critical coronary occlusive disease, cerebrovascular or renovascular disease, or other impairments in organ flow autoregulation. After aortic crossclamping, MAP is generally reduced to reduce warm noncoronary blood flow to the heart through the pericardium and pulmonary and venous drainage, while still maintaining adequate perfusion pressures to other vital organs. The pump flow rate is a surrogate for cardiac output on bypass, so MAP is a product of the pump flow rate and SVR. The pulmonary arterial mean pressure should be less than 15 mmHg, and the CVP should be less than 5 mmHg.

Assuming no technical issues with monitoring lines, systemic arterial hypotension on bypass can occur as a result of either low SVR or low pump flow. Low SVR can occur as a result of vasodilator therapy, anesthetic agents, anaphylaxis, sepsis, transfusion reactions, or acute adrenal insufficiency (Addisonian crisis). Low blood viscosity due to anemia or hemodilution (as is frequently seen upon initiation of bypass) also decreases the effective SVR. Low pump flow can result from technical malfunction, excessive venting or cardiotomy suction, cannula occlusion or kinking, or aortic dissection.

Similarly, hypertension on bypass can arise from disorders that lead to either a high SVR or excessive pump flow. High systemic arterial pressures on bypass can lead to cerebral hemorrhage or aortic dissection, so a MAP greater than 100 mmHg is generally treated aggressively by reducing pump flow, increasing the concentration of volatile anesthetic agent, or initiating vasodilator therapy. Causes of high SVR include vasoconstriction from catecholamine release, exogenous vasoconstrictors, inadequate anesthetic depth, hypothermia, preexisting hypertension, thyroid storm, pheochromocytoma, and malignant hyperthermia.

An elevated pulmonary artery pressure most commonly results from collapse of the nonperfused lung around the tip of the PA catheter and is resolved by gently withdrawing the PA catheter a few centimeters. However, pulmonary artery hypertension can also be a sign of left ventricular distension, which can lead to myocardial ischemia, subendocardial necrosis, and pulmonary edema. If the left ventricle is distended on the surgical field, adequate left ventricular drainage should be reestablished by improving venous drainage, venting the left ventricle or pulmonary artery, administering additional cardioplegia, or in rare cases, initiating total circulatory arrest.

The adequacy of tissue perfusion on CPB is evaluated via arterial blood gas measurements, urine output, and mixed venous oxygen levels. Serial arterial blood gases are drawn during CPB to assess for hypoxemia, electrolyte abnormalities, anemia, and lactic acidosis. Arterial hypoxemia can reflect an inadequate oxygen sweep rate, oxygenator malfunction, or transpulmonary shunting of blood. In the absence of hypoxemia, reduced urine output, worsening metabolic acidosis, or mixed venous hypoxemia (less than 70 %) likely represents inadequate pump flow. Oliguria on bypass (less than 1 ml/kg/h) may indicate inadequate renal perfusion and should be communicated to the perfusionist. Other potential causes of oliguria, such as postrenal obstruction, renal vasoconstriction, and hypothermia, should be excluded. Hemoglobinuria on bypass can reflect red blood cell trauma, transfusion reactions, or a water leak in the heat exchanger. A low mixed venous oxygen saturation is a sign of decreased tissue oxygen delivery (inadequate pump flow, excessive hemodilution) or increased tissue oxygen consumption (hyperthermia, shivering, malignant hyperthermia, thyrotoxicosis).

Malpositioning of the arterial cannula can manifest at any time during the bypass run. Aortic dissection can result from the cannula being embedded in the aortic wall rather than in the lumen. Management of this complication requires stopping CPB, placing a new arterial cannula, recommencing CPB, and repairing the dissected segment. A malpositioned aortic cannula can also direct flow preferentially toward one of the carotid arteries, leading to unilateral facial blanching, pupillary dilation, and conjunctival chemosis. These symptoms should be assessed periodically during bypass and communicated to the surgeon, who may need to reposition the cannula. Factitious hypertension can be registered on a

right radial or brachial arterial line if the aortic cannula is directed toward the innominate artery.

Monitoring patient temperature is crucial in order to confirm adequate cooling and rewarming during CPB. Temperature should measured in multiple locations, as rapid cooling and rewarming can lead to significant temperature differences between well-perfused tissues (core temperature) and the highly vasoconstricted periphery (shell temperature). Rapid rewarming can also cause gas bubbles because oxygen is less soluble in blood as temperature increases. Nasopharyngeal and tympanic membrane probes reflect brain temperature, while a rectal probe will reflect shell temperature. A bladder probe on the Foley catheter will reflect renal temperature only if urine output is adequate. A thermistor PA catheter may provide unreliable readings with low blood flow during CPB. Nasopharyngeal temperature probes should be placed prior to heparinization to prevent epistaxis.

In recent times, many cardiac operations are done with either warm CPB or passive cooling to 33–35 °C. The decision to pursue hypothermia during bypass requires weighing the benefits of cerebral protection, decreased metabolism, and lower pump flows against the risks of coagulopathy and a prolonged bypass time. Lower temperatures require longer times for cooling and rewarming. During mild-to-moderate hypothermia (30–32 °C), MAP can be generally maintained between 50 and 70 mmHg. Deep hypothermia (18–25 °C) can be accomplished with a lower MAP range (as low as 30–40 mmHg) in patients without altered flow regulation. Urine production during cold bypass can be used as a marker of renal perfusion; low urine output can be addressed by increasing pump flow or using vasoconstrictors to increase MAP into the patient's autoregulatory range. Hypothermia decreases anesthetic requirements, but rewarming is associated with an increased risk of awareness and recall. Additional doses of amnestic medications and muscle relaxants may need to be administered prior to rewarming.

Neurological Protection

Neurological injury and postoperative neurocognitive dysfunction are widely known sequelae of cardiac surgery. The etiology of these complications is multifactorial, encompassing preoperative neurological condition, comorbid diseases, surgical factors, exposure to anesthesia, and exposure to CPB. The incidence of clinically significant neurologic deficits or stroke is approximately 2–6 % for CABG and rises to 4–13 % for open cardiac chamber (e.g., valve replacement) operations. Subtler neurocognitive impairments, such as decreased concentration, impaired memory, and reduced spatial orientation, have been demonstrated in as many as 80 % of patients within one week after undergoing CABG on bypass. Up to 35 % of patients retain some level of cognitive deficit one year after surgery. Risk factors that predispose to an increased risk of postoperative neurological deficits include advanced age (greater than 70 years), preexisting cerebrovascular disease, extensive aortic atherosclerosis, diabetes, perioperative hemodynamic instability, prolonged CPB (longer than 90 min), and repeated aortic instrumentation.

Overt cerebrovascular accidents occur as a consequence of focal ischemia and appear to be related to gaseous or particulate emboli. Embolization during cardiac surgery can propagate from aortic atheroma, intraventricular thrombi, valvular calcifications, and entrained air bubbles. Open chamber cardiac procedures present a higher risk of focal embolic ischemia than closed chamber procedures.

In contrast to focal ischemia, global ischemia appears to be related to cerebral hypoperfusion. Watershed areas, the boundary areas between regions of brain perfused by major cerebral arteries, are at particular risk of ischemia from rapid severe hypoperfusion. Diabetes and previous cerebrovascular accidents impair cerebral autoregulation, predisposing patients to neurological injury during intraoperative periods of decreased cerebral perfusion. While intraoperative hypothermia reduces cerebral metabolic oxygen consumption and can be neuroprotective, the deep hypothermia (15–18 °C) used in circulatory arrest also induces vasoparesis that can also inhibit cerebral autoregulation. In addition, systemic inflammatory responses are potentiated during rewarming, and hyperthermia greater than 37 °C may also increase the risk of neuropsychological dysfunction.

A variety of pharmacologic agents have been studied with the goal of preventing neuronal injury during bypass. To date, none of these agents have risen to the level of standard practice. Indeed, the usage of different forms of neuroprotective prophylaxis varies widely across different institutions. Inducing burst suppression with thiopental, propofol, or isoflurane is purported to decrease neurological sequelae, though the risk of focal ischemia persists. Furthermore, administering these agents can increase the need for inotropic support and delay emergence from anesthesia and postoperative neurologic assessment. Despite extensive study, the preemptive administration of corticosteroids, calcium channel blockers, lazaroids (21-aminosteroids), *N-methyl-D-aspartate* (NMDA) antagonists, and free radical scavengers has not been definitively shown to improve postoperative neurological outcomes.

Preparing for Termination of CPB

Several conditions must be met before the patient can be weaned successfully from CPB. Rewarming to a core temperature of at least 36 °C should be completed. However,

rapid rewarming can increase the temperature gradient between well-perfused organs and highly vasoconstricted peripheral tissues. Premature separation from bypass can lead to prolonged hyperthermia after cessation of active rewarming as the warmer, vessel-rich core equilibrates with the cooler, vessel-poor periphery. Persistent post-bypass hypothermia can also interfere with normal platelet function and the coagulation cascade, increasing bleeding complications.

Rewarming of the myocardium is accomplished by a final infusion of warm cardioplegia (the "hotshot"). As the cardiac muscle itself approaches normothermia, spontaneous electrical activity may resume. Many clinicians will administer lidocaine (100–200 mg) or magnesium sulfate (1–2 g) prior to removal of the aortic crossclamp to reduce the risk of ventricular fibrillation during rewarming. A heart rate of 70–100 beats/min in sinus rhythm is usually sufficient to maintain adequate cardiac output. Bradycardia may respond to anticholinergic or inotropic support, but in most cases, epicardial pacing leads will be placed, and an external pacemaker will be used to set a desired heart rate. Patients with stiff, poorly compliant left ventricles are more dependent on the atrial kick to maintain adequate cardiac output, so atrioventricular pacing may be required. Significant sinus tachycardia should be treated with either volume administration or appropriate medication. Supraventricular tachycardias often require synchronized cardioversion with internal paddles.

Adequate mechanical ventilation and oxygenation must be established before separation from bypass. Before restarting the ventilator, the lungs should be reexpanded and atelectatic alveoli recruited with a few sustained manual breaths while verifying bilateral lung expansion. Overzealous lung inflation in patients with internal mammary artery grafts can cause graft avulsion. Minor elevations in arterial carbon dioxide tension can cause significant increases in pulmonary vascular resistance that can compromise right ventricular function. A higher respiratory rate than usual may be needed to maintain P_aCO_2 below 40 mmHg in the post-bypass period.

Electrolyte abnormalities commonly occur during CPB and should be treated. Administration of calcium can inhibit the action of inotropes and, in rare instances, cause coronary vasospasm or augment myocardial reperfusion injury. Therefore, while calcium administration can help treat hypocalcemia and hyperkalemia, routine administration after bypass is not recommended. Anemia less than 7.0 g/dL should be treated before separation from CPB to improve oxygen carrying capacity and myocardial oxygen delivery.

The heart and any coronary bypass grafts should be scrupulously deaired before removal of the aortic crossclamp. Failure to do so can lead to embolization into the coronary circulation (causing acute heart failure), the carotid arteries (causing stroke), or other distal organs. The left atrium and ventricle should be examined by TEE for air bubbles, which often collect near the left ventricular apex. Resuming ventilation can also mobilize retained air from the pulmonary venous circulation. Intracavitary air can be dislodged by manual agitation of the heart and evacuated via needle aspiration or the aortic root vent. Putting the patient in Trendelenburg position and bilateral carotid artery compression can also help minimize entry of air bubbles into the cerebral circulation.

Although the right atrium and right ventricle are visible on the surgical field, TEE is invaluable in visualizing all four chambers during the effort to separate from bypass. Ventricular end-diastolic chamber size can be used to assess volume status of the heart. CVP and pulmonary artery pressure readings provide another indication of filling pressures and ventricular preload. Newly implanted prosthetic valves should be evaluated for annular motion, significant regurgitation, and perivalvular leaks, any of which can lead to cardiac dysfunction in the post-bypass period. Overall contractility and changes in segmental wall motion should be assessed in comparison to the pre-bypass exam. Poor ventricular contractility on TEE may indicate the need for inotropic support and additional preload to improve forward cardiac output prior to weaning from bypass. Severely impaired contractility may require preemptive insertion of an intra-aortic balloon pump (IABP).

Separation from CPB

Separation from CPB involves gradually transferring the mechanical work of producing cardiac output from the bypass pump to the heart. As the heart assumes a greater fraction of the total mechanical work, the arterial pressure waveform becomes more pulsatile. A decrease in pulsatility during separation from bypass suggests left ventricular failure. The diastolic blood pressure reflects vascular tone and indicates coronary perfusion pressure. Post-bypass changes in diastolic compliance make PCWP less reliable than TEE as a monitor of left ventricular filling. CVP provides a measure of right heart filling pressures, while the difference between the pulmonary artery mean pressure and CVP reflects the work performed by the right ventricle.

In order to wean the patient from bypass, the venous return line is first partially occluded. This increases right atrial pressure and directs blood into the right ventricle. Preload increases, causing cardiac output to increase by the Frank–Starling effect. Careful adjustment of venous line occlusion helps maintain optimal left ventricular preload. Next, the pump flow rate is gradually decreased, allowing the patient's native cardiac output to increase to maintain total aortic blood flow. As the heart performs more work, the venous line can be further occluded to provide adequate preload while still maintaining adequate volume in the pump reservoir. If systolic blood pressure and preload remain

adequate, then the venous line is occluded completely, pump flow is stopped, and CPB is terminated. Alternatively, patients with good cardiac function may tolerate more aggressive weaning by abruptly clamping the venous line, then reducing pump flow as the heart begins contracting in reaction to the sudden, steep increase in venous filling.

Post-CPB Hemodynamic Management

After separation from bypass, the combination of invasive pressures, TEE imaging, and visual inspection of the surgical field provides an overall assessment of cardiovascular status that helps guide supportive therapy. If systemic tissue perfusion and ventricular contractility appear adequate, then increases in blood pressure likely reflect increases in afterload. In this setting, high systolic pressures should be avoided in order to reduce surgical bleeding and strain on suture lines. Hypertension can be managed by increasing the depth of anesthesia or by starting an arterial vasodilator (such as nitroprusside or nicardipine).

Hypotension can reflect inadequate filling, ventricular failure, or peripheral vasodilation. If ventricular contractility and chamber size appear adequate on TEE, and cardiac index is appropriate (at least 2 L/min/m^2), then persistent hypotension is likely a result of very low SVR. Causes of inappropriate vasodilation include previous exposure to ACE inhibitors or calcium channel blockers, acidosis, sepsis, and hyperthermia. Administration of a vasoconstrictor, such as phenylephrine or norepinephrine, coupled with judicious volume administration, can improve SVR and increase blood pressure. Hemodilution and anemia decreases blood viscosity, reducing the apparent SVR. Treatment consists of diuresis and transfusion of red blood cells.

Hypovolemic patients will present with hypotension, low filling pressures, and underfilled ventricles on TEE. If ventricular function remains normal, then transfusion of small amounts of pump blood via the aortic cannula can increase preload and significantly improve cardiac output. If cardiac function after separating from bypass is adequate, then prompt removal of the venous cannula can improve venous return to the right side of the heart. Blood from the venous cannula can then be added to the pump reservoir and transfused to the patient via the arterial cannula. Continuous volume infusion should be avoided to prevent overdistension of the heart.

Left ventricular failure after CPB can arise from a variety of causes, including inadequate coronary blood flow, obstruction of coronary artery grafts, coronary vasospasm, myocardial ischemia, valvular disorders (including prosthetic valve dysfunction), hypoventilation, hypoxemia, and reperfusion injury. In these situations, inotropic therapy is indicated. The most common first-line inotropic agents are epinephrine and dobutamine. Milrinone may be added if the patient does not show significant improvement with a first-line inotrope. If SVR is also decreased, phenylephrine or norepinephrine may also be needed to maintain an acceptable blood pressure.

Patients with pulmonary hypertension, either as a primary diagnosis or secondary to pulmonary embolus, intracardiac shunts, or severe mitral valve dysfunction, have a higher risk of developing right ventricular failure post-bypass. Right ventricular failure can also occur with right ventricular ischemia, infarction, or outflow tract obstruction. Dobutamine or milrinone can be administered to improve right ventricular contractility and decrease pulmonary vascular resistance. Pulmonary vasodilation is also desirable and can be accomplished by increasing the respiratory rate, avoiding hypoxemia and acidosis, and administering inhaled nitric oxide.

Severe ventricular function may require reinstituting CPB as a temporizing measure until adequate inotrope concentrations can be achieved. Ischemic changes on ECG or TEE should alert the surgeon to possible coronary artery obstruction or graft occlusion. Prosthetic valve malfunction, perivalvular leaks, and significant valvular stenosis or regurgitation should also be ruled out. Ventricular dysfunction that does not improve with aggressive pharmacologic inotropic support may warrant mechanical support measures, including IABP insertion, cannulation for ECMO, or implantation of a ventricular assist device.

Reversal of Anticoagulation

After a satisfactory surgical outcome, hemodynamic stability, and adequate hemostasis are achieved, heparin anticoagulation is reversed with protamine. Protamine, a strong base, binds to heparin, a strong acid, to produce a neutral, inactive salt that is eliminated via the reticuloendothelial system. In most cases, 0.5–1.5 mg of protamine is administered for every 100 units of heparin given. While some practitioners give a standard dose of protamine for every patient, others choose to titrate protamine in response to serial ACT measurements. Once one-third to one-half of the protamine is given, cardiotomy suction is discontinued to prevent excessive protamine from being introduced into the circuit. The surgeon also can remove the aortic cannula at this time. The ACT is checked 3–5 min after the protamine infusion is completed, and additional protamine is given if the ACT has not returned to a normal range. Additional protamine may also be required after infusion of blood recovered from the pump reservoir, which may contain residual heparin. Because protamine is a stand-alone anticoagulant, overdosing it may be counterproductive. Heparin concentration assays can help determine the correct dose of protamine, particularly in patients who received multiple doses of heparin while on bypass.

Protamine is associated with several types of adverse reactions, most of which can be minimized by slow administration (over 10–20 min) in a dilute infusion. Administering protamine slowly may also prevent heparin rebound or reheparinization, a poorly understood phenomenon that may be attributed to redistribution of heparin from peripheral tissues into the central circulation. Protamine can be safely administered either centrally or peripherally. Rapid protamine infusion is associated with transient vasodilation and hypotension that can be treated with volume administration and vasoconstrictors. Acute cardiovascular collapse can occur as a result of anaphylactic reactions in patients previously exposed to protamine or similar antigens (e.g., NPH insulin), or from nonimmunologic anaphylactoid reactions. The most serious reaction to protamine is sudden, catastrophic pulmonary hypertension leading to right ventricular collapse and systemic hypotension. Patients who experience this chain of events may require emergent reheparinization and reinstitution of CPB. Some surgeons choose to administer protamine directly into the left atrium in an attempt to avert this complication; the effectiveness of this tactic is dubious at best. In patients with known severe protamine reactions, spontaneous termination of heparin activity over time with supportive blood transfusions may be required.

Safe anesthetic care includes developing procedures to prevent the accidental yet devastating administration of protamine while the patient is still on bypass. Examples of such procedures include storing heparin and protamine vials in separate locations, having non-anesthesia personnel prepare and keep the protamine infusion until needed, and waiting until the surgeon requests protamine before drawing the medication.

Post-CPB Bleeding

Persistent bleeding after separation from bypass can occur as a result of inadequate heparin reversal, inadequate control of surgical bleeding, thrombocytopenia, platelet dysfunction, and preexisting or newly acquired coagulopathy. Hypothermia, hemodilution, and prolonged exposure to synthetic extracorporeal surfaces during CPB exacerbate the decline in both the quantity and function of platelets and coagulation factors. Diffuse oozing from suture sites and tissue surfaces after surgical hemostasis and reversal of heparin is a sign of thrombocytopenia or impaired platelet function, often requiring platelet transfusion. Desmopressin (DDAVP, 0.3 μg/kg) increases the release of factor VIII and von Willebrand factor from vascular endothelium. It can reverse platelet defects and reduce blood loss in selected groups of patients, but no evidence exists to support its routine use to limit bleeding after cardiac surgery. Depletion of coagulation factors can be treated with FFP or recombinant factor concentrates, while fibrinogen deficits can be treated with cryoprecipitate.

Ideally, the decision to transfuse platelets or other blood products should be justified by results of laboratory tests. However, persistent blood loss may necessitate administration of these products before test results are available, particularly if continued oozing is preventing timely closure of the chest. Also, empiric administration may be deemed necessary in the case of dilutional thrombocytopenia and coagulopathy after massive red cell transfusion.

Postoperative Management

Patient Transport

The end of surgery marks the beginning of one of the most intimidating and dangerous periods in cardiac perioperative care. Transporting a critically ill patient from the operating room to the intensive care unit (ICU) requires continual vigilance and attention to detail. Just as in the operating room, anesthesia providers should be prepared at all times during transport to address significant changes in the patient's cardiac and respiratory status. Creating standardized protocols to allocate tasks during transport, communicate important information, and hand off patient care duties can help reduce errors and improve efficiency.

The key to safe, successful patient transport is advance preparation. Before starting the transport process, the receiving team in the ICU should be alerted to prepare for the patient. The anesthesia team should ensure the availability of a working transport monitor, supplemental oxygen, and a self-inflating bag valve mask. Infusion pumps, pacemakers, and other devices should have adequate battery power to last the duration of transport. Intravenous fluids and infusions should be available in sufficient quantities to support the patient's needs until ICU personnel have completed their intake procedures. At least one injection port should always be easily accessible for drug administration. A well-ordered kit of vasoactive medications and emergency airway equipment should be prepared.

Transferring the patient from the operating table to the transport bed can be associated with significant fluid shifts, arrhythmias, and hemodynamic instability. The operating room is the best setting to handle these changes, and the patient should not be removed from the operating room until reasonably stable. During transport, the patient monitor should be easily visible and audible to all personnel. Hemodynamic monitoring must be maintained continuously; at the very least, arterial blood pressure, pulse oximetry, and ECG should be monitored throughout transport. Within the context of available resources, enough people should be recruited to transport the patient so that each person can focus on one set of tasks without unnecessary distraction. For example, a single anesthesia provider should not have to

administer a vasoconstrictor while also ventilating the patient and steering the bed. This is particularly crucial when moving very obese patients or those with extra equipment, such as IABP consoles or nitric oxide delivery systems.

Upon arrival in the ICU, designated personnel should connect the patient to the ventilator, reconfirm bilateral breath sounds, and transfer patient monitors and infusions in a methodical fashion. Prioritization of tasks is critical. Reestablishment of adequate ventilation, oxygenation, and cardiac monitoring should take precedence over routine patient care tasks such as drawing blood for laboratory tests or completing paperwork. The anesthesia provider should identify the nurse accepting responsibility for the patient and provide a brief report, including the patient's baseline cardiac status, comorbid conditions, surgical procedure, adverse intraoperative events, current drug therapy, and expected postoperative issues.

Management in the ICU

The primary goal of management within the first few hours after surgery is to maintain stable hemodynamic parameters while observing for signs of postoperative bleeding. Patients often suffer from relative hypovolemia for several hours after surgery and may require volume resuscitation to maintain an adequate blood pressure. However, decreases in blood pressure can also be caused by myocardial ischemia or peripheral vasodilation. Hypertension can develop after surgery as preoperative antihypertensive medications or intraoperative anesthetic agents wear off. Provided adequate coronary and distal organ perfusion is maintained, hypertension should be treated promptly to avoid exacerbating bleeding from raw tissue surfaces and suture lines. Equilibration of temperature between the core and periphery can lead to hypothermia and shivering, greatly increasing tissue oxygen demand, hypercarbia, and myocardial oxygen consumption. Active warming strategies should be employed to prevent ischemia and cardiac compromise.

While drainage from chest tubes may initially be brisk, it should taper off within the first few hours after surgery. Particularly in patients previously exposed to aspirin or other antiplatelet therapy, laboratory tests can help differentiate platelet dysfunction or a bleeding diathesis from postsurgical blood loss. In the absence of known coagulopathy, chest tube output exceeding 200–300 mL/h in the first two hours after surgery or sustained drainage of 100–200 mL/h thereafter justifies surgical reexploration. Accumulation of blood in the chest cavity can lead to cardiac tamponade and hemodynamic instability requiring emergency drainage.

Cost containment pressures have encouraged the wider adoption of measures to fast-track patients after cardiac surgery. Additional benefits of fast-tracking include reduced ventilator-associated complications, improved patient comfort, and earlier ambulation and rehabilitation therapy. Protocols to wean patients from mechanical ventilation within 6–12 h after surgery, even in comparatively sick patients, are now relatively commonplace. Nonetheless, cardiac surgery increases postoperative physiologic shunting and atelectasis. Surgical entry into the chest cavity reduces total lung capacity, forced expiratory volumes, and functional residual capacity for weeks after surgery. Cold cardioplegia infusion can injure the left phrenic nerve and temporarily impair diaphragmatic function. The decision to extubate a patient must be based on an assessment of oxygenation, ventilation, airway patency, protective reflexes, and muscle strength, not on arbitrary time parameters. Electrolyte abnormalities, hypothermia, dysrhythmias, significant bleeding, and high-dose vasoactive support should all be resolved before extubation is contemplated. Whether the patient is extubated in the ICU or, less commonly, in the operating room, supplemental oxygen, aggressive pulmonary toilet, incentive spirometry, and noninvasive positive-pressure ventilation should be used to prevent atelectasis, hypoxemia, and hypercarbia.

Hemodynamically stable patients without significant postoperative bleeding who have undergone CABG should receive aspirin within 6–24 h after surgery to help preserve vein graft patency. Patients who presented with ACS prior to CABG should be restarted on dual antiplatelet therapy, which is associated with decreased recurrence of myocardial infarction and improved survival.

If a continuous insulin infusion was started in the operating room, it should be continued into the postoperative period with a goal of maintaining serum glucose $\leq$180 mg/dL. This level of glycemic control should be continued for the duration of the patient's ICU care. Patients without a preoperative diagnosis of diabetes who have persistent serum glucose levels $\geq$180 mg/dL after CPB also need insulin infusion therapy and may require endocrinology consultation. Regardless of diabetic status, more aggressive glycemic control ($\leq$150 mg/dL) is warranted in patients whose ICU care is prolonged due to ventilator dependence, renal replacement therapy, or the need for medical or mechanical inotropic support. Before discharge from the ICU, the patient should be transitioned to a scheduled subcutaneous insulin regimen with a target blood glucose level $\leq$180 mg/dL in the peak postprandial state and $\leq$110 mg/dL in the fasting and premeal states. Once these targets are reached consistently, preoperative oral hypoglycemic medications can be restarted and insulin dosages reduced accordingly.

Postoperative Analgesia

Perioperative myocardial ischemia is most commonly observed in the immediate postoperative period. CPB stimulates the production of stress-response hormones, and higher circulating catecholamine levels persist into the postoperative

period. In addition, increased cardiac sympathetic stimulation exacerbates the imbalance between coronary arterial blood flow and myocardial oxygen demand. Aggressive postoperative pain management can reduce the neurohormonal stress response and reduce the incidence and severity of postoperative myocardial ischemia. Attenuation of the postoperative stress response can also help mitigate alterations in platelet activation and immune responses. Patients may expect much higher levels of pain after cardiac surgery than what they actually experience; as a result, patient satisfaction ratings with postoperative analgesia may not accurately correlate with the physiologic sequelae of persistent pain stimuli.

Many techniques to provide analgesia after cardiac surgery are available, all of which have benefits and drawbacks. Combining multiple techniques that work by different mechanisms (multimodal analgesia) may achieve more profound analgesia with a more favorable risk profile. Intravenous opioids have a long and proven history of efficacy in the cardiac setting. Local anesthetics can be infused via indwelling catheters inserted at the sternal incision site. The intense localized analgesia provided by these catheters can promote early ambulation and reduce the time to hospital discharge, but reports of infection and tissue necrosis raise questions about their long-term safety. Intercostal, intrapleural, and paravertebral nerve blocks do not appear to be reliably potent enough to constitute the sole method of postoperative pain control, but they can serve as convenient adjuncts to other techniques. Nonsteroidal anti-inflammatory drugs (NSAIDs) and cyclooxygenase (COX) inhibitors provide relief from incisional pain that is poorly treated by opioids, but questions remain about adverse effects on platelet aggregation, renal tubular function, and gastric mucosal function. The α-adrenergic agonists, clonidine and dexmedetomidine (Precedex), can enhance postoperative analgesia and potentially decrease myocardial ischemia, but they are also associated with postoperative sedation, bradycardia, and vasodilation.

Administration of intrathecal morphine prior to heparinization for CPB can provide successful postoperative analgesia without delaying early extubation. The addition of intrathecal clonidine appears to improve these effects. However, intrathecal opioids do not reliably attenuate the postoperative stress response. In contrast, intrathecal local anesthetics can produce a thoracic cardiac sympathectomy, but the adverse hemodynamic effects associated with total spinal anesthesia render this technique unsuitable for cardiac surgery. Thoracic epidural opioids or local anesthetics, administered either before heparinization or postoperatively, produce reliable analgesia and facilitate early extubation. Thoracic epidural local anesthetics can also attenuate the postoperative stress response and induce thoracic cardiac sympathectomy, effectively improving the myocardial oxygen supply–demand ratio. However, it remains unclear whether neuraxial techniques provide clinically meaningful effect on outcomes beyond enhanced analgesia.

Off-Pump and Minimally Invasive Cardiac Surgery

Off-pump coronary artery bypass grafting (OPCAB) came into prominence in the 1990s as a method of surgical revascularization that presumably avoided the neurologic, embolic, and systemic inflammatory complications of CPB. Improvement in epicardial stabilization devices allowed surgeons to perform the meticulous work of coronary graft anastomosis on a normothermic, beating heart. Early experience focused on single- and double-bypass surgery in low-risk patients, promoting OPCAB as a method to facilitate early recovery and discharge from the hospital. Over time, OPCAB came to be seen as a viable method for performing multiple bypasses in patients at high risk of complications from CPB. These include patients with severe renal disease who may not tolerate the systemic inflammatory response to CPB, patients with severe lung disease who may return to baseline after prolonged lack of ventilation, and patients at risk of embolic stroke from the aortic cannulation and crossclamp sites. The prevalence of OPCAB as compared to on-pump CABG continues to vary across different institutions and even among different surgeons.

While the avoidance of the physiologic effects of CPB has been the primary consideration for medical personnel, patients are more often concerned about postoperative recovery from a full sternotomy. Partly because of this, minimally invasive cardiac surgical techniques are under continual development. Minimally invasive direct coronary artery bypass (MIDCAB) surgery, sometimes called "keyhole" cardiac surgery, is a variant of OPCAB that employs instruments inserted through a mini-thoracotomy incision. Totally endoscopic coronary artery bypass (TECAB) surgery is a more recent advancement in which the surgeon uses a robot to perform the operation through three or four small incisions in the chest wall. Hybrid cardiac surgery, combining minimally invasive coronary grafting with percutaneous coronary stenting in the same procedure, has also been performed at some centers.

Setup of the operating room for OPCAB is similar to that for standard CABG. Because an OPCAB may need to be converted to a CABG on bypass, the CPB circuit is assembled, though typically not primed until needed, and a perfusion team is immediately available. Heparin doses and ACT targets generally mirror those of on-pump CABG, though some centers use lower ACT targets for off-pump CABG.

Like other cardiac surgical patients, patients undergoing OPCAB should have large-bore intravenous access and invasive arterial pressure monitoring. The need for additional invasive monitors depends on the patient's baseline ventricular function, the presence of comorbid conditions, and in some cases, provider and institutional preference.

Patients with well-preserved ventricular function undergoing only one or two grafts are unlikely to require extensive invasive monitoring. The worse the ventricular function and the more grafts that are planned, the more likely it is that a PA catheter (with or without continuous cardiac output functionality) will provide useful information to guide inotropic or vasopressor therapy. A central venous introducer with an obturator allows the option of placing a PA catheter later if intraoperative events warrant one. TEE allows direct visualization of volume loading status and changes in contractility, but lifting of the heart out of the chest for surgical exposure of graft targets can make images difficult or impossible to obtain. For certain minimally invasive operations, TEE guidance may be required for placement of specific cannulas or a transvenous coronary sinus catheter for retrograde cardioplegia.

Treating hypothermia is more difficult without access to the heat exchanger on CPB. Therefore, to prevent complications from hypothermia and facilitate early recovery, it is imperative in OPCAB to prevent heat loss. Methods to keep the patient warm include increasing the ambient room temperature, minimizing patient exposure prior to surgical draping, applying forced-air warming devices, using fluid warmers, and reducing fresh gas flows.

Anesthetic induction and maintenance follow the same guidelines as in patients with ischemic disease undergoing other types of heart surgery. In contrast to on-pump CABG, manipulation of the heart during OPCAB subjects the patient to major hemodynamic changes throughout the operation. Without the functional "safety net" that CPB provides, the anesthesia team must remain continuously alert and responsive to marked changes in heart rhythm, cardiac filling, and blood pressure. Lifting the heart to access distal graft targets can compress the right ventricle, kink the great vessels, and seriously reduce venous return. Placing the patient in a head-down (Trendelenburg) position, volume loading, inotropes, and vasopressors can help mitigate the effects of decreased venous return. In severe situations, adequate surgical exposure may not be possible, and conversion to on-pump CABG may become necessary. In contrast, vasodilators may be required to prevent hypertension when the surgeon applies the partial aortic crossclamp and begins work on proximal anastomosis.

Reviewing the cardiac catheterization findings and planned sequence of grafting with the surgeon preoperatively can help the anesthesiologist anticipate the intraoperative response to surgical occlusion of different coronary arteries. An artery with very high-grade stenosis that provides inadequate blood flow at rest is likely to be associated with collateral flow from adjacent regions; as a result, occlusion of this vessel during grafting may be surprisingly well tolerated. In contrast, less severely occluded arteries—particularly those with proximal stenosis—may still be responsible for resting flow to a large area of myocardium, so surgical occlusion of these vessels may lead to severe ventricular compromise. Close communication between the surgeon and anesthesiologist is absolutely vital in these cases. The surgeon should always tell the anesthesiologist what he or she intends to do next so the anesthesia team can be prepared to respond to hemodynamic changes. Similarly, the anesthesiologist should continually observe the surgical field and inform the surgeon of changes in the patient's status and response to interventions. Uncoordinated management can lead to serious complications that prolong the operation or necessitate emergency institution of CPB.

Early recovery and prompt extubation are appropriate and beneficial goals for postoperative care in off-pump and minimally invasive procedures. Maintenance of anesthesia with an inhaled agent or total intravenous anesthesia, coupled with judicious use of opioids, can facilitate early awakening from general anesthesia. Isoflurane may also have a beneficial role in protecting myocardium from ischemic damage during lengthy periods of coronary occlusion. Local anesthetic infusion catheters, non-narcotic analgesics, and multimodal analgesic regimens can provide postoperative pain relief and encourage early mobility while minimizing respiratory depression. Various centers around the world have developed experience with OPCAB using neuraxial techniques as an adjunct to or even in place of general anesthesia, allowing cardiac surgery to be performed in some cases on awake, communicative patients. Although such techniques may help expedite postoperative recovery and hospital discharge and thus expand access to advanced cardiac surgery in resource-constrained environments, they have yet to find widespread favor in the United States.

Ischemic Heart Disease

Coronary Perfusion

Although the heart constitutes less than 1 % of total body weight, it is responsible for nearly 7 % of the body's basal metabolic oxygen consumption. As in other vascular beds, blood flow to the myocardium is a function of the arteriovenous pressure gradient and local vascular resistance. Flow through the coronary arteries varies over the course of the cardiac cycle. Unlike other tissues, however, contraction of the left ventricle during systole generates sufficient wall tension to obliterate coronary blood flow. The magnitude of this throttling effect on left ventricular coronary blood flow is greatest in the subendocardium, which puts it at highest risk of coronary hypoperfusion. Therefore, perfusion of the left ventricle occurs primarily during diastole, as opposed to during systole and diastole for the right ventricle. Left ventricular end-diastolic pressure (LVEDP) can exceed CVP, so

LVEDP becomes the venous component of the arteriovenous pressure gradient. Left ventricular coronary perfusion pressure, then, is approximately DBP—LVEDP.

In addition, the heart extracts a much larger percentage of oxygen from coronary blood flow (60–70 %) than do other tissues (about 25 %). Consequently, the heart lacks the ability to compensate for increased oxygen demand through increased oxygen extraction from the blood. Coronary vasodilation remains the primary compensatory mechanism when oxygen supply is compromised. Autoregulation helps couple coronary blood flow closely to myocardial metabolic oxygen requirements, thus maintaining myocardial oxygen tension within a very narrow range. Endogenous chemical factors such as adenosine and nitric oxide are responsible for the metabolic regulation of coronary perfusion. Vascular smooth muscle also adjusts intrinsically in response to changes in intravascular distending pressures to help maintain constant flow. Sympathetic and parasympathetic inputs provide secondary regulation of coronary blood flow.

Myocardial ischemia results from an imbalance between metabolic oxygen demand and supply to the myocardium. Decreased oxygen supply can arise from hypoperfusion due to atherosclerosis, severe aortic stenosis or insufficiency, coronary vasospasm or thrombosis, severe hypotension, anemia, or hypoxemia. The most critical determinants of myocardial oxygen consumption are contractility, heart rate, and wall tension. Increased myocardial oxygen demand can occur with severe hypertension, tachycardia, or left ventricular hypertrophy. Tachycardia is particularly detrimental to oxygen supply–demand balance because it decreases coronary blood flow by shortening diastole, while also increasing myocardial oxygen demand.

Coronary Artery Disease

The predominant cause of ischemic disease is coronary artery disease (CAD) due to atherosclerosis, a leading cause of death in the industrialized world. Major risk factors include age, male sex, smoking, hypertension, hyperlipidemia, diabetes, and a family history of CAD. Other contributors include obesity, a history of peripheral vascular or cerebrovascular disease, and a sedentary lifestyle.

The most common presenting symptom of CAD is angina. As a coronary artery becomes progressively occluded, distal segments dilate to compensate for reduced blood flow. Patients may remain completely asymptomatic throughout this process. Maximum compensatory dilation is usually achieved once approximately 70–75 % of the artery is occluded. The dilated distal segments generally provide adequate blood flow to meet myocardial oxygen demand at rest but not with activity. The increase in myocardial oxygen demand with activity leads to exertional angina. Patients with more extensive collateralization will tolerate more severe coronary occlusion before feeling symptoms.

Though classically described as substernal chest pain radiating to the neck and back, angina can be highly variable, encompassing epigastric pain, transient shortness of breath, burning sensations, nausea, and palpitations. Women present more often than men with atypical symptoms of ischemia, at times delaying diagnosis and treatment. Patients with limited cardiac reserve may have orthopnea, paroxysmal nocturnal dyspnea, or decreased exercise tolerance, even without significant pulmonary disease. Patients with autonomic neuropathy from diabetes are at high risk of asymptomatic (silent) ischemia. Stenotic epicardial coronary lesions are also at risk of transient vasospasm and transmural ischemia in some patients upon variable degrees of activity or emotional distress (Prinzmetal's angina). CAD can also lead to myocardial infarction (MI), ventricular dysfunction, CHF symptoms (ischemic cardiomyopathy), arrhythmias, and sudden death.

Specialized testing for CAD is of limited benefit in asymptomatic patients and should not be used as routine screening methods. They can, however, help determine perioperative risk and the need for coronary angiography and intervention in patients with symptoms or known lesions. Noninvasive stress testing is recommended in patients with active cardiac conditions undergoing noncardiac surgery, and it may be beneficial in patients with multiple risk factors and poor functional capacity, or in patients with risk factors undergoing vascular or other moderate risk surgery. Tests such as Holter monitoring, myocardial perfusion scans, and stress ECG and echocardiography should not be ordered unless their findings will alter patient care. The definitive test for evaluating CAD remains coronary angiography.

Coronary revascularization modalities include percutaneous coronary intervention (PCI, encompassing balloon angioplasty, stent insertion, atherectomy, and brachytherapy) and coronary artery bypass grafting (CABG). Current recommendations suggest a benefit from coronary revascularization in patients with stable angina who have significant left main coronary artery disease, severe three-vessel disease, or severe two-vessel disease with a left ventricular ejection fraction less than 50 %. Patients with unstable angina, acute ST-segment elevation MI, or non-ST-segment elevation MI can also benefit from revascularization.

Intra-aortic Balloon Pump

The intra-aortic balloon pump (IABP or "balloon pump") is an indwelling mechanical device that is designed to improve both myocardial oxygen perfusion and coronary blood flow. The balloon pump is a long, cylindrical polyethylene balloon that is inserted over a guidewire through the femoral artery

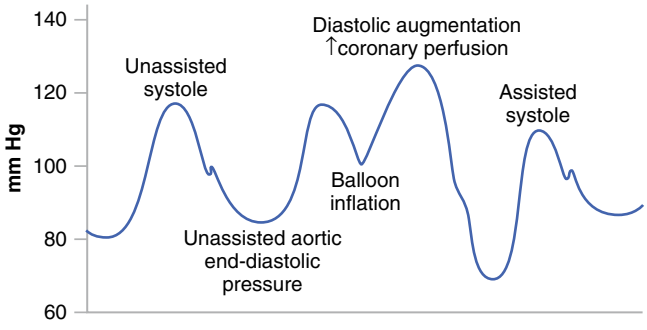

Fig. 26.9 Effects of intra-aortic balloon pump (IABP) on arterial pressure

and deployed in the descending aorta under either fluoroscopic or echocardiographic guidance. The balloon pump is connected to a control console that monitors the cardiac cycle via either the patient's ECG or an arterial pressure transducer at the balloon tip. The computerized mechanism rapidly inflates the balloon with helium during diastole and deflates the balloon during systole. Helium is used because its low viscosity promotes rapid movement into and out of the balloon, and because it is less likely than air to cause an embolus if the balloon ruptures. Proper positioning of the balloon pump is critical in order to minimize complications. The tip of the IABP should be positioned approximately 2 cm distal to the left subclavian artery. Malposition can lead to occlusion of subclavian flow and left arm ischemia.

The counterpulsation of the balloon pump provides two benefits to ventricular function (Fig. 26.9). First, inflation during diastole markedly increases diastolic blood pressure. This provides a higher driving force for blood through the coronary arteries, increases coronary perfusion pressure, and improves myocardial oxygen delivery. Second, rapid deflation of the balloon pump during systole creates a vacuum effect in the descending aorta, acutely decreasing afterload and increasing forward flow. As a result, cardiac output can be maintained with reduced left ventricular effort and reduced myocardial oxygen consumption. The overall effect is an improved myocardial oxygen supply/demand balance.

The IABP is often used in patients in cardiogenic shock to reduce myocardial ischemia and improve cardiac output. Patients with unstable angina, severe left main coronary artery disease, or severe left ventricular dysfunction may have a balloon pump placed prior to revascularization. Also, patients undergoing CABG who are difficult to wean from bypass may benefit from balloon pump counterpulsation as they continue to recover from myocardial injury.

Absolute contraindications to balloon pump insertion include severe aortic valve insufficiency, aortic dissection, and severe aortoiliac occlusive disease. Diastolic inflation in the setting of severe aortic valve insufficiency would severely increase left ventricular wall tension and increase myocardial oxygen demand, worsening left ventricular ischemia. Balloon pump insertion into a dissected aorta carries the risks of placement in the false lumen and aortic rupture. The balloon pump can dislodge large thrombi or atheroma in the aortoiliac system, leading to distal embolic complications. Aortic aneurysms and prosthetic aortic or aortofemoral grafts present a relative contraindication to placement. Blood return through the driveline indicates balloon rupture. A ruptured balloon pump presents a serious embolic risk from thrombus adhering to the device and should be removed promptly.

Valvular Heart Disease

Mitral Regurgitation

Mitral regurgitation is the most prevalent form of valvular heart disease. Mitral regurgitation reduces forward stroke volume by allowing backward flow of blood from the left ventricle into the left atrium during systole. The most common cause of mitral regurgitation is mitral valve prolapse, a result of myxomatous degeneration (pathologic degradation of the connective tissue) of the valve components. The stretched and elongated leaflets fail to come together properly when the valve closes, prolapsing instead into the left atrium and causing regurgitation. Connective tissue disorders, such as Ehlers–Danlos syndrome and Marfan syndrome, can lead to mitral valve prolapse in the same manner.

Other disorders can lead to either acute or chronic mitral valve regurgitation. Myocardial ischemia or infarction can cause papillary muscle dysfunction or rupture of a papillary muscle or a chorda tendinea, any of which can precipitate acute mitral regurgitation. Bacterial infective endocarditis can also cause acute regurgitation by damaging or distorting any part of the mitral valve apparatus. Chronic mitral regurgitation can arise from dilation or calcification of the mitral annulus or from restricted leaflet motion. Rheumatic fever, now a rare cause of mitral valve disease, usually causes combined mitral regurgitation and stenosis. Mitral regurgitation with otherwise normal valve components, also called functional mitral regurgitation, can occur from any condition that causes left ventricular dilation and mitral annulus stretching, such as aortic insufficiency, dilated cardiomyopathy, and noncompaction (spongiform) cardiomyopathy.

In acute mitral regurgitation, the total stroke volume must increase to accommodate both forward cardiac output and retrograde flow into the left atrium. By the Frank–Starling mechanism, increasing EDV helps increase ejection fraction because increased ventricular preload stretches the myocardium and allows more forceful contractions. This results in left ventricular dilation and increased EDV. The regurgitant

volume causes both volume and pressure overload of the left atrium. Increased left atrial pressures impede drainage from the pulmonary veins, leading to pulmonary congestion. Patients with acute regurgitation typically present with signs and symptoms akin to decompensated CHF, such as dyspnea, orthopnea, and pulmonary edema. Cardiogenic shock may be present in patients who have acute mitral regurgitation due to papillary muscle or chorda tendinea rupture.

If mitral regurgitation develops over several months or years, or if acute mitral regurgitation remains untreated, then the patient will enter the chronic compensated phase of the disease. During this phase, cardiac architecture changes to improve the low forward cardiac output and pulmonary congestion seen in the acute phase. The left ventricle develops eccentric hypertrophy, which, in tandem with increased diastolic volume, increases stroke volume sufficiently to bring forward cardiac back to near-normal levels. Volume overload of the left atrium causes left atrial dilation. This improves atrial compliance, decreases filling pressures, and improves drainage from the pulmonary veins. Patients with chronic compensated mitral regurgitation may experience improved symptoms and exercise tolerance.

Over time, however, the left ventricle will become unable to contract adequately to make up for its volume overloaded state, and stroke volume will decrease. Decreased forward cardiac output leads to increased left ventricular end-systolic volume and higher left-sided filling pressures. As the left ventricle dilates, wall stress increases, and concurrent dilation of the mitral annulus worsens the severity of mitral regurgitation. Severe mitral regurgitation is accompanied by reversal of pulmonary vein flow. Patients once again develop symptoms of pulmonary congestion and CHF. In addition, dilation of the left ventricle and left atrium put the patient at higher risk of arrhythmias and thrombus formation.

The severity of mitral regurgitation is quantified by the regurgitant fraction, the percentage of left ventricular stroke volume that flows retrograde into the left atrium (i.e., the regurgitant stroke volume as a percentage of total stroke volume). A regurgitant fraction of less than 30 % represents mild regurgitation, fractions of 30–60 % represent moderate regurgitation, and fractions greater than 60 % represent severe disease. The regurgitant fraction can be assessed via cardiac catheterization or echocardiography. Echocardiography also allows visualization of specific structural defects in the valve and can help guide possible surgical interventions.

Afterload reduction, though non-curative, improves forward flow by decreasing the regurgitant fraction. Hypertension should be treated aggressively with diuretics and sodium restriction. Vasodilators such as ACE inhibitors and hydralazine can be beneficial in patients with chronic mitral regurgitation and can delay the need for surgery in patients with mild regurgitation. Normotensive patients with acute mitral insufficiency can also benefit from afterload reduction therapy with drugs such as nitroprusside or nicardipine.

Patients with moderate or severe mitral regurgitation will likely require surgery to improve their symptoms. Surgery is indicated in patients with chronic mitral regurgitation who have left ventricular ejection fraction less than 60 %, newly diagnosed atrial fibrillation, or severe pulmonary hypertension (pulmonary artery systolic pressure greater than 50 mmHg at rest or 60 mmHg with activity). Valve repair is generally preferable to replacement, which carries an increased risk of myocardial ischemia, thromboembolism, endocarditis, and prosthetic failure. Percutaneous techniques to repair the mitral valve (such as a transcatheter clip to plicate the leaflet tips in a manner akin to the surgical Alfieri stitch) are under ongoing development and may provide an alternative treatment option for high-risk patients who would otherwise be poor candidates for open-heart surgery.

Anesthetic management of patients with mitral regurgitation should be guided by the severity of valvular disease and the degree of left ventricular dysfunction and pulmonary compromise. The presence of large *v* waves on the pulmonary arterial waveform can help judge the severity of regurgitation. Patients with severe regurgitation can develop increased pulmonary pressures that lead to right heart failure, so pulmonary vasoconstriction from hypercapnia, hypoxia, and nitrous oxide administration must be scrupulously avoided. The heart rate should be maintained within a range of 80–100 beats/min. Bradycardia is detrimental to patients with mitral regurgitation, as it increases left ventricular volume, reduces forward cardiac output, and increases regurgitant fraction. While small increases in preload can help ensure adequate forward stroke volume, administration of large amounts of fluid in some patients can dilate the mitral annulus and increase the regurgitant fraction. Acute increases in systemic vascular resistance also increase the regurgitant fraction and reduce forward cardiac output. Nitroprusside is commonly used to decrease afterload and improve cardiac index in these patients, but nitroglycerin may be preferable in patients with acute mitral regurgitation as a consequence of ischemic disease.

Maintaining forward stroke volume requires maximum contraction of the eccentrically hypertrophic left ventricle. Inotropic agents can reduce regurgitant fraction by both constricting the mitral annulus and improving ventricular contractility. Patients with acute mitral regurgitation from papillary valve rupture may require inotropic support and IABP placement preoperatively. After mitral valve replacement, the loss of the low-pressure outlet to the left atrium can increase left ventricular wall tension, compromising ejection fraction. Inotropic support or IABP counterpulsation may be necessary to support the left ventricle as it adjusts to postsurgical changes.

Most anesthetic regimens are well tolerated in patients with mitral regurgitation who have well-preserved left ventricular dysfunction. High-dose opioid induction, for example, is an appropriate choice provided bradycardia is avoided. Isoflurane, which decreases systemic vascular resistance and can increase heart rate, is useful for maintenance of anesthesia, though patients with severely reduced left ventricular function may be sensitive to its myocardial depressant effects at high concentrations.

Mitral Stenosis

In adults, mitral stenosis almost universally occurs as a delayed result of rheumatic disease, which causes scarring and fibrosis of the leaflet edges. Scarring and fusion can progress to the commissures and chordae tendinae, resulting in a calcified mitral valve apparatus. About two-thirds of cases occur in women. Rheumatic mitral stenosis is often accompanied by mitral regurgitation or aortic regurgitation. Less commonly, vegetations from infective endocarditis can increase the chance of mitral stenosis. Mitral stenosis is the most common valvular lesion in pregnancy.

Patients are typically asymptomatic after an acute episode of rheumatic fever. However, over the course of 10–30 years after the initial episode, the progression of mitral stenosis reduces the valve orifice area from the normal 4–6 cm^2 to 1.5–2.5 cm^2. Patients at this mild level of stenosis may report symptoms only during heavy exertion. With moderate stenosis (valve area 1.0–1.5 cm^2), symptoms may present with mild exertion. Left atrial dilation can lead to atrial fibrillation. Because atrial contraction contributes 30 % of left ventricular filling in mitral stenosis, atrial fibrillation can significantly reduce cardiac output and precipitate heart failure. CHF can also develop in response to high cardiac output states, such as pregnancy, fever, thyrotoxicosis, or anemia. Patients who progress to critical mitral stenosis (valve area <1.0 cm^2) have symptoms at rest. Increased left atrial pressure leads to chronic pulmonary hypertension and right ventricular dilation. The dilated right ventricle causes a leftward shift of the intraventricular septum, exacerbating the already reduced cardiac output from the chronically underloaded left ventricle. Continued right ventricular dilation can cause tricuspid regurgitation and peripheral venous congestion.

Patients report symptoms consistent with CHF, such as chronic or exertional dyspnea, orthopnea, and paroxysmal nocturnal dyspnea. About 10–20 % of patients with mitral stenosis report angina, but it is poorly predictive of concomitant CAD. Palpitations may be present in patients with atrial fibrillation. Patients with atrial fibrillation are also at a high risk of systemic thromboembolic events. Hemoptysis can occur as a result of disruption of pulmonary and bronchial veins. Left atrial distension and pulmonary artery enlargement can cause compression of the left recurrent laryngeal nerve, presenting as hoarseness. Severe right-sided heart failure can manifest as peripheral edema, hepatomegaly, and ascites. Although progression from initial onset to appearance of symptoms can take decades, further progression to severe disability (such as NYHA class IV heart failure) can take less than 10 years, and incapacitated patients survive less than 5 years without surgery.

Treatment options for symptomatic mitral stenosis include medical management, mitral valve replacement surgery, and percutaneous transseptal balloon valvuloplasty. Medical management is based on treating concomitant conditions, such as CHF, atrial fibrillation, and hypertension. Anticoagulation is usually required for patients with atrial fibrillation or a history of embolic events. NYHA class III or IV heart failure is an indication for mitral valve replacement surgery. Balloon valvuloplasty is associated with restenosis of the mitral valve over the course of 5–15 years and, therefore, does not provide a permanent cure for the disease. However, it is a valuable treatment option for carefully selected patients, such as pregnant women or elderly patients who are poor surgical candidates.

Nearly any anesthetic regimen can be used effectively in patients with mitral stenosis as long as sufficient forward flow is ensured. Adequate preload is required to maintain forward flow across the stenotic mitral valve, and hypovolemia can be detrimental. However, in patients with elevated left atrial pressures, overly aggressive fluid administration can exacerbate CHF and lead to severe pulmonary edema. Careful intravenous fluid management, then, is mandatory. Inotropic support may be required to maintain right and left ventricular contractility and promote forward flow. Reducing afterload has little appreciable effect on forward flow because the stenotic mitral valve acts as the limiting factor for stroke volume and cardiac output. Severe decreases (as can occur with spinal or epidural anesthesia) can also compromise coronary perfusion and increase myocardial work. Therefore, normal afterload should be maintained in these patients, and vasopressors may be required after anesthetic induction to maintain adequate vascular tone. As in mitral regurgitation, patients with severe mitral stenosis have increased pulmonary artery pressures and can be very sensitive to the effects of hypoxia, hypercapnia, acidosis, and nitrous oxide.

Sinus rhythm should be maintained if it is present preoperatively. Tachycardia shortens the diastolic period during which mitral flow occurs, so left atrial pressure must increase in order to maintain cardiac output. Maintaining sufficient diastolic time allows for adequate loading of the left ventricle. At the same time, severe bradycardia is counterproductive since stroke volume is relatively fixed. Judicious administration of opioids or β-blockers can help maintain a favorable heart rate intraoperatively. Sudden supraventricular tachycardia can lead to rapid hemodynamic deterioration and required immediate cardioversion.

Aortic Insufficiency

Aortic insufficiency (aortic regurgitation) can result from abnormalities of either the aortic valve or the aortic root. Acute insufficiency can arise from infective endocarditis, trauma, or aortic dissection (from retrograde extension of the dissection flap; see Diseases of the Thoracic Aorta below). About half of all cases of chronic aortic insufficiency occur as a result of aortic root dilation (annuloaortic ectasia). The vast majority of these cases are idiopathic, but aortic root dilation can also occur with aging, hypertension, syphilitic aortitis, cystic medial necrosis, osteogenesis imperfecta, rheumatoid and psoriatic arthritis, and Behçet's disease. A congenitally bicuspid aortic valve can present with aortic insufficiency as well as aortic stenosis.

Regardless of the underlying cause, aortic insufficiency leads to left ventricular systolic and diastolic volume overload. Patients with chronic aortic insufficiency can remain asymptomatic for many years. In the early stages of chronic insufficiency, the increased volume load causes both increased wall thickness and cavity diameter, resulting in eccentric hypertrophy. End-diastolic pressures remain relatively normal because the slow increase in EDV is accompanied initially by an increase in ventricular compliance. Along with peripheral vasodilation, this helps keep myocardial oxygen demand relatively stable. As aortic insufficiency progresses (regurgitant fraction about 40–60 % of stroke volume), continued dilation and hypertrophy lead to irreparable myocardial damage and left ventricular dysfunction. Patients report symptoms of CHF and pulmonary congestion. ACE inhibitors and diuretics can be used to reduce afterload, offload the left ventricle, and increase forward ejection fraction. If left heart failure worsens further, the decreased diastolic blood pressure can impair coronary blood flow. Angina may develop as an indication of myocardial ischemia. Poor cardiac output and coronary perfusion cause sympathetically mediated peripheral vasoconstriction, worsening cardiac output even further. Once irreversible left ventricular dysfunction occurs, even valve replacement surgery may be inadequate to improve the patient's condition.

In acute aortic insufficiency, the sudden increase in the volume load of the left ventricle stimulates an increase in sympathetic tone. In addition to tachycardia and improved contractility, fluid retention increases preload to the left ventricle. However, these changes may not be sufficient to preserve cardiac output. The acutely overloaded left ventricle cannot compensate through hypertrophy or dilation, and increased filling pressures are transmitted through the pulmonary circulation. Patients usually present with sudden hypotension, CHF, and pulmonary edema. Medical management consists of inotropic and vasodilator therapy, but patients will continue to deteriorate rapidly without emergency surgery.

Patients with aortic insufficiency require preload augmentation to maintain adequate forward flow; venodilators can reduce preload and significantly impair cardiac output. In contrast, afterload reduction therapy with arteriodilators benefits the left ventricle by reducing stroke work and decreasing end-diastolic pressure. Bradycardia should be avoided, as it increases the regurgitant fraction of stroke volume. While slight increases in heart rate improve cardiac output, severe tachycardia can increase myocardial oxygen demand and induce ischemia. A heart rate range of 80–100 beats/min appears to be optimal. Maintaining adequate contractility may require administration of inotropic agents. IABP counterpulsation will severely increase regurgitant flow and is absolutely contraindicated in aortic insufficiency.

The choice of anesthetic regimen should be based on the need to preserve preload, improve contractility, avoid bradycardia or severe tachycardia, and prevent peripheral arterial constriction. Judicious premedication can help avoid increases in systemic vascular resistance associated with anxiety. Inhalational agents are peripheral vasodilators and are a good choice for maintaining general anesthesia. Patients with severely compromised left ventricular function may better tolerate opioid-based regimens. When treating hypotension associated with anesthetic induction, vasoconstrictors should be used very carefully to avoid detrimental increases in systemic vascular resistance.

Aortic Stenosis

Aortic stenosis can arise from progressive thickening or calcifications of the cusps, leading to restricted opening and a decreased valve orifice area. Rheumatic valvular disease resulting from streptococcal infection was the most common cause of aortic stenosis in the past. Today, however, the most common cause of aortic stenosis in adults is calcification of a congenitally bicuspid aortic valve, in which the commissure between two of the three normal cusps failed to form completely. In addition, progressive calcification of a normal aortic valve can lead to fusion of two cusps along their commissure, creating functionally bicuspid valvular pathology.

Aortic stenosis increases the left ventricular systolic pressure required to maintain forward flow into the systemic circulation, leading to compensatory, concentric left ventricular hypertrophy. The greater muscle mass of the left ventricle increases myocardial oxygen consumption. At the same time, the severely stenotic aortic valve limits the amount of blood that can be ejected during systole, in effect creating a fixed cardiac output and a decrease in coronary perfusion pressure. Coronary perfusion is also impeded by the increase in left ventricular end-diastolic pressure. Stiffening of the thicker myocardium decreases left ventricular compliance, leading to diastolic dysfunction.

As stenosis becomes critical, the hypertrophic left ventricle also dilates, increasing EDV along with end-diastolic pressure. Cardiac output decreases further due to a decrease in left ventricular ejection fraction. The combination of increased end-diastolic pressure and volume increases myocardial work, further worsening the imbalance between myocardial oxygen supply and demand and leading to CHF. Further ischemia puts the patient at risk of hemodynamic collapse and sudden death.

The aortic valve orifice normally has an area of 2.5–3.5 cm^2, which corresponds to a valve index (valve area over body surface area) of 2 cm^2/m^2. A valve index of 0.5 cm^2/m^2 or less indicates a critically stenotic valve. As the severity of stenosis increases, a transvalvular pressure gradient develops between the left ventricle and the aortic root. This gradient can be measured by echocardiography or cardiac catheterization and, along with reported symptoms, helps determine the need for valve replacement surgery. Patients with aortic stenosis may report angina with exertion arising from an unmet increase in myocardial oxygen demand with activity. In the absence of concomitant CAD, patients are unlikely to report angina at rest. Insufficient cardiac output with activity can also lead to syncope.

Patients with aortic stenosis can remain asymptomatic for years or even decades before needing surgery. However, symptomatic patients will generally die within 5 years without treatment. The mainstay of treatment is surgical aortic valve replacement, which can be performed with a smaller sternotomy than most other heart operations. Several alternative interventions exist, in various stages of development and popularization, to treat patients who may otherwise be poor surgical candidates. Percutaneous balloon valvuloplasty is often used in children with congenital aortic stenosis, but eventual restenosis limits its use in adults. The apicoaortic conduit (or aortic valve bypass) is an alternative operation that nearly eliminates the pressure gradient across the aortic valve by installing a bypass conduit from the left ventricular apex to the descending aorta through a left thoracotomy. By avoiding the aorta and base of the heart, this operation is associated with a reduced incidence of postoperative stroke and arrhythmias. Finally, transcatheter aortic valve implantation (TAVI) involves the catheter-guided deployment of a self-expanding prosthetic valve within the existing valve annulus.

Anesthetic goals in patients with aortic stenosis include avoidance of tachycardia, maintenance of normal sinus rhythm, and supporting preload and afterload. Because the stenotic lesion renders cardiac output fixed, decreases in afterload do not improve forward flow. On the contrary, increased systemic vascular resistance is required to provide adequate coronary perfusion to the hypertrophic left ventricle. Decreases in contractility, as can occur with β-blockers, can be detrimental. Extremes of heart rate are poorly tolerated. Tachycardia can decrease coronary perfusion, while bradycardia limits cardiac output in the context of fixed stroke volume. However, a lower range of heart rate (50–70 beats/min), which allows adequate time for systolic ejection across the stenotic valve, appears to be optimal. Supraventricular arrhythmias severely compromise left ventricular filling and should be treated rapidly.

Any anesthetic agent that causes peripheral vasodilation, myocardial depression, or tachyarrhythmias should be used with caution. A potent vasoconstrictor, such as phenylephrine or vasopressin, should always be readily available to treat reductions in systemic blood pressure. Premedication should be administered cautiously, if at all, in patients with severe stenosis, as even slight decreases in systemic vascular resistance can lead to rapid hemodynamic deterioration. A patient with critical disease may become dependent on afterload to maintain systemic perfusion, and minimal sedation for anxiolysis can cause complete cardiovascular collapse. More so than in any other cardiac condition, a cardiac surgeon and perfusionist should be present and prepared to commence emergency CPB if the patient rapidly deteriorates upon induction.

Severe aortic stenosis is a relative contraindication to neuraxial anesthesia. Spinal and epidural anesthesia can cause hypotension through decreases in preload and afterload. However, in less severe stenotic disease, the hemodynamic risks of neuraxial anesthesia should be weighed against the benefits of avoiding general anesthesia and airway instrumentation in certain patients (e.g., pregnant patients for cesarean section). Epidural anesthesia may be preferable to single-dose spinal anesthesia, as medications can be titrated more slowly and rapid hemodynamic changes avoided. Reductions in blood pressure should be treated with vasoconstrictors and fluids.

Combined Valvular Lesions

The hemodynamic goals of anesthetic management for various valvular lesions are summarized in Table 26.11. Patients with multiple valvular disorders present a special challenge for anesthetic management. Patients frequently present for surgical repair or replacement of multiple diseased valves that may, individually, call for conflicting hemodynamic goals. Reviewing the patient's symptoms, preoperative assessment, and diagnostic test results should help to identify the most hemodynamically significant lesion. An alternative strategy is to assess, prior to sedation or induction, the range of blood pressure and heart rate within which the patient is least symptomatic, and then attempt to maintain similar hemodynamics throughout induction and maintenance of anesthesia.

Table 26.11 Goals of hemodynamic management in valvular disease

Disease	LV preload	Heart rate	Contractility	SVR	PVR
Mitral regurgitation	Variable	↔ or ↑	↔	↓	↓
Mitral stenosis	↑	↓	↔	↔	↓
Aortic insufficiency	↑	↑	↔	↓	↔
Aortic stenosis	↑	↔ (sinus rhythm)	↔	↑	↔
	RV preload	**Heart rate**	**Contractility**	**SVR**	**PVR**
Tricuspid regurgitation	↑	↔ or ↑	↔	↔	↓
Tricuspid stenosis	↑	↔ or ↓	↔	↑	↔

LV left ventricle, *RV* right ventricle, *SVR* systemic vascular resistance, *PVR* pulmonary vascular resistance, ↑ increase, ↓ decrease, ↔ maintain

Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM), sometimes called idiopathic hypertrophic subaortic stenosis (IHSS), is a primary disease of the myocardium that occurs in about 0.2–0.5 % of the population. It is an autosomal dominant trait commonly involving a genetic mutation of a sarcomere protein in the cardiac myocyte, leading to increased extracellular fibrosis and altered intracellular calcium handling.

Patients with HCM have some degree of asymmetric left ventricular hypertrophy, in contrast to the concentric hypertrophy of severe aortic stenosis or chronic severe hypertension. Asymmetric septal hypertrophy, up to 20–30 mm thick, occurs in about two-thirds of patients with HCM. Variable obstruction of the left ventricular outflow tract occurs and can be detected as a late systolic murmur on auscultation. Decreased ventricular filling and increased myocardial filling worsen the obstruction. Myocardial hypertrophy and altered myocyte architecture lead to increased left ventricular stiffness, which can progress to diastolic dysfunction. Increased diastolic pressure reduces coronary blood flow, while the increased myocardial muscle mass and variable outflow tract obstruction increase oxygen consumption, leading to myocardial ischemia.

The dynamic outflow obstruction occurs as a result of systolic anterior motion (SAM) of the anterior leaflet of the mitral valve into the left ventricular outflow tract. This phenomenon was previously thought to arise from the increased velocity in the narrowed outflow tract creating a Venturi effect, sucking the anterior mitral valve leaflet against the septum. Recent echocardiographic studies, however, have demonstrated that asymmetrical hypertrophy alters the position of the mitral valve, exposing the anterior leaflet to abnormal systolic flow patterns that cause SAM. The mitral valve leaflet does not get pushed into the outflow tract until after the aortic valve opens at the start of systole. As systole progresses, increased left ventricular pressure overcomes the obstruction caused by SAM. This flow pattern can be detected on physical examination as a double pulsation upon carotid artery palpation (bifid pulse).

Symptoms of HCM can include fatigue, reduced exercise tolerance, dyspnea, angina, palpitations, light-headedness, or syncope. Angina is a sign of inadequate myocardial perfusion. Dyspnea often indicates diastolic dysfunction and elevated left-sided filling pressures. Symptoms can mimic those of CHF, but diuretics are contraindicated in HCM, as decreased circulating volume exacerbates the dynamic outflow obstruction. Many patients remain asymptomatic until they initially present with sudden cardiac death. HCM is perhaps best known as a leading cause of sudden cardiac death in otherwise healthy young athletes. Family-specific genetic testing of patients with known HCM can help identify relatives at risk of the disease.

Anesthetic management of patients with known HCM is aimed at minimizing outflow tract obstruction. Adequate intravascular volume should be maintained to prevent collapse of the outflow tract, and hypovolemia should be avoided. Myocardial contractility should be reduced with β-blockers. Vasodilation can compromise coronary blood flow and lead to ischemia.

Cardiac Tamponade

Cardiac tamponade (or pericardial tamponade) is a physiologic condition that arises when increased pericardial pressure impairs diastolic filling of the heart. Tamponade typically results from accumulation of fluid inside the pericardial sac. Normally, the pericardial sac contains about 25–50 mL of fluid. Additional fluid (blood, pus, or other fluids) can accumulate as a result of trauma (blunt or penetrating), infection, or malignancy. Less common causes include acute MI, aortic dissection, iatrogenic injury (e.g., catheter or lead placement), radiation injury, connective tissue disorders, and uremia. Postoperative bleeding from graft suture lines, sternotomy edges, and generalized coagulopathy leads to tamponade in about 3–6 % of cardiac surgical patients. Tamponade can also occur after cardiac surgery if chest tubes become obstructed with thrombus.

As the pericardial space fills with fluid, the pericardial sac stretches to accommodate the increased volume. If the rate of filling exceeds the ability of the pericardium to expand, the increased pressure inside the pericardium will compress the cardiac chambers, impeding their ability to fill during diastole. The increase in pericardial pressure is a function of the volume of fluid and the rate of accumulation. Acute tamponade can occur with as little as 100 mL of rapid fluid accumulation. In contrast, in chronic conditions such as cancer, up to 1,000 mL of fluid can collect in the pericardial sac without significantly raising pericardial pressure.

A pericardial thrombus or mass will exert pressure in a localized area of the heart, while a generalized fluid collection will exert pressure across all four chambers equally. The relatively thin-walled atria and right ventricle are at higher risk of diastolic compression from increased pericardial pressure. As pericardial pressure rises, filling pressures fall, leading to equalization of CVP and diastolic pressures across all four chambers. Bowing of the interventricular septum to the left decreases stroke volume. Reflex sympathetic activation causes an increase heart rate and contractility in an effort to preserve cardiac output. Sympathetic stimulation also leads to arterial vasoconstriction, increasing SVR to help preserve systemic blood pressure. As pericardial pressure increases, stroke volume becomes relatively fixed, meaning cardiac output becomes primarily dependent on heart rate. As pericardial pressure increases further, right ventricular end-diastolic pressure exceeds CVP, compromising forward flow and leading rapidly to cardiogenic shock.

Acute cardiac tamponade can present as sudden hypotension, tachycardia, and tachypnea. The patient may complain of dyspnea, orthopnea, or light-headedness. The classic Beck's triad of hypotension, distended neck veins, and muffled heart sounds, though pathognomonic for cardiac tamponade, is present in only a minority of cases. Pulsus paradoxus (a drop in arterial blood pressure greater than 10 mmHg on inspiration) is often present. The chest radiograph may show an enlarged or globular heart shadow. ECG changes are generally nonspecific and may include generalized ST-segment changes and decreased voltage in all leads (owing to the intervening fluid). Swinging of the heart within a very large pericardial effusion can cause alternating increases and decreases in wave magnitude on the ECG, called electrical alternans. Echocardiography is the most readily useful diagnostic modality in tamponade. It allows direct visualization of atrial and right ventricular diastolic collapse, localization and quantification of the pericardial effusion, and guidance during pericardiocentesis or surgical exploration. Tamponade should be strongly suspected in a postsurgical patient with a CVP that approximates the mean pulmonary arterial pressure and an underfilled left ventricle on TEE.

Definitive treatment of tamponade remains pericardial drainage, either by subxiphoid pericardiocentesis or by surgical decompression via sternotomy or thoracotomy. Anesthetic management in cardiac tamponade depends on the acuity and severity of the patient's condition. The overriding goals are to maintain venous return, prevent bradycardia, and preserve sympathetic tone in order to avoid catastrophic decreases in cardiac output (The popular mnemonic, "Keep the patient full, fast, and tight," is helpful.). Large-bore intravenous access is mandatory. An arterial line and other invasive monitors are highly desirable, but placing them must not delay surgical intervention on an unstable patient. Trendelenburg (head-down) position can worsen symptoms and should be avoided during central line placement; ultrasound guidance can be useful. Intravenous fluids, inotropes, and vasoconstrictors are beneficial only if sufficient filling pressures exist to provide forward cardiac output. If tamponade has progressed to the point of diastolic dysfunction and cardiogenic shock, then pericardial drainage alone will restore venous drainage and improve hemodynamics.

Anesthetic induction should be deferred until the patient is prepped and draped, equipment is available, and the surgeon is ready to make incision. Any anesthetic agent that decreases heart rate, myocardial contractility, or vasomotor tone is potentially lethal in a patient with cardiac tamponade. Ketamine and scopolamine are valid options for induction. Mechanical ventilation with positive-pressure ventilation can increase intrathoracic pressure enough to obliterate venous return. Intubation with topical anesthesia in a spontaneously breathing patient may be preferable, though coughing and hypoxemia will also worsen the patient's condition. The best option in a truly unstable patient may be subxiphoid pericardiocentesis under local anesthesia only. Drainage of as little as 100 mL of fluid may improve hemodynamics sufficiently to permit conversion to general anesthesia and invasive line placement. An intubated postsurgical patient in shock may require immediate reopening of the chest for hematoma evacuation at the ICU bedside.

Diseases of The Thoracic Aorta

Surgical conditions of the thoracic aorta are manifold and consist of aortic aneurysms, aortic occlusive disease, developmental abnormalities (such as coarctation and vascular rings), and acute aortic syndromes. The latter category includes aortic dissections, traumatic aortic transections, intramural hematomas, and penetrating atherosclerotic ulcerations.

Aortic Dissection

An aortic dissection occurs when blood leaves the normal lumen through an intimal tear and penetrates the aortic wall. The blood separates the layers of the aortic wall, usually

between the intima and media, to produce a dissecting hematoma. High, sustained intraluminal pressure generates hydraulic stresses that can extend the dissection flap in an antegrade or retrograde direction, producing a false lumen of variable length along the aortic wall. Intimal tears leading to acute dissection most often occur in the ascending aorta, apparently in relation to the high mechanical shear forces present there. However, a small proportion of patients with dissection on autopsy have no discernible intimal tear. In these cases, it has been hypothesized that rupture of the vasa vasorum in the aortic wall caused the formation of a medial hematoma that subsequently ruptures into the intimal layer.

The most common and consistent inciting factor in aortic dissection is systemic hypertension, particularly in elderly patients. Hypertension accelerates degenerative changes in the aorta, predisposing the patient to the development and propagation of intramural hematomas. Cystic medial necrosis is a primary degenerative process that commonly occurs in various hereditary connective tissue disorders, such as Marfan syndrome and Ehlers–Danlos syndrome. Patients with these conditions are at risk of developing aortic aneurysms and acute dissections early in life. Younger patients can also develop aortic dissection in association with a congenitally bicuspid aortic valve, congenital aortic stenosis, or coarctation of the aorta. Pregnancy increases blood volume, cardiac output, and blood pressure, increasing the risk of aortic dissection. Dissection can also occur as an iatrogenic complication from aortic cannulation for CPB, coronary angiography, transcatheter procedures, or IABP insertion.

Left untreated, an aortic dissection flap can extend to four locations of immediate concern:

1. The aortic root and valve. This causes valvular incompetence and sudden, severe aortic insufficiency. The sudden volume overload of the left ventricle leads to severe left heart failure and pulmonary edema. Even localized dissection of the aortic root can alter the suspensory support of the aortic valve annulus and cause aortic insufficiency.
2. The coronary arteries. The right coronary ostium is more commonly affected than the left. The aortic dissection flap can occlude the ostium or propagate into the coronary artery itself, causing acute myocardial ischemia.
3. The pericardium or pleura. This produces cardiac tamponade or hemothorax, respectively.
4. The carotid or subclavian arteries. This can lead to acute neurological ischemia, stroke, or upper extremity ischemia. In addition, obstruction of arterial branches to the spine can produce paraplegia.

The most common presenting symptom of aortic dissection is sudden, severe pain. The pain is frequently described as tearing or stabbing, may migrate as the dissection flap propagates, and is greatest in magnitude at the time of inception (in contrast to pain from myocardial infarction). However, acute dissection is painless in approximately 20 % of patients, and up to half of patients die before a correct diagnosis is made, so a high index of clinical suspicion is warranted. Neurohumoral responses to the intense pain can manifest as pallor, sweating, nausea, and vomiting. Even in the setting of hypertension, patients may appear to be in shock.

Aortic dissections are generally classified by either the DeBakey or Stanford system (Fig. 26.10). The DeBakey classification system categorizes the dissection based on the site of the original intimal tear and the extent of the dissection flap. Both DeBakey type I and II dissections originate from an intimal tear in the ascending aorta, with DeBakey type I dissections involving the distal arch and descending aorta, while DeBakey type II dissections remain confined to the ascending aorta proximal to the innominate artery. DeBakey type III dissections originate from an intimal tear in the descending aorta and typically propagate distally (Table 26.12).

The Stanford classification identifies whether the dissection involves the ascending aorta (Stanford A) or does not (Stanford B), regardless of the origin of the intimal tear. The Stanford classification is more commonly used in modern practice, as it is simpler and more closely mirrors the surgical decision-making process. Type A dissections generally require primary, typically emergent, surgical repair due to the risk of further propagation of the dissection flap under the high shear forces of the ascending aorta. On the other hand, type B dissections are primarily treated medically, possibly in anticipation of either open or endovascular graft repair. Primary surgical repair of type B dissections is typically avoided except in cases of leakage, rupture, severe pain, or compromised end-organ perfusion (e.g., kidneys or mesentery). Further categorization of acute type B dissections has been proposed in order to guide medical therapy and identify those patients at higher risk of mortality, though further clinical validation is still needed.

The most common types of dissection are the DeBakey Types I and II and the Stanford Type A. Regardless of the need for acute surgical intervention, early and aggressive control of blood pressure is mandatory. Blood pressure is reduced to a target SBP of 100–120 mmHg or MAP of 60–80 mmHg, and heart rate is maintained between 60 and 80 beats/min. The left radial artery or femoral artery is used for arterial blood pressure monitoring as clamping of the innominate artery may be required during the surgery. It is just as important to control tachycardia in order to reduce cardiac ejection velocity, a critical determinant of the rate of rise in aortic pressure and intraluminal shear forces. Nitroprusside infusion alone can actually increase heart rate and ejection velocity. Therefore, intravenous arterial vasodilators, such as nicardipine or nitroprusside, should be combined with β-blockade. Esmolol is a suitable choice for infusion, as it has a very short duration of action and is therefore eminently titratable. Bradycardia, however, should be avoided if aortic insufficiency is present.

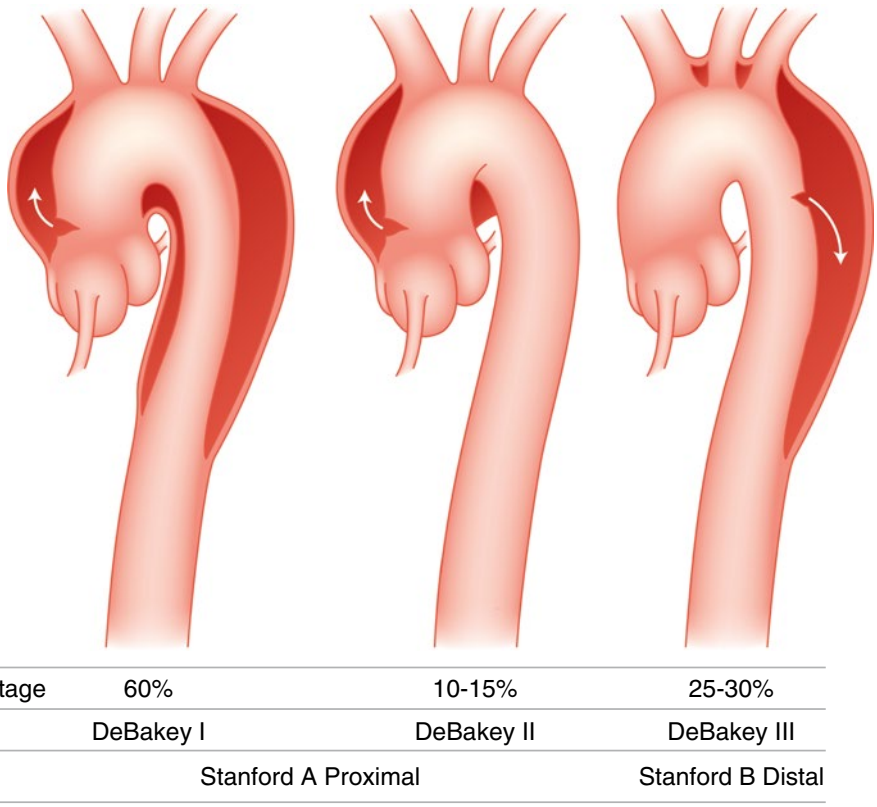

Fig. 26.10 Classification of aortic dissection

Table 26.12 Classification system for aortic dissection

DeBakey classification	
Type I	Originates in ascending aorta, propagates at least to the aortic arch and often beyond it, most common in patients <65 years of age, most lethal
Type II	Originates in and is confined to the ascending aorta
Type III	Originates in descending aorta, rarely extends proximally but will extend distally, most common in elderly patients with atherosclerosis and hypertension
Stanford classification	
Type A	Involves the ascending aorta and/or aortic arch, and possibly the descending aorta, it includes DeBakey types I and II
Type B	Involves the descending aorta or the arch (distal to the left subclavian artery), no involvement of the ascending aorta, it includes DeBakey type III

Thoracic Aortic Aneurysms

An aortic aneurysm involves the pathologic dilation of all three layers (intima, media, and adventitia) of the aortic wall. Thoracic aortic aneurysms are less common than those of the abdominal aorta. Aneurysms most commonly result from either atherosclerotic disease or cystic medial necrosis. Ascending aortic aneurysms are also commonly associated with congenital bicuspid aortic valves, chronic aortic dissection, systemic vasculitis, rheumatoid arthritis, syphilis, and primary bacterial infection (mycotic aneurysms). Pseudoaneurysms, dilated areas that do not involve all three layers of the aortic wall, can occur in areas of aortic trauma, infection, cannulation, or suturing. Systemic hypertension enhances aneurysm formation.

About 40 % of patients who present with thoracic aortic aneurysms are asymptomatic and are discovered as incidental findings. Symptoms arise from the cardiovascular consequences of aortic insufficiency or coronary artery impingement, thromboembolic manifestations of nonlaminar blood flow, or local mass effects from the expanding aneurysm. Chest and back pain can be caused by impingement on other intrathoracic structures. Compression of the superior vena cava can impair venous return and cause venous congestion in the head and neck. Aortic arch and descending thoracic aneurysms can compress or deviate

the trachea or left mainstem bronchus, producing dyspnea, wheezing, and hemoptysis that can be worse in the supine position. Recurrent laryngeal nerve compression can cause hoarseness.

The major risk of aortic aneurysms is rupture, leading to rapid exsanguination, cardiovascular collapse, and death. A sudden increase in pain may be a harbinger of acute expansion and impending rupture. The risk of rupture increases with aneurysm size. Asymptomatic aneurysms greater than 6 cm in diameter, and those expanding at a rate greater than 1 cm/year are generally repaired on an elective basis. Symptomatic ascending aortic aneurysms and those associated with severe or symptomatic aortic insufficiency require urgent surgery. Aortic rupture and contained leak are surgical emergencies.

Anesthetic Considerations

The primary goal of surgery for an aortic dissection, aneurysm, or rupture is to control hemorrhage. Once surgical control is achieved, the diseased aorta is repaired, and blood flow to major arterial branches is restored. Surgical treatment consists of removing and replacing the diseased portions of the ascending aorta and arch with an artificial graft. If necessary, the aortic valve is resuspended or replaced, the coronary arteries are reimplanted into the aortic root, and major arterial branches are reanastomosed to the prosthetic graft.

Continued control of blood pressure during the transition from preoperative to intraoperative management is essential. Patients undergoing emergency aortic surgery frequently have other cardiovascular and systemic diseases that may not have been fully evaluated in advance, such as CAD, cerebrovascular disease, COPD, diabetes, and renal impairment. Anesthetic induction and maintenance should be chosen with the goal of maintaining a stable blood pressure and minimizing the adverse effects of any acute valvular disorders or myocardial ischemia. The likely presence of a full stomach should be considered when planning airway management for emergency aortic repair.

Placement of arterial lines should take into account the planned location of the aortic crossclamp and arterial cannulation. Obstruction of blood flow to the subclavian or innominate arteries during aortic arch repair can render radial and brachial arterial lines unusable. Surgery on the ascending aorta and aortic arch often requires femoral arterial cannulation for bypass. Dilation of the ascending aorta or arch can place the aorta in close proximity to the sternum, increasing the risk of traumatic injury and massive hemorrhage during sternotomy. In some cases, the femoral artery and vein are cannulated and partial CPB initiated prior to sternotomy.

Anesthetic management of thoracic aortic surgery shares many features with that of cardiac surgery. However, thoracic aortic operations are associated with longer crossclamp times and prolonged periods of hypothermia, both of which contribute to large intraoperative blood losses. Operations on the aortic arch require temporarily occluding blood flow to the cerebral circulation and are performed using deep hypothermic circulatory arrest (DHCA). The patient is cooled to 15–18 °C, severely reducing cerebral metabolic oxygen consumption during the period that circulation is stopped. Stopping the CPB pump and partially draining the patient's blood volume provides a bloodless field to maximize surgical exposure. Intraoperative electroencephalography (EEG), cerebral oximetry, and other monitors are often used to assess adequacy of cerebral protection and recovery. Retrograde cerebral perfusion (RCP) via the superior vena cava can provide oxygen and energy substrates to brain tissue and evacuate air emboli from cerebral vessels, potentially reducing postoperative morbidity while allowing for prolonged periods of circulatory arrest in complex arch reconstructions. There is little evidence to support the efficacy of various medications often employed intraoperatively as neuroprotective agents, such as barbiturates, propofol, corticosteroids, mannitol, and phenytoin. Minimizing the duration of arrest appears to have the greatest influence on postoperative neurological recovery.

Cardiovascular Trauma

Cardiac injury is a relatively common occurrence in thoracic trauma. Although traumatic injuries are classically divided into blunt and penetrating, the clinical sequelae of blunt and penetrating cardiac trauma frequently overlap, and such patients are often managed similarly. Cardiac trauma is also frequently associated with injury to other organs, often requiring patients to undergo emergency noncardiac surgery prior to addressing their cardiac injuries.

The most common type of cardiovascular trauma is blunt aortic injury, most commonly resulting from rapid deceleration, as in a motor vehicle accident. Under such severe traction, the aorta most commonly ruptures just distal to the left subclavian artery at the aortic isthmus. At this location, the aorta is anchored by the ligamentum arteriosum (the remnant of the fetal ductus arteriosus), the left mainstem bronchus, and the intercostal arteries. However, aortic rupture can occur anywhere along the length of the thoracic aorta. Complete transection of the aorta usually results in death at the scene of the accident from rapid exsanguination. Even in patients with incomplete or contained transection who arrive at the hospital alive, mortality prior to surgical repair approaches 50 %.

Computed tomography angiography (CTA) is the favored diagnostic modality for aortic injury, with sensitivity and specificity approaching 100 %. CTA is also convenient in patients with multiple traumatic injuries who already undergo generalized CT scanning. TEE has similar sensitivity and specificity at detecting injury at the aortic isthmus and can detect concomitant cardiac injury; however, the air interface from the left mainstem bronchus obstructs much of the ascending aorta, the aortic arch, and great vessels. Furthermore, TEE is heavily operator dependent, requires sedation in the awake patient, and may be unsuitable in patients with esophageal or craniofacial trauma.

Traditionally, blunt aortic injury to the aortic isthmus has been repaired via open left thoracotomy, an extensive operation involving single-lung ventilation, aortic crossclamp, possibly partial left heart bypass (and associated anticoagulation), and significant blood loss. More recently, thoracic endovascular aortic repair (TEVAR) has been successfully performed for blunt aortic injury and is associated with significantly reduced bleeding, neurological injury, morbidity, and mortality.

Blunt trauma can also cause rupture of the pericardium, myocardium, or valves. Myocardial contusion, the most common anatomic result of blunt cardiac trauma, is difficult to diagnose in the immediate posttraumatic period but can lead over time to arrhythmias. An abnormal EKG upon admission correlates with the development of further cardiac complications and can suggest the need for further diagnostic testing. Serum cardiac enzyme levels can help diagnose cardiac contusions, but their ability to predict further cardiac complications is less clear, and their utility is severely diminished in the presence of massive noncardiac muscle injury. TEE is useful for detecting the decreased regional wall motion associated with contusions, as well as focal intramural echolucencies indicative of myocardial hematoma.

A specific type of blunt cardiac trauma, *commotio cordis* ("agitation of the heart"), can occur in the absence of cardiac contusion or preexisting cardiac disease. Blunt impact to the anterior chest wall (as can occur during a fall, brawl, or contact sports) within an electrically vulnerable phase during ventricular repolarization can precipitate a ventricular arrhythmia and sudden death. Increased public awareness of sudden cardiac death, plus the more widespread availability of automated external defibrillators and CPR training, appears to have increased survival.

Penetrating trauma most commonly injures the right ventricle, which is relatively large and positioned most anteriorly in the chest cavity. The right-sided chambers are more likely to be ruptured in trauma than their corresponding left-sided chambers. However, penetrating injuries can affect any cardiac structures, and multiple chambers are often affected. Unlike atrial tears, the thicker ventricular myocardium will sometimes close small puncture wounds spontaneously, sometimes leading to retained foreign bodies (e.g., bullets or shrapnel). The presence of an intracardiac foreign body may pose a significant psychological burden to the patient, but unless the object presents an embolic risk or threatens nearby structures, it is not necessarily removed.

Hemopericardium with resultant tamponade is the most common initial finding in penetrating cardiac injuries. However, gunshot wounds tend to create larger defects and more primary bleeding than tamponade. The classic signs of pericardial tamponade (pulsus paradoxus, jugular venous distension, Kussmaul's signs, muffled heart sounds, and widened cardiac silhouette on chest radiograph) are often absent in trauma because of severe concomitant hypovolemia. Rarely, pericardial disruption can lead to herniation and strangulation of the left atrial appendage or, in extreme cases, the entire heart.

Acute valvular abnormalities can occur after blunt or penetrating trauma. Acute severe aortic insufficiency is the least well tolerated, as the left ventricle must eject its stroke volume while exposed to high aortic systolic pressure, thus massively increasing left ventricular wall tension and myocardial oxygen demand. In acute mitral insufficiency, on the other hand, the left ventricle is partly decompressed by ejecting the regurgitant volume during systole into the left atrium. Acute mitral insufficiency rapidly leads to increased pulmonary edema and pulmonary hypertension. In contrast, acute tricuspid insufficiency is relatively well tolerated, possibly because less force (and therefore less myocardial injury) is needed to disrupt the more anteriorly located tricuspid valve.

Coronary arteries can also be injured in blunt or penetrating trauma. Coronary artery injury can lead to distal ischemia from hypoperfusion, dissection, fistula formation, or hemopericardium and tamponade. Fistulas most commonly affect the left anterior descending artery or the first diagonal branch, and can be arteriovenous or arteriocameral (into a chamber, most commonly the right atrium and right ventricle).

Cardiac Transplantation

Cardiac transplantation is performed as a treatment for patients with end-stage heart failure, most commonly resulting from ischemic cardiomyopathy or idiopathic dilated cardiomyopathy. Less common reasons for transplantation include other cardiomyopathies (viral, infiltrative, or postpartum) and complex congenital heart disease. About 2,000 heart transplantation procedures are performed in the United States each year.

Although heart transplant candidates typically undergo a thorough evaluation and ongoing management by a specialized heart failure team, the transplant operation itself occurs under emergent circumstances depending on donor organ

availability. The need to minimize the donor organ ischemic period limits the time available for the preoperative anesthetic evaluation, as prolonged donor organ ischemia is associated with poorer outcomes. Ideally, anesthetic preparation and induction are timed so that CPB can be started immediately upon arrival of the donor heart. Donor hearts from patients with hepatitis B or C and HIV are excluded for transplantation.

Preoperative Issues

Preoperatively, measurement of pulmonary vascular resistance (PVR) is important. A heart transplanted into a patient with a high PVR may lead to right ventricular failure. High PVR is treated with pulmonary vasodilators, and patients who show improvement in PVR may safely undergo the transplantation.

Chronic systemic hypoperfusion and venous congestion in the setting of end-stage heart failure can cause hepatic and renal dysfunction. Perioperative coagulopathy, electrolyte abnormalities, and azotemia from diuretic therapy may be present. If present preoperatively, any inotropic infusions, IABP, and ventricular assist device should be continued until CPB is started. Patients with chronic heart failure have elevated circulating catecholamine levels and become preload dependent, and even small doses of sedatives or other vasodilators can lead to rapid cardiovascular collapse. Slow circulation times commonly cause a delayed response to anesthetic agents. Reduced preoperative fasting time and preoperative administration of oral immunosuppressive agents increases the risk of aspiration during induction and airway management.

The New Heart

Anesthesia for cardiac transplant is managed similarly to other cardiac procedures (balanced anesthesia technique with small doses of fentanyl and etomidate for induction, muscle relaxant—pancuronium, invasive monitoring, TEE). Patients are placed on CPB for the surgery. Before the recipient's heart is removed, the central venous catheter or the pulmonary artery catheter is withdrawn into the internal jugular vein. The catheter may be refloated once the new heart is transplanted.

The cardiac autonomous plexus is transected during orthotopic transplantation, leaving the newly transplanted heart completely denervated. However, the ECG may still show two P waves, one from the recipient's SA node (but no effect on heart function), and the other from the donor's heart. Pharmacologic agents that act indirectly through autonomic stimulation of the heart (e.g., phenylephrine, atropine) are generally ineffective; direct-acting agents show unchanged or even increased activity. Infusion of a direct-acting chronotropic agent (e.g., isoproterenol, dobutamine, epinephrine) and epicardial pacing are often used immediately after aortic crossclamp removal to maintain an adequate heart rate; permanent pacemaker implantation may be required long term. Heart rate is not affected by opioids, cholinergics and anticholinergics, pancuronium, and meperidine.

Partial sympathetic activity begins to reestablish itself within a year of transplantation, but there is a lack of comparable parasympathetic activity. The result is a relatively high resting heart rate (90–110 beats/min) in the post-transplant patient, with no reflex heart rate response to systemic blood pressure changes or vagal maneuvers. Systemic hypertension frequently results from the neurohormonal activation associated with cardiac denervation and immunosuppression. Changes in cardiac output arise from increases in stroke volume rather than heart rate and are mediated via direct-acting catecholamines secreted by the adrenal glands. The transplanted patient may exhibit diminished or delayed responses to physiologic or surgical stress. Denervation of cardiac pain fibers also increases the likelihood of asymptomatic myocardial ischemia.

Complications

Right heart failure is a leading complication during and after heart transplantation and must be diagnosed and treated early to avoid severe morbidity or death. Causes of right heart dysfunction include preexisting pulmonary hypertension, pulmonary vasospasm, acute tricuspid or pulmonic insufficiency, and donor-recipient size mismatch. Depending on severity, right heart failure may be improved with avoidance of hypercarbia (hyperventilation), correction of electrolyte abnormalities, inotropic support, pulmonary vasodilation, or right ventricular assist device implantation. Other complications include cardiac arrhythmias, hypovolemia, left ventricular dysfunction, and anastomotic obstruction.

Postoperative Care

Patients are extubated usually in the ICU in the absence of hemodynamic instability and other complications. Cardiac transplant patients require lifelong immunosuppression and are at a higher risk of infection and renal toxicity. Immunosuppressive therapy can lead to atypical presentations of infection, without fever or leukocytosis. Furthermore, chronic corticosteroid therapy can cause adrenal suppression, thrombocytopenia, and soft tissue changes that can affect airway anatomy. Anesthesia personnel should adhere to strict aseptic technique throughout the transplant operation and any subsequent procedure on the transplant recipient, particularly when handling intravenous injection ports and infusion lines.

Clinical Review

1. Preload is closely represented by
   A. End-systolic volume
   B. End-diastolic volume
   C. Stroke volume
   D. Cardiac index
2. Coronary perfusion pressure is
   A. Diastolic BP – LVEnd systolic pressure
   B. Diastolic BP – LVEnd diastolic pressure
   C. Systolic BP – LVEnd systolic pressure
   D. Pulse pressure
3. The sinoatrial node is most commonly supplied by the
   A. Right coronary artery
   B. Left coronary artery
   C. Left circumflex artery
   D. Posterior descending artery
4. A 25-year-old man is brought to the trauma center after sustaining a gunshot wound to the chest. The patient has narrow pulse pressure, jugular venous distention, muffled heart sounds, and pulsus paradoxus. The most likely diagnosis is
   A. Cardiogenic shock
   B. Tension pneumothorax
   C. Cardiac tamponade
   D. Right ventricle perforation
5. A 58-year-old man underwent coronary artery bypass grafting. Initial output from the mediastinal chest tube was 350 ml/h. The drainage then appeared to stop, but the mean arterial pressure dropped to 40 mmHg, and the CVP increased to 18 mmHg. The most appropriate next step is
   A. Placement of intra-aortic balloon pump
   B. Administration of intravenous norepinephrine infusion
   C. Administration of packed red blood cells
   D. Surgical exploration of the mediastinum
6. The primary aim to insert an intra-aortic balloon pump is to
   A. Increase myocardial contractility
   B. Decrease afterload
   C. Increase coronary blood flow
   D. Increase preload
7. Anticoagulation in a patient with heparin-induced thrombocytopenia can be achieved by using
   A. Purified heparin
   B. Argatroban
   C. Enoxaparin
   D. Ticlopidine
8. Fall in the platelet count during cardiopulmonary bypass is most likely due to
   A. Hemolytic transfusion reaction
   B. Sequestration
   C. Dilutional thrombocytopenia
   D. Heparin-induced thrombocytopenia
9. The most sensitive indicator of left ventricular myocardial ischemia is
   A. ST-segment changes in lead V5 of the ECG
   B. Appearance of V waves on the pulmonary capillary wedge pressure tracing
   C. Sustained elevation of the pulmonary capillary wedge pressure
   D. Wall-motion abnormalities on the echocardiogram
10. Preferable anesthetic to use in a patient with hypertrophic cardiomyopathy scheduled for left ventricular myectomy under general anesthesia is
    A. Ketamine
    B. Isoflurane
    C. Halothane
    D. Fentanyl-N_2O

Answers: 1. B, 2. B, 3. A, 4. C, 5. D, 6. C, 7. B, 8. B, 9. D, 10. C

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Vascular Anesthesia

27

Joshua Hensley and Kathirvel Subramaniam

The seventeenth-century physician Thomas Sydenham said, "You are as old as your arteries." Vascular surgery involves surgery on vessels throughout the body, from the aorta and great vessels to the arteries and veins extending into the extremities. Vascular patients often carry with them multiple comorbidities, and they are frequently involved in high-risk procedures that can pose specific challenges to the anesthesiologist. The anesthesiologist plays a critical role in the care of vascular patients, and it is important to understand the challenges and techniques needed for their proper care before, during, and after any surgical intervention.

Preoperative Evaluation

A thorough review of the central nervous system is essential for vascular patients. Patients should be asked about previous transient ischemic attacks/cerebrovascular accidents, seizures, syncope, existing neurologic deficits, and any neurologic workup they have undergone. Neurologic deficits should be assessed and documented.

As vascular disease affects the entire body, a complete cardiovascular evaluation is warranted. Pertinent morbidities include hypertension, coronary artery disease, congestive heart failure, valvular heart disease, and arrhythmias. In a detailed history of medical therapy (including beta-blockers), recent changes in symptoms and interventions for each disease process should be ascertained. All recent cardiac testing such as EKG, echocardiography, stress testing, and cardiac catheterization should be reviewed. Further cardiac testing can be guided by ACC/AHA Guidelines (chapter on preoperative evaluation).

Chronic obstructive pulmonary disease (COPD) is common among patients with vascular disease, the most common cause being smoking. Medication regimen, oxygen requirements, recent respiratory tract infections, and hospitalizations for exacerbations are pertinent questions during the interview. Pulmonary studies such as chest X-ray, CT scan, and PFTs should be reviewed.

Many patients with vascular disease will have some form of renal dysfunction. It is important to assess the degree of dysfunction and volume status preoperatively and if there have been any recent changes. Dialysis regimens should be reviewed to optimize the patient's volume and electrolyte status. Diabetes is a common risk factor for the development of vascular disease. Diabetic patients should be asked about their medication regimen and the last administered dose.

Recent hemoglobin, hematocrit, platelet count, and coagulation profile should be performed prior to surgery. Patients may have genetic bleeding disorders, be on oral anticoagulant medications, or have disease processes that make them more susceptible to bleeding. Blood product availability should be addressed (type and screen/cross) prior to surgery.

Abdominal Aortic Aneurysm

Arterial aneurysm is a progressive dilation of all three layers of the aorta, by at least 50 % of the expected diameter (usually greater than 3 cm). Common etiologies include atherosclerosis (usually descending aorta) and medial necrosis (usually ascending aorta); other reasons are traumatic, genetic and infectious (pseudo aneurysms). All these factors contribute to inflammation and plaque formation, which causes dilation of the arterial wall (Fig. 27.1). Loss of elastin and increased serum elastase activity have been found in many patients with aortic aneurysms.

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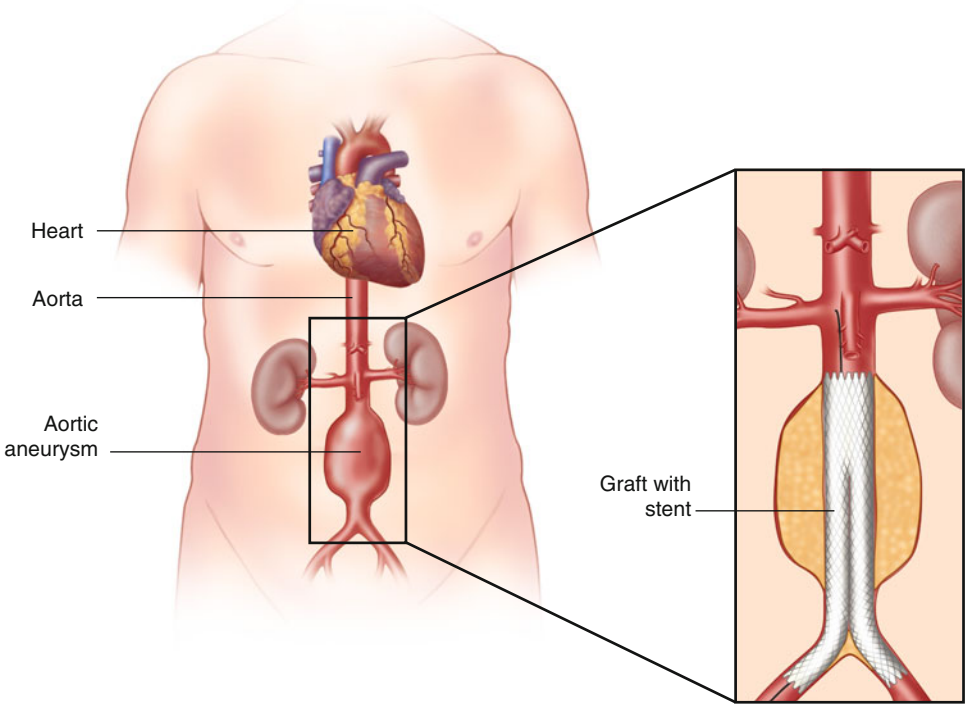

Fig. 27.1 Abdominal aortic aneurysm and insert showing a graft repair

Most abdominal aortic aneurysms (AAA) are silent clinically and are discovered incidentally during physical examination. Symptoms, if present, may include back, abdominal, or flank pain. Ultrasound and CT scans are commonly used for evaluation of AAA. Rupture of aortic aneurysms is associated with mortality rates >70 %. Therefore, aneurysms that are 3–5 cm should be closely monitored. The risk of rupture is directly related to the size of the aneurysm, rapid expansion, and female gender.

Surgery is indicated for aneurysms >5 cm, development of neurologic deficits, and involvement of the aortic valve and coronary arteries (ischemia). The abdominal aorta is approached through a median laparotomy with the patient in the supine position (transperitoneal approach), or via a retroperitoneal approach (right lateral decubitus, left side up), which is used mainly for suprarenal aneurysms. For high-risk patients, endovascular repair may be undertaken. In future, laparoscopic AAA repair appears to be a promising technique.

Anesthetic Management

Standard ASA monitors are applied for surgery on the aorta. EKG should monitor leads II and V5 (for ischemia). A Foley catheter is routinely placed to monitor urine output. Arterial catheters are placed in all patients. These allow for rapid assessment of blood pressure, management with appropriate medication/interventions (cross clamping), and frequent laboratory analysis. Placement sites should be coordinated with the surgeon according to his/her approach/technique. Dynamic variation in the arterial wave form with positive pressure ventilation may be observed as an indicator of volume status.

Venous access should include at least one large-bore peripheral IV and central venous access (CVP or PA catheter, more commonly a triple lumen catheter). This allows for infusion of vasoactive/ionotropic medications, resuscitative fluids/blood products, and measurement of central venous pressure. Transesophageal echocardiography may be used to monitor cardiac function, guide fluid management, and detect myocardial ischemia and for anatomical assessments on the aorta, heart, and lungs. Cerebrospinal fluid drains are usually reserved for surgery on the thoracic aorta. Somatosensory evoked potentials and motor evoked potentials have been used during surgery on the aorta to detect spinal cord ischemia.

General anesthesia is required for surgery on the aorta. An epidural is commonly placed preoperatively, but is usually used for analgesia after the aortic cross clamp is removed and the patient is stabilized. The goal of anesthetic induction is to avoid wide variations in blood pressure and heart rate. During induction, blood pressure may drop significantly secondary to hypovolemia and limited cardiac reserve. However, with intubation, heart rate and blood pressure may increase. Therefore, induction medications should be tailored to avoid hemodynamic instability. Patients with ruptured AAA may be severely hypovolemic, and therefore, profound hypotension may occur with induction of anesthesia. Induction should occur with the abdomen prepped, the

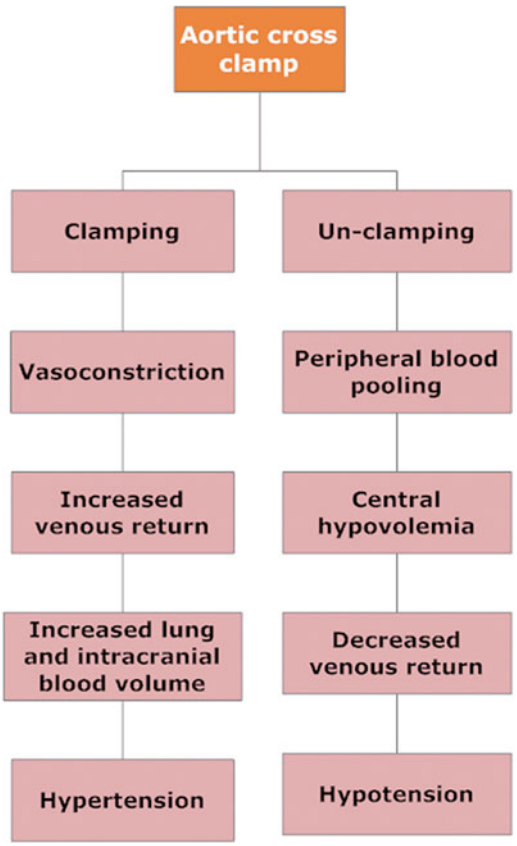

Fig. 27.2 Physiologic effects of aortic cross clamping and unclamping

drapes placed, and the surgeon ready to enter the abdomen to gain control of the aorta and raise the blood pressure.

Most surgical approaches can be facilitated by using a single-lumen endotracheal tube. A double-lumen tube or endobronchial blocker may be used for surgery on the thoracic aorta to improve surgical exposure. Anesthesia is usually maintained by using volatile anesthetic agents, muscle relaxants, and narcotics.

Cross Clamping of the Aorta

Cross clamping of the aorta causes an immediate increase in systemic vascular resistance (vasoconstriction) and afterload and also venous return and mean arterial pressure (Fig. 27.2). This response is directly proportional to the level of aortic clamping with infrarenal<suprarenal<thoracic. These changes are mediated by an impedance to blood flow and increased circulating catecholamines. Vasodilating drugs (volatile inhalational agent, nitroglycerin, nitroprusside) may be used to counteract this response and decrease the afterload strain placed on the heart. Monitoring of cardiac function and hemodynamics is critical during this portion of the surgery. It should be remembered that any vasodilating drugs used to treat proximal hypertension will exacerbate hypotension and ischemia distal to the aortic clamp.

Unclamping is associated with hypotension secondary to decreased systemic vascular resistance and venous return (peripheral shift of blood volume), washout of ischemic metabolites, and vasoplegia. Treatment options include fluid loading prior to unclamping, vasoactive/ionotropic medications (phenylephrine), and gradual release of the cross clamp.

Postoperative Management

Postoperatively, patients are admitted in the intensive care unit. Patients who are hemodynamically stable may be extubated in the operating room. Epidural analgesia is initiated for pain control and helps to decrease requirements for intravenous opioids, improve lung function, and decrease the duration of postoperative ileus. For additional pain control, intravenous narcotics and nonsteroidal anti-inflammatory drugs should be used as needed.

Symptoms and signs of myocardial ischemia (adequate beta-blocker therapy), renal function, bleeding, mesenteric or bowel ischemia (blood in stool), or neurologic impairment should be followed closely. Bleeding is major concern during aortic surgery. Anatomic sources include acute rupture, leaking anastomotic sites, or perforation of surrounding organs or vasculature. Constant observation of the field and communication with the surgeon are critical aspects of management. Other sources of bleeding include hypothermia, dilution of coagulation factors, disseminated intravascular coagulation, inadequate anticoagulant reversal, and platelet dysfunction.

Postoperative renal failure, which is more common in patients with preexisting renal disease, is a major complication following aortic surgery and may be the strongest predictor of mortality. Renal failure is more common with suprarenal than infrarenal aortic clamping. Pharmacologic interventions to prevent renal failure include the administration of mannitol (0.5 g/kg) or furosemide (prior to cross clamping), and fenoldopam or low-dose dopamine (after release of cross clamp). None, however, have been shown to decrease the risk of renal failure. Other interventions include limiting cross clamp time, mild hypothermia (infusion of 4 °C Ringer lactate), and adequate hydration and maintaining adequate perfusion pressure (avoid hypotension).

Paraplegia secondary to spinal cord ischemia is a major concern after thoracic aortic repair. Long cross clamping times associated with interruption of blood flow or hypoperfusion from the anterior spinal artery leads to spinal cord ischemia. There is loss of motor and pin-prick sensation, but preservation of vibration and proprioception. Spinal cord ischemia may be prevented by monitoring somatosensory and motor evoked potentials. Methods to decrease the incidence of paraplegia are extracorporeal circulation, use of heparin-coated shunts, placement of CSF lumbar drain, administration of methylprednisolone and mannitol, mild hypothermia, and decreased cross clamping time.

Endovascular Aortic Repair

Endovascular stent grafting is an alternative to open aortic repair. With the development of new graft material and technology, almost any portion of the aorta can be stented. The aorta is typically accessed through a femoral or iliac artery. Under fluoroscopy, the diseased portion of the aorta is identified, surround vascular branches are mapped, and the graft deployed. Once in place, the graft is assessed for leak or rupture. As compared to open aortic repair, endovascular aortic repair is associated with decreased blood loss, fluid shifts, and cardiac, renal, and pulmonary morbidity. It also decreases the length of ICU and hospital stay. Although short-term outcome may be improved, on 1-year follow-up, there is no significant difference in outcomes.

Other than standard ASA monitors, a large-bore intravenous line, and an arterial catheter, is usually placed for continuous measurement of blood pressure and laboratory analysis. General, regional (spinal, epidural, or combined), or local anesthesia can be used for endovascular aortic repair. The choice usually depends on the patient, surgeon, or anesthesiologist. Vasoactive medications and blood products should be readily available. Complications of endovascular aortic repair are listed in Table 27.1. In the event of difficulty with repair, preparation and planning must be made for possible conversion to open aortic repair.

Table 27.1 Complications of endovascular aortic repair

Complication	Etiology
Renal failure	Contrast dye or occlusion of renal artery by graft
Mesenteric ischemia	Occlusion of mesenteric arteries
Paraplegia	Occlusion of artery of Adamkiewicz
Endoleak-leak around graft in aneurysmal sac	Inadequate seal, backflow, defective fabric
Aortic rupture	Surgical manipulation

Carotid Artery Stenosis

The carotid arteries supply blood flow to the anterior circulation of the brain, while the vertebral arteries supply blood flow to the posterior circulation of the brain. These two circulations communicate at the Circle of Willis via the posterior communicating arteries. The Circle of Willis functions as a source of collateral blood flow in the event of occlusion of one of its contributing branches.

Carotid stenosis results from progressive build-up of plaque in the wall of the carotid artery, the most common site being the origin of the internal carotid artery (Fig. 27.3). The deleterious nature of atheromatous plaque in the carotid artery is twofold. Firstly, progressive narrowing of the lumen restricts blood flow through the artery. Secondly, this area is a potential source for thromboembolism to the brain.

Symptoms of carotid stenosis may manifest as an asymptomatic bruit, transient ischemic attack (TIA), or a stroke. A neurological deficit persisting for more than 24 h is defined as a stroke, whereas a deficit resolving within 24 h is defined as TIA. Patients may present with contralateral muscle weakness, paresthesias, aphasia, and dysarthria. Amaurosis fugax or transient monocular blindness can also be a presenting symptom, which is caused by embolic obstruction of the ophthalmic artery.

Carotid endarterectomy is usually indicated in patients with more than 70 % occlusion. Symptomatic patients with 30–70 % occlusion are also candidates for surgery. While most patients are elderly, the presence of angina and uncontrolled hypertension increases the risk of surgery. Patients should continue taking their medications until the day of surgery (except diuretics and antidiabetic medications in the morning of the surgery). Myocardial infarction is the most common cause of mortality, whereas neurological deficit (stroke) is the most common cause of morbidity.

Anesthetic Management

Regional Anesthesia

Regional anesthesia involves performing superficial and deep cervical plexus block (C2–C4). Local infiltration of the

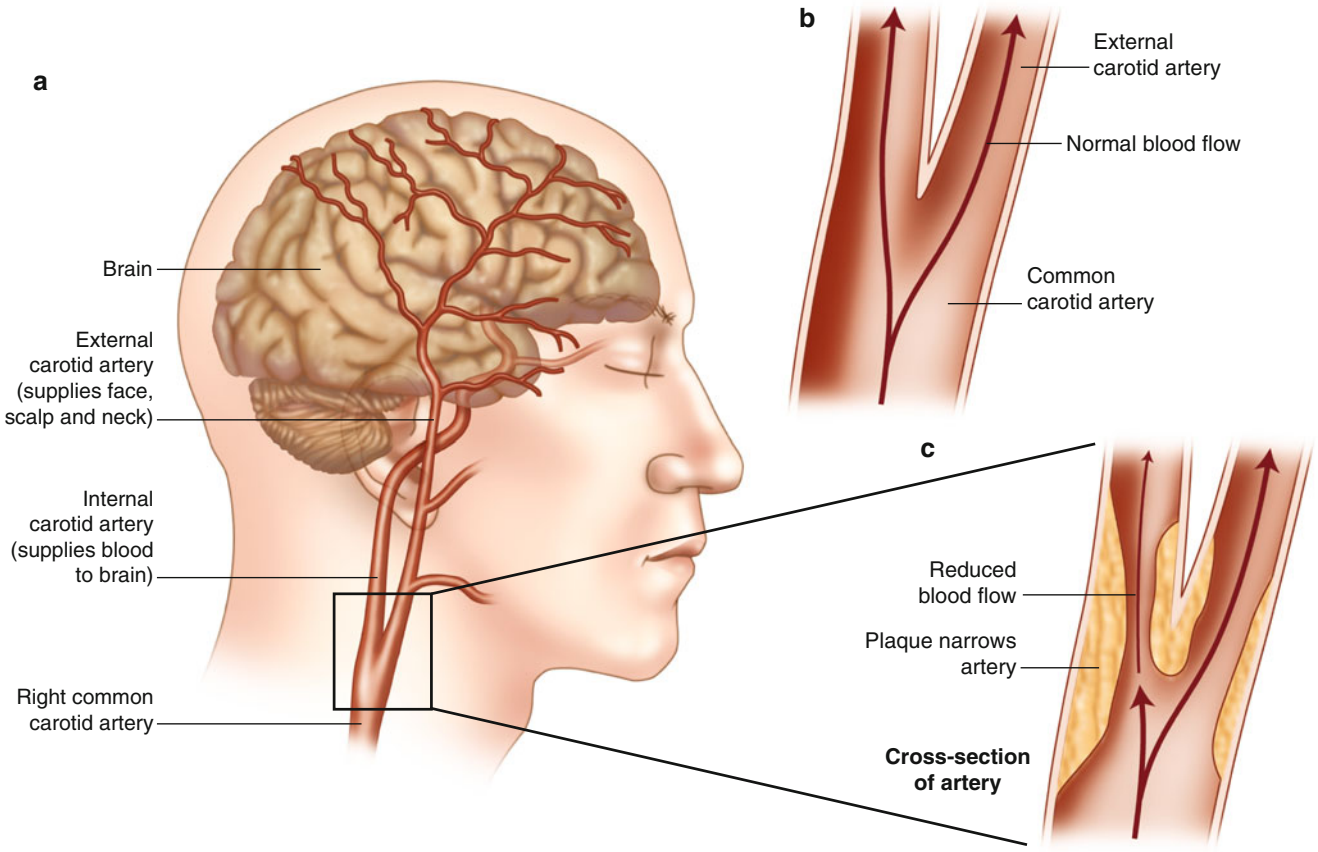

Fig. 27.3 (**a**) Carotid arteries supplying blood to the brain, (**b**) normal carotid arteries, (**c**) plaque formation at the origin of internal carotid artery

surgical field with lidocaine by the surgeon may also be performed. Advantages of regional anesthesia are (1) neurologic examination of an awake patient (speech, contralateral hand grip, level of consciousness) and (2) the avoidance endotracheal intubation and consequent hemodynamic changes. Disadvantages of regional anesthesia include (1) a non-secured airway that may be difficult to manage during surgery, (2) complications of regional anesthesia (intrathecal spread or phrenic nerve involvement), and (3) an uncooperative patient (the patient may become combative if neurologic deficits arise).

General Anesthesia

General anesthesia entails intravenous induction and placement of an airway device, an endotracheal tube, or LMA. The advantages of general anesthesia are the (1) presence of a secured airway and (2) avoidance of an anxious or combative patient in the event of neurologic changes. Disadvantages of general anesthesia include (1) hemodynamic changes encountered during endotracheal intubation and surgery and (2) relying on neurologic monitors to detect ischemia. A combination of general and regional anesthesia may be performed, which may reduce postoperative opiate requirement and increase patient satisfaction.

Standard ASA monitors are used for carotid artery surgery. The electrocardiogram should monitor leads II and V5, and ST segments to detect myocardial ischemia. One large peripheral IV should be adequate, as large fluid shifts and blood loss are not anticipated. Direct arterial catheterization is indicated as acute changes in blood pressure can be assessed and treated. Central venous access, pulmonary artery catheterization, and TEE may be used as necessary.

There are multiple modalities used for neurologic monitoring during CEA. Under regional anesthesia (minimal sedation), the patient can be frequently assessed for changes in mental status, speech, or motor function. Under general anesthesia, common monitors used to detect ischemia include electroencephalography (EEG), somatosensory evoked potential (SSEP), cerebral oximetry, and transcranial Doppler. It should be noted that these monitors are not without fault and their use does not reduce the risk of perioperative stroke.

The goal of anesthetic induction is to maintain hemodynamic stability, that is, to avoid tachycardia and excessive drop in mean arterial blood pressure, to help maintain adequate cerebral perfusion. Heart rate and blood pressure should be kept within 10 % of baseline. Abrupt changes that occur during induction or intubation should be treated

immediately to prevent deleterious effects on the heart and brain. General anesthesia is commonly induced with propofol, etomidate, or a combination of both the agents. For airway management, an endotracheal tube may be secured with the help of muscle relaxants (succinylcholine, vecuronium, or rocuronium).

Anesthesia is usually maintained with oxygen, a volatile anesthetic inhalational agent, and a short-acting opiate (fentanyl). Nitrous oxide may also be used to supplement maintenance of anesthesia. The use of nitrous oxide will decrease the requirements of volatile inhalational anesthetic agent; however, cerebral blood flow increases with its use. Normocapnia is maintained during surgery, as hypercapnia can cause intracerebral steal, where as hypocapnia decreases cerebral perfusion. It may be preferable to use glucose-free intravenous solutions for hydration because of the adverse effects of excessive glucose on the brain.

Neurologic Protection

For the awake patient under regional anesthesia, neurologic changes can occur during any portion of the surgery, but are most common during carotid artery cross clamping. The surgeon will request administration of intravenous heparin (5,000–7,500 units) before cross clamping. Neurologic changes should be managed by alerting the surgeon, providing adequate cerebral perfusion pressure by raising the blood pressure with vasoactive medications (phenylephrine) and/or by placement of a shunt by the surgeon. Distal stump pressure of less than 50 mmHg is usually an indication of shunt placement. It should be, however, noted that placement of shunt increases the risk of thromboembolic events. Pharmacologic cerebral protection with benzodiazepines and barbiturates (thiopental) has also been used during CEA. The benefit is thought to be derived from their coupled decrease of cerebral oxygen consumption and cerebral blood flow.

Cardiovascular Protection

Patients undergoing CEA are at increased risk for myocardial ischemia. Therefore, hypotension, hypertension, and tachycardia should be prevented. Hypotension is treated with an alpha agonist such as phenylephrine (decreases heart rate, 40–100 mcg bolus) or ephedrine (increases heart rate, 5–10 mg bolus). An intravenous infusion of phenylephrine may have to be started to maintain mean arterial blood pressure. Hypertension, which is more common after removal of the cross clamp and during emergence from anesthesia should be treated with short-acting vasodilators (nitroglycerin or nitroprusside), beta-blockers (esmolol or metoprolol), hydralazine, or a calcium channel blocker (nicardipine). In addition, traction on the carotid sinus may stimulate the baroreceptors causing hypotension and bradycardia. Treatment options include release of the traction, infiltration with local anesthetic (lidocaine) by the surgeon, and judicious use of medications such as atropine or glycopyrrolate.

Postoperative Management

Complications of CEA include neurological deficit, myocardial ischemia or infarction, persistent hypertension, hematoma formation and airway compromise, and recurrent laryngeal nerve and cranial nerve injury (facial, hypoglossal). Patients should be monitored closely for neurologic deficits postoperatively. New onset of deficits may herald a thromboembolic event or disruption at the surgical site. The surgeon should be made aware immediately so that quick interventions can be made. Hypertension is common following CEA secondary to ipsilateral baroreceptor dysfunction. Hypertension should be treated aggressively, as described above, to prevent hyperperfusion injury, bleeding, and hematoma formation, which may result in airway compromise.

Carotid Artery Stenting

An alternative to CEA is carotid angioplasty and/or stenting. This technique may be used for patients considered high risk for CEA. This procedure is performed in awake patients to allow constant neurologic examinations. Anesthesiologists are generally asked to provide sedation and maintain hemodynamic stability. These procedures may be performed at an off-site location such as a vascular suite in the radiology department.

In these procedures, access to the arterial circulation is gained through the femoral or radial artery. An endovascular catheter is passed under fluoroscopy to the area of carotid stenosis. At this point, the stenotic area is angioplastied and/or stented. Complications related to this procedure are microembolism, bradycardia and hypotension (secondary to carotid sinus baroreceptor stimulation), and arterial dissection. Filter devices have been developed, which are placed distal to the stenotic area in an attempt to decrease the incidence of microembolism. It should be mentioned that there is no difference in surgical outcomes between CEA and carotid stenting.

Anesthesia for Peripheral Vascular Disease

Peripheral vascular disease (PVD) results in an acute or chronic decrease in blood flow to the extremities causing ischemia (Fig. 27.4). Etiologies include atherosclerosis, embolism, and vasculitis. Risk factors include diabetes

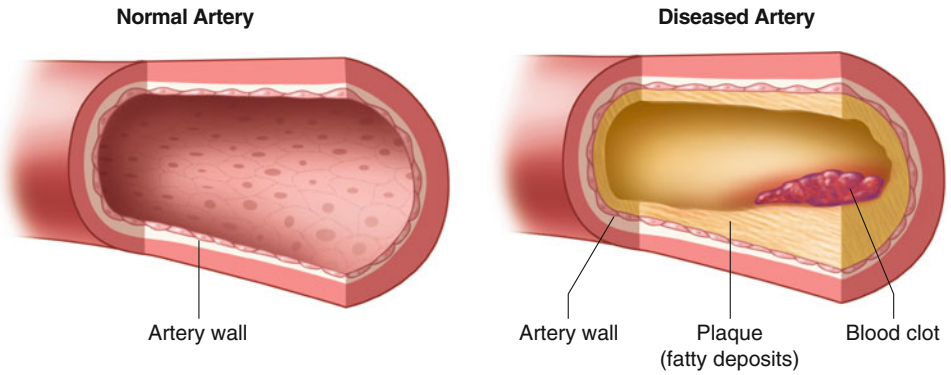

Fig. 27.4 Normal and diseased artery causing peripheral vascular disease

mellitus, hypertension, tobacco use, dyslipidemia, systemic vasculitis, and a family history. The signs and symptoms are claudication, pain, nonpalpable pulses, edema, cyanosis, atrophy, and hair loss.

Surgical technique consists of either an "open vascular repair" or an "endovascular repair." In open vascular repair, the diseased portion of the vasculature is exposed by surgical dissection. Blood flow proximal to lesion is interrupted by cross clamping. At this point, the lesion can either be bypassed by a graft or endarterectomy performed. Endovascular procedures begin by gaining access to the vascular system proximal or distal to the obstructive lesion. Under fluoroscopy, the clot may be retrieved or angioplasty (+/− stent) may be performed. Unsuccessful or complicated endovascular procedures may be converted to open procedures.

Anesthetic Management

Standard ASA monitors are used during all peripheral vascular procedures. Further monitoring may be quite extensive and resemble the setup for aortic procedures. The invasiveness of the procedure and patient comorbidities will determine monitor selection and placement.

Patients with PVD usually have multiple comorbidities of the cardiovascular system. EKG leads II and V should be monitored for myocardial ischemia. A favorable balance of myocardial oxygen supply and demand should be maintained during surgery. Hypertension and hypotension should be a treated with appropriate drugs and fluid administration.

Bleeding is always a concern during vascular surgery. Anatomic sources include the surgical site, leaking anastomotic sites, or perforation of surrounding structures. Endovascular procedures may be converted to open procedures if arterial dissection or perforation occurs. Patients taking anticoagulant medications prior to surgery and/or given anticoagulants such as heparin, perioperatively, may also contribute to increased bleeding. Therefore, routine testing of the coagulation status is essential (INR < 1.4).

Regional Anesthesia

Advantages of regional anesthesia include avoidance of hemodynamic changes associated with general anesthesia and endotracheal intubation, improved graft patency, decreased used of narcotics, and reduced incidence of respiratory and cardiovascular complications. However, regional anesthesia may not be appropriate for all patients. Patients who are hypercoagulable or cannot tolerate lying flat for long periods may not be candidates for regional anesthesia alone. For surgery, a single shot spinal anesthetic may be administered with bupivacaine, 1:200,000 epinephrine, and preservative-free morphine. Epidural anesthesia may also be performed, but usually is not necessary,

General Anesthesia

Advantages of general anesthesia include a secured airway and the elimination of patient tolerance as it concerns to positioning. Regional anesthesia can also be considered as an adjunct to general anesthesia. It should be noted that there is no difference in overall mortality between regional and general anesthesia for peripheral vascular surgery.

Neuraxial Anesthesia

This technique can provide excellent surgical anesthesia and postoperative analgesia. However, many vascular patients do not meet the criteria for neuraxial anesthesia secondary to anticoagulant medications and positioning tolerance. In addition, the tissues may be inflamed, for example, an ankle block may not be performed for toe amputation if the tissues are inflamed or gangrenous.

Postoperative Management

Pain can have multiple etiologies postoperatively. Surgical pain, compartment syndrome, or graft occlusion can all cause pain in the postoperative period. While graft occlusion and compartment syndrome must be treated surgically, surgical pain can be treated with regional and neuraxial

nerve blockade and opioids. NSAIDs are typically avoided secondary to increased risk of bleeding. Patients undergoing endovascular procedures are at an increased risk of acute renal injury secondary to contrast dye used during fluoroscopy. Volume status, electrolytes, kidney function, and urine output should be monitored in the postoperative period.

Clinical Review

1. The most common site of abdominal aortic aneurysm is
   A. Suprarenal
   B. Infrarenal
   C. Pararenal
   D. Aorto-iliac
2. Congestive heart failure during aortic surgery is more likely to occur with
   A. Aortic cross clamping
   B. Aortic cross un-clamping
   C. Induction of anesthesia
   D. Aortic graft placement
3. Most significant predictor of postoperative renal failure in patients undergoing AAA repair is
   A. Long aortic cross-clamping time
   B. Decreased renal perfusion pressure
   C. Large size aneurysm
   D. Existing preoperative renal dysfunction
4. All are true statements regarding carotid endarterectomy, EXCEPT
   A. The most common site of stenosis is the origin of internal carotid artery
   B. The most common cause of mortality is myocardial infarction
   C. Postoperative stroke can be prevented by using electroencephalography or somatosensory evoked potential monitoring
   D. Postoperatively, hypertension is more common than hypotension
5. True statement regarding anesthetic management of carotid endarterectomy is
   A. Blood pressure should be maintained within 10 % of baseline
   B. Hypotension is desirable to provide the surgeon with a bloodless field for surgery
   C. Surgery can be performed by performing an interscalene block
   D. The most common cause of mortality is stroke

Answers: 1. B, 2. A, 3. D, 4. C, 5. A

Further Reading

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Thoracic Anesthesia

28

Lundy Campbell and Jeffrey A. Katz

Thoracic anesthesia encompasses the care of patients undergoing thoracic surgery, as well as patients with diseases of the respiratory system undergoing non-thoracic surgical procedures. This chapter is written with the goal of helping the clinician deliver superb anesthetic care to both of these patient groups. To facilitate understanding this topic, selected concepts of basic respiratory physiology, as well as disease states encountered in patients with lung disease, will be discussed. Finally, the intraoperative management of patients undergoing thoracic surgical procedures will be covered.

Respiratory Anatomy and Physiology

Within the scope of thoracic anesthesia practice, patients with significant lung disease are often encountered, and many thoracic surgical procedures involve single-lung ventilation. Significant perturbations in patients' baseline respiratory function are frequently seen; therefore an understanding of basic respiratory physiology is important. Specifically, familiarity with oxygen and carbon dioxide transport and understanding shifts in the oxyhemoglobin dissociation curve, as well as the concepts of shunt and dead space, are essential knowledge for the thoracic anesthesiologist.

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Anatomy

The thorax or rib cage consists of two lungs, each surrounded by pleura. The right lung has three lobes, whereas the left lung as two lobes. Each lung lobe is divided into segments, 22 on the right and 20 on the left (total of 42). The diaphragm is the primary muscle of respiration, accounting for 75 % of the respiratory effort. Accessory muscles of respiration include the intercostal, sternocleidomastoid, scalene, and the pectoralis muscles. The pharyngeal muscles mainly maintain the patency of the upper airway. Inspiration is an active process, while expiration is usually passive and driven by elastic recoil of the lungs.

The upper airway consists of the nose, mouth, and the pharynx, and has the main functions of humidification and filtering of the air. The trachea begins at the level of C6 or the cricoid cartilage, and is about 11–13 cm in length in adults. At the level of T5, the trachea divides into the right- and left-main bronchus. The right-main bronchus diverges from the trachea at an angle of 25°, while the left-main bronchus diverges at 45°. The right-main bronchus is shorter but wider than the left (Figs. 28.1 and 28.2). The right upper lobe bronchial orifice is about 1–2.5 cm from the carina, while the left upper lobe bronchial orifice is 5 cm from the carina.

After the tracheal division into the right and left bronchus, there are subsequent divisions—total of 23 generations of divisions. The first 17 divisions carry gas but do not take part in gas exchange. Also, the respiratory mucosa gradually changes from ciliated columnar to cuboidal and finally to flat alveolar epithelium, where gas exchange takes place. Similarly, the airways gradually lose their cartilaginous support and finally their smooth muscle content.

Alveoli sacs begin to appear about the 17th generation/division. Each alveoli sac contains about 17 alveoli, which are thin walled and in close contact with the pulmonary capillaries. The alveoli are made up of Type I cells, which take part in gas exchange, and Type II cells, which produce surfactant. Type I cells form tight junctions preventing passage of large

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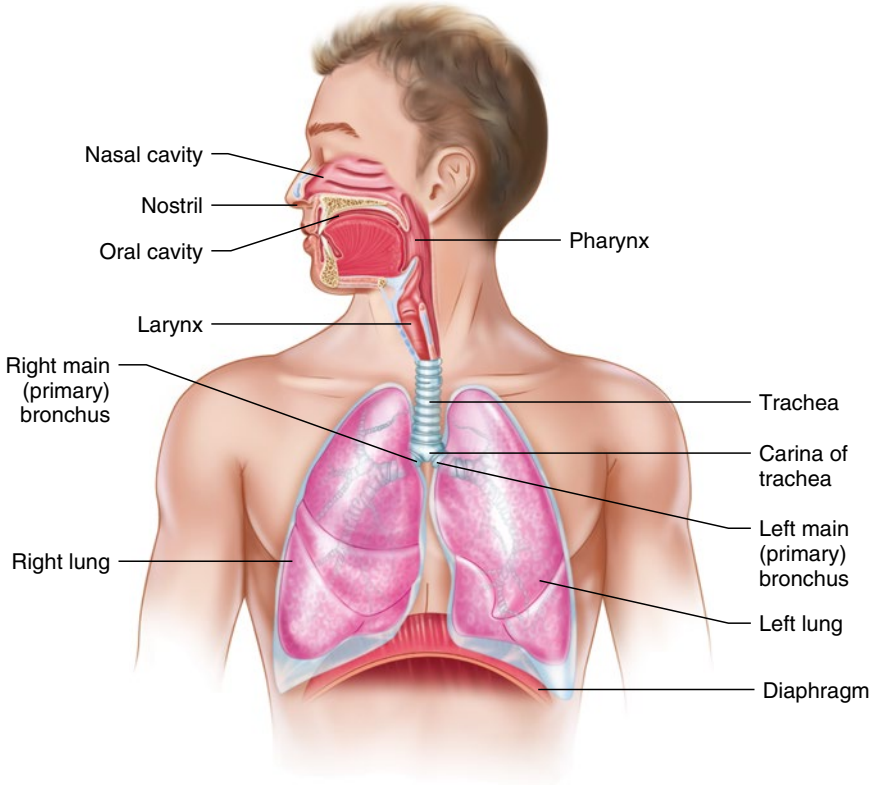

Fig. 28.1 Anatomy of the respiratory system

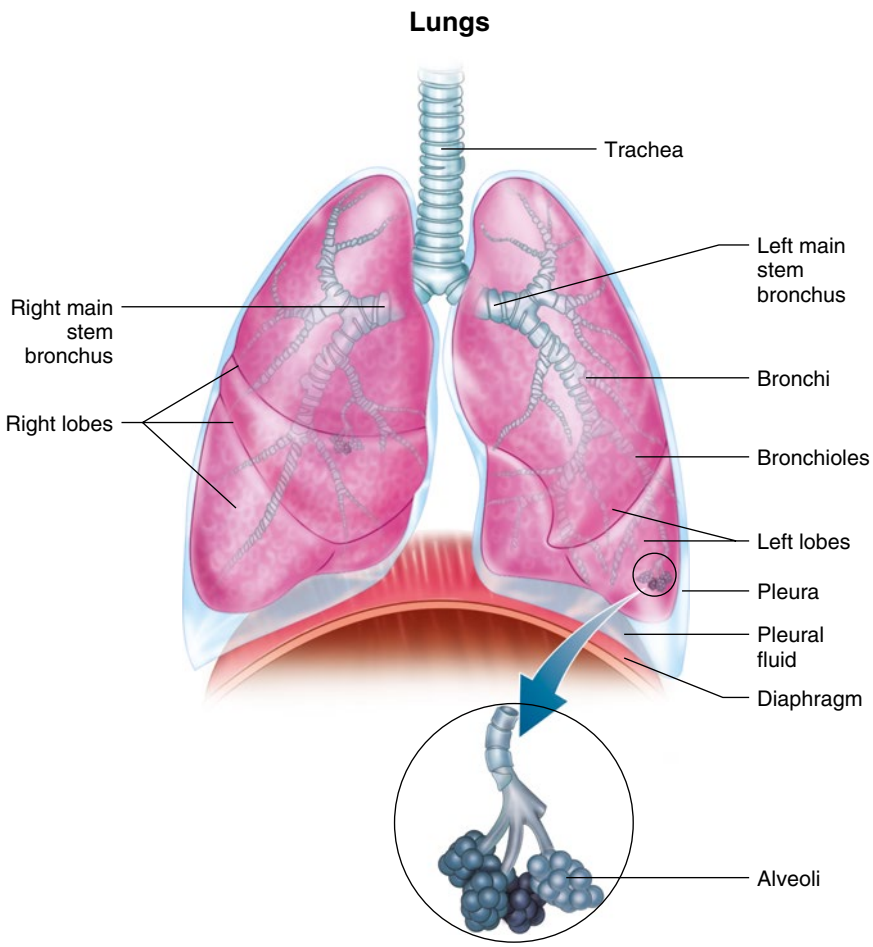

Fig. 28.2 Tracheobronchial tree anatomy

molecules, such as albumin, into the alveolus. Type II cells can divide and replace damaged Type I cells. The interstitial space contains mainly elastin and collagen.

Blood is supplied to the lungs by both the bronchial and the pulmonary arteries. The bronchial arteries arise from the aorta and provide nutritive needs of the airways. The pulmonary arteries arise from the right ventricle and form a capillary network, which takes part in gas exchange (O_2 uptake and CO_2 elimination). The pulmonary veins then supply oxygenated blood to the left atrium.

The tracheobronchial tree is innervated by both the parasympathetic (vagus nerve) and sympathetic nervous systems (beta-2 and alpha-1, primarily). Parasympathetic stimulation causes bronchoconstriction and increase in secretions, while sympathetic stimulation causes bronchodilation and decrease in secretions. The diaphragm is innervated by the phrenic nerves (C3–5).

Physiology

The lungs have various important physiological functions which are summarized in Table 28.1.

Control of Breathing

Respiratory Centers

Breathing is controlled neuronally by respiratory centers located in the medulla and pons. The dorsal respiratory group in the medulla is responsible for inspiration, while the ventral respiratory group is responsible for expiration. While the medulla is responsible for the basic respiratory rhythm, the pontine centers seem to fine-tune the respiratory rate and rhythm. The lower pontine (apneustic) center is excitatory, while the upper pontine (pneumotaxic) center is inhibitory (Fig. 28.3).

Table 28.1 Functions of the airway and lungs

Gas exchange
Alter pH of blood
Humidification and filtration of air
Surfactant production
Secretion of immunoglobulin-A to fight infections
Secretion of mucus which has antimicrobial substances
Metabolism of norepinephrine, serotonin, bradykinin, prostaglandins
Synthesis of angiotensin-converting enzyme, which converts angiotensin I to active angiotensin II
Lungs have high content of heparin and plasminogen activator—causing breakdown of fibrin debris

Sensors

CO_2 crosses the blood–brain barrier (BBB) and causes a decrease in cerebrospinal fluid (CSF) pH. The central chemoreceptors sense the change in pH, and compensate for the change by causing an increase in minute ventilation, thereby returning the CO_2 back to normal (Fig. 28.4). Over the course of few days bicarbonate is transported across the BBB to return the pH of CSF to normal, which decreases the minute ventilation. It should be noted that while increasing $PaCO_2$ tension leads to an increase in minute ventilation, very high $PaCO_2$ tension (>80 mmHg) causes depression of respiration, which is called CO_2 narcosis. Furthermore, under anesthesia the $PaCO_2$ at which ventilation is Zero, that is, the highest arterial CO_2 tension at which there is no spontaneous ventilation, is called the apneic threshold.

Peripheral chemoreceptors, which are located in the carotid bodies and the aortic arch, also modulate respiration (Fig. 28.5). Stimulation of peripheral chemoreceptors (decreases in PaO_2 or pH, or increases in $PaCO_2$ levels) leads to an increase in minute ventilation. The peripheral chemoreceptors interact with the central respiratory centers via the glossopharyngeal nerves. Of the stimuli, the carotid bodies are most sensitive to changes in the PaO_2 (especially below $PaO_2 < 50$ mmHg), while the central chemoreceptors are most sensitive to changes in the $PaCO_2$.

Other receptors that modulate respiration, though to a minor extent, are the stretch receptors located in the smooth muscle of airways, and irritant receptors located in the tracheobronchial

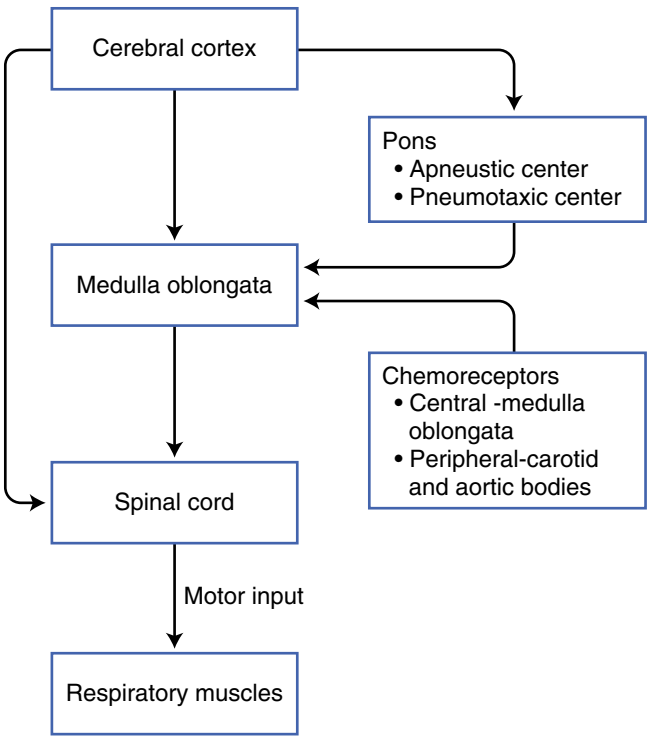

Fig. 28.3 Neuronal control of breathing

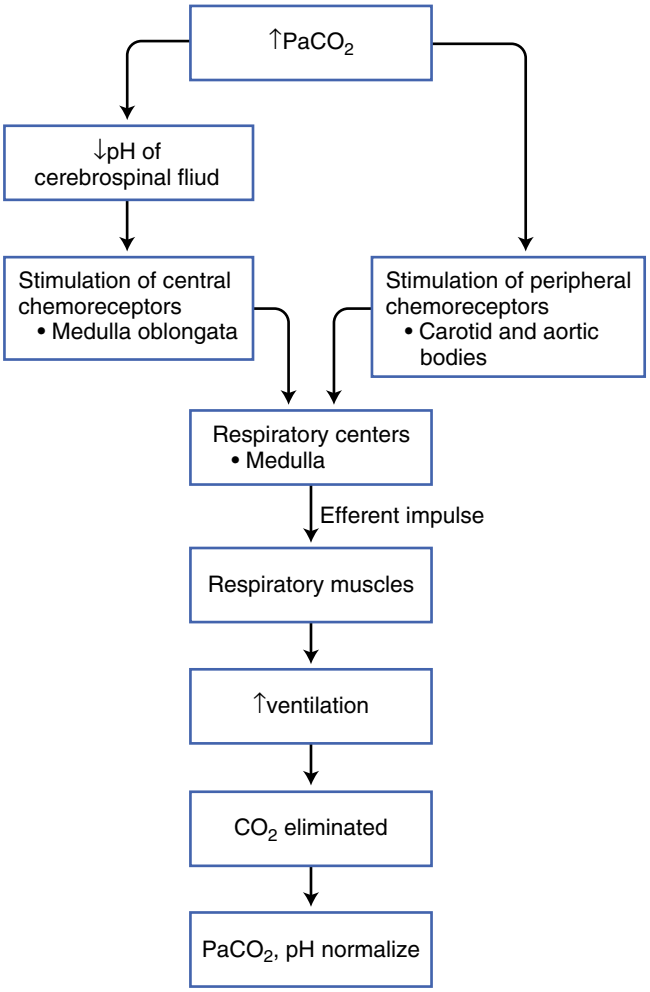

Fig. 28.4 Chemical control of breathing

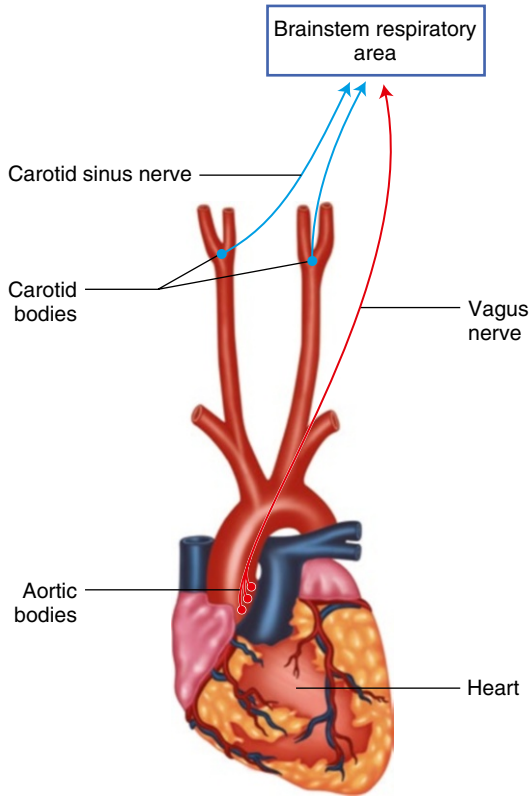

Fig. 28.5 Peripheral chemoreceptors

mucosa. Stretch receptors prevent the lung from excessive expansion (inhibition of inspiration) and excessive deflation (shortening of expiration). Input from the stretch receptors is carried to the brain (centrally) by the vagus nerve. Irritant receptors produce bronchoconstriction or tachypnea in response to stimulation by smoke, dust, or light anesthesia.

Lung Compliance and Work of Breathing

The elastic properties of the chest wall and the lung make them move in opposite directions; the chest wall expands outwards, while the lungs recoil inwards. The chest wall and the lungs each has its own compliance, which is defined as the change in volume/change in pressure.

$$\text{Lung compliance} = \text{Change in lung volume} / \text{Change in transpulmonary pressure}$$

$$\text{Chest wall compliance} = \text{Change in chest volume} / \text{Change in transthoracic pressure}$$

Total pulmonary compliance (lung and chest wall) is about 100 ml/cm H_2O. Lung compliance is affected by lung volume, pulmonary blood flow, and pulmonary diseases. Lung compliance can be referred to be either static or dynamic. Static lung compliance is the change in volume for any given applied pressure, while dynamic lung compliance is the compliance of the lung at any given time during actual movement of air. The compliance of the lungs is different on inspiration and expiration for identical volumes, which is referred to as hysteresis. Compliance is greatest at moderate lung volumes, and much lower at volumes which are very low or very high.

In a normal awake patient, on inspiration of 500 ml of tidal volume, the transpulmonary pressure increases from 0 to 5 cm H_2O (Fig. 28.6). Potential energy is stored during inspiration (active process), which is spent during expiration (passive process). Work of breathing can be calculated as:

$$\text{Work of Breathing} = \text{pressure} \times \text{volume}$$

As shown in Fig. 28.6a, the work of breathing equals the area in the triangle ABC plus the shaded area. Triangle ABC represents the work to overcome elastic resistance, while the shaded area represents the work to overcome airflow resistance. In an anesthetized patient with COPD (Fig. 28.6b), increased work is required to overcome both the elastic

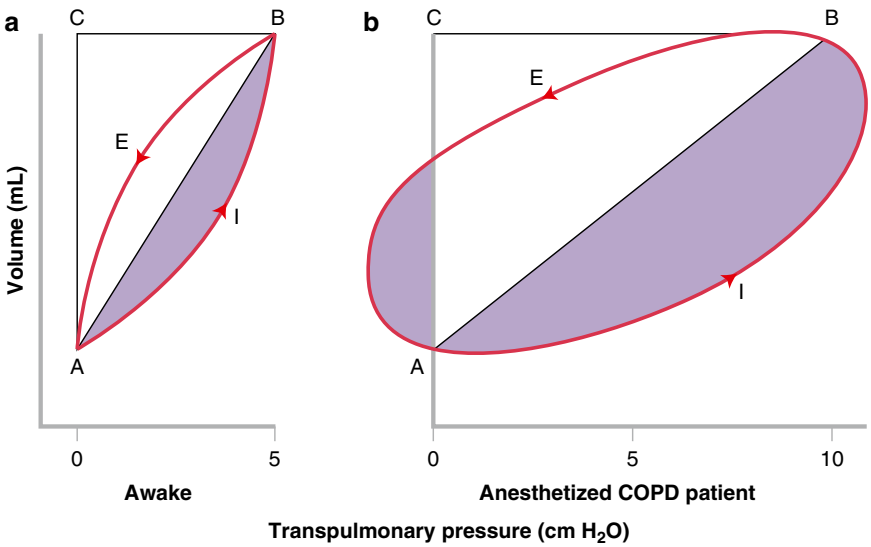

Fig. 28.6 Work of breathing. Lung volume plotted against transpulmonary pressure. (**a**) Normal awake patient with lung compliance (slope of AB) of 100 ml/cm H_2O, (**b**) Anesthetized patient with COPD with lung compliance (slope of AB) of 50 ml/cm H_2O (*I* inspiration, *E* expiration). See text for more description

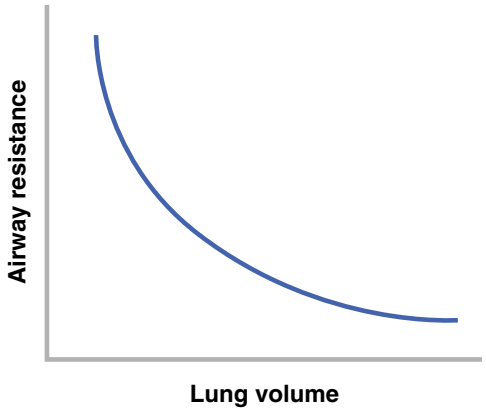

Fig. 28.7 Inverse relationship between airway resistance and lung volume

resistance (triangle ABC) and the airflow resistance (shaded area). During expiration about half the air leaves passively, while the other half of the air has to be forced out. This requires energy, which increases the work of breathing. Therefore, an anesthetized patient with COPD has decreased lung compliance, increased elastic resistance (ABC), and increased airflow resistance during inspiration and expiration.

Airflow Resistance

High airway resistance leads to a decrease in lung volume (Fig. 28.7). The flow of gas in the lungs can be laminar or turbulent. A gas that is flowing laminar has the highest velocity in the center and decreased velocity in the periphery, which usually occurs in smaller airways. Turbulent flow occurs at high gas flows and is inversely proportional to the airway diameter. Turbulent gas flow usually occurs in larger airways, and is seen at branching (sharp angles) airway points. Airflow resistance is higher in the conducting medium-sized bronchi (Fig. 28.8). Larger bronchi have low airway resistance due to their larger caliber, while terminal

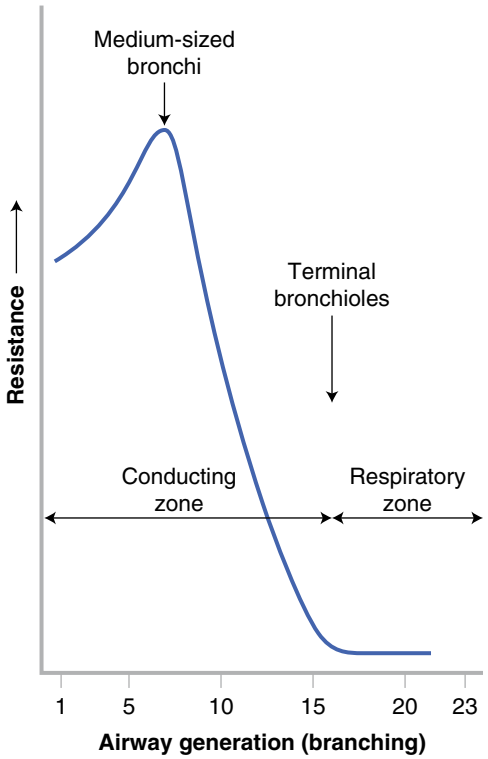

Fig. 28.8 Airway resistance is highest in medium-sized bronchi, and decreases starting about the seventh generation

smaller bronchi have low airway resistance because of their increased cross-sectional area.

The Reynolds number can be used to predict laminar or turbulent flow. Reynolds number less than 1,000 predicts laminar flow, whereas a number greater than 1,500 predicts turbulent flow.

$$\text{Reynolds number} = \frac{\text{Linear velocity} \times \text{Diameter} \times \text{Gas density}}{\text{Gas Viscosity}}$$

A gas, such as helium, which has a low density to viscosity ratio, will have a lower Reynolds number than air at the same velocity and therefore provide laminar flow. A helium–O_2 gas mixture can be used to decrease turbulent flow and airway resistance to gas flow. Airflow resistance is usually not increased with the induction of general anesthesia, per se. However, conditions that do lead to an increase in airflow resistance under anesthesia include upper airway obstruction, laryngospasm, secretions or mucus plug, bronchospasm, use of small size ETTube, and obstruction of breathing apparatus (kinking of ETTube).

Lung Volumes and Flow-Volume Loops

Pulmonary function tests are used to diagnose, or monitor disease progression or treatment. Patients presenting for major surgeries, especially with existing lung disease, often undergo pulmonary function tests. However, it should be noted that PFTs are not routinely ordered for preoperative evaluation. Spirometry is commonly used to measure lung volumes and flows. Lung volumes and capacities are summarized in Fig. 28.9 and Table 28.2.

Functional Residual Capacity

This is the volume of air in the lungs at the end of a normal expiration. The FRC is directly proportional to height, greater in upright than supine position, is higher in males (10 %) than females, and is reduced in obese people (increased abdominal mass). Preoxygenating a patient with 100 % O_2 increases their oxygen reserve, as the 21 % oxygen in air for the FRC (2,200 ml) is replaced with 100 % oxygen. As normal oxygen consumption is about 250 ml/min, more time is available if there is a problem of ventilating the patient on induction of general anesthesia. Induction of anesthesia reduces the FRC by about 15–20 % (400 ml). Many factors are responsible for this decrease in FRC, such as loss of muscle tone causing the diaphragm to shift cephalad, an increase in intrathoracic blood volume, a Trendelenburg (head down) position, and a change in thoracic cavity shape.

Closing Capacity (CC)

This is the volume at which the small airways begin to close. These airways lack cartilaginous support and need radial traction provided by the surrounding tissues for their patency. Higher CC means more intrapulmonary shunting as the small airways continue to be perfused but not ventilated.

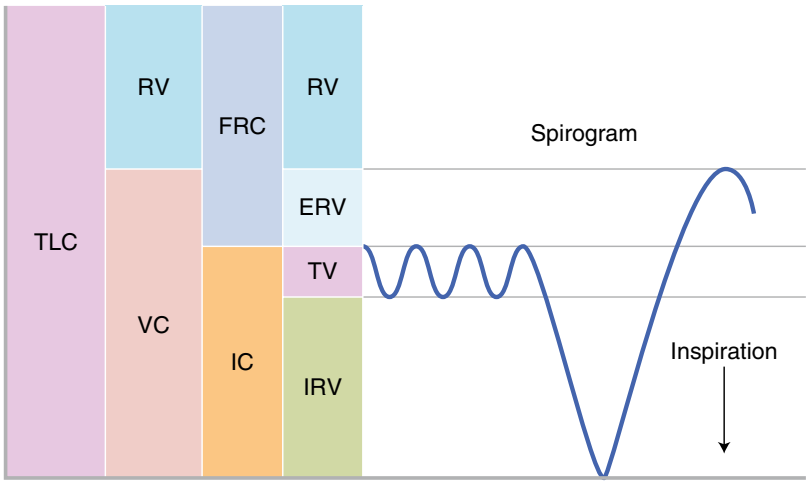

Fig. 28.9 Lung volume and capacities

Table 28.2 Lung volumes and capacities for a healthy 70 kg male

Volume/capacity	Definition	Value
Tidal volume (TV)	Volume of air inspired during normal breathing	500 ml
Inspiratory reserve volume (IRV)	Volume of air forcibly inhaled after a normal tidal volume breath	3,000 ml
Expiratory reserve volume (ERV)	Volume of air forcibly exhaled after expiration of normal tidal volume	1,000 ml
Residual volume (RV)	Volume of air remaining in the lungs after a forced exhalation (ERV)	1,200 ml
Functional residual capacity (FRC)	Volume of air remaining in the lungs after a normal expiration	2,200 ml (ERV + RV)
Inspiratory capacity (IC)	Maximum volume of air that can be inspired	3,500 ml (TV + IRV)
Vital capacity (VC)	Volume of air that can be fully expired after a full inspiration	4,500 ml (TV + IRV + ERV)
Total lung capacity (TLC)	Maximum volume of air in the lungs	5,700 ml (TV + IRV + ERV + RV, or VC + RV)

Therefore, people with higher CC are prone to hypoxemia. The CC increases with age, and is less than the FRC, but by the age of 45 years CC approximates FRC, and exceeds FRC by age 65 years.

Pulmonary function tests commonly measure the above lung volumes and capacities. Commonly used terms for PFTs include:

- Forced vital capacity (FVC): volume of air that can be exhaled forcefully and quickly after maximal inhalation. Measuring forced vital capacity provides information of airway resistance
- Forced expiratory volume (FEV): volume of air that can be exhaled with force in one breath. The volume of air can be measured at 1 s (FEV_1—normal 3.2 L), 2 s (FEV_2), or 3 s (FEV_3)
- FEV_1/FVC ratio: normal is ≥75–80 %. In obstructive lung disease both the FEV_1 and FVC are reduced, but the FEV_1 is reduced to a greater extent than FVC, so the ratio is low. In restrictive lung disease both FEV_1 and FVC are reduced proportionally, so the ratio may be normal.
- Forced mid-expiratory flow 25–75 % ($FEF_{25–75\ \%}$): Measurement of air flow halfway through an exhalation. Both FEV1 and FVC are effort dependent; however, $FEF_{25–75\ \%}$ is effort independent and may be a more reliable measurement of obstruction.
- Peak expiratory flow (PEF): Measurement of how quickly one can exhale
- Maximum voluntary ventilation (MVV): maximum volume of air that can be breathed in and out during 1 min
- Diffusion capacity for carbon monoxide: normal is >80 %

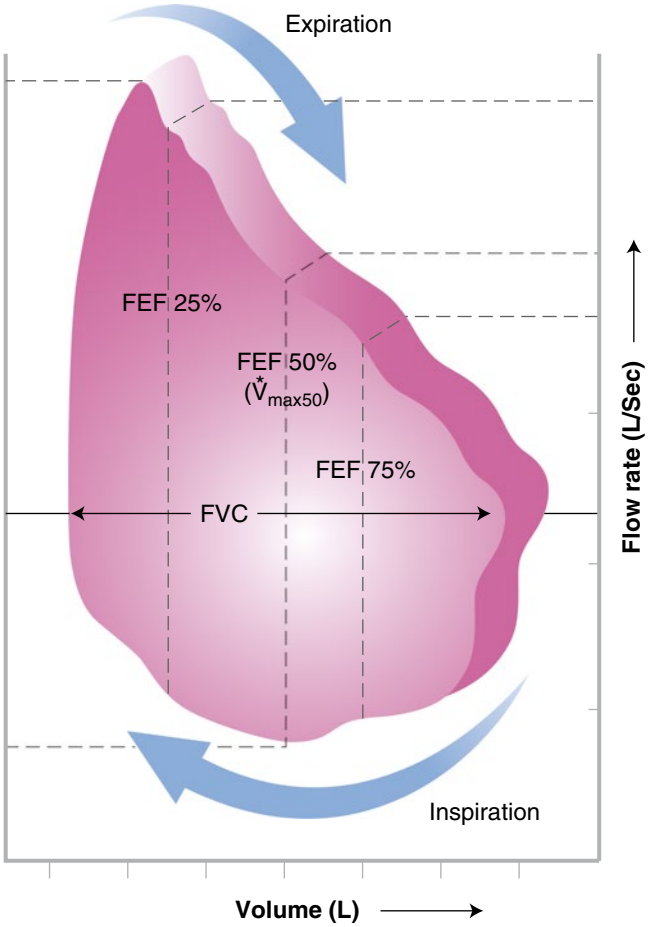

Fig. 28.10 A typical flow-volume loop

Flow-Volume Loops

Flow-volume loops can be used to identify the presence of pulmonary disease (obstructive or restrictive), or airway obstruction. A flow-volume loop is generated (Fig. 28.10) by making the patient inhale deeply to TLC, then forcefully exhaling to empty the lungs to residual volume, and then quickly inhaling again to reach TLC. Flow (both expiratory and inspiratory) is plotted on the *Y* axis and the volume on the *X* axis. The normal expiratory portion of the flow–volume curve is characterized by a rapid rise to the peak flow rate, followed by a nearly linear fall in flow as the patient exhales toward residual volume. In contrast, the inspiratory curve is a relatively symmetrical, saddle-shaped curve. Changes in the contour of the loop can aid in the diagnosis and localization of airway diseases: obstructive, restrictive, or presence of tumors (Fig. 28.11).

Physiologic Dead Space

During inspiration, a portion of the gas remains in the upper airway, where no gas exchange takes place. This space is called the anatomical dead space. The remainder of the gas is used as alveolar ventilation. However, all the alveoli do not take part in gas exchange, as they may not be perfused. This space is called alveolar dead space. The total dead space, that is, the sum of the anatomical and alveolar dead space, is called physiological dead space. Physiological dead space is approximately 1/3rd of the tidal volume, and is about 150 ml in adults or roughly 2 ml/kg. It can be calculated by the Bohr's equation:

$$\text{Physiologic Dead space Vd / Vt} = \frac{PaCO_2 - ETCO_2}{PaCO_2}$$

where $PaCO_2$ is the arterial CO_2 tension and $ETCO_2$ is the expired CO_2 tension. Factors affecting dead space are summarized in Table 28.3. $ETCO_2$ is used as a measure of $PaCO_2$, and the gradient between $ETCO_2$ and $PaCO_2$ is 5–7 mmHg ($PaCO_2$ is higher, normal $PaCO_2$ is 35–45 mmHg). This gradient is increased in diseased states and during some surgeries (laparoscopy).

Alveolar Oxygen Tension

Inspired oxygen tension is reduced by water vapor in the breath in the upper airway. Therefore, alveolar oxygen

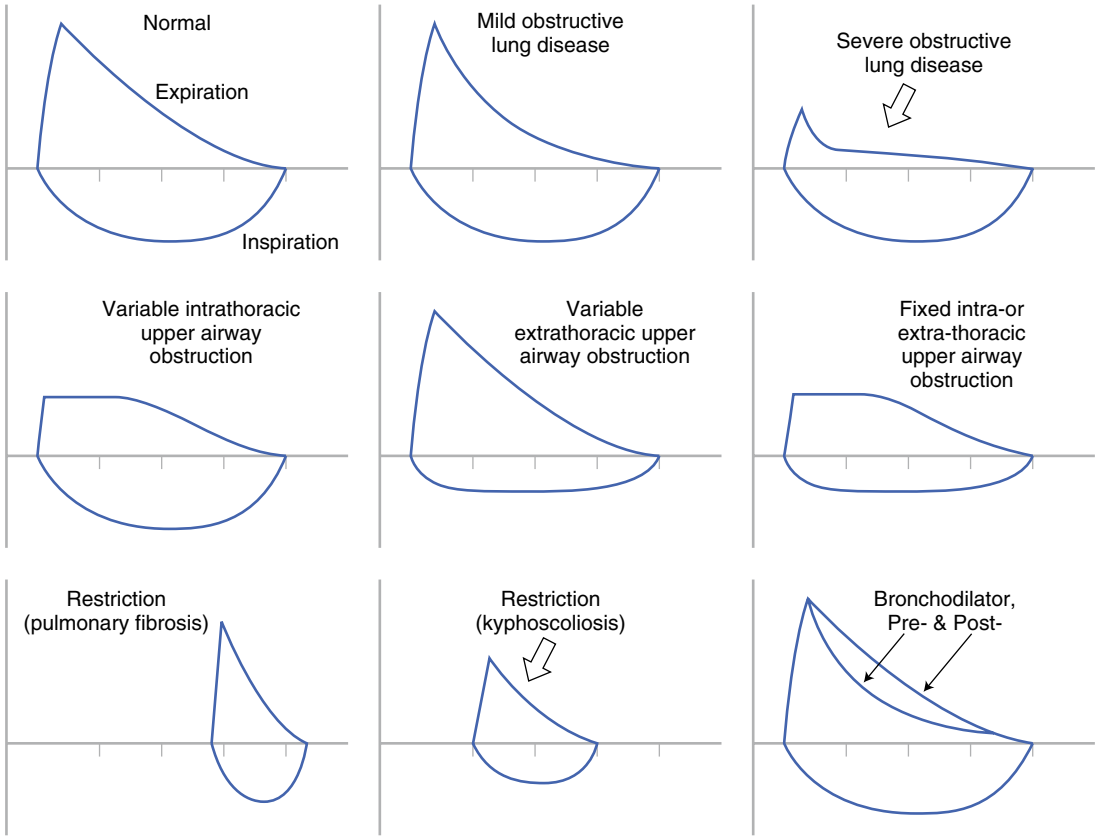

Fig. 28.11 Flow-volume loops in various conditions

Table 28.3 Factors affecting physiologic dead space

Increase	Decrease
Upright position	Supine position
Age	Artificial airway
Positive pressure ventilation	
Anticholinergic drugs	
Hypotension	
COPD	

tension is lower than the inspired oxygen tension. Alveolar gas is also diluted by residual alveolar gas from previous breaths and the addition of CO_2. Alveolar gas oxygen tension can be calculated as:

$$PAO_2 = PiO_2 - \frac{PaCO_2}{RQ}$$

$$PiO_2 = FiO_2 \times (PB - PH_2O)$$

where PiO_2—inspired oxygen tension, PAO_2—alveolar oxygen tension, $PaCO_2$—arterial oxygen tension, RQ—respiratory quotient (normal 0.8) is the ratio of CO_2 produced/O_2 consumed, FiO_2—delivered oxygen, PB—atmospheric pressure, PH_2O—water vapor pressure). Furthermore, normal alveolar–arterial oxygen tension gradient (A-a gradient) is 15–20 mmHg. Normal PaO_2 is 80–100 mmHg, and hypoxemia ($PaO_2 < 60$ mmHg) results in an increased A-a gradient. Intrapulmonary shunting (no ventilation but perfusion) increases the gradient, while increasing mixed venous oxygen tension decreases the A-a gradient.

Hypoxic Pulmonary Constriction

Pulmonary hypoxia leads to vasoconstriction in the lung, called hypoxic pulmonary constriction (HPV). This effect is opposite to the systemic circulation. The end result is optimal perfusion in those areas of the lungs which are adequately ventilated. HPV leads to decreased shunting and preventing further hypoxemia.

HPV is an autoregulatory mechanism, which diverts blood flow from the atelectatic lung toward the remaining normoxic or hyperoxic ventilated lung. HPV maintains the PaO_2 by decreasing the amount of shunt flow that can occur through hypoxic lung. HPV is of high importance when the percentage of hypoxic lung is intermediate (30–70 %), which is the case during single-lung ventilation. HPV is of little importance when very little of the lung is hypoxic (near 0 %) because the shunt will be small (normal 1–2 %), or when most of the lung is hypoxic (near 100 %), as there is no significant normoxic region to which the hypoxic region can divert blood flow. Factors which inhibit HPV are listed in Table 28.4.

Table 28.4 Factors inhibiting hypoxic pulmonary vasoconstriction

Very high or very low pulmonary artery pressures
Hypocapnia
High or low mixed venous oxygen tension
Pulmonary infections
High airway pressures, high PEEP
Low FiO_2, or prolonged administration of high FiO_2 (>50 %)
Vasodilators—nitroprusside, nitroglycerin, dobutamine, calcium channel blockers, volatile inhalational agents >1.0 MAC

Table 28.5 Mixed venous oxygen saturation in various conditions

High mixed venous oxygen saturation
• Increased oxygen delivery
– Increasing FiO_2
• Decreased oxygen demand
– Hypothermia, sepsis, left to right shunting, high cardiac output
Low mixed venous oxygen saturation
• Decreased oxygen delivery
– Anemia, hemorrhage (low Hb)
– Hypoxia (decreased arterial oxygen saturation)
– Hypovolemia, shock, arrhythmias (decreased cardiac output)
• Increased oxygen demand/consumption
– Hyperthermia, pain, shivering

Mixed Venous Oxygen Saturation

Blood is returned to the heart via the superior and inferior vena cava, and the coronary sinus. Blood then flows to the lungs from the right ventricle and into the pulmonary artery. Therefore, a blood sample obtained from a pulmonary artery catheter denotes a mixed venous oxygen sample. Venous blood has a PO_2 of 40 mmHg and a Hb saturation of 75 % (60–80 %). MvO_2 in various conditions is summarized in Table 28.5. MvO_2 can be calculated by the following formula. Clinical relevance of continuous MvO_2 monitoring includes use as a surveillance, early warning system, and to guide and adjust therapy.

$$MvO_2 = SaO_2 - \left(1.34 \times Hb \times 10 \times VO_2 / CO\right)$$

(SaO_2—arterial oxygen saturation, Hb is expressed in mg/L, hence a factor of 10, VO_2—oxygen consumption per minute, CO—cardiac output)

Oxygen Transport

Approaching the topic of cardiopulmonary physiology from the concept of oxygen delivery is often most helpful. O_2 delivery refers to the amount of oxygen that is transported or delivered to the tissues, and is expressed in milliliters of oxygen per minute. O_2 delivery depends on two separate but interconnected concepts: First, the amount of oxygen that is actually carried in the blood, or the oxygen content, and second, the rate of blood (with associated oxygen) that is carried to the tissues (or cardiac output). Adult O_2 stores are about 1,500 ml, and O_2 consumption is about 250 ml/min. During anesthesia, it is imperative that O_2 delivery and CO_2 removal are maintained. This is frequently quite difficult to accomplish in patients with severe lung disease who are undergoing thoracic surgical procedures.

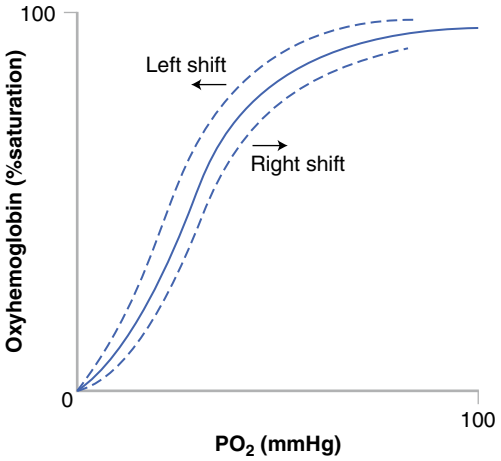

Fig. 28.12 Oxygen hemoglobin dissociation curve

Blood oxygen content is based on two factors, the amount of oxygen bound to hemoglobin (Hb), and to a much lesser extent, the amount of dissolved oxygen. The basic equation for blood oxygen content is:

$$\text{Blood } O_2 \text{ content} = \left(Hb \times 1.34 \times SaO_2\right) + \left(0.003 \times PaO_2\right),$$
$$\text{where } 1.34 \times SaO_2 \text{ equals \% } O_2 \text{ bound to Hb}$$

As can be seen from the equation, the primary determinant of oxygen content is the Hb-bound portion, which depends on the amount of hemoglobin and the oxygen saturation. Oxygen binds to Hb in a cooperative fashion, meaning as oxygen binds, it changes the conformation of the Hb molecule such that it facilitates further binding. This effect is seen in the "S" shape of the O_2–Hb dissociation curve with its associated hysteresis. As the PO_2 increases, oxygen binds more readily and the saturation, or % of oxygen bound to hemoglobin, rises rapidly until around 90 % where it begins to level off. The shape of the curve is altered or shifted under certain physiologic circumstances.

- The curve is shifted to the left (meaning oxygen is more tightly bound to hemoglobin) under the conditions of alkalosis, decreased temperature, or decreased levels of 2,3 diphosphoglycerate (DPG)—a by-product of glycolysis. Carbon monoxide or cyanide poisoning and methemoglobinemia resulting from nitrates/sulfonamides also shift the curve to the left.
- The curve is shifted to the right (meaning oxygen is less tightly bound at a given PO_2) under the conditions of acidosis, hyperthermia, and increased 2,3 DPG (Fig. 28.12).

An easy way to remember this is by recalling that tissues that are more metabolically active have increased temperature and CO_2 (acid) production, and therefore need more oxygen delivered to them. Nature has provided for this by rightward shift of the O_2–Hb dissociation curve with associated decreased affinity for oxygen and easier oxygen unloading to these active tissue beds.

Carbon Dioxide Transport

Approximately 80 % of CO_2 transport occurs as bicarbonate ion, and rest 10 % each as dissolved and bound to amino groups on hemoglobin (carbamino-hemoglobin). Adults have about 120 L of CO_2 stores. CO_2 released from the red cell is acted on by the enzyme carbonic anhydrase (CA) to form carbonic acid (H_2CO_3), which dissociates into bicarbonate and hydrogen ions (Fig. 28.13).

$$CO_2 + H_2O \xrightarrow[CA]{\Leftrightarrow\Leftrightarrow} H_2CO_3 \Leftrightarrow\Leftrightarrow HCO_3^- + H^+$$

Oxyhemoglobin (presence of oxygen) has a lower affinity to bind to CO_2, and conversely deoxyhemoglobin (absence of oxygen) has a higher affinity to bind to CO_2. In tissue beds, where O_2 is consumed and its concentration is low, CO_2 binds more readily to hemoglobin. Therefore, venous blood has more CO_2 content than arterial blood. This property is known as the Haldane effect, and is responsible for increased CO_2 transport by hemoglobin.

The reverse holds true in the lungs, where O_2 levels are high and CO_2 is preferentially off-loaded. Because CO_2 is eliminated, the concentration of H^+ is low in the lungs, which drives the binding of Hb to oxygen. The binding of Hb to oxygen further releases H^+ ions, driving the formation and elimination of CO_2. This property is known as the Bohr Effect, which refers to the inverse relationship between oxygen and hydrogen ion affinity for Hb. The two properties, the Haldane and Bohr effect, work in concert to increase O_2 loading and CO_2 off-loading in the lungs, and O_2 release and CO_2 binding in the tissues.

Another interesting property is the Chloride (Hamburger) shift. Bicarbonate is continually produced in the red cells. To prevent the red cell from becoming alkalotic, the bicarbonate ions are transported out and chloride ions are transported in. This maintains electrical neutrality, and is termed as chloride shift.

Ventilation–Perfusion

Effect of Position on Ventilation and Perfusion

In an upright position, the lower portions of the lungs are most ventilated and perfused, while in the supine position the dependent portions receive the highest ventilation and perfusion. Each lung can be divided into three zones (Fig. 28.14), which have a gradient between three pressures, the alveolar, the pulmonary arterial, and the pulmonary venous pressures. Zone 1 has the highest amount of dead space as the alveolar pressure is higher than the arterial/venous pressure, thereby occluding the pulmonary capillaries. Pulmonary capillary flow is intermittent in zone 2, while in zone 3 it is continuous.

Alveolar ventilation is on average 4 L/min, whereas perfusion is about 5 L/min. Therefore, normal *V/Q* ratio is 0.8. Most of the lung areas have a *V/Q* of 0.8–1.0, but *V/Q*s can range from 0.3 to 3.0. Theoretically, a *V/Q* of "0" means no ventilation, while a *V/Q* of "infinity" means no perfusion. The former is referred as a intrapulmonary shunt, while the latter is referred as alveolar dead space. Increase in the number of low *V/Q* units leads to hypoxemia, while an increase in high *V/Q* units leads to hypercarbia. The concentration of any gas in the alveolus is dependent on the rate of its addition (perfusion) and the rate of its removal (ventilation).

Nondependent areas of lung have higher *V/Q*s than do dependent areas of lungs, as the nondependent areas are ventilated better, while the dependent areas are perfused better.

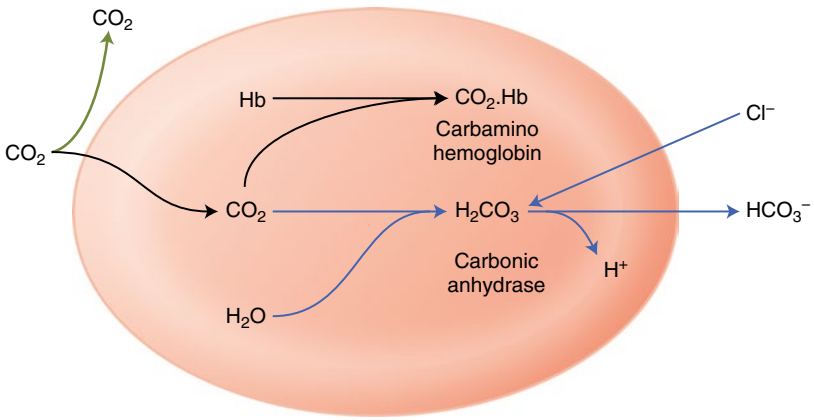

Fig. 28.13 Carbon dioxide transport and chloride shift

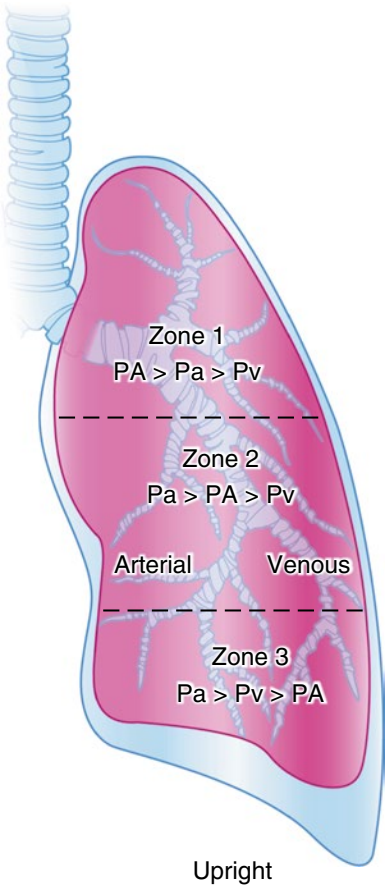

Fig. 28.14 Zones of the lung showing the relationship between alveolar (PA), pulmonary artery (Pa), and pulmonary venous (Pv) pressures

Shunt and dead space fall under the general heading of ventilation–perfusion (*V/Q*) mismatch. Essentially, there is a mismatch in the amount of pulmonary blood flow compared to the amount of alveolar ventilation within the lung. *V/Q* mismatch may occur globally throughout the lung or, more commonly, only in regional areas of the lung. In fact, it is quite possible to have areas of normal *V/Q*, areas of low *V/Q* (*Q* > *V* or shunt), and areas of high *V/Q* (*V* > *Q*, or dead space) all at the same time.

Venous Admixture (Low *V/Q* and Shunt)

Venous admixture refers to a process where pulmonary blood flow exceeds alveolar ventilation thus encompassing areas of lung with both low *V/Q* and shunt (*V/Q* = 0). A common clinical scenario causing pure shunt is pneumonia with alveolar flooding due to pus, debris, and/or fluid such that no ventilation takes place in the affected respiratory unit. Increased venous admixture due to right to left shunting occurs with single-lung ventilation in thoracic surgery. During the initiation of single-lung ventilation the patient experiences a fixed shunt of the non-ventilated side. Over time, the alveolar PO_2 on the non-ventilated side falls, and hypoxic pulmonary vasoconstriction increases, thereby redirecting blood flow to the ventilated side with an associated reduction in the degree of shunt. Other etiologies of low *V/Q* are shown in Table 28.6.

Table 28.6 Etiology of high and low *V/Q* mismatch

High *V/Q* (Dead space)	Low *V/Q* (Shunt)
Pulmonary embolism	Chronic bronchitis, asthma
Chronic obstructive pulmonary disease	Hepatopulmonary syndrome
Shock-pulmonary vascular hypotension	Pulmonary edema
Tumors	Pneumonia
Pneumothorax	Significant atelectasis
High airway pressures	Large pleural effusion, pneumothorax, hemothorax
	Acute respiratory distress syndrome

The amount of shunt is reflected in the arterial oxygen partial pressure PaO_2. In shunt physiology, the PaO_2 falls significantly, whereas the $PaCO_2$ remains normal to only slightly elevated. In mild/small shunt, increasing the FiO_2 will increase the PaO_2, but in a large shunt enriching the inspired oxygen up to 100 % will not reverse the low PaO_2. The reason for this is based on the oxygen content of the blood. Even with hypoxic pulmonary vasoconstriction, portions of the lung that are perfused and ventilated can only take up oxygen to a certain extent. Once hemoglobin is fully saturated, adding more oxygen will only increase the dissolved O_2 content by the factor of $0.003 \times PaO_2$. This additional oxygen will not make up for the areas of lung that remain poorly ventilated with little or no gas exchange.

The reason the $PaCO_2$ does not fall is more complicated. The CO_2 content in the blood is kept much more constant than the oxygen content between the arterial and venous systems. The arterial $PaCO_2$ is typically around 40 mmHg, whereas the venous $PaCO_2$ is only around 45 mmHg. The $PaCO_2$ has to be kept tightly controlled in order to keep blood pH relatively constant throughout the body. Therefore, there is simply not a huge difference between the $PaCO_2$ in areas of the lung that have a low *V/Q* and those that are normal. Even with a very large shunt fraction, when the blood mixes in the pulmonary vein, the $PaCO_2$ is only marginally elevated, and simply increasing the respiratory rate slightly will return the $PaCO_2$ to a normal value.

High *V/Q* and Dead Space

High *V/Q* refers to ventilation–perfusion abnormalities which are characterized by areas of lung with high ventilation relative to perfusion (*V/Q* > 1), and impaired CO_2 elimination. As discussed before, this is referred to as alveolar dead space. Pure dead space (opposite of shunt) are areas where ventilation infinitely exceeds pulmonary perfusion (*V/Q* = infinity). The classic example of increased dead space is a pulmonary embolism. In this case, the area of lung that is

perfused by the blocked pulmonary artery receives no blood flow, and therefore no gas exchange takes place, and this is referred to as wasted/dead space ventilation. Other etiologies of high *V/Q* are shown in Table 28.6.

In dead space physiology, the $PaCO_2$ rises dramatically, but the PaO_2 does not fall nearly so far. The $PaCO_2$ rises because there is significant wasted ventilation. The amount of change in the $PaCO_2$ depends on the amount of dead space, as well as on the physiologic reserve of the individual. Patients will increase minute ventilation in an attempt to normalize their $PaCO_2$, and will do so until they begin to fatigue, causing the minute ventilation to fall and the $PaCO_2$ to rise further. The PaO_2 level is maintained by blood flow being diverted to other areas of the lung that have a normal *V/Q*. In these areas *Q* will increase but so will ventilation in order to keep the $PaCO_2$ constant. *V/Q* will be matched in these areas until the patient starts to fatigue, which will then cause the PaO_2 to fall. The PaO_2 can be normalized with the addition of supplemental oxygen.

Diseases of the Pulmonary System

Obstructive Airway Diseases

Obstructive airway diseases can be divided into two major forms: asthma and chronic obstructive pulmonary disease (COPD). These two diseases are fairly common, affecting millions of Americans, and are responsible for a large percentage of the US healthcare budget.

Asthma

Asthma is rapidly rising in prevalence. In 2011, it was estimated that 1 in 12 or 8 % of the general US population had asthma. This corresponds to approximately 25 million Americans, and is estimated to cost $56 billion dollars annually. Asthma does not affect the population equally. Children are more likely than adults to have asthma, and there is an increased prevalence in African Americans versus Caucasians or Hispanics. In fact, the prevalence is estimated to be 1 in 6 among black children.

Asthma, which is typified by chronic airway inflammation and hyperreactivity, causes a variable degree of airway obstruction, most seen on exhalation. Asthma has four major pathologic features:

- Variable airflow obstruction (dyspnea, cough, wheezing)
- Airway inflammation (edema, secretions)
- Hyperresponsiveness of the airways to specific triggers such as cold, exercise, aspirin, and allergens (pollen, dust, pollutants, chemicals) may be seen in otherwise asymptomatic patients.
- Reversibility (or at least partial reversibility) of airway obstruction with inhaled bronchodilators

On exposure to a trigger, typically two processes happen: a parasympathetic (vagal response), and release of chemical triggers, such as histamine, bradykinin, prostaglandins (PGE_2/$F_2\alpha$/D), and leukotrienes, which all lead to bronchoconstriction. Bronchoconstriction combined with mucosal edema and secretions leads to an increase in airflow resistance.

Signs and Diagnosis

Patients with asthma typically present with cough, shortness of breath, and/or wheezing. However, these symptoms may be quite variable, as the degree of inflammation, airflow obstruction, or hyperresponsiveness is unique in each individual. Prolonged or severe asthmatic attacks markedly increase the work of breathing and lead to muscle fatigue and shunting with increase in the number of areas of low *V/Q* ratios. Hypoxemia leads to tachypnea, which drives down the $PaCO_2$. Therefore, a patient having an asthmatic attack, with a normal or elevated $PaCO_2$, is often a sign of impending respiratory failure. Severe respiratory obstruction may also be associated with ST-segment changes and heart strain.

Typically, asthma begins early in life for most patients and is characterized by risk factors such as atopy, recurrent wheezing, or a parental history of asthma. The initial diagnosis of asthma is most typically made by the presence of expiratory wheezing on physical exam. Confirmation of this diagnosis is usually done by spirometry demonstrating airflow obstruction, and also by bronchoprovocation of airway hyper-responsiveness with methacholine and bronchodilation with inhaled albuterol.

There is a subgroup of approximately 5–10 % of asthmatics who have severe or refractory asthma as defined by the American Thoracic Society (ATS). Despite the small percentage of severe asthmatics, these patients experience most of the significant morbidity associated with this disease. The ATS has established major and minor criteria for the diagnosis of severe asthma. A patient can be classified as having severe or refractory asthma if they demonstrate at least one major and two of the minor criteria.

- The major criteria for severe or refractory asthma are the continuous (or near continuous) use of oral corticosteroids, or needing high-dose inhaled corticosteroids
- The minor criteria include the need for daily treatment with a bronchodilator, persistent airway obstruction (FEV_1 less than 80 % predicted), or peak expiratory flow variability greater than 20 %
- Additional minor criteria include the need for urgent care visits for asthma, use of 3 or more steroid bursts in a year, increase in corticosteroid use, prompt deterioration in function, or a near fatal asthma event in the past

Pulmonary function studies and peak expiratory flow measurements demonstrate evidence of airflow obstruction and are the mainstay of diagnosis and monitoring of therapy.

Besides reduction in FEV, there is an increase in FRC, RV, and TLC. Reversibility of obstruction after administration of a bronchodilator helps to confirm a diagnosis of asthma. An increase in FEV_1 % predicted of more than 12 % and greater than 0.2 L has historically been used as the criteria for bronchodilator responsiveness and variability of airflow obstruction. However, current data suggest that this may not be the "gold standard" criteria, since in a recent study only slightly more than 50 % of asthmatics met this standard. Therefore, a more holistic approach is needed to make an accurate diagnosis of asthma. This should include a combination of patient history, symptoms, and pulmonary functions tests on a case by case basis.

Treatment

The National Heart Lung and Blood Institute (NHLBI) has set guidelines for the effective treatment of asthma. This treatment has been divided into four components of care: Assessment and monitoring, education, controlling environmental factors and comorbid conditions, and finally, pharmacologic therapy. Additionally, the NHLBI has divided pharmacologic therapy into three distinct age groups: 0–4 years of age, 5–11 years of age, and those patients 12 years and older. The actual details of treatment for each of these groups are beyond the scope of this chapter, but in general the goal of pharmacotherapy is along a stepwise approach.

Initially, inhaled corticosteroids (beclomethasone, triamcinolone) should be initiated for effective long-term control (maintenance therapy) of asthma symptoms. If symptoms persist, then bronchodilator therapy with a β_2-selective agonist (albuterol) is added to the treatment regimen. These agents stimulate the receptors to increase the activity of the enzyme adenylate cyclase, which leads to an increase in the concentration of cAMP. Additionally, patients may also be treated with ipratropium, an anticholinergic drug acting on muscarinic receptors.

During severe asthma exacerbations, intravenous therapy with glucocorticoids (hydrocortisone, methylprednisolone, followed by oral prednisone) is the mainstay of therapy. It should be remembered that glucocorticoids take about 4–6 h to take effect. In rare circumstances, when life-threatening status asthmaticus persists despite aggressive pharmacologic therapy, it may be necessary to consider general anesthesia (isoflurane or sevoflurane) in an attempt to produce bronchodilation. However, giving an inhaled anesthetic agent can be problematic if a patient is in severe status asthmaticus, since their respiratory function may be so compromised that drug delivery becomes unreliable. When general anesthesia is needed during severe asthmatic exacerbations, intravenous ketamine maybe an effective approach because of its sympathomimetic action and relaxation of increased airway smooth muscle tone. However, ketamine markedly increases secretions which may limit its usefulness in this situation.

Anesthetic Considerations

Preoperative Preparation

- Thorough history and physical examination, with inquiry about any emergency room visits or hospitalization for asthmatic attacks, and steroid therapy. Absence of wheezing should be noted by chest auscultation. A chest radiograph may be useful for assessing air trapping (hyperinflation leading to hyperlucent lung fields).
- Pulmonary function studies (normal values-FEV_1>3 L for men and 2 L for women, FEV_1/FVC> 75 %, PEFR>200 L/min) obtained before and after bronchodilator therapy may be indicated in the asthmatic patient who is scheduled for a thoracic or abdominal operation.
- Measurement of arterial blood gases before proceeding with elective surgery is a consideration if there are questions about the adequacy of ventilation or arterial oxygenation. Hypocapnia is indicative of moderate disease, while hypercapnia is indicative of severe disease.
- Essentially, the patient should be evaluated prior to surgery to see if their lung function is well controlled, and if not, additional medications should be started in an attempt to do so.
- All asthmatics who have persistent symptoms should be treated with either inhaled or systemic corticosteroids (depending on the severity of their airflow obstruction), in addition to scheduled doses of inhaled β_2 agonists.
- Patients who are on an inhaled corticosteroid or who have received an oral corticosteroid within 6 months of surgery may benefit from a short 24 h pulse of steroids (hydrocortisone 100 mg every 8 h).
- Premedication with benzodiazepine may be used cautiously to decrease anxiety. Anticholinergics (glycopyrrolate) are only used in the presence of copious secretions. H_2 blocker administration (ranitidine, famotidine) causes unopposed action of H_1 receptors, which can produce bronchoconstriction.

Choice of Anesthesia

- Regional anesthesia is often preferred when the surgery is superficial or on the extremities. Although regional anesthesia is likely to result in lower complication rates compared to general anesthesia, bronchospasm has been reported in asthmatics undergoing a spinal anesthetic, as blockade of sympathetic fibers (T_{1-4}) may lead to bronchoconstriction.
- Another reasonable approach to avoid tracheal intubation is to use an LMA, whenever safe and feasible in asthmatic patients.
- If tracheal intubation is required, the goal during induction and maintenance of general anesthesia in patients with asthma is to depress airway reflexes in order to avoid bronchoconstriction in response to mechanical stimulation.

Before tracheal intubation, a sufficient depth of anesthesia should be established to minimize bronchoconstriction with stimulation of the upper airway. In the asthmatic patient, rapid intravenous induction of anesthesia is most often accomplished with the administration of propofol or ketamine. Propofol may blunt tracheal intubation-induced bronchospasm in patients with asthma. Likewise, ketamine (1–2 mg/kg IV) is an excellent alternative selection for rapid induction of anesthesia, due to its bronchodilator effects noted above.

Sevoflurane and isoflurane are potent volatile anesthetics that depress airway reflexes and do not sensitize the heart to the cardiac effects of sympathetic nervous system stimulation produced by β_2 agonists and theophylline. Bronchodilation with sevoflurane and isoflurane is due to the production of nitric oxide and prostanoids by the normal airway epithelium. Desflurane may be associated with increased secretions, coughing, laryngospasm, and bronchospasm due to in vivo airway irritation. However, at 1 MAC or more, all potent inhaled anesthetics achieve bronchodilation, so it is unlikely that desflurane is contraindicated in the asthmatic.

Intravenous lidocaine (1–2 mg/kg) is sometimes used to blunt airway reflexes in anesthesia, and although case reports suggest that bronchodilation results from intravenous lidocaine, the clinical significance of this is unclear. Studies comparing the effects of intravenous lidocaine with inhaled albuterol given prior to tracheal intubation demonstrate mixed results. Therefore, in the asthmatic patient undergoing tracheal intubation, premedication with inhaled albuterol should be the first choice of therapy to prevent intubation-induced bronchoconstriction.

Intraoperatively, the PaO_2 and $PaCO_2$ can be maintained at normal levels by mechanical ventilation of the lungs at a slow respiratory rate to allow adequate time for exhalation. This slow breathing rate can usually be facilitated by increasing the inspiratory flow rate, thereby lengthening the time for exhalation. Positive end-expiratory pressure (PEEP) should be used cautiously, due to the inherent, impaired exhalation in the presence of narrowed airways and the possibility of worsening preexisting auto-PEEP.

At the conclusion of elective surgery, the trachea may be extubated while the depth of anesthesia is still sufficient to suppress airway reflexes. Following administration of anticholinesterase drugs to reverse the effects of nondepolarizing neuromuscular blocking drugs, bronchospasm may occur but is not usual, which may reflect decreased airway resistance effects of administered anticholinergics. When extubation is delayed for reasons of safety until the patient is awake, e.g., in the presence of gastric contents, intravenous administration of lidocaine may decrease the likelihood of airway stimulation due to the endotracheal tube in an awake patient.

Intraoperative Bronchospasm

The frequency of perioperative bronchospasm in patients with asthma is low if patients are asymptomatic from their asthma at the time of surgery. When bronchospasm does occur intraoperatively, it is usually due to factors other than an acute asthma exacerbation. Therefore, it is important to first consider other causes of obstruction, such as a mechanical obstruction or excessive secretions, prior to initiating treatment for intraoperative bronchospasm. Bronchospasm that is due to asthma often responds to deepening of anesthesia alone (volatile agent, propofol). If bronchospasm persists despite an increase in the concentration of delivered anesthetic drugs, albuterol should be administered by attaching a metered dose inhaler to the anesthetic delivery system, and administration of intravenous corticosteroids should be considered. In an emergency, *intravenous epinephrine* may be required to relieve the bronchospasm.

Chronic Obstructive Pulmonary Disease

The CDC estimates that 15 million Americans are afflicted with COPD, and as of 2011, it was listed as the 3rd leading cause of death in the United States. Of note, it is estimated that approximately 50 % of adults with diminished respiratory function are not aware that they may have COPD (are asymptomatic), so the actual prevalence of this disease may be even greater.

COPD is characterized by a progressive chronic inflammation of the lower airways and lung parenchyma, and expiratory flow obstruction, which is not fully reversible with bronchodilators. The foremost cause of COPD is long-term exposure to tobacco smoke. Other irritants such as pollution and repeated pulmonary infections also contribute to the development of COPD, but to a much lesser extent. COPD encompasses two distinct entities, emphysema and chronic bronchitis (Table 28.7).

- Emphysema is caused by destruction of alveoli, respiratory bronchioles, and small airways with resultant loss of elastic recoil of the lungs. Normally, the elastic recoil keeps the airways open during exhalation by radial traction; however, in emphysema the diminished elastic recoil predisposes the airways to collapse prematurely during exhalation at higher lung volumes, thereby increasing airway resistance.
- Chronic bronchitis is defined as cough and sputum production for 3 months in each of 2 successive years in a patient with risk factors, most commonly cigarette smoking. Chronic hypoxemia may lead to early development of pulmonary hypertension and resultant right heart failure.

It has been estimated that 25 % of surgical patients smoke, and a further 25 % of surgical patients are ex-smokers, making COPD an important diagnosis to consider preoperatively.

Table 28.7 Differences between Emphysema and chronic bronchitis

Parameter	Emphysema	Chronic bronchitis
Coughing and sputum production	+	+++
Erythrocytosis	Normal hematocrit	Present
$PaCO_2$	Normal	High
Elastic recoil	Decreased	Normal
Pulmonary HTN, Cor pulmonale	Late	Early

Table 28.8 GOLD classification of COPD

Classification of severity of airflow limitation in COPD (Based on post-bronchodilator FEV_1)		
In patients with $FEV_1/FVC < 70$ %		
GOLD 1	Mild	$FEV_1 \geq 80$ % predicted
GOLD 2	Moderate	50 % $\leq FEV_1 < 80$ % predicted
GOLD 3	Severe	30 % $\leq FEV_1 < 50$ % predicted
GOLD 4	Very severe	$FEV_1 < 30$ % predicted

FEV1 forced expiratory volume in one second, *FVC* forced vital capacity, *COPD* chronic obstructive pulmonary disease

The **G**lobal Initiative for Chronic **O**bstructive **L**ung **D**isease (GOLD) guidelines provide criteria for diagnosis and classification of severity for patients with symptoms of chronic cough, sputum production, or exposure to cigarette smoke (Table 28.8).

There is little utility in preoperative pulmonary function tests in patients with COPD since there is scant correlation of these tests with postoperative outcome. Hypercapnia and hypoxemia as detected by arterial blood gases may also help identify patients with severe airflow obstruction. A better predictor than PFT for postoperative risks assessment is through the use of the BODE index, as proposed by Celli et al. The Bode index is a multidimensional grading system used to assess the respiratory and systemic extent of COPD and is a better predictor of mortality than using FEV_1 % alone. Patients with higher BODE scores are at higher risk for death. This grading system is based on four variables, and ranges from 0 to 10 points:

- (B) **B**ody mass index (0 point for >21, 1 point for ≤21)
- (O) Severity of airflow **O**bstruction (0–3 points, FEV1 % predicted >65/>64–50/>49–36/<35)
- (D) Functional **D**yspnea (0–4 points, as per the MMRC dyspnea scale)
- (E) **E**xercise capacity as assessed by a 6-min walk test (0–3 points for walking a distance of >350/349–250/249–150/<149 m)

The modified medical research council dyspnea scale (MMRC) classifies dyspnea as follows: 0—Dyspneic with strenuous exercise, 1—Dyspneic on walking up a slight hill, 2—Dyspneic on walking on level ground with stopping occasionally due to breathlessness, 3—Must stop for breathlessness after walking 100 yards or after a few minutes, 4—Cannot leave house and become breathless on dressing/undressing,

Treatment of patients with COPD is supportive and consists of cessation of smoking and administration of bronchodilators (β_2 adrenergic agonists, glucocorticoids, and/or ipratropium). Antibiotics are administered in the presence of a pulmonary infection. Patients with PaO_2<60 mmHg (hypoxemia) require supplemental oxygen. Patients with chronic hypoxemia may also require home oxygen supplementation (1–2 L/min via nasal cannula). It should be remembered that oxygen should be administered carefully to patients dependent on their hypoxic respiratory drive (patients with CO_2 retention). Elevation of PaO_2 can eliminate their hypoxic drive causing respiratory depression, which will further elevate their $PaCO_2$.

Anesthetic Considerations

There is no "right way" to provide anesthesia for patients with COPD. Rather, knowledge of the underlying pathophysiology of the disease and the individual patient characteristics allow the clinician to tailor the anesthetic to fit the patient. The patient's respiratory status should be optimized before surgery, as described above under management of asthma. Optimization of the patient includes cessation of smoking, correction of hypoxemia, treatment of bronchospasm, pulmonary toilet to mobilize and reduce secretions, and treatment of infections. Other investigations include a chest radiograph, arterial blood gas, and PFTs, as necessary. Patients with PFT values less than 50 % of predicted are at a greater risk for development of postoperative pulmonary complications.

Regional anesthesia is preferable over general anesthesia, but a high block level may cause a decrease in lung volumes and loss of use of accessory muscles of respiration and produce an ineffective cough, which can lead to hypoxemia. General anesthesia consists of adequate preoxygenation, use of an inhalation agent, and avoidance of nitrous oxide, Nitrous oxide is avoided in patients with bullae and pulmonary hypertension, as rupture of bullae can lead to a pneumothorax. One should have a high degree of suspicion for development of a tension pneumothorax. Signs of a tension pneumothorax include hypoxemia, hypotension, high peak airway pressures, decreasing tidal volumes, and absent breath sounds/chest movement on side on the pneumothorax. Placing a needle in the second intercostal space in the midclavicular line can be life saving. This is followed by placing a chest tube by the surgeon.

Since hypoventilation is a frequent component of many patients with COPD, it is important to use narcotics judiciously to prevent further depression of the patient's respiratory drive. Additionally, intraoperative hyperventilation can lead to severe alkalosis with associated decreased cerebral

blood flow, as well as difficulty with extubation due to depressed respiratory drive at the time of extubation. A reasonable approach to management is to obtain a room air arterial blood gas prior to induction of anesthesia, which allows the anesthesiologist to gain an awareness of the patient's baseline $PaCO_2$ and pH values. Ventilation during the surgery can be guided by periodically assessing the $PaCO_2$ and pH, which at the end of the case will help to guide the suitability for extubation.

Patients with COPD do not require a specific ventilation strategy, but the use of relatively low tidal volumes with long expiratory times (slow rate) can help reduce ventilator associated trauma. PEEP can often be beneficial as it may help stent airways open that are at risk of collapse from loss of elastic recoil. Nitrous Oxide should be avoided as it may increase the risk of gas trapping in emphysematous bullae and risk their rupture, as described above. Inspired oxygen should be kept at a reasonable level to provide a margin of safety, but too much oxygen may worsen *V/Q* mismatch and may lead to severe postoperative absorption atelectasis in poorly ventilated respiratory areas.

Restrictive Lung Diseases

These diseases include acute respiratory distress syndrome (ARDS), aspiration pneumonitis, pulmonary infections, and chronic interstitial lung diseases producing pulmonary fibrosis, such as idiopathic pulmonary fibrosis, sarcoidosis, radiation pneumonitis, and drug induced (bleomycin). Lung volumes are reduced, with proportional decreases in FEV_1 and the FVC, so the FEV_1/FVC ratio is normal (Table 28.9). The lung compliance is reduced in restrictive lung diseases.

If possible, surgery should be deferred in the presence of an acute infection. If surgery is to be done in an emergency, the ventilation and oxygenation should be optimized (FiO_2, PEEP, diuretics, vasodilators, inotropes). Peak airway pressures should be kept below 30 cm H_2O to avoid barotrauma, the tidal volume should be reduced (5 ml/kg) with a faster respiratory rate.

Patients with chronic disease present with dyspnea, nonproductive cough, fine crackles over lung bases, and in late stages, with evidence of right ventricular failure and pulmonary hypertension. Chest imaging may show a ground glass or honeycomb appearance. Certain patients may be receiving glucocorticoids and immunosuppressive therapy. Patients with restrictive lung disease are prone to developing rapid hypoxemia on induction of anesthesia, and development of oxygen-induced toxicity. Therefore, the FiO_2 may be kept to a minimum with toleration of oxygen saturation of about 90 %.

Table 28.9 Lung volumes and capacities in obstructive and restrictive lung disease

Lung parameter	Obstructive	Restrictive
FEV_1	Decrease (↓↓)	Decrease (↓)
FVC	Decrease (↓)	Decrease (↓)
FEV_1/FVC	Decrease	Normal
FRC	Increase	Decrease
RV	Increase	Decrease
TLC	Increase	Decrease
FEF 25–75 %	Decrease	Normal

FEV1 forced expiratory volume in 1 s, *FVC* forced vital capacity, *FRC* functional residual capacity, *RV* residual volume, *TLC* total lung capacity, *FEF* forced expiratory flow

Pulmonary Hypertension

Pulmonary arterial pressure is considered normal between 8 and 20 mmHg. Pulmonary hypertension (PH) is, therefore, defined as a sustained elevation of the pulmonary artery pressure greater than 25 mmHg at rest, or more than 30 mmHg during exercise, with a mean pulmonary wedge pressure and left ventricular end-diastolic pressure of less than 15 mmHg. The etiology of PH can be quite variable. The WHO has proposed five distinct etiologies of PH:

- Group I is pulmonary arterial hypertension, and comprises of idiopathic, collagen vascular diseases, HIV, congenital shunts, etc. This group comprises a minority of cases.
- Group II is pulmonary venous hypertension and is due to left-sided heart disease. This is the most common cause of PH.
- Group III is pulmonary hypertension associated with hypoxemia, and is due to pulmonary disease and chronic high altitude exposure.
- Group IV is pulmonary hypertension due to chronic thrombotic or embolic disease.
- Group V consists of most other causes including sarcoidosis, tumors, etc.

Indicators of significant disease include dyspnea at rest, chronic hypoxemia, syncope, metabolic acidosis due to low cardiac output, and signs of right heart failure on physical examination. Diagnostic evaluation of PH includes echocardiogram, a chest X-ray, and evaluation for possible known etiologies, such as a spiral CT for pulmonary embolism, pulmonary function testing for underlying pulmonary disease, and right heart catheterization. Right heart catheterization still remains the gold standard for diagnosis as it accurately measures the pulmonary artery pressure, as well as the cardiac output and left-sided filling pressures. In addition, the pulmonary artery catheter is used to determine response to vasodilators, which is an important first step in therapy.

Long-standing pulmonary hypertension results in elevated right heart pressures, with associated RV hypertrophy and eventual RV failure, if untreated. The right ventricle is dependent upon the systemic arterial pressure for perfusion via the right coronary artery. As the right ventricular function worsens due to pressure overload, cardiac output drops as less blood is delivered to the left heart. Systemic pressure then begins to fall to the point that the RV becomes ischemic. Rapid RV failure then ensues with eventual cardiac arrest and death. Chest compressions are typically not very effective in restoring blood flow through the high resistance pulmonary circuit.

Anesthetic Considerations

Care of the patient with significant pulmonary hypertension requires careful monitoring of both cardiac output and pulmonary artery pressure. A pulmonary artery catheter is usually required for the intraoperative management of this patient population. Minimizing triggers which increase pulmonary vascular resistance such as hypoxemia and hypercarbia and stresses such as cold and pain is essential. Nitrous oxide use is avoided in patients with PH. In addition, preserving cardiac output by providing adequate preload, avoiding arrhythmias and hypotension, and maintaining systemic afterload to sustain right ventricular perfusion is absolutely necessary.

Options for treatment of pulmonary hypertension during surgery include inhaled nitric oxide (0–20 ppm), inhaled prostacyclin, and IV phosphodiesterase inhibitors such as milrinone. Beta agonists, such as dobutamine or epinephrine, may be required to improve cardiac contractility to preserve cardiac output during surgery. Vasopressin is a good choice for improving systemic afterload, and thereby improving right heart ventricular perfusion, as it is believed to spare constriction in the pulmonary and coronary vascular beds.

The goals of care in the postoperative period are essentially the same as for intraoperative management. Avoidance of triggers which worsen pulmonary arterial resistance and maintenance of adequate cardiac output is essential. Excellent pain control is mandatory, but judicious use of narcotics is also necessary as they may worsen hypoxia and hypercarbia. Regional analgesia, such as a thoracic epidural, is typically an excellent adjunct for pain control. Morbidity and mortality in the postoperative period are significant concerns, as possible etiologies include pulmonary vasospasm, increases in pulmonary arterial pressures, fluid shifts, cardiac arrhythmias, and heightened sympathetic tone due to pain.

Obstructive Sleep Apnea

Obstructive sleep apnea (OSA) is a serious disorder that is associated with significant comorbidity and postoperative complications in patients undergoing surgical procedures. Currently OSA is estimated to occur in roughly 3–7 % of adult men and 2–5 % of adult women. The actual prevalence may be significantly higher since it is suspected that 70–80 % of patients with OSA remain undiagnosed. The incidence of OSA increases with age, obesity, smoking, and alcohol use. Obesity is the most significant risk factor for developing OSA. A body mass index greater than 30 kg/m^2 or a neck circumference greater than 44 cm positively correlates with severe OSA.

OSA is associated with severe comorbidities including systemic hypertension, coronary artery disease, congestive heart failure, pulmonary hypertension, stroke, and impaired glucose metabolism. Chronic episodes of hypoxemia are thought to be the most likely mechanism for cardiac comorbidities associated with OSA. Impaired glucose metabolism is associated with OSA, but not independently from obesity, so it is difficult to tell if it is a true independent comorbidity of OSA.

It is not surprising that patients with OSA are at higher perioperative risk. Hypertension, coronary artery disease, congestive heart failure, and pulmonary hypertension have all been well correlated with higher surgical risk and worse outcomes in patients with these conditions. Adverse neurologic outcome after surgery is also seen in patients with OSA, as a high incidence of OSA has been reported among stroke patients undergoing rehabilitation. Stroke patients with OSA have significant cognitive and functional impairment compared to stroke patients without OSA. Aside from stroke risk, OSA has also been demonstrated to increase the risk of postoperative delirium in non-demented older patients. Delirium has been seen in multiple studies to be associated with increased morbidity and mortality and a possible predictor of long-term cognitive decline and dementia.

Anesthetic Considerations

The typical risk factors for OSA, namely obesity and/or a large neck circumference, also increase the possibility of difficulty securing the airway. A thorough examination of the airway should be performed in all OSA patients with close attention paid to the size of the pharyngeal space as well as neck circumference. Deposition of fat in the pharynx decreases the airway size and increases the likelihood of obstruction. Pharyngeal fat is reflected in the patient's neck circumference and is strongly correlated with OSA and difficulty with direct laryngoscopy.

Regional anesthesia may be preferable in cases where general anesthesia is not an absolute necessity. To avoid hypoventilation and airway obstruction, the use of sedation during regional anesthesia should be minimized or avoided altogether. If a deeper level of anesthesia is required, then the airway should be secured to ensure adequate patency throughout the case. Tracheal intubation can be facilitated by

thorough preparation for a likely difficulty airway. The patient should be positioned on a ramp if they have significant upper body obesity to improve the view via laryngoscopy. Other techniques for securing a difficult airway should be readily available including an LMA, a fiberoptic bronchoscope, and/or a video laryngoscope. The typically obese patient with OSA also presents the additional challenge of a reduced FRC, with rapid oxygen desaturation following induction of anesthesia, and while attempting intubation.

Once the airway is secured, plans should be made for the eventual extubation of the patient. Minimizing the use of long-acting respiratory depressants such as narcotics and benzodiazepines will help facilitate the return of airway patency. The use of non-narcotic adjuncts such as intravenous acetaminophen, ketorolac, lidocaine, or ketamine can help alleviate pain and not depress the respiratory drive further. Close monitoring of the patient in the recovery room or ICU for signs of airway obstruction or hypoventilation is mandatory. The use of noninvasive ventilation strategies such as CPAP or BiPAP may be required to safely transition the patient from the OR to the hospital environment.

Thoracic Surgery

The major challenges in anesthesia for thoracic surgery are establishing adequate separation of the lungs, maintaining acceptable gas exchange, and ensuring circulatory stability during one-lung anesthesia. One-lung anesthesia involves the deliberate ventilation of the dependent, or nonoperative, lung by isolating its bronchus from that of the operative, or nondependent, lung using specially designed endotracheal tubes. In addition, thoracotomy incisions are associated with severe pain and potentially deleterious changes in cardiopulmonary physiology after surgery, such as profound hypoventilation due to pain from the incision. Some of these physiologic changes can be minimized by thoracic epidural analgesia for effective postoperative pain control.

Preoperative Assessment

Patients undergoing thoracic surgery are at high risk of developing postoperative pulmonary complications, particularly if there is coexisting underlying pulmonary disease. Risk factors associated with increased perioperative morbidity and mortality include the extent of lung resection (pneumonectomy > lobectomy > wedge resection), preexisting pulmonary disease, smoking, obesity, age >70 years, experience of the operating surgeon, and predicted poor postoperative pulmonary function.

Preoperative preparation starts with a thorough history and physical examination. Lung surgery is most commonly performed for malignant lung tumors; non-small cell carcinomas (80 %), and small cell carcinomas (20 %). Patients with lung tumors commonly present with weight loss, cough, dyspnea, wheezing, and hemoptysis, Presence of fever and sputum production indicate the development of pneumonia, while compression of recurrent laryngeal nerve leads to hoarseness of voice. Other signs include Horner's syndrome from involvement of the sympathetic chain, dysphagia from compression of esophagus, superior vena cava syndrome, pleuritic chest pain from pleural involvement, or pericardial effusion from cardiac involvement. Metastasis may occur to the brain, bone or liver.

Small cell carcinoma may be associated with Lambert–Eaton syndrome (proximal myopathy in which muscle strength increases with repeated effort) and ectopic hormone production (ACTH—Cushing's syndrome, vasopressin-hyponatremia, parathyroid-hypercalcemia). Since most small cell carcinomas have already metastasized by the time they are diagnosed, they are preferably treated with radiation and chemotherapy. Non-small cell carcinomas are preferably treated by surgical resection.

Preoperative testing includes arterial blood gas analysis, and chest radiography, CT scans and MRI are performed to determine the extent of tumor, and the amount of tracheal or bronchial deviation. A baseline EKG is done as perioperative supra ventricular arrhythmias (tachycardia) are common due to surgical manipulation of the right atrium. Patients with associated cardiac disease undergo echocardiography and stress testing.

Patients with lung disease should have minimal sedation as it can further aggravate hypoxemia. Glycopyrrolate is commonly administered to reduce secretions and help with airway visualization. For effective postoperative pain control, a thoracic epidural catheter may be placed preoperatively while the patient is sedated but conscious. Patients undergoing thoracotomy should have a large bore IV (18/16G), and an intra-arterial catheter in place to permit continuous monitoring of systemic blood pressure and periodic measurement of arterial blood gases and pH. Although somewhat controversial, a central venous catheter may be helpful for guiding intravenous fluid replacement during extensive operations such as pleuro-pneumonectomies, or if the use of inotropes or vasopressors is anticipated. A catheter should be inserted into the bladder of patients who are expected to undergo long operations associated with blood loss or receiving large amounts of intravenous fluids.

Smoking Cessation

Smoking increases airway irritability and secretions, decreases mucociliary transport, and increases the incidence of postoperative pulmonary complications. Tobacco smoke contains carbon monoxide (CO) which binds to Hb to form carboxyhemoglobin. CO has approximately a 250-fold greater affinity for hemoglobin than oxygen, thereby keeping Hb in its bound conformation and reducing

oxygen dissociation and associated O_2 delivery to tissues. Cessation of smoking for 12–24 h before surgery decreases the level of carboxyhemoglobin, shifts the oxyhemoglobin dissociation curve to the right, and increases oxygen availability to tissues. However, improvement in mucociliary transport, small airway function, optimal wound healing, and decreases in sputum production require prolonged abstinence (8–12 weeks) from smoking. The incidence of postoperative pulmonary complications in patients undergoing thoracic surgery decreases when abstinence from cigarette smoking is longer than 8 weeks.

Determination of Resectability

To determine resectability, the tumors are anatomically staged by chest radiography, CT scan, bronchoscopy, and mediastinoscopy. Tumors that have spread to the contralateral side are usually not resectable. The extent of surgery should maximize the chances of cure, but at the same time allow for adequate residual pulmonary function. Lobectomy is the most commonly performed procedure (mortality 3 %), while wedge or segmental resection is performed for smaller lesions. Pneumonectomy (mortality 6 %) is performed for extensive lesions, and for lesions involving the right or left bronchus.

Spirometric testing is commonly used as the first step to evaluate the suitability of patients for lung resection surgery. Spirometric testing is accomplished by having the patient breathe at normal tidal volumes, take in a maximal inspiration, and then breathe out a forced maximal exhalation. Maximal patient effort is essential in getting good, reliable, and reproducible results. Many values are obtained by spirometry including the forced vital capacity (FVC), total lung capacity (TLC), forced expiratory volume in one second (FEV_1), and the diffusion capacity of the lung for carbon monoxide (DLCO).

Most of these values are not particularly important as preoperative predictors of surgical outcome, but two values, the FEV_1 and DLCO, do stand out as predictors of surgical risk. The FEV_1 and DLCO have been shown to be predictive in many studies to determine suitability for lung resection. The ACCP has published guidelines for the workup of patients who are being considered for lung resection surgery. A preoperative FEV_1 of 1.5 L for lobectomy or 2 L for pneumonectomy is the cutoff for average risk, while patients with FEV_1 values below this are considered to be at increased perioperative risk. In a similar manner, a DLCO of 80 % predicted is cutoff for average risk, as patients with less than this value (<40 % predicted) are considered to have a higher than average surgical risk (Table 28.10).

In patients who do have a low FEV_1 or DLCO, further workup should be performed to help accurately assess risk prior to lung resection surgery. This group of patients should have an estimate made of predicted postoperative lung function. This can be achieved by either simply counting the number of functional lung segments to be removed (the anatomic method), or more precisely, through *V/Q* scans or quantitative CT scans.

Table 28.10 High-risk preoperative criteria for pneumonectomy

FEV_1	<2 L
Predicted postoperative FEV_1	800 ml or <40 % predicted
FEV_1/FVC	<50 % predicted
Maximum oxygen consumption during exercise	VO_2 < 10 ml/kg/min
Predicted postoperative diffusion capacity for carbon monoxide (DLCO)	<40 %
Arterial blood gas	Room air PaO_2 < 50 mmHg, $PaCO_2$ > 45 mmHg

For those patients in whom a predicted postoperative FEV_1 or DLCO yields a value that is less than 40 %, formal cardiopulmonary exercise testing to establish maximum oxygen consumption (VO_{2max}) is recommended. A value of VO_{2max} less than 15 ml/kg/min places the patient in the high-risk group. Clearly, the lower the VO_{2max} the less likely the patient will tolerate a surgical resection. If formal exercise testing is not available, suitable alternatives such as a 6-min walk test, stair climb, or a shuttle-walk test may be used. Patients who cannot climb one flight of stairs or complete 25 shuttles are likely to have a VO_{2max} less than 10 ml/kg/min, and are at very high risk for respiratory complications and mortality following lung resection.

Separation of the Lungs (One-Lung Anesthesia)

Separation of the lungs is perhaps the most important anesthetic procedure for patients undergoing thoracic surgery (Table 28.11). Separation permits intraoperative one-lung ventilation, greatly facilitating the surgical procedure. Double-lumen endobronchial tubes (DLT), and bronchial blockers (BB) with single-lumen endotracheal tubes, enable anatomical isolation of the lungs and facilitate lung separation.

Anatomic Considerations

Tracheobronchial anatomy should first be assessed by reviewing preoperative radiologic studies. In addition, bronchoscopy is very helpful prior to surgery to detect abnormal anatomy that may complicate lung separation. For example, a markedly distorted carina or a proximal endobronchial tumor may necessitate fiberoptic-guided endobronchial intubation.

Tracheobronchial dimensions in general are approximately 20 % larger in men than women. In adults, the trachea is about 11–13 cm in length and begins at the level of C6 or the cricoid cartilage. At the level of T5, the trachea divides into the right- and left-main bronchus. The right-main bronchus diverges from the trachea at an angle of 25°, while the left-main bronchus diverges at 45°. The right-main bronchus

is shorter but wider than the left. The right upper lobe bronchial orifice is about 1–2.5 cm from the carina, while the left upper lobe bronchial orifice is 5 cm from the carina. Although there is variation in tracheal and bronchial widths among the population, within individual patients a significant correlation between tracheal and bronchial widths has been determined: Bronchial diameter is predicted to be 0.68 of tracheal diameter. The implications of these dimensional relationships are the following: (1) a left-sided DLT is preferred because uniform ventilation to all lobes will most likely be achieved and (2) measurement of tracheal width from postero-anterior chest roentgenogram can help select the size of a left-sided DLT.

Table 28.11 Indications for lung separation

Prevent contamination or spillage
Infection
Hemorrhage
Unilateral bronchopulmonary lavage
Control of the distribution of ventilation and/or PEEP
Bronchopleural fistula
Unilateral lung cyst or bullous disease
Severe hypoxemia due to asymmetric lung disease
Enhance surgical exposure
Pneumonectomy/lobectomy/wedge resection
Thoracic aneurysm repair
Esophageal resection
Anterior mediastinal exploration with hilar extension
Lung transplantation
Procedures on the thoracic spine

Left-Sided DLT

The left-sided DLT is the most reliable and widely used approach for endobronchial intubation in one-lung anesthesia. Several manufacturers, such as Mallinckrodt and Rusch, manufacture clear, disposable PVC tubes. The DLT consists of two lumens, a longer blue bronchial lumen with a high pressure–low volume cuff, and a shorter clear tracheal lumen with a low pressure–high volume cuff. In general, a 35/37 French tube can be used for most adult females, and a 39/41 French for most adult males. This corresponds to an internal diameter of 5.0, 5.5, 6.0, and 6.5 mm, respectively. A typical left-sided DLT is shown in Fig. 28.15. Although there is no specific guide to the correct size of a DLT, rough DLT sizing is listed in Table 28.12. A proper size DLT should pass through the airway easily, causes no trauma, aligns well with the intended bronchus, and forms a good seal with both the tracheal and bronchial cuffs.

Advantages of DLT, because of their larger size, over other techniques include the ability to pass suction catheters to clear secretions, application of CPAP to the operative lung, and the ability to pass a pediatric fiberoptic scope with ease. Care should be taken to not overinflate the bronchial cuff, as it may lead to mucosal ischemia. It is prudent to deflate the bronchial cuff when one-lung ventilation is not required.

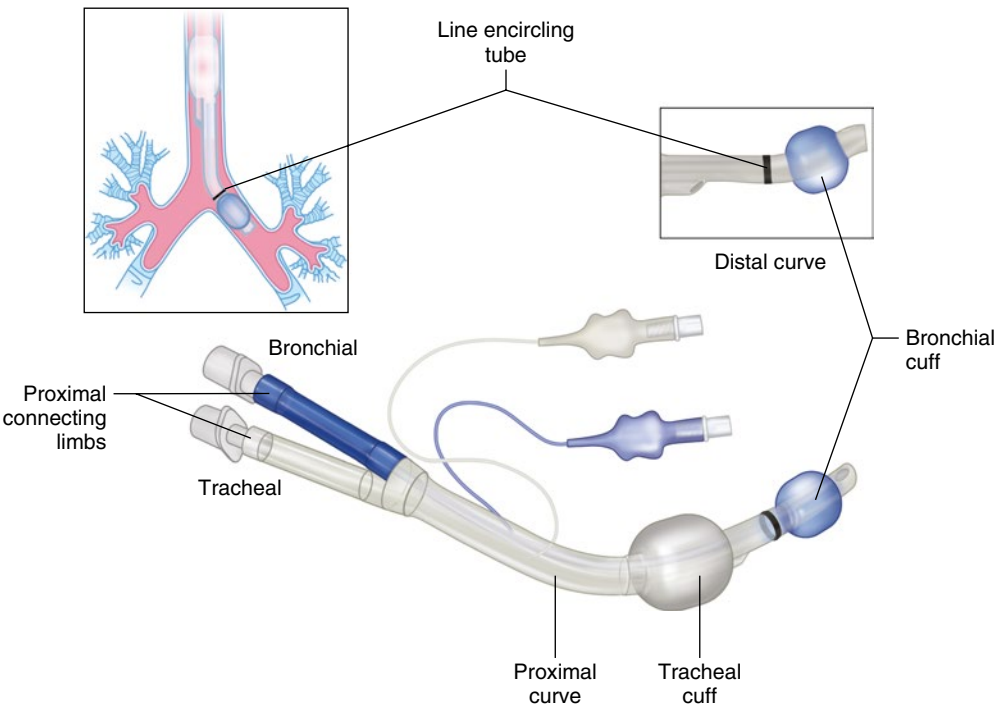

Fig. 28.15 Left-sided double-lumen endobronchial tube. Note the distal *black line* and the *insert* showing its position at the carina

Table 28.12 Rough sizing of double-lumen tube

Parameter	Patient	Tube size (French)
Tracheal width (mm) on chest X-ray	18 mm	41
	16 mm	39
	15 mm	37
	14 mm	35
Patient height	≥ 6 ft	41 (male), 39 (female)
	5′5″–5′11″	39 (male), 37 (female)
	≤5′4″	37 (male), 35 (female)
Age	<14 years	26–35

Insertion Technique

Endobronchial intubation is usually accomplished by direct laryngoscopy following induction of general anesthesia and neuromuscular blockade. The tube is held so that the distal bronchial curve faces anteriorly, while the proximal curve is to the right. The bronchial cuff is inserted through the vocal cords, and the stylet is removed. Next, while advancing, the tube is rotated 90° to the left, directing the bronchial lumen to the left-main bronchus, so that the blue proximal connecting bronchial lumen is on the patient's left side, and the clear proximal connecting tracheal lumen is on the patient's right side. The tube is advanced until a moderate resistance to further passage is encountered. Force should never be used during advancement of the tube; resistance usually indicates impingement within the main-stem bronchus. If any difficulty or resistance in placing or advancing the DLT is encountered, then a fiberoptic scope can be inserted through the bronchial lumen and the DLT is placed under direct vision. The tracheal cuff is inflated with 5–10 ml of air, while the bronchial cuff is inflated with 1–2 ml of air.

An estimate of the appropriate depth of placement of a DLT can be based on the patient's height. The average depth of insertion referenced to the corner of the mouth is 29 cm for patients 170 cm tall, and for each 10 cm increase or decrease in height, average depth of placement correspondingly changes by 1 cm. In addition, correct DLT position must be confirmed by chest auscultation and by fiberoptic visualization. Intraoperatively, if clamping or stapling of the left main-stem bronchus is necessary, the DLT is withdrawn under fiberoptic guidance to above the carina, and ventilation of the right lung is continued through the bronchial lumen. This approach may be used for lung separation during a left pneumonectomy.

Algorithm for Determining Proper Left-Sided DLT Position (Fig. 28.16)

While physical examination (auscultation) to confirm left-sided DLT position is widely used, and considered by many to be a reliable method to verify correct position, several clinical studies using fiberoptic assessment have shown malpositioning of left-sided double-lumen tubes in 20–48 % of cases. Perhaps the most important tool to facilitate

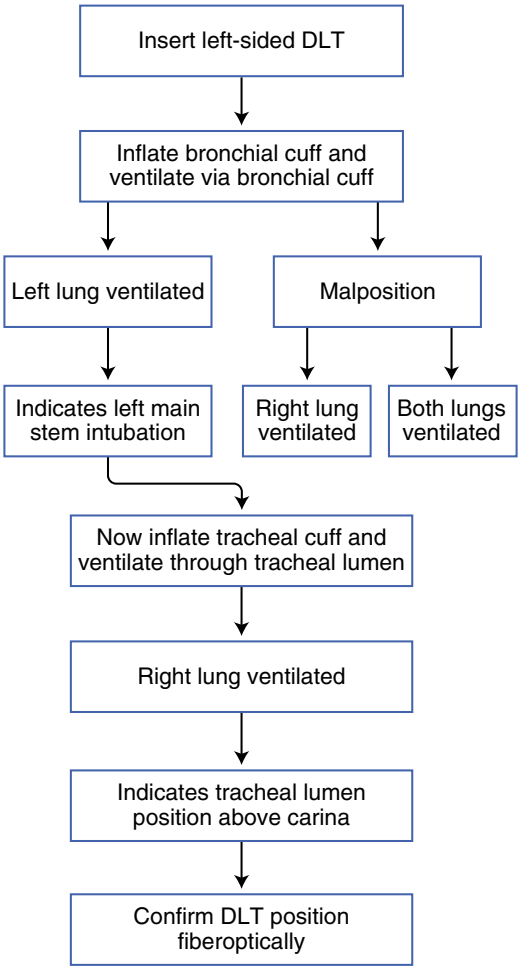

Fig. 28.16 Algorithm for determining the position for a left-sided double-lumen endobronchial tube. A sequence of cuff inflations and positive pressure ventilations is performed to confirm tube position and functional isolation of the lungs. The sequence starts by inflating the bronchial cuff slowly with 0.5–1 ml of air. Initial ventilation through the bronchial lumen should produce left lung ventilation. A malpositioned tube could result in either the right lung or both lungs being ventilated. Confirmation of ventilation of the left lung indicates that the bronchial lumen has entered the left-main bronchus. Next, the tracheal cuff is inflated. Ventilation through the tracheal lumen should produce only right lung ventilation, indicating that the tracheal lumen is above the carina. Fiberoptic visualization confirms or aids in correct tube positioning

confirmation of a DLT position is fiberoptic bronchoscopy. A 3.6 mm fiberscope is initially passed through the tracheal lumen. Correct position of the tube is confirmed by:

- Visualizing the carina
- Non-obstructed view of the right main-stem bronchus
- Takeoff of the right upper lobe bronchus
- Blue bronchial cuff below the carina (Fig. 28.17a)
- Visualization of the line encircling the tube. This line is 4 cm from the distal lumen, and it should ideally be positioned at or slightly above the carina. Fiberoptic visualization through the bronchial lumen reveals the bronchial carina and the left lower and upper lobes (Fig. 28.17b).

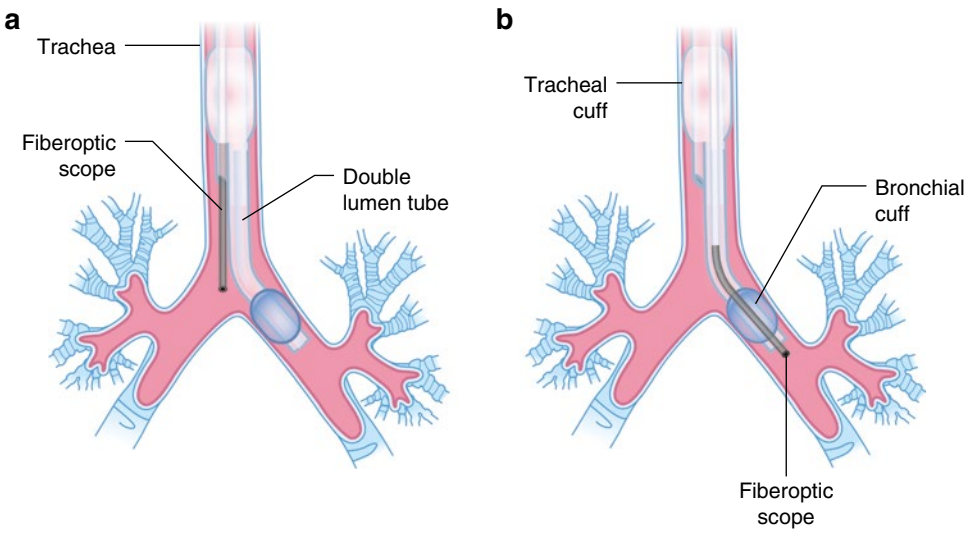

Fig. 28.17 Fiberoptic visualization confirming correct position of left-sided double-lumen tube. (**a**) Fiberoptic scope inserted through the tracheal lumen. (**b**) Fiberoptic scope inserted through the bronchial lumen

Malpositioned Left-Sided DLT

A malpositioned left-sided DLT may occur during initial placement, following surgical positioning, or during surgery. A malpositioned tube is usually detected by clinical signs and changes in lung mechanics. The tube may be too deep, not deep enough, or in the right side. When the tube is too deep, the blue bronchial cuff may not be visible, and it may occlude the left upper bronchial opening. When the tube is not deep enough, the bronchial cuff may be in the trachea (above the carina) and will occlude ventilation of the right bronchus. Deflating the bronchial cuff and advancing the tube into the left bronchus will solve the problem. During initiation of one-lung ventilation, peak inspiratory airway pressure should increase by approximately 50 % when compared to two-lung ventilation at the same tidal volume. When the DLT is malpositioned, peak inspiratory airway pressure will increase by approximately 75 %. Two algorithms define three types of malpositioned left-sided DLTs (Fig. 28.18a, b).

Right-Sided DLT

The short and variable distance of the right upper lobe orifice from the main carina makes the use of a right-sided DLT undesirable for most procedures requiring lung separation. A small change in the position of the tube results in either inadequate lung separation and/or collapse of the right upper lobe. Nevertheless, there are some situations in which it is best to avoid intubation of the left-main bronchus, e.g., in circumstances in which the left-main bronchus is obstructed by tumor, disrupted following trauma, or distorted secondary to a thoracic aortic aneurysm. Right-sided DLTs are designed to incorporate a separate opening in the bronchial lumen to allow ventilation of the right upper lobe (Fig. 28.19). Confirmation of correct right-sided DLT position using physical examination alone results in a 90 % chance of malposition, with most being too deep.

Proper positioning of the right-sided tube must include fiberoptic guidance. The right-sided DLT is inserted into the distal trachea, and the fiberscope is inserted through the bronchial lumen. The tip of the scope is flexed anteriorly to visualize the center of the right upper lobe. The scope is then returned to neutral position viewing the bronchus intermedius. The tube is advanced until the rim of the bronchial lumen comes into view. The fiberscope is withdrawn and its tip flexed anteriorly to visualize the upper lobe through the ventilation slot. The fiberscope is next passed through the tracheal lumen for inspection of the bronchial cuff at the carina and opening of the left-main bronchus. Following lateral positioning of the patient for surgery, fiberoptic inspection should be performed because tube dislodgment is common.

Bronchial Blockers

Lung separation can also be effectively achieved using a single-lumen endotracheal tube and fiberoptically guided placement of a bronchial blocker (BB) via the single-lumen tube. The BB technique can be useful if postoperative ventilation will be required, eliminating the need to exchange the DLT for a single-lumen tube. Using a BB is especially useful when managing a difficult airway. In patients requiring an awake fiberoptic intubation where DLT placement may be difficult or impossible, using a BB may be the only practical approach to lung separation. Confirmation of proper BB position should include fiberoptic bronchoscopy.

A recent study found that all bronchial blockers were equivalent in the degree of lung isolation they provided. However, bronchial blockers required significantly more repositioning for correct placement than did DLTs. Additionally, because of the small size of bronchial blocker, the lung collapses more slowly and sometimes partially when compared to a DLT. Three blocker systems are available, the Univent Bronchial Blocker Tube, the Arndt Endobronchial Blocker, and the Cohen Endobronchial Blocker.

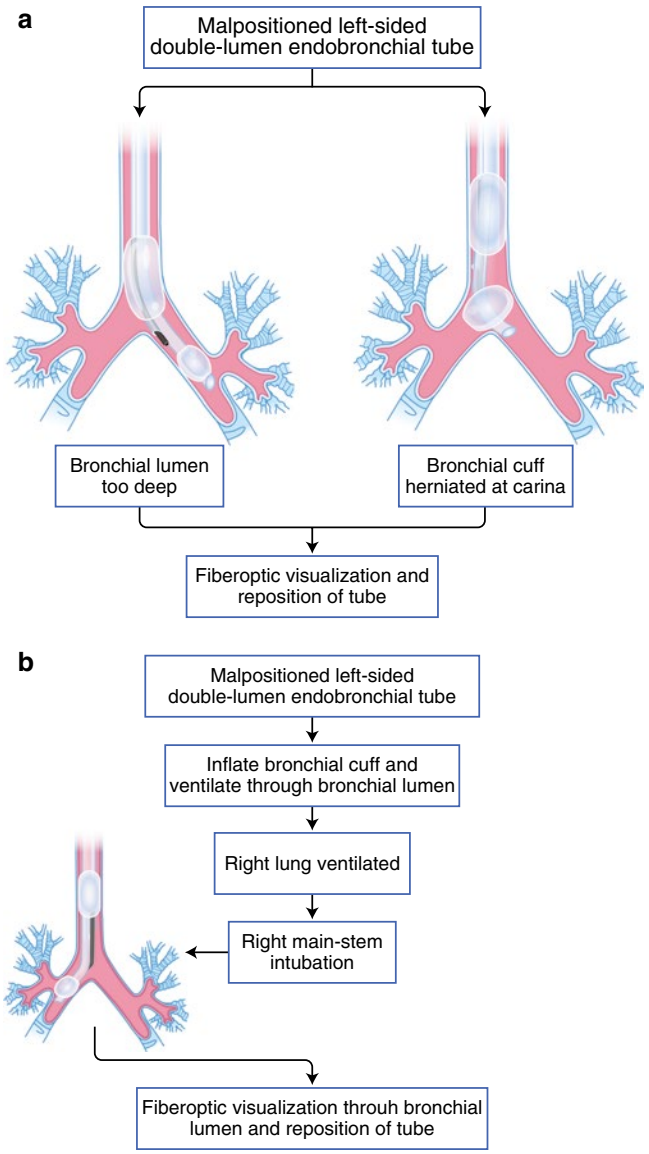

Fig. 28.18 Malpositioned left-sided DLT. (**a**) Ventilation through the bronchial lumen results in left lung ventilation, but ventilation of the right lung through the tracheal lumen results in increased resistance. Fiberoptic visualization through the tracheal lumen identifies either a bronchial lumen that is too deep in the left main-stem bronchus or a bronchial cuff that has herniated over the carina. Repositioning is accomplished with fiberoptic guidance. (**b**) The left-sided DLT is accidentally inserted into the right-main bronchus. Ventilation through the bronchial lumen results in right-lung ventilation. Repositioning of the tube is accomplished by advancing the fiberscope through the bronchial lumen and guiding the tube into the left main-stem bronchus

Univent Bronchial Blocker: The Univent BB Tube has two compartments, a large main lumen for conventional air passage, and a small lumen embedded in the anterior wall permitting passage of the moveable BB, which has a high pressure–low volume cuff (Fig. 28.20). The two fused lumens add to the external diameter of the Univent tube. The blocker is a relatively stiff catheter that has an internal channel measuring 2 mm through which oxygen may be insufflated for CPAP, or secretions could be cleared. Following tracheal intubation with the blocker retracted, initial positioning is accomplished by the tube rotation method. Rotating the tube to the right or left positions rotates the blocker too, so it may be advanced into the corresponding main-stem bronchus. Fiberoptic visualization should be used to confirm appropriate main-stem intubation and to guide the depth of insertion. For right-sided placement, the blocker is positioned in such a way that when the cuff is inflated it partially herniates into the right upper lobe (Fig. 28.21a). For left-sided placement, the blocker should be inserted adequately deep into the left main-stem bronchus to minimize dislodgment into the trachea with surgical manipulation (Fig. 28.21b).

Arndt Endobronchial Blocker: The Arndt Endobronchial Blocker set (Cook®) consists of a wire-guided endobronchial catheter and a multi-airway adapter allowing independent passage of the blocker and fiberscope (Fig. 28.22). The blocker (sizes-9 French/78 cm, 7 F/65 cm, 5 F/50 cm) and a pediatric fiberscope are placed coaxially through a conventional endotracheal tube (minimal size ETTube 8.0, 7.0, 4.5 mm ID, respectively). The blocker is coupled to the fiberscope through the guide loop (protruding at the distal end of the catheter). Once coupled, the fiberscope is advanced into the desired main bronchus. The blocker is advanced while steadying the fiberscope until the guide loop is seen to exit the end of the scope. The fiberscope is then retracted, and endobronchial placement of the blocker is confirmed. After final positioning of the patient, endobronchial blockade is visualized by inflating the 3-cm-long elliptical cuff with approximately 6 ml of air, and the guide loop is removed. Once the wire is removed, the central channel (1.4 mm) can be used for suctioning or CPAP. When using this blocker, it is important to use an appropriate sized ETTube.

Cohen Endobronchial Blocker: The Cohen Flextip Endobronchial Blocker consists of a 9 French external diameter catheter, is 62 cm in length, and contains a 1.6 mm diameter central lumen. Unlike the Arndt blocker, the Cohen blocker does not require a guide loop for placement. Rather, it has a 3 cm soft nylon deflecting tip with a pear-shaped high volume, low pressure balloon at the tip. Placement is accomplished via the deflecting tip, which is controlled by counterclockwise rotation of a wheel positioned at the proximal end of the blocker. A 180° rotation of the wheel results in a 90° deflection of the tip. Like the Arndt blocker, the Cohen blocker uses the same Arndt Multi-Port Adapter (Cook Critical Care) to permit simultaneous ventilation, fiberoptic bronchoscopy, and manipulation of the bronchial blocker. Both the Arndt and Cohen endobronchial blockers have a central lumen to permit insufflation of oxygen if required for intraoperative hypoxia.

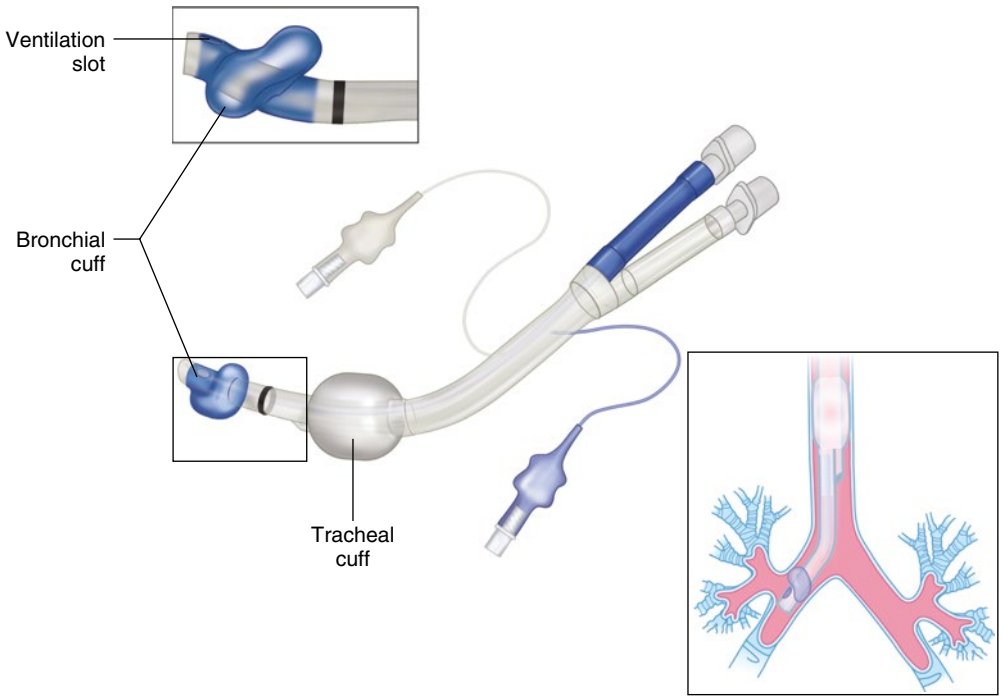

Fig. 28.19 Right-sided double-lumen endobronchial tube

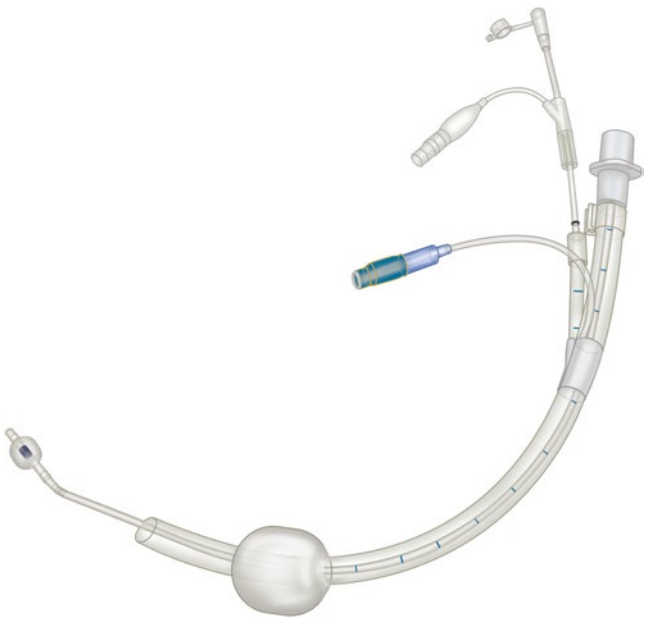

Fig. 28.20 Univent endobronchial blocker

Management of Anesthesia

There are five main goals of anesthesia in thoracic surgery: To produce controlled levels of narcosis and analgesia, to suppress cough and reflex airway activity, to maintain protective reflexes such as hypoxic pulmonary vasoconstriction, to ensure satisfactory blood–gas exchange and cardiovascular stability, and to recover rapidly from anesthesia to avoid postoperative respiratory depression. A practical approach is through a balanced technique with general anesthesia using a potent volatile anesthetic supplemented with intravenous narcotics, along with controlled ventilation.

A thoracic epidural is commonly placed preoperatively for thoracotomies and lung resection surgeries. For epidural placement, the patient should be sitting upright with the head rested on a pillow on a table. Sedation (midazolam, fentanyl) and O_2 supplementation may be provided, as necessary. After placement of the epidural catheter a test dose is given. The epidural may be bolused intraoperatively (2 % lidocaine, 0.25 % bupivacaine or 0.5 % ropivacaine) for pain control. Postoperatively, a patient controlled narcotic-local anesthetic epidural analgesic infusion (PCEA) is started for pain management (typically, a mixture of fentanyl 2 mcg/ml-bupivacaine 1.25 mg/ml, 6–8 ml/h, 2–3 ml boluses every 6–10 min, 4 h limit of 80 ml).

Induction

After adequate preoxygenation, anesthesia is induced with an intravenous anesthetic (propofol). Endotracheal intubation is facilitated by administering succinylcholine or a nondepolarizing agent (rocuronium, vecuronium). If the surgeon initially performs a bronchoscopy, a large single-lumen ETT is inserted 8.0–9.0, which is then changed to a double-lumen tube for the surgery.

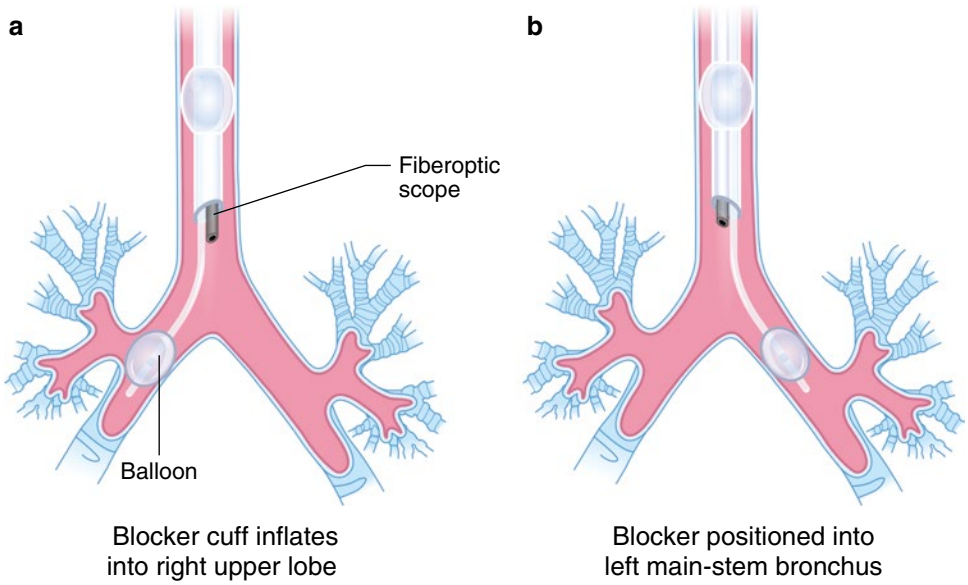

Fig. 28.21 Positioning of Univent bronchial blocker, **a** and **b**

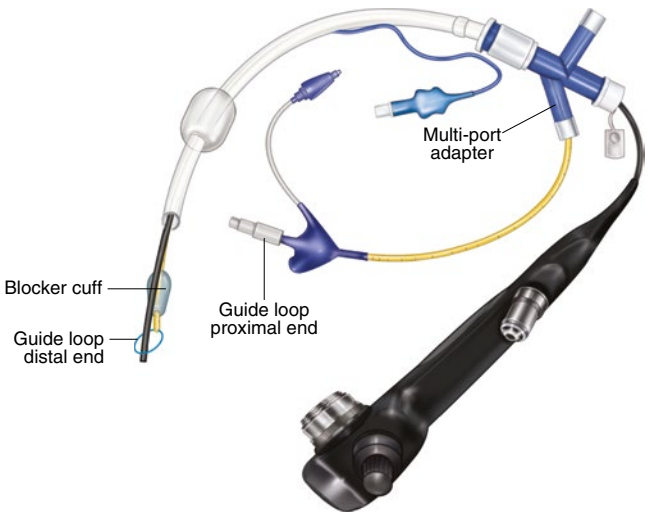

Fig. 28.22 Arndt endobronchial blocker. The Arndt endobronchial blocker and pediatric scope are connected through a multi-port airway adapter. The blocker is coupled to the scope through the guide loop at the distal end of the blocker. Once coupled, the pediatric scope and blocker are advanced into the main bronchus of the lung to be blocked

Positioning

Following induction, the patient is then positioned in the lateral decubitus position (Fig. 28.23). The arms are padded and positioned so that stretching is avoided. The upper arm is put in a support or pillows are placed between the arms. An axillary role is positioned in the dependent axilla to prevent compression of the brachial plexus. The patient's eyes and dependent ear are checked for compression. A bean bag is commonly used to maintain the patient in the lateral decubitus position. The surgeon also asks that the operating table be flexed.

Maintenance

Anesthesia is maintained with oxygen, a narcotic (usually fentanyl), a nondepolarizing muscle relaxant, and a volatile agent. Morphine or hydromorphone are avoided as they are long acting and may cause respiratory depression. If a thoracic epidural is used for pain control intraoperatively, then the amount of intravenous opioid that is administered is reduced. A nondepolarizing neuromuscular blocking drug is administered to facilitate controlled ventilation of the lungs and improve surgical exposure by maximizing mechanical separation of the ribs. Depression of airway reflexes is an important benefit of the volatile anesthetics. This class of agents can also be rapidly eliminated at the conclusion of surgery, allowing rapid recovery from anesthesia. In addition, volatile anesthetics minimally inhibit regional hypoxic pulmonary vasoconstriction and thus aid in the maintenance of arterial oxygenation during one-lung anesthesia. Due to its intrinsic sympathomimetic effects, ketamine may also be useful for induction of anesthesia in emergency thoracotomy situations associated with hypovolemia (blunt trauma, gunshot, and stab wounds).

Administration of intravenous fluids is usually restricted to maintenance requirements and replacement of blood loss. This is because excessive fluid administration with the patient in the lateral position may lead to a gravity-dependent transudation of fluid into the dependent lung known as a "lower lung syndrome" leading to hypoxemia.

Conclusion of Surgery

Near the conclusion of the surgery, when the chest is closed, initiation of spontaneous ventilation may be instituted. This will help to gauge the tidal volume of the patient and determine adequate pain control by noticing the patient's respiratory rate. Hyperinflation of the lungs is important to remove

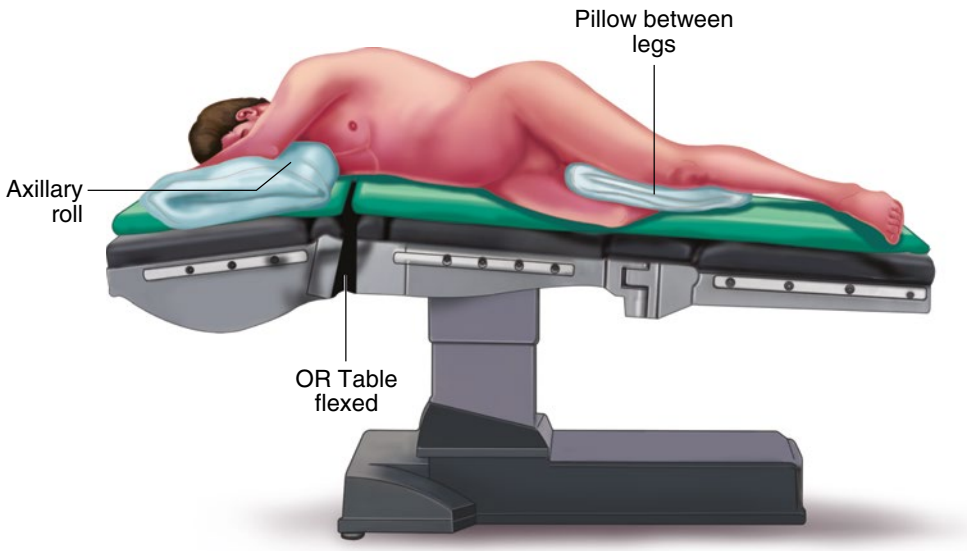

Fig. 28.23 Lateral decubitus position for thoracotomy

air from the pleural space at the conclusion of thoracic surgery. Furthermore, alveoli incised during segmental resection of the lungs continue to leak air into the pleural space, necessitating the placement of chest tubes to minimize the air leak and promote continued expansion of the lung. Chest tubes should be set to continuous suction and must not be allowed to kink, because sudden increases in intrathoracic pressure, as with coughing, may increase the air leak and cause a tension pneumothorax.

Placement of a chest tube is not necessary after pneumonectomy. Intrapleural pressure on the operated side is adjusted by aspirating air to slightly below atmospheric pressure. Excessive negative pressure should be avoided because the mediastinum may shift to the nonoperated side resulting in operated lung hyperinflation. Excessive positive pressure in the pneumonectomized space will compress the residual lung and may lead to hypotension and cardiac output compromise. Nevertheless, many thoracic surgeons prefer the placement of a balanced-drainage system, especially following complicated pneumonectomy. This system allows continuous drainage of the operated hemithorax while maintaining physiologic intrathoracic pressures of −5 cm H_2O.

The balanced-drainage system has three compartments: (1) a collection bottle for fluid, (2) a positive pressure regulator (water seal), where intrathoracic pressure exceeding 1 cm H_2O relative to atmosphere is vented, and (3) a negative pressure regulator (a reverse water seal), where air inflow into the system will occur when pleural pressures are more negative than 10–13 cm H_2O. Unlike the standard Pleur-Evac no suction is applied. The balanced-drainage system chest tube provides for drainage of the postpneumonectomy space in complicated cases while avoiding mediastinal shifts following pneumonectomy.

The trachea may be extubated when the adequacy of spontaneous ventilation is confirmed and protective upper airway reflexes have returned. In otherwise healthy patients, extubation of the trachea may be performed at the conclusion of surgery, especially if adequate pain relief (thoracic epidural analgesia) has been instituted. If mechanical ventilation of the lungs must be continued into the postoperative period, it will be necessary to replace the DLT with a single-lumen tube. This can be accomplished with changing the DLT to a single-lumen tube over a tube exchanger, or alternatively by performing direct laryngoscopy. The patient is then transferred to the recovery room or the ICU.

Gas Exchange During One-Lung Ventilation

Intrapulmonary distribution of blood flow is regulated by gravity, lung volume, and regional pulmonary vascular resistance (PVR). As a result, in the lateral decubitus position, the dependent lung receives a greater proportion of the cardiac output (~60 %). During thoracotomy and mechanical ventilation of both lungs, the proportion of tidal ventilation to the operated (nondependent) lung increases because the lung and thorax compliance in this hemithorax is greater once the chest is opened. In contrast, the dependent lung has low compliance and a low ventilation-per-unit lung volume. Furthermore, the dependent lung is compressed due to pressure from abdominal contents and the weight of the mediastinum, which is no longer offset by the sub-atmospheric pressure in the nondependent hemithorax. These factors, combined with the inhalation of soluble gases, promote atelectasis in the dependent lung. Thus, the nondependent lung is well ventilated but poorly perfused (high ventilation-to-perfusion or *V/Q* ratio) and the dependent lung is well perfused but poorly ventilated (low *V/Q*), Fig. 28.24, Table 28.13. These *V/Q* imbalances lead to altered pulmonary gas exchange.

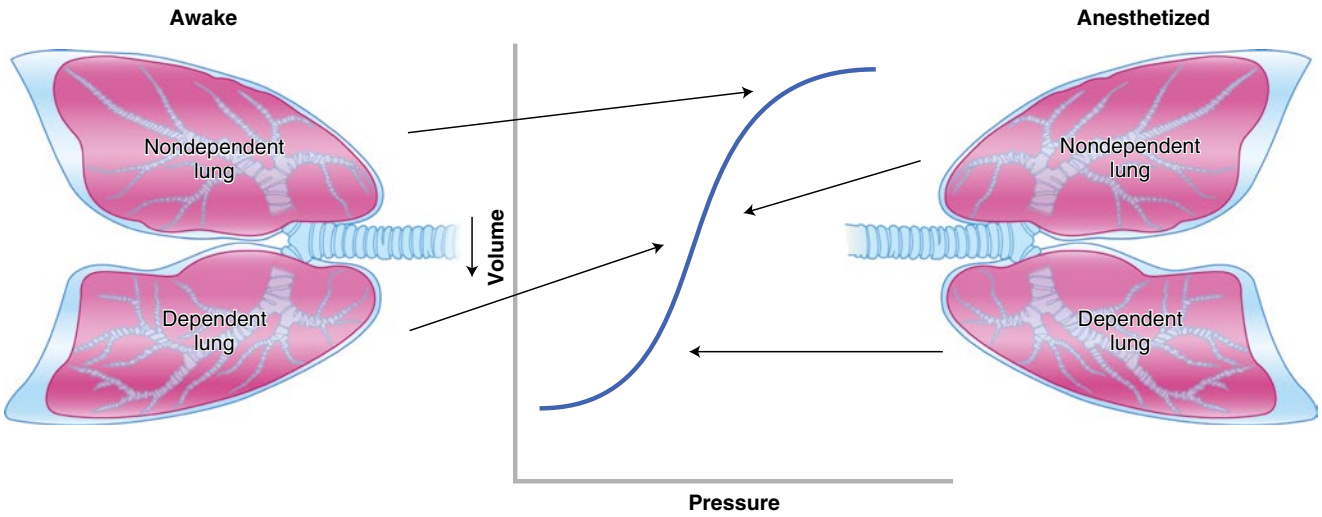

Fig. 28.24 Ventilation in the lateral decubitus position in an awake and anesthetized patient. With induction of anesthesia the lung has moved down the compliance curve

Table 28.13 Lung mechanics in the lateral position

Patient	Ventilation	Chest	Lung	*V/Q* mismatch
Awake	Spontaneous	Closed	Dependent lung better ventilated and perfused than nondependent lung	Minimal
Anesthetized	Spontaneous	Closed	Dependent lung better perfused, nondependent lung better ventilated (reduction in FRC by anesthesia)	Increased
Anesthetized	Paralyzed	Closed	As above, added weight of abdominal organs and mediastinum against the dependent lung	Further increased
Anesthetized	Paralyzed	Open	Dependent lung better perfused, further increase in ventilation to nondependent lung	Worsening

The major disadvantage of one-lung anesthesia is the introduction of an iatrogenic right-to-left intrapulmonary shunt by the continued perfusion of both lungs while only one lung, the dependent lung in the lateral decubitus position, is ventilated (Fig. 28.25). In one representative study, mean PaO_2 at an FiO_2 of 0.99 was approximately 400 mmHg (range 300–500 mmHg) during two-lung ventilation and decreased to a value of approximately 200 mmHg (range 45–450 mmHg) during one-lung ventilation. Following the initiation of one-lung ventilation, PaO_2 decreases progressively during the first 20 min and remains relatively constant thereafter.

The wide variability of PaO_2 and shunting during one-lung ventilation is the result of multiple factors affecting the distribution of blood flow between the lungs. Blood flow is decreased through the nondependent collapsed lung by the effects of gravity, from hypoxic pulmonary vasoconstriction, and by surgical compression. In addition, blood flow diversion may have already occurred in the nondependent lung due to an increase in regional PVR as a result of the underlying pulmonary disease. Although gravity directs more than

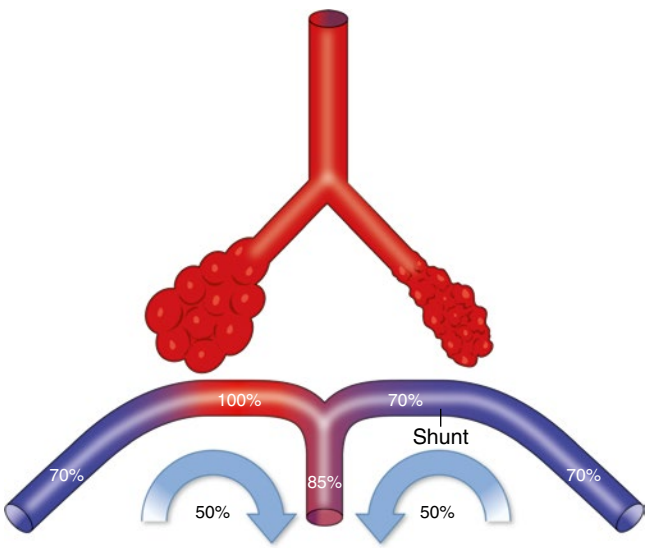

Fig. 28.25 Shunting of blood with ventilation of single lung. Venous blood returning to the lungs (saturation of 70 %), oxygenation of the blood in one lung (saturation 100 %), and shunting of blood in the non-ventilated lung

Table 28.14 Summary of the approach to the management of one-lung ventilation

1.	Deliver a high FiO_2
2.	Initiate tidal ventilation with 5–7 ml/kg
3.	Adjust respiratory frequency to maintain minute ventilation at approximately the same level during two-lung ventilation to keep $PaCO_2$ at baseline
4.	Continuous pulse oximetry and measure arterial blood gases after 15–20 min of one-lung ventilation and thereafter as indicated
5.	Response to hypoxemia:
	(a) Reconfirm proper position of double-lumen tube by fiberscope
	(b) Apply recruitment maneuver to dependent lung
	(c) Titrate 5–10 cm H_2O PEEP to the dependent lung
	(d) Reinflate nondependent lung and insufflate oxygen with CPAP (0–5 cm H_2O)
	(e) Clamp or ligate pulmonary artery or segment of pulmonary artery to nondependent lung during pneumonectomy or lobectomy
	(f) Reposition to semi-lateral decubitus position, if surgery is in supine position
	(g) Resume two-lung ventilation if hypoxemia is uncorrected

half the blood flow to the dependent lung, compensatory factors secondary to underlying disease may increase PVR in the dependent lung as well, thus preventing blood flow diversion from the nondependent collapsed lung.

Management of One-Lung Ventilation

The recommended approach to the management of ventilation during one-lung anesthesia is summarized in Table 28.14. Arterial hypoxemia is a common occurrence during one-lung ventilation (OLV), and an FiO_2 of nearly 1.0 is usually required. Nevertheless, arterial hypoxemia cannot be completely prevented. In approximately 25 % of patients the PaO_2 is ≤80 mmHg, and in 10 % of patients the PaO_2 is ≤60 mmHg.

Two-lung ventilation should be used for as long as possible. On initiation of one-lung ventilation the tidal volume should be reduced slightly to keep from over-distending the ventilated, dependent lung. Any problem on initiation of one-lung ventilation, such as high peak airway pressures or low tidal volumes, usually indicates malposition of the DLT. Proper positioning of the DLT should be confirmed by the fiberoptic scope. Also, dislodgment of the tube is not uncommon following positioning of the patient and again with surgical manipulation. During one-lung ventilation, ventilation should be monitored closely and modified based on pulse oximetry and arterial blood gas analysis.

Several approaches can be followed to improve oxygenation during one-lung ventilation. Continuous positive airway pressure (CPAP 5–10 cm H_2O) applied to the nondependent lung is the most effective approach to improve oxygenation. This level of CPAP results in minimal lung inflation and should not interfere with surgery. Nevertheless, discontinuing CPAP prior to lung stapling may be required to minimize postoperative air leaks. Notably, CPAP applied to the nondependent lung may not be useful, e.g., during certain procedures such as thoracoscopy, bronchopleural fistula repair, sleeve resection, or massive pulmonary hemorrhage.

Since atelectasis in the dependent lung is an important factor contributing to hypoxemia during one-lung anesthesia, ventilation strategies to the dependent lung may be attempted to improve arterial oxygenation. An alveolar recruitment maneuver (sustained increase in peak pressure up to 40 cm H_2O for 5–10 breaths) often results in an initial increase in PaO_2. If an improvement in PaO_2 is not sustained, PEEP may be applied to the dependent lung. PEEP may improve oxygenation due to recruitment of atelectatic lung, which offsets its pressure effect of blood flow redistribution to the nondependent collapsed lung. However, in some circumstances, when PEEP is applied to the dependent lung, it may result in a decreased PaO_2 due to increased PVR of the dependent lung, resulting in blood flow diversion to the nondependent collapsed lung (Fig. 28.26). Depending on the stage of surgery, clamping of the pulmonary artery will decrease the shunt fraction, thus improving oxygenation.

Some controversy exists regarding the optimal tidal volume during one-lung ventilation (OLV). Historically, it was felt that tidal volumes of 8–10 ml/kg were required to maintain oxygenation during OLV, and decreasing tidal volumes to 5–6 ml/kg would promote atelectasis and resultant hypoxemia. Recent evidence suggests that tidal volumes of 8–10 ml/kg during OLV may cause acute lung injury, whereas smaller tidal volumes seem to be less deleterious. To counter the loss of recruitment with lower tidal volumes and thereby increase the PaO_2, the use of PEEP to the ventilated lung has been advocated.

Similarly, the optimal value of PEEP continues to be disputed. Some authors suggest that similar PaO_2 levels can be achieved by decreasing the tidal volumes from 10 ml/kg to 5 ml/kg and simultaneously increasing PEEP from 5 to 10 cm, as mentioned above. It seems clear that ventilation with lower tidal volumes (approximately 5 ml/kg) while on OLV is preferred if arterial oxygen levels remain acceptable.

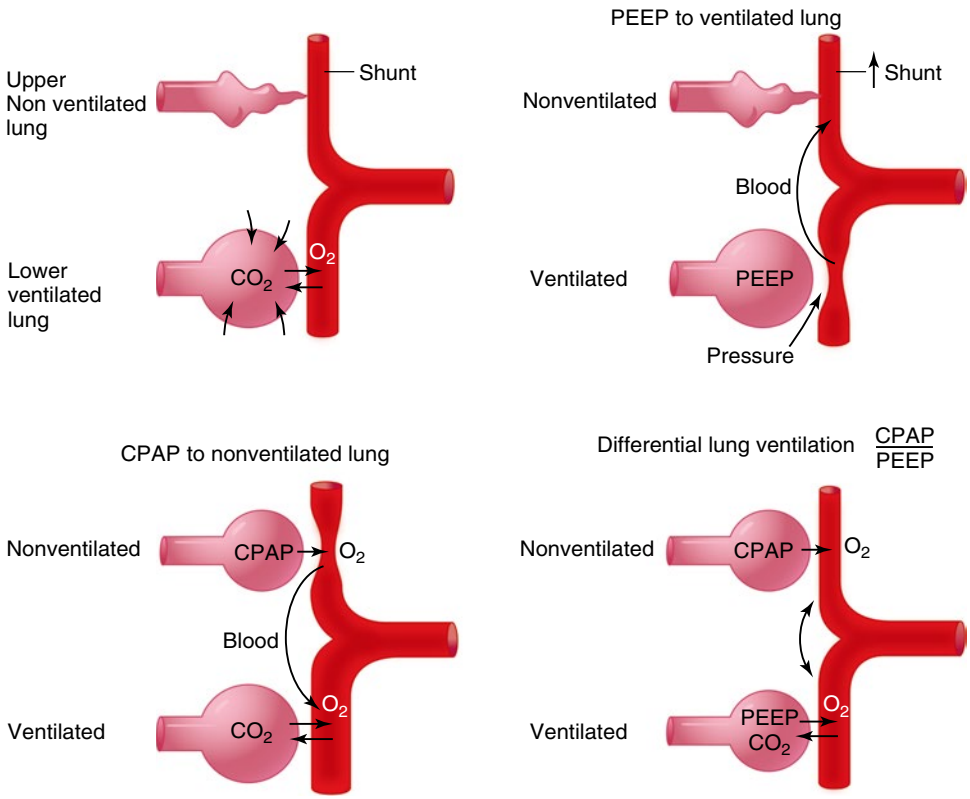

Fig. 28.26 Effect of various ventilation management strategies during single-lung ventilation

Postoperative Care and Pulmonary Complications

Patients are extubated as early as possible to decrease the risk of barotrauma (rupture of the suture line), and decrease the incidence of infection. After extubation patients are taken to the recovery room, and then to a close care unit or the ICU. Patients who are not extubatable may be directly taken to the ICU from the operating room. Postoperative pulmonary complications after thoracic surgery are often characterized by arterial hypoxemia from atelectasis, often followed by pneumonia. The severity of these complications parallels the magnitude of decreases in vital capacity and functional residual capacity. Presumably, decreases in these lung volumes interfere with generation of an effective cough and contribute to atelectasis. The net effect is decreased clearance of secretions from the airways, leading to arterial hypoxemia and pneumonia. Incentive spirometry may help to improve lung function.

In addition, thoracotomy is known to produce intense postoperative pain due to skeletal muscle transection and possible rib removal during surgery. Pain decreases respiratory effort, which results in atelectasis, contributes to the development of the stress response and increased sympathetic tone, and increases cardiac morbidity. Thoracic epidural analgesia offers a unique opportunity for the anesthesiologist to improve postoperative recovery following thoracotomy. By delivering local anesthetics and narcotics to a limited dermatomal distribution, this technique results in profound segmental analgesia, improved pulmonary function, earlier extubation, and early mobility in the postoperative period. In addition, the decreased sympathetic tone caused by thoracic epidural analgesia may also provide myocardial protection in patients with coronary artery disease.

About 3 % of thoracotomies are complicated with postoperative bleeding. Chest tube drainage >200 ml/h, a falling hematocrit, hypotension, and tachycardia are all signs of excessive bleeding. Supraventricular tachyarrhythmias are common postoperatively in patients who underwent a thoracotomy.

Special Circumstances

Mediastinoscopy

Mediastinoscopy is often performed before thoracotomy to establish the diagnosis and/or resectability of lung carcinoma. The procedure consists of making a small incision just above the sternal notch, and inserting a mediastinoscope into the patient's pretracheal space. Mediastinoscopy is performed under general anesthesia. A large bore IV is placed preoperatively, and an arterial line may also be placed preoperatively depending on the patient's condition. Anesthesia is maintained

with oxygen, volatile agent, fentanyl, and a nondepolarizing neuromuscular blocking agent. The pulse oximeter/arterial line is placed on the right hand as the innominate artery (right side) may be compressed by the surgeon.

Hemorrhage and pneumothorax are the most frequently encountered complications of this procedure. Severe hemorrhage, although quite rare, can be life threatening as many of the great vessels of the thorax are within reach of the mediastinoscope. The most likely injured vascular structures include the azygos vein, innominate artery, and pulmonary artery. Initial control of bleeding should be through compression and packing of the wound, but if this fails to control bleeding, or if hemorrhage is severe, then an immediate sternotomy or thoracotomy is indicated.

Positive pressure ventilation of the lungs during mediastinoscopy is recommended to minimize the risk of venous air embolism (risk is greater during spontaneous ventilation). The mediastinoscope can also exert pressure against the right subclavian artery/innominate artery, causing the loss of a pulse distal to the site of compression and an erroneous diagnosis of cardiac arrest. Likewise, unrecognized compression of the right carotid artery has been proposed as an explanation for postoperative neurologic deficits that may occur after this procedure. Therefore, the pulse oximeter is placed on the right hand to monitor this complication. Bradycardia during mediastinoscopy may occur due to stretching of the vagus nerve or trachea by the mediastinoscope. This is treated by repositioning the mediastinoscope, followed by intravenous administration of atropine if bradycardia persists.

Thoracoscopic Surgery

Thoracoscopy is the insertion of a thoracoscope into the thoracic cavity and pleural space for the purpose of obtaining a lung or pleural biopsy, performing a wedge resection or lobectomy, pleurodesis, or other procedure. The bulk of thoracic surgery is now performed thoracoscopically in much the same way that laparoscopic procedures dominate general surgery. In a similar fashion, there are a few anesthetic differences that must be taken into account when performing thoracoscopic versus a classic open thoracic surgery.

First, because the surgical approach is much less invasive, there is typically less postoperative pain, and there may be a lesser need for postoperative epidural analgesia. The decision of whether or not to place a preoperative epidural needs to be based on the likelihood of converting the procedure to an open thoracotomy, as well as the anticipated difficulty in the placement of a postoperative epidural should the need arise. For example, there is a greater risk of conversion to an open procedure in a thoracoscopic lobectomy than in a wedge resection.

Second, adequate surgical exposure may be more difficult via a thoracoscopic approach. Because the surgeon has limited access to the intrapleural cavity, excellent lung separation is vital. The surgeon cannot retract a partially ventilated lung segment that may be in the surgical field of view. The choice of a DLT over a bronchial blocker may be warranted and desired by most surgeons to allow suction of the operative lung and, thereby achieve better lung collapse and visualization. However, in a blinded study of both open and thoracoscopic surgeries, surgeons could not distinguish between a BB and a DLT regarding the quality of lung isolation, but the time to complete lung collapse was significantly longer when using a BB versus a DLT. Finally, intraoperative hypoxia may be worse during thoracoscopic surgery since maneuvers to improve shunting through the operative lung, such as restricting blood flow to the pulmonary artery or CPAP, are usually not possible.

Bronchopleural Fistula

Bronchopleural fistula (BPF) is a direct connection between an airway and the pleural space. It happens following lung resection, pulmonary barotrauma, or by rupture of a lung abscess into the pleural cavity. Most patients are treated conservatively with antibiotics and chest tube drainage. Chest tube drainage of the pleural space is necessary to maintain a negative pleural pressure and avoid the development of a tension pneumothorax. When conservative treatment fails, surgical closure of the BPF is performed. This may involve over sewing the affected airway, placement of a muscle flap, covered stenting, or glue closure. General anesthesia using a DLT is performed to isolate the normal lung, and prevent cross contamination. When possible, extubation and negative pressure breathing is preferable to allow the BPF to close and heal.

Tracheal Resection

Patients presenting with obstructing tumors of the trachea are occasionally scheduled for tracheal resection surgery. Currently, many of these tumors are treated more conservatively with laser resection and tracheal stenting; however surgical resection of the trachea is still performed in specific circumstances where a complete tumor resection may offer a cure or long-term palliation. The procedure consists of removing a portion of the patient's trachea with the associated obstructing mass. It is this obstructing mass that presents the greatest challenge to the anesthesiologist. Control of the airway distal to the mass is essential throughout this procedure and may be quite difficult to accomplish.

The preoperative CT scan should be reviewed prior to the procedure to determine the degree of airway obstruction and location (both proximal and distal extent) of the mass. Induction of anesthesia consists of a slow inhalation induction with sevoflurane, maintenance of spontaneous ventilation, and

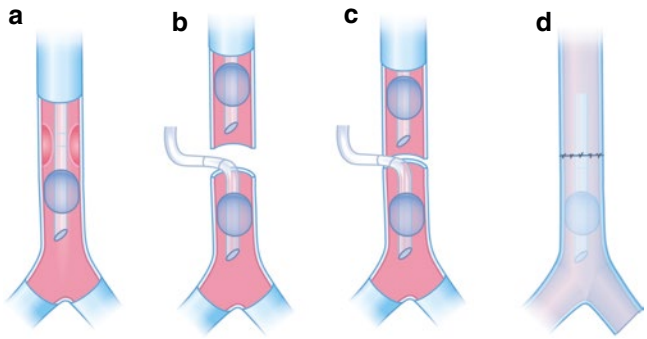

Fig. 28.27 Airway management during tracheal resection. (**a**) The trachea is intubated beyond the level of the obstructing mass. (**b**) Once the trachea is incised, an endotracheal tube is inserted in the distal airway from the surgical field and cross-table ventilation is commenced, (**c**) Ventilation via the surgical field is continued until the anastomosis of the tracheal back wall is finished. (**d**) The endotracheal tube is then advanced distal to the suture line and the trachea anastomosis is completed

avoiding use of neuromuscular blocking agents. An endotracheal tube needs to be advanced to the point where the cuff can be inflated beyond the mass to ensure adequate ventilation throughout the procedure. If the mass is quite distal in the airway, a long, small-internal caliber endotracheal tube may be needed to reach this point. Once the airway is secured, the surgeon will then incise and remove the portion of the trachea containing the mass. In order to continue ventilation at this point, an endotracheal tube is placed by the surgeon in the distal trachea and the cuff is inflated. During anastomosis of the airway, the trachea is re-intubated from the oropharynx and the tube is positioned so it is distal to the anastomosis. An illustration of airway management during the entire procedure is shown in Fig. 28.27.

At the end of the procedure, the surgeon may suture the patient's chin to their chest with a Grillo stitch to remove tension and avoid hyperextension of the neck with associated traction on the trachea. The patient is usually extubated immediately after surgery. An alternative approach to this method of airway management during tracheal resection is to place the patient on femoral cardiopulmonary bypass during the portion when the trachea is being excised. Cardiopulmonary bypass may also be helpful in cases where the initial airway management is extremely difficult or impossible due to the nature of the obstructing mass.

Lung Transplantation

Lung transplantation frequently offers difficult challenges to the thoracic anesthesiologist. Patients scheduled for lung transplant are obviously quite ill and typically have severe respiratory acidosis and significant hypoxia. The most typical indications for lung transplantation include obstructive disease such as end-stage emphysema, or cystic fibrosis, as well as restrictive diseases such as interstitial lung disease, sarcoid, or scleroderma. Many of these patients with restrictive disease also have severe pulmonary hypertension, and may have associated right heart failure.

Typically, both the left and right lungs are transplanted, except in the older patient (age greater than 60), where a single lung is usually transplanted. Bilateral lung transplantation has not been shown to offer a significant survival benefit in the older (age greater than 60 years) population. The surgery is performed essentially as a series of two pneumonectomies with intervening reattachment of the donor lungs and may be conducted either on or off cardiopulmonary bypass (CPB). There are advantages and disadvantages of either technique.

Off-Bypass

When performed off-bypass, an arterial blood gas is analyzed as each lung is separately ventilated. The lung with the poorest gas exchange is transplanted first, and the 2nd lung transplanted thereafter. Off-bypass transplantation has the advantages of decreased bleeding due to less required anticoagulation, diminished cytokine activation, and an associated decrease in the risk of transfusion. It is important in transplant patients to limit blood transfusion as much as possible to decrease the risk of alloimmunization. However, since each lung is sequentially removed and then replaced with a donor organ, there are periods when the patient is surviving on one lung only. Initially the patient is ventilated on a single native lung, and if their lung function is poor enough, they may not tolerate single-lung ventilation even for a brief period of time. If the patient has hypoxia and/or hypercarbia at baseline, this will most likely get significantly worse on single-lung ventilation.

Right heart pressure may dramatically increase as 100 % of the patient's cardiac output has to go through the remaining lung. This situation is made even worse if the patient has preexisting pulmonary hypertension or right heart failure. Once the first transplanted lung is sutured in, the patient will again be ventilated on a single lung, in this case it is the newly transplanted lung, while the contralateral lung is being transplanted. At this point, the new lung usually has adequate gas exchange, but forcing the entire cardiac output through it may increase the risk of reperfusion injury. If reperfusion injury does occur, gas exchange may fall dramatically and severe pulmonary edema may occur.

On CPB

When transplantation is performed on CPB, the patient is typically placed on bypass via femoral or central cannulation. Usually, the patient is kept warm, and no cardioplegia is given. Once both lungs are removed and transplanted, the patient is weaned back off of CPB. Lung transplantation performed this way has several advantages over the off-bypass technique. In very sick or unstable patients, CPB allows the

surgeon better exposure by draining the heart, and there is less worry of unstable hemodynamics, severe hypoxia or hypercarbia. In addition, by transplanting on bypass, full blood flow through the pulmonary artery only occurs after both transplanted lungs have been anastomosed, thus minimizing high blood flow through one lung only, and the associated risk of reperfusion injury. Disadvantages of CBP include increased bleeding, cytokine activation, stroke risk, and a high likelihood of blood transfusion.

Clinical Review

1. Factors decreasing functional residual capacity include all, except
   A. Change from upright to supine position
   B. Obesity
   C. Pregnancy
   D. Infant compared to an adult
2. The FEV_1/FVC ratio is decreased in
   A. Chronic obstructive pulmonary disease
   B. Acute respiratory distress syndrome
   C. Sarcoidosis
   D. Radiation lung fibrosis
3. Normal mixed venous oxygen saturation is (%)
   A. 60
   B. 75
   C. 90
   D. 100
4. Ciliary transport returns to normal within following weeks after cessation of smoking
   A. 1
   B. 2
   C. 4
   D. 8
5. Hypoxic pulmonary vasoconstriction is inhibited by all of the following, except
   A. Nitroprusside
   B. Diltiazem
   C. Propofol
   D. Sevoflurane (2 MAC)
6. On initiation of single-lung ventilation with a double-lumen endotracheal tube, high peak airway pressures are seen. Your next step would be to
   A. Add PEEP to the ventilated lung
   B. Add CPAP to the non-ventilated lung
   C. Suction the endotracheal tube to clear any secretions
   D. Insert a fiberoptic scope
7. In an anesthetized patient in the lateral decubitus position with a closed chest, the
   A. Nondependent lung is better ventilated and perfused
   B. The dependent lung is better ventilated and perfused
   C. The dependent lung is better perfused, and the nondependent lung is better ventilated
   D. The dependent lung is better ventilated, and the nondependent lung is better perfused
8. High-risk patients for lung resection have all the following parameters, except
   A. Postoperative predicted $FEV_1 < 800$ ml
   B. Postoperative predicted diffusion capacity of carbon monoxide of 80 %
   C. PaO_2 less than 50 mmHg
   D. $PaCO_2$ more than 45 mmHg
9. For mediastinoscopy, the pulse oximeter should be placed on the
   A. Right hand
   B. Left hand
   C. Right or left hand
   D. Right or left foot
10. For single-lung ventilation, advantage of using a bronchial blocker over a double-lumen tube is
    A. Patient can be taken to the ICU without changing the endotracheal tube
    B. Rapid deflation of the lung
    C. Ease of placement
    D. Bulky

Answers: 1. D, 2. A, 3. B, 4. D, 5. C, 6. D, 7. C, 8. B, 9. A, 10. A

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Neuroanesthesia

29

Brian Gierl and Ferenc Gyulai

Tissues in the human body require oxygen supply and blood flow to maintain homeostasis. The human brain is subject to a number of physical and physiological constraints that limit its reserve and magnify the impact of pathologic insults. The purpose of this chapter is to provide an understanding of the brain's physiology and provide strategies for manipulating it during anesthesia and critical care. Specific topics discussed include cerebral protection, traumatic brain injury, and anesthesia for specific procedures, such as craniotomy for subarachnoid hemorrhage, tumor resection, and management of traumatic brain injury.

Neurophysiology

The term neurophysiology encompasses two important aspects: (1) the cellular physiology of the brain and its response to anesthetic agents and (2) the neurophysiologic monitoring tests that are used to monitor the function of the brain and spinal cord, perioperatively. The brain is a collection of neurons that generate their own energy and use it for electrical conduction and cellular maintenance. The brain is intolerant to ischemia and requires a continuous supply of oxygen (20 % of total body oxygen consumption) and glucose (primary energy source for the brain) to meet the cerebral metabolic rate, which is usually expressed in terms of oxygen consumption ($CMRO_2$).

Normal $CMRO_2$ is about 3.5 ml/100 g/min (50 ml/min) in adults. Any interruption of cerebral blood flow greater than 3–10 min can cause brain ischemia. Therefore, anesthesiologists plan combinations of anesthetic and vasoactive agents to minimize ischemic damage by providing sufficient cerebral perfusion to meet a reduced $CMRO_2$.

Cerebral blood flow (CBF) averages about 50 ml/100 g/min (750 ml/min) in adults, which is about 20 % of the cardiac output. It is important to know that CBF increases with metabolic activity, and CBF below 25 ml/100 g/min is associated with cerebral ischemia.

Cerebral perfusion is determined by the driving force for flow, which is known as the cerebral perfusion pressure (CPP). The normal CPP is about 100 mmHg, and CPP below 50 mmHg usually indicates brain ischemia. The CPP is the difference between the high-pressure arterial blood on one side of the brain tissue and the low-pressure venous blood on the downstream side. Because the brain is perfused throughout the cardiac cycle, the mean arterial pressure (MAP) represents the driving force, while the central venous pressure (CVP) represents pressure downstream from the system. However, in the presence of intracranial hypertension, the intracranial pressure (ICP) can exceed the CVP, thereby replacing CVP as the downstream pressure. Since normal ICP is only about 10 mmHg, CPP is mainly dependent upon MAP. However, moderate to severe increases in ICP can significantly reduce CPP even in the presence of normal MAP:

$$\mathrm{CPP} = \mathrm{MAP} - \mathrm{CVP}\left(\text{when CVP} > \mathrm{ICP}\right)$$

$$\mathrm{CPP} = \mathrm{MAP} - \mathrm{ICP}\left(\text{when ICP} > \mathrm{CVP}\right)$$

Autoregulation of CBF

The two internal carotid arteries supply ~70 % of CBF, while the vertebral arteries, which form a single midline basilar artery, supply the remaining 30 %. These three arteries form a heptagonal arterial loop known as the circle of Willis that distributes blood throughout the brain (Fig. 29.1). In theory, this redundancy protects the brain from disruptions in

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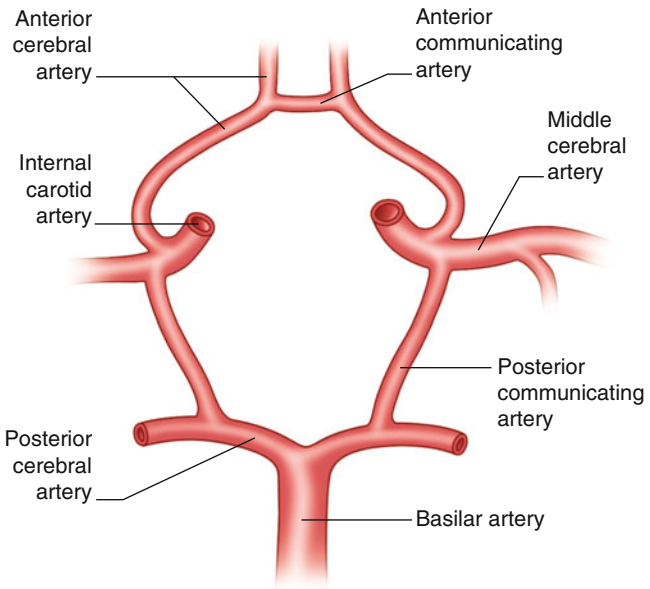

Fig. 29.1 Circle of Willis

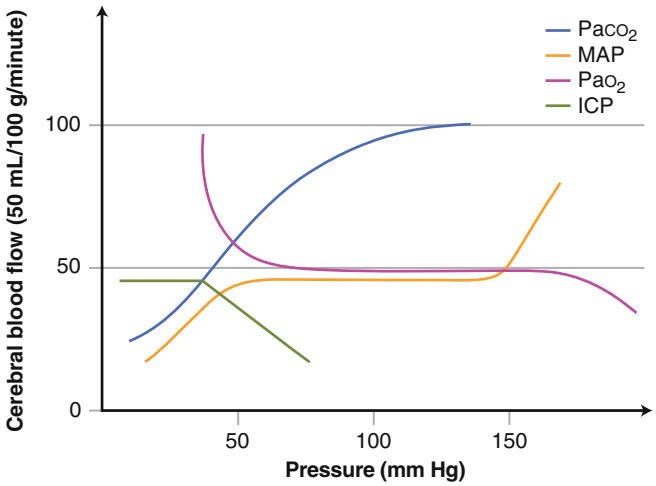

Fig. 29.2 The impact of MAP, ICP, $PaCO_2$, and PaO_2 on CBF. Notice that the brain autoregulates CBF across a wide range of MAP and $PaCO_2$ (*MAP* mean arterial pressure, *ICP* intracranial pressure, *CBF* cerebral blood flow)

blood flow through any one artery. However, a complete and symmetric circle of Willis is present only in ~40 % of the population. Therefore, this necessitates cerebral monitoring (SSEPs, EEG) during many intracranial procedures.

The CPP range for autoregulation is often cited as 50–150 mmHg, but significant variation exists across the population. The presence of chronic hypertension may increase these limits to a higher range of pressures, 80–180 mmHg or higher. Thus, a patient with chronic hypertension might experience cerebral ischemia at a CPP of 60 mmHg, whereas an individual without a history of hypertension or intracranial pathology is unlikely to experience ischemia at that pressure. The above two equations imply that CBF is a linear function of CPP, but the flow through healthy brain has multiple intricate and interdependent controls to manipulate cerebral blood flow as listed below (Fig. 29.2):

1. Metabolic–perfusion coupling diverts blood flow to metabolically active brain regions so that the oxygen supply matches the demand. This response is robust and remains intact in comatose patients. The mechanism is not well understood, but metabolic by-products (hydrogen ions, ionic gradients, nitric oxide, prostaglandins) likely play a role in producing the vasodilation.
2. Healthy cerebral vasculature responds to increased MAP with vasoconstriction that reduces cerebral blood volume (CBV) and ICP. The opposite is also true: A decreased MAP leads to vasodilation in an effort to maintain perfusion. Autoregulation alters arteriolar tone to provide a stable CBF over a range of CPP. Autoregulation is impaired to various degrees after stroke, hemorrhage, traumatic brain injury (TBI), and extremes of temperature. Multiple factors play a part in autoregulation—thus, no single target can be manipulated to restore autoregulation.
3. Autonomic innervation of large cerebral vessels: This theory purports that parasympathetic stimulation increases CBF (vasodilation), while sympathetic activation decreases CBF (vasoconstriction), independent of associated changes in MAP or CPP. Whether this mechanism is clinically relevant is controversial.
4. $PaCO_2$ reactivity: CBF is directly proportional to $PaCO_2$ between arterial tensions of 20–80 mmHg, with CBF changing 1–2 ml/100 g/min for every mmHg change in $PaCO_2$. Dissolved carbon dioxide diffuses across the blood–brain barrier and alters the pH of the cerebrospinal fluid (CSF). A decrease in the dissolved CO_2 (e.g., hypocapnia secondary to hyperventilation) causes CSF alkalosis that leads to arteriolar constriction reducing CBV and ICP. When the opposite occurs, that is, increased dissolved CO_2 levels, it leads to a relative CSF acidosis accompanied by smooth muscle relaxation with increased CBF, CBV, and ICP. Since hypercapnia increases ICP, it is strictly avoided in neuroanesthesia.
5. PaO_2 reactivity: CBF reacts to a lesser extent to changes in PaO_2 than to $PaCO_2$. Hyperoxia is associated with minimal decreases in CBF (10–15 %), but hypoxemia ($PaO_2 < 60$ mmHg) leads to a profound increase in CBF.
6. Temperature: CBF changes by 5–7 % for every degree Celsius change in temperature. Hypothermia decreases CBF and cerebral metabolic rate, while hyperthermia has opposite effects.

Intracranial Pressure

The cerebrospinal fluid (CSF) is an ultrafiltrate of the plasma. CSF is produced at a rate of about 20 ml/h, or 500 ml/day, with a total volume of about 150 ml. It is a clear and

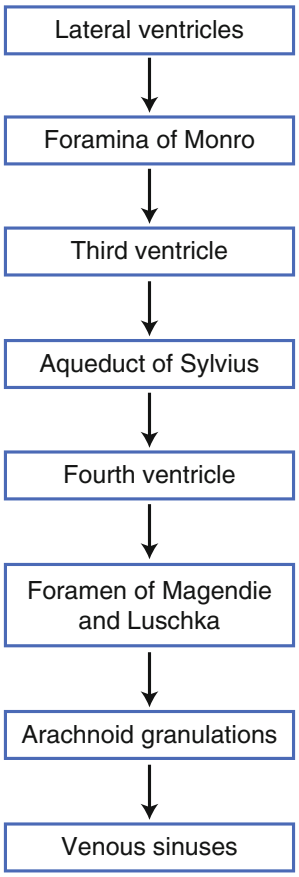

Fig. 29.3 Circulation of cerebrospinal fluid

colorless fluid produced in the brain by modified ependymal cells in the choroid plexus (about 50–70 %), while the remainder is formed around blood vessels and along ventricular walls. The CSF flows in a pulsatile manner and circulates as shown in Fig. 29.3.

Normal CSF pressure is about 8–15 mmHg with the patient lying on the side and 16–24 mmHg with the patient sitting up. In newborns, CSF pressure ranges from 4.4 to 7.3 mmHg, about half that of adults. The CSF acts as a cushion or buffer for the brain and provides mechanical and immunological protection to the brain. It provides buoyancy to the brain by decreasing its effective mass from 1,400 to 47 g. The CSF also protects the brain tissue from injury and prevents brain ischemia. The CSF provides nutrients and clears metabolic waste from the central nervous system through the blood–brain barrier.

The cranial vault is a fixed space that provides protection but also represents a physical constraint that often results in increased ICP that reduces CPP. The vault contains the brain, blood, and CSF, with both the blood and CSF being incompressible. In the average adult, the skull encloses a total volume of about 1,500 ml (1,200 ml brain, 150 ml CSF, and 150 ml blood) (Fig. 29.4). The Monro–Kellie hypothesis states that the sum of the intracranial volumes of blood,

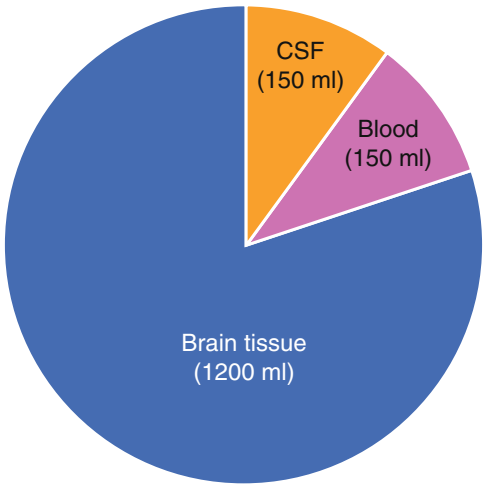

Fig. 29.4 Contents of the cranial vault

brain, CSF, and other components is constant. To prevent an increase in ICP, any increase in the volume of one component must be compensated by a reciprocal decrease in the volume of another component. Sufficient buffering capacity (elastance) exists to allow for minor changes in the volume of any one component (tumor, CSF, extravascular blood, or edema) without significantly altering the ICP (Fig. 29.5).

Initially the increased ICP shifts venous blood out of the skull; however, it is the extracranial shift of CSF that provides long-term adaptation to chronically increased ICP. An extraventricular drain (EVD) can be inserted by a neurosurgeon at the bedside to drain CSF through the ventricles, to both monitor and reduce the ICP. When these fluid shifts fail to control ICP, it increases and leads to reduced CPP. The brain's response to reduced CPP is vasodilation to reestablish blood flow, but vasodilation increases CBV and ICP, which further worsens ischemia via a positive feedback loop (Fig. 29.6). Without emergent intervention, the compensatory mechanisms will be exhausted, and further ICP increase may force the brain out of an opening in the skull (herniation).

Common causes and clinical signs of increased ICP are summarized in Tables 29.1 and 29.2, respectively. Brainstem ischemia is a late sign of intracranial hypertension and raises the possibility of brain herniation and the associated demise. Because the brainstem regulates its own perfusion, brainstem ischemia triggers an increase in cardiac efferent activity, resulting in hypertension. Carotid baroreceptors sense the hypertension and transmit a signal to the brainstem via the glossopharyngeal nerve (CN IX) and initiate a parasympathetic response via the vagus nerve (CN X) that results in bradycardia. Hypertension and bradycardia in the presence of intracranial hypertension are known as Cushing's phenomenon. This is actually a protective mechanism, and the hypertension itself should only be treated if the patient's systolic pressure is excessive or accompanied by organ dysfunction.

Strategies to Reduce ICP (Fig. 29.7)

1. Head elevation: Elevating the patient's head increases jugular venous drainage and reduces cerebral venous pressure and volume, which in turn reduces ICP. This effect is maximized at a 30° angle, with further elevation decreasing the cerebral arterial pressure and reducing perfusion. Head elevation should be avoided in patients with hypovolemia, as it may further decrease blood pressure and reduce CPP.
2. Hyperosmolar therapy: Increases blood osmolality so that water diffuses down its concentration gradient from the brain's extracellular space into the bloodstream. The result is a decreased total brain volume and increased elastance. Mannitol or hypertonic saline (3–23 %) is often used for this purpose in patients with an intact blood–brain barrier.

   Mannitol not only decreases brain volume but also decreases blood viscosity, which increases oxygen delivery to the brain. However, care should be taken when administering mannitol to cardiac-compromised patients, as it initially increases intravascular blood volume by drawing water into the bloodstream, which may cause congestive heart failure (CHF). Secondly, excessive diuresis with mannitol may cause hypovolemia. Maintaining euvolemia is of prime importance, and as such the maximum recommended serum osmolality is 320 mOsm/l. Mannitol is given in a dose of 0.25–1 g/kg and starts lowering ICP within 5 min, with a peak effect in 30–60 min and duration of action of 2–6 h.

   Hypertonic saline is especially useful in hypovolemic and hypotensive patients. Adverse effects of administration include hypernatremia and hypervolemia, which may cause CHF, bleeding secondary to decreased platelet aggregation and prolonged coagulation times, hypokalemia, and hyperchloremic acidosis. Rapid administration of hypertonic saline, in the presence of hyponatremia, may increase the risk of central pontine myelinolysis.
3. Hyperventilation: It can be used to temporarily reduce elevated ICP until medical therapy or a surgical intervention can remedy the underlying cause. In ICU patients with elevated ICP, hyperventilation has been used to produce hypocapnia for extended periods. However, existing data suggests that hypocapnea should only be used for brief periods of time, in order to either stop impending herniation or to alter total intracranial volume to provide surgical exposure.

   Hypocapnea causes a change in CSF pH; however, the buffering mechanisms in the CSF return the pH to normal after 4–8 h. Over that time, both CBV and ICP slowly

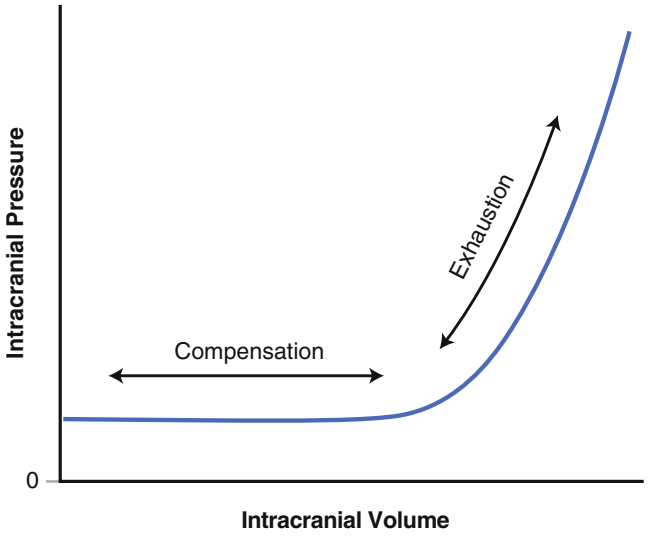

Fig. 29.5 Intracranial elastance. As the intracranial volume increases, compensation mechanisms are exhausted and small changes in volume drastically increase the ICP

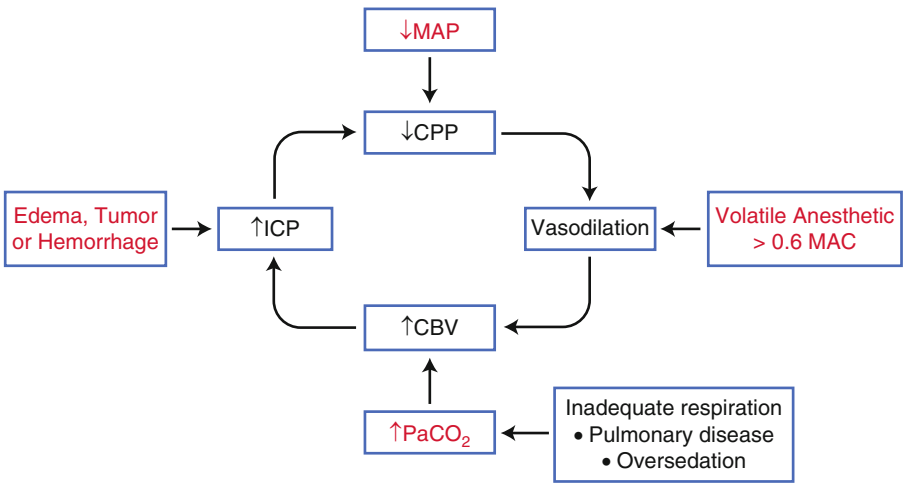

Fig. 29.6 The relationship of pathology, vasodilation, and neurophysiology on cerebral perfusion. A decrease in MAP or an increase in the volume of intracranial contents decreases perfusion, and the corresponding vasodilation worsens the pathologic state (MAP mean arterial pressure, CPP cerebral perfusion pressure, CBV cerebral blood volume, ICP intracranial pressure)

normalize, and further hypocapnea is required to reduce CBV. Without intervention, a return to eucapnea ($PaCO_2$ ~ 40 mmHg) will cause CSF acidosis that will increase CBF and CBV. If an area of the brain was damaged, the resulting hyperemia may lead to a reperfusion injury with edema or intraparenchymal hemorrhage.

Table 29.1 Causes of increased intracranial pressure

Intracranial	• Brain tumor • Cerebral edema, increased cerebral blood volume • Aneurysm rupture • Head injury • Hematoma (subdural, epidural) • Stroke • Hydrocephalus • Benign or idiopathic intracranial hypertension • Pneumocephalus • Abscess, cysts
Extracranial	• Hypoventilation (hypercarbia, hypoxia) • Hypertension (pain, coughing) • Hypotension (hypovolemia) • Airway obstruction • Seizures • Hyperpyrexia • High altitude • Hepatic failure

Table 29.2 Clinical signs of increased intracranial pressure

Early	• Headache • Vomiting • Mental status changes • Seizures • Pupil dysfunction • Cranial nerve dysfunction • Sunsetting sign
Late	• Further deterioration in consciousness • Papilledema, pupillary dilation with decreased response to light • Bulging fontanels • Posturing, decreased spontaneous movements • Cushing's triad (hypertension, bradycardia, irregular respiration)

Other changes that limit the therapeutic benefits of hyperventilation include:

(a) Hypocapnea causes a leftward shift of the oxyhemoglobin dissociation curve and reduces oxygen delivery to tissues.
(b) Vasoconstriction induced by hypocapnea reduces oxygen delivery to damaged ischemic tissue.
(c) Hypocapnea has a limited impact on CBV and ICP. Of the 150 ml of CBV, only ~1/3rd of it (50 ml) is arterial with only a fraction of that blood in CO2-reactive arterioles. The result is that if hypocapnea is used to reduce CBF by 30 %, CBV is reduced only by ~7 %, which represents ~1 % of total intracranial volume at the expense of a dramatic reduction in perfusion.

4. Steroid therapy: Steroids may be used (dexamethasone) to decrease brain swelling and for stabilizing the cell membrane in patients with increased ICP due to mass lesions, such as brain tumors and abscesses, inflammation, and infections. However, corticosteroids are not indicated in the management of increased ICP after traumatic brain injury.
5. Seizures: They increase cerebral metabolic rate and the ICP and hence should be aggressively managed.
6. Sedation and analgesia: Agitation and pain increase ICP. Therefore, providing anxiolysis (midazolam, propofol) and adequate analgesia (morphine) is an important aspect in the management of ICP.
7. Adequate ventilation: Optimal respiratory management to prevent hypoxia and hypercarbia is extremely important. A ventilated patient may require neuromuscular blockade for effective ventilator use and prevention of raised ICP. It should be noted that excessive PEEP can increase ICP by decreasing venous return and increasing cerebral venous pressure.
8. Barbiturate coma: Refractory cases of increased ICP may require inducing a barbiturate coma and hypothermia. However, a rebound increase in ICP may occur when discontinuing these therapies.

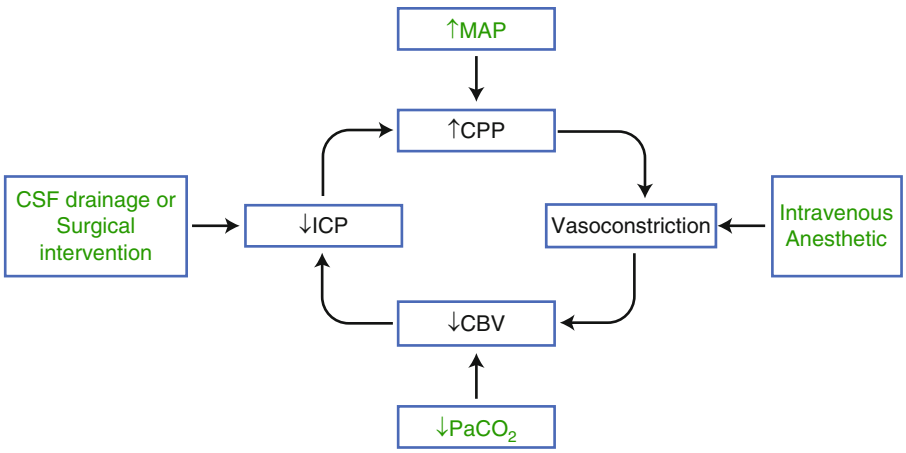

Fig. 29.7 Physiologic, anesthetic, and surgical interventions to reduce intracranial pressure (MAP mean arterial pressure, CPP cerebral perfusion pressure, CBV cerebral blood volume, ICP intracranial pressure)

9. Surgical interventions: To reduce intracranial pressure include removing an intracranial mass or hemorrhage, decompressive craniectomy, or draining excess CSF via a ventriculostomy catheter. Resecting portions of the cranium and underlying dura nullifies the Monro–Kellie doctrine such that the brain is no longer confined to the skull.

Effects of Anesthetics on Cerebral Physiology

All anesthetic agents impact $CMRO_2$, cerebral arteriolar tone, and the brain's reactivity to changes in carbon dioxide tension, with resultant changes in CBF, CBV, and ICP (Table 29.3).

Intravenous Anesthetics

Thiopental, propofol, and etomidate reduce $CMRO_2$ and CBF in tandem. Barbiturates produce vasoconstriction, which reduces CBF and $CMRO_2$ in normal brain tissue. Blood flow is redistributed to ischemic areas, which remain dilated (reverse steal phenomenon). The maximal reduction in CBF and $CMRO_2$ is about 50–60 %, after which the EEG becomes isoelectric. All these changes lead to a decrease in the ICP. When the cranium has been opened during an intracranial procedure, CBF reduction produced by these agents improves surgical exposure. In addition to reducing the ICP, barbiturates have anticonvulsant properties. However, methohexital, which is commonly used for inducing patients for electroconvulsive therapy (ECT), activates seizure foci when used in smaller doses. Higher doses of methohexital have similar anticonvulsant properties as thiopental.

Propofol has similar actions to thiopental: producing reductions in ICP and having anticonvulsant properties. The advantage of using propofol is its short duration of action: however, it produces more hypotension than thiopental, which can significantly reduce cerebral perfusion pressure, especially in cardiac-compromised patients. Etomidate, like thiopental and propofol, reduces both the CBF and ICP. However, etomidate produces adrenal suppression and is associated with myoclonic movements on administration.

The effects of ketamine are different than other intravenous induction agents. Ketamine increases CBF (cerebral vasodilation), which leads to an increase in ICP. Ketamine increases activity in the limbic system and decreases activity in other brain areas, so-called dissociative anesthesia.

Opioids minimally impact CBF and $CMRO_2$. Fentanyl is usually preferred over morphine in neuroanesthesia, because of the latter's slow onset and prolonged duration of action. Excessive administration of opioids, however, may cause respiratory depression, which may increase the $PaCO_2$ and the ICP. Benzodiazepines lower CBF and $CMRO_2$; however, their effects are milder compared to barbiturates. Benzodiazepines are usually agents of first choice for treating seizures. The duration of action of benzodiazepines is longer compared to other intravenous induction agents.

Muscle relaxants do not directly affect brain physiology. However, some muscle relaxants cause a release of histamine, which causes cerebral vasodilation and an increase in CBF and ICP. Succinylcholine increases muscle spindle activity, which transiently increases the ICP. This effect is usually blunted by prior administration of the intravenous induction agent or a small defasciculating dose of a nondepolarizing muscle relaxant.

Inhalational Anesthetics

All volatile anesthetics depress $CMRO_2$ with increasing doses. Volatile anesthetics also produce cerebral vasodilation with resultant increase in CBF. However, at concentrations <0.6 MAC, the vasodilatory effect is minimal, and anesthesiologists commonly utilize volatile anesthetics for their easy titrability and fast, predictable elimination. Concentrations >0.6 MAC are avoided because they lead to dose-dependent cerebral vasodilation that increases CBF, CBV, and ICP. This is commonly referred to as uncoupling of $CMRO_2$ and CBF. Volatile anesthetics increase blood flow to normal areas

Table 29.3 Effects of common anesthetic agents on neurophysiology

Anesthetic agent	CBF	$CMRO_2$	ICP	Comments
Thiopental	↓	↓↓	↓	No longer available in the USA
Etomidate	↓	↓	↓	Adrenal suppression is a concern
Propofol	↓	↓	↓	May decrease MAP profoundly
Ketamine	↑↑	↑	↑↑	Undesirable neuroanesthetic
Midazolam	↓	↓	↓	Variable reaction to small doses
Fentanyl	↓	–	↓	Long-duration infusions may cause hypercarbia
Remifentanil	↓	–	↓	Half-life ~3–5 min, effective for periods of intense stimulation
Nitrous oxide	↑↑	↑	↑	Controversial neuroanesthetic
Desflurane, isoflurane, sevoflurane	<0.6 MAC –	↓	–	$PaCO_2$ reactivity preserved
	>0.6 MAC ↑	↓↓	↑	Vasodilation and increased CBF and ICP
Halothane	↑↑	↓	↑	Extreme cerebral vasodilation

of the brain; therefore, ischemic brain areas see a decline in their perfusion (steal phenomenon). Among volatile anesthetics, halothane increases CBF the greatest and decreases the $CMRO_2$ the least.

Nitrous oxide (N_2O) has been shown to mildly increase $CMRO_2$ and CBF. When combined with a volatile anesthetic, these effects are additive. N_2O is also known to rapidly diffuse into closed spaces that may cause a rapidly expanding venous air embolism or a pneumocephalus. However, it has been found that the use of N_2O does not significantly change outcomes when used during craniotomies. Some anesthesiologists still use N_2O for its rapid titrability and analgesic properties.

Anesthesia for neurosurgical patients is often a combination of a low-dose volatile anesthetic (<0.6 MAC) and an intravenous anesthetic infusion to provide favorable CBV. Since the residual effects of anesthetics can hinder the postoperative evaluation of neurosurgical patients, a combination of fast-offset agents is often preferred. One common combination is 0.6 MAC of sevoflurane/desflurane, combined with propofol and remifentanil infusions.

Vasoactive Drugs

Catecholamine infusions are commonly used in patients to maintain MAP and CPP. When the CPP is within the range of autoregulation and the blood–brain barrier is intact, catecholamine infusions do not impact CBF. However, in pathologic areas, CBF may be a linear function of CPP, and slight changes in CPP could dramatically impact tissue perfusion. Phenylephrine and norepinephrine are common choices of vasopressors for neuroanesthesia.

When the blood–brain barrier (BBB) is compromised, epinephrine can interact directly with pathologic tissues and increase $CMRO_2$. Because dopamine is involved in the hypothalamic–pituitary axis, its infusions are typically avoided. Direct cerebral vasodilators such as hydralazine and nitroprusside have a greater impact on CBF and ICP. Oral nimodipine and parenteral nicardipine are cerebral vasodilators that are hypothesized to reduce cerebral vasospasm in blood vessels serving pathologic tissue.

Cerebral Protection

Pathophysiology of Cerebral Ischemia

The mechanism of the cerebral ischemia is important to the pathogenesis of the disease. For example, cardiac arrest causes global ischemia without collateral flow, causing neuronal depolarization within minutes. In subarachnoid hemorrhage, there is focal ischemia as well as an adjacent area that receives some, albeit reduced, collateral perfusion. The ischemic area is known as the core and the adjacent area the penumbra. The imbalance between perfusion and $CMRO_2$ in the penumbra must be restored in a timely manner so that it can be saved.

No matter the cause, ischemic cells release toxic products and the excitatory amino acid glutamate that increase energy consumption at the border between the ischemic core and the penumbra, leading to depolarization in adjacent cells. In a futile attempt to repolarize, these cells consume their energy stores leading to expansion of the ischemic core and further injury (Fig. 29.8). This mechanism of injury is known as cortical spreading depression and commonly occurs in ischemic tissue after subarachnoid hemorrhage (SAH) and traumatic brain injury (TBI).

A dramatic change in the balance between oxygen metabolic supply and demand, such as a regional decrease in CPP or a seizure, can trigger a large group of at-risk cells in the

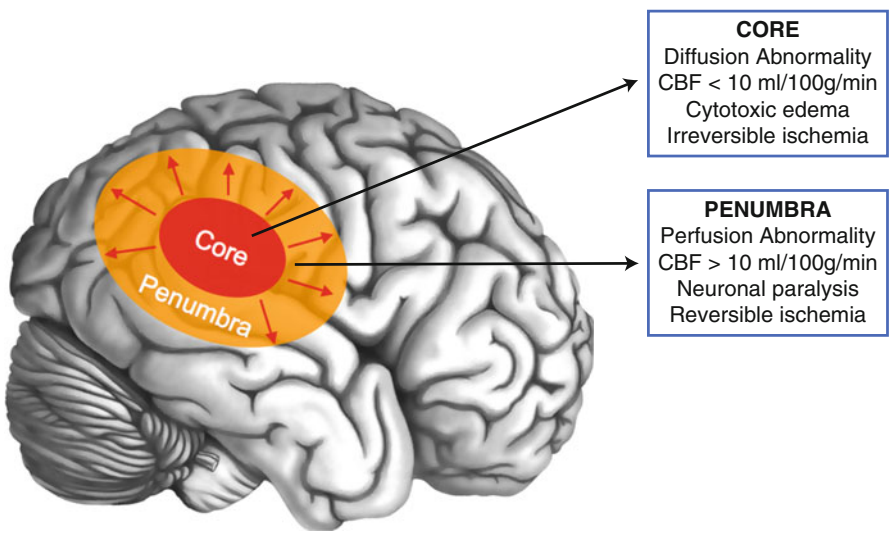

Fig. 29.8 Pathophysiology of cerebral ischemia

penumbra to depolarize. The depolarization of an already injured cell can be massive with large influxes of Na^+ and Ca^{++}. The energy required to remove these ions can double the $CMRO_2$. If this metabolic requirement is not met, K^+ and organic anions (notably glutamate) flow out of the cell where they enhance depolarization of local cells by reducing the K^+ potential and opening excitatory channels in surrounding cells. This mechanism spreads the depression. Hemorrhaged blood increases extracellular K^+, which increases the energy required for repolarization. Free hemoglobin also reduces nitric oxide (NO), inhibiting vasodilation and activating apoptotic pathways, leading to increased risk of ischemia. Water diffuses down the sodium and calcium gradients, which leads to edema and further pathology.

If the CBF–$CMRO_2$ coupling mechanism is still intact, the spreading depolarization is counteracted with spreading hyperemia. Hyperemia lasts for only a few minutes, which is just enough time for perfusion to match the increased metabolic demand so that the neurons can recover (repolarize). Hyperemia is followed by a period of oligemia with failures of CBF–$CMRO_2$ coupling and $PaCO_2$ autoreactivity that lasts for a few hours.

Strategies for Cerebral Protection

Cerebral protection (CP) is a term that refers to strategies to prevent long-term deterioration of CNS function after some insult. That insult may be planned, such as surgery, or impromptu as in cardiac arrest, a cerebrovascular accident (CVA), traumatic brain injury (TBI), or spinal cord injury. These conditions occur frequently, with 750,000 CVAs and 1.7 million TBIs per year in the USA alone. Several strategies have been evaluated for cerebral protection, with the hope that instituting therapies prior to the insult (prevention) may increase their efficacy.

For decades physicians have been exploring means to protect neural tissue from ischemic injury. They initially focused on limiting oxygen demand (decreasing $CMRO_2$), so that the reduced oxygen supply as a result of ischemia could match the $CMRO_2$. Maximal $CMRO_2$ reduction that can be achieved is ~60 %, which coincides with cessation of electrical activity and burst suppression on EEG. Animal study protocols that dosed volatile and intravenous agents to achieve burst suppression protected neural tissue from ischemic injury of brief to moderate duration. However, the tissue died several days later.

When these experiments were repeated and antiapoptotic drugs were administered a few days after the insult, the cells survived. Further experiments determined that only 1/3 of the barbiturate dose that is required to achieve an isoelectric EEG provided near-maximal protection. Therefore, neuroprotection is accomplished by a different, as yet undefined, mechanism that may include reductions in the stress response, slowing the apoptotic cascade, or encouraging axonal regeneration. Several triggers and pathways of apoptosis have been elucidated, including calcium dysregulation, free radical damage, and cytokine release by CNS macrophages (microglial cells). All activate enzymes that cause apoptosis. Multiple laboratory studies have shown that by blocking a single pathway, apoptosis can be delayed.

Table 29.4 Strategies for cerebral protection

Maintain optimal cerebral perfusion pressure
Normal or slightly elevated arterial blood pressure
Prevent increases in ICP
Maximize oxygen-carrying capacity (hematocrit 33 %)
Avoidance of hyperglycemia (blood sugar <200 mg/dl)
Maintain normocarbia

Anesthetic agents have been shown to provide varying degrees of neuroprotection either by reducing the metabolic demand and the stress response or by blocking steps in the apoptosis cascade. Anesthetics reduce metabolic demand by hyperpolarization of mitochondrial potassium ion channels; reduce excitation secondary to GABA agonism, NMDA antagonism, and reduced glutamate release; and reduce $CMRO_2$ that both saves energy for cellular maintenance and limits free radical formation and membrane oxidation. Strategies for cerebral protection are summarized in Table 29.4.

Anesthetic Agents

In animal studies, volatile anesthetics provided neuroprotection when administered within 1 h of the onset of mild to moderate ischemia; however, the benefits have not been demonstrated in human clinical trials. Potential antiapoptotic mechanisms of volatile anesthetics include reducing calcium influx to limit apoptotic kinase activation and increasing nitric oxide (NO) levels to induce antiapoptotic kinases. Propofol reduces metabolic demand and also acts as a free radical scavenger. Lidocaine inhibits sodium channel opening and may impede the spreading depolarization. Unlike other anesthetics, etomidate has been shown to increase infarct size in models of ischemia, which may be due to a reduction in NO levels.

Hypothermia

Hypothermia is another technique for neuroprotection. The mechanism is simple: $CMRO_2$ declines 5–7 % for each degree Celsius decline in body temperature. Following cardiac arrest, hypothermia dramatically reduces morbidity due to brain damage and is the standard of care. However, hypothermia hinders coagulation, oxygen–hemoglobin dissociation, and the immune response and was determined to be "neither effective nor unsafe" for brain surgery and TBI. In the acute phase of treatment following SAH, the potential benefits of a trend toward reduced infarct size was offset by

complications that were related to decreased immune system function and coagulopathy. Hyperthermia in the acute phase of injury has a negative impact on mortality in all types of ischemic brain insults. The stress response to SAH or TBI commonly causes hyperthermia, and guidelines recommend that it be treated aggressively with anti-inflammatory medications and direct temperature modulation.

Other Agents

Multiple anti-inflammatory agents have been tested with inconclusive results, including corticosteroids, lipid peroxidation scavengers, statins, and glutamate inhibitors. Corticosteroid therapy has only been shown to improve outcome in patients who suffered spinal cord trauma. It has been shown to improve functional recovery so that patients regain their ability to use 1 or 2 additional spinal cord levels. The other drugs were not efficacious in clinical trials. Patients who are already taking statin drugs experience a poorer outcome when these drugs are stopped after an ischemic insult. However, initiating statin therapy after an insult has not been shown beneficial.

Nimodipine and nicardipine, which are calcium channel blockers, have been used to reduce vasospasm-mediated ischemia after SAH or TBI. Meta-analysis has shown that their effects were either beneficial or equivocal, suggesting that calcium dysregulation was responsible for neuronal damage. Although other investigations of calcium antagonists, including magnesium, have proven to be inconclusive, both nimodipine and magnesium are commonly administered as an attempt at neuroprotection given their benign side effect profile.

Cerebral Monitoring

The evaluation of patients with ischemic brain injury is complicated by the multifaceted nature of the disease and the need for invasive mechanical ventilation with sedation and possibly muscle relaxation. Imaging studies can be used to track changes, but these are expensive in terms of both cost and resource utilization and often require that the patient be placed at risk during transport to the scanner. Clinicians seek robust tests that would define the severity of initial injury in order to (1) guide therapy, (2) predict functional recovery, (3) diagnose secondary brain injury as it occurs, and (4) track the response to treatment. There are many promising modalities under development, but a simple and reliable standard for monitoring has yet to be defined.

S100B is the most studied protein biomarker for traumatic and ischemic brain insults. It is released from damaged CNS cells and has a plasma half-life of ~30 min before renal excretion. The presence of S100B is a sensitive indicator of BBB disruption. S100B levels predict infarct volume as well as functional outcome after CVA. It can predict post-concussion symptoms in minor TBI and functional outcomes in severe TBI. Most promising of all, serum S100B concentration may predict increases in ICP up to 24 h before they occur, allowing aggressive therapy to be implemented. Clearly, more studies are necessary before serum S100B levels are used for clinical decision making, but the noninvasive nature of the test is very desirable.

Monitors have been developed to evaluate neurophysiologic parameters such as intracranial pressure, tissue oxygenation, as well as the function of neural pathways. Monitors vary based on their invasiveness and their ability to provide a therapeutic intervention. A monitor is effective if it can be coupled to a therapeutic intervention to improve outcome:

1. Intracranial pressure monitoring: The pressure inside the skull is measured by invasive monitors that are inserted through burr holes that are drilled into the skull (burr-hole craniotomies). Recent innovations allow for continual monitoring of MAP and ICP to continually calculate CPP. The pressure reactivity index (PRi) evaluates autoregulation by comparing changes in ICP with those in MAP during positive pressure mechanical ventilation. The loss of autoregulation is a harbinger of increased ICP and clinical deterioration:
   (a) The subdural bolt can monitor ICP, but without an ability to treat intracranial hypertension.
   (b) An extraventricular drain (EVD) can be inserted into a lateral ventricle to both monitor ICP and drain CSF in order to treat intracranial hypertension.
2. Tissue oxygenation monitoring: Monitors are available to measure local, regional, or global brain oxygenation:
   (a) Intraparenchymal probes measure the partial pressure of oxygen in brain tissue ($PbtO_2$) within a ~1 cm radius of the probe tip. Again, the regional nature of this measurement limits the usefulness of the technique.
   (b) Microdialysis catheters (MDCs) are intraparenchymal probes that evaluate the extracellular lactate/pyruvate ratio (LPR), which measures oxygen availability in brain tissue. An elevated LPR correlates with (1) a reduction in $CMRO_2$ as measured on PET scan and (2) clinical outcome. This associates mitochondrial dysfunction with cell death, suggesting that cells die from a lack of energy production.
   (c) Near-infrared spectroscopy (NIRS) utilizes light diffusion and scatter to measure relative ratios of oxy- and deoxyhemoglobin to determine a regional tissue oxygenation index. The NIRS monitor uses multiple detectors so that it can monitor brain tissue without interference from the scalp and cranium. Large-scale clinical trials of NIRS are under way to determine its clinical usefulness.
   (d) Oxygen saturation of the venous blood draining from the head into the bulb of the jugular vein ($SjvbO_2$) can

be measured and compared to arterial saturation to define oxygen extraction. $S_{jvb}O_2$ should range between 60 and 80 %. High oxygen extraction ratios are predicted by an $S_{jvb}O_2 < 55$ % and indicate that global ischemia is present. However, this technique is invasive and only measures global extraction rates. The presence of complete regional ischemia without collateral flow will not likely alter $S_{jvb}O_2$. Therefore, regional ischemia is likely to go undetected and this limits the specificity of $S_{jvb}O_2$.

3. Regional perfusion monitoring: Hemispheric CBF can be monitored via transcranial Doppler (TCD) ultrasound. TCD uses a special pulsed Doppler ultrasound that allows the probe to focus at a specific tissue depth, for example, the middle cerebral artery. Traditionally, the bulky equipment and need for a hands-on technician have limited its usefulness, but recent advances in technology have made continual TCD possible.
4. Neural pathway monitoring: Surface electrodes placed on the scalp and over individual peripheral nerves can monitor whether the neural pathways are intact. These are important in both intracranial and spinal surgeries (for EEG monitoring, see chapter on patient monitoring):
   (a) Somatosensory evoked potentials or SSEPs monitor (dorsal spinal cord columns) sensory pathways from the cerebral cortex through the thalamus and posterior spinal cord to the peripheral nerve. High doses of volatile anesthetics (>1 MAC) depress the amplitude and latencies of SSEPs. N_2O decreases amplitude but not the latency of SSEPs. Evoked potentials are preserved with the administration of barbiturates. Propofol and etomidate increase SSEP amplitude and latency in high doses. Ketamine increases wave amplitude, while opioids increase latency and may increase wave amplitude. Muscle relaxants have no impact on sensory nerve function and, therefore, do not alter SSEPs.
   (b) Electromyographic potentials (EMGs) monitor motor pathways from the cerebrum to a peripheral muscle via the anterior spinal cord. EMG monitoring requires that the tested muscle respond to such stimulation, and, therefore, neuromuscular blockade is not used when monitoring EMGs.

A non-paralyzed patient might move during light anesthesia, which can have serious consequences during neurosurgery. Therefore, when muscle relaxants are not used, the extra anesthetic depth must be provided by using a combination of agents at a combined ~2 MAC. Volatile anesthetics depress SSEPs at levels greater than 1 MAC, so they are usually combined with infusions of remifentanil and propofol to provide deep (2 MAC) anesthesia. A vasoconstrictor (usually phenylephrine) may be infused to counteract the vasodilation caused by the deep anesthesia.

Anesthetic Considerations for Neurosurgical Procedures

Craniotomy for Tumors

Craniotomies are commonly performed for a variety of pathologies. Neoplasms which grow slowly remain asymptomatic for a longer time than the rapidly growing ones. Clinical signs and symptoms of intracranial tumors include headache, seizures, decline in neurologic function, focal neurological deficits, cerebellar dysfunction (ataxia, nystagmus), brainstem compression (cranial nerve palsies, abnormal respiration), and an increase in ICP.

Preoperative Evaluation

A thorough history and physical examination is mandatory. Physical examination should include mental status assessment and neurologic examination for any sensory or motor deficits. The patient's medications should be reviewed (anticonvulsants, diuretics, corticosteroids). Laboratory evaluation should include measurements of glucose (hyperglycemia) and electrolytes. The patient should be assessed for presence of increased ICP, presence of cerebral edema (CT scan, MRI), a midline shift greater than 0.5 cm, and ventricular size. Premedication should be carefully administered to patients with intracranial pathologies, as it may cause respiratory depression and hypercapnia, which increase cerebral blood flow and worsen the ICP. Anticonvulsant therapy should be continued perioperatively.

Monitoring

Standard ASA monitors are applied including a Foley catheter so as to measure the urine output and the effect of diuretics. Intra-arterial blood pressure monitoring is mandatory (may be placed preoperatively) as there may be wide swings in blood pressure which have to be controlled promptly. To accurately assess cerebral perfusion pressure, the arterial pressure transducer is zeroed at the level of the external auditory meatus.

Patients should at least have one large-bore IV. Central venous access is done to monitor CVP and to infuse vasoactive medications. Sites commonly used for CVP monitoring include the subclavian vein or the median basilic vein (long catheter used for this vein). The internal jugular vein is avoided as it may interfere with venous drainage from the brain and also the surgical exposure. If the patient has neurologic deficits (stroke), neuromuscular monitoring should be done on the normal side and not on the affected extremity, as the twitch response in the affected extremity may not be depressed by neuromuscular-blocking drugs.

If the surgeon has inserted a ventriculostomy drain or a subdural bolt (under local anesthesia), the ICP can be monitored.

The transducer is again zeroed at the level of the head. Additionally, the CSF may be drained to decrease the ICP.

Induction of Anesthesia

Induction should be performed in a controlled manner. Both hypertension and hypotension should be avoided. The goal is to avoid increasing the ICP and maintaining the cerebral perfusion pressure. An excessive increase in the BP causes the ICP to increase, which decreases cerebral perfusion and increases the risk of herniation. Similarly, hypotension or hypovolemia can also lead to a decrease in the cerebral perfusion pressure.

The patient is preoxygenated adequately. This is followed by administering fentanyl (2–5 mcg/kg), lidocaine (1–1.5 mg/kg, to blunt the effects of stimulation by endotracheal intubation), and a precurarization dose of neuromuscular-blocking drug if succinylcholine is used. Anesthesia is induced by administering propofol (1–2 mg/kg) or etomidate (0.2–0.3 mg/kg), followed by a neuromuscular-blocking drug (succinylcholine [1–2 mg/kg] or rocuronium [0.6–0.9 mg/kg]/vecuronium [0.1 mg/kg]) to facilitate endotracheal intubation. Succinylcholine may increase transiently the ICP and its use may be avoided. If EMGs or motor evoked potentials are monitored, then the muscle relaxants are not redosed after their intubating dose. Hyperventilation may be used during the induction to decrease the ICP ($PaCO_2$ of about 30 mmHg).

It is important to note that head-holder pins cause intense adrenergic stimulus, which necessitates to increase the depth of anesthesia (propofol, narcotic, volatile anesthetic). Postinduction hypotension can be treated with phenylephrine or ephedrine. Hypertension is treated by increasing the depth of anesthesia (volatile agent, propofol) or administering labetalol or esmolol, as the case may be. Use of vasodilators (nitroglycerine, nitroprusside, hydralazine) is avoided until the dura is opened.

Positioning

Patients are usually positioned supine for craniotomy. The head is elevated 15–30° to facilitate venous and CSF drainage. The head should not be twisted more than 45° to one side as this may impede venous drainage via the jugular veins. The endotracheal tube and the anesthesia circuit should be well secured to prevent accidental disconnection. As the operating table would be turned 90–180°, the anesthesia circuit should be of proper length. All pressure points should be protected with adequate padding. Intravenous and monitoring lines should have adequate length and be properly secured.

Surgery performed in the sitting position, as for posterior fossa lesions, has its own complications, such as pneumocephalus and venous air embolism. Preoperatively, all patients should be evaluated for a patent foramen ovale, as it can cause embolism from the right atrium to the systemic circulation. As the CSF is lost during surgery, air can enter the subarachnoid space and cause a pneumocephalus. This can compress the brain and delay or prevent awakening of the patient. Secondly, since the operative site is above the level of the right atrium, air can enter the veins and cause embolism. If the air bubbles reach the pulmonary circulation in the lungs and are not cleared rapidly, the pulmonary artery pressure rises and causes a decrease in the cardiac output.

Clinical signs of air embolism include hypotension, tachycardia, a rising $PaCO_2$, and a falling $ETCO_2$ (because of a decrease in the cardiac output). Monitors to detect air embolism include transesophageal echocardiography (most sensitive monitor) and precordial Doppler probes. Additionally, TEE can also be used to assess cardiac function. The Doppler probe is placed over the right atrium, which is to the right of the sternum between the third and the sixth ribs. Hearing roaring sounds, rather than the regular swishing sounds, indicates venous air embolism.

Use of N_2O should be avoided, especially for sitting craniotomies, as it can cause expansion of the air bubble. The treatment of venous air embolism includes immediately informing the surgeon, who floods the field with saline, discontinuation of N_2O, an attempt to aspirate the air from the central venous catheter, fluid administration, and BP support. If these attempts are unsuccessful, preparations for CPR have to be done.

Maintenance of Anesthesia

Anesthesia is maintained with oxygen, fentanyl, a volatile agent (<1 MAC), and a muscle relaxant (rocuronium/vecuronium). Some anesthesiologists prefer to also use N_2O for its anesthetic and analgesic properties. It should be noted that N_2O increases cerebral blood flow (offset by hyperventilation) and will interfere with motor evoked potential monitoring. N_2O can also increase the volume of intracranial air space and is usually turned off before the dura is closed. For long-duration surgeries, the endotracheal tube cuff pressure may increase when using N_2O.

An alternative to using a volatile agent, TIVA may be used, which includes infusing propofol (100–200 mcg/kg/min). If EMGs or motor evoked potentials are *not* monitored, then the muscle relaxant is administered by bolus injections or via an infusion (titrated to one twitch of train of four). Regarding ventilation, normocapnia should be maintained, and the airway pressures should not be excessive as they can increase the ICP. Fluids should be replaced with glucose-free crystalloid solutions (lactated Ringer's or normal saline). It should be noted that excessive crystalloid administration may worsen cerebral edema. Colloids (5 % albumin, hetastarch) may be used to replace volume deficits.

Emergence

Patients are usually extubated at the end of the surgery, unless the patient's condition does not warrant extubation or

the ICP is still elevated. Similar to induction, the extubation procedure should be smooth, and one should prevent patient bucking which can precipitously increase the ICP. A small dose of propofol (20–30 mg) or lidocaine (1 mg/kg) may be given to smoothen the extubation. Patients should be adequately suctioned and the muscle relaxant reversed prior to extubation. Patients who are left intubated are admitted to the ICU, and for them adequate sedation and muscle paralysis are needed. Neuromuscular function assessment (moving the extremities) and mental status should be documented on the anesthesia record.

Traumatic Brain Injury

About 1.7 million people suffer trauma annually, and 30 % of trauma patients suffer neurologic injury. Most patients are young and male. TBIs are a heterogeneous group of injuries, and many factors influence the neurological outcome, including the patient's medical history and the physiologic response to both the injury and various treatments. Treatment of the CNS insult itself is still lacking and is often the limiting factor in recovery. TBIs can result in complete recovery, permanent disability, or death.

Pathophysiology of TBI

The pathophysiology of TBI is not well defined. Trauma causes primary brain damage due to mechanical forces on individual axons, capillaries, and the blood–brain barrier. This damage leads to secondary damage that includes pathologic neuronal excitation, brain edema, intracranial hematomas, and dysfunctional CBF autoregulation. From the time that the trauma occurs, these pathologies evolve over several days to cause ischemia and secondary injury.

The blood–brain barrier (BBB) is a barrier between the circulatory system and the brain extracellular fluid. It occurs along the capillary network where the capillary endothelial cells form tight junctions. The BBB allows glucose and small hydrophobic molecules (O_2, CO_2, hormones) to pass through, while preventing the passage of bacteria and large hydrophilic molecules. Disruption or dysfunction of the BBB can result in cerebral edema (Table 29.5). In most instances, cytotoxic and vasogenic edema occur together. Cytotoxic edema is dominant immediately following an injury or infarct, but gives way to a vasogenic edema that can persist for several days or weeks.

Evaluation of TBI

TBI evaluation is limited to physical examination and radiographic evaluation because there are no biomarkers for neurologic dysfunction or ischemia. Intubation is often essential to provide care to a TBI patient (mechanical ventilation to avoid hypercarbia) and requires sedation. This complicates the physical examination, which is the primary evaluation of the CNS and its response to treatment.

Patients with moderate/severe injury and those with mild injury but with LOC should be evaluated for TBI by a computed tomography (CT) of the head. Although a head CT has a relatively poor sensitivity for intracranial hypertension, intracranial hypertension is likely in the presence of a midline shift, a hematoma, any change in ventricle shape or size, or a loss of gray–white differentiation. Obliteration of the basal cisterns normally occurs before ventricular collapse, making cistern evaluation a meaningful part of CT evaluation.

Table 29.5 Types of cerebral edema

Vasogenic	• Most common form • Disruption of blood–brain barrier • Increased permeability of small vessels • Fluids and proteins leak from the vascular system into the extracellular space • White matter swelling > gray matter swelling • Occurs in trauma, intracranial tumors, focal inflammation, late stages of cerebral ischemia, hypertensive encephalopathy
Cytotoxic	• No disruption in blood–brain barrier • Cellular brain edema • Increased permeability of cell membranes due to cellular injury (disruption of sodium–calcium ion pumps due to lack of oxygen or glucose) • Accumulation of sodium and calcium intracellularly followed by accumulation of water • Gray matter swelling > white matter swelling • Occurs in early stages of cerebral ischemia/stroke, with metabolic toxins (dinitrophenol, hexachlorophene), severe hypothermia, cardiac arrest, pseudotumor cerebri
Hydrostatic	• Disruption of CSF–brain barrier • CSF spreads into extracellular space, mainly the white matter • Edema (CSF) contains no protein • Seen in obstructive hydrocephalus
Osmotic	• Dilution of plasma decreases serum osmolality • Higher CSF and extracellular brain osmolality causes water to move into the brain • Caused by excessive water intake, hyponatremia, SIADH, hemodialysis

Predictors of Outcome

The Glasgow Coma Scale (GCS) is commonly used to assess the severity of injury and correlates well with outcome. The GCS evaluates patient's motor, verbal, and eye response to physical examination (Table 29.6). Initial GCS motor scores, pupillary response, and CT findings are the most powerful predictors of outcome. However, the GCS score has several limitations. The GCS is nonlinear with greater weight placed on motor response, and the verbal response score is often omitted for a "T" in an intubated patient. The GCS is also insensitive to subtle changes of consciousness that may be harbingers of neurologic deterioration.

The Full Outline of UnResponsiveness (FOUR) score was developed to remedy the shortcomings of the GCS. The FOUR score places equal weight on four variables: eye response, motor response, brainstem response via pupillary reflexes, and respiratory pattern. In some studies, it has been shown to be a better predictor of brain damage and to respond more quickly to changes in consciousness.

Classification and Clinical Signs of TBI

- Mild—GCS 13 or higher, posttraumatic amnesia of <1 day, and no loss of consciousness or LOC of less than 30 min
- Moderate—GCS of 9–12, PTA 1–7 days, and LOC 30 min–24 h
- Severe—GCS 8 or less, PTA >7 days, and LOC >24 h, requires intubation

Signs of TBI include confusion, disorientation, amnesia, headache, dizziness, vision disturbances, ringing in ears, nausea and vomiting, or speech problems. These are more pronounced in cases of moderate and severe TBI. Severe TBI can ultimately result in cerebral herniation. Signs of cerebral herniation on physical examination include dilated and unreactive pupils, asymmetric pupils, or extensor posturing or no motor response. Elevated ICP can result in herniation of the uncus over the tentorium. There the uncus compresses the oculomotor nerve (CN III) and presents as a lack of reaction to bright light (<1 mm response) or a baseline asymmetry of >1 mm between the pupils due to inhibition of the parasympathetic fibers that travel on its surface. It can progress to complete blockade of CN III function that is recognized as a fixed and dilated ipsilateral pupil or *blown pupil*. Without therapy, the entire CN III input can be abolished, causing inferior and temporal pupillary deviation.

Table 29.6 Glasgow Coma Scale

Motor	Verbal	Eye opening
6. Spontaneous	5. Oriented	4. Spontaneous
5. Localizes to pain	4. Confused	3. Verbal stimuli
4. Withdraws to pain	3. Inappropriate	2. Painful stimuli
3. Decorticate posturing	2. Incoherent	1. No response
2. Decerebrate posturing	1. No verbalization (intubated[a])	
1. No movement		

[a]Intubated patients are appointed a verbal score of 1 with a modifier "t" added to their score to indicate their intubated status [e.g., a 6 t for a patient who is intubated (1-nonverbal), does not open their eyes (1), and withdraws with painful stimuli (4)]

Similarly, frontal swelling can cause the cingulate gyrus to herniate over the tentorium. This compresses the anterior cerebral artery (or the anterior communicating artery) and disrupts blood supply to the internal capsule, as evidenced by extensor posturing or a lack of movement after painful stimulation of the extremities. Cingulate herniation is a harbinger of further herniation and necessitates immediate therapy; therefore, motor responses are an essential part of the evaluation of the patient with TBI.

Preoperative Management

The emergent therapy for TBI focuses on minimizing secondary insults by maintaining adequate oxygen delivery to injured brain tissue. In the acute phase, trauma patients often suffer from systemic hypotension, hypoxemia, and hypercarbia that worsen the secondary injury. A retrospective review of TBI patients found hypotension (systolic pressure <90 mmHg) on arrival to the emergency department as a stronger predictor of poor outcome or death than hypoxia ($PaO_2 < 60$ mmHg).

The presence of electrocardiographic abnormalities (T-wave and ST segment changes) is common in head injury patients and likely represents disturbances in autonomic function rather than cardiac injury. Patients with TBI are at increased risk for DVT, but it should be noted that antithrombotic prophylaxis also increases the risk of intracranial hemorrhage. Radiographic studies should not gain priority over clinical management of the patient. Every patient should be stabilized prior to any radiographic studies.

Anesthesiologists are frequently called to the emergency room to manage ventilation in head injury patients. All head injury patients should be considered to have a full stomach. Patients should be adequately preoxygenated, which is followed by rapid sequence induction with cricoid pressure (propofol/etomidate, muscle relaxant—succinylcholine/rocuronium). Coexisting cervical spine injury is relatively common (10 % incidence) and warrants careful in-line stabilization during endotracheal intubation. In patients suspected of a difficult airway, an awake fiberoptic intubation or tracheostomy is performed.

Intraoperative Management

Monitoring modalities include intra-arterial, central venous, or pulmonary artery monitoring and intracranial monitoring. Anesthesia is maintained with oxygen, volatile agent, fentanyl, and a muscle relaxant. N_2O is avoided if air trapping is a concern. Hyperventilation is avoided as it decreases CBF.

Hypotension is treated with phenylephrine/ephedrine and fluid management to maintain CPP at about 70 mmHg. Treatment of hypertension is avoided until the dura is opened. Treatment of hypertension before the dura is opened may blunt the protective Cushing's reflex. At the conclusion of the surgery, the patients are extubated, if stable, or left intubated, if unstable or having ICP issues.

The presence of hypotension is usually associated with intra-abdominal injuries. In the presence of bleeding, volume resuscitation should be adequate and at the same time not lead to cerebral edema. Volume resuscitation is the initial therapy for hypotension after TBI and the choice of fluid is important. Hyperosmolar fluids have the potential to both replace volume and increase plasma oncotic pressure, which has the potential to pull water from the interstitial space and reduce brain edema. However, large studies that compared initial resuscitation with isotonic (0.9 %) to hypertonic (7.5 %) saline found no difference in mortality or functional neurologic outcome at 6 months. In another study, initial resuscitation with 5 % albumin led to a poorer outcome in the setting of vasopressor-enhanced CPP. The hematocrit should be maintained at least 33 % to maximize oxygen delivery. A vasopressor may have to be used to maintain the arterial pressure.

Hyperglycemia is deleterious to the injured brain tissue, and therefore, glucose-containing solutions should be avoided. The brain responds to hyperglycemia by increasing metabolism without regard for oxygen availability. This can lead to significant increases in lactate production and local acidosis, both of which are deleterious to brain tissue. Therefore, glucose-containing solutions are only administered to treat hypoglycemia.

Guidelines for TBI Treatment

The following are the US National Guideline Clearinghouse and NICE guidelines for the treatment of TBI:

1. Hyperventilation should only be used as a temporizing measure to reduce ICP: prophylactic hyperventilation is not recommended. In the first 24 h after TBI, hyperventilation to $PaCO_2 < 25$ mmHg mediates hypoperfusion and ischemia. Hyperventilation and relative hypocarbia are only recommended in the setting of impending herniation.
2. Sedatives should only be used to reduce $CMRO_2$ in the presence of intracranial hypertension despite medical and surgical therapies.
3. Hyperthermia is associated with poor outcome due to increased $CMRO_2$ and CBF, leading to ischemia, inflammation, and edema formation. However, prophylactic hypothermia is not associated with improved outcome.
4. Seizures should be treated immediately with anticonvulsants.
5. Blood pressure should be monitored and hypotension (systolic blood pressure <90 mmHg) avoided.
6. Oxygenation should be monitored and hypoxia ($PaO_2 < 60$ mmHg or O_2 saturation <90 %) avoided.
7. Mannitol is effective in reducing ICP in the management of traumatic intracranial hypertension. Current evidence is not strong enough to make recommendations on the use, concentration, and method of administration of hypertonic saline for the treatment of traumatic intracranial hypertension.

The Brain Trauma Foundation (BTF) recommends that intracranial hypertension (>20 mmHg) be treated by increasing CPP to perfuse edematous tissue. Studies of the impact of CPP on outcome showed that increasing MAP *and* decreasing ICP improved outcome as compared to increasing MAP alone. The BTF's first published recommendations proposed a CPP >70 mmHg, but the high MAP required to achieve that CPP was associated with ARDS, and the target CPP was revised downward to 50–70 mmHg. Of note, TBI patients often display autonomic dysfunction with significant variations in both blood pressure and heart rate; a coexisting loss of cerebrovascular autoreactivity is common. Any loss of autoregulation is indicative of a poorer outcome.

When intracranial hypertension persists despite medical management, physicians may apply an alternative (and less widely accepted) strategy known as oxygen-directed therapy, or Lunde therapy. Proponents of the Lunde concept argue that edema at the injury site is responsible for secondary ischemic injury due to reduced venous outflow. They also argue that increasing MAP (and thus CPP) via increasing SVR decreases perfusion by (1) reducing cardiac output and (2) exacerbating the edema by increasing capillary pressure. In response, Lunde practitioners supplement oncotic pressure via infusions of 5–20 % albumin to increase plasma oncotic pressure to reduce edema. Angiotensin II and β-blockers are combined with α2-agonism in order to limit vasospasm and transcapillary pressure and reduce edema formation. Rather than targeting a specific CPP, the CPP is manipulated in response to tissue oxygenation levels. Preliminary and retrospective studies have shown favorable outcomes in TBI patients who received Lunde therapy. Clearly, this therapy warrants further randomized controlled trials.

Finally, decompressive craniectomy is a surgical intervention employed for intracranial hypertension. It is typically employed when a patient presents with signs of imminent herniation or a patient's neurological examination deteriorates despite maximal medical therapy. It involves resecting a portion of the skull in order to nullify the Monro–Kellie doctrine by allowing the brain tissue to expand, thereby decreasing ICP while increasing CPP.

Summary of TBI Management

The evaluation of TBI begins with physical examination. Treatment begins with fluid resuscitation with isotonic crystalloid. Fever and hyperglycemia are very deleterious and warrant aggressive treatment. Hyperventilation is only indicated in

the setting of catastrophic herniation. If a CT scan is indicated and shows a lesion consistent with or the potential to increase ICP, it may be treated with an EV drain or craniotomy to avoid further ischemic injury. Hypertonic therapy may include mannitol or hypertonic saline, which should be repeated every 4–6 h with concurrent electrolyte monitoring.

As in SAH, the traumatically injured brain progresses through different stages of injury, and despite the normalization of ischemic conditions, injured tissue may progress to necrosis or apoptosis. There is no proven therapy to provide neuroprotection. Many clinicians advocate the use of oxygen-directed therapy when the patient's condition continues to deteriorate despite these therapies. However, no single monitor or therapeutic strategy has been shown to improve outcome, and research into this important pathology continues.

Subarachnoid Hemorrhage and Cerebral Aneurysms

About 2–3 % of individuals have cerebral aneurysms, and these patients are at risk for aneurysm rupture with intracerebral hemorrhage or subarachnoid hemorrhage (SAH). The most common cause of SAH is rupture of a saccular aneurysm at branch points of the circle of Willis. These incidents account for <10 % of strokes, but because they have a high morbidity and strike middle-aged individuals (40–60 years), they cause as much long-term disability as ischemic strokes.

Risk factors: Female sex, hypercholesterolemia, alcoholism, and cigarette smoking are risk factors for aneurysm formation, which in turn increase the risk of aneurysm rupture and SAH. Women and African-Americans suffer increased morbidity after rupture for unclear reasons. Prodromal symptoms suggesting enlargement and impending rupture include headache (the worst kind), eye pain, visual field defects, and cranial nerve palsies (CN III and CN VI). The body's stress response to SAH includes increased neurogenic sympathetic activity as well as increased catecholamines. These changes commonly cause non-life-threatening arrhythmias and, rarely, result in a stunned myocardium with or without neurogenic pulmonary edema.

*Size and location***:** of the aneurysm determines the risk of rupture and the need for intervention. While small aneurysms (<7 mm) may be monitored with serial CT examinations, larger aneurysms, especially those in the vertebrobasilar or posterior circulation, benefit from intervention. A patient's history of aneurysm rupture is highly predictive of the future rupture of coexisting aneurysms. Angiograms are performed for the presence and evaluation of coexisting aneurysms, which are considered during treatment of a ruptured aneurysm or after surgical clipping of a non-ruptured aneurysm.

Prognostic factors: Patient's age, GCS score on admission, and subarachnoid blood volume on presenting CT scan are the major prognostic factors after SAH. Hunt and Hess developed a simple scale to grade SAH symptoms on a scale of 1–5. The scale has been used extensively to determine treatment, but it loosely correlates with outcome. Several other scales have been developed on the basis of modern outcomes data to predict outcome and guide therapy. Acute phase mortality after aneurysm rupture is approximately 15 %. One-fifth of SAH survivors suffer from global cognitive impairment 1 year after their event. Outcome is worsened by fever, the use of blood transfusion, and the development of delayed cerebral ischemia:

Grade I—asymptomatic or mild headache—11 % (mortality)
Grade II—moderate to severe headache or CN III palsy—26 %
Grade III—confusion and drowsiness—37 %
Grade IV—stupor—71 %
Grade V—coma—100 %

Pathophysiology

After an aneurysm rupture, cerebral perfusion falls acutely and drastically via two mechanisms. First, blood shunting through the rupture site reduces cerebral blood flow, and secondly, the shunted blood increases regional ICP which further hinders perfusion. The exposure of blood to extravascular tissue initiates clot formation at the aneurysm's rupture site, which may result in clotting of the entire aneurysm. Blood flow gradually normalizes, but 30 % of untreated ruptured aneurysms rebleed in the first 6 months with the highest incidence within 24 h of the initial bleed.

A second period of delayed cerebral ischemia (DCI) occurs in about 30 % of the patients. This usually occurs 5–9 days after the acute phase of aneurysm rupture. The etiology of DCI is controversial. Classically, the etiology of DCI was described as cerebral vasospasm, as the best clinical outcomes were seen with calcium channel blockers nimodipine or nicardipine. However, despite improved clinical status, nimodipine treatment did not significantly reduce vasospasm. More doubt is cast on vasospasm as an etiology for cerebral ischemia because the temporal correlation between vasospasm and DCI is poor, and the area of dysfunctional tissue may or may not occur in areas perfused by the spastic artery. Other etiologies proposed for DCI include apoptosis and spreading depolarization.

Medical Management

Acute phase management after SAH includes limiting the systolic blood pressure to 140 mmHg to reduce the risk of rebleeding. The fluid of choice for resuscitation and maintenance is 0.9 % NaCl. Half of patients experience a febrile response to their SAH, and hyperthermia increases the risk of poor outcome by four times. Temperature should be

maintained at less than 37 °C. Euglycemia is desired with a target glucose of 80–120 g/dl. Patients who present with a seizure should receive seizure prophylaxis with phenytoin or levetiracetam.

Patients who suffer an SAH usually have a history of hypertension, and the SAH often worsens this state. Vasospasm occurs most commonly on days 5–9 in patients who present with Hunt–Hess grades 4 or 5. Nimodipine and magnesium infusions are used for vasospasm prophylaxis and blood pressure control. TCD, CT angiography, or brain MRI is recommended on days 4–14 in high-risk patients to evaluate for vasospasm. If vasospasm is found, it can be treated with a direct intra-arterial infusion of vasodilating drugs or intracerebral stents.

Treatment of DCI

The use of hypervolemia, hypertension, and hemodilution (HHH therapy) has been widely advocated to increase perfusion in areas at risk for vasospasm due to SAH. It is discussed here with the intention of describing the theory and presenting evidence behind each of these three components. Several clinical trials failed to show that HHH improves tissue perfusion after ischemic injury, which is not surprising given the previous discussion above regarding vasospasm after SAH:

- Hypervolemia: Adequate fluid resuscitation is necessary to optimize cardiac output in all patients. Hypertension is a risk factor for SAH, and these patients are commonly hypovolemic at baseline due to endogenous natriuretic peptides and diuretic therapy. One recent study showed that 1/3 of patients with SAH were either moderately or severely hypovolemic, defined as a circulating blood volume <60 ml/kg. Fluid resuscitation to normovolemia has been associated with improved outcome. However, hypervolemia does increase complications in this population, which include cerebral edema, pulmonary edema, and CHF.
- Hypertension: Hypertension definitely increases CPP and CBF. Tissue perfusion in areas adjacent to an SAH is often pressure passive due to dysfunctional autoregulation, meaning that CBF has a linear relationship with CPP. One study of SAH patients with diagnosed vasospasm demonstrated increased CBF when cardiac output was increased via dobutamine infusion. Studies have shown that induced hypertension increases the oxygen concentration in brain tissue, and studies are under way to assess its clinical impact.
- Hemodilution: The reduced blood viscosity provided by hemodilution increases blood flow through capillaries during pressure-passive flow. This is especially apparent in the vasospastic and edematous vessels that are present in the penumbra that surrounds an area of SAH. Because hemodilution also reduces hemoglobin concentration, a target hematocrit of 30–33 % is believed to provide optimal oxygen delivery. Further hemodilution will reduce the oxygen-carrying capacity of blood. Patients presenting with SAH often have cardiac and pulmonary comorbidities, which necessitate a higher hematocrit.

Anesthetic Considerations for Cerebral Aneurysm Surgery

Surgeries performed between post-aneurysm-rupture days 4 and 14 are associated with a greater incidence of symptomatic vasospasm. Therefore, surgeons avoid non-emergent procedures in this period. The primary interventions for cerebral aneurysms are craniotomy with surgical clipping or endovascular coiling to ablate the aneurysm. While clipping carries a higher risk of intraoperative morbidity, coiled aneurysms have a higher risk of rebleeding. Smaller aneurysms are more likely to rupture during coiling because the wall may be injured when the coil is deployed into a small space, while larger aneurysms are more likely to rupture due to increased wall tension. Posterior circulation aneurysms are particularly likely to rupture and are difficult to access via endovascular coiling; therefore, they are often clipped.

Besides basic preparation for surgery (history, physical, lab work), blood should be crossmatched and be immediately available for transfusion, if needed. Monitors for cerebral aneurysm clipping include invasive monitors and intra-arterial and central venous monitoring. Additionally, a precordial Doppler ultrasound should be placed for any craniotomy that will approach the dural venous sinuses in order to detect venous air embolism.

All patients are adequately preoxygenated. Premedication is generally avoided as it may cause respiratory depression and hypercapnia. Precurarization with a small dose of muscle relaxant (rocuronium 5–10 mg) is beneficial as it reduces the transient ICP increase seen with succinylcholine administration.

Induction of anesthesia (with propofol/etomidate, fentanyl, lidocaine, muscle relaxant for intubation) should focus on maintaining cerebral perfusion pressure to ischemic areas, while avoiding hyperemia and sudden increases in BP that can lead to aneurysm rupture. These increases in BP may occur during endotracheal intubation or surgical stimuli. Therefore, an adequate depth of anesthesia should be maintained throughout.

Anesthesia is maintained with oxygen, volatile agent, fentanyl, and a muscle relaxant. Once the dura is opened, mannitol is commonly infused to reduce brain volume and the need for surgical retraction during aneurysm clipping. The initiation of the infusion should take into account the fact that the effect is delayed until 20–30 min after the infusion is initiated. Hypernatremia should be avoided in the setting of SAH as it can lead to pulmonary edema and CHF. The blood pressure is maintained on the lower side of normal before aneurysm clipping and normal/high normal after clipping.

The patient is hyperventilated before clipping, and normocarbia is then maintained. Normothermia is maintained as hypothermic protocols have not been shown to improve outcome after aneurysm clipping. Attempts are made to extubate the patient at the conclusion of the surgery. If not, the patients are taken to the ICU.

Controlled hypotension may be used during aneurysm clipping, as it reduces transmural tension across the aneurysm. Controlled hypotension also decreases blood loss and improves surgical exposure. Controlled hypotension, with a target MAP of 60–70 mmHg, can be achieved with a slightly head-up position, using an inhalational volatile agent and hypotensive agents (nitroglycerine, nitroprusside).

Although rare, aneurysm rupture can be a catastrophic complication of aneurysm surgery. Rapid changes in the transmembrane pressure (sudden drainage of CSF or hyperventilation) or surgical trauma may cause aneurysm rupture. Aneurysm rupture leads to a decrease in MAP in the cerebral circulation, resulting in immediate global ischemia. The hemorrhage also obscures the ruptured aneurysm, making vessel control difficult and death imminent. The treatment is a sharp decrease in cardiac output that may be achieved by a bolus of nitroglycerine, which greatly reduces the cardiac preload, controlling BP (MAP 40–60 mmHg), and burst suppression (using propofol). Adenosine dosed at 15–30 mg may stop the heart for up to 60 s (place defibrillator pads preoperatively on the patient).

Catastrophic aneurysm rupture is avoided by isolating the aneurysm from the circulation prior to clipping. However, this usually involves temporary clipping of the vessels of the circle of Willis that may lead to ischemia. An increased MAP improves collateral brain perfusion when temporary clips are in place. A bolus dose of propofol prior to clipping may decrease $CMRO_2$ to improve the O_2 supply/demand ratio. Antifibrinolytics, such as epsilon aminocaproic acid, may be used to stabilize the existing clot prior to endovascular coiling, but their use is controversial.

Other Surgeries

Other neurosurgeries that are performed include:

- Transnasal transsphenoidal pituitary tumor—This procedure can be done endoscopically or via craniotomy if the tumor is large. Since the tumor is located near cavernous sinuses, intraoperative bleeding may be significant.
- Ventriculoperitoneal shunt—to drain CSF into the peritoneal cavity, usually performed under general anesthesia.
- Brain biopsy—under local/general anesthesia.
- Resection of seizure focus—involves temporal lobectomy, is usually performed awake (with mild sedation) so that the patient can communicate.
- Stereotactic radiosurgery—delivery of radiation to a tumor.
- Ommaya reservoir—implantation of a chemotherapy reservoir under the scalp.
- Deep brain stimulator—Electrode placed deep into the brain (hypothalamus) to treat certain disorders, such as parkinsonism, usually performed awake with mild sedation.
- Arteriovenous malformations—An arteriovenous malformation (AVM) is a low-pressure drop connection that allows blood to bypass local capillary beds and reach the veins (direct arteriovenous connection). They often present as intracerebral hemorrhage between the ages of 10 and 30 years. The vascular beds that lie adjacent to the AVM vasodilate in order to maximize local perfusion and often lose the ability to autoregulate blood flow. Treatment of AVM includes embolization and radiation and surgical excision when the prior are not successful. AVM resections are often associated with extensive blood loss, and therefore, large-bore IVs and intra-arterial blood pressure monitoring are necessary. After AVM resection, the surrounding tissue is at risk for hyperemia injury that may include edema or even hemorrhage. Thus, the blood pressure should be controlled after resection until the vasculature recovers.

Clinical Review

1. Change in cerebral blood flow (100 g/min) for each 1 mmHg change in $PaCO_2$ is:
   A. 1 ml
   B. 3 ml
   C. 5 ml
   D. 10 ml
2. The mean arterial pressure is 70 mmHg, the intracranial pressure is 12 mmHg, and the central venous pressure is 14 mmHg. The calculated cerebral perfusion pressure (mmHg) is:
   A. 44
   B. 56
   C. 58
   D. 96
3. The following drug increases intracranial pressure:
   A. Propofol
   B. Etomidate
   C. Pancuronium
   D. Succinylcholine
4. The administration of the following solution should be avoided in head injury patients:
   A. Albumin
   B. Hetastarch
   C. Dextrose
   D. O^- red blood cells

5. If you need to perform a wake-up test, intraoperatively, to assess neurologic function, you would prefer to use the following volatile agent:
   A. Isoflurane
   B. Halothane
   C. Sevoflurane
   D. Desflurane
6. Sedation may increase intracranial pressure by causing:
   A. Hypercapnia
   B. Hypocapnia
   C. Hypoxia
   D. Acidosis
7. Nitrous oxide affects intracranial pressure by:
   A. Increasing it
   B. Decreasing it
   C. No effect
   D. Initial increase, followed by a decrease
8. The HHH therapy to treat cerebral vasospasm consists of:
   A. Hypertension, hypervolemia, and hemodilution
   B. Hypertension, hypervolemia, and hypocapnia
   C. Hypertension, hypocapnia, and hemodilution
   D. Hypertension, hypervolemia, and hypercapnia
9. The following therapy is not used to treat high intracranial pressure:
   A. Mannitol
   B. Hypotonic saline
   C. Furosemide
   D. Hyperventilation
10. Cushing's triad seen in a head injury patient consists of:
   A. Hypotension, tachycardia, and irregular respiration
   B. Hypotension, bradycardia, and tachypnea
   C. Hypertension, bradycardia, and irregular respiration
   D. Hypertension, tachycardia, and bradypnea

Answers: 1. A, 2. B, 3. D, 4. C, 5. D, 6. A, 7. A, 8. A, 9. B, 10. C

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Ambulatory Anesthesia

30

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and Ashish Sinha

Ambulatory surgery refers to surgical procedures that are done on a day-care basis, where patients are discharged home the same day of admission and do not require hospitalization. Due to low cost economics, ambulatory surgical procedures are being increasingly performed in recent years (Table 30.1). The cornerstone of ambulatory practice is early and rapid recovery of the patient. Newer surgical and anesthesia techniques, postoperative pain management advances, and optimal prophylaxis of postoperative nausea and vomiting (PONV) have largely been responsible for improved ambulatory care. Increasing surgical procedures performed under monitored anesthesia care (MAC), regional anesthesia techniques, and general anesthesia techniques with short-acting drugs are the basis of the early discharge. At the same time, safety of the patient is paramount, and therefore, various guidelines and recommendations have been formulated.

Advantages and Risks

As mentioned above, ambulatory anesthesia and office-based anesthesia have gained popularity in the recent years because of their low cost, comfort, and convenience to patients. Other advantages include ease of scheduling, maintenance of patient privacy, decreased risk of nosocomial infections, and relatively more personal attention to the patient.

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However this subspecialty has also developed its own risk profile. Possible compromise of patient safety in the interest of efficiency is possible. Office-based procedures have an overall complication rate of 0.24 %, and factors that contribute to this problem include limited availability of anesthesia personnel, inadequate availability of anesthesia and resuscitation equipment, and lack of backup personnel and expert consultation. Although the mortality rate of office-based anesthesia is lower (1:400,000) as compared to in-hospital anesthetics (1:250,000), the fact partly contributing to this statistic is that office-based anesthesia usually involves young, healthy patients with no or few comorbidities.

To ensure patient safety, certain prerequisites for the facility where these surgeries are being done have been established. These include regular checkup and maintenance of ventilators and availability of age-appropriate resuscitation equipment, difficult airway and malignant hyperthermia carts, drugs for resuscitation in the event of a cardiac arrest or an emergency, and a defibrillator with a battery backup. To manage these problems, regulations are in place for office-based anesthesia (ASA-SAMBA regulations), as well as the existence of a number of accreditation organizations for ambulatory anesthesia facilities (Accreditation Association for Ambulatory Health Care or AAAHC and American Society for Accreditation of Ambulatory Surgical Facilities or AAASF).

Patient Selection

Patient selection is the key to procedures being safely performed in the ambulatory care center. Most of the patient mix is of ASA I and II patients. Surgery for patients who are >ASA III classification may not be performed in an ambulatory care setting, unless the surgery is minor. These ASA III patients usually have a history of congestive cardiac failure, unstable angina, severe pulmonary disease (COPD, asthma), renal failure, or uncontrolled hypertension or diabetes mellitus.

One should be mindful of the risks factors that increase the complication rate for surgeries performed in the ambulatory

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Table 30.1 Surgical procedures commonly done under ambulatory anesthesia care

• Cosmetic surgeries: breast reduction or augmentation, rhinoplasty, liposuction, blepharoplasties
• Orthopedic surgeries such as arthroscopies, carpal tunnel release
• Endoscopic procedures such as colonoscopies
• Minor urological procedures
• Mini-laparoscopic procedures
• Dental procedures
• Ophthalmic procedures: cataracts, strabismus repair
• ENT procedures: tonsillectomy, myringotomy, septoplasty

Table 30.2 Preoperative evaluation for ambulatory procedures

1. Abnormalities of any organ system, optimization of any medical illness
2. Current medications
3. Airway assessment, associated obesity, obstructive sleep apnea
4. History of previous anesthetics and any adverse events in the patient or family member
5. Alcohol and substance abuse, current or in the past
6. Last oral intake, follow appropriate NPO guidelines
7. Presence of a responsible person to take the patient home and care for him/her at home
8. Patient education regarding risks, anesthetic plan, and postoperative course

care center. These risks factors include extremes of age, morbid obesity, history of smoking, presence of comorbidities, site and duration of the surgery, controllability of postoperative pain, excessive fluid losses, need for general endotracheal anesthesia, distance of the ambulatory center from an emergency service center, and escort availability for the patient.

One of the most important patient-related factors for consideration in ambulatory anesthesia service is the availability of a responsible person who can take the patient home and care for the patient at home. In the pediatric age group, prematurity with post-gestational age <60 weeks is a contraindication for same-day surgery (increased incidence of apnea). Morbidly obese patients with a BMI of >35 kg/m^2 may only have procedures done with mild sedation. Patients with pulmonary disease or suspected sleep apnea should have satisfactory oxygen saturation on room air.

Preoperative Evaluation for Ambulatory Procedures

A thorough preoperative evaluation (Table 30.2) along with an informed written consent is a must. Patients are contacted by the surgery center at home preoperatively by telephone or the patient sends in a filled questionnaire. This is done to identify any risk factors and to ensure that the patient is medically optimized before the surgery. Appropriate laboratory results should also be available on the day of the surgery.

Anesthesia Techniques in the Ambulatory Care Setting

Monitored Anesthesia Care With or Without Local Anesthesia

Varying levels of sedation with local anesthesia (breast biopsy, inguinal hernia repair, hemorrhoidectomy) or without local anesthesia (colonoscopies, endoscopies) can be used. While performing MAC, one should be aware that the dose of sedatives required to achieve a particular depth of anesthesia is different for each patient and that there is no objective measurement of anesthesia depth. While a light plane of anesthesia may not provide adequate comfort to the patient and decrease cooperation from the patient, a deep plane of anesthesia may render a patient uncooperative. Respiratory depression from oversedation accounts for many complications (hypoxia and brain injury). Backup airway management equipment should be available at all times.

MAC is usually performed by using anxiolytic and sedative drugs (midazolam, fentanyl, propofol), injection of local anesthetics (usually by the surgeon), and providing supplemental oxygen. A deeper plane of anesthesia may be required (bolus of propofol) when the surgeon injects the local anesthetic. Goals of MAC are minimal/adequate depression of consciousness (allowing rapid recovery) and providing anxiolysis, sedation, and analgesia.

Regional Anesthesia

Peripheral nerve blocks, intravenous regional anesthesia (IVRA), or spinal anesthesia may be used for ambulatory surgeries. Peripheral nerve blocks are extremely popular and are performed preoperatively using mild sedation. These blocks are nowadays commonly performed with ultrasound guidance, which has decreased the complication rate. Commonly used local anesthetics for nerve blocks include bupivacaine, ropivacaine, and lidocaine. IVRA is usually performed using 0.5 % preservative-free lidocaine. For spinal anesthesia, lidocaine is avoided due to the increased incidence of transient neurological symptoms. The benefits of regional anesthesia techniques include lower cost, excellent surgical conditions, excellent postoperative analgesia, and low incidence of PONV.

Nerve block catheters can be very effective for postoperative pain relief. Local anesthetic infusion via popliteal, interscalene, or femoral catheters can provide pain relief for about 4 days. Patients can be sent home on a local anesthetic infusion if the patients are appropriately interested and are educated about the pump function and signs of local anesthetic

toxicity and have a responsible adult at home to take care of them. Postoperatively, patients receiving upper extremity nerve blocks should have the blocked extremity placed in a sling, while patients receiving lower extremity nerve blocks should receive coaching on using crutches for walking. Additionally, all ambulatory centers should be equipped with intravenous lipid emulsion to counteract the effects of local anesthetic toxicity.

General Anesthesia

For some procedures, such as laparoscopic surgery, general anesthesia is performed. Use of drugs of short duration of action and prophylaxis against PONV are most important.

Preoperative Fasting

Light meals up to 6 h and clear fluids up to 2 h preoperatively are allowed. Carbohydrate-rich clear fluids decrease thirst and hunger sensations and anxiety. Breast milk for 4 h and infant formula for 6 h are allowed preoperatively before surgery.

Premedication

Drugs commonly used for premedication include:

1. Benzodiazepines: Midazolam is commonly used for anxiolysis and sedation. In adults, midazolam 2–4 mg intravenously may be used preoperatively, or oral diazepam 2–5 mg the night before or on the day of surgery helps to control anxiety. For pediatric patients, oral midazolam in doses of 0.25–0.5 mg/kg (maximum 20 mg) makes the child cooperative and decreases parent separation and stranger anxiety. In appropriate doses these drugs cause minimal cardiorespiratory depression; however, it is recommended that supplemental oxygen be administered with pulse oximetry monitoring when using these drugs.
2. Beta-blockers: These drugs (metoprolol, atenolol) reduce the sympathetic and catabolic response to surgery. They have also been found to decrease the postoperative requirement of analgesics. Beta-blockers should be continued on the day of surgery.
3. Alpha-2 agonists: These drugs not only decrease the requirement of opioids but also decrease intraoperative blood loss and PONV. Clonidine has also been found to decrease postoperative ileus when given epidurally.
4. Opioids: While opioids prevent the hypertensive response to intubation, they can also be used to provide postoperative analgesia (OxyContin 10 mg PO administered preoperatively).
5. NSAIDs: NSAIDs like celecoxib (400 mg) orally in adults and acetaminophen orally/rectally in children, given preoperatively, help to reduce postoperative pain. Intravenous acetaminophen and ibuprofen are useful adjuncts in postoperative pain management.
6. GI prophylaxis: This includes administration of famotidine (20 mg PO/IV) or ranitidine (150 mg PO/50 mg IV) and prophylactic antiemetics such as ondansetron (4 mg), dexamethasone (4–8 mg), and a scopolamine patch. A scopolamine patch is not applied for patients at the extremes of age.

Induction of Anesthesia

1. Propofol, because of its rapid onset and elimination, is the obvious choice for induction and sometimes maintenance of anesthesia. Residual CNS effects after propofol last for only 1 h, whereas that with thiopental can last for as much as 5 h. To decrease the pain on propofol injection, using bigger veins, adding lidocaine, and administration of 0.1 mg/kg of ketamine before administering propofol are all variably helpful.
2. Ketamine has an added advantage of being an analgesic and provides dissociative anesthesia without obtunding the respiratory drive. It also increases the blood pressure and causes dysphoric reactions. Administering midazolam (or propofol) helps to decrease ketamine's dysphoric actions. Clonidine helps to blunt its hypertensive effect, while glycopyrrolate decreases the secretions.
3. For children who do not allow placement of an IV line before induction of anesthesia, inhalational induction with sevoflurane is used. If an IV line is required before induction of anesthesia, ketamine may be administered intramuscularly to obtund the patient.

Maintenance of Anesthesia

Desflurane and sevoflurane, based on their blood-gas partition coefficients, provide faster recovery from anesthesia compared to isoflurane and are the preferred agents for maintenance of anesthesia for ambulatory surgical patients. Total IV anesthesia with propofol and remifentanil/dexmedetomidine not only obviates the need for a bulky anesthesia machine but also decreases OR pollution, incidence of PONV, and awakening times. Bispectral index (BIS) may be used to monitor the dose of maintenance agents.

Any of the intermediate-acting muscle relaxants, vecuronium, rocuronium, or cisatracurium, may be used to provide muscle relaxation. Neuromuscular blockade should be completely reversed at the end of surgery.

Pain Management

Multimodal analgesia is the key for management of pain in the ambulatory care setting. This includes administering drugs and performing peripheral nerve blocks (with or without continuous infusion via catheters—see above). The aim is to minimize the use of opioids and their adverse postoperative effects like nausea and vomiting, pruritus, respiratory depression, constipation, and urinary retention.

(a) NSAIDs: They are the first-line analgesics for ambulatory surgical patients. Increased risk of bleeding is a concern; however, for most surgeries this is usually not an issue. Typical doses are 30–60 mg IV of ketorolac for adults and acetaminophen (children aged 3–12 years, 120–240 mg orally and adults, single dose up to 1,000 mg, daily maximum of 4,000 mg).
(b) Opioids
- Remifentanil: This newer opioid has a short time of onset (1–1.5 min) and a short duration of action (3–4 min). Its metabolism is by ester hydrolysis and is not dependent on the function of either the liver or the kidney. Although remifentanil is very useful for short duration intense procedures, drawbacks of this drug are the lack of postoperative analgesia and its price.
- Fentanyl: Being a shorter-acting agent, it is the preferred opioid for ambulatory surgeries. For postoperative pain, 25 mcg of fentanyl is administered, repeated every 5 min, until the pain is controlled (up to 2 mcg/kg for children).
- Oral acetaminophen (300 mg) with codeine (30 mg), given every 4 h as necessary.

PONV Prophylaxis

One of the major goals of ambulatory anesthesia is reduction in the incidence of PONV, so that the patient can be discharged home. Risk factors for PONV include younger age, nonsmoker, female gender, history of PONV or motion sickness, use of opioids intraoperatively, and the type of surgery (breast surgeries; ear, nose, and throat surgeries; or laparoscopic surgeries). Adequate hydration, minimal use of opioids, and use of TIVA are helpful to prevent PONV. Acupressure at P6 acupressure point (at the level of wrist) may also be used. Combination therapy with the drugs listed may be used: 5HT3 antagonists (ondansetron, 4 mg IV), droperidol (0.625 mg IV), metoclopramide (10–20 mg IV), dexamethasone (4–8 mg IV), promethazine (Phenergan, 12.5–25 mg IM/6.25 mg IV), transdermal scopolamine patch, and clonidine.

Fluid Management

Adequate fluid management is important in ambulatory surgeries since it helps to reduce PONV, dizziness, drowsiness, and thirst and increases patient readiness for discharge. However, this can be tricky since patients arrive with variable fasting times and have variable intraoperative fluid and blood loss. Excessive hydration, coupled with salt and water retention due to surgical stress, can lead to cardiac and pulmonary dysfunction along with tissue hypoxia leading to impaired wound healing.

Special Procedures

1. Liposuction: This technique involves lysis of the fat cells using a hypotonic solution with 1:100,000 epinephrine for hemostasis. This technique also uses tumescent anesthesia in which 35–55 mg/kg of 0.05–0.1 % of lidocaine is used. As much as 70 % of the infiltrate is absorbed which may cause problems such as lidocaine and epinephrine toxicity, pulmonary edema, organ perforation, hypothermia, infection, hemorrhage, hypotension, and skin ulceration. It is recommended that the aspirant should be limited to 5 l, and in case of more than 4 l of aspirant is to be employed, a Foley catheter should be inserted.
2. Facial surgeries: These commonly include blepharoplasty, facelift, and rhinoplasty. These surgeries carry risk of OR fires since the surgeon uses electrocautery and operates close to the oxygen source (masks/nasal cannulas) that supply supplemental oxygen to the patient. Therefore, for these surgeries supplemental oxygen should be used carefully and when necessary (as indicated by pulse oximetry). Additionally, the skin preps used are flammable, and therefore, the prep solutions should be allowed to dry completely for at least 3 min before commencing with the surgery. The drapes should not be allowed to tent to prevent formation of oxygen reservoirs.
3. Bariatric surgery: This type of surgery may be done in the ambulatory care setting for patients with a BMI < 35 kg/m^2. Patients with a BMI > 35 kg/m^2 are usually operated in a hospital setting.

Discharge Criteria

A variety of scoring systems are available to assess discharge readiness of patients (please see Chap. 41). Discharge readiness of patients is summarized in Table 30.3. If these criteria are not met, then the patient may have to be admitted.

Factors that can delay patient discharge from the ambulatory surgery center include elderly patients, female gender, history of renal failure or congestive heart failure, long duration of surgery with general anesthesia, and postoperative issues such as uncontrolled pain, PONV, CNS dysfunction, and lack of presence of an escort to take the patient home.

Oral intake and voiding of urine prior to discharge is not mandatory in ambulatory patients. However, patients who have not voided after about 6 h after discharge should be instructed to return to the hospital/emergency room. Patients with a bladder volume >500 ml (as measured by ultrasound) should have straight catheterization done prior to discharge.

Table 30.3 Discharge criteria for ambulatory surgical patients

• Stable vital signs (blood pressure, heart rate, oxygen saturation, temperature)
• An alert and oriented patient
• Adequate control of pain
• Adequate control of nausea
• Absence of bleeding
• Patient can adequately ambulate
• Patient must avoid use of alcohol or sedatives and hazardous machinery and driving for at least 24 h postoperatively
• Patient should receive discharge instructions and a prescription from the surgeon
• An adult should be available to ride the patient home. At home a responsible adult must be present to take care of the patient

Fast Tracking

Fast tracking refers to a multimodal package of techniques which aim to decrease the length of postoperative stay. The patient bypasses the regular recovery room (phase I) and is directly admitted postoperatively to the phase II recovery unit. The patient should be awake, with stable vital signs, and is not anticipated to have significant postoperative issues (pain, nausea, CNS dysfunction).

The speedy postoperative recovery has been shown to decrease cardiorespiratory morbidity, and the minimal hospital stay improves the economics. Fast tracking advocates use of minimal invasive surgery (with transverse or oblique incisions rather than vertical incisions) and minimal use of nasogastric tubes, apart from other anesthetic principles discussed above.

Clinical Review

1. Factors that can delay patient discharge from the ambulatory surgery center include all, EXCEPT:
   A. Male gender
   B. Age of 70 years
   C. Long duration of surgery with general anesthesia
   D. Lack of presence of an escort to take the patient home
2. Risks factors that increase the complication rate for surgeries performed in the ambulatory surgical center include all, EXCEPT:
   A. Extremes of age
   B. Morbid obesity
   C. Site and duration of the surgery
   D. Administering a peripheral nerve block
3. The following pediatric premature patient may not have a surgical procedure in an ambulatory care setting:
   A. Post-gestational age <60 weeks
   B. Post-gestational age <70 weeks
   C. Post-gestational age <80 weeks
   D. Post-gestational age <90 weeks
4. Patients having surgery in an ambulatory surgical center should not have a body mass index (kg/m^2) greater than:
   A. 28
   B. 30
   C. 35
   D. 38

Answers: 1. A, 2. D, 3. A, 4. C

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Non-operating Room Anesthesia

31

Carlee Clark

Every year the number of nonsurgical procedures performed in sites other than the operating room increases, as does the involvement of the anesthesia team in the care of the patients. As more procedures move toward the minimally invasive, the anesthesia team will be faced with providing quality care in potentially unfamiliar areas. Each non-OR site has its own unique anesthetic challenges and can either be secondary to the patient, the procedure, or the location. The change in venue can create technical, communication, and operational difficulties for anesthesiologists. Several closed-claim analyses evaluated complications in anesthetics performed in remote locations versus the operating room. The patients in remote locations were older and sicker with complications occurring most commonly in the endoscopy suite and the cardiology/electrophysiology labs. Those in non-OR sites had higher severity of injury with the most common complication being over sedation. The challenge of non-operating room anesthesia (NORA) is to deliver an anesthetic of the same quality as the operating room, and the best way to approach this is systematically.

Patient Selection

Patients undergoing a NORA procedure may be relatively healthy, but rarely is the anesthesia team asked to be involved in the care of such patients. The anesthesia team is commonly consulted on patients with:

- Significant comorbidities (patients with coronary artery disease, pulmonary hypertension, morbid obesity, obstructive sleep apnea (OSA), chronic obstructive pulmonary disease (COPD), or solid tumors which can compress or invade major organs)
- New acute illnesses (infections or sepsis, acute bleeding intra-abdominal/intra-cerebral, myocardial ischemia)
- Psychiatric disease (patients resistant to sedatives, chronic alcohol, or recreational drug abuse)
- Movement disorders (patients with movement disorders may not be difficult to sedate, but may require an anesthesiologist to help ensure immobility for certain procedures)
- A history of difficulty to sedate
- Presence of a difficult airway

All patients should have a thorough preoperative anesthesia evaluation including an investigation of their past medical history, past anesthetic history, and airway and physical examination. Communication with the proceduralist about their needs and expectations for the procedure is very important and should occur as early as possible, preferably before seeing the patient. Discussions with the proceduralist should include questions regarding the patient position, the use of radiologic equipment, the need for immobility or paralysis, the expected length of the case, and the postprocedural plan (intensive care unit (ICU) or recovery area). An anesthetic plan should then be formulated by determining the unique needs of the patient, taking into consideration the anticipated procedure and the environment.

Environment

The American Society of Anesthesiologists created guidelines for the preparation and execution of out-of-OR anesthetics (Table 31.1). The sites where anesthesia personnel may find themselves vary greatly: it could be an endoscopy suite, a practitioner's office, an intensive care unit, or a radiology suite. All of these sites need to be held to the standards of the operating room, the key elements being the following:

1. Comprehensive preprocedural anesthetic assessment and informed consent
2. Understanding and agreement on the procedure at hand and anesthetic plan

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Table 31.1 ASA guidelines for non-operating room anesthetizing locations

Anesthetic equipment	• Self-inflating bag for PPV providing at least 90 % oxygen • Drugs, supplies, and equipment for intended level of anesthetic • Monitoring equipment to allow adherence to standards for basic anesthetic monitoring • Administration of inhaled anesthetics requires an anesthesia machine equivalent to those in the operating room and maintained with the same standards
Adequate lighting	• Requires illumination of the patient, monitors, and equipment • Battery-powered backup available
Building and safety codes	• All should be observed
Electrical outlets	• Sufficient for machine and monitors • Isolated electrical power or ground fault circuit interrupters if "wet location"
Oxygen	• Reliable source and quantity • Backup cylinder—checked and full
Postanesthesia care facilities	• Appropriate postanesthesia management • Adequately trained staff • Appropriate equipment for safe transport
Resuscitation equipment	• Emergency drugs • Defibrillator • Cardiopulmonary resuscitation equipment
Scavenging	• Adequate and reliable when administering anesthetic gases
Staff	• Adequately trained staff for support • Reliable means of two-way communication to request assistance
Suction	• Adequate and reliable
Sufficient space	• Space for personnel and equipment • Easy access to patient, machine, and monitors

3. Standardized ASA monitoring and anesthetic equipment allowing for maximal patient safety and comfort
4. Emergency equipment in an easily identified and accessible location (code cart, defibrillator, and difficult airway cart)
5. Adequate access to equipment and personnel in case of emergencies/difficulties
6. Postprocedural care in a setting similar to a postanesthesia care unit (PACU) with appropriately trained nursing staff

Radiologic Procedures

Radiologic procedures put patients at risk for radiation and this should be part of the informed consent given by the proceduralist. Procedures utilizing radiologic equipment also put the personnel in the room, including the anesthesia team, at risk for radiation exposures. It is imperative that all members of the anesthesia team wear appropriately sized protective led aprons, thyroid shields and goggles, and their radiation safety detection badges. In addition, some procedural areas have protective screens available when utilizing fluoroscopy. These screens should be placed between the source of radiation and the anesthesia personnel.

Interventional Radiology

Interventional radiology (IR) procedures vary a great deal (Table 31.2), but very frequently they are emergent and are needed in unstable patients. Almost 70 % of the procedures are urgent and booked less than 48 h ahead of time. Most scheduled IR procedures are performed with physician- or nurse-administered sedation; however, these emergent cases frequently require the involvement of an anesthesiologist or anesthesia team. In addition, patients with significant comorbidities may need anesthesia involvement to optimize their medical condition in a way that allows for their procedure to be completed. Preprocedural assessment and discussion with the interventionalist is imperative to developing a safe and realistic anesthetic plan.

Table 31.2 Common interventional radiology procedures

Angiography
Angioplasty
Embolization
Gastrostomy tubes
Intravascular ultrasound
Foreign body extraction
Needle biopsy
Inferior vena cava filters
Injection of clot-lysing agents
Catheter insertion
Cancer treatment

Interventional procedures require patients to be in the supine, prone, or even lateral positions, sometimes for extended time periods. Most interventional procedures require the placement of needles into blood vessels, organs, or spaces, and to decrease adverse outcomes, the patients need to be still, whether it is a result of cooperation or

sedation. The ability to cooperate is instrumental in these procedures, and many patients with dementia and psychiatric disorders, inpatients with delirium, or pediatric patients may be unable to cooperate. Because of these situations, many patients may require deep sedation or even general anesthesia (GA) with a laryngeal mask airway (LMA) or endotracheal tube depending on the patient comorbidities and length of procedure. Many of the emergent cases may involve hemodynamically unstable patients. This is often a result of sepsis, hepatic failure, or gastrointestinal or postsurgical bleeding. Procedures such as arterial embolization, abscess drainage, TIPS, or portal sclerotherapy necessitate the need for anesthesiology involvement due to the potential for continuous patient monitoring and resuscitation, in addition to the anesthetic.

Other potential issues during interventional procedures are hypothermia, which mostly affects elderly and pediatric patients, and radiation exposure. It is important to monitor the patient's temperature throughout the procedure, in addition to having the ability to change room temperature or apply forced warm-air heating devices. Patients are at higher risk for hypothermia during longer procedures. According to most manufacturers, the temperature tolerance of the computers and machinery is 68° F, and therefore, the thermostat should be set to this level.

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) procedures are unique among the NORA locations, in that they are used solely for diagnostic testing (Fig. 31.1). This will likely change in the future as many interventionalists plan to use the new 3-Tesla (3 T) units to perform procedures similar to those done with a CT scan. MRI studies can be several hours in duration depending on what part of the body is being imaged, and it is essential that the patient remain immobile for optimal imaging. Anesthesia involvement is common in pediatric patients with the inability to cooperate or lay still and adult patients with claustrophobia or anxiety.

The preprocedural assessment of the patient and discussion with the radiology team should uncover the need for anesthetic involvement and allow for appropriate planning. These patients can require anything from moderate sedation to a GA, and this will be determined for each patient individually. Regardless, most patients receive propofol for sedation, with a total intravenous anesthesia technique used for general anesthesia. At times, the risks/benefits of GA should be discussed with the radiologist, patient, and their family if the information gained by the study will not change the patient's outcome.

The MRI suite is quite unique in the challenges it presents to anesthetic personnel. Airway equipment (including laryngoscopes), medication pumps, poles, monitors, the anesthesia machine, and cart must all be MRI compatible. Many radiologic suites have an induction room separate from the procedure rooms where the patient can be attached to monitors, an IV started and then safely placed under sedation or under general anesthesia with airway securement. Patients would then be transported to the MRI suite and transferred to the MRI table. If an MRI-compatible machine or medication pump is not available, then they must be located outside the room with adequate extensions for intravenous tubing and breathing circuits. Organization of intravenous or arterial lines, monitoring cables, and either supplemental oxygen tubing or the ventilator circuit is important so they are not dislodged while moving the patient. During the MRI exam, patients are always located in a separate room, but patient

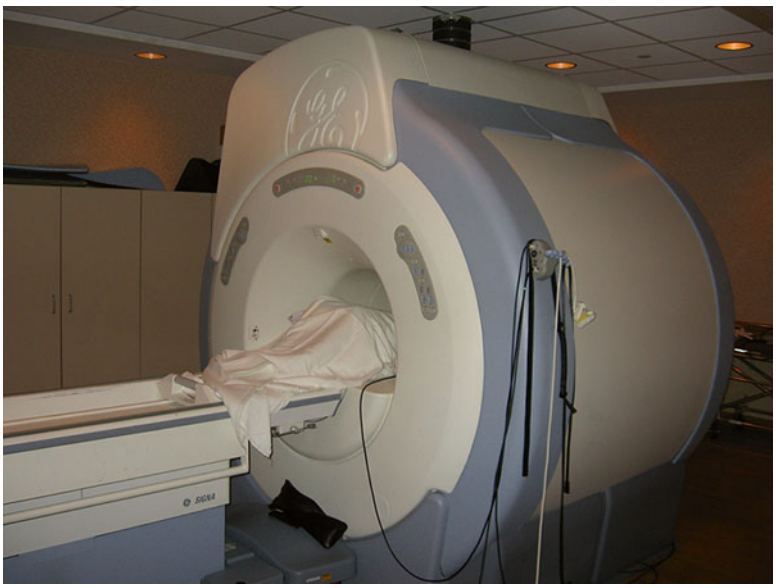

Fig. 31.1 A magnetic resonance imaging scanner. Note the remoteness of the patient from the surroundings

Table 31.3 Contraindications for MRI

Absolute contraindications	Relative contraindications
Automatic implanted cardiac defibrillators (AICD)	Cochlear implants
Pacemakers	Insulin pumps
Metallic splinters in the eye	Nerve stimulators
Electronically activated implanted pumps	Mechanical heart valves
Metallic surgical clips (CNS)	Metallic surgical clips (body)

and patient monitors must be viewed at all times via a window or video screen.

Complications to be concerned about include oversedation or apnea leading to the need to emergently obtaining and maintaining the airway. One cannot emergently enter the MRI suite as the magnet has to be turned off before anyone can enter, which takes time. Patients with cardiovascular disease, particularly arrhythmias or coronary artery disease, may be difficult to monitor given the ECG interference from the MRI machine. Pediatric patients at higher risk for adverse events during propofol administration were those undergoing longer procedures, those with American Society of Anesthesiologist's physical status, or those with airway abnormalities.

All staff working in MRI should undergo MRI safety training as to not bring harm to themselves or the patients. Any patient with ferrous implants may not safely undergo an MRI for risk of dislodging the device. Common devices prohibiting patients from undergoing an MRI are listed in Table 31.3. Titanium implants or clips are considered safe for MRI. Patients with tattoos should be warned that they are at risk for burn injury as some tattoo ink contains high amounts of ferrous oxide.

Computerized Tomography

Computerized tomography (CT) scans can be used for diagnostic and/or interventional procedures. Diagnostic procedures are quite quick and patients typically do not require the administration of sedation or analgesia. Those nontypical patients are identical to patients requiring anesthetic involvement for MRI: psychiatric illnesses, anxiety, movement disorders, intellectual disabilities, or chronic pain. For these patients, sedation, analgesia, and possibly even GA may be needed in order to complete the study. Other patients requiring anesthetic involvement are those who are hemodynamically unstable or those already intubated from the OR, emergency room (ER), or ICU.

Interventional procedures may take longer than diagnostic studies, in addition to the possibility of causing new pain, worsening pain, or injury to organs and blood vessels. The patient and procedural considerations are similar to those described previously in the interventional radiology section, as the interventional radiologists frequently perform CT-guided procedures. Procedures involving the lung parenchyma may require general endotracheal anesthesia and occasionally a double-lumen endotracheal tube for bronchial lesions. Patients should be evaluated for a pneumothorax and compromised ventilation prior to extubation following pulmonary biopsies or ablations.

Anesthesia personnel may be asked to intervene after a failed sedation attempt. This happens commonly in patients with acute or chronic pain, alcohol or recreational drug use, or anxiety and is complicated because the patient has likely already received sedative or analgesic agents and will be difficult to interview. Best practice would be to delay or cancel the case to allow for an appropriate preoperative evaluation of the patient and creation of an optimal anesthetic plan. Anesthetic challenges given the location of the patient are similar to those for MRI, excluding the need for compatible equipment.

Interventional Neuroradiology

Interventional neuroradiologic procedures are increasing in number and commonly performed prior to or in conjunction with neurosurgical procedures (Table 31.4). Cerebral angiography is performed for the diagnosis and potentially the treatment of cerebral aneurysms with coiling. Large intracranial tumors are imaged and the vascular supply embolized prior to surgery to improve surgical conditions and decrease intraoperative blood loss. Most healthy patients can tolerate cerebral angiography with nurse-administered sedation. Elective stenting, coiling, or embolization of cerebral aneurysms require general endotracheal anesthesia, invasive blood pressure monitoring with an arterial line, and two well-functioning IVs.

Neurointerventional procedures are one of the most common sources of emergent or urgent procedures requiring anesthetic coverage. These patients have typically sustained a CVA from a ruptured or leaking aneurysm or AVM and require emergent angiography with coiling or embolization, which may be followed by a trip to the operating room. Other emergent procedures are those for vasospasm, where postoperative craniotomy patients are taken for angiography for diagnosis and treatment of vasospasm. All emergent procedures or

Table 31.4 Common interventional neuroradiology procedures

Cerebral aneurysm	Meningiomas
Brain arteriovenous malformations (AVM)	Epistaxis
Carotid-cavernous fistula (CCF)	Paragangliomas
Dural arteriovenous fistula	CVA
Extracranial (brachiocephalic) atherosclerosis	Spinal and paraspinal vascular malformations
Extracranial tumors	Traumatic vascular lesions
Head and neck tumors	Intracranial arterial vasospasm
Intracranial atherosclerosis	Vertebral body tumors
Juvenile nasopharyngeal tumor	Vertebral body compression fractures

unstable patients require general endotracheal anesthesia to provide patient immobility and placement of an arterial line for close hemodynamic monitoring.

Logistically, anesthetics in the neuroradiology suite take planning as the anesthesiologist does not have close proximity to the patient or the airway. All breathing circuits, IV, and arterial line tubing must have the appropriate extensions. Arterial lines are commonly used for hemodynamic monitoring and tight blood pressure control and may be slaved off the percutaneous sheath placed by the interventionalist.

Patient complications to be concerned about are acute intracranial bleeding with resulting intracranial hypertension and hemodynamic instability. Anesthetic personnel must be prepared to treat intracranial hypertension and to optimize cerebral perfusion pressure if acute bleeding occurs. There is radiation exposure, so all anesthetic personnel should wear their radiation badge and protective lead with a thyroid shield and stay behind the provided shield.

Endoscopic Procedures

Utilization of anesthesia services for patients undergoing endoscopic procedures is increasing. Many patients requiring monitored anesthesia care for endoscopic procedures are healthy, but have requested to be "asleep," while others have already had a failed attempt at sedation. Patients with chronic gastrointestinal disorders or other comorbidities, such as hepatic failure with ascites, gastroparesis, or obstructive sleep apnea, warrant close hemodynamic or airway monitoring. Many patients with chronic gastrointestinal disorders suffer from chronic pain and may be difficult to sedate with only nurse-administered sedation. Invasive procedures such as endoscopic retrograde cholangiopancreatography (ERCP), esophageal stenting or dilatations, and small bowel enteroscopies can be painful and may require deep sedation or a general endotracheal anesthetic. The procedure length is operator and patient dependent, which may affect the type of sedation or anesthesia required for a particular patient and procedure.

The majority of endoscopic procedures are elective cases scheduled well in advance. When possible, these patients should be seen in the preanesthesia clinic by anesthesia personnel. During this preprocedural visit, the anesthesiologist should determine the procedure to be performed and the reasoning behind the anesthesia request. The anesthesiologist should contact the endoscopist with any questions regarding complexity of the upcoming procedure and with any other logistical questions. Endoscopic procedures are often done for patients who are not surgical candidates or for palliation. It is not uncommon for a patient on the heart transplant or liver transplant list to present for endoscopic screening. Patients with head and neck cancers may present for feeding tube placement. These patients are at high risk for periprocedural complications and, depending on the facilities and resources available, may be candidates for having their procedures completed in the operating room.

Inpatients are frequently added on to the daily schedule and may be appropriate for a procedure in the endoscopy suite, or they may be an ICU patient and undergo the procedure at the bedside. Inpatients typically have more acute illnesses and deserve a thorough preprocedural assessment and discussion with the endoscopist regarding the procedural plan. It is not uncommon for these inpatients to require some preprocedural workup or medical optimization, and this should be discussed with the endoscopy team.

Upper and lower endoscopies are commonly performed under moderate to deep sedation by administering small doses of midazolam or fentanyl and then utilizing continuous propofol infusions. Some patients may only require small doses of midazolam and fentanyl in order to tolerate the procedure, especially a lower endoscopy. The expectations of the level of sedation should be discussed with the patient and endoscopist prior to the procedure. ERCPs are performed in the prone position, which can compromise ventilation in certain patient populations. Many ERCP patients do not need airway securement, but be cautious in those with aspiration or pulmonary risk factors. GA is often utilized for the longer or more painful procedures or in any patient where the risks of moderate to deep sedation outweigh the benefits.

The presence of an endoscope, sedation, and patient positioning can easily lead to airway obstruction in any patient, so careful consideration should be given to the securement of

the airway for patients at high risk for airway complications: OSA, morbid obesity, oropharyngeal abnormalities, or COPD. Easy access to the patient's airway is essential because patients may need a chin lift or jaw thrust to relieve airway obstruction. In 2009, the ASA released a statement on respiratory monitoring during endoscopic procedures and recommended the use of end-tidal carbon dioxide (ETCO2) monitoring in patients receiving sedation and special attention to airway compromise in patients undergoing ERCP. Both outpatients and inpatients are often dehydrated secondary to their bowel preparation, liquid diet, and NPO status. Patients frequently require volume resuscitation and/or phenylephrine administration during their anesthetic. Patients are at risk of bleeding and viscous perforation during both upper and lower endoscopy procedures and may require transfer to the operating room. ERCP procedures are commonly performed in patients with biliary infections, who may become septic during the procedures.

Radiation Oncology

Many radiation oncology procedures require the services of anesthesiologists to make procedures and postprocedural pain more tolerable for cancer patients. Radiation requires patients to remain immobile, and as previously stated, certain patient populations may be unable to cooperate without the involvement of an anesthesia team. Many of the procedures take place in the operating room or procedural suites, but may require the transportation of the patient between the two. Each patient should undergo a thorough preoperative assessment, and all members of the care team, in addition to the patient and family, should review all available options prior to proceeding. Every attempt should be made to avoid frequent short general anesthetics by discussing alternative techniques or medication regimens (5 days a week for 5–7 weeks).

Radiation oncologists treat many forms of cancer, and it may be in patients prior to surgery or in nonoperable patients. For unresectable cervical and uterine carcinoma, the treatment is usually short outpatient treatments over several days. General endotracheal anesthesia is utilized for many cases, as the patient is placed in the lithotomy position after induction and airway securement. An LMA could be placed in patients at low risk for hypoventilation in the lithotomy position. The radiation oncology team places tandem and ovoids and then confirms appropriate placement using CT imaging. After the dosimetrist completes calculations, the treatment is administered and then all instrumentation is removed from the patient. The patient is then awakened, extubated, and then taken to the PACU. Most patients are discharged the same day. Patients requiring MRI for dosimetry planning will need to be transported. It should be decided with the patient and the radiation oncologist if the patient will undergo GA or epidural anesthesia to allow for safer transportation between the OR and the MRI.

Interstitial implants require that radiation be given continuously for 48–72 h, and it is common to place lumbar epidurals with either intravenous sedation, for placement of the implants and postoperative pain management. Epidurals remain in place and a continuous infusion of dilute local anesthetic with or without narcotic (hydromorphone or fentanyl) is maintained until the course of radiation is completed and the instrumentation removed. The patient should be rounded on each day by either the pain or regional anesthesia service.

Prostate cancer can be treated either surgically or with brachytherapy. Brachytherapy requires the placement of irradiated seeds under GA. These patients are also in lithotomy position for needle placement. CT scanning is used for placement confirmation and dosimetry calculations. After seed placement, the instrumentation is removed and the patient is awakened and taken to the PACU. Patients are typically admitted overnight and discharged home the next morning.

Cardiology Procedures

Cardioversion

Cardioversion is commonly an elective procedure performed in the cardiac procedural area for patients in chronic atrial fibrillation but at times can be emergent in the ED or ICU. Each patient should have a thorough preprocedural workup focusing on his or her current cardiac functional status. Patients presenting for cardioversion often have an extensive cardiac history and typically have been NPO for 8 h. The patient should be on telemetry, with noninvasive blood pressure monitoring (NIBP), pulse oximetry, and capnography. Supplemental oxygen should be administered via a nonrebreather mask.

The procedure is painful, so patients should be sedated for the procedure as long as they are hemodynamically stable. Cardioversion only lasts a few seconds, so the goal for the anesthetic is to provide a short intravenous general anesthetic. Low doses of propofol (30–50 mg) are an option and allow for quick recovery. Etomidate can be used for patients with hemodynamic instability, but it often produces myoclonus and, hence, is not a popular choice. Hypotension, if occurs, should be treated with fluids or small boluses of phenylephrine. Brief airway obstruction may occur in patients with or without OSA. A chin lift, jaw thrust, or nasal airway will be helpful in relieving the obstruction until the sedation wears off. Emergency airway and resuscitation

equipment should be immediately available. After the cardioversion, the patient will be monitored by the cardiology nursing staff and then discharged once fully awake.

Coronary Angiography

Elective cardiac catheterization procedures are commonly performed with nurse-administered sedation. Pediatric patients may require an anesthesiologist depending on the age of the patient and the cardiac lesion. Adults undergoing emergent cardiac catheterization may require intubation and a general anesthetic if the patient presented in or evolved into respiratory failure or hemodynamic compromise.

Administering anesthesia to pediatric patients with congenital lesions (corrected or uncorrected) or post-heart transplant requires a thorough understanding of their cardiac anatomy. Discussions should be with the cardiologist, the patient, and the patient's family in order to understand the needs for the procedure. Depending on these discussions, the patient may undergo either moderate sedation or general anesthesia.

Requests for intubation and/or general anesthesia in adult cath lab patients frequently involve patients who are unstable and have a full stomach. There may not be an anesthesia machine or a ventilator immediately available in the cath lab, so the cardiology support staff in the procedure room should be asked to get any additional equipment needed. If available, another member of the anesthesia team may need to be called for help. The patient will likely need transport directly to the operating room or ICU.

Other Non-OR Procedures

ICUs, EDs, and diagnostic imaging frequently request anesthesia staffing for bedside procedures. Percutaneous, open tracheostomies and endoscopic procedures are frequently performed at the bedside in ICUs to minimize complications from patient transport. Endoscopic procedures may be emergent or urgent, and the patients are frequently hemodynamically unstable, intubated, and on the ventilator. Procedures in the ED may be related to painful fracture reductions. Diagnostic imaging needs typically involve the difficulty to sedate patient or the patient with significant comorbidities making the patient too high risk for sedation administration by the proceduralist.

The request for anesthetic administration may come without helpful information about the patient's current state or comorbidities. The urgency of the procedure may hinder the anesthesia team's ability to do a thorough preprocedural assessment, but all effort should be put toward doing a focused workup and assessment of the patient prior to the administration of anesthesia. Appropriate monitoring and emergency equipment (including airway equipment if the patient is not already intubated) should always be immediately available.

Summary

The number of NORA procedures are increasing and becoming a significant aspect of anesthesiology practice. The perimeter of anesthesiology practice continues to evolve to include these new arenas, but the same standards for OR anesthetics must be applied in order to optimize patient safety and minimize complications.

In order to develop and execute a safe anesthetic plan for patients in these areas, the patient, the procedure, and the environment must all be considered. Patients will frequently have comorbidities prohibiting them from nurse-administered sedation or psychiatric disorders, anxiety, dementia, or movement disorders that require the involvement of an anesthesia team. Each patient should have a thorough preprocedural anesthetic assessment, and the proceduralist should be approached to answer any questions about the procedure at hand. Each anesthetic should be tailored to the individual patient, procedure, and procedural environment. The monitoring of each patient should be in adherence with ASA standards and include ETCO2 monitoring, without which recognition of apnea has been shown to be delayed. Every NORA procedural area should have immediate access to emergency equipment such as oxygen, suction, resuscitation medication, and equipment.

Postprocedural care should be in a recovery facility with the same postoperative standards as those in the PACU. Full anesthetic report should be given to the nurse assuming care of the patient, and the patient should be extubated, spontaneously ventilating, awake, and hemodynamically stable before handing over care. The patient should remain in the recovery facility until meeting criteria for discharge. Contact information for the anesthesia personnel should be available in case of any anesthesia-related complications.

Transport of patients between procedural areas and ICUs is a challenging procedure in itself and is routinely the responsibility of the anesthesiologist. For successful transportation of patients, communication with nursing staff both in the procedure area and in the patient care unit is essential. All patients should be attached to transport monitoring including telemetry, NIBP, and pulse oximetry. Intubated patients should be transported with capnography or carbon dioxide detectors, if possible, to aide in detection of unintentional extubation.

Clinical Review

1. Patients that an anesthesiologist can be called upon to administer anesthesia outside the main operating room include:
   A. Pediatric patients
   B. Patients unable to lay still
   C. ASA III and IV patients
   D. All of the above
2. The most commonly used anesthetic induction agent for cardioversion is:
   A. Etomidate
   B. Propofol
   C. Midazolam
   D. Thiopental
3. A 44-year-old patient is to undergo colonoscopy in the endoscopic suite. The patient had a similar procedure 1 week ago without the presence of an anesthesiologist, and the procedure was listed as failed. Your most likely choice of anesthesia technique would be:
   A. Intravenous sedation with midazolam and fentanyl
   B. General endotracheal tube anesthesia
   C. Intravenous sedation with propofol
   D. General anesthesia with laryngeal mask airway
4. Contraindications of magnetic resonance imaging (MRI) include all of the following, *EXCEPT*:
   A. Automated implanted cardiac defibrillators
   B. Metallic splinters in the eye
   C. Pacemakers
   D. Claustrophobia
5. True statement for non-operating room anesthesia procedures is:
   A. As these procedures are short, only a brief preanesthetic evaluation may suffice.
   B. Since most procedures are performed under intravenous sedation, the anesthesia machine and emergency airway equipment may only be brought from the main operating room when needed.
   C. Patients need not be NPO before short procedures.
   D. All procedures in remote locations should have the same patient preparation and recovery parameters as procedures in the main operating room.

Answers: 1. D, 2. B, 3. C, 4. D, 5. D

Further Reading

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Hepatic and Gastrointestinal Diseases

32

Kasia Petelenz Rubin

The gastrointestinal tract (GI) and the liver are important organs which are involved in the absorption and metabolism of nutrients, drugs, and toxins. Diseases involving the GI tract and the liver, therefore, affect every organ in the human body. Anesthesiologists must be familiar with the anatomy, physiology, and disease states affecting the GI tract and the liver, to provide optimal care to the surgical patient.

The Liver

Anatomy and Physiology

The liver is located in the abdomen to the right of the stomach, overlying the gallbladder. Blood supply to the liver consists of two large blood vessels, the hepatic artery and the hepatic portal vein. The hepatic portal vein carries venous blood from the spleen and GI tract, while the hepatic artery supplies arterial blood to the liver. The hepatic artery supplies 25 % of total hepatic blood flow but 50 % of the oxygen supply. The portal vein provides 75 % of total hepatic blood flow and the remaining 50 % of the oxygen supply. The total blood flow to the liver is approximately 25 % of the cardiac output, or 100 mL/100 g/min. Blood flows through the liver sinusoids and empties into the central vein. Nerve supply to the liver is by sympathetic fibers ($T_{6–11}$), as well as parasympathetic fibers (vagus nerve).

The simple external anatomy of the liver hides an internal complexity (Fig. 32.1). The central area where the common bile duct, the hepatic portal vein, and the hepatic artery proper enter is called the porta hepatis. This area then divides into left and right branches, constituting the left and right lobes of the liver. Anatomically, the liver is composed of eight segments, each supplied by a portal triad—portal vein, hepatic artery, and bile duct. These segments divide into four sectors separated by segments that contain the three main hepatic veins. The terminal portal triads are at each corner of a hepatic lobule. Microscopically, the hepatic lobule is the structural basis for the metabolic and secretory functions of the liver (Fig. 32.2). It is made up of a terminal hepatic venule, surrounded by four to six terminal portal triads. Hepatocytes are aligned one cell thick, surrounded on each side by endothelial-lined and blood-filled sinusoids. Blood flows from the terminal portal triad through the sinusoids into the terminal hepatic venule.

Liver anatomy and function are intricately related. Liver functions include regulation of blood coagulation, synthesis of hormones, erythrocyte breakdown, carbohydrate metabolism, lipid and amino acid metabolism, and immunologic function. Corticosteroids, aldosterone, estrogen, androgens, insulin, and antidiuretic hormone are all inactivated by the liver. The unique structure of the hepatic lobule, and a hepatocyte location within the liver, is critical to its function. Periportal hepatocytes, in what is termed zone 1, are located close to the terminal vascular branches of the portal vein and hepatic artery. These hepatocytes are supplied by blood with a high nutritional content returning from the GI circulation. These zone 1 hepatocytes contain large mitochondria and have high concentrations of Krebs cycle enzymes. They are involved in gluconeogenesis, beta-oxidation of fatty acids, amino acid catabolism, ureagenesis, synthesis of cholesterol, and bile acid secretion. Hepatocytes in the centrilobular or perivenular area (zone 3) are most distant from the terminal vascular branches. Because of their location, these hepatocytes are involved in anaerobic work: glycolysis and lipogenesis. They are involved in general detoxification and biotransformation of drugs. These cells are most sensitive to injury from systemic hypoperfusion, hypoxemia, and accumulation of toxic by-products.

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Preoperative Examination of the Patient with Liver Disease

Currently, endstage liver disease affects more than three million individuals in the United States. Liver dysfunction has historically been due to chronic viral (B or C) or alcoholic hepatitis. Alcohol is the most common cause of cirrhosis of liver. However, the incidence of nonalcoholic fatty liver disease is increasing due to the obesity epidemic. Though the overall presence of cirrhosis in this population is low, it does increase the number of patients with liver disease that are encountered in routine anesthetics. Patients presenting to the operating room should be screened for the possibility of liver disease with questions of prior blood transfusion, illicit drug use, alcohol intake, and family history of liver disease (Table 32.1). Physical examination can identify signs of liver disease such as jaundice, spider telangiectasia, ascites, or dilated abdominal veins. Preoperative workup includes blood count, coagulation studies, and a complete metabolic panel (Table 32.2). Two primary indicators of liver dysfunction are a serum albumin <2.5 mg/dl and

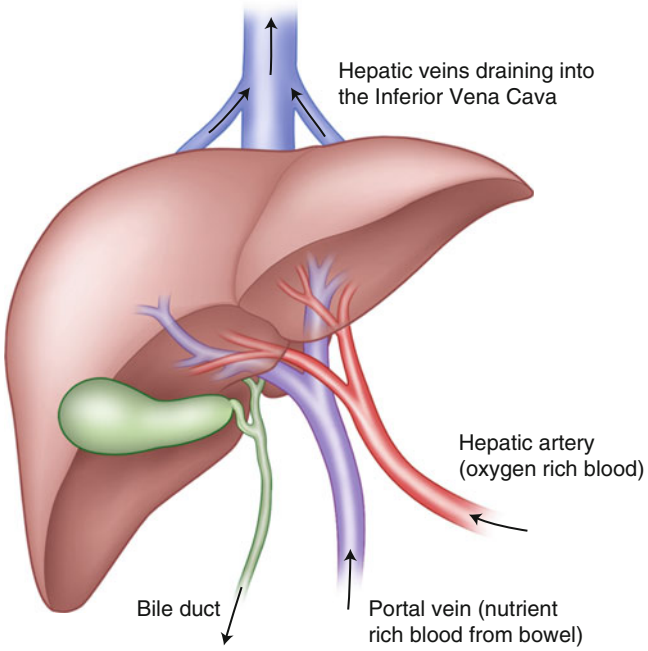

Fig. 32.1 Functional anatomy of the liver

Table 32.1 Key aspects of history and physical examination to consider in liver disease

History of alcohol use and alcoholic hepatitis
Features of portal hypertension
Ascites
Esophageal or gastric varices
Renal function
Hepatic encephalopathy
Presence of acute liver failure
Calculated Child–Turcotte–Pugh and/or MELD score
Prior liver biopsy—cirrhosis present?
Liver transplantation evaluation

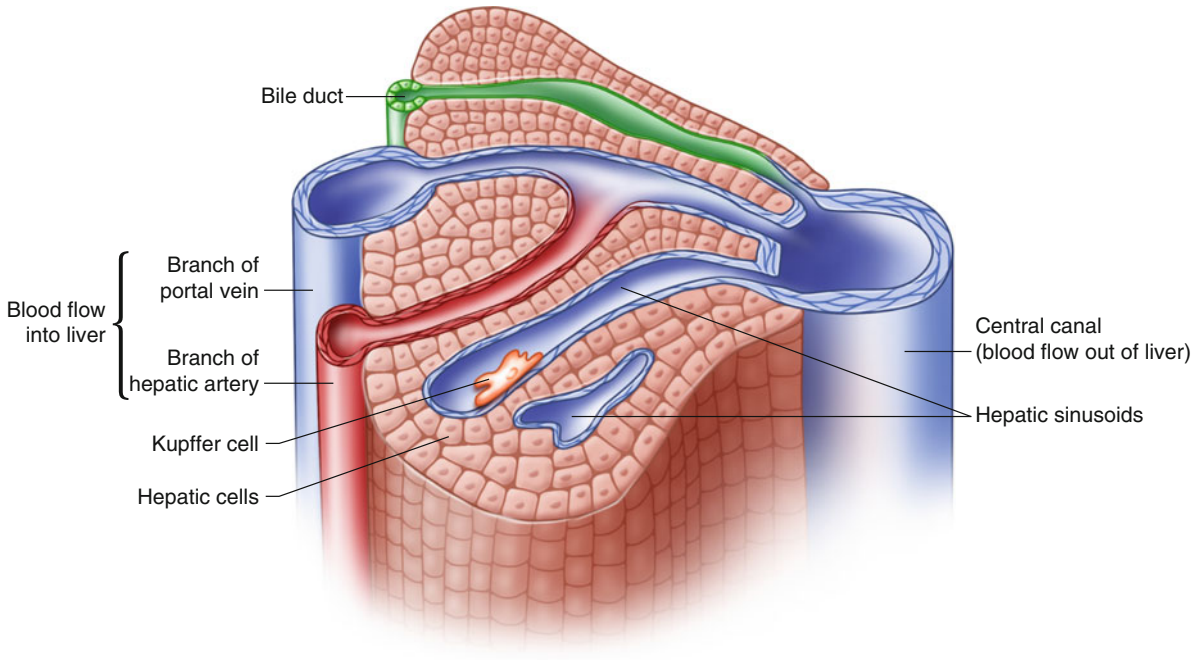

Fig. 32.2 A hepatic lobule

Table 32.2 Liver function tests

Serum bilirubin	Normal < 1.5 mg/dl Jaundice with > 3.5 mg/dl Postoperative jaundice most commonly due to production of bilirubin as a result of resorption of large hematoma/red cell breakdown following transfusion
Serum ALT and AST	ALT is more liver specific, while AST is also found in the heart, kidneys, and skeletal muscle
Serum alkaline phosphatase (AP)	AP is also found in the bones, small bowel, and kidneys. Mild elevation, hepatocellular injury; high elevation, biliary obstruction
Serum albumin	Normal 3.5–5.5 mg/dl, half-life 2–3 weeks
Blood ammonia	Elevations with hepatocellular damage
Prothrombin time	Normal 11–14 s

ALT alanine aminotransferase, *AST* aspartate aminotransferase

a prolonged prothrombin time >14 s/INR > 1.5. However, some centers also use prealbumin as a marker for liver disease, since it has a short half-life of just 2 days.

Acute hepatitis is viewed as a strict contraindication to elective surgery because of the associated high complication and mortality rate. Delay of urgent surgery should also be considered until an episode of acute liver injury resolves, such as in acute alcoholic hepatitis. Patients with mild chronic hepatitis with no evidence of portal hypertension and well-preserved hepatic function generally may proceed with elective surgery. However, patients with significant portal hypertension may be at higher risk of postoperative complications.

Classification of Liver Dysfunction

There are two main classification systems for liver disease that aim to stratify patients with liver dysfunction. The Child–Turcotte–Pugh system (CTP), initially developed in 1964, assesses patients using serum albumin level, serum bilirubin level, ascites, encephalopathy, and prothrombin time (Table 32.3). This value is then assigned as a Class A (good, 4 % 3-month mortality), B (intermediate, 14 % 3-month mortality), or C (poor, 51 % 3-month mortality). The CTP is easy to calculate and is historically verified. It was a key consideration in the transplant algorithm, until it became supplanted by the Model for End-Stage Liver Disease (MELD) score in 2002. The MELD score is calculated from the objective values for the serum bilirubin level, serum creatinine level, and INR. The values are weighted by relative mortality influence, with greatest weight given to renal function.

Anesthetic Considerations in End-Stage Liver Disease

It is important to understand the physiology behind liver disease and minimize the risks when surgery is necessary in the presence of liver disease.

Table 32.3 Child–Turcotte–Pugh score

Characteristic	1 point	2 points	3 points
Ascites	None	Controlled	Refractory
Encephalopathy	None	Controlled	Dense
Albumin (g/L)	>3.5	2.8–3.5	<2.8
Bilirubin (mg/dL)	<2	2–3	>3
INR	<1.7	1.7–2.3	>2.3
Class A, 5–6 points; Class B, 7–9 points; Class C, 10–15 points			

Cardiovascular: Patients with end-stage liver disease typically have a hyperdynamic circulation characterized by an elevated heart rate, increased stroke volume, and low peripheral vascular resistance. This combination of factors leads to a high cardiac output. Though the total blood volume is increased, the central "effective" volume is decreased. Some causes of cirrhosis are also associated with disease-induced cardiomyopathy, such as alcoholic liver disease. These patients may have atypical cardiovascular presentations in the face of their chronic liver disease. They present with congestive heart failure and decreased peripheral blood flow.

Pulmonary Dysfunction: This complication of end-stage liver disease is due to intrapulmonary vascular dilations. There is a decrease in oxygenation with a $PaO_2 < 70$ mmHg (hypoxemia) or PAO_2–PaO_2 gradient >22 mmHg on room air that is associated with intrapulmonary vascular dilation. Patients may hyperventilate producing a respiratory alkalosis. The triad of increased alveolar–arterial oxygen gradient, and evidence of intrapulmonary vascular dilations is defined as the hepatopulmonary syndrome (HPS). Supplemental oxygen is unable to increase PaO_2 significantly when large arteriovenous communications are the primary cause of hypoxemia. Survival of patients with HPS compared with cirrhotic patients of the same CTP class without HPS is dramatically lower. In addition, the presence of significant ascites causes elevation of the diaphragm leading to decreased lung volumes (FRC) and a restrictive ventilatory defect.

Electrolyte Abnormalities: Hyponatremia is common, due to a relative water overload rather than total body sodium

depletion. Water restriction may help regain normal serum sodium levels. Diuretics that increase free water clearance are used in severe cases. Saline solution is infused in cases of severe hyponatremia complicated by seizures. Infusion of saline solution temporarily increases serum Na^+ levels but can worsen ascites and increase fluid retention. Hypokalemia is seen frequently due to urinary potassium excretion, secondary to an increase in circulating aldosterone. Diuretic therapy may also contribute to hypokalemia. Management consists of oral KCl supplementation and withholding K-wasting diuretics. It is important that renal function be preserved perioperatively and excessive diuresis avoided.

Endocrine: Glucose intolerance and insulin resistance are often seen. This is usually due to the liver's impaired ability to degrade insulin. Abnormal thyroid function tests may be discovered. This usually reflects altered hepatic metabolism of the thyroid hormones and a decreased production of plasma binding proteins.

Coagulation Defects: In chronic and acute liver diseases, many changes in the coagulation pathway occur. This can be due to a number of factors including abnormal platelet numbers and function, decreased synthesis of coagulation factors, and vitamin K deficiency. There is a decrease in the levels of factors II, V, VII, IX, and X, protein C, protein S, and antithrombin III. Thrombocytopenia commonly occurs due to increased platelet sequestration. Decreased thrombopoietin synthesis by the disease liver also contributes. Decreased platelet adhesiveness and impaired aggregation are also well described, with unknown etiology. It is unclear if these changes actually increase the bleeding risk, as the decrease in the procoagulant system is mirrored by a simultaneous decrease of the fibrinolytic system. Thus, despite significant coagulation abnormalities as assessed by standard laboratory tests, clinical bleeding may not be evident. Surgical procedures are performed on cirrhotic patients often without the need for any blood products, despite the presence of end-stage liver disease with significant thrombocytopenia and platelet abnormalities.

Portal Hypertension this complication results from an increased hepatic vascular resistance to portal blood flow, typically occurring in the hepatic sinusoids. Hepatic vascular changes are due to cirrhotic changes in the liver and a reaction to the hyperdynamic state caused by systemic vasodilation and volume expansion. Over time, this resistance gradient leads to the formation of portosystemic collaterals (sites—gastroesophageal, periumbilical, retroperitoneal, hemorrhoidal). These develop by dilation and hypertrophy of vascular channels. This is the root cause of the development of esophageal varices.

Ascites: Ascites is the accumulation of fluid in the peritoneal cavity. It is a common consequence of many forms of cirrhosis, due to a combination of portal hypertension, hypoalbuminemia, and sodium/water retention. Three theories underlie its pathogenesis:

- The *underfill* hypothesis states that cirrhosis-related hepatic venous drainage is blocked due to portal hypertension leading to the ascitic fluid formation. This fluid formation decreases the effective intravascular volume, leading to further sodium and water retention by the kidney, perpetuating the cycle.
- The *overflow* hypothesis states that portal hypertension leads to sodium and water retention despite an overfilled vasculature, increasing the total plasma volume. This increased intravascular volume leads to portal hypertension via increased portal hydrostatic pressure. The lower plasma oncotic pressure leads to translocation of fluid from the splanchnic circulation.
- The theory of peripheral vasodilation states that splanchnic arterial vasodilation occurs secondary to the production of vasodilatory mediators in the setting of liver failure. In order to maintain systemic perfusion in the face of an enlarged intravascular compartment, the kidney retains sodium and water, thus increasing the total ascitic fluid volume.

In spite of differences in proposed etiology, ascites is treated with sodium- and fluid-restrictive diets. Aldosterone antagonists (potassium-sparing spironolactone) allow for diuresis and volume reduction. Large-volume (4–6 L) paracentesis is effective in removal of large amounts of ascitic fluid in the setting of refractory ascites. This allows for an immediate improvement in cardiac output, as pressure on the inferior vena cava and right atria is released. Subsequent circulatory dysfunction, however, may occur up to 24 h later with relative hypovolemia occurring due to progressive reaccumulation of ascites with a resultant decrease in filling pressures. Administration of a plasma expander, such as albumin, may prevent the relative hypovolemia. Re-equilibration of the intravascular volume occurs 6–8 h after the removal of a large volume of ascitic fluid.

The clinical implications of the ascites vary. Ascites may impede the patient's respiratory function and increase the patient's risk for aspiration. Patients with acute deterioration of pulmonary function or tense ascites may benefit from preoperative drainage in an elective or semi-urgent situation. In an emergency, laparotomy itself will lead to release of ascites fluid.

Hepatorenal Syndrome: This is a prerenal failure that is characterized by intense vasoconstriction of the renal circulation and low glomerular filtration (oliguria), with preserved renal tubular function and normal renal histology. HRS can be brought about by gastrointestinal bleeding, dieresis, sepsis, or major surgery. There are two types of hepatorenal syndrome. Type I develops rapidly over a few weeks and is progressive with a high mortality rate, and often needing a liver transplantation. Type II follows a less acute course and is mainly seen in patients that are resistant to diuretic therapy.

Hepatic Encephalopathy: Severe hepatocellular damage can lead to accumulation of toxins such as ammonia, mercaptans, and phenols, which are normally metabolized by the liver. This can lead to hepatic encephalopathy characterized by mental status changes, asterixis, hyperreflexia, and an inverted plantar reflex. Hepatic encephalopathy can be precipitated by GI bleeding, sepsis, vomiting, and excessive diuresis. Treatment should be aggressive and consists of supportive care, lactulose (osmotic laxative), and neomycin (inhibits ammonia production by intestinal bacteria).

Anesthetic Management of End-Stage Liver Disease

Patients with advanced liver disease have alterations in pharmacokinetics and pharmacodynamics of all medications. For example, cerebral uptake of benzodiazepines is increased, due to a leaky blood brain barrier. By contrast, pharmacologic responses to catecholamines and other vasoconstrictors are decreased. Induction drugs and muscle relaxants have increased dose requirements due to increased volume of distribution.

Intraoperative Monitoring: Depending on the surgery performed, it may warrant consideration of an arterial line and central line in addition to standard ASA monitors. An arterial line provides immediate measurement of the patient's hemodynamic status in the setting of large volume shifts. It also provides access for intra- and postoperative lab draws. A central line provides an indication of cardiac filling pressures. The ability to monitor intravascular fluid volume is especially important in situations of underlying cardiovascular instability, hepatorenal syndrome, dehydration, and anticipated intercompartmental fluid shifts.

Induction of Anesthesia: Rapid sequence induction is typically recommended for patients with increased intra-abdominal pressure due to the presence of ascites. Although severe liver dysfunction can decrease cholinesterase activity and may prolong the effect of succinylcholine, this is rarely clinically significant. In hepatorenal syndrome, however, plasma potassium levels may preclude the use of succinylcholine. Cisatracurium and rocuronium may be beneficial to use for muscle relaxation, in order to avoid prolongation of muscle paralysis due to dysfunction of hepatic metabolism.

Maintenance of Anesthesia: One must be aware that liver injury can be worsened with hypoxia, the stress response, drug toxicity, and infection. Therefore, adequate hepatic oxygenation must be ensured throughout the procedure. In addition, anemia should be avoided. Arterial hypotension should be prevented by adequate blood and volume replacement and by avoiding relative overdoses of anesthetics or other blood pressure-lowering agents.

Postoperative Care: The management of the patient with liver disease is very challenging, affecting all major organ systems. Operations on CPT Class B or C patients should only be performed if the benefit–risk ratio is deemed absolutely necessary. The patient's cardiovascular status must be assessed preoperatively and considered separately in risk stratification for anesthesia. Finally, intensive care unit observation is recommended for the first postoperative night, due to the many hemodynamic shifts that may be expected to occur in the first 6–12 h after surgery.

Liver Transplantation

Candidates for a liver transplant undergo a rigorous preoperative evaluation with multiple specialists including: a transplant surgeon, hepatologist, transplant anesthesiologist, psychiatrist, dietitian, and social worker. The appropriateness of liver transplant for each candidate is determined, and then a formal transplant listing is submitted to the national transplantation organization. Organ allocation priority is based on the MELD score with additional points awarded for specific indications. This is an effort to maintain an equitable system of allocation. Nationwide, the 3-year patient survival rate after transplantation is about 73 %. Contraindications to liver transplantation include but are not limited to: significant coronary artery disease, cardiac dysfunction, moderate to severe pulmonary hypertension, uncontrolled infection or sepsis, active alcohol abuse, advanced malignant hepatic disease or metastatic disease, and markedly elevated intracerebral pressure in the presence of acute hepatic failure.

Preoperative Preparation: Immediately prior to transplant, preoperative labs should include a hematocrit, electrolytes, bilirubin, albumin, prothrombin time (PT), partial thromboplastin time (PTT), fibrinogen, and a blood type and cross. The blood bank should be notified immediately with a massive transfusion protocol available: 10–20 units of red blood cells, 5–10 units of fresh frozen plasma, 4–10 units of single donor platelets, and 10 units of cryoprecipitate. Rapid sequence induction is often performed due to the emergency nature of the procedure, plus the significant ascites that is usually present. Monitors required for the procedure are: 2–3 large-bore IV catheters, a radial arterial line, a rapid transfusion catheter, and a central venous pressure monitor. In a patient with known pulmonary hypertension, either a preinduction or pre-incision pulmonary artery catheter should be placed, or transesophageal echocardiography can be used. Every patient must have a Foley bladder catheter to aid in volume status monitoring. Normothermia is maintained with fluid warmers and forced-air heating blankets.

Surgical Procedure: The surgical procedure is divided into three stages: (1) the dissection phase, which mobilizes the vascular structures around the liver and isolates the common bile duct; (2) the anhepatic phase, in which the native liver is excised and clamped from circulation; and (3) the

neohepatic phase, in which vascular clamps are removed from the liver graft, the hepatic artery anastomosis is completed, and closure begins. Each phase is associated with unique anesthetic management issues.

During the dissection phase, blood loss is very high. Crystalloid and colloid replacement is necessary. Diuresis should be established early in the dissection phase to facilitate fluid management. This diuresis provides some renal protection in anticipation of renal ischemia during the anhepatic period. Commonly used drugs are loop diuretics, mannitol, and fenoldopam. At this time, the organ donor liver is prepared on a separate table.

During the anhepatic phase, many physiologic disturbances occur. During this time, complete liver vascular occlusion is established with the clamping of the hepatic artery, portal vein, and infrahepatic and suprahepatic vena cava. In order to maintain cardiac preload, blood flows through the collateral circulation. In some centers, veno-venous bypass (VVBP) is used. VVBP is established with cannulation of the femoral and portal veins. Diversion is to the suprahepatic vena cava through the axillary or subclavian vein. Most North American centers rarely use VVBP, as patients often tolerate volume loading and low-dose vasopressor infusion to a target CVP of 10–20 mmHg during the anhepatic phase. Also, during the anhepatic phase a profound acidosis develops. Hypocalcemia develops due to citrate accumulation from administered blood products. Hyperkalemia often occurs; it is treated with forced diuresis, beta-adrenergic agonists, insulin and glucose, and alkalinization by hyperventilation and administration of sodium bicarbonate. Significant swings in serum glucose may be expected as the liver normally regulates blood glucose, and it is functionally removed from circulation during the anhepatic phase: no gluconeogenesis can occur. Fluid management is challenging. Overly aggressive fluid management during the anhepatic phase can lead to fluid overload with cardiopulmonary compromise during reperfusion. Frequent blood gas monitoring and correction of parameters optimizes patient outcomes.

Prior to the neohepatic or reperfusion phase, the vascular clamps are removed in a staged fashion. The most critical part of the reperfusion phase is the removal of vascular clamps from the liver graft. Communication between the anesthesia and surgical teams is imperative at this point. Prior to clamp removal, all emergency drugs and blood products should be available. Sodium bicarbonate should be prepared to treat the acid load from the grafts. Calcium chloride is administered preemptively to counteract the effects of the elevated potassium as it is flushed out of the donor graft. With the removal of the portal vein clamp, significant hemodynamic instability ensues. Commonly, hypotension with a further drop of already low SVR occurs. Reduced cardiac contractility, arrhythmias, profound hypotension, and hyperkalemic arrest are reported complications of the reperfusion syndrome. After initial reperfusion, the hepatic artery anastomosis is completed, the gallbladder is removed, and the bile duct is reconstructed.

Predictors of graft success include low transfusion requirements, intraoperative bile and urine production after introduction of the donor liver into circulation, decreased cardiac output and increased SVR in the first hour of reperfusion, and the lack of calcium requirements despite FFP infusion. After adequate hemostasis is obtained, the abdomen is closed. Tracheal extubation may be performed if patients meet standard extubation criteria. Postoperative care is accomplished in the intensive care unit. The postoperative course is dictated by the degree of immediate liver function and the level of recovery of the presurgically compromised organs, that is, hepatorenal or hepatopulmonary syndrome.

Laparoscopic Surgery

Laparoscopic, or minimally invasive surgery, is a technique in which operations within the abdomen, pelvic, or retroperitoneal cavities are performed through small 1–1.5 cm incisions. A laparoscope which contains a video camera and a fiber-optic light source is inserted into the belly, and the abdomen is insufflated with carbon dioxide or another inert gas. This elevates the abdominal wall above the internal organs and creates a working space for the surgeon to perform the procedure. Procedures commonly performed via laparoscopy include: cholecystectomy, appendectomy, inguinal hernia repair, antireflux surgery, colectomy, and even nephrectomy. Laparoscopic surgery has even been adapted for bariatric procedures and gynecologic and urologic surgeries. Physiologic changes affecting anesthetic management are common due to the CO_2 insufflation required.

Physiologic Changes During Laparoscopy

Cardiovascular: At increased intra-abdominal pressures (IAP) >10 mmHg, there is an increase in venous return from compression of sequestered blood in the splanchnic venous bed (Fig. 32.3). The pressure on the venous vasculature leads to an increased central venous pressure, pulmonary capillary wedge pressure, and right- and left-side cardiac filling pressures. In turn, this leads to an increase in cardiac output and arterial pressure. However, following this initial rise in venous return, a steady state of decreased blood circulation occurs due to the continued increased IAP. This continued compression exerts its effects on the arterial vasculature and capillaries and increases afterload, SVR, and arterial pressure. Stroke volume and cardiac output decrease. Heart rate

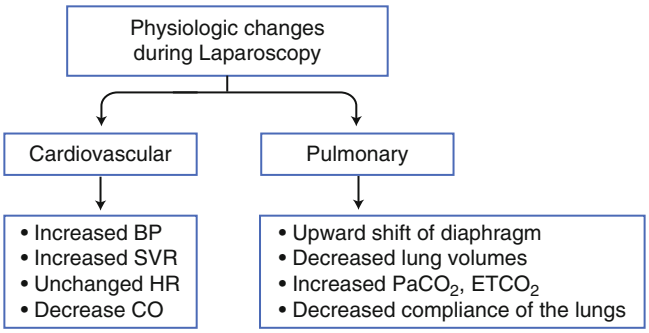

Fig. 32.3 Physiologic changes during laparoscopic surgery

rises initially in response to the increased SVR and arterial blood pressure, but in otherwise healthy patients, this is transient and short lived. These cardiovascular changes vary with the level of IAP. Higher IAP, over 20 mmHg, leads to a more significant decrease in venous return due to compression of the inferior vena cava, thereby, decreasing the cardiac output significantly.

Respiratory: With increased IAP, the abdominal organs exert weight on the diaphragm, and the excursion of the diaphragm into the abdomen is decreased. Functional residual capacity, vital capacity, and pulmonary compliance all drop Peak airway and plateau pressures increase upwards of 75 %. These effects are exacerbated with Trendelenburg positioning. Hypercarbia and hypoxemia may be caused by ventilation/perfusion mismatch due to a decrease in diaphragmatic excursion caused by the pneumoperitoneum. The partial pressure of arterial carbon dioxide progressively increases to reach a plateau about 30 min after the onset of CO_2 insufflation. This is secondary to multiple factors: absorption of CO_2 from the peritoneal cavity, impairment of pulmonary ventilation and perfusion by mechanical factors such as abdominal distention, and Trendelenburg position. Absorption of the carbon dioxide can worsen hypercarbia and acidosis, though this can be offset with increased ventilation. Although healthy patients generally tolerate these physiologic changes quite well, patients with obesity or chronic obstructive pulmonary disease may be at high risk of pulmonary decompensation. Poor CO_2 diffusion and elimination in patients with COPD can lead to significant increases of $PaCO_2$. Obese patients may not have an appropriate ventilator response to the increased $PaCO_2$. This may be difficult to monitor as $PETCO_2$ may not correlate with $PaCO_2$ in patients with underlying pulmonary disease.

Renal: Oliguria is often seen with increases in intra-abdominal pressure during laparoscopy. As IAP increases, compressive effects on the renal vasculature, renal parenchyma, and inferior vena cava reduce the effective renal blood flow (ERBF) and renal venous outflow. At a typical intra-abdominal pressure of 15 mmHg, urinary output decreases by as much as 64 %, GFR by 21 %, and ERBF by 26 %. If IAP cannot be decreased, volume expansion and slight fluid overload are generally reasonable treatment options.

Anesthetic Considerations

Laparoscopic procedures are usually done under general endotracheal anesthesia. Some anesthesiologists use a laryngeal mask airway (ProSeal LMA), with the advantage of reduced postoperative analgesia requirements and decreased incidence of postoperative nausea and vomiting (PONV). However, other anesthesiologists are reluctant to use an LMA for laparoscopic procedures because of the risk of regurgitation and pulmonary aspiration of gastric contents, due to increased intra-abdominal pressures and positive pressure ventilation.

All patients receive standard ASA monitors. Patients with significant comorbidities may need invasive monitoring and frequent blood gas analysis. Capnography is used intraoperatively to monitor the adequacy of ventilation. The normal gradient of 3–5 mmHg between $PaCO_2$ and $ETCO_2$ is disrupted during laparoscopic procedures due to CO_2 insufflation. Hence, if one desires to measure an accurate $PaCO_2$, an arterial blood gas analysis is required.

Additionally, a Foley catheter and an orogastric tube are inserted to decompress the bladder and the stomach, respectively. Anesthesia is maintained with opioids, volatile inhalational agent, and a nondepolarizing muscle relaxant. Use of N_2O is avoided as it may cause bowel distention and increase the incidence of PONV. Since insertion of the trocar by the surgeon is a blind procedure, the patient should have adequate muscle relaxation to prevent injury to the inferior vena cava or the aorta, prior to trocar insertion. Trocar insertion may be also associated with a vagal response (bradycardia).

Intraoperative hypertension should be treated with adequate pain control (fentanyl and morphine or hydromorphone), deepening the anesthesia (volatile agent), and if necessary labetalol or metoprolol. Since laparoscopic procedures are associated with a high incidence of PONV, patients are usually administered dexamethasone and ondansetron intraoperatively. A scopolamine patch may be applied behind the ear preoperatively.

Postoperatively, some surgeons discharge the patients from the recovery unit, while other surgeons discharge the patients after 24 h. Laparoscopic procedures are associated with reduced postoperative pulmonary complications than open procedures. Adequate pain control should be achieved, and antiemetics should be administered postoperatively. Patients may have an increased risk of deep vein thrombosis. Bile duct injuries usually cause pain and jaundice, which may need re-exploration.

Risks Associated with Laparoscopic Surgery

The most significant risks unique to laparoscopic surgery are trocar injuries to blood vessels, resulting in hemorrhage; bowel injury, resulting in peritonitis if unrecognized; or urinary tract injury with transaction of the ureter. The first step in a laparoscopic surgery requires obtaining access to the peritoneal cavity. Adequate muscle relaxation should be provided prior to this step. This abdominal entry accounts for 40 % of all laparoscopic complications. Most often, this is performed blindly with a Veress needle: a stab incision is made at the umbilicus, followed with the blind passage of the needle into the abdominal cavity. The open technique allows a surgeon to incise the peritoneum under direct vision; a wedge-shaped Hasson trocar establishes a seal to allow CO_2 insufflation. However, the open technique is not immune to complications of major vascular injuries and bowel injuries with trocar placement. The risks of such injuries are increased in obese patients or those with prior abdominal surgery and the presence of significant adhesions. Rapid recognition of vascular injury is the key to preventing a catastrophic outcome, as an emergency midline laparotomy may have to be performed to achieve hemostasis.

CO_2 embolism is a rare but dramatic complication that can lead to sudden cardiovascular collapse. It is associated with a mortality rate as high as 28.5 % and survivors may have significant neurologic deficits. CO_2 embolism is caused by the direct entry of insufflated CO_2 gas into the arterial or venous system. Diagnosis of CO_2 embolism may be difficult as the presentation mimics that of other complications, with hypotension, hypoxia, and decreased end-tidal carbon dioxide (Table 32.4).

Extravasation of CO_2 during laparoscopic abdominal procedures may result in pneumomediastinum, pneumopericardium, and pneumothorax. CO_2 can pass retroperitoneally through potential spaces causing subcutaneous and ocular emphysema. Intraoperative treatment of extraperitoneal CO_2 insufflation includes the use of positive end-expiratory pressure (PEEP), increased minute ventilation, and increased inspiratory pressures to decrease the abdominal gradient. Lowering IAP pressures of CO_2 insufflation may prevent these complications. Postoperatively, entrapped CO_2 gas will diffuse out in about 24 h with 100 % oxygen and adequate ventilation. An upright sitting position aids the diffusion. Significant subcutaneous emphysema may lead to airway compromise, which may delay extubation.

Table 32.4 Diagnosis and management of CO_2 embolism

Diagnosis	
Cardiovascular signs	Hypotension, tachycardia, dysrhythmias
Electrocardiogram	Tachycardia, dysrhythmias
Capnogram	Fall in $ETCO_2$
Pulse oximetry	Decreased saturation
Auscultation	Mill wheel murmur
Precordial Doppler	Disruptive flow
TEE	Presence of bubbles
Management	
Stop insufflation, saline irrigation by surgeon	
Move patient to left lateral decubitus Trendelenburg position	
Aspirate air via central venous catheter	
Cardiopulmonary support	

Bariatric Surgery

The prevalence of obesity, defined as a body mass index (BMI) > 30 kg/m^2, has increased dramatically in the last decade. Currently, 35.7 % of the adult US population is obese by this definition and 80 % of this obese population has a debilitating comorbidity related to obesity. Because meaningful weight loss in the morbidly obese is difficult to achieve, surgical weight loss procedures allow for a sustained weight loss and significant improvement in obesity-associated comorbidities. The gold standard surgical treatment of obesity is the Roux-en-Y gastric bypass (Fig. 32.4). It involves anastomosing the proximal gastric pouch to a segment of the proximal jejunum, bypassing most

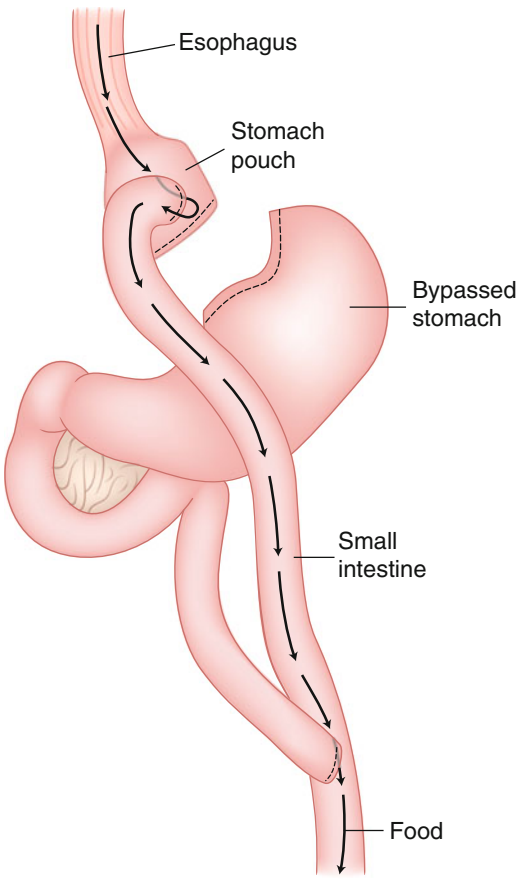

Fig. 32.4 Roux-en-Y gastric bypass

the stomach and the entire duodenum. It combines the effects of gastric restriction with a modest degree of malabsorption to lead to significant weight loss. Patients considering bariatric surgery must have failed nonsurgical treatments. Intraoperative and preoperative management focuses on the organ systems most affected by the patient's obesity.

Preoperative Preparation

Preoperative evaluation should consist of airway examination (difficult airway/difficult mask ventilation), presence of comorbidities (cardiovascular, pulmonary), laboratory tests, and medication compliance (insulin, oral agents, diuretics).

Cardiovascular: Systemic and pulmonary hypertension must be evaluated. Symptoms of pulmonary hypertension include dyspnea on exertion, fatigue, and syncope. These symptoms may be difficult to obtain in a sedentary patient; a dobutamine echo may best evaluate underlying cardiac pathology. The presence of mild to moderate pulmonary hypertension warrants avoidance of nitrous oxide and maintenance of adequate oxygenation; the inhalational agents are beneficial in that they cause bronchodilation and inhibit hypoxic pulmonary vasoconstriction.

Respiratory: Oxygen consumption and carbon dioxide production are increased in the obese patient. There is a decreased expiratory reserve volume (ERV) and a decrease in functional residual capacity (FRC) in the upright position. FRC is reduced to the extent that it approaches residual volume (RV). Such a reduction in FRC means that closing volume exceeds the FRC and airway closure can occur within normal tidal volume breaths. This is exacerbated in the supine position. Under anesthesia, the FRC of the obese patient decreases even further (Fig. 32.5). This results in ventilation/perfusion abnormalities and hypoxemia.

Obstructive Sleep Apnea (OSA): OSA is defined as a complete cessation of airflow that lasts 10 or more seconds in spite of efforts to maintain ventilation (apnea), occurring five or more times per hour of sleep, and accompanied by at least a 4 % decrease in SpO_2. Hypopnea is defined as a partial reduction of airflow greater than 50 %. Polysomnography provides results in the form of an apnea/hypopnea index (AHI) which is calculated by the number of episodes of apnea/hypopnea per total sleep time. The severity is defined as mild (AHI 5–15), moderate (AHI 15–30), or severe (AHI >30). Moderate to severe OSA is known to place a patient at significant risk for the development of systemic and pulmonary hypertension, left ventricular hypertrophy, cardiac arrhythmias, and cognitive impairment.

OSA and obstructive sleep hypopnea occur 12–30 times more often in obese than nonobese patients. The percentage of morbidly obese patients with OSA ranges in the literature

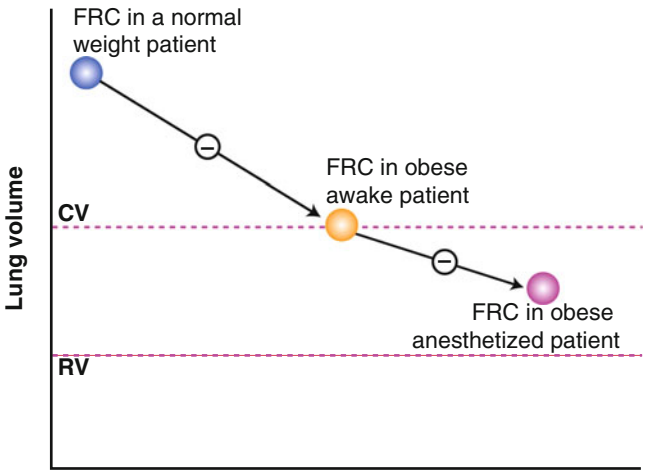

Fig. 32.5 Relationship of functional residual capacity (FRC) and closing volume (CV) in a normal and obese patient. Note that in an obese patient, the FRC approaches the closing volume, which causes airway closure with normal tidal volume breaths (RV, residual volume)

from 12 to 40 %. Preexisting OSA is thought to increase morbidity and mortality from respiratory complications. These upper airway obstruction and oxygen desaturation events are worse under the effects of residual anesthetics and postoperative analgesic agents. They can be minimized with the use of the patient's home continuous positive airway pressure (CPAP) device.

Associated with OSA is the obesity hypoventilation syndrome (OHS). It is characterized by chronic hypercarbia ($PaCO_2$ >45 mmHg) with a decreased respiratory drive, the presence of sleep apnea, and hypersomnolence. OHS may progress to Pickwickian syndrome which is defined as hypercarbia, hypoxia, polycythemia, and pulmonary hypertension with eventual biventricular failure.

Obese patients who do not have a known history of OSA should be screened preoperatively with the STOP questionnaire and treated appropriately prior to any elective surgery. Detecting OSA is important, as these patients show an increased sensitivity to the respiratory depressant effects of benzodiazepines and opiates. Chronic CPAP use (>1 month) has been shown to reverse the cardiac and respiratory effects of OSA; deferring nonurgent surgery until CPAP use is established as beneficial.

The "STOP" questionnaire

S	Do you snore loudly?
T	Do you often feel tired or sleepy during the day?
O	Has anyone ever observed you stop breathing during sleep?
P	Do you have or are you being treated for high blood pressure

If patients answer "yes" to two or more of these questions, they are considered as high risk for OSA

Intraoperative Considerations

Patients may be premedicated with anxiolytics. However, patients with OSA may be sensitive to these medications. Prophylaxis for gastric aspiration is usually provided by administering famotidine, ranitidine, or omeprazole. Intravenous access is obtained by inserting one or two large-bore IV catheter (16–18G).

Monitors for bariatric surgery procedures, besides the standard ASA monitors (including a Foley catheter), may include central and arterial cannulations. Arterial blood gases evaluate oxygenation and carbon dioxide retention and provide data for weaning from postoperative ventilation. Patient size may also preclude use of a noninvasive blood pressure cuff due to poor fit on conically shaped arms or lack of appropriately sized cuffs.

In the operating room, *positioning* of obese patients may be difficult to accomplish. Prior to sedation and movement of the patient onto the operating room table, the weight capacity of the table must be assessed. Many OR tables will hold up to 500 kg, but some have weight limits of only 205 kg. Extra width is often necessary, and a bean bag may be a useful positioning device. Pressure areas should be well padded and stretch positions avoided, as pressure sores and neural injuries are more common in this group of patients.

Induction must consider the risks of difficult endotracheal intubation. Neck circumference alone is an independent predictor of a difficult airway in morbidly obese patients. A neck circumference greater than 60 cm represents a 35 % chance of difficult intubation. Failed intubation can occur in as many as 5 % of attempted surgeries on morbidly obese patients with OSA. To complicate matters, these patients have a small FRC and desaturate quickly. An awake fiberoptic intubation should be considered in patients who are 75 % over ideal body weight. If a difficult airway is not suspected, a rapid sequence induction may be indicated. As obese patients have an increased intra-abdominal pressure and an increased fasting gastric volume, they should be considered a "full" stomach. "Stacking" blankets for induction positioning will facilitate intubation by placing the chin at a higher level than the chest. The goal is to create an imaginary horizontal line connecting the sternal notch to the external auditory meatus; this allows for the best possible view with direct laryngoscopy.

Maintenance of anesthesia is done by using opioids, volatile agent, and a muscle relaxant. Consideration must be given to the altered pharmacodynamics and pharmacokinetics in the morbidly obese patient. Lipophilic drugs should be dosed according to actual body weight, with increased loading doses. Clearance will be slowed due to slow extraction from the adipose tissue reservoir. Lipophilic drugs include propofol, benzodiazepines, and fentanyl. Hydrophilic drugs, on the other hand, should be dosed according to an adjusted body weight, which is between the actual and ideal body weight. Hydrophilic drugs include vecuronium and succinylcholine. Remifentanil and desflurane are two useful drugs which can be used for maintenance of anesthesia, as the metabolism of remifentanil is via nonspecific plasma esterases and desflurane is a very insoluble volatile agent (fast on–off).

Table 32.5 Criteria for routine awake extubation

Subjective
Follows verbal commands
Clear oropharynx/hypopharynx of secretions
Intact gag reflex
Sustained head lift for 5 s, sustained hand grasp
Adequate pain control
Minimal end-expiratory concentration of inhaled anesthetics
Objective criteria
Vital capacity >10 mL/kg
Peak voluntary negative inspiratory pressure > 20 cm H_2O
Tidal volume > 6 mL/kg
Respiratory rate < 35 breaths/min
Stable hemodynamics
Sustained tetanic contraction (5 s)
Alveolar–arterial PaO_2 gradient on 100 % FIO_2 < 350 mmHg

Extubation criteria for bariatric surgery patients are the same as for nonobese patients (Table 32.5). These patients may need CPAP or BiPAP in the recovery room and continuing overnight in the intensive care unit, to prevent postoperative airway obstruction and improve postsurgical atelectasis. Achieving postoperative pain control is of prime importance in these patients. Additionally, patients are administered subcutaneous heparin to prevent deep vein thrombosis.

Given the epidemic of obesity, it is incredibly difficult for meaningful, sustained weight loss to occur with only dietary and lifestyle changes. Surgical interventions for obese individuals are becoming increasingly common, and it is imperative that the anesthesiologist be equipped to handle this ever-growing patient population.

Emergency Abdominal Surgery

Management of patients who present for emergent intra-abdominal surgery requires the rapid coordination between the surgeon, the anesthesiologist, and the primary medical team. The urgency of care for the surgical disease must be balanced with medical optimization needed to tolerate anesthesia. Metabolic alterations range from mild perfusion deficits to severe shock. Shock may be hypovolemic, as in the case of trauma; septic, as in the case of intestinal ischemia; or multifactorial, as in a patient with a bowel perforation and peritonitis who subsequently has a myocardial infarct. Early goal-directed resuscitation is begun preoperatively and continued throughout the operation. Prior to taking the patient to the operating room, advance directives must be reviewed, especially in light of the changing risks of perioperative

morbidity and mortality. Correction of fluid deficits and electrolyte abnormalities is of prime importance. Specific issues to consider in sepsis and trauma in the setting of an emergent abdominal surgery are discussed in greater detail below.

Sepsis

Patients with sepsis need source control as soon as their hemodynamic status allows for surgical intervention. The etiologies of intra-abdominal sepsis that result in a trip to the operating room vary, including gastrointestinal perforation, incarcerated hernia, bowel obstruction, and mesenteric ischemia. Aggressive resuscitation with fluids and even blood component therapy may be necessary.

Induction of the anesthesia in septic patients must take into account alteration in drug metabolism, increased risk of cardiovascular toxicity, and enhanced patient sensitivity to sedative effects. Patients have unstable hemodynamics due to hypovolemia, cardiac dysfunction, impaired vasoregulation, and possibly even adrenal insufficiency, leading to a high sensitivity to induction agents. Ketamine is often used in the septic patient, as it does not depress ventilation and produces bronchodilation. Etomidate is often considered due to its relative stable hemodynamic profile, but due to its potential of adrenal suppression after even one dose, it should not be chosen as a first-line agent. Propofol's vasodilating effects may be mitigated with concurrent administration of an alpha-1 agonist; a lower dosing may be indicated.

Sepsis is often associated with hyperglycemia that is detrimental to outcome. It is prudent to maintain blood glucose less than 150 mg/dl in accordance with the surviving sepsis campaign guidelines. Care, however, must be taken to avoid over administration of insulin. A single episode of hypoglycemia with glucose less than 40 mg/dL has been correlated with increased mortality, prompting early termination of two large trials.

Though septic patients are often febrile, severe sepsis may also be associated with hypothermia. The triad of hypothermia, acidosis, and coagulopathy significantly increases a patient's mortality. Therefore, hypothermia should be aggressively corrected. Forced-air warming is sometimes limited by surface area exposure; therefore, intraoperative fluid warming becomes key to maintaining normothermia. It is prudent to consider warming blankets in the intensive care unit prior to operative transport.

Trauma

In Americans ages 1–44 years, unintentional injury (trauma) is the number 1 cause of death. Through advances in prehospital care during the "golden hour," more patients are surviving and coming to the operating room for stabilization and subsequent procedures. The "damage control abdomen" is a strategy used in trauma that has been adopted to allow for initial stabilization of life-threatening hemorrhage and fecal contamination. Damage control resuscitation (DCR) decreases the amount of time the unstable patient spends in the OR. DCR leaves abdominal fascia open, and a return to the OR is planned after the patient is stabilized for closure and repair of non-life-threatening injuries. DCR improves immediate survival outcomes and decreases the number of cases whose course is complicated by abdominal compartment syndrome (ACS).

The aggressive initial large-volume crystalloid resuscitation by the anesthesiologist often results in intra-abdominal hypertension and the development of abdominal compartment syndrome due to the development of the systemic inflammatory response syndrome (SIRS) and visceral edema. Intraoperative signs of ACS include hypothermia, acidosis (base deficit greater than 14 mmol/L), hemoglobin less than 8 g/dL, and oliguria. Immediate surgical decompression usually results in prompt improvement in hemodynamic instability and organ dysfunction. Aggressive diuresis following DCR can improve oxygenation and ventilation and will allow for earlier closure of the abdominal fascia.

The initial perioperative physiology following trauma is due to hypoperfusion secondary to hemorrhagic shock. Resuscitation of the intravascular and extravascular spaces is required. Particular attention must be paid to the correction of hypothermia, acidosis, and coagulopathy (which significantly increase mortality). Optimization of fluid management and correction of coagulopathy may prevent up to 20 % of trauma-related deaths. Over the past 15 years, the accepted view on trauma resuscitation has been to limit crystalloid; instead, a near even balance of packed red blood cells, fresh frozen plasma, and platelets is transfused. Even after a seemingly adequate initial resuscitation at the time of injury, trauma patients often remain hypotensive. A systemic inflammatory immune response is common, with a degree of vasodilation contributing to persistent inflammation, immunosuppression, and catabolism. After adequate fluid resuscitation, introduction of a vasopressor may be necessary to combat the vasodilation associated with this inflammatory response.

The care of the patient in the setting of acute abdominal emergency requires close communication between the surgeon, medical team, and anesthesiologist. Optimization of fluid status, maintenance of normothermia, and the use of appropriate blood products and vasoactive agents improve patient outcomes tremendously.

Clinical Review

1. The following is most likely an indicator of significant liver dysfunction:
   A. Serum albumin 3.0 mg/dL
   B. Serum bilirubin 3 mg/dL
   C. Prothrombin time 16 s
   D. Deficiency of factor VIII
2. Oxygen is supplied to the liver by
   A. Portal vein
   B. Hepatic artery
   C. Both A and B
   D. Portal artery
3. Patients with cirrhosis of liver have
   A. Increased cardiac output
   B. Peripheral vasoconstriction
   C. Preserved renal function
   D. Deficiency of factor VIII
4. Initial step in management of CO_2 embolism is
   A. Immediate irrigation of the wound with saline
   B. Turning the patient to left lateral decubitus position and aspirating air from a central venous line
   C. Maintenance of blood pressure and cardiac output
   D. Stop insufflation
5. Obesity hypoventilation syndrome is characterized by all of the following, *EXCEPT*:
   A. Hypercarbia
   B. Hypoxia
   C. Anemia
   D. Pulmonary hypertension

Answers: 1. C, 2. C, 3. A, 4. D, 5. C

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Renal and Urinary Tract Diseases

33

Arielle Butterly and Edward A. Bittner

Urologic surgery includes a wide spectrum of procedures ranging from minor outpatient endoscopic procedures to major procedures that can cause marked physiologic disturbances. Many patients undergoing these procedures have underlying renal dysfunction and associated comorbid medical conditions. Preoperative optimization of patients with renal dysfunction and comorbid disease, knowledge of specific complications associated with the operative procedures, and implications for the various positions that the patient may be subjected to during surgery are essential elements for the anesthesiologist caring for patients undergoing urologic surgery. Since regional anesthesia is often employed during urologic surgery, the anesthesiologist must be aware of the spinal levels that conduct nociceptive input from the genitourinary urinary system.

Anatomy of the Genitourinary System

The kidneys are located in the retroperitoneal space between the T_{12} and L_4 vertebrae, with the right kidney lying slightly lower than the left one because of the presence of the liver (Fig. 33.1). The adrenal glands are located above each kidney. The kidneys are surrounded by a fatty capsule that fills the space inside the loosely applied renal fascia. The renal blood vessels generally lie anterior to the pelvis of the kidney, although some branches may pass posteriorly. One renal artery and vein supply each kidney. The renal arteries arise directly from the aorta immediately inferior to the superior mesenteric artery. Each kidney has an outer cortex and inner medulla. The medial border of each kidney comprises the hilum which opens into the renal pelvis. The ureters originate at the renal pelvis and course down the psoas across the iliac vasculature to the bladder. During development, the rudimentary kidneys are close together and may fuse to give rise to a horseshoe kidney. This organ is unable to ascend, held in place by the inferior mesenteric artery, and when present it remains as a pelvic organ.

Autonomic innervation of genitourinary tract consists of sympathetic fibers (originating from T_8–L_1) and parasympathetic fibers (vagal nerve and nerves originating from $S_{2–4}$), which serve to modulate renal perfusion, peristalsis, and sphincter tone (Table 33.1). Efferent nerves for both parasympathetic and sympathetic innervation of genitourinary systems originate from the spinal cord as splanchnic nerves, combining at several major nerve plexus which then innervate visceral organs. Sympathetic stimulation serves to inhibit peristalsis and increase sphincter tone while parasympathetic stimulation serves the opposite functions. Innervation of the intra-abdominal components of the genitourinary system, the kidney, and the ureter is primarily thoracolumbar (T_8–L_2), while the nerve supply of the pelvic organs, the bladder, the prostate, the seminal vesicles, and the urethra is primarily lumbosacral with some lower thoracic input (T_{10}). Nerve supply to the testicles is via the ilioinguinal nerve and genital branch of the genitofemoral nerve for the anterior scrotum. These nerve branches originate from T_{10} to L_2. The posterior portion of the scrotum is innervated from $S_{1–4}$.

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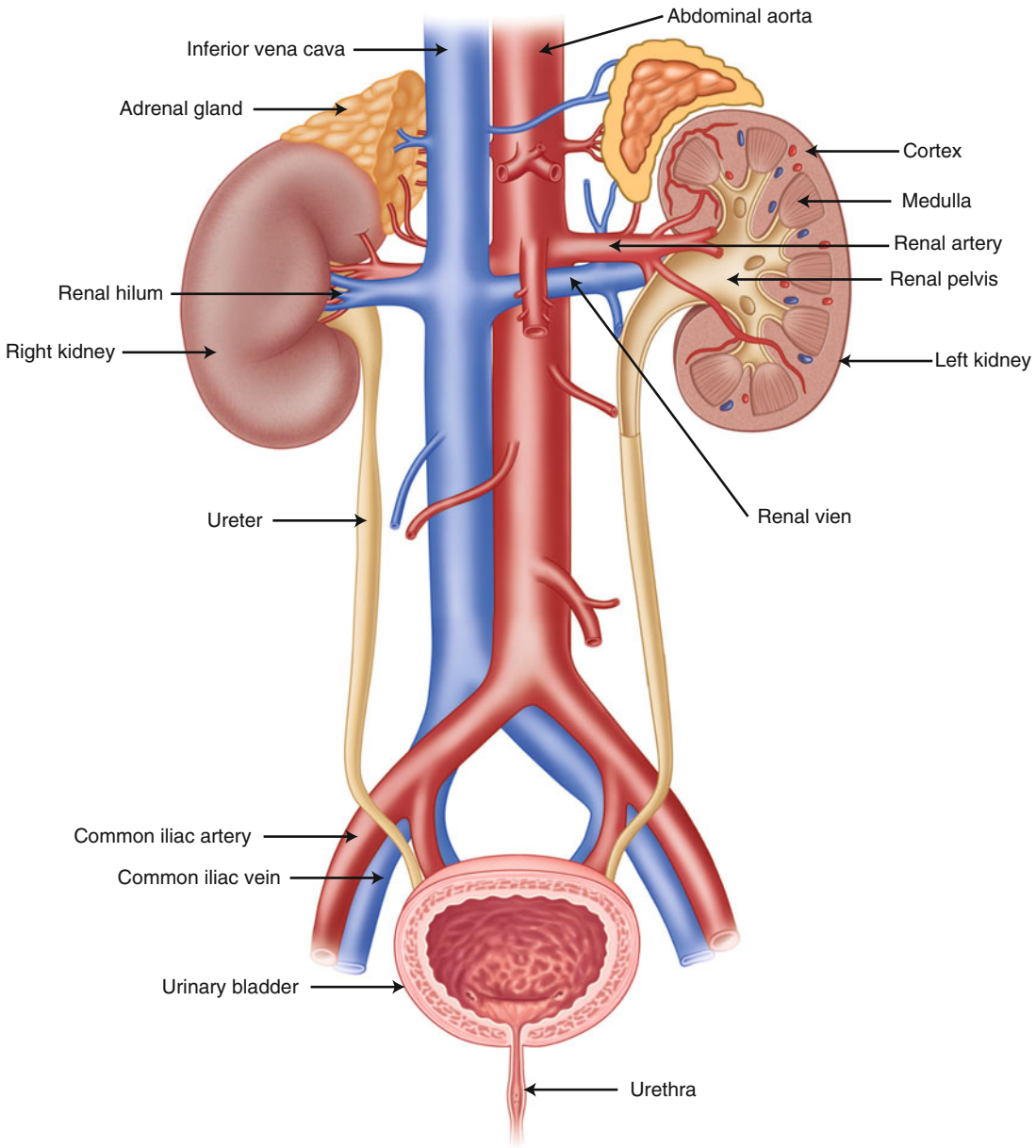

Fig. 33.1 Anatomy of the kidney and urinary system

Renal Physiology

The functions of the kidney are numerous including feedback mechanisms that maintain fluid balance, osmolarity, electrolyte content and concentration, and acidity within narrow limits. Extracellular solutes are tightly regulated, including sodium, potassium, hydrogen ion, bicarbonate, and glucose. The kidney also generates ammonia and glucose, and eliminates nitrogenous and other metabolic waste, including urea, creatinine, and bilirubin, as well as toxins and many classes of drugs. Finally, circulating hormones secreted by the kidney influence regulation of systemic blood pressure, red blood cell generation, and calcium homeostasis. The adrenal glands, sitting atop of the kidneys, are a major endocrine organ producing mineralcorticoid (aldosterone), glucocorticoids (cortisol), and sex steroids (androgens). The medulla of the adrenal glands is directly innervated by presynaptic sympathetic fibers and release systemic epinephrine in response to sympathetic stimulation.

Each kidney contains approximately one million nephrons, the functional units of the kidney (Fig. 33.2). The nephron is a tubular structure that is segmented into specialized parts, including the glomerulus, proximal convoluted tubule, loop of Henle, distal convoluted tubule, and a collecting duct that drains into the renal pelvis and ureter. The glomerulus, a

Table 33.1 Autonomic and sensory innervation of the genitourinary system

Organ	Sympathetics	Parasympathetics	Spinal levels of pain conduction
Kidney	T_8–L_1	CN X (vagus)	T_{10}–L_1
Ureter	T_{10}–L_2	$S_{2–4}$	T_{10}–L_2
Bladder	T_{11}–L_2	$S_{2–4}$	T_{11}–L_2 (dome), $S_{2–4}$ (neck)
Prostate	T_{11}–L_2	$S_{2–4}$	T_{11}–L_2, $S_{2–4}$
Penis	$L_{1–2}$	$S_{2–4}$	$S_{2–4}$
Scrotum	NS	NS	$S_{2–4}$
Testes	T_{10}–L_2	NS	T_{10}–L_1

NS not significant for nociceptive function

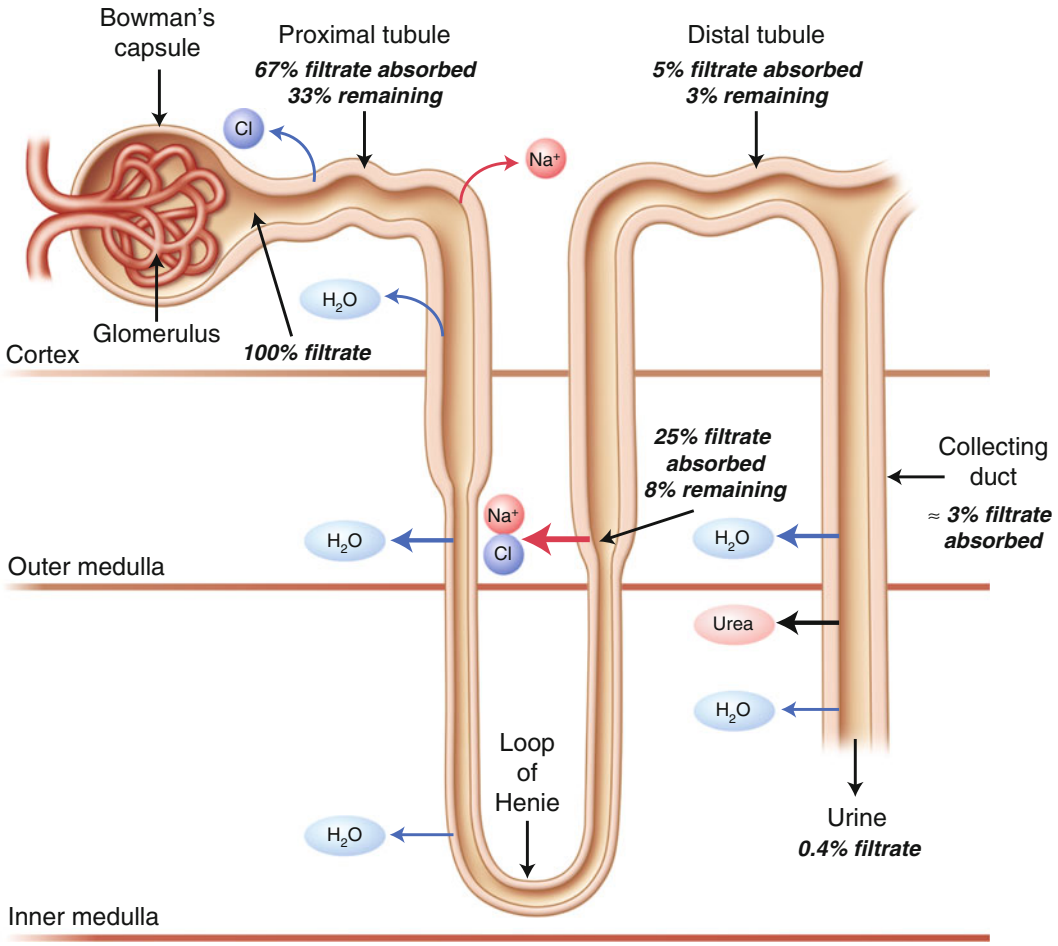

Fig. 33.2 Structure and function of the nephron

permeable tuft of capillaries, serves as the interface between blood and kidney. It is cupped by Bowman's capsule, the most proximal component of the nephron, thereby, providing a large surface area for filtration of blood into the nephron. Blood flow to the glomerulus is regulated through the afferent and efferent arterioles, which adjust the glomerular filtration pressure. Depending on this filtration pressure, fluid (approximately 120 mL/min) is filtered into the Bowman's capsule and then passes into the tubules.

The glomerular capillary endothelium, glomerular basement membrane, and visceral epithelium of Bowman's capsule are responsible for creating the filtration barrier. All three layers are negatively charged and fenestrated. Filtration through the glomerulus is dependent on particle size and charge (cations readily filtered, while anions repelled and remain in the blood) and the hydrostatic pressure in the tuft (determined by afferent and efferent arterioles). Examples of molecules that are freely filtered are water, sodium, urea,

glucose, and insulin. Larger molecules that are not filtered include hemoglobin and proteins (albumin). Injury to the kidney can result in disruption of the charge and fenestrations such that proteins are filtered, resulting in proteinuria.

The permeable large surface area of the glomeruli allows approximately 180 L of protein-free fluid to be filtered by the kidneys each day. However, almost 99 % of this filtrate is reabsorbed in the tubules of the nephrons. Unlike the glomerulus (which depends on perfusion pressure, particle size, and charge for passive filtration), the tubules depend on specialized active pumps to generate local environments of diffusion gradients. The tubule can be divided into several segments in which these local environments occur, allowing highly regulated solute and fluid absorption. Sodium is actively transported via triphosphate (ATP) pumps into the interstitium, while water follows passively across an osmolar gradient (Loop of Henle). Urine and plasma osmolality are regulated by a feedback mechanism in the loop of Henle: increased interstitial sodium concentrations which result from hypovolemia lead to an increased reabsorption of water and a decrease in urine output.

The glomerular filtration rate (GFR) describes the rate at which fluid is filtered by the kidneys.

Ideally the GFR is measured by clearance of a molecule that is freely filtered at the glomerulus, but neither secreted nor absorbed in the renal tubule. The gold standard molecule for GFR measurement is inulin (derived from Jerusalem artichoke, chicory, and dahlias), which is impractical for clinical use. Instead, due to ease of measurement, creatinine is used. Creatinine slightly overestimates true GFR because some creatinine is also secreted by renal tubules. Normal GFR is 120–130 mL/min/1.73 m^2, with a decline with age by approximately 1 mL/min/1.73 m^2 per year after the third decade. A GFR of 60 represents loss of approximately half of the adult level of normal kidney function.

Renal Blood Flow and Autoregulation

The kidneys are the best-perfused organ per gram of tissue in the body and receive 20 % of the cardiac output. Renal blood flow is heterogeneous with the renal cortex receiving approximately 80 % of renal blood flow, and the renal medulla receiving only about 20 %. As a result, the medulla is particularly susceptible to ischemia during periods of decreased renal blood flow. Several overlapping control mechanisms exist to regulate renal blood flow and GFR by altering tone of the afferent and efferent arterioles of the glomerulus and broadly include: autoregulation, the rennin–angiotensin–aldosterone system, and neurohumeral system.

Autoregulation

Global renal blood flow is autoregulated and is kept constant at a mean arterial pressure of 50–150 mmHg in normotensive patients. The mechanism for autoregulation is thought to be due to direct myogenic activity of the afferent arteriole in response to blood pressure. With increased blood pressure the afferent arteriole contracts (thereby reducing blood flow), and with reduced blood pressure the arteriole dilates, thereby, maintaining perfusion in low blood pressure states. Autoregulation fails when the mean arterial pressure falls below 50 mmHg at which point perfusion becomes pressure dependent.

Renin–Angiotensin–Aldosterone System

The renin–angiotensin –aldosterone system (RAAS) plays key role in salt and water reabsorption by the nephron (Fig. 33.3). The RAAS is regulated by the juxtaglomerular apparatus (JGA), a specialized group of cells adjacent to the afferent arteriole, and the macula densa, a specialized group of tubule cells located in the ascending limb of the loop of Henle. The JGA releases the enzyme renin in to the bloodstream which is responsible for production of angiotensin I in the liver. Angiotensin I is converted to active angiotensin II in the lung by angiotensin converting enzymes (ACE) which then stimulates aldosterone production by the adrenal gland. Aldosterone acts on tubule cells to increase intravascular volume and salt absorption. Therefore, renin catalyzes the rate limiting step in the production of angiotensin II; thus, it is plasma renin levels that determine angiotensin II levels. Cells of the macula densa act as chemosensors for filtrate passing through the tubule, and modulate the activity of JGA. The macula densa senses sodium chloride (NaCl) concentration, which is directly related to tubular flow rate (the higher the rate the higher the NaCl concentration). A decrease in NaCl concentration strongly stimulates secretion of renin from the JGA, thereby, increasing GFR.

In addition to its role in salt and water absorption, angiotensin II has significant effects on renal vasculature and GFR. Importantly, it causes increased vasoconstriction of the efferent arteriole relative to the afferent arteriole, which results in a higher hydrostatic pressure in the glomerulus, thereby, increasing filtration. However, in states of very high angiotensin II secretion, the differential in constriction of the afferent and efferent arterioles is lost, and GFR decreases. The stimulation of renin release during times of increased sympathetic activity is an important mechanism of maintaining GFR despite reduced renal blood flow resulting from catecholamine-induced vasoconstriction. In addition to the JGA-macula densa mechanism, renin secretion is also directly stimulated by a decrease in arterial pressure, which is thought to be due to direct stimulation of baroreceptors in the afferent arteriole responding to changes in wall stretch, and by circulating catecholamines which act on β-adrenergic receptors on the JGA cells.

Autonomic System

Catecholamines (norepinephrine and epinephrine) act on renal vascular α_1 receptors leading to reduced renal blood flow by

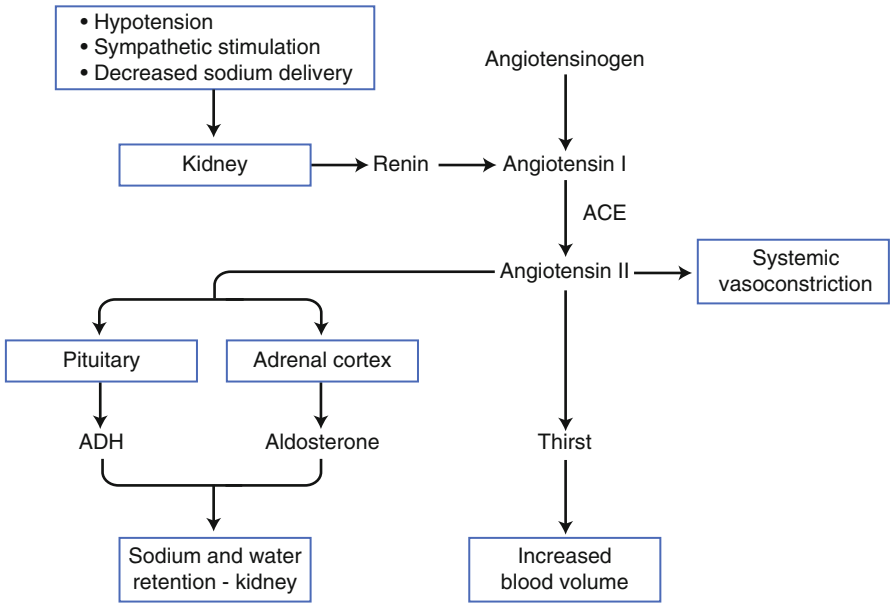

Fig. 33.3 The renin–angiotensin–aldosterone system

vasoconstriction. GFR is maintained during sympathetic activation by the RAAS activity, which disproportionately increases efferent arteriole constriction. The renal vasculature also contains dopaminergic receptors which cause vasodilation in response to activation. These dopaminergic receptors are the site of action of dopamine and fenoldopam, which are sometimes used to "protect" the kidney in times of high norepinephrine-induced vasoconstriction.

Prostaglandins

Prostaglandins are synthesized in the kidney and lead to afferent arteriole dilation. This dilation is an important mechanism of maintaining renal perfusion during systemic hypotension. Nonsteroidal inflammatory drugs (NSAIDs) block prostaglandin synthesis resulting in their nephrotoxic properties.

Atrial Natriuretic Peptide (ANP)

ANP is released by atrial myocytes in response to atrial stretch and beta receptor stimulation. ANP acts on the renal vasculature by dilating the afferent arteriole and possibly constricting the efferent arteriole of glomeruli, thereby, increasing GFR and promoting fluid elimination. ANP also antagonizes the action of aldosterone in the collecting duct, and the release of angiotensin, further reducing Na and H_2O reabsorption.

Effects of Anesthesia on Renal Function

The primary effects of anesthesia and surgery on renal physiology occur through changes in GFR. Fluctuations in blood pressure can have a major effect on renal blood flow and GRF through vasodilation, which reduces renal blood flow when blood pressure falls below autoregulation range, and vasoconstriction (surgical stress), which induces sympathetic activation and alters renal perfusion by stimulating renin/angiotensin/aldosterone release. Clinical studies have failed to identify the superiority of one anesthetic technique over another in the general surgery population. Repeated insults from nephrotoxins in conjunction with ischemic injury or preexisting renal dysfunction are usually required to result in acute kidney injury.

Volatile anesthetics in general cause a decrease in GFR caused by a decrease in renal perfusion pressure either by decreasing systemic vascular resistance or cardiac output (e.g., halothane). This decrease in GFR is exacerbated by hypovolemia, and the release of catecholamines and antidiuretic hormone, as a response to painful stimulation during surgery. Some older inhalational anesthetics (methoxyflurane, enflurane) may, however, have a directly nephrotoxic effect from their metabolic breakdown to free fluoride ions. High intra-renal fluoride concentrations may impair the concentrating ability of the kidney and lead to non-oliguric renal failure. Sevoflurane is also associated with production of nephrotoxic Compound A (a vinyl ether), which is a degradation product formed during low flow anesthesia (<2 L/min) with interaction of sevoflurane with the carbon dioxide absorbent. Although nephrotoxic effects of compound A has been shown in animal models, they have not been shown to be significant in humans. Sevoflurane is considered safe even in patients with renal impairment as long as prolonged low-flow anesthesia is avoided. Isoflurane is metabolized to insignificant amounts of fluoride.

Opiates and benzodiazepines have minimal effect on renal function. Nonsteroidal anti-inflammatory drugs may be nephrotoxic through their inhibition of the production of prostacyclin. Some antibiotics commonly used during the

perioperative period, particularly the aminoglycosides, can also be nephrotoxic. Aminoglycosides are filtered in the proximal tubule and bind to tubular membranes resulting in cellular injury. Toxicity is proportional to high trough levels of the drug. Other antibiotics such as β-lactams (penicillins, cephalosporins) can also cause interstitial nephritis.

Positive-pressure ventilation used during general anesthesia can decrease cardiac output leading to release of catecholamines, renin, and angiotensin II, which results in reduced renal blood flow and GFR. The use of regional anesthetic techniques that achieve a sympathetic block of levels $T_{4–10}$ may be beneficial to patients with kidney disease, or those at high risk for postoperative kidney injury, as the sympathetic blockade attenuates catecholamine-induced renal vasoconstriction and suppresses cortisol and epinephrine release. However, care should be taken to maintain normovolemia and normotension to avoid decreases in renal perfusion associated with the regional anesthetic associated sympathetic blockade. Epidural anesthesia has minimal effects on renal blood flow in healthy volunteers as long as normotension and isovolemia are maintained.

Effects of Surgery on Renal Function

Surgical factors can have a significant impact on renal physiology. Insufflation of the abdomen during laparoscopic surgery can reduce venous return and cardiac output resulting in a decrease in renal blood flow and GFR. The increased intra-abdominal pressure during laparoscopic surgery also may be transmitted directly to the kidneys resulting in further reduction of renal blood flow. Aortic cross-clamping or occlusion of the inferior vena cava can drastically reduce renal blood flow. Suprarenal clamping of the aorta not only reduces blood flow to the kidneys but may also loosen aortic plaque resulting in renal embolism. Interestingly, there is also a reduction in renal blood flow with infra-renal aortic clamps, possibly through renal vasospasm or reduction in cardiac output resulting from the large increase in resistance due to clamping. Cardiopulmonary bypass is associated with renal dysfunction as a result of hypotension, microemboli, and inflammation. Use of off-pump coronary bypass grafting may cause renal injury comparable to cardio-pulmonary bypass, as the results of clinical trials have been equivocal.

The use of intravenous contrast during procedures which require angiograms can result in nephrotoxicity. Intravenous contrast induces renal injury through hemodynamic effects, direct contrast medium molecule tubular cell toxicity, and endogenous biochemical disturbances such as an increase in oxygen-free radicals and/or a decrease in antioxidant enzyme activity. Contrast-induced nephropathy is prevented by adequate hydration. Use of *N*-acetylcysteine (free radical scavenger) may help in preventing renal injury. Importantly, radiocontrast dye is an osmotic diuretic, which may increase urine output and actually worsening the renal injury through dehydration.

Renal Failure

Acute Kidney Injury

Approximately 1 % of patients undergoing general surgical procedures develop acute kidney injury (AKI). Patients developing perioperative AKI are more likely to be male, older, diabetic, and have a history of congestive heart failure, hypertension, ascites, or preoperative renal insufficiency. Emergency surgery doubles and intraperitoneal surgery more than triples the risk for postoperative AKI. Patients who develop AKI have a higher risk of postoperative morbidity and mortality. Additional patient and surgical risk factors for development of perioperative AKI are listed in Table 33.2.

Acute kidney injury is characterized by an acute decline in GFR, associated with disturbances in fluid, electrolyte, and acid–base balance. Acute kidney injury commonly results from multiple insults and is often, but not always, reversible. A change in nomenclature from acute renal failure to acute kidney injury has allowed a more accurate characterization of the spectrum of disease from subclinical injury to complete organ failure. Classification of AKI is commonly described by the RIFLE or AKIN criteria. The RIFLE criteria for AKI contain five categories (risk, injury, failure, loss, and end-stage kidney disease rifle). The first three categories are defined by either percent change of serum creatinine or urine output criteria. The Acute Kidney Injury Network (AKIN) subsequently introduced a definition of AKI based on the observation that even smaller absolute changes of serum creatinine may affect morbidity and mortality.

- Risk—serum creatinine 1.5 times the baseline, and urine output < 0.5 mL/kg/h for 6 h
- Injury—serum creatinine 2 times the baseline, and urine output < 0.5 mL/kg/h for 12 h
- Failure—serum creatinine 3 times the baseline, and urine output < 0.5 mL/kg/h for 24 h
- Loss—persistent loss of renal function > 4 weeks
- End-stage—persistent loss of renal function > 3 months

Acute kidney injury is commonly divided into three categories based on etiology (Table 33.3):

1. Prerenal (adaptive state to reduced perfusion through hypotension or dehydration, where structure and function of kidney remain intact)
2. Intrinsic (cytotoxic injury with destruction of nephron anatomy and function)
3. Postrenal (state of obstructive urine flow).

Table 33.2 Risk factors for perioperative AKI

Preexisting renal insufficiency
Congestive cardiac failure
Hypertensive or diabetic nephropathy
Sepsis, shock
Nephrotoxic drugs—radiocontrast dye, aminoglycoside antibiotics, cyclosporin, NSAIDs
Surgeries—kidney transplant, cardiopulmonary bypass, aortic cross-clamping
Advanced age

Table 33.3 Causes of acute kidney injury

Prerenal failure—State of low renal perfusion, nephron intact	– Hypovolemia (blood loss, dehydration) – Hypotension (Abdominal compartment syndrome) – Shock (CHF, Sepsis) – Unabated systemic/renal vasoconstriction (ACE inhibitors, NSAIDS, high sympathetic tone, high dose pressors)
Intrinsic failure—State of nephron cell death from toxins/ischemia	– Vascular: Renal infarction, embolism – Tubular (ATN): Ischemia from prolonged prerenal state, nephrotoxins (aminogylcosides), rhabdomyolisis – Glomerular: Glomerulonephritis, vasculitis
Postrenal failure—State of urinary flow obstruction	– Prostatic obstruction – Ureteral obstruction (stone, clot) or injury – Extraureteral obstruction

Renal failure also is classified according to urine flow rates, so the terms *oliguric* (<400 mL urine output in 24 h), *nonoliguric* (>400 mL urine output in 24 h), and *polyuric renal failure* are often encountered. Prerenal, intrinsic, and postrenal causes of failure can present as oliguric or non-oliguric failure, but more commonly present as oliguric failure. In some cases, patients with AKI may have normal or high (>2.5 L/day) urine flow rates, but have biochemical abnormalities that are similar to the abnormalities occurring in patients with low urine output. Their management is generally less complex than that of oliguric patients because fluid balance is easier to maintain.

Reversible prerenal AKI and acute tubular necrosis caused by medullary ischemia (intrinsic AKI) are two ends of a continuum. Initially, hypotension or dehydration leads to reduction in renal perfusion. Prerenal failure ensues and the kidney compensates by retention of solute and water leading to oliguria (<0.5 mL/kg/h) and a state of prerenal azotemia. This compensation increases tubular workload and decreases medullary blood supply. Prerenal azotemia is a reversible state; however, persistence of this state or an additional renal insult will eventually lead to irreversible ischemic injury and death of tubular cells characteristic of intrinsic renal failure. Urine output then decreases despite adequate intravascular volume, leading to accumulation of waste products. The traditional division of prerenal versus intrarenal azotemia is artificial, but may help guide treatment options, especially if further hydration may potentially reverse the condition.

Table 33.4 Parameters used to distinguish between prerenal and renal causes of acute kidney injury

Parameters	Prerenal	Renal
Fraction of sodium filtered	<1 %	>2 %
Ratio of serumBUN/creatinine	>20	<20
Urine sodium (meq/L)	<20	>40
Urine osmolality (mosm/L)	>500	<400

Indices used to distinguish between prerenal and renal causes of AKI are provided in Table 33.4. The fractional excretion of sodium (FE_{Na}) is a commonly used to differentiate prerenal azotemia from acute tubular necrosis.

FE_{Na} is calculated as $(Urine_{Na}/Plasma_{Na})/(Urine_{Creatinine}/Plasma_{Creatinine})$

A FE_{Na} <1 % is consistent with prerenal azotemia, while a FE_{Na} >3 % is consistent with the development of ATN. Notably, the calculation of a FE_{Na} is only useful in patients with *oliguric* renal failure, without preexisting renal failure, who have not received a diuretic. Urine sediment/microscopy is also useful in differentiating ATN from prerenal azotemia, where the presence of muddy brown casts and renal tubular epithelial cells is highly associated with development of ATN. The number of casts and epithelial casts per high power field may also be correlated with the degree of ATN. Once acute renal failure is established, there is no intervention that has proven beneficial to expedite the recovery of renal function. In most cases renal function recovers spontaneously within a few days. However, it is essential to avoid further renal injury and improve the impaired physiologic functions to prevent progression to chronic renal failure.

Prevention of Perioperative Kidney Injury

A number of strategies have been proposed to preserve renal function in the perioperative period. Most of these practices are based on tradition, anecdotal information, or extrapolation from animal studies rather than double blinded randomized controlled trials in humans. A summary of strategies to reduce or prevent the development of perioperative acute kidney injury is provided in Table 33.5.

Monitoring for Acute Kidney Injury

Current ability to monitor renal function and detect early stages of kidney injury remains poor. Serum creatinine levels and urine output remain the most reliable and practical monitors in the perioperative period. In the dynamic environment of the operating room, large fluid shifts often occur in

Table 33.5 Strategies to reduce or prevent the development of perioperative acute kidney injury

Oxygen delivery maintenance	Maintaining hematocrit, cardiac output
Prevention of vasconstriction	Maintaining adequate preload, use of ACE inhibitors
Renal vasodilation	Measure atrial natriuretic peptide, use dopamine?
Maintaining renal tubular flow	Diuretics—mannitol, furosemide

addition to autonomic effects of anesthetics and surgical stimulation that greatly alter renal physiology and subsequent urine output. Therefore, hemodynamic monitoring may be the best tool currently available to prevent renal injury intraoperatively. In future, specific biomarkers known to be released by the kidney during times of injury may be helpful in detecting early renal dysfunction.

Urine Output

Though urine output is used intraoperatively to monitor renal function, it does not reliably predict the development of postoperative AKI. Adequate urine output (>0.5 mL/kg/h) is usually associated with adequate renal function, while anuria is a sign of severe renal injury unless there is postrenal obstruction. Low urine output may have various causes. Low urine output caused by hypovolemia may be secondary to easily reversible prerenal azotemia, which can progress to intrinsic AKI if left untreated. Intra-abdominal surgery, especially laparoscopic, causes a decrease in renal blood flow and urine output that does not necessarily represent significant renal injury.

Blood Urea Nitrogen

The blood urea nitrogen (BUN) concentration is not a direct correlate of reduced GFR. BUN is influenced by a number of conditions, independent of the glomerular filtration rate, including exercise, bleeding, steroids, and massive tissue breakdown. It is important to note that BUN is not elevated in kidney disease until the GFR is reduced to almost 75 % of normal. Normal BUN/serum creatinine ratio is 10:1.

Creatinine

Measurements of creatinine provides valuable information regarding general kidney function. Serum creatinine measurements reflect glomerular function, and creatinine clearance is a specific measure of GFR. Creatinine clearance can be calculated as follows that accounts for age-related decreases in GFR, body weight, and sex:

$$\text{Creatinine clearance}\left(\text{mL}/\text{min}\right) = \frac{\left(140-\text{age}\right)\times \text{wt}\left(\text{kg}\right)}{\text{Serum creatinine}\left(\text{mg}/\text{dl}\right)\times 72}\left(\times\, 0.85 \text{ for females}\right)$$

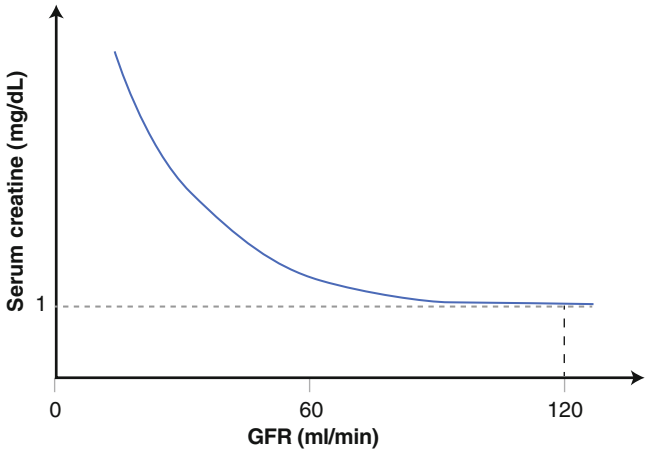

Fig. 33.4 Relationship between glomerular filtration rate (GFR) and serum creatinine

It is important to recognize that because there is such a wide range in normal creatinine values, a small change of serum creatinine level may represent large changes in GFR. Therefore, excretion of drugs dependent on renal clearance may be significantly decreased despite what might seem to be only slightly elevated serum creatinine values. Serum creatinine requires time to accumulate, and in the immediate perioperative period serum creatinine may even be decreased from preoperative levels because of dilution. Furthermore, although creatinine measurements reflect glomerular function, it does not have a direct or linear relationship with actual glomerular function and GFR, as it may not begin to rise until nearly half of the kidney's nephrons are dysfunctional (Fig. 33.4). Serum creatinine level is, therefore, a marker of renal function and not injury.

Since creatinine is partially secreted in the renal tubule, it will slightly overestimate true GFR. Furthermore, creatinine is generated by muscle, thus malnourished elderly patients may have normal serum creatinine measurements despite low actual GFRs. Given the inverse logarithmic relationship between creatinine and GFR, it is also important to understand that a rise in creatinine from 1 to 1.2 may actually represent a 50 % reduction in GFR, while a rise of creatinine from 4 to 8 may represent a relatively much smaller loss of nephrons.

Biomarkers

The lack of early biomarkers of AKI has resulted in a delay in initiating therapies. Several promising novel biomarkers of renal function and injury have been studied and have shown promising results for AKI, with potentially high sensitivity and specificity. These include a plasma panel (neutrophil gelatinase-associated lipocalin and cystatin C) and a urine panel (neutrophil gelatinase-associated lipocalin, interleukin 18, and kidney injury molecule-1). It is likely that these biomarkers of AKI will be useful for timing the initial

insult, assessing the duration of AKI (analogous to the cardiac panel for evaluating chest pain), and for predicting overall prognosis with respect to dialysis requirement and mortality. It is also likely that the AKI panels will help distinguish between the various types and pathogeneses of AKI. Studies to validate the sensitivity and specificity of these biomarker panels in clinical samples from large cohorts and from multiple clinical situations are ongoing.

Chronic Kidney Disease

Chronic kidney disease (CKD) is defined as kidney damage with a GFR <60 mL/min/1.73 m^2 present for more than 3 months, and is characterized by a progressive course of worsening renal function. Kidney damage may be diagnosed by proteinuria (caused by diabetes or hypertension), abnormalities in urine sediment, abnormalities on imaging studies (polycystic kidneys, hydronephrosis), or abnormal serum and urine laboratory values. CKD is characterized into five stages, which are dependent on the GFR.

- Stage 1: GFR > 90 (normal)
- Stage II: GFR 60–89 (mild failure)
- Stage III: GFR 30–59 (moderate failure)
- Stage IV: GFR 15–29 (severe failure)
- Stage V: GFR < 15 (end-stage failure)

Normal GFR is 120–130 mL/min/1.73 m^2, which declines with age by approximately 1 mL/min/1.73 m^2 per year after the third decade. A GFR of 60 mL/min/1.73 m^2 represents loss of approximately half of the adult level of normal kidney function. These patients with decreased renal reserve (non-dialysis-dependent chronic kidney disease) are often asymptomatic and frequently do not have elevated blood levels of creatinine or urea. However, these patients are at increased risk of developing end-stage renal disease (ESRD). ESRD is the term used to describe a clinical syndrome characterized by renal dysfunction that would prove fatal without renal replacement therapy. ESRD patients have GFRs <15 mL/min/1.73 m^2.

Chronic kidney disease results in severe alteration of homeostasis in virtually every physiologic system (Table 33.6). Loss of the intricate regulatory system of the kidney results in water, electrolyte, acid–base, metabolic, and multiple-organ system dysfunction. The ability to concentrate or dilute urine in chronic renal disease is often impaired, resulting in hypernatremia or hyponatremia, respectively. This may also result in fluid overload and derangements in calcium, magnesium, and phosphorus metabolism. Hypoalbuminemia may also be present if significant proteinuria develops.

Metabolic acidosis results as hydrogen ions accumulate from inability of the kidney to excrete titratable acids. Patients with CKD have a limited ability to buffer an endogenous acid load, such as may occur in shock states, hypovolemia, or with an increase in catabolism. Compensation for metabolic acidosis in patients with CKD results in a shift of hydrogen ions intracellularly, and a subsequent shift of potassium ions extracellularly. There is a rightward shift in the hemoglobin–oxygen dissociation curve (increase in 2, 3-DPG levels and metabolic acidosis). This shift effect, coupled with the effect of drugs that elevate potassium levels (ACE inhibitors, angiotensin receptor blockers, NSAIDS, β-blockers) can result in dangerously elevated serum potassium levels. Importantly, the hyperkalemia seen in CKD is usually chronic in nature, and therefore, better tolerated than an acute rise of potassium in AKI patients.

Severe kidney dysfunction can result in a uremic syndrome which is characterized by dysfunction of multiple organ systems (cardiovascular, pulmonary, gastrointestinal,

Table 33.6 System effects of chronic kidney disease

Neurologic system
– Encephalopathy
– Autonomic/peripheral neuropathy
Cardiovascular system
– Sodium and water retension, hypertension, and LVH
– Cardiomyopathy, CHF
– Accelerated atherosclerosis
– Pericarditis
– Complications of AV fistula/shunts (heart failure, limb ischemia, steal syndrome)
– Calciphylaxis and vascular calcification resulting in valvular heart disease and calcified atherosclerotic lesions
Pulmonary system
– Pulmonary edema
– Pleural effusion
– Restrictive pulmonary dysfunction
– Hyperventilation due to metabolic acidosis
Hematologic system
– Anemia
– Platelet dysfunction
– Prothrombotic tendency (hypercoagulable and reduced fibrinolysis)
Gastrointestinal system
– Gastrointestinal bleeding
– Delayed gastric emptying
– Anorexia, nausea/vomiting, reduced protein intake, malnutrition
Musculoskeletal system
– Renal osteodystrophy
Immune system
– Acquired defects in both cellular and humoral immunity
Endocrine system
– Peripheral insulin resistance
– Decreased insulin clearance
– Secondary and tertiary hyperparathyroidism, vitamin D deficiency
Fluid and electrolye homeostasis
– Hypernatremia/hyponatremia (more common)
– Hyperkalemia
– Hyperphosphatemia
– Hypocalcemia
– Hypermagnesemia
– Volume overload
– Dehydration

hematologic, neurologic, and endocrine) due to the systemic effects of toxins that cannot be eliminated, which is in addition to loss of normal functions of the kidney. Encephalopathy can result in severe cases of uremia, which is manifested as asterixis, lethargy, mental status changes, seizures, and coma. Patients with uremic syndrome often require frequent or continuous dialysis.

A number of cardiovascular changes can occur as a result of uremic syndrome, due to the effects of volume overload, high renin–angiotensin activity, autonomic nervous system hyperactivity, acidosis, and electrolyte disturbances. Hypertension may be seen due to increased sodium absorption and renin effects. Myocardial dysfunction and congestive heart failure can result from increased cardiac oxygen demand (hypertension, fluid overload) in the setting of reduced oxygen supply (due to anemia). Pericarditis can occur secondary to the effects of uremia or dialysis, with pericardial tamponade developing in up to 20 % of the latter group. Other cardiovascular changes include accelerated atherosclerosis and development of arrhythmias.

Pulmonary problems associated with severe CKD are limited to changes in lung water and control of ventilation. Restrictive pulmonary dysfunction is commonly seen in patients with renal failure. Pulmonary edema and pleural effusions can result from fluid overload and increased pulmonary capillary permeability, which are usually responsive to dialysis. Chronic metabolic acidosis is responsible for the hyperventilation seen in patients with ESRD, but increased lung water and poor pulmonary compliance can also stimulate hyperventilation.

Altered gastrointestinal mucosal integrity can result in gastrointestinal bleeding and delayed gastric emptying. Anemia of CKD occurs as a result of reduced levels of erythropoietin, reduced red cell survival, ongoing gastrointestinal blood loss, and iron or vitamin deficiencies. Coagulopathy can result due to uremic platelet dysfunction. Acquired defects in both cellular and humoral immunity due to renal disease, and exacerbated by dialysis, result in increased susceptibility to infection and sepsis (impaired platelet and white cell function). Abnormal glucose tolerance occurs due to peripheral resistance to insulin. Importantly, insulin clearance is markedly reduced in renal dysfunction. Secondary hyperparathyroidism can occur in response to hypocalcemia.

Patients with CKD often have a hemoglobin of 6–8 g/dL. This anemia is due to decreased erythropoietin production by the kidney and decreased red cell production and survival. Often, the anemia is well tolerated, and preoperative interventions to correct the anemia are usually not undertaken, unless absolutely necessary. Compensatory mechanisms to correct the anemia in CKD patients include increase in cardiac output, increase in tissue blood flow, and a rightward shift of the hemoglobin–oxygen dissociation curve. Additionally, these patients are administered erythropoietin to improve the anemia.

Anesthetic Considerations for Patients with Renal Disease

Priorities for anesthetic management of patients with renal dysfunction involve the prevention of acute kidney injury and optimization of multisystem organ dysfunction associated with the kidney disease. Considerations for management of patients with CKD can be divided into those related to altered pharmacodynamics and those relating to changes in organ systems as a result of systemic toxicity. As described above, renal dysfunction affects the physiology of nearly all organ systems and can result in severe metabolic and electrolyte derangements. This global dysfunction must be individually considered when caring for patients with either acute or chronic renal dysfunction.

The history and physical examination, besides routine evaluation, should include information of the last dialysis (if pertinent), evaluation of fluid status (volume overload or hypovolemic—which may occur after dialysis) and electrolyte panel (potassium—mandatory especially after dialysis, sodium, calcium, magnesium), including bicarbonate, which can help assess the level of acidosis when an arterial blood gas is not available, complete blood panel (CBC), echocardiogram if available (given concurrent cardiac disease and possible pericardial effusion). Use or avoidance of renally eliminated drugs must also be considered.

Although anesthetics do not usually harm the kidneys with their direct effects, indirect effects combined with hypovolemia, shock, nephrotoxin exposure, or other renal vasoconstrictive states can lead to renal dysfunction. If the chosen anesthetic technique causes a protracted reduction in cardiac output or sustained hypotension that coincides with a period of intense renal vasoconstriction, renal dysfunction or failure can result. Avoiding intraoperative renal insults and maintaining isovolemia, adequate cardiac output, and renal perfusion pressure are the best interventions to prevent postoperative AKI, and are more important than the choice of a specific anesthetic technique. This is true for either general or regional anesthesia. There are no comparative studies demonstrating superior renal protection or improved renal outcome with general versus regional anesthesia.

Pharmacologic Considerations

Significant renal impairment may affect the absorption, metabolism, and excretion (pharmacokinetics) of commonly used anesthetic agents (Table 33.7). An altered pharmacodynamic effect should be anticipated in patients with kidney dysfunction. Acute or chronic kidney dysfunction may affect absorption of a drug. For example, a reduced first-pass effect through the gastrointestinal tract and liver is associated with increased serum levels of oral beta-blockers

Table 33.7 Pharmacologic considerations for commonly used perioperative drugs in patients with chronic kidney disease

Drug class	Considerations
Inhalational anesthetics	Sevoflurane has a potentially nephrotoxic metabolite (compound A)
Intravenous anesthetics	
Benzodiazepines	Potentiated clinical effect in CKD. Certain metabolites are pharmacologically active and accumulate with repeated dosing
Barbiturates	Exaggerated clinical effect in CKD. Need to reduce induction dose
Propofol	Effects are not prolonged in CKD
Etomidate	CKD does not alter clinical effects
Ketamine	CKD does not alter clinical effects
Opioids	May have increased and prolonged effect in CKD. Active metabolites may prolong action with chronic administration: Morphine-6-glucuronide (morphine metabolite) has potent analgesic and sedative effects. Normeperidine (meperidine metabolite) has neurotoxic effects. Hydromorphone-3-glucuronide (hydromorphone metabolite) can cause cognitive dysfunction and myoclonus. Fentanyl has no active metabolites
Muscle relaxants and reversal agents	
Succinylcholine	Standard dose of succinylcholine raises serum K + 0.5–0.8 mEq/L, this rise is usually not seen in CKD patients. Succinylcholine is not contraindicated in CKD if the serum K + is not elevated
Nondepolarizing agents	Many nonpolarizing NMBs result in prolonged effects due to reliance on renal excretion Cisatracurium or rocuronium are preferable in CKD
Cholinesterase inhibitors	Decreased elimination in CRF and half-life is prolonged Half-life prolongation is similar or greater than the duration of blockade from long acting NMBs, so recurarization is rarely seen
Vasoactive drugs	
Catecholamines	Catecholamines with α-adrenergic effects constrict renal vasculature and may reduce renal blood flow
Sodium nitroprusside	Metabolized by the kidney and excreted as thiocyanate. Toxicity from thiocyanate accumulation is more likely in CKD
Digoxin	Excreted in urine resulting in increased risk of toxicity in CKD
Antibiotics	Penicillins, cephalosporins, aminoglycosides, vancomycin are predominately dependent on renal elimination. Loading dose is unchanged but maintenance doses are substantially reduced

and opioids in patients with kidney dysfunction. In addition, hepatic metabolism of drugs is difficult to predict in the setting of renal failure because some hepatic enzymes are inhibited, whereas others are induced. Also, accompanying liver disorders may alter the relationship of drug clearance with GFR. Additionally, many drugs effects are altered in renal disease possibly through reduced protein binding, acidotic environment, impaired biotransformation, changes in the blood brain barrier, or interaction with toxins of azotemia. Lipid soluble drugs are poorly ionized and must undergo metabolism by hepatic transformation to water soluble forms before elimination by the kidney. Ionized drugs tend to be eliminated unchanged by the kidney and their duration of action may be prolonged with kidney dysfunction. Therefore, changes in pharmacologic action of drugs result from inability of the kidney to excrete the drugs or their metabolites.

The duration of action of many drugs administered by bolus or short-term infusion is determined mainly by redistribution, rather than elimination. Consequently, the loading dose of drugs does not need to be altered significantly in kidney dysfunction (unless there is increased pharmacodynamic effect). However, with repeated dosing or long term infusion, the duration of action of drugs is dependent on elimination. Consequently, maintenance doses of drugs with significant renal excretion should be reduced. If a drug depends solely on the kidney for clearance, then a simple approach to drug dosing involves a calculated percentage reduction in dosage that matches the reduction in GFR. An estimated clearance derived from serum creatinine is usually adequate for these purposes. Unfortunately, clearance of most medications involves a more complex combination of both hepatic and renal function, and drug level measurement or algorithms for specific drugs are often recommended.

Patients with renal disease are sensitive to barbiturates and benzodiazepines secondary to decreased protein binding; however, the effects of propofol are not as affected. Etomidate effects may be increased by reduced protein binding, which increases the level of unbound, active drug. Ketamine is metabolized by the liver and partially excreted in the kidney; thus renal impairment may lead to buildup of metabolites. Some narcotic agents may have increased and prolonged effect in CKD. Active metabolites may prolong action with chronic administration: Morphine-6-glucuronide (generated from morphine) has potent analgesic and sedative effects; normeperidine (generated from meperidine) has neurotoxic effects. Therefore, fentanyl and hydromorphone are better choices.

Inhalational agents are minimally affected by CKD disease. Low flow sevoflurane is not currently recommended for long procedures due to possible renal toxicity, though this has not been shown to affect humans. Other commonly administered IV medications dependent on renal clearance are H_2 blockers (ranitidine, famotidine) and metoclopramide. Many antimicrobial agents must be dosed according to renal function. Nonsteroidal anti-inflammatory agents should be avoided in renal insufficiency or AKI as they may exacerbate renal injury.

Muscle relaxants are variably affected by renal disease. Succinylcholine can be used if the patient's serum potassium level is normal, but is best avoided if the potassium level is unknown. A standard dose of succinylcholine raises serum K^+ level by 0.5–0.8 mEq/L, which usually does not rise in patients with CKD. Steroidal neuromuscular blocking agents (NMBA), such as vecuronium and rocuronium, are mostly metabolized in the liver, but also partially dependent on renal elimination. Thus, the duration of action of these drugs may be increased in CKD. Non-steroidal NMBAs such as cisatracurium and atracurium are eliminated in a non-organ-dependent manner in the blood stream by Hoffman elimination and plasma esterases, and therefore, their duration of action is not significantly altered by renal disease. Long acting NMBAs such as pancuronium are very much dependent on renal elimination, and their duration may be significantly prolonged by renal disease. Neuromuscular reversal agents rely on renal excretion and, therefore, their effects will be prolonged. However, half-life prolongation of reversal agents in renal disease is similar or greater than the duration of blockade from long acting NMBAs; therefore, recurarization is rarely seen.

Common Urologic Procedures

Positioning for Urologic Surgery

Lithotomy Position

This is commonly used for transurethral procedures and consists of hip and knee flexion with legs placed in stirrups or leg rests. Lower extremity neuropathies are a complication of this position. Injury of common peroneal nerve can result from compression of the side of the lower extremity against the leg rest. Strain can also be placed on the obturator, lateral femoral cutaneous nerves, and sciatic nerves in this position. To avoid neuropathies, compression of the legs should be avoided by adequately padding the legs, with the hips not flexed more than 90°. Back pain from lithotomy may result from loss of lordosis in this position. Rarely, compartment syndrome can be seen in the lower extremity when blood flow is compromised from leg rests.

Trendelenberg Position

Trendelenburg (head down) position is often used in urologic procedures to assist in perineal exposure, and/or facilitate laparoscopic or robotic surgery. A number of physiologic changes occur in response to Trendelenburg positioning including increased downward force of the abdominal contents on the thorax, which reduces lung volumes resulting in atelectasis, increased intracranial pressure, and cardiovascular changes.

Lateral Flexed Position

The lateral position with flexion and kidney rest elevation is often used to facilitate access to the kidney. An axillary roll is often placed between the chest and table to prevent brachial plexus injury. A bean bag is used under the patient, which can be shaped to prevent the patient from rolling. Physiologic changes associated with this position include reduced systemic blood pressure and cardiac output, which may be a result of aorta/IVC compression.

Cystoscopy and Ureteroscopy

Cystoscopy and ureteroscopy are used to evaluate for hematuria, renal calculi, bladder pathology, and may also be performed as an access point to the ureters to place ureteral stents. Cystoscopy, as a single procedure, is commonly performed under sedation or general anesthesia with an LMA. It is important to know that electrocautery may stimulate the obturator nerve, causing a sudden jerk of the leg and subsequent potential puncture of the bladder by the cystoscope. This obturator reflex is not prevented by even spinal anesthesia, but can be reliably blocked by muscle paralysis during general anesthesia.

Transurethral Resection of Prostate

Transurethral resection of the prostate (TURP) is performed to relieve urinary obstruction in patients with benign prostatic hypertrophy, who are usually older than 60 years. Often patients have comorbid cardiovascular and pulmonary conditions, and hence they should be thoroughly evaluated before the surgery. A resectoscope is inserted through the urethra and prostatic tissue is resected with an electrically powered cutting-coagulating metal loop. In order to facilitate resection of prostatic tissue, irrigation fluid is continuously instilled. Since electrolyte solutions disperse electric current and render electrocautery ineffective, alternative hypotonic solutions are used, which include glycine and sorbitol–mannitol. Although water provides excellent visibility, its absorption can, however, lead to water intoxication and volume overload.

The resection results in disruption of venous sinuses, allowing the absorption of irrigant systemically. Factors that influence the amount of irrigation fluid absorbed include the duration of resection, irrigant hydrostatic pressure, prostatic

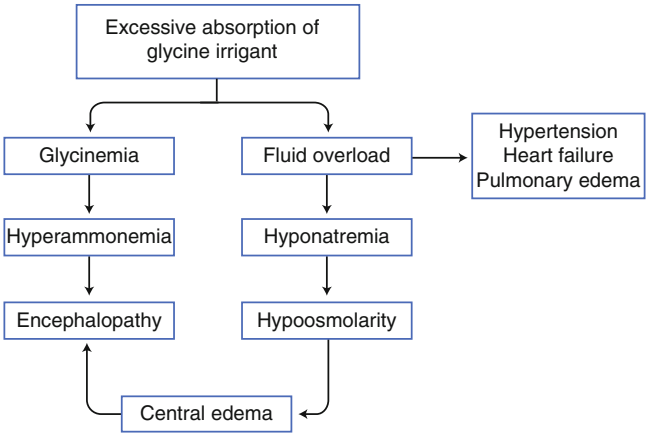

Fig. 33.5 Pathophysiology of TURP syndrome

venous pressure, and the number and size of the venous sinuses breached. Excessive absorption of irrigant can result in a collection of cardiovascular and neurologic signs and symptoms referred to as TURP syndrome.

TURP Syndrome

Development of manifestations is related to the volume of the irrigation fluid absorbed, intrinsic toxicity and temperature of the irrigation fluid, and plasma hypo-osmolarity. About 25 mL/min of irrigation fluid is absorbed on average; therefore, longer the procedure more is the irrigant volume absorbed. This can lead to congestive heart failure and pulmonary edema (Fig. 33.5). Also, large volumes of irrigation fluid absorbed can lead to hypothermia and postoperative shivering, which increases myocardial oxygen demand. Intrinsic toxicity of the irrigation solutions include: Glycine—an inhibitory neurotransmitter, can cause hyperammonemia and transient visual loss and sorbitol–mannitol—hyperglycemia and infection associated with sorbitol and acute volume expansion and osmotic diuresis associated with mannitol. Finally, excessive fluid absorption can lead to hyponatremia, which when severe can lead to seizures and mental status changes.

Treatment of TURP syndrome consists of elimination of excess water and prevention of hypoxemia and hypoperfusion. Fluid restriction and diuresis are used for treatment. Hypertonic saline may be considered only in patients with severe hyponatremia (usually serum sodium <120 meq/L). Depending on the severity of symptoms, cardiovascular and ventilatory support may be required. Therapy should be guided by regular measurements of serum sodium and osmolarity. Although advances in surgical techniques including laser ablation, bipolar electrocautery, and new irrigation fluids have minimized the incidence of TURP syndrome, it remains relevant because of the associated morbidity and mortality.

Other complications associated with TURP syndrome include:

- Bleeding: Bleeding during TURP is common as a result of disruption of venous sinuses, and dilutional thrombocytopenia. Rarely, disseminated intravascular coagulation may result from the release of thromboplastin from the prostate. Assessment of the amount of blood loss during TURP is difficult because of irrigant dilution, but roughly averages 200–300 mL (3–5 mL/min).
- Bacteremia: bacteremia may occur due to absorption of bacteria through open venous sinuses, often associated with the chronic indwelling catheters or inadequately treated prostatitis. This can lead to septicemia. Prophylactic antibiotics are commonly administered perioperatively.
- Perforation: Perforation of the bladder during TURP is more likely to occur during difficult resections as a result of direct injury from the resectoscope. Bladder perforation may also result from over-distention of the bladder with the irrigation fluid. Extraperitoneal perforation is more common and may be manifested as suprapubic fullness, abdominal spasm, or pain in the periumbilical, inguinal, or suprapubic areas. Intraperitoneal bladder perforation, a less frequent event, may cause symptoms such as upper abdominal pain or symptoms related to diaphragmatic irritation including shoulder pain, dyspnea, hiccups, nausea, restlessness, bradycardia, and hypotension.

TURP is commonly performed under spinal or general anesthesia (LMA). Regional anesthesia may reduce the incidence of postoperative venous thrombosis, and is also less likely to mask the signs and symptoms of bladder perforation or TURP syndrome. Regional anesthesia may not be performed in patients with prostatic carcinoma with metastasis to the bones (back pain). No difference in morbidity and mortality has been reported comparing general vs. regional anesthesia for TURP. Common causes of mortality after TURP are pulmonary edema, myocardial infarction, and renal failure.

Extracorporeal Shock Wave and Laser Lithotripsy

Extracorporeal shock wave lithotripsy (ESWL) uses acoustic shock waves to fragment stones located in the upper ureters or kidneys. First generation lithotripters involved immersion of the patient in a water bath. They were cumbersome and provided challenges due to need for anesthetizing a patient in a water bath as well as the hemodynamic changes that were associated with water immersion. Newer lithotripters utilize a water cushion which is placed in direct contact with the patient's skin. Stones are localized for ESWL with intraoperative fluoroscopy or ultrasound.

Anesthetic regimens used commonly for lithotripsy include general anesthesia (LMA) or monitored anesthesia

care (propofol, fentanyl, midazolam). General anesthesia offers the advantages of control of patient movement, while the ventilation can be controlled to decrease stone movement with respiration. Postoperative pain after ESWL is usually minimal. Potential complications of ESWL include cardiac arrhythmias precipitated by shock waves, renal hematoma resulting from collateral damage to the renal vasculature, and pulmonary or intestinal damage. Fever and sepsis can occur after ESWL, which are more common in patients with infected urinary tracts.

Laser lithotripsy is used for ureteral stones that are low in the ureter and not amenable to extracorporeal shock wave lithotripsy. A pulsed dye laser is directed at the stones, which releases pulsatile energy that causes stone disintegration. The beam is carried over a bare wire passed through a rigid ureteroscope. The bare laser wire is sharp and so a risk of ureteral perforation exists. Ideally, general anesthesia with paralysis should be maintained to avoid patient movement. If regional anesthesia is chosen, a spinal level of $T_{8–10}$ is required. These lasers are not well absorbed by red blood cells or other tissues, which provides safety against tissue coagulation or thermal injury. Because the laser beam is reflective, the user, other personnel, and the patient should wear protective eyeglasses. Since some hematuria usually occurs, intravenous hydration is recommended.

Radical Surgery

Radical nephrectomy, radical cystectomy, and radical prostatectomy share common features, such as they are lengthy procedures, potentially associated with sudden and significant blood loss, and carry a risk for perioperative renal dysfunction. Many patients are elderly, have a smoking history, with comorbid cardiovascular and pulmonary diseases.

Prostatectomy

Radical prostatectomy for cancer has traditionally been performed by open laparotomy, but laparoscopic and robotic-assisted techniques are being used more frequently. In the commonly used retropubic approach, a low midline incision facilitates removal of the prostate, seminal vesicles, ejaculatory ducts, and a section of bladder neck. The bladder neck is then anastamosed to the urethra. Hemorrhage is a major complication of this surgery, and should be considered when determining the need for monitoring and IV access. Patients undergoing radical prostatectomy are placed supine in the Trendelenburg position with their back extended, which elevates the pubis above the head. Air embolism from entrainment of gas through open prostatic veins positioned above the heart has been reported. These procedures are commonly done under general anesthesia, but epidural and spinal anesthesia have also been used successfully for radical prostatectomy.

Cystectomy

Radical cystectomy is performed for invasive bladder tumors. General anesthesia is the standard anesthetic management with epidural anesthesia for postoperative analgesia. Generally, a low midline incision is made to access the bladder, with subsequent removal of the bladder, peritoneum, lower ureters, prostate (and uterus, ovaries, and anterior vaginal wall in women). Partial resection of the bladder is usually not favored due to a high recurrence rate. A type of urinary diversion or bladder reconstruction is then performed, which often involves fashioning a neo-bladder by using a segment of ileum or colon anastomosed to the native urethra. If this approach is not possible due to urethral or prostatic involvement, then diversions using an ileal conduit or cutaneous urostomy may be performed. Hyperchloremic metabolic acidosis may develop with colonic and ileal conduits. Radical cystectomy is associated with large fluid shifts and carries a high risk of hemorrhage. Adequate venous access and monitoring should be employed.

Nephrectomy

Radical nephrectomy is the usual treatment for renal cell cancer as these tumors are not that responsive to chemotherapy and radiation therapy. The procedure involves excision of the kidney, associated adrenal gland, surrounding fascia with ligation of the renal artery and vein. The surgery can be performed as an open procedure or laparoscopically. Partial nephrectomy is considered for patients with small lesions, bilateral tumors, or for patients at high risk due to comorbid diseases. In these cases laparoscopic surgery may be particularly beneficial. In laparoscopic approaches the kidney can either be accessed via a transperitoneal or retroperitoneal approach.

A number of physiologic alterations can occur due to positioning and the surgical procedure intraoperatively. For surgery, the patient is usually positioned in the lateral flexed position to allow flank, subcostal, or thoracoabdominal exposure. A decrease in blood pressure may occur with patients in the lateral kidney rest position due to compression of the aorta/inferior vena cava. Respiratory changes include decreases in thoracic compliance, tidal volume, vital capacity, and functional residual capacity. Dependent atelectasis is common and may lead to hypoxemia. Pneumothorax may occur and can have significant respiratory and hemodynamic consequences intraoperatively.

In 5–10 % of patients, the tumor extends into the renal vein, inferior vena cava, and the right atrium. Tumor extension into the inferior vena cava and atrium occurs more frequently with right-sided renal cell carcinoma. Several problems can occur in these patients, ranging from circulatory failure as a result of complete occlusion of the vena cava by the tumor to acute pulmonary embolization of tumor frag-

ments during surgery. Cardiopulmonary bypass is often required to prevent tumor embolization. If the tumor involves the vena cava, a thoraco-abdominal incision is favored to allow exposure of the IVC. Intraoperative blood loss can be significant due to the size and vascularity of the tumor, and therefore, patients should have adequate IV access and invasive monitoring. Combined general-epidural anesthesia is commonly used to provide effective anesthesia and postoperative analgesia, especially with an upper abdominal or thoracoabdominal incision.

Laparoscopic Techniques and Robotic Techniques

Laparoscopic techniques are increasing being used in urologic surgery instead of traditionally open procedures such as prostatectomy, cystectomy, nephrectomy, pyeloplasty, adrenalectomy, and stone extraction. Anesthetic considerations are similar to those for laparoscopy procedures in general surgery, although unique issues also exist. General anesthesia with controlled ventilation is the anesthesia of choice for laparoscopic urology surgery as increases in arterial carbon dioxide tension can be mitigated by respiratory ventilator changes. Because the urogenital structures are mainly retroperitoneal, the large retroperitoneal space and its communications with the thorax and subcutaneous tissue are exposed to the insufflated gas. As a result subcutaneous emphysema frequently develops, which may extend up to the head and neck. In severe cases this subcutaneous emphysema may result in pharyngeal swelling, which could compromise the upper airway (important for decision to extubate). Despite adequate hydration, patients undergoing laparoscopic surgery may develop intraoperative oliguria, which can occur due to the effects of increased pressure from CO_2 insufflation exerted on the retroperitoneal space leading to compromised renal perfusion. The intraoperative oliguria is often followed by diuresis when the insufflation is discontinued.

Robotic assisted laparoscopic surgery has been promoted for its minimal invasiveness with comparable clinical outcomes to open procedures. During robotic laparoscopic surgery, the surgeon is stationed away from the operating room table, while working at a computer station. Advantages of the robotic laparoscopic surgery include improved visualization allowing greater surgical precision and dexterity. Robotic assisted radical prostatectomy has been associated with reduced blood loss and postoperative pain compared with open radical prostatectomy. Disadvantages of robotic procedures include larger diameter ports, and a significant learning curve, compared to standard laparoscopic surgery. Anesthetic concerns with robotic assisted laparoscopic surgery are related to the need for steep head-down position and pneumoperitoneum, which can result in hypercarbia, hypoxemia, increased intraocular and intracranial pressures, decreased perfusion pressure to lower extremities, and positional injuries.

Patients with Spinal Cord Pathology

Spinal cord injury is frequently associated with neurogenic bladder dysfunction predisposing patients to urinary retention, vesico-uretero reflex, urinary tract infections, and nephrolithiasis. Consequently, urologic procedures are common in this unique patient population. It should be noted that these patients are at risk for development of autonomic hyperreflexia (AH). AH is a condition that can occur in patients with spinal cord injury at the T_6 level or higher, and is manifested by acute onset of sympathetic hyperactivity in response to stimuli below the spinal cord lesion. The syndrome may appear at any time from a few months to years after the spinal cord injury. Common precipitants of AH include bladder distension, bladder infection, severe constipation, or insertion of a cystoscope. The pathophysiology involves a stimulus below the level of the cord injury, which triggers a peripheral sympathetic response. Normally this reflex is inhibited by descending signals from the parasympathetic system, but this signaling is interrupted by the spinal cord injury. The result is uninhibited sympathetic outflow below the spinal lesion leading to severe vasoconstriction and hypertension. Neuraxial anesthesia may be beneficial over general anesthesia for patients at risk for AH, since it will block the afferent pathway to this reflex.

Renal Transplant

Progression of renal disease often results in the need for renal replacement therapy (dialysis), and ultimately transplantation. With the advent of immunosuppressive drugs, the kidneys have become one of the most commonly transplanted organs. In 2008, approximately 80,000 patients were awaiting kidney transplantation in the United States, with an average waiting time of more than 3 years. Renal transplant is notably important in both cost reduction and reduced mortality of patients with end stage renal disease (ESRD). Renal transplant reduces mortality by 40–60 % compared to those who remain on dialysis. The donor kidney can either be cadaveric or from a living donor, with majority of transplants occurring from a deceased donor. If the kidney is from a living donor, both surgeries are performed at the same time in different operating rooms.

Anesthetic management entails optimizing therapy for a patient with comorbidities, coordinating dialysis, and understanding the pharmacokinetic and pharmacodynamic effects of drugs administered to patients with ESRD. Pretransplant evaluation should involve evaluation of concurrent disease, correction of electrolyte imbalances and coagulopathy, volume status, and if necessary, dialysis before surgery may be indicated. The most common cause of ESRD is diabetes followed by hypertension. Important preoperative considerations in patients undergoing renal transplant are summarized in Table 33.6, as described for patients with chronic kidney disease.

The surgical procedure is usually performed with the patient in the supine position with a lower quadrant curvilinear incision. The donor kidney is implanted retroperitoneally into the iliac fossa. After exposure of the iliac vasculature, the external iliac artery and vein are clamped and three anastomosis are created: between the external iliac artery and the renal artery, external iliac vein and the renal vein, and the donor ureter to the bladder. The clamps are then released allowing perfusion to the donor kidney.

General endotracheal anesthesia is generally performed for this procedure. Selection of monitors is determined by the patient's comorbid conditions. Important anesthetic considerations for kidney transplant include:

- Rapid sequence intubation may be desirable due to concurrent gastric dysmotility.
- Drugs dependent on renal clearance should be used cautiously as the donated kidney will not have optimal function intraoperatively.
- Fluid status is especially important during renal transplant as immediate urine output from the donor kidney is directly related to donor success. Both lactated ringers and normal saline can safely be used for maintenance fluids. Patients who have recently undergone dialysis may be volume depleted, which can compromise blood flow to the donated kidney. Dopamine, mannitol, or furosemide may be administered intraoperatively to improve urine output; however, convincing scientific evidence of their benefit is lacking.
- Avoidance of hypotension is also crucial because renal graft function is dependent on perfusion pressure. Vasopressors, especially α-agonists, may interfere with renal perfusion.
- Serum electrolyte concentrations should be monitored closely intraoperatively.
- Ninety percent of living donor transplants and 40–70 % of cadaveric transplants produce urine immediately. A decrease in urine output during surgical closure can result from impingement of the graft, vessel, or ureter, and should be investigated.

Clinical Review

1. Renin is secreted by the
   A. Proximal tubule
   B. Renal capillary system
   C. Macula densa
   D. Juxtaglomerular apparatus
2. The effects of the following muscle relaxant are minimally affected by renal failure
   A. Cisatracurium
   B. Rocuronium
   C. Succinylcholine
   D. Vecuronium
3. All of the following metabolic abnormalities may be commonly present in a patient with renal failure, EXCEPT
   A. Hypocalcemia
   B. Hypophosphatemia
   C. Hypermagnesemia
   D. Hyperuricemia
4. End-stage renal failure is associated with a GFR of less than (mL/min/1.73 m^2)
   A. 90
   B. 60
   C. 30
   D. 15
5. Glycine solutions used for irrigation during TURP can cause
   A. Hyperglycemia
   B. Excitatory CNS effects
   C. Hyperammonemia
   D. Infections
6. Compensatory mechanism/s for anemia in patients with chronic kidney disease include
   A. Increase in cardiac output
   B. Increase in tissue blood flow
   C. Rightward shift of hemoglobin-oxygen dissociation curve
   D. All of the above

Answers: 1. D, 2. A, 3. B, 4. D, 5. C, 6. D

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Endocrine Diseases

34

Paul K. Sikka

Endocrine diseases frequently present major clinical anesthetic problems. Extensive knowledge of the pathophysiology of the endocrine condition is required to manage and formulate an anesthetic plan. This chapter describes the pathophysiology and anesthetic considerations of various endocrine diseases that anesthesiologists may encounter during their practice, with the aim to provide optimal anesthetic care.

Diabetes Mellitus

Diabetes mellitus (DM) is the most common endocrine disease. It is prevalent among 25 million people in the USA. DM occurs due to a lack/inaction of insulin, which is secreted in response to blood glucose levels, by the β-cells of the islet of Langerhans of the pancreas. Insulin is an anabolic hormone that increases glycogenesis, protein, and triglyceride synthesis. One of the most important functions of insulin is to increase the uptake of glucose into the cells. Therefore, lack of insulin leads to hyperglycemia. DM may be classified as listed in Table 34.1.

Clinical Effects of Hyperglycemia

Chronic uncontrolled blood glucose levels can lead to effects in virtually every organ system leading to increased morbidity and mortality in diabetic patients (Fig. 34.1). Preoperative evaluation of a diabetic patient should focus on the following factors.

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- Hyperglycemia leading to ketoacidosis/nonketotic hyperosmolar coma
- Interference with wound healing (decreased granulation tissue formation, fibroblast proliferation and collagen synthesis, and capillary proliferation)
- Increased incidence of wound infection (decrease in phagocytosis and chemotaxis of the polymorphonuclear cells)
- Thrombus formation (platelet aggregation due to increase in the production of thromboxane and inhibition of plasminogen activator)
- Cardiac effects (silent myocardial infarction, hypertension, coronary artery disease, congestive cardiac failure, diastolic dysfunction)
- Neurological effects including stroke and peripheral neuropathy (glucose presence increases anaerobic metabolism leading to increased lactic acid levels, and intracellular acidosis aims to keep glucose levels normal during surgery for head injury/stroke patients)
- Prone to lung infections (pneumonia)
- Retinopathy, cataract formation
- Peripheral vascular disease
- Renal insufficiency
- Autonomic imbalance

A thorough history and physical examination (including functional status), laboratory testing, chest radiograph (cardiomegaly), and an electrocardiogram (silent myocardial infarction) are essential in evaluation of diabetic patients. Noninvasive and invasive cardiac testing may be necessary in high-risk patients. Blood sugar control in the previous 3–4 weeks can be assessed by measuring hemoglobin A_{1C} level (normal 4–6 %). Medications taken by patients should be inquired. In addition, patients may be taking either insulin or oral hypoglycemic agents. Patients with DM may have restricted movements at the temporomandibular (TMJ) and atlanto-occipital joints, thereby potentially making laryngoscopy difficult. The presence of obesity may further aid to problems in airway management.

Patients should be instructed to continue their antihyperglycemic regimen until the evening prior to their surgery, and

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Table 34.1 Types of diabetes mellitus

	Type I/juvenile/insulin dependent	Type II/maturity onset/ non-insulin dependent	Gestational	Stress related
Age	Children, young adults	Adults	Pregnant women	Usually adults
Etiology	Immune mediated/idiopathic	Resistance/deficiency to insulin	Hormones/lack of insulin	Stress of surgery/hospitalization causing insulin lack/resistance, hormone[a] related
Insulin therapy	Required	May be required/oral hypoglycemics	May be required	May be required
Ketoacidosis	Yes	Hyperosmolar nonketotic coma	No	No
Body weight	Normal to thin	Overweight to obese	Overweight to Obese	Normal to obese

[a]Hormones include corticosteroids, growth hormone, glucagon, and catecholamines (epinephrine and norepinephrine)

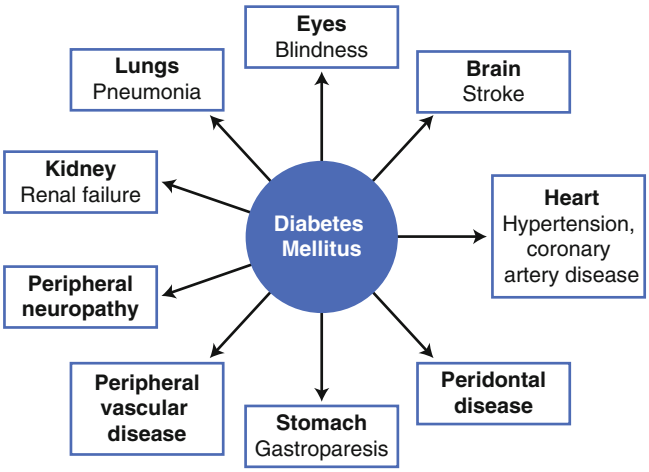

Fig. 34.1 Complications of diabetes mellitus

Table 34.2 Insulin time chart

Insulin	Preparation	Onset of action	Peak effect	Duration
Rapid acting	Lispro (Humalog)	<15 min	1 h	3–5 h
	Aspart (Novolog)			
	Glulisine (Apidra)			
Short acting	Regular (Humulin L, Novolin R)	30–60 min	2–3 h	3–6 h
Intermediate acting	NPH (Humulin N, Novolin N)	1–2 h	4–9 h	14–20 h
Long acting	Glargine (Lantus)	1 h	6–16 h	24 h
	Detemir (Levemir)			
Inhaled powder	Human insulin (Exubera)	<30 min	1–2 h	6–8 h

perhaps skip the AM dose or receive half their morning insulin dose on the day of surgery (see chapter on preoperative evaluation), to prevent hypoglycemia (insulin time chart, Table 34.2). Patients on insulin pump (baseline insulin infusion of short-acting insulin) may be continued on their basal regimen. It is important to remember that patients on metformin may be more prone to developing lactic acidosis. Therefore, metformin may be stopped 24 h before surgery and restarted postoperatively. Blood glucose level (finger stick) should be checked prior to taking a diabetic patient to the operating room. Also, surgery in DM patients should be scheduled as early in the morning, as possible.

Autonomic Imbalance

Autonomic neuropathy occurs in 20–40 % of patients with diabetes mellitus. Patients lack compensatory mechanisms to deal with hemodynamic fluctuations and hypoxia and are prone to sudden cardiac death, arrhythmias, and myocardial infarction. Signs and symptoms of autonomic imbalance include lack of pulse rate variability with respiration, resting tachycardia, orthostatic hypotension, lack of sweating, gastroparesis, impotence, and bladder dysfunction. Orthostatic hypotension may be demonstrated by a positive tilt test (decrease in blood pressure approximately 30 mmHg when moving from a supine to an upright position). Bradycardia may be unresponsive to atropine or ephedrine and may require administration of epinephrine.

Ketoacidosis

High blood glucose levels can lead to a life-threatening condition called diabetic ketoacidosis. This usually occurs in type I diabetics, but can also occur in type II diabetics. Due to the lack of insulin, there is profound hyperglycemia with blood glucose levels up to 500 mg/dl. There is an increase in anaerobic metabolism leading to an accumulation of ketone bodies (acetoacetate, β-hydroxybutyrate). Infection is the commonest precipitating factor in causing diabetic ketoacidosis.

Signs and Symptoms of Diabetic Ketoacidosis

- Anion-gap metabolic acidosis
- Nausea and vomiting, thirst (hypovolemia)
- Abdominal pain, constant urination (diuretic effect of glucose)
- Dyspnea
- Agitation, confusion, and ultimately coma

Treatment of Diabetic Ketoacidosis

- Intravenous regular insulin, 0.2 units/kg bolus, followed by an infusion of 5–10 units/h or 0.1 units/kg/h.
- The blood glucose levels are gradually reduced at a rate of not more than 100 mg/dl/h.
- Blood glucose levels are measured every 30 min–1 h (may require an arterial line for repeated blood samples).
- Urine output and vital signs are monitored.
- When the blood glucose reaches 250 mg/dl, a D_5W infusion is started to prevent hypoglycemia from occurring.
- Hydration (aggressive)—normal saline 500–1,000 ml/h initially.
- Electrolyte replacement, especially potassium as insulin carries glucose and potassium into the cell.

Nonketotic Hyperosmolar Hyperglycemic Coma

This syndrome usually occurs in elderly patients with type II DM. This clinical condition is characterized by:

- High blood glucose levels >600 mg/dl.
- Hyperglycemic diuresis and dehydration-plasma hyperosmolality >330 mOsm/L.
- Reduced brain water may cause seizures, confusion, and coma.
- Acute renal failure and lactic acidosis.
- There is enough insulin to prevent formation of ketone bodies.
- Treatment includes fluid administration, potassium supplementation, and insulin.

Hypoglycemia

Hypoglycemia is the most feared complication in patients with DM. DM patients may not tolerate blood glucose levels lower than 50 mg/dl, as they have chronically elevated blood glucose levels. Hypoglycemia leads to catecholamine secretion causing sweating, tachycardia, and hypertension. Central nervous symptoms may include dizziness, seizures, and coma. Hypoglycemia may be difficult to recognize in anesthetized patients, those taking beta blockers, or in patients with severe autonomic neuropathy. Renal failure prolongs the duration of action of insulin and hypoglycemic agents, making these patients prone to developing hypoglycemia. Treatment includes a high degree of suspicion and prompt administration of 50 ml of 50 % dextrose intravenously.

Intraoperative Blood Glucose Management

Although the lowest blood glucose level prior to surgery in DM patients is under debate, the general consensus is to proceed with surgery with a blood glucose level between 100 and 200 mg/dl. Patients with a blood glucose level greater than 180 mg/dl may be given regular (short-acting) insulin, keeping in mind that 1 unit of regular insulin (subcutaneously/intravenously) will decrease the blood glucose level by about 25–30 mg/dl.

Blood glucose levels should be measured intraoperatively every 45 min–1 h. Mild to moderately elevated blood glucose levels may be managed by small doses of regular insulin. Higher blood glucose levels (>400 mg/dl) are managed by running an insulin infusion, adequate hydration and potassium supplementation. This is because insulin increases the uptake of glucose and potassium into the cells, thereby, leading to hypoglycemia and hypokalemia in the plasma.

Postoperative Care

A blood glucose level should be measured in the recovery room before discharging the patient. Pain, nausea, and vomiting should be treated appropriately. It is important to remember that nausea and vomiting in a patient with DM may be a sign of severe hyperglycemia. Similarly, hypoglycemia should also be watched for and treated aggressively. Patients should be started on an insulin sliding scale or their oral antihyperglycemic regimen once oral intake is begun. Comorbid conditions, such as hypertension, coronary artery disease, and renal failure, should be taken into account in treating DM patients.

Thyroid Disorders

Hyperthyroidism

Overactivity of the thyroid gland causes increased secretion of thyroid hormones resulting in hyperthyroidism. Hyperthyroidism causes increased metabolism in almost every organ of the body (Table 34.3). Thyroid hormone secretion is controlled by the anterior pituitary and the hypothalamus. Figure 34.2 depicts the negative feedback mechanism regulating thyroid hormone secretion.

Table 34.3 Clinical manifestations of hyperthyroidism

Neurological	Anxiety, nervousness, fine tremor, fatigue, hyperactivity, irritability, sweating, heat intolerance
Ophthalmic	Exophthalmos in Grave's disease, eyelid lag, eyelid retraction
Cardiac	Palpitations, arrhythmias (tachycardia, atrial fibrillation)
Miscellaneous	Weight loss with increased appetite, hair loss, loss of libido, diarrhea, osteoporosis, polyuria, polydipsia

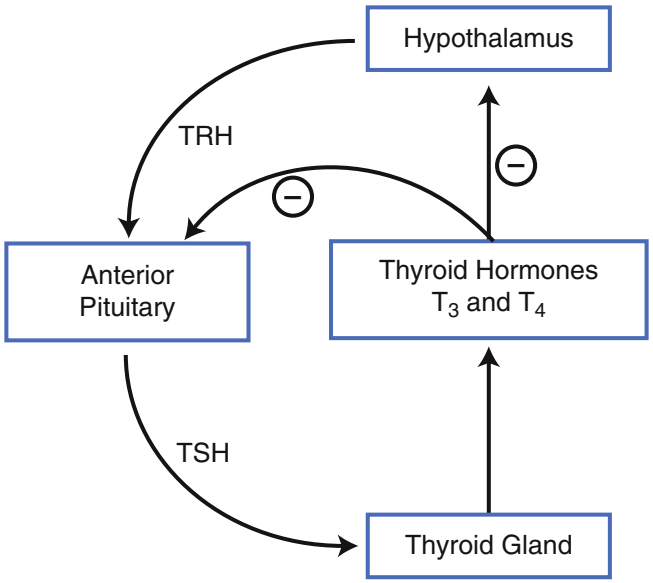

Fig. 34.2 Regulation of thyroid hormone secretion via a negative feedback mechanism. *TRH* thyroid-releasing hormone, *TSH* thyroid-stimulating hormone

Causes

The most common cause of hyperthyroidism is Graves's disease. This is an autoimmune disease with hyperfunctioning of the entire thyroid gland. It is caused by circulating thyroid-stimulating IgG antibodies which stimulate the production of the thyroid hormones. Other causes of hyperthyroidism include presence of hyperactive nodules (hot thyroid nodules), inflammation (thyroiditis), amiodarone (a drug with similar structure to thyroxine), and thyroid carcinoma.

Diagnosis

- Measuring levels of thyroid-stimulating hormone (TSH), total and free thyroxine (T_4), and total and free triiodothyronine (T_3)
- Measuring thyroid-stimulating antibodies (Graves's disease) and antithyroid peroxidase (Hashimoto's thyroiditis)
- Radioactive iodine uptake by the thyroid gland and thyroid scan

A low TSH and high thyroid hormone levels confirm then diagnosis of hyperthyroidism. Primary pituitary failure may also produce a low TSH level (rare)—euthyroid sick syndrome.

Treatment

- Temporary—antithyroid hormone synthesis medications—methimazole and propylthiouracil, and beta blockers like propranolol, which control both beta adrenergic symptoms and also block the peripheral conversion of T_4 to T_3
- Permanent—radioactive iodine I-131 thyroid ablation or subtotal/total thyroidectomy (large goiter, compression of the neck structures, thyroid cancer)

Table 34.4 Complications of thyroidectomy

Unilateral RLN damage, one cord midline	Hoarseness
Bilateral RLN damage, midline vocal cords	Total airway obstruction, aphonia—secure airway emergently
Superior laryngeal nerve damage	Hoarseness, pulmonary aspiration risk
Hematoma	Airway compromise
Inadvertent parathyroidectomy	Hypocalcemia, laryngospasm
Thyroid storm	Life-threatening emergency

RLN recurrent laryngeal nerve

Anesthetic Considerations

Patients should be euthyroid before surgery. Non-emergent surgery should be avoided unless the patient is euthyroid. Preoperative thyroid medications, including beta blockers (heart rate less than 85/min), should be continued in the perioperative period. For emergency surgery, the heart rate can be controlled with esmolol (infusion of 100–300 mcg/kg/min). Preoperative evaluation should include a thorough airway evaluation, as patients with goiter may have airway difficulties and tracheal deviation. It may be prudent to avoid addition of epinephrine to local anesthetic solutions for regional anesthesia.

- Premedication: midazolam, narcotics (avoid anticholinergics).
- Induction: A large goiter may warrant awake intubation with a reinforced endotracheal tube. Thiopental/propofol can be used for induction (avoid ketamine). General endotracheal anesthesia is usually administered for surgery. Alternatively, an LMA can be used which allows visualization of vocal cords via a fiberoptic scope in a spontaneously breathing patient. Hyperthyroid patients are frequently hypovolemic, which may cause hypotension during induction.
- Maintenance: Intraoperatively, the heart rate, cardiac function, body temperature, and fluid status should be closely monitored. Esmolol can be used to treat tachycardia, while sympathomimetic drugs (desflurane, ketamine, pancuronium) should be avoided. Patients with hyperthyroidism may have associated myopathy or myasthenia gravis warranting for close muscle relaxation monitoring. Patients with exophthalmos should have their eyes carefully taped to avoid injury. It is important to note that MAC is unchanged in hyperthyroid patients.

Complications of Thyroidectomy

Complications of thyroidectomy are listed in Table 34.4. To minimize RLN injury, one can use specialized endotracheal tubes with external wires to detect EMG activity from electrical stimulation of the RLN. In addition, visualization of

Table 34.5 Treatment of thyroid storm

Hydration
Supplemental oxygen
Antipyretics, cooling blankets
Hydrocortisone—decreases peripheral conversion of T_4 to T_3
Propylthiouracil—blocks thyroid hormone synthesis
Potassium iodide—blocks release of thyroid hormones
Propranolol—blocks effects of released thyroid hormones
Treatment of underlying cause—infection, diabetic ketoacidosis

Table 34.6 Clinical manifestations of hypothyroidism

Metabolism	Slow, increased sensitive to drugs
Neurologic	Fatigue, intolerance to cold, hypotonia, delayed tendon reflexes, depression, slow speech, hoarseness of voice, hair loss
Cardiac	Bradycardia, decreased cardiac output and cardiac contractility, decreased intravascular volume, peripheral edema
Respiratory	Goiter, dyspnea, sleep apnea, decreased ventilatory drive
Miscellaneous	Weight gain and anorexia, constipation, decreased libido, menstrual irregularities

vocal cords by a fiberoptic bronchoscope through an LMA can be used by the anesthetist to confirm vocal cord response to electrical stimulation of the RLN by the surgeon.

Thyroid storm is a rare but life-threatening exacerbation of hyperthyroidism. It is a hypermetabolic state, which occurs due to sudden and massive release of thyroid hormones into the circulation. It may occur intraoperatively, but usually occurs 6–24 h postoperatively. Precipitating factors include acute illness or infection, trauma, surgery, or radioiodine therapy. Signs and symptoms (may mimic malignant hyperthermia) include anxiety, sweating, tachycardia, hyperthermia, arrhythmias, myocardial ischemia, and congestive cardiac failure. Treatment of thyroid storm is summarized in Table 34.5.

Hypothyroidism

Decreased functioning of the thyroid gland with decreased thyroid hormone secretion leads to hypothyroidism. Diagnosis of hypothyroidism is made by measuring levels of TSH, T4, and T3. An elevated TSH level with a low or normal thyroid hormone level confirms the diagnosis. Clinical symptoms and signs of hypothyroidism are usually slow to develop (Table 34.6).

Causes

Hypothyroidism can result from chronic (Hashimoto's) thyroiditis (common cause in the USA), due to treatment of hyperthyroidism (drugs, radioiodine, or surgery), deficiency of dietary iodine (common cause worldwide), administration of lithium, postpartum thyroiditis, pituitary disorders (decreased release of TSH), and hypothalamic disorders (decreased release of thyrotropin-releasing hormone).

Treatment

The aim of treatment is normal TSH and thyroid hormone levels. Hypothyroidism is treated with oral replacement of levothyroxine (L-T_4), synthetic combination of L-T_4 and L-T_3, or a desiccated thyroid extract (porcine/natural L-T_4 and L-T_3). Half-life of T_4 is about 7 days, while that of T_3 (faster acting than T_4) is about 1.5 days. For emergency treatment, thyroxine can be given intravenously (100–500 mcg). Intravenous thyroxine should be cautiously used in patients with coronary artery disease, as it can cause myocardial ischemia.

Myxedema coma is an extreme form of hypothyroidism and a medical emergency. It presents with the features of hypothyroidism, as well as a depressed level of consciousness (coma), profound hypothermia, hypoventilation, hypotension, hyponatremia (SIADH), and occasionally seizure activity and CHF. The disease is most common in the elderly and is usually precipitated by infection (sepsis, pneumonia), trauma, or surgery. It is treated with intravenous levothyroxine, ECG monitoring for ischemia, ventilatory support, external rewarming, electrolyte and fluid management, and steroid (hydrocortisone) administration (possibility of coexisting impaired adrenal function).

Anesthetic Considerations

Patients with mild to moderate hypothyroidism can undergo elective surgery. However, elective surgery in patients with severe hypothyroidism should be done only when they have achieved a euthyroid state. Regional anesthesia may be a reasonable choice for anesthesia as long as intravascular volume is maintained. Patients requiring emergency surgery should be treated with intravenous levothyroxine, though with cardiac monitoring.

- Premedication: Sensitive to midazolam, narcotics. Patients have delayed gastric emptying and may benefit from metoclopramide and H_2 antagonists.
- Induction: Thiopental, propofol, or ketamine (latter especially for severe hypothyroidism). Since hypothyroid patients have decreased cardiac output and intravascular volume, profound hypotension can occur on induction. For refractory hypotension, steroids should be administered as coexisting adrenal insufficiency is common.
- Maintenance: Fluid and electrolyte balance and body temperature regulation. Presence of skeletal muscle weakness can make these patients sensitive to muscle relaxants. MAC remains unchanged.
- Since recovery from general anesthesia may be slow. Extubation should be done when the patient is normothermic, awake, and breathing adequately.

Table 34.7 Clinical manifestations of hypercalcemia

Neurologic	Fatigue, depression, confusion, decreased pain sensation
Skeletal	Bone pains, muscle weakness, osteopenia, vertebral body fractures
Cardiac	Hypertension, arrhythmias, shortened QT interval
Renal	Nephrolithiasis, renal tubular acidosis, polyuria, polydipsia
Gastrointestinal	Nausea and vomiting, anorexia, constipation, peptic ulcer, pancreatitis

Parathyroid Disorders

Hyperparathyroidism

The parathyroid gland secretes the parathyroid hormone (PTH) which regulates plasma calcium and phosphate levels. Hyperparathyroidism (an increased secretion of PTH) can be primary, secondary, or tertiary:

- Primary hyperparathyroidism, the most common cause of hypercalcemia, occurs from overactivity of the parathyroid glands. The most common cause is an adenoma and rarely a carcinoma. Primary hyperthyroidism can be a part of multiple endocrine neoplasia (MEN).
- Secondary hyperparathyroidism occurs when chronic hypocalcemia stimulates PTH secretion, for example, in chronic renal failure. It is commonly accompanied by deficient vitamin D synthesis and hyperphosphatemia.
- Tertiary hyperparathyroidism occurs when autonomous oversecretion of PTH persists despite correction of the underlying disease, for example, after renal transplantation. There is loss of response to serum calcium levels.

Symptoms and Signs

Most patients are asymptomatic with hypercalcemia found incidentally. Persistent hypercalcemia leads to clinical manifestations as summarized in Table 34.7. Since calcium is involved in neurotransmission, many early symptoms are neurologic in origin.

Diagnosis

Levels of parathyroid hormone are measured by parathyroid immune assay. In addition, serum calcium, phosphorous, and vitamin D levels are measured. Diagnosis of the type of hyperparathyroidism is summarized in Table 34.8.

Treatment

Hypercalcemia can be life threatening. The mainstay of treatment of hypercalcemia is hydration (normal saline-250–500 ml/h), furosemide, avoiding thiazide diuretics, and administration of bisphosphonates (pamidronate, zoledronate).

- Primary hyperparathyroidism—surgery is the definitive treatment and has a high cure rate.

Table 34.8 Diagnosis of hyperparathyroidism

Hyperparathyroidism	PTH level	Serum calcium	Serum phosphorous
Primary	High	High	Low
Secondary	High	Low or normal	High

PTH parathyroid hormone

- Secondary hyperparathyroidism—treatment is medical consisting of calcium and vitamin D supplementation and phosphate restriction. When conservative treatment is inadequate and the symptoms are severe, parathyroidectomy is performed as subtotal (portion of one gland is left in situ) or total (parathyroidectomy with autograft placement in the forearm).
- Tertiary hyperparathyroidism—the parathyroid glands usually return to normal size and function within 12 months, and surgery is rarely necessary.

Anesthesia Considerations

- Bilateral neck exploration—identification and resection of enlarged parathyroid glands. The adequacy of resection can be assessed by measuring declining intraoperative PTH levels. General anesthesia with endotracheal intubation is most commonly employed, though an LMA could be considered. It is important to maintain adequate hydration, urine output, and vigilant ECG monitoring. The response to nondepolarizing muscle relaxants may be variable. Patients with skeletal muscle weakness may have decreased muscle relaxant requirements, while hypercalcemia itself may antagonize the drug's effect. Special care in positioning may be needed for patients with severe osteoporosis. The vocal cords may be evaluated during extubation to rule out recurrent laryngeal nerve injury.
- Minimally invasive parathyroidectomy—since most patients with primary hyperparathyroidism have a solitary adenoma, unilateral neck exploration or "minimally invasive parathyroidectomy" (MIP) may be performed. Patients first undergo preoperative localization of the adenoma with Tc-99 m sestamibi scintigraphy. In addition, ultrasound is used to delineate parathyroid anatomy. Patients have a lower incidence of postoperative hypocalcemia and shorter operative stay. Anesthesia for MIP may be general or regional. Regional anesthesia is done using a superficial or deep cervical plexus block.

Complications of Parathyroidectomy

- Transient hypocalcemia—paresthesias of the lips and fingertips. Treatment is with oral calcium supplementation begun the night of surgery.
- Severe hypocalcemia—treatment for symptomatic patients (serum calcium < 0.8 mM) consists of an initial bolus of calcium gluconate/chloride followed by a continuous intravenous infusion, oral or intravenous calcitriol (vitamin D), and magnesium supplementation. It is important to remem-

Table 34.9 Symptoms and signs of hypocalcemia

Mild	Tingling of lips/fingers/toes, muscle cramps, dry hair, brittle nails, weak tooth enamel
Severe	Muscle spasms (tetany), seizures, laryngospasm (airway maintenance), bronchospasm, arrhythmias, QT prolongation, hypotension

ber that 1 g of calcium gluconate supplies 9.3 mg, and 1 g of calcium chloride supplies 27.2 mg of elemental calcium. Magnesium levels must also be monitored as hypomagnesemia aggravates hypocalcemia.

- Postoperative inspiratory stridor—can occur due to laryngeal edema (racemic epinephrine, corticosteroids), hematoma, hypocalcemia, and recurrent laryngeal nerve palsy.
- Operative failure and persistent hyperparathyroidism may complicate 0–5 % of initial explorations.

Hypoparathyroidism

Hypoparathyroidism results from decreased functioning of the parathyroid gland. This results in hypocalcemia (Table 34.9) due to decreased secretion of PTH. Causes of hypoparathyroidism include removal or trauma during thyroid surgery, autoimmune destruction, hemochromatosis, and DiGeorge syndrome. Diagnosis is established by measuring serum calcium, albumin, phosphorous, and PTH levels. Treatment is as described above.

Uncommon Endocrine Disorders

SIADH

Syndrome of inappropriate antidiuretic hormone (ADH) hypersecretion is associated with excessive release of ADH (vasopressin) from the posterior pituitary gland. ADH is produced in the hypothalamus and released from the pituitary gland. ADH acts in the distal tubule and collecting ducts in the kidneys to cause retention of water. Decreased secretion of ADH will allow the kidneys to increase the urine output, whereas increased secretion will conserve water, dilute the solute, and decrease the urine output.

Therefore, the major stimulus for ADH secretion is an increase in serum osmolality or a decrease in extracellular volume. Other factors such as pain, nausea, positive pressure ventilation, and hyperthermia can also affect ADH release. ADH can also constrict arterioles in splanchnic, coronary, and renal blood vessels. Causes of SIADH are listed in Table 34.10.

Clinical Manifestations of SIADH

- Dilutional hyponatremia and associated signs (normal serum sodium = 135–145 meQ/L)

Table 34.10 Causes of SIADH

Small-cell lung cancer
Infections—meningitis, pneumonia, brain abscess
Central nervous system—head trauma, multiple sclerosis, brain tumors
Drugs—phenothiazines, chlorpropamide, clofibrate, carbamazepine
Hypothyroidism
Postoperative pain

  - Serum sodium 125–135 meQ/L—nausea, vomiting, headache, confusion, irritability, and muscle weakness
  - Serum sodium < 125 meQ/L—manifestations mentioned above plus seizures and coma
- Oliguria

Diagnosis

- Hyponatremia (serum sodium < 135 mEq/L)
- Serum osmolality < 270 mOsm/kg
- Concentrated urine (U_{Osm} > 300 mOsm/L)
- Urine sodium > 20 mEq/L, FeNa > 1 %
- Decreased (dilutional) serum uric acid, low BUN, and albumin

Treatment

- Treatment of underlying cause
- Fluid/water restriction to about 1,500 ml/day
- Intravenous saline or hypertonic saline (3 %) for patients with severe hyponatremia. The rate of sodium correction should not exceed 12 mEq/L in the first 24 h or 0.5 mEq/L/h so as to minimize the risk of central pontine myelinolysis. Sodium deficit can be calculated as per the following formula:

$$\text{Sodium deficit} = \text{desired sodium-measured sodium} \times 0.6 \times \text{weight in kg}$$

- Furosemide administration for dieresis.
- Lithium and demeclocycline may be used for the treatment of chronic hyponatremia as they interfere with the ability of renal tubules to concentrate urine.

It is important to remember that in SIADH from subarachnoid hemorrhage, fluid restriction may worsen the condition as it can cause cerebral vasospasm and infarction secondary to hypotension.

Diabetes Insipidus

Decreased secretion/effectiveness of ADH results in diabetes insipidus (DI). It is characterized by excretion of large amounts of diluted urine (polyuria) and excessive thirst (polydipsia). DI can be central, nephrogenic, or gestational. Causes of DI and clinical manifestations are listed in Tables 34.11 and 34.12, respectively.

- Central DI—results from decreased production or release of ADH.

Table 34.11 Causes of diabetes insipidus

A. Central
Idiopathic—no known cause
Surgery—transsphenoidal resection of pituitary adenoma
Head trauma
Brain tumors
Sarcoidosis
B. Nephrogenic
Hypercalcemia
Lithium toxicity
Amyloidosis
Hereditary—X-linked genetic defect

Table 34.12 Clinical manifestations of diabetes insipidus

Polyuria
Polydipsia
Signs of dehydration—dry, scaly skin, muscle cramps, fatigue, dizziness
Anorexia
Delayed growth

- Nephrogenic DI—results from insensitivity of the kidneys to ADH caused by the inability of ADH to act normally on the kidneys. Clinically DI is characterized by polydipsia and polyuria which may be accompanied by hypovolemia and hypernatremia (dehydration) if access to free water is restricted. Laboratory studies include serum sodium and osmolarity along with urine sodium and osmolarity.
- Gestational—occurs during pregnancy. The placenta produces vasopressinase in excess, an enzyme which breaks down ADH causing loss of water conservation.

Diagnosis

The diagnosis of DI can be established by the following tests:

- Serum electrolytes—hypernatremia (due to dehydration), blood glucose level (to differentiate from diabetes mellitus), and bicarbonate and calcium levels.
- Urine analysis—dilute urine with low specific gravity and low osmolarity.
- Fluid deprivation test—patients with DI continue to urinate large amounts of dilute urine in spite of withholding fluids.
- Desmopressin test—to differentiate between central and nephrogenic DI. On administering desmopressin (injection, nasal spray, oral tablet), if it causes a reduction in urine output, then the kidneys are responding normally to ADH (central DI). However, If there is no effect on urine output or osmolarity, then the defect lies in the kidneys.
- MRI—to diagnose brain tumors.

Treatment

Anesthetic considerations involve correcting fluid deficits and existing electrolyte abnormalities, especially hypernatremia. Elective surgery should be delayed until sodium levels are below 150 mEq/L.

- Central DI—treatment of the cause and administration of desmopressin, either intravenously, orally, or by nasal spray. Some studies have suggested the use of carbamazepine for the treatment of central DI.
- Nephrogenic DI—desmopressin is ineffective. Hydrochlorothiazide, a thiazide diuretic, can be used to treat nephrogenic DI. It acts in the distal tubule to cause diuresis and loss of sodium. This leads to a decrease in the plasma volume, leading to increased absorption of water in the proximal tubules. Consequently, less water now reaches the distal tubule causing conservation of water.
- Gestational DI—responds to treatment by desmopressin. Resolution occurs 4–6 weeks after delivery.

Cushing's Syndrome

Cushing's syndrome is caused by excess of cortisol in the body. The most common cause of Cushing's syndrome is exogenous administration of glucocorticoids (for treatment of asthma, rheumatoid arthritis, or immunosuppression). Cushing's syndrome can also be caused by adrenocorticotropic hormone (ACTH)-producing tumors. Cushing's *disease* is specifically caused by an ACTH-producing benign pituitary adenoma. Excess cortisol can also be produced by adrenal gland tumors.

Signs and symptoms of Cushing's syndrome include central obesity (sparing of the limbs), moon facies, buffalo hump (fat pads along the collar bone and back of the neck), muscle wasting and weakness, osteoporosis, telangiectasia (dilation of capillaries), hyperpigmentation, sweating, hirsutism (facial male pattern hair growth), reduced libido, menstrual irregularities, hypercalcemia, insulin resistance and glucose intolerance, persistent hypertension, depression or psychosis, and mental status changes.

Diagnosis of Cushing's syndrome can be established by a dexamethasone suppression test (administration of dexamethasone does not lead to decreased cortisol levels), a 24 h urinary cortisol level, a 24 h salivary cortisol level, physical examination, and MRI of the brain and adrenal glands. Treatment includes tapering off exogenous steroid therapy and surgery for any tumors. Anesthetic considerations include correcting electrolyte abnormalities (hypokalemia), administration of spironolactone (a potassium-sparring diuretic) to decrease volume overload and prevent hypokalemia, difficult mask ventilation and recognizing airway abnormalities, difficult IV access, and easy bruising (careful positioning).

Addison's Disease

Addison's disease, or chronic adrenal insufficiency, is caused by insufficient production of glucocorticoids by the adrenal

glands. Often it is also associated with insufficient mineralocorticoid production. Adrenal insufficiency may result from a defect anywhere in the hypothalamic-pituitary-adrenal axis. The most common cause of Addison's disease is autoimmune destruction of the adrenal gland. Other causes of adrenal destruction include tuberculosis, amyloidosis, hemorrhage, metastasis of cancer cells, and congenital under development of adrenal glands.

Patients with Addison's disease may remain asymptomatic until 90 % of the adrenal gland has been destroyed. Clinical manifestations of Addison's disease include chronic fatigue, muscle weakness, mood changes, weight loss, nausea, vomiting, diarrhea, hyperpigmentation, and a craving of salty foods (sodium). Patients often have orthostatic hypotension and associated medical conditions such as type I diabetes mellitus, goiter, and vitiligo (all part of autoimmune polyendocrine syndrome). Associated mineralocorticoid deficiency can cause hyperkalemia, hyponatremia, hypovolemia, and metabolic acidosis. Acute Addisonian crisis or adrenal crisis is a medical emergency, which presents as refractory hypotension, shock, dehydration, abdominal pain, severe vomiting, syncope, hypoglycemia, and seizures.

Treatment of Addison's disease involves lifelong replacement of cortisol (glucocorticoids-steroids such as prednisone, hydrocortisone) and aldosterone (mineralocorticoids-fludrocortisone). Treatment of adrenal crisis involves intravenous administration of glucocorticoids, hydration, prevention of hypoglycemia, maintaining electrolyte balance, and treatment of any precipitating cause (infection, surgery, trauma).

Perioperative Steroid Use and Replacement

Since anesthesia blunts the normal physiologic adrenal response to surgery, patients who are on long-term steroid therapy may require supplementation in the perioperative period. Current guidelines suggest:

A. Patients who have not taken steroids in the last 3 months do not usually require perioperative supplementation.
B. Patients who have taken 10 mg of prednisone/equivalent in the last 3 months usually require perioperative supplementation.
   - Minor surgery (hernia)—25 mg hydrocortisone at induction of anesthesia.
   - Moderate surgery (hysterectomy, cholecystectomy)—patients regular preoperative steroid dose, plus 25 mg hydrocortisone at induction, plus 100 mg hydrocortisone for 24 h.
   - Major surgery—patients regular preoperative steroid dose, plus 25 mg hydrocortisone at induction, plus 100 mg hydrocortisone/day for 2–3 days.

Relative potency of hydrocortisone < prednisone < methylprednisolone < dexamethasone = 30:5:4:1.

Chronic steroid use depresses the hypothalamic-pituitary-adrenal axis and hence the need for steroid supplementation. It is important to remember that possible side effects of intraoperative steroid use include impaired wound healing, psychiatric disturbances, and glucose intolerance. Although the risk of perioperative acute adrenal insufficiency is quite small, but since it is a potentially life-threatening condition, the benefit of steroid supplementation outweighs its risks.

Pheochromocytoma

Pheochromocytoma is a rare neuroendocrine tumor originating in the chromaffin cells of the adrenal gland medulla. Besides the adrenal medulla it can also originate anywhere in the ganglia of the sympathetic nervous system chain. Although pheochromocytomas are primarily catecholamine (epinephrine and norepinephrine)-secreting tumors, they may also secrete other substances such as dopamine, serotonin, calcitonin, and ACTH. These tumors usually manifest in the 3rd–6th decade of life and are usually unilateral. About 1/4th of the tumors occur as part of multiple endocrine neoplasia (MEN associated with parathyroid adenomas and medullary thyroid carcinoma).

Clinical manifestations of pheochromocytoma include signs and symptoms of sympathetic nervous system hyperactivity, such as the classic triad of headache, diaphoresis, and palpitations, plus presence of tachycardia, severe hypertension (sporadic), anxiety, cardiac arrhythmias, heart failure, stroke, and renal failure. Ideally the diagnosis will be known preoperatively if the patient is scheduled for surgery to remove the tumor, or it may be previously unrecognized. Therefore, it is important that anesthesiologists be familiar with the disease, its presentation, and its management.

Diagnosis is established by a 24 h urine analysis for metanephrines and vanillylmandelic acid (VMA), plasma-free metanephrines, and imaging (CT scan, MRI, MIBG-a functional scan using an iodine-123 metaiodobenzylguanidine, PET scan). The clonidine suppression test can be used to aid in the diagnosis of pheochromocytoma. When clonidine is administered, it should lead to suppression of the sympathetic nervous system with decreased catecholamine levels. However, in patients with pheochromocytomas, clonidine administration does not decrease plasma catecholamine levels.

Preoperatively, the patient's blood pressure should be controlled. These patients are volume depleted with an elevated hematocrit, and hence replacement of intravascular volume is necessary (a drop in hematocrit is indicative of adequate replacement of intravascular volume). Additionally, cardiac and renal function status should be determined.

Preoperative antihypertensives to control blood pressure include alpha blockers (phenoxybenzamine, prazosin, doxazosin), beta blockers (propranolol, labetalol), and calcium channel blockers (nifedipine). It is important to remember that blood pressure control should be started with alpha

blockers and then followed with beta blockers. This is because administration of beta blockers *first* will lead to unopposed alpha agonist vasoconstriction causing hypertension.

Surgery to remove the tumor can be done open or laparoscopically. Intraoperatively, the aims are to maintain normal hemodynamics (large bore IV, arterial line, central line), avoid drugs that stimulate the sympathetic nervous system (ketamine, ephedrine, pancuronium), maintain hydration, and avoid hypoglycemia-hypotension (after tumor removal). Severe intraoperative hypertension or tachycardia can be controlled with phentolamine, sodium nitroprusside, and esmolol. Postoperative management again includes maintaining stable hemodynamics, hydration, glucose, and electrolyte balance.

Clinical Review

1. Treatment of diabetic ketoacidosis with insulin will most likely cause:
   A. Hyperkalemia
   B. Hypokalemia
   C. Hypernatremia
   D. Hyponatremia
2. All of the following are signs of autonomic imbalance in a diabetic patient, except:
   A. Gastroparesis
   B. Bradycardia
   C. Orthostatic hypotension
   D. Lack of sweating
3. In a hyperthyroid patient the following inhalational agent may be avoided during surgery:
   A. Desflurane
   B. Sevoflurane
   C. Isoflurane
   D. Halothane
4. Following thyroidectomy, total airway obstruction can occur with damage to:
   A. Superior laryngeal nerve, unilaterally
   B. Recurrent laryngeal nerve, unilaterally
   C. Recurrent laryngeal nerve, bilaterally
   D. Superior laryngeal nerve, bilaterally
5. Minimum alveolar concentration of a volatile inhalational agent in a hypothyroid patient is:
   A. Increased
   B. Decreased
   C. Unchanged
   D. Increased or decreased
6. The parathyroid hormone regulates the plasma level of:
   A. Calcium
   B. Phosphate
   C. Both calcium and phosphate
   D. Neither calcium nor phosphate
7. Hypoparathyroidism may cause all of the following, except:
   A. Tetany
   B. Laryngospasm
   C. Hypotension
   D. Shortening of the QT interval
8. Rapid correction of plasma sodium in a patient with SIADH can most likely lead to:
   A. Diffuse cerebral degeneration
   B. Brain herniation
   C. Central pontine myelinolysis
   D. Cerebral edema
9. Perioperative steroid replacement should be given to all patients who have taken steroids in the last:
   A. 1 month
   B. 3 months
   C. 6 months
   D. 1 year
10. Blood pressure in patients with pheochromocytoma should be controlled with:
    A. Alpha blockers
    B. Beta blockers
    C. Alpha blockers, then followed with addition of beta blockers
    D. Beta blockers, then followed with addition of alpha blockers

Answers: 1. B, 2. B, 3. A, 4. C, 5. C, 6. C, 7. D, 8. C, 9. B, 10. C

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Neurological and Neuromuscular Diseases

35

Brian Gierl and Ferenc Gyulai

For anesthesiologists nervous system pathologies are important for a number of reasons. These reasons are defined by the essential components of anesthesia: immobility, analgesia, unconsciousness, and suppression of autonomic reflexes. These components provide the context in which neurological disorders should be considered by the anesthesiologist. This chapter will specifically focus on the interaction of movement disorders with anesthetic management. In order to facilitate understanding of these interactions, a simplified yet fundamental structure of the motor pathway is discussed below.

The Motor Pathway

The voluntary motor signal originates in the upper motor neurons (UMNs) comprised by the pyramidal neurons of the motor strip in the frontal lobe. The axons of the UMNs constitute the pyramidal tract, which transmits the signal onto the lower motor neurons (LMNs) in the ventral horn of the spinal cord. The axons of the LMNs in turn take the signal to the neuromuscular junction (NMJ), where neuronal impulses translate into muscle contraction as the final manifestation of the initial idea to move (Fig. 35.1). Movement disorders result from dysfunction anywhere along this pathway.

Immobility, which is accomplished partially by general anesthetics and fully by muscle relaxants, is one of the most important components of general anesthesia. Therefore, neurological and neuromuscular pathologies and their treatment require special consideration from the anesthesiologist so that the patient can be recovered safely with appropriate return of motor, respiratory, and bulbar muscle functions. As a conceptual framework, these pathologies are grouped as whether the primary lesion occurs in the UMN or LMN (Table 35.1), at the neuromuscular junction (NMJ), or in the muscle. The presence of a lesion in one area often causes distinct pathologic changes in and of itself, in addition to associated alterations in areas that are of concern to the anesthesiologist.

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Motor Neuron Diseases

The motor neuron diseases are a group of acquired or congenital disorders characterized by loss of motor neuron input to muscle causing muscle weakness. The location of the nerve lesion—i.e., UMN or LMN—is important to the pathology of the disease, the identification of comorbidities, and the response to muscle relaxants. Initially, both UMN and LMN lesions result in weakness with decreased deep tendon reflexes (DTRs). After several days, muscles affected by UMN lesions are termed spastic because patients develop increased tone and increased DTRs, whereas fasciculations and atrophy occur in muscles affected by LMN lesions.

Denervation causes immature acetylcholine receptors (AChRs) to proliferate on the surface of myocytes. These immature receptors mature only with appropriate reinnervations and are hyperresponsive to stimulation with use of succinylcholine, a depolarizing neuromuscular muscle relaxant. Exposure to succinylcholine has the potential to cause hyperkalemia and/or rhabdomyolysis in patients with both UMN and LMN lesions, and therefore, it should be avoided. Hyperkalemia can cause abnormal cardiac conduction, including ventricular tachycardia and asystole. Secondly, the large and lasting stimulus allows calcium to collect in the myocyte, resulting in a state of continual contraction that may cause damage to both the cell membrane and intracellular myoglobin. Rhabdomyolysis may occur when these damaged cells leak myoglobin into the circulation.

Motor neuron diseases cause muscle weakness with a variety of clinical sequelae. Perhaps most importantly, they depress respiratory muscle function and cause bulbar muscle weakness (muscles of the tongue and oropharynx that perform deglutination/swallowing). Weakness of respiratory muscles, besides weakening the cough reflex, can eventually cause

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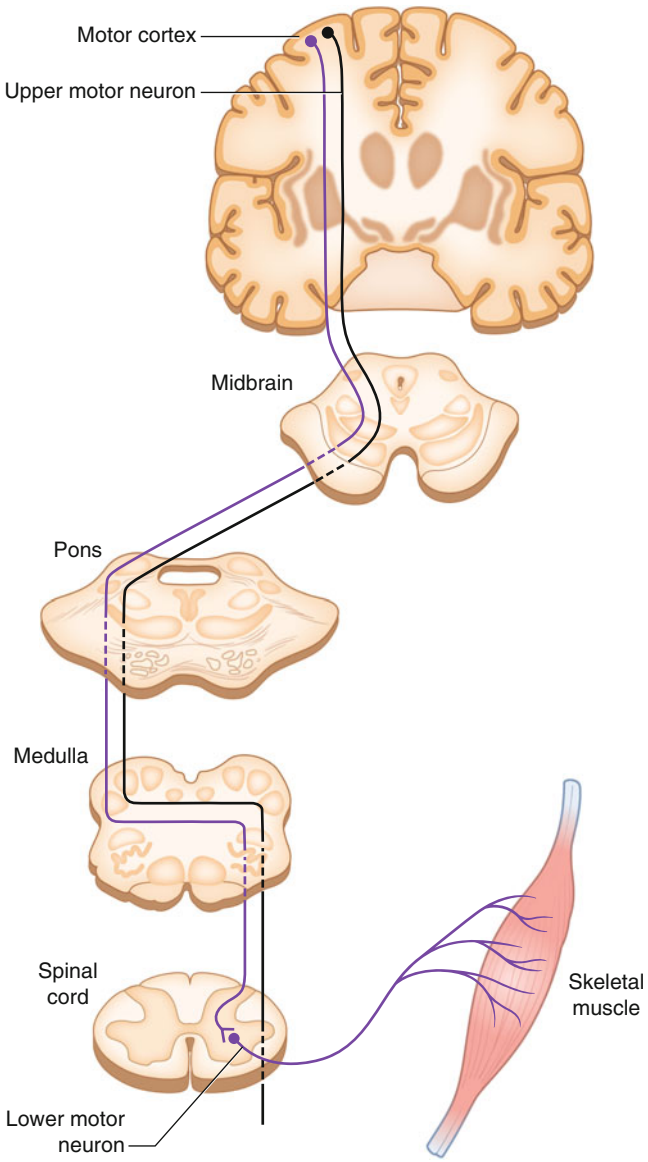

Fig. 35.1 Motor neuron pathway

respiratory failure, whereas bulbar muscle weakness increases the risk of aspiration and predisposition to pneumonia. These debilities make these patients highly sensitive to muscle relaxants. In addition, residual neuromuscular blockade further increases the likelihood that postoperative mechanical ventilation (POMV) will be required for respiratory insufficiency or airway protection in a patient who chronically struggles with these issues. Regional anesthesia and sedation is an alternative technique to avoid muscle relaxants. However, any respiratory compromise due to a high spinal or phrenic nerve block may cause muscle weakness with respiratory insufficiency and unplanned intubation. Also, sedation may lead to hypoventilation that may not be tolerated.

UMN Lesions

With baseline weakness due to UMN denervation, these patients may not tolerate any residual weakness after muscle relaxant dosing. This is especially true when relaxation is monitored on an affected upper extremity. Succinylcholine is best avoided in any disease affecting UMNs, for fear of causing severe hyperkalemia with massive depolarization. The use of a low-dose muscle relaxant for "precurarization" does not prevent the development of hyperkalemia. UMN lesions may complicate neuraxial regional anesthesia by increasing inflammation and neuron damage or by decreasing the efficacy of the blockade.

Spinal Muscle Atrophy

Spinal muscle atrophy (SMA) is an autosomal recessive disease that results in muscle weakness due to malfunction of the "survival motor neuron (SMA) gene" with loss of UMNs in the brainstem and spinal cord. The disease is classified into four forms based upon the age of onset (infantile, 0–6 months; intermediate, 6–18 months; juvenile, >18 months; and adulthood). The infantile and intermediate onset individuals have a shorter life span.

Patients present with hypotonia and absent reflexes. The limpness can be characterized as a "floppy baby syndrome." An electromyogram will show fibrillation and muscle denervation, and genetic testing will show bi-allelic deletion of exon 7 of the SMN1 gene. Patients have developmental delay (difficulty in sitting, walking, swallowing) but no mental retardation. Poor feeding leads to a lower than normal weight. Patients develop multiple contractures. Respiratory

Table 35.1 Differential signs of upper motor (UMN) and lower motor neuron (LMN) disease

Sign	UMN disease	LMN disease
Location	Lesion located in the CNS, within the brain and spinal cord	Lesion located in the peripheral nervous system, outside the brain and spinal cord
Weakness	Present	Present
Atrophy	Mild atrophy	Present
Fasciculations	None	Present
Tone	Increased	Decreased
Reflexes	Increased	Decreased
Babinski's sign (plantar response)	Extensor (up going toe)	Normal or absent

Table 35.2 Diseases affecting muscle relaxant response

Disease	Response to succinylcholine	Response to non-depolarizing muscle relaxants (NDMR)
Myasthenia gravis	May require increased dosage, and prone to phase II block (similar to that produced by NDMR)	↑ sensitivity
Eaton Lambert syndrome	↑ sensitivity	↑ sensitivity
Amyotrophic lateral sclerosis	↑ K+	↑ sensitivity
Spinal cord injury	↑ K+ (3 days-9 months)	Resistance in distal muscles
Duchenne muscular dystrophy	↑ K+	↑ sensitivity
Myotonia dystrophica	↑ K+	↑ sensitivity
Multiple sclerosis	↑ sensitivity/↑K+	↑ sensitivity
Guillain-Barre syndrome	↑ K+	↑ sensitivity
Parkinsonism	↑ sensitivity	↑ sensitivity
Hemiplegia	↑ K+	Resistance on affected side
Cerebral palsy	↑ sensitivity	Resistance
Burns	↑ K+	Resistance
Critical illness polyneuropathy	↑ K+	↑ sensitivity

↑ sensitivity *means* decrease the dose, ↑K+ means *do not* administer

complications (pneumonia) are the leading cause of death due to loss of strength of the pulmonary muscles and accumulation of secretions (weak cough).

There is no known cure for spinal muscular atrophy, and therefore, care is symptomatic. Because of weak spine muscles, patients develop kyphosis and scoliosis. SMA patients greatly benefit from physiotherapy. To relieve the pressure of the deformed spine on the lungs, spinal fusion may be performed in SMA patients. Once the respiratory muscles are weakened significantly, SMA patients may require BiPAP or even a tracheostomy. For difficulty in feeding, a feeding tube may be eventually required. Future treatments include gene therapy (to correct SMN gene function), stem cell therapy, and SMN gene activation.

Spinal Cord Injury

Although the manifestations of spinal cord injury (SCI) can be severe, modern medical treatment has increased survival rates, and rehabilitation has allowed people with SCI to live active lives. In the *acute* phase, these patients can present with neurogenic shock secondary to the loss of sympathetic input from the brainstem to levels below the injury. There is loss of sensation, flaccid paralysis, and loss of reflexes below the level of injury. Traumatic injuries, beyond those suffered to the central nervous system (CNS), may add a component of hypovolemic shock (hypotension and bradycardia). Patients with SCI above $C_{3–5}$ require ventilatory assistance (phrenic nerve). An awake fiber-optic intubation with the head in the neutral position may be required. Succinylcholine may cause hyperkalemia if used after 48 hours of SCI (Table 35.2). For management of the acute phase, we emphasize that (1) spinal cord edema can reduce tissue perfusion and, therefore, a MAP of greater than 80 mmHg is recommended, (2) hypervolemia due to over-resuscitation can exacerbate cord edema, and (3) high-dose intravenous corticosteroids reduce cord edema and allow patients to regain function of a more distal spinal cord segment.

Patients with SCI above the 6th thoracic vertebra often develop autonomic dysreflexia/hyperreflexia in the *subacute and chronic* phase (Fig. 35.2). With this condition, noxious stimuli below the transection are transmitted to sympathetic fibers by spinal interneurons, which cause local vasoconstriction (dry, pale skin), catecholamine release, and hypertension. The carotid baroreceptors are stimulated which initiate a parasympathetic response from the brain causing vasodilation (sweating, flushing) and bradycardia (even cardiac dysrhythmias) above the lesion (the response cannot be transmitted down because of the transection). Therefore, the pathologic sympathetic response is unabated because there is no supraspinal input to attenuate it. Uncontrolled sympathetic stimulation causes hypertension, which may be severe and lead to headache, myocardial ischemia, cardiomyopathy, seizures, or retinal, intracerebral, or subarachnoid hemorrhages. Further, the sympathetic stimulation is amplified by hyperresponsive receptors in the denervated tissue. Denervated tissue also predisposes these patients to pressure ulcers.

These patients frequently present for urologic procedures due to bladder dysfunction and may react to urethral stimulation and bladder distention with autonomic hyperreflexia and catecholamine release. In order to block noxious stimuli below the transection, spinal anesthesia (severe hypotension may occur) or deep general anesthesia (avoid succinylcholine, hypothermia) are effective during procedures. Sustained hypertension may be treated with nitroglycerin or nitroprusside. Several studies have evaluated the effect of SCI on MAC. If the surgery is performed at the level of the lesion, MAC is unchanged. However, for surgery below the level of the SCI, MAC is reduced by 20–30 %.

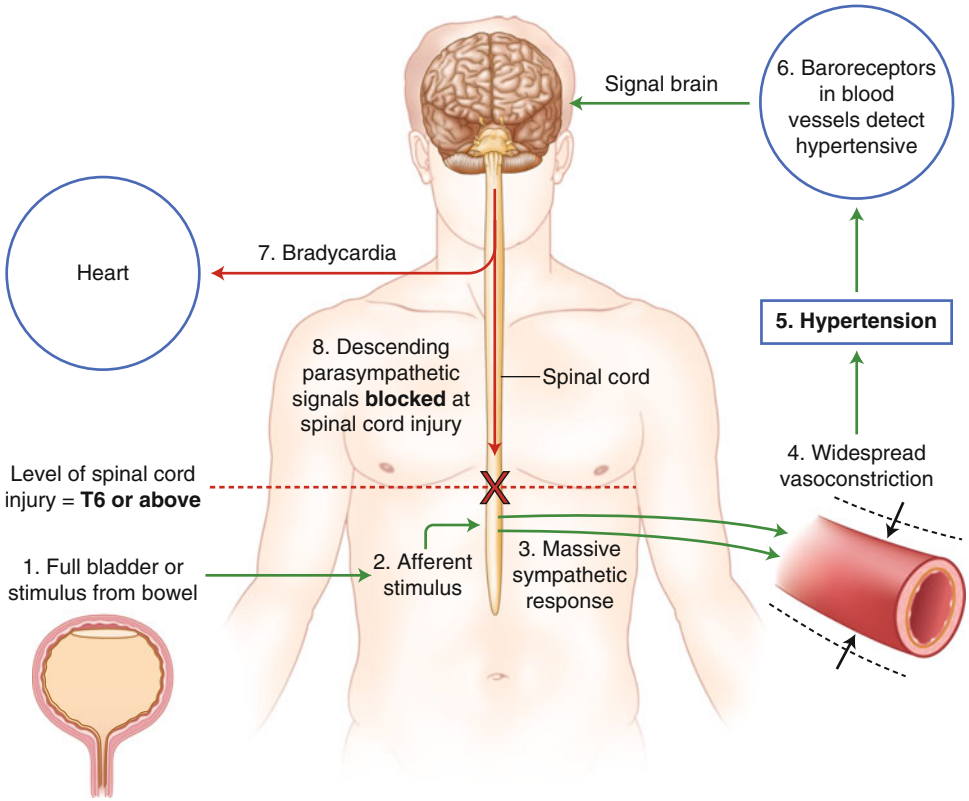

Fig. 35.2 Spinal cord injury and mechanism of autonomic hyperreflexia

Syringomyelia

Syringomyelia is the development of a fluid-filled cavity in the spinal cord (Fig. 35.3). It most commonly occurs at the cervical level and is marked clinically by neuropathic pain, numbness, weakness and muscular atrophy of the hands, and loss of temperature sensation. However, tactile sense is preserved (i.e., there is sensory dissociation). Many patients have Arnold-Chiari malformation. Treatment typically involves placement of a ventriculoperitoneal or thoracolumbar-peritoneal shunt that relieves symptoms by increasing CSF compliance. Anesthetic concerns for these patients include maintenance of spinal cord perfusion and pathologic reactions to muscle relaxants.

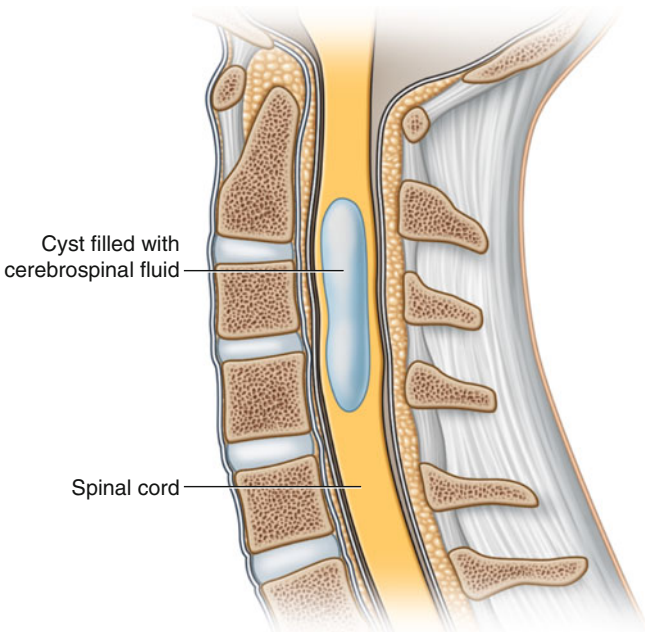

Fig. 35.3 Syringomyelia

LMN Lesions

LMN lesions occur commonly in combination with UMN lesions. Examples of only LMN diseases include progressive muscular atrophy and progressive bulbar palsy. Similarly to UMN lesions, succinylcholine is best avoided in patients with these lesions, since AChR upregulation may cause severe hyperkalemia with excessive depolarization. With the presence of baseline weakness due to LMN denervation, these patients may not tolerate any residual weakness after muscle relaxant dosing. Neuraxial regional anesthesia may cause trauma to peripheral nerves. Therefore, it should be used with caution, if at all, in patients with lower motor neuron disease because the diseased nerve may not tolerate any trauma or inflammation.

Combined UMN and LMN Lesions

Often pathology is confined to both upper and lower motor neurons, and therefore, the patient has effects from both types of lesions.

Amyotrophic Lateral Sclerosis

Amyotrophic lateral sclerosis (ALS) is the most common motor neuron disorder. It is a neurodegenerative disease of unknown etiology characterized by both UMN and LMN lesions. It often presents in the 5th–6th decade of life with fasciculations of the hands and bulbar muscles and progresses to spastic weakness of the extremities, bulbar weakness, and dysphagia. Eventually, patients lose all voluntary muscular control. Cognitive impairment is generally spared. The most common cause of death is respiratory failure due to respiratory muscle weakness, aspiration, and the inability to clear secretions. Late in the course of the disease, patients may require a feeding tube for nutrition and positive pressure ventilation to extend their life. Riluzole (Rilutek) is the only treatment that has been found to improve survival, but only to a modest extent. It may lengthen survival by several months. Anesthetic considerations for patients with ALS include autonomic dysfunction that can lead to hemodynamic instability requirement of postoperative mechanical ventilation (POMV). Succinylcholine should be avoided, and non-depolarizing muscle relaxants should be used sparingly, if at all.

Friedreich's Ataxia

Friedreich's ataxia is a congenital disease where a trinucleotide expansion repeat causes misfolding of a mitochondrial protein that leads to degeneration of the spinocerebellar and pyramidal tracts. In addition to ataxia and spasticity, these patients may also develop paravertebral muscle weakness that can lead to kyphoscoliosis with respiratory dysfunction. Two-thirds of the patients develop hypertrophic cardiomyopathy. Classically, this disease presents shortly after birth, and patients succumb to cardiac or respiratory failure in the 3rd decade of life. The age of onset varies inversely with the number of repeats, and recently, a late onset variant has been identified.

Multiple Sclerosis

Multiple sclerosis (MS) affects young adults between the ages of 20–40 years, being more common in women. MS is an inflammatorydisease in which the myelin sheaths (which increase the speed and efficiency of neuronal signaling) around the nerve axons are damaged, leading to demyelination and scarring. The result is plaques in demyelinated regions that manifest as paresthesias and spastic muscle weakness due to damage to nerves in the spinal cord. Symptoms and signs of MS are listed in Table 35.3. The optic nerves are often a target, leading to optic neuritis. Plaques and brain inflammation increase susceptibility to seizures. The exact cause of MS is not known, but MS is more common in families, with decreased exposure to sunlight (vitamin D deficiency), stress, smoking, low uric acid, exposure to environmental toxins, and viral infections. The natural course of the disease is one of flairs and remissions, with inflammation and hyperthermia leading to flairs, and pregnancy leading to a remission (for unclear reasons). In extreme cases, patients may experience respiratory insufficiency and dysphagia. Limb weakness may develop late in the course of the disease.

Table 35.3 Clinical manifestations of multiple sclerosis

System	Symptoms and signs
Central nervous system	Fatigue, cognitive impairment, depression
Visual	Diplopia, optic neuritis
Speech	Dysarthria
Throat	Dysphagia
Musculoskeletal	Muscle weakness, spasms, ataxia
Sensation	Pain, paresthesias, tingling
Bowel	Incontinence, diarrhea
Urinary	Incontinence, increased frequency
Lhermitte's sign	Electrical sensation that runs down the back when bending the neck

Baseline spasticity can be treated with dantrolene or baclofen, both of which can impact liver function tests and alter the pharmacokinetics of other drugs. MS patients are hypercoagulable and aggressive thromboprophylaxis should be implemented. Treatment of acute attacks includes administration of methylprednisolone, and in severe cases plasmapheresis. Other treatments include administration of interferon, mitoxantrone (immunosuppressant), natalizumab, and fingolimod. Neurorehabilitation is important for functional deficits and disability. Patients' symptoms may be exacerbated in response to perioperative stressors, including blood pressure and temperature changes (prevent hyperthermia). The loss of upper motor neurons can lead to sensitivity to depolarizing drugs. There are case reports of spinal anesthesia exacerbating MS. One explanation for this is that demyelinated axons may be more sensitive to local anesthetic toxicity. Epidural, other regional techniques, and general anesthesia have not been implicated in MS exacerbations.

Charcot-Marie-Tooth Disease

Charcot-Marie-Tooth (CMT) is a group of illnesses that are characterized by myelin deficiency (either quantitative or qualitative) that causes peripheral nerve dysfunction, with progressive muscular atrophy and loss of touch sensation. It is one of the most common inherited neuromuscular diseases. Patients suffer from muscle weakness that can cause respiratory dysfunction with increased likelihood that POMV will be required after intubation. Patients with significant muscle denervation may be hyperresponsive to depolarizing neuromuscular blocking drugs. The severity of cardiomyopathy seen in CMT patients increases with age and enhances the sensitivity to negative inotropes. Skeletal

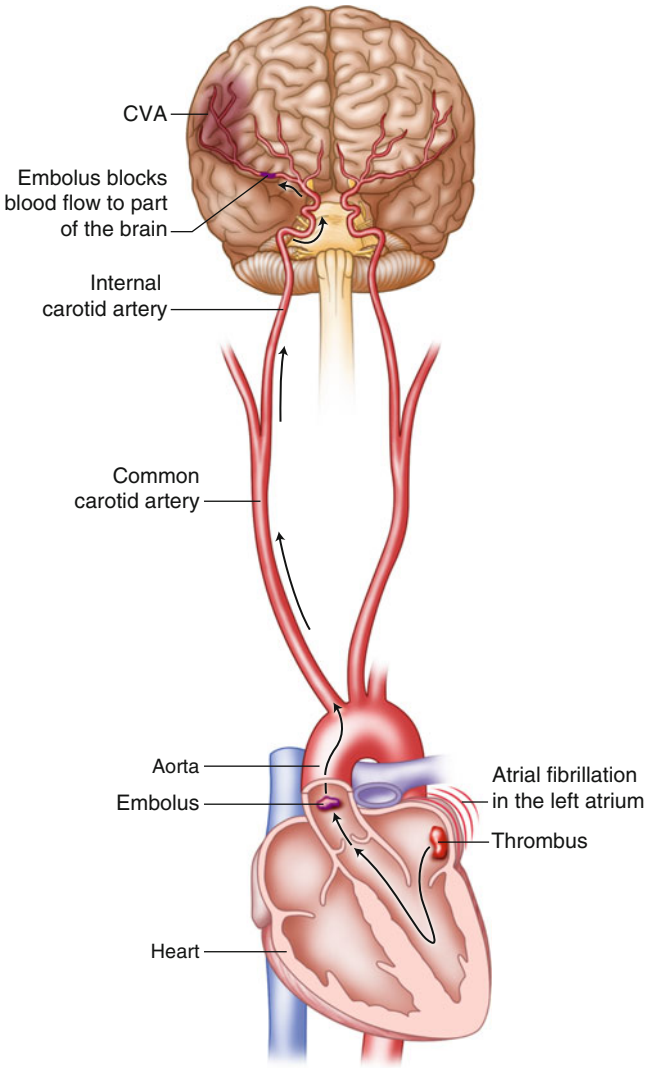

Fig. 35.4 Mechanisms of cerebrovascular accident (CVA)

muscle deformities can be severe, resulting in difficult patient positioning or scoliosis that may reduce FVC. The loss of myelin produces the greatest impact on longer nerves, and therefore, the symptoms of the disease progress from distal to proximal. The clinical effects of a peripheral nerve block may be magnified by the preexisting neuropathology.

Cerebrovascular Disease

In the United States alone, 800,000 people suffer strokes annually and cost the economy ~$70 billion. Cerebrovascular disease (CVD) refers to both occlusive disease (i.e., carotid or vertebral artery stenosis) and potentially hemorrhagic lesions, including intracranial aneurysms and arteriovenous malformations (Fig. 35.4). Patients often have a history of transient ischemic attacks (TIAs), which are defined as transient neurological impairment lasting less than 24 h, with no residual neurological impairment.

Occlusive disease is more common in surgical patients for non-neurosurgical procedures and will be the focus here. Lesions with hemorrhagic concerns are discussed in the Neuroanesthesia chapter. Occlusive CVD is a common cause of perioperative cerebrovascular accidents (CVA), aka stroke. The etiology of these CVAs is either thrombotic or embolic. Perioperative CVAs in patients for noncardiac, non-neurosurgical procedures occur in 4–8 % of patients over the age of 60, and 60 % of these are thrombotic in nature. Perioperative inflammation doubles perioperative CVA mortality to 25 %, as compared to the ~10 % mortality seen in non-perioperative patients. The role of inflammation rather than a reduction of cerebral perfusion is evidenced by the fact that <10 % of CVAs occur intraoperatively, and in fact, most present on postoperative day #1. It is recommended that all nonurgent procedures be postponed 2–6 months after a CVA. This period allows: (1) the inflammation to subside and (2) the normalization of pressure-passive flow (i.e., return of cerebrovascular autoregulation). Although initiating statin therapies post-CVA has not been shown to be therapeutic, acute statin withdrawal increases morbidity by eightfold.

Atrial fibrillation (AFib) is a common etiology of thrombotic stroke, and some authors theorize that perioperative stress and electrolyte imbalance can trigger paradoxical AFib that may go unrecognized. The presence of AFib is certainly a risk factor for thromboembolism. Recent recommendations for anticoagulation in patients with AFib include the modified CHADS2 score, also known as the CHADS2-VASC. Here, the patient is assigned a point each for CHF, HTN, diabetes mellitus, vascular disease (peripheral artery disease, MI, aortic plaque), age 65–74 years, and sex (female) and 2 points each for age ≥75 years or a history of TIA/CVA. The presence of any two points in the setting of AFib warrants anticoagulation.

The presence of extracranial carotid artery stenosis (CAS), with or without a bruit, has not been shown to increase the risk of CVA. CVA data has led to recommendations against surgical intervention for CAS <60 %, with interventions for higher grade stenosis only in the presence of bilateral disease or other risk factors (e.g., diabetes mellitus). Echolucent plaques are associated with CVA. Statins and anti-inflammatory drugs should be used to stabilize echolucent plaques and reduce emboli.

Embolic strokes (air, fibrin, calcium debris) are particularly common after cardiac or carotid artery surgery. These CVAs are characterized as watershed infarcts with ischemic areas in the distal circulation thought to be caused by the large number of emboli produced by these procedures (especially cardiac bypass). The impact is exaggerated due to low cerebral blood flow that is common in patients undergoing these procedures.

In summary, CVAs in patients with CVD are best prevented by maintaining a high cerebral perfusion pressure in order to ensure perfusion to the watershed regions in the presence of altered CBF autoregulation. The benefits from appropriate perfusion include adequate oxygen delivery, toxic metabolite

removal, and debris clearance. When using muscle relaxants intraoperatively, neuromuscular blockade should be monitored with a nerve stimulator in the non-affected extremity. Succinylcholine should be avoided in chronically debilitated patients (proliferation of acetylcholine receptors) as it may cause hyperkalemia. Administration of antiplatelet agents immediately after surgery reduces clot formation but must be balanced by the risk of postoperative bleeding. Aspirin is superior to clopidogrel in this regard and is usually started 2–6 h postoperatively. The role of anesthetics in neuroprotection has not shown to be beneficial in large-scale human trials and is discussed in the chapter of Neuroanesthesia.

Neuromuscular Junction Lesions

Several conditions limit the transmission of neuronal impulses to muscles at the neuromuscular junction (NMJ), resulting in muscle weakness. Myasthenia means muscle weakness, and therefore, these diseases are termed myasthenic syndromes.

Lambert-Eaton Syndrome

Lambert-Eaton myasthenic syndrome (LEMS), although rare, is the most common myasthenic syndrome. It is an autoimmune disorder whereby the body produces IgG antibodies (usually in response to small cell lung cancer) to the voltage-gated calcium channels, which disrupts their normal alignment at the nerve terminus. This limits calcium influx, which decreases ACh release. The inflammation increases the width of the NMJ, which increases exposure to acetylcholine esterase (AChE) and further decreases the amount of ACh that reaches the AChRs. Clinically, these patients present with weak proximal limb muscles and reduced DTRs. Muscle strength improves with effort, which is in *contrast* to myasthenia gravis. Late stage diaphragmatic dysfunction can result in respiratory failure. Bulbar function is usually preserved, and ocular symptoms are rare. Because the antibodies also bind calcium channels on autonomic ganglia, these patients experience autonomic dysfunction (orthostatic hypotension) and anticholinergic symptoms that include a dry mouth and constipation. Patients with LEMS are very sensitive to succinylcholine and non-depolarizing neuromuscular blocking drugs, and hence these should be avoided.

Congenital Myasthenic Syndromes

The congenital myasthenic syndromes (CMS) are less common and involve protein mutations that can hinder ACh release or binding. The AChR themselves or the proteins that localize them to the NMJ are most often altered, but a myotonic form of the disease also exists. These syndromes are termed seronegative LEMS because patients suffer similar clinical consequences as LEMS, but there are no antibodies. The drug 3,4-diaminopyridine (3,4-DAP) appears to be effective in patients affected by LEMS or CMS. By blocking the voltage-gated potassium channels, 3,4-DAP prolongs the action potential so that calcium channels remain open for a longer duration allowing more ACh release to stimulate the muscle (the drug increases ACh release and overcomes the lack of ACh in seropositive LEMS and the lack of organized AChR in seronegative LEMS).

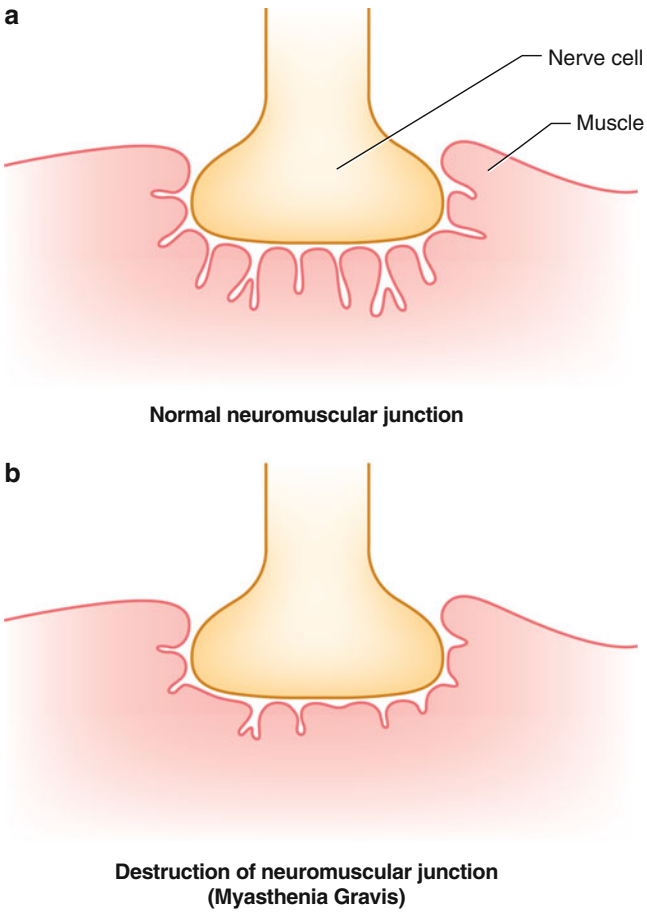

Fig. 35.5 Neuromuscular junction. (**a**) Normal. (**b**) Myasthenia gravis

Myasthenia Gravis

Myasthenia gravis (MG) is a disorder in which antibodies are generated against the AChR, or less commonly, against the protein that clusters the AChRs at the postsynaptic junction (Fig. 35.5). This results in inactivation or destruction of the AChRs leading to skeletal muscle weakness and easy fatigability. MG presents in women in their 3rd decade and in men in their 6th decade of life. About 60–65 % of the patients with MG have a hyperplastic thymus gland, and another 10 % of patients have thymomas. Muscle strength

improves with rest but decreases rapidly with effort. MG typically is marked with exacerbations and remissions. Often the presence of infection, stress, and pregnancy can precipitate exacerbations. MG can affect either a group of muscles or be generalized. Ocular muscle involvement, which is common, causes ptosis and diplopia. Bulbar muscle involvement (laryngeal and pharyngeal muscles) can lead to dysphagia and increased risk of pulmonary aspiration.

Anticholinesterase drugs (anti-AChE) are the mainstay of treatment of MG. These drugs increase the ACh concentration to overcome the lack of AChR so that the patient can maintain adequate muscular function. Other forms of treatment include glucocorticoids, immunosuppressants, plasmapheresis, and thymectomy. The most common anti-AChE drug used to treat MG is pyridostigmine. However, excessive dosage of anti-AChE drugs can precipitate "cholinergic crisis" (increased muscle weakness, muscarinic symptoms—sweating, salvation, bronchial secretions, bradycardia, miosis). It is important to differentiate a cholinergic crisis from a myasthenic crisis (weakness of skeletal muscles due to MG), which can be done by using the drug edrophonium. After administering edrophonium increased muscle weakness indicates cholinergic crisis, whereas improvement in muscle strength indicates myasthenic crisis.

Anesthetizing patients with MG has several challenges. Preoperative forced vital capacity (FVC) predicts the postoperative course, with FVC < 60 % of predicted value for patient height, weight, age, and sex predicting the need for prolonged POMV. If the patient can tolerate skipping a dose, then anti-AChE drugs are usually withheld on the morning of surgery and dosed at the end of the procedure. If the patient cannot tolerate skipping the morning anti-AChE dosage, the muscle relaxant effects of a deep anesthetic achieved via propofol or a volatile agent may provide sufficient relaxation for the procedure. It is important to remember that many drugs can cause acute weakness (aka myasthenic crisis), including aminoglycoside antibiotics, beta-blockers, and sodium channel blockers including local anesthetics.

- Patients with MG are very sensitive to premedication with opioids or benzodiazepines.
- Anesthesia is usually induced with propofol and maintained with a volatile inhalational agent.
- Muscle relaxants are usually avoided. Patients with MG may be resistant to the effects of succinylcholine (increased dose if used) or may exhibit a prolonged effect. Patients with MG are highly sensitive to non-depolarizing muscle relaxants (NDMB), and even a precurarization dose may cause paralysis. NDMBs, if used, should be short acting and used in small doses and with extreme caution (monitoring with a nerve stimulator).

For pregnant patients with MG, regional anesthesia is commonly employed with care taken to prevent a high level block.

Muscular Lesions

Muscular Dystrophy

The muscular dystrophies are X-linked recessive disorders that are characterized by a reduced amount (Becker's muscular dystrophy, BMD) or a complete absence (Duchenne's muscular dystrophy, DMD) of the muscle protein dystrophin (a protein which provides structural stability to the cell membrane in muscles). The disease affects males, while females are carriers. DMD presents by 5 years, while BMD presents in the 2nd decade of life. Progressive skeletal muscle weakness leads to gait disturbances, contractures, and kyphoscoliosis, which in turn limit respiratory reserve (restrictive ventilatory defect) and physical activity (wheel chair bound). Cardiac muscle fibers are also affected with dilated cardiomyopathy occurring in the teenage years in DMD patients and in the 20s in BMD patients. Although these are X-linked recessive disorders, female carriers can exhibit a mild myopathy evidenced by an elevated creatinine kinase level and cardiac dysfunction. The most common causes of death are related to the cardiomyopathy, respiratory insufficiency, or a combination of the two. Physical inactivity can mask myocardial dysfunction, which may be disproportional to the muscle weakness.

Muscular dystrophies were formerly, and incorrectly, associated with an increased risk of malignant hyperthermia (MH) based upon the reaction of these patients to the administration of succinylcholine or volatile anesthetics. However, recent evidence has shown that these patients do not exhibit the hypermetabolic state that is required for the diagnosis of MH. In these patients, the damaged muscle is continually regenerating, and therefore, it expresses a juvenile acetylcholine receptor. Stimulation due to succinylcholine, a depolarizing neuromuscular blocker, causes a strong muscle contraction, which can lead to muscle damage with myoglobin release as well as hyperkalemia. It has been proposed that volatile anesthetics accelerate the cell membrane breakdown that is characteristic of the disease. With either class of drugs, the resulting potassium leak and rhabdomyolysis cause renal dysfunction that itself worsens the hyperkalemia.

Myotonia

The myotonias are a small group of rare muscular disorders that are characterized by slow muscle relaxation after a contraction. A particular sodium channel in skeletal muscle, SCN4A is crucial for muscle depolarization. Different mutations in this specific channel can cause aberrant responses to a variety of stimuli, including hyperkalemic periodic paralysis, hypokalemic periodic paralysis, paramyotonia congenita (PMC), potassium-aggravated myotonia, and congenital myasthenic syndrome.

Hyperkalemic periodic paralysis (hyperKPP) is caused by a SCN4A mutation that results in prolonged channel activation and elevated resting membrane potential. Anything that makes the already elevated membrane potential more positive can prevent repolarization, causing myotonia that may be followed by a period of weakness. An episode can occur in response to several triggers that include potassium ingestion, cold and shivering, fasting, and glucocorticoid administration. The attacks last from 15 to 60 min and fortunately do not typically involve the bulbar muscles or impact respiratory function. Laboratory studies may show elevated plasma potassium (4.5–8.0 meq) during attacks.

Paramyotonia congenita is similar to hyperKPP. However, the triggers are physical exertion in cold weather, with the patient's plasma potassium level remaining normal/high during attacks. It is called paramyotonia because the weakness worsens with exercise (paradoxical), as opposed to myotonia congenita in which strength builds with exercise/repetition.

Patients with hypokalemic periodic paralysis (hypoKPP) suffer attacks of paralysis that vary in frequency, with some individuals experiencing attacks daily, while others only a few times in their lifetime. Such attacks may last from hours to a day and may include the bulbar and respiratory muscles. Oral potassium without a carbohydrate load is therapeutic (monitor EKG), while acetazolamide is frequently prophylactic. Recurrent attacks can lead to permanent muscle damage. Two different mutations have been linked to the hypoKPP phenotype. One of these is the SCN4A sodium channel that was discussed above. Other studies have implicated alterations in the voltage-gated calcium channel (Ca 1.1) as an etiology of hypoKPP. Because the Ca 1.1 channel activates the ryanodine receptor (RYR1), this disorder is associated with malignant hyperthermia (MH), although the relationship between hypoKPP and MH is unproven. Diligence precludes the use of volatile anesthetics and depolarizing muscle blocking drugs in these patients. The mechanism of the paralysis is not clear but unlike hyperKPP, hypokalemia is the cause of the disorder. HypoKPP attacks can be caused by insulin released after carbohydrate-rich meals that drives potassium into cells. In the perioperative period, the release of catecholamines due to preoperative anxiety, intraoperative surgical stress, or cold exposure can cause hypokalemia that can lead to weakness with increased sensitivity to NMBDs.

Malignant Hyperthermia

Malignant hyperthermia (MH) is a clinical syndrome in which a calcium imbalance leads to a hypermetabolic state in skeletal muscle. It more commonly occurs in the pediatric population. MH is thought to be caused by a rare (~1:2,000) genetic mutation that affects the ryanodine receptor 1 (RYR1) on the sarcoplasmic reticulum's calcium channel. Excessive calcium leads to continual contraction, and to remove this excess calcium, the cell responds by expending energy (increased O_2 consumption and CO_2 production, depletion of ATP stores). The syndrome is characterized by tachycardia/dysrhythmias, hypercarbia, hyperthermia, and muscle rigidity. Increased $ETCO_2$ is the hallmark and one of the earliest signs, while fever is often a late sign. Lab values may show hypercalcemia, hyperkalemia, increased creatinine kinase, myoglobin, and a mixed metabolic and respiratory acidosis. Eventually, renal failure, pulmonary and cerebral edema, and coagulopathies may occur.

Volatile inhalational anesthetics, intense exercise, or thermal stress are clearly implicated as causing MH episodes in susceptible persons. Succinylcholine may trigger MH as well, but some authors question whether the effects after succinylcholine administration is truly MH or due to hyperkalemia. Because very low levels of volatile anesthetics can trigger and propagate an episode, the first line of treatment of MH is to stop all volatile anesthetics. The patient is maintained on TIVA and bag-mask ventilation from a separate oxygen source. A circuit may be prepared by continual flushing for an extended period of time, but modern anesthesia machines contain a large amount of plastic that makes purging volatile anesthetics difficult, and an adequate purging procedure has still not been well defined. A charcoal filter has recently been developed to remove the volatile anesthetics.
Dantrolene blocks the RYR receptor and thus is the therapy of choice for MH. Dantrolene inhibits calcium release from the sarcoplasmic reticulum and interferes with muscle contraction. It is given in a dose of 2.5 mg/kg intravenously (up to 10 mg/kg) every 5–15 min until the symptoms subside. Calcium channel blocking drugs should be avoided with dantrolene use as they may cause severe hyperkalemia. In addition, the MH patient is kept well hydrated (intravenous fluids), furosemide may be administered to prevent renal damage from myoglobinuria, and cooling measures are instituted in presence of fever. The most frequent complications of MH are an altered level of consciousness, cardiac dysfunction, and pulmonary edema. Their frequency increases 1.5 × per 1 °C increase in temperature and 1.6 × per 30-min delay of dantrolene dose. Central core disease, multiminicore disease, and nemaline rod myopathy are all descriptors of the histological appearance of muscle biopsies that indicate MH susceptibility.

Neurological Diseases

Parkinsonism

Parkinsonism is a neurodegenerative disease evident in people 60–70 years of age. Parkinsonism is characterized by progressive loss of dopamine in the substantia nigra. A

decrease in dopaminergic activity is accompanied by an increase in cholinergic activity, with effects on the extrapyramidal system. Symptoms and signs of parkinsonism include a cogwheel rigidity, muscle stiffness and pains, fixed facial expression, postural instability, shuffling gait, resting (pill-rolling) tremor, and bradykinesia. All these eventually lead to physical incapacitance and dementia.

Parkinsonism can be primary (unknown cause) or secondary. Secondary parkinsonism can be due to a viral infection (encephalitis), carbon monoxide or cyanide poisoning, or head trauma (pugilistic). Parkinsonism may also be associated with other neurological disorders such as Huntington and Alzheimer's disease. Symptoms of parkinsonism can be controlled by both medical and surgical therapies. The most commonly used drug for treatment of parkinsonism is levodopa, which is a precursor of dopamine. It is commonly used in combination with carbidopa, a decarboxylase inhibitor, which retards the breakdown of levodopa. Other medications used to treat parkinsonism include selegiline (MAOI), which decreases the breakdown of dopamine, and bromocriptine and pergolide (dopamine agonists). Surgical procedures are used to treat parkinsonism in patients who have failed to respond to medications. These procedures include pallidotomy (destroying globus pallidus, which is involved in motor control) or cryothalamotomy (destroying the area of the brain that produces tremors by inserting a probe into the thalamus). Pallidotomy may improve symptoms such as tremors, rigidity, and bradykinesia. Restorative surgery, which is still in experimental stage, replaces the lost dopaminergic neurons of the patient with dopamine producing fetal brain tissue.

Antiparkinsonism medications should be continued in the perioperative period. Care should be taken to avoid antidopaminergic medications, such as phenothiazines, droperidol, and metoclopramide. Anticholinergics (benztropine) and antihistaminics (diphenhydramine) can be used for acute exacerbation of symptoms. Patients may have dementia, so appropriate consent for surgery should be obtained. Patients are usually intravascularly depleted and may show signs of autonomic instability; therefore, hypotension with induction of anesthesia may occur. Hypotension can be safely treated with phenylephrine (an alpha agonist). Patients with parkinsonism may show increased sensitivity to muscle relaxants, and hence these should be used judiciously.

Alzheimer's Disease

Alzheimer's disease (AD) is the most common form of dementia affecting about 2 % of people above the age of 85 years. Early symptoms are often mistakenly thought to be "age-related" concerns, with the most common symptom being difficulty in remembering recent events. As the disease advances, symptoms include confusion, irritability and aggression, language problem (loss of vocabulary), and long-term memory loss. As the disease progresses further, the patients often withdraw from family and society. When AD is suspected, the diagnosis is usually confirmed from the patient's history, tests that evaluate behavior, and thinking abilities, often followed by brain imaging (CT, MRI, PET, SPECT).

The exact cause of Alzheimer's disease is still not known. It is characterized by loss of neurons and degenerative changes in the cerebral cortex, which leads to atrophy. Several hypotheses exist, which include cholinergic hypothesis (decreased synthesis of acetylcholine), amyloid hypothesis (amyloid plaques in the brain), and tau hypothesis (tau protein abnormalities causing neurofibrillary tangles). Plaques are dense, mostly insoluble deposits of beta-amyloidpeptide and cellular material around the neurons, while neurofibrillary tangles are aggregates of the microtubule-associated protein tau which has become hyperphosphorylated and accumulates inside the nerve cells.

There is no known treatment for Alzheimer's disease. Care is mainly supportive, which includes psychosocial interventions (behavior-, emotion-, cognition-, and stimulation-oriented approaches). With advancement of disease, different medical issues can appear, such arousal, dental disease, pressure ulcers, malnutrition, hygiene problems, and respiratoryinfections. While disease progression cannot be halted with current pharmaceutical interventions, cognitive impairment can be improved with acetylcholinesterase inhibitors (tacrine, rivastigmine, galantamine, donepezil) and memantine (NMDA receptor antagonist).

Patients presenting to the operating room may not be able to give their own consent for the surgery, as they may be confused, disoriented, and uncooperative. Because of age and memory loss, patients may be sensitive to premedication with benzodiazepines and opioids. Scopolamine should be avoided as it may add to the confusion. Regional anesthesia may be appropriate for cooperative patients. When general anesthesia is instituted, it is important to remember that general anesthesia may lead to postoperative confusion. Patients with advanced AD may need proper positioning and padding of the extremities.

Guillain-Barre Syndrome

The Guillain-Barre syndrome (GBS) most commonly follows a viral or gastrointestinal infection. GBS is characterized by acute inflammatory demyelinating polyneuropathy, with an immunologic reaction to the myelin sheath of peripheral nerves. There is sudden onset of ascending motor paralysis, with weakness and aching pain beginning in the hands and feet and progressing to the trunk. Facial nerve weakness is common. Sensory loss may involve loss of proprioception (position sense) and complete loss of deep tendon reflexes

Table 35.4 Causes of seizures

Idiopathic
Intracranial tumors
Stroke
Head injury
Congenital brain defects
Infections—meningitis, encephalitis, abscess
Metabolic and electrolyte abnormalities
Medications—cocaine, amphetamine
Withdrawal—alcohol, opioids

(areflexia). Respiratory muscle and bulbar (dysphagia) involvement may occur. Treatment includes administration of intravenous immunoglobulins or plasmapheresis, with most patients recovering completely in days to a few weeks. Anesthesia concerns include pulmonary complications, autonomic instability, and risk of hyperkalemia with succinylcholine.

Seizure Disorder

Seizures are changes in behavior or attention brought about by abnormal synchronized electrical activity in the brain. Causes of seizures are listed in Table 35.4. The increased electrical activity may be due to excessive stimulation (excitatory neurotransmitter glutamate release) or loss of inhibition (decreased GABA activity). Seizures are termed epileptic when they occur repeatedly. Seizures can be classified as generalized, localized or focal or partial, and petit mal.

- Generalized tonic-clonic seizure: a generalized tonic-clonic seizure usually has three phases, namely, the aura, the actual seizure, and a postictal phase.
  - Aura: many patients have an aura before the seizure. The aura can be a change in vision, taste, smell, sensory changes, hallucinations, or dizziness.
  - Seizure: with the onset of the seizure, there is muscle rigidity followed by violent muscle contractions and loss of alertness/consciousness. Symptoms that can also occur during the seizure include biting the cheek or tongue, clenched teeth or jaw, incontinence (urine/stool), and difficulty in breathing.
  - Postictal phase: the seizure is followed by a postictal phase which is characterized by sleepiness (for about an hour), amnesia for the event, headache, confusion, and weakness of one side of the body for a few minutes to hours (Todd's paralysis).
- Focal/partial seizures: these seizures are localized up to varying extent. They are classified as simple partial seizures when a localized part of the body has motor, sensory, or autonomic symptoms. When these seizures are accompanied by impairment in consciousness, they are called complex partial seizures. Focal seizures may include abnormal muscle contraction (muscle contraction/relaxation-clonic activity), may affect one side of the body (leg, face, or other area), abnormal head movements, abnormal mouth movements, lip smacking, abnormal sensations (numbness, tingling, crawling sensation), or hallucinations.
- Petit mal seizures: these seizures most commonly occur in people under the age of 20 years, usually in children of ages 6–12 years. They may occur with other types of seizures, such as generalized tonic-clonic seizures, twitches or jerks (myoclonus), or sudden loss of muscle strength (atonic seizures). These last only a few seconds and most commonly involve staring episodes or "absence spells." These spells may occur many times a day, interfere with school and learning, and may go unnoticed for weeks or months. During the seizure, the person may stop an activity and then resume the activity being unaware of the seizure. For example, a person may stop walking and start again a few seconds later or stop talking in mid-sentence and start again.

Preoperatively, antiseizure medications should be continued. If the medication cannot be given orally, then it should be administered intravenously. If an intravenous form of the medication is not available, then an equivalent dose of another antiseizure medication should be administered intravenously. The type of seizure and the antiseizure drugs taken by the patients should be documented. If a seizure occurs outside the operating room, the airway should be maintained, and drugs should be administered to stop the seizure (diazepam 5–10 mg, propofol 50 mg, or phenytoin 500 mg slowly). Attempts should be made to correct any metabolic or electrolyte abnormalities that are evident preoperatively. It is important to remember that withdrawal from alcohol and narcotics can lead to seizures. Patients who are on antiseizure medications but are having seizures often should have the medication blood levels checked. CBC and liver parameters should be checked, in case of bone marrow suppression or hepatotoxicity.

Intraoperatively, certain drugs with epileptogenic potential should be avoided (methohexital). Accumulation of laudanosine, a metabolite of cisatracurium, can cause seizures. Phenobarbital causes hepatic microsomal enzyme induction, which may alter the metabolism of several other medications that the patient may be taking. It is important to know that phenytoin and carbamazepine may decrease the duration of non-depolarizing neuromuscular blockade. Postoperatively, antiseizure medications should be restarted on a regular schedule.

Critical Illness Polyneuropathy/Myopathy

Critical illness polyneuropathy/myopathy is a recently described illness of unknown cause that is characterized by

denervation muscular atrophy that usually affects limb muscles. The accessory muscles of respiration may also be impacted, which can lead to respiratory insufficiency. It develops as a complication of severe trauma or infection, while the patients are in the intensive care unit. It presents in ~50 % of patients who have been ventilated for 1 week in the presence of an inflammatory condition (SIRS, ARDS, sepsis, etc). Presence of hyperglycemia and extended use of muscle relaxants or steroids increase its incidence. The muscle weakness may persists after the discontinuation of muscle relaxants and extend the time to wean the patient from ventilator support.

Psychiatric Disorders

A psychiatric disorder or mental illness is defined as a behavioral pattern causing suffering or an impaired ability to function, physically or socially, in ordinary life. The anesthesiologist should be familiar with common mental disorders, as the mental illness and medications used to treat these disorders can alter the management of anesthesia.

Depression

- Disorder of mood (sadness), pessimism, cognitive function, lack of sleep and energy, sexual dysfunction, and suicidal ideation.
- Treatment—pharmacotherapy, ECT for resistant and suicidal cases, and psychotherapy.

Pharmacotherapy—Antidepressants are continued preoperatively:

– Tricyclic antidepressants increase the concentration of neurotransmitters (norepinephrine, dopamine, and/or serotonin) in the synaptic cleft by inhibiting their reuptake (Fig. 35.6). Examples are doxepin (Sinequan), amitriptyline (Elavil), and clomipramine (Anafranil).

Side effects include anticholinergic (dry mouth, blurred vision, urinary retention), cardiac effects (tachycardia, T-wave flattening, prolongation of QT interval), exaggerated response to vasopressors, and sympathetic stimulation (pancuronium, meperidine, epinephrine, ketamine, which should be used carefully). Potentiation of anticholinergic effects and postoperative delirium can occur when used with atropine or scopolamine:

– Selective serotonin reuptake inhibitors—fluoxetine (46 Prozac), paroxetine (Paxil), sertraline (46 Zoloft), and citalopram (Celexa). These drugs have little or no anticholinergic/cardiac side effects. Side effects include headache, agitation, insomnia, weight gain, and sexual dysfunction.
– Monoamine oxidase inhibitors (MAOIs)—inhibit MAO enzyme, which metabolizes the neurotransmitters. At least two types of MAO isoenzymes, MAO-A and MAO-B, exist. Only MAO-A enzyme inhibitors are effective in the treatment of depression. MAO-B inhibition leads to hypertensive reaction on ingestion of tyramine-containing foods (cheese, red wine). Examples are nonselective MAO inhibitors [phenelzine (Nardil), tranylcypromine (Parnate)] and MAO-A inhibitor (moclobemide). Selegiline, a nonselective MAO inhibitor, has fewer or no diet restriction when applied transdermally.

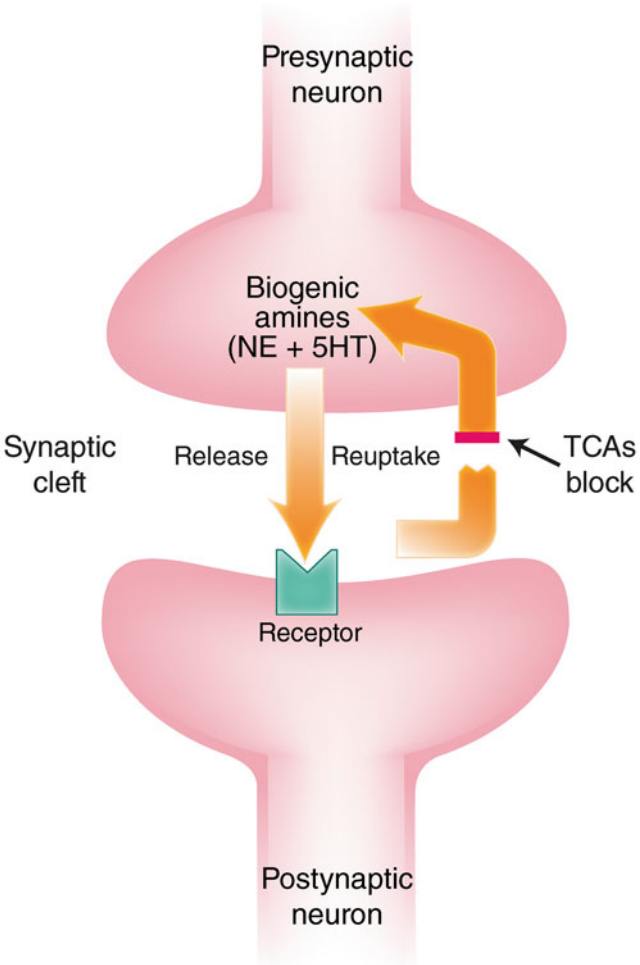

Fig. 35.6 Mechanism of action of antidepressants: inhibit the reuptake of neurotransmitters in the synaptic cleft

Side effects include hypertensive crisis [can occur when taking these drugs with indirect sympathomimetics (ephedrine) or tyramine-containing foods (cheese, red wine)], orthostatic hypotension, agitation, tremor, muscle spasms, and seizures:

– Others—dopamine reuptake inhibitor, bupropion (Wellbutrin); serotonin and norepinephrine reuptake inhibitor, venlafaxine (Effexor) and mirtazapine (Remeron)
– Herbal—St. John's wort: it induces hepatic enzymes, which may reduce blood levels of other drugs. It should be discontinued 2 weeks prior to surgery.

Table 35.5 Protocol for electroconvulsive therapy

Patient preparation	History and physical, consent, equipment
Monitors	Standard monitors—ECG, blood pressure, pulse oximeter
Drugs and bite block	Drawn up and ready
Preoxygenation	3–5 min via face mask
Premedication choice	Ketorolac 30 mg IV—for postoperative muscle pains
	Glycopyrrolate 0.2 mg IV—antisialogogue, prevents or treats bradycardia
	Esmolol 10–20 mg IV/metoprolol 2–3 mg IV—for heart rate and blood pressure control
Induction	Propofol (1–1.5 mg/kg)/methohexital (0.5–1 mg/kg)—drug of choice as it activates seizure foci
Additional blood pressure cuff	(Usually on the leg) to monitor muscle activity is inflated
Muscle relaxation	Succinylcholine 0.25–1 mg/kg, one can monitor muscle twitch fade if desired
Ventilation	Controlled, positive pressure via face mask. Hyperventilation causing hypocarbia can enhance seizure duration
Bite block	Inserted
Administration of shock	All personnel clear from bed/metal
Ventilation after shock	Resumed
Patient to recovery unit	After adequate spontaneous ventilation
Postoperative issues	Rule out hypoxia, agitation (treat with lorazepam/midazolam), confusion, headache (treat with NSAIDs)

Bipolar Disorder

Mania (elation, hyperactivity) alternates with depression. Drugs used to treat bipolar disorder include lithium, lamotrigine, valproic acid, and carbamazepine. Lithium has a narrow therapeutic index (0.8–1.2 meq/l). Side effects of lithium include T-wave changes, hypothyroidism, and toxicity (confusion, tremor, muscle weakness prolongation of neuromuscular blockade, hypotension, seizures, wide QRS complex, and AV block). Blood levels of lithium should be checked preoperatively.

Schizophrenia

Disordered thinking, hallucinations, delusions, and paranoia occur (likely) due to increased dopamine activity in the brain. Antipsychotics are used to treat schizophrenia. Examples include haloperidol, chlorpromazine, and the newer atypical agents, such as risperidone, clozapine, and olanzapine. Side effects include orthostatic hypotension, extrapyramidal effects, parkinsonism-like manifestations, and prolongation of QT interval. Agranulocytosis, though rare, most commonly occurs with the atypical antipsychotic clozapine.

Neuroleptic Malignant Syndrome

This syndrome is characterized by muscle rigidity, hyperthermia, and rhabdomyolysis after ingestion of antipsychotic drugs. The syndrome may occur hours or weeks after ingestion of antipsychotics, and, in the severe form, presents in a similar picture to malignant hyperthermia. Dopamine blockade by these drugs in the basal ganglia leads to impaired thermoregulation and other manifestations. The muscle biopsy test is normal in these patents, unlike patients with malignant hyperthermia. The mortality rate with the syndrome is about 30 %, with death occurring due to renal failure or cardiac arrhythmias. Patients can be treated with dantrolene or bromocriptine (a dopamine agonist).

Electroconvulsive Therapy

- Indications—severe depression, catatonia, schizophrenia, acute mania, suicidal intentions
- Contraindications—unstable cardiac disease (recent MI), recent stroke, increased ICP, intracranial tumor, pregnancy, severe glaucoma, or retinal detachment

An ECT course is usually 6–9 treatments, administered 2–3 times per week. A maintenance ECT may be performed once a week or once a month to prevent relapse. Electrical shock is applied to one (unilateral) or both (bilateral) cerebral hemispheres, with the aim of producing a therapeutic seizure lasting 30–60 s (Table 35.5). General anesthesia with muscle relaxation is employed for ECT to prevent musculoskeletal injuries that can occur due to the violent seizure. Hyperventilation (hypocapnia) or a caffeine infusion (125–250 mg) can be used to prolong the seizure. The physiological effect of an ECT is an initial short-lived bradycardia (parasympathetic response), followed by sustained tachycardia and hypertension for a few minutes (sympathetic response). A common adverse effect of ECT is memory loss (more common with bilateral ECTs).

Clinical Review

1. Autonomic hyperreflexia may be completely abolished by:
   A. Liberal local anesthesia
   B. Spinal anesthesia
   C. Epidural anesthesia
   D. General anesthesia

2. The following type of anesthesia may be more likely to cause exacerbations of symptoms in a patient suffering from multiple sclerosis:
   A. Local anesthesia
   B. Spinal anesthesia
   C. Epidural anesthesia
   D. General anesthesia
3. In patients suffering from myasthenia gravis:
   A. Neostigmine is commonly used to differentiate a cholinergic from a myasthenic crisis.
   B. There is overexpression of acetylcholine receptors.
   C. Duration of action of succinylcholine may be shortened.
   D. Patients may be more resistant to the action of succinylcholine.
4. Mainstay of treatment of malignant hyperthermia is the administration/institution of:
   A. Calcium channel blockers
   B. Furosemide
   C. Active cooling
   D. Dantrolene
5. The following medication is contraindicated in patients suffering from parkinsonism:
   A. Metoclopramide
   B. Verapamil
   C. Digoxin
   D. Bromocriptine
6. Phenytoin, when used to treat seizure disorders, may have the following effect on non-depolarizing neuromuscular blockade:
   A. Cause phase 1 block
   B. Cause phase 2 block
   C. Shorten
   D. Prolong
7. A cerebrovascular accident is most commonly the following in nature:
   A. Hemorrhagic
   B. Embolic
   C. Thrombotic
   D. Traumatic

Answers: 1. B, 2. B, 3. D, 4. D, 5. A, 6. C, 7. C

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Ophthalmic Surgery

36

Scott Berry and Kristin Ondecko Ligda

Ophthalmologic surgeries present unique and specific challenges to the anesthesiologist. The patient population can present at extremes of age, from an infant for strabismus surgery to an elderly patient for cataract surgery. Because most patients undergoing ophthalmologic surgeries are elderly and present with multiple medical comorbidities, a thorough understanding of past medical history and current medications is essential to prevent potential adverse events. Successful delivery of anesthesia requires a fundamental knowledge of ocular physiology, intraocular pressure management, ocular and systemic effects of common medications, the oculocardiac reflex, and intraocular gas expansion. Similar to the ophthalmologic procedures themselves, anesthesia for ophthalmic procedures is both delicate and complex.

Oculocardiac Reflex

This reflex arc consists of the trigeminal nerve (mainly the ophthalmic division of cranial nerve (CN V)) forming the afferent limb, which synapses with the visceral motor nucleus of the vagus nerve (CN X) in the reticular formation of the brain stem to form the efferent limb of the reflex arc (Fig. 36.1). The reflex is elicited primarily by external pressure on the globe, traction of the extraocular muscles (medial rectus), conjunctiva, or orbital structures, and also potentially by performing an ophthalmic regional block (i.e., retrobulbar block). The most common manifestation of this reflex is sinus bradycardia, but a wide variety of cardiac dysrhythmias may occur such as atrioventricular blockage, junctional rhythms, ventricular bigeminy, or asystole.

The oculocardiac reflex is more prominent in the pediatric population, and it is thought to be due to increased vagal tone of children. In children, some anesthesiologists recommend prophylactic treatment with intravenous (IV) atropine (0.02 mg/kg) or glycopyrrolate (0.01 mg/kg) just prior to the surgical stimulus. Prophylaxis with IV atropine is currently not warranted for adults due to the risk of inducing cardiac dysrhythmias and conduction abnormalities (i.e., left bundle branch block, ventricular tachycardia, or ventricular fibrillation). Should bradycardia or other dysrhythmia occur, the first step should be to ask the surgeon to stop the surgical stimulus. Next, the patient's anesthetic depth, oxygenation, and ventilation should be re-evaluated. These steps often correct the dysrhythmia. If the conduction abnormality continues, then IV atropine can be considered. With repeated manipulation of the extraocular muscles, the reflex is less likely to occur, which is thought to be due to fatigue of the reflex arc.

Intraocular Pressure

Formation and Drainage of Aqueous Humor

The ciliary body, located in the posterior chamber of the eye, is responsible for production of two-thirds of the aqueous humor. Most of the aqueous humor is produced by an active secretory process of the carbonic anhydrase and the cytochrome oxidase systems. The remainder is produced by passive filtration of vessels on the anterior surface of the iris. Aqueous humor flows from the posterior chamber through the pupillary aperture into the anterior chamber. The aqueous humor drains out of the eye via the trabecular meshwork and then into Schlemm's canal either directly or indirectly through a network of venous channels (Fig. 36.2). Venous drainage of aqueous humor eventually leads to the superior

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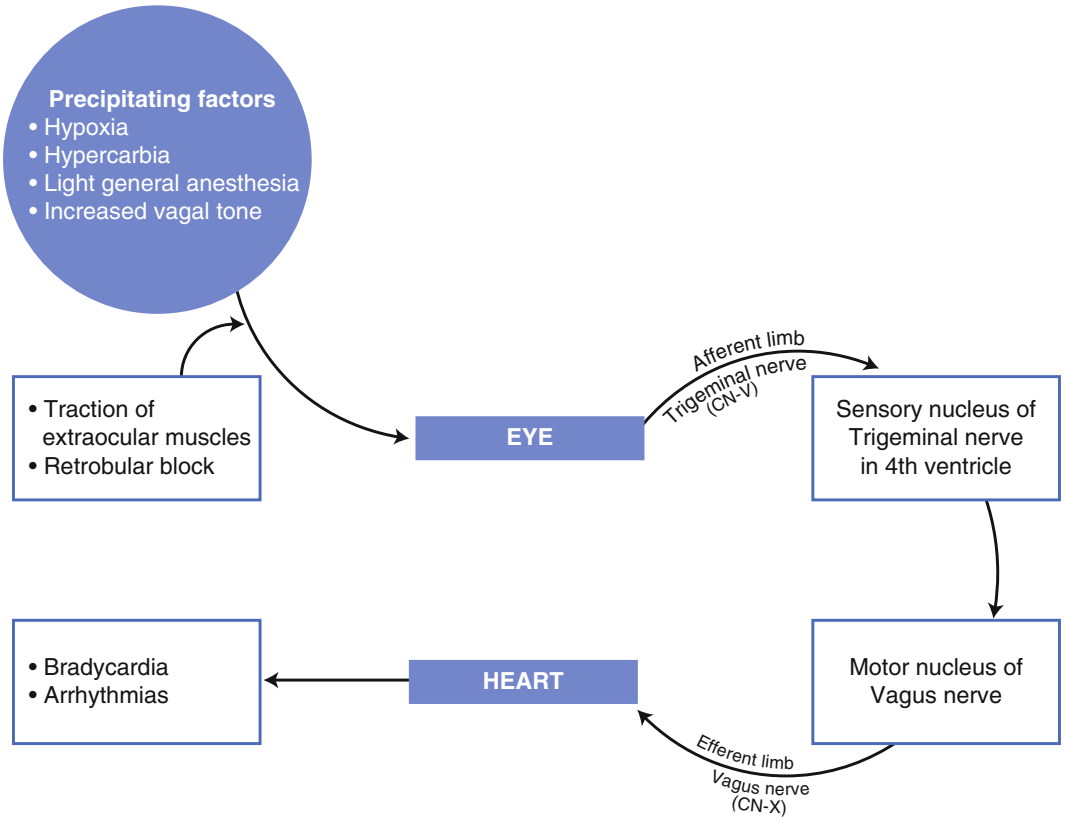
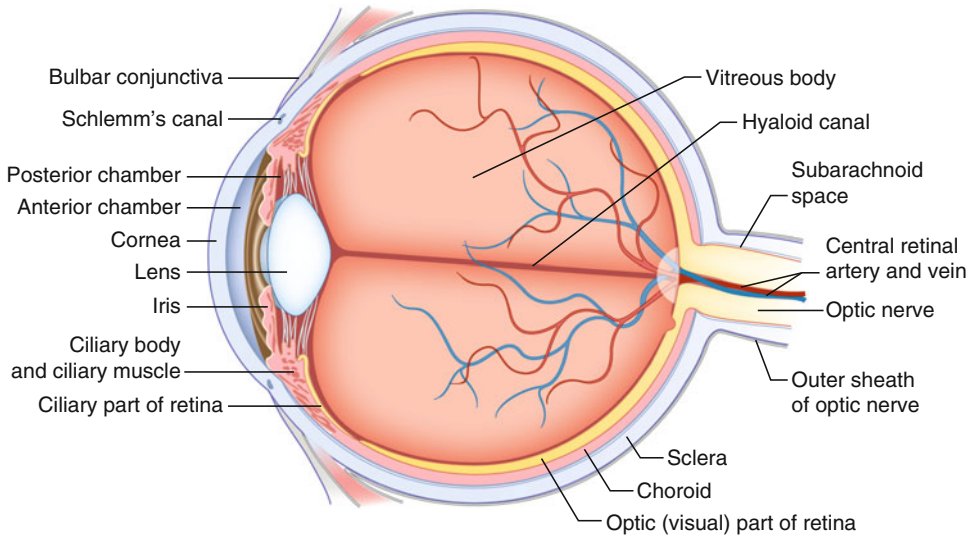


Fig. 36.1 The oculocardiac reflex. The trigeminal nerve is the afferent limb, and the vagus nerve is the efferent limb

Fig. 36.2 Ocular anatomy



vena cava and the right heart. Venous congestion (right heart failure, Valsalva maneuver, and elevated central venous pressures) will prevent aqueous humor drainage and can lead to elevated intraocular pressures.

Normal intraocular pressure (IOP) ranges from 10 to 20 mmHg. IOP will vary by 1–2 mmHg with each heartbeat and will vary by 2–5 mmHg throughout the day, with higher pressures noted after awakening. Factors that influence IOP include external pressure on the globe by the extraocular muscles and orbicularis oculi muscle, venous congestion preventing drainage of aqueous humor, orbital tumor, scleral rigidity, intraocular fluid (i.e., blood, aqueous humor), and changes in intraocular contents that are semisolid (i.e., lens, vitreous humor). Maintenance of normal IOP is vital for proper functioning of the structures of the eye. Once the globe has been penetrated, the IOP is comparable to that of atmospheric pressure.

Glaucoma

Glaucoma is caused by an obstruction to the outflow of aqueous humor, leading to elevated IOP. This causes decreased perfusion of the optic nerve with eventual loss of function and blindness. There are two types of glaucoma: open angle (most common) and closed angle. Open-angle glaucoma is caused by reduced flow of aqueous humor through the trabecular network, often presents in the elderly population, and affects the eyes bilaterally. First-line treatment consists of ophthalmic drops that produce miosis and trabecular stretching. A trabeculectomy is commonly performed under monitored anesthesia care. General anesthesia is often warranted if a goniotomy, cyclocryotherapy, or glaucoma seton implant is performed. In closed-angle glaucoma, the iris is pushed or pulled up against the posterior corneal surface, completely blocking the trabecular meshwork and preventing the drainage of aqueous humor. Surgical intervention may be necessary.

Effects of Anesthesia on Intraocular Pressure

The majority of anesthetics decrease IOP. Almost all central nervous system depressants also decrease IOP (inhalational agents, barbiturates, tranquilizers, opioids, neuroleptics, propofol, etomidate). The exact mechanism of action is unknown. The effect of ketamine on IOP is still debated. Ketamine remains a poor choice for many ophthalmologic procedures due to its side effects such as nystagmus and blepharospasm. Non-depolarizing muscle relaxants decrease intraocular pressure. Intravenous succinylcholine has been shown to increase IOP by approximately 8 mmHg within 1–4 min of administration. This increase in IOP is transient and resolution occurs within 7 min. Expulsion of vitreous from an open globe injury has been reported after use of IV succinylcholine. Pretreatment with non-depolarizing muscle relaxant is controversial.

Intravenous hypertonic solutions (i.e., mannitol and dextran) increase plasma osmotic pressure and decrease the formation of aqueous humor, thereby decreasing IOP. Intravenous acetazolamide inhibits the enzyme carbonic anhydrase, which decreases the formation of aqueous humor and decreases IOP. Hypoxia and hypercarbia elevate IOP, while hypocarbia and hypothermia decrease IOP.

Anesthetic Considerations

Regional Anesthesia

Many ophthalmologic procedures can be performed under regional anesthesia. The most common regional techniques are retrobulbar and peribulbar blocks. These typically provide adequate analgesia and akinesia of the eye. They are usually performed in conjunction with a facial nerve block to prevent squinting and allow placement of a lid speculum. Ophthalmologists often perform these blocks; however, they may also be performed by an anesthesiologist. Patient cooperation is required for completion of both retrobulbar and peribulbar blocks. Peribulbar blocks are thought to have fewer complications compared to retrobulbar blocks because the needle does not penetrate the cone formed by the extraocular muscles, as in a retrobulbar block. Some of the complications of a retrobulbar block include retrobulbar hemorrhage, globe perforation, oculocardiac reflex, injection into optic nerve sheath (and spread into the CSF) causing apnea, convulsions, optic nerve injury or atrophy, respiratory arrest, acute neurogenic pulmonary edema, and trigeminal nerve block. These regional techniques are typically not performed for procedures that will last longer than 2 h from the time of the initial block.

Goals of Monitored Anesthesia Care and General Anesthesia

For ophthalmologic procedures, the depth of anesthesia must be closely monitored. Intraoperative patient movement is the leading cause of both eye injury and anesthesiologist liability for ophthalmologic procedures. Therefore, for monitored anesthesia care, patients must be cooperative, be able to remain still and maintain their airways comfortably without coughing, and be able to respond appropriately and communicate with the anesthesiologist. Patients must also be at a comfortable temperature to avoid shivering.

For general anesthesia, a smooth induction, control of intraocular pressure, a smooth intraoperative course, preventing patient coughing and movement, and avoidance/management of the oculocardiac reflex are all essential components. Extubation should be performed prior to the patient coughing or gagging on the endotracheal tube to prevent an increase in intraocular pressure. Intravenous or endotracheal lidocaine given 1–2 min prior to extubation may help decrease coughing upon extubation. Multimodal antiemetic therapy should be utilized to prevent nausea and vomiting in the postoperative period. Total IV anesthesia with propofol may be selected if a patient is at high risk for postoperative nausea and vomiting.

Systemic Effects of Ophthalmic Drugs

Many ophthalmologic drugs are given as topical eye drops. These medications are often in much higher concentrations compared with direct systemic dosing. The systemic absorption of topical eye drops is greater than that of subcutaneous absorption but less than that of intravenous administration. An anesthesiologist must be aware that systemic absorption of these topical medications can have adverse effects (Table 36.1).

Table 36.1 Common ophthalmologic medications and their potential adverse reactions

Medication	Potential adverse reaction
Acetazolamide (decreases AH production)	Diuresis, hypokalemic metabolic acidosis
Atropine (mydriasis)	Tachycardia, flushing, central anticholinergic syndrome
Cyclopentolate	Disorientation, psychosis, convulsions, dysarthria
Echothiophate (miosis)	Prolongation of effects of mivacurium and succinylcholine (reduces activity of plasma cholinesterase), bronchospasm, bradycardia
Epinephrine	Hypertension, tachycardia, cardiac dysrhythmias, headache
Phenylephrine (pupillary dilation)	Hypertension, headache, reflex bradycardia
Scopolamine	Dryness, central anticholinergic syndrome
Timolol	Bradycardia (atropine-resistant), bronchospasm, exacerbation of congestive heart failure due to beta-blocking activity

Ocular Injuries During Anesthesia

Corneal abrasions are the most common eye injury during anesthesia. Proper taping of the eyes prior to mask ventilation and intubation may help prevent such injuries from occurring. Other injuries include hemorrhagic retinopathy, retinal ischemia (prone position with pressure on the eye), ischemic optic neuropathy, cortical blindness, acute glaucoma, chemical injury, or injury due to lasers used on the surgical field. Ischemic optic neuropathy can occur due to decreased oxygenation of the optic nerve, which results from decreased perfusion of the optic nerve. Perfusion pressure of the optic nerve (PON) is the difference between the mean arterial pressure and intraocular pressure (PON = MAP-IOP). Proper eye protection should always be evaluated for each surgical case, and frequent evaluation of external pressure on the eye should be performed, especially in both the prone and jackknife positioning. An anesthesiologist must be vigilant to reduce the risk of ocular injuries during anesthesia. Institutional policies should be followed should an ocular injury be suspected.

Specific Ophthalmic Procedures

Intraocular Gas Expansion and Retinal Detachment Surgery

Surgical correction of a retinal detachment may consist of the ophthalmologist injecting a gas bubble into the vitreous to aid mechanical reattachment of the retina. This gas may consist of air, sulfur hexafluoride, perfluoropropane, or octafluorocyclobutane. It is highly recommended to terminate the use of nitrous oxide 15 min prior to injection of the gas bubble. Nitrous oxide is over 30 times more soluble than nitrogen (78 % constituent of air) and 117 times more soluble than sulfur hexafluoride. Nitrous oxide will diffuse into the injected gas bubble and cause a rapid expansion of the bubble. If the globe is closed, then intraocular pressure will increase. Later discontinuation of the nitrous oxide will lead to reabsorption of the gas, a decrease in intraocular pressure, and possible detachment of the recently corrected retina. An injected bubble will be absorbed by the body in approximately 5 days for air, 10 days for sulfur hexafluoride, and over 30 days for perfluoropropane. Therefore, the use of nitrous oxide should be avoided if a patient requires anesthesia within these time frames of gas reabsorption to avoid expansion of the gas bubble and the negative sequelae associated with this process.

Traumatic Open Eye Injury

An open globe injury presents a unique clinical scenario where an anesthesiologist must balance a risk of aspiration in a trauma patient with assumed full stomach and further eye injury from elevated IOP and possible extrusion of eye contents. For premedication, the patient should receive a proton pump inhibitor, H_2 blocker, or sodium bicitrate to elevate gastric pH and reduce gastric acid production. A prokinetic agent (metoclopramide) may also be useful to promote gastric emptying. A rapid sequence induction (RSI) with propofol and non-depolarizing muscle relaxant decreases the risk of aspiration and may lead to decreased IOP. A twitch monitor may be used at time of RSI to evaluate when the muscle relaxant's effect is optimal for intubation to avoid coughing and gagging. Succinylcholine is not indicated given the risk of elevated IOP and potential extrusion of eye contents. If a patient is suspected of being a difficult airway, then a discussion must take place with the ophthalmologist to discuss the risks and benefits. Regional anesthesia with MAC or an awake fiberoptic intubation may be warranted in the patient with a difficult airway.

Strabismus Surgery

This is the most common pediatric operation performed in the United States and involves significant manipulation of the extraocular muscles, which may elicit the oculocardiac reflex or lead to increased risk for postoperative nausea and vomiting. Multimodal antiemetic therapy is necessary. Anesthesia may be provided with a laryngeal mask airway or endotracheal intubation. Succinylcholine has been shown to alter the forced duction test (FDT), which is used to assess eye movement during strabismus surgery, and ophthalmologists should wait 20 min after administration of succinylcholine prior to performing the FDT.

Clinical Review

1. First step in the management of an oculocardiac reflex is
   A. Administration of atropine
   B. Administration of glycopyrrolate
   C. Communicating with the surgeon
   D. Maintaining the airway, breathing, and circulation
2. The following drug prolongs the action of succinylcholine
   A. Acetazolamide
   B. Echothiophate
   C. Cyclopentolate
   D. Scopolamine
3. The following muscle relaxant may not be used for inducing general anesthesia in a patient with traumatic open eye injury
   A. Succinylcholine
   B. Midazolam
   C. Pancuronium
   D. Diazepam
4. The most common ophthalmic injury during anesthesia is
   A. Retinal ischemia
   B. Ischemic optic neuropathy
   C. Cortical blindness
   D. Corneal abrasion
5. The strategies to prevent high intraocular pressure during anesthesia include all, EXCEPT
   A. Avoid pressure on the eye globe
   B. Prevent coughing
   C. Adequate depth of anesthesia before laryngoscopy
   D. Administration of succinylcholine to provide muscle relaxation

Answers: 1. C, 2. B, 3. A, 4. D, 5. D

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Ear, Nose, and Throat Surgery

37

M. Christopher Adams and Edward A. Bittner

Otorhinolaryngologic procedures comprise some of the most commonly performed surgical procedures for adults and children. These procedures range from simple day-surgery operations such as myringotomy to complex head and neck reconstruction surgery performed in specialized centers. A wide range of anesthetic techniques are routinely provided for otorhinolaryngologic surgery including mask anesthetics, spontaneous or jet ventilation, difficult airway management, controlled hypotension, and extubation during deep levels of anesthesia. Safe conduct of anesthesia for these procedures requires understanding and knowledge of the common pathologies involved and the surgical procedures that will be performed. The diversity and complicated nature of these procedures require a high level of cooperation between the anesthesia and surgical teams since access to the airway is often shared.

Although otorhinolaryngologic surgery is often performed on an outpatient basis and is generally straightforward, it has potential for a disproportionate number of complications. Factors contributing to these potential complications are listed in Table 37.1. These potential complications are best avoided through preoperative assessment and preparation, meticulous airway management, vigilance, and timely intervention before problems become severe. This chapter provides an overview of the anesthetic management for some commonly performed otolaryngologic procedures and describes some unique considerations for patients undergoing this type of specialized perioperative care.

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Middle Ear Surgery

Middle ear disease requiring surgery affects patients of all ages. Common middle ear surgeries in children include myringotomy, tympanoplasty, and mastoidectomy, whereas common middle ear surgeries in adults include tympanoplasty, stapedectomy or ossiculoplasty, mastoidectomy, and removal of cholesteatoma. Some of these procedures can be performed under local anesthesia, although general anesthesia is often required. Primary anesthetic considerations include attention to patient positioning, facial nerve preservation, adequate hemostasis, use of nitrous oxide, smooth emergence, and prevention of PONV.

Myringotomy and Tympanostomy Tube Placement

Myringotomy and tympanostomy tube placement are used to improve middle ear aeration and hearing in patients with chronic otitis media (OM). Preoperative evaluation should assess for signs and symptoms of upper respiratory tract infection (URI) since URI often accompanies otitis media and is associated with increased airway reactivity. Some patients with chronic OM may show signs of obstructive sleep apnea due to adenoidal hypertrophy. Since the primary surgical population is pediatric and operative time is brief, a mask induction with sevoflurane is frequently followed with the patient breathing spontaneously with the head positioned to one side. Premedication is often avoided since its effects will outlast the duration of the procedure. Intranasal fentanyl can be added to oral or rectal acetaminophen to provide analgesia, as many practitioners perform this anesthetic without placing an intravenous line.

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DOI 10.1007/978-1-4939-1737-2_37,

Table 37.1 Factors which may contribute to increased complications with ENT surgery

• Airway is shared with surgeon
• Patient is often positioned away from anesthesia provider
• Airway irritability or obstruction due to presence of blood or secretions or frequent URIs
• Presence of congenital abnormalities of the airway
• Potential for blood loss leading to hypovolemia
• High incidence of nausea and vomiting

Myringoplasty, Tympanoplasty, and Mastoidectomy

Myringoplasty is performed to repair a perforation of the tympanic membrane, while tympanoplasty is performed to reconstruct the tympanic membrane. Mastoidectomy is performed to remove infected air cells within the mastoid bone. Anesthetic considerations for these procedures are similar and include minimization or avoidance of the use of nitrous oxide, need for a bloodless surgical field, facial nerve monitoring, and high incidence of PONV. There are, however, particular concerns for maintenance of and emergence from anesthesia.

The facial nerve runs through the middle ear in close relation to the ossicles and through the mastoid before emerging from the skull. Therefore, it is at risk for injury during otologic procedures and, accordingly, intraoperative monitoring of evoked facial nerve electromyographic activity is often employed. This requires avoidance of long-acting neuromuscular blockers, which may mandate a deeper plane of anesthesia so as to ensure immobility.

For maintenance of anesthesia, nitrous oxide is frequently avoided since normal venting of middle ear pressure can be compromised by trauma, inflammation, edema, or congenital abnormalities, resulting in an increase in middle ear pressure. Conversely, the abrupt cessation of nitrous oxide can result in rapid resorption, creating a net negative pressure within the middle ear. These pressure changes may result in alteration of middle ear anatomy, displacement of surgical grafts, and potential rupture of the tympanic membrane. Additionally, nitrous oxide may contribute to the risk of postoperative nausea and vomiting. Consequently, nitrous oxide should be used with caution and for indications that cannot be met with other approaches.

A bloodless operative field is essential as even a few drops of blood can obscure the surgical field. Techniques to minimize bleeding include head-up tilt 15–20° to avoid venous obstruction, epinephrine infiltration by the surgeon, and controlled hypotension (MAP< 10–20 % of normal). It is desirable to avoid coughing by the patient on emergence as this increases the risk of postoperative bleeding and displacement of finely positioned prosthetics. As such, extubating/removal of the LMA under a deep plane of anesthesia is commonly performed. As mentioned previously, postoperative nausea and vomiting are common after middle ear surgery. A multimodal pharmacologic approach to both prophylaxis and treatment is needed. Ensuring adequate hydration, avoiding nitrous oxide and use of TIVA can also help to reduce PONV.

Nasal and Sinus Surgery

Common nasal and sinus surgical procedures include rhinoplasty (functional and/or cosmetic), functional endoscopic sinus surgery, and skull base approaches to neurosurgical procedures. Newer developments in endoscopic surgeries include stereotactic guidance systems, which permit real-time guidance of surgical instruments based on imaging. Superficial nasal surgery can be performed in a physician's office with local anesthesia or sedation while general anesthesia is used for longer and more invasive procedures in order to provide immobility, airway protection, and amnesia. A special consideration in nasal surgery is the use of vasoconstrictors such as cocaine or epinephrine administered by the surgeon to reduce bleeding. These agents may have profound effects on the cardiovascular system including tachycardia, hypertension, and arrhythmias. These effects are particularly significant in the elderly and in patients with preexisting cardiac disease.

Anesthetic Considerations

For induction of anesthesia, attention should be given to patient factors that may render positive pressure mask ventilation difficult or serve as a contraindication to its use. Obstructive processes involving the nasal passages may eliminate that route for ventilation. Patients who present with nasal cerebrospinal fluid leaks from trauma, prior skull base surgery, or invasive tumors should not receive positive pressure mask ventilation, as this can lead to bacterial translocation, pneumocephalus, and herniation.

Endotracheal intubation is most commonly used for nasal, septal, and sinus surgery. An oral RAE endotracheal tube secured to the lower mandible is frequently utilized to permit full access to the surgical field. In rhinoplasty, it is important to secure the tube in the midline without tension, to prevent distortion of the natural appearance of the nose. For facial surgery particular attention should be given to protecting the eyes, preferably with fully occlusive dressings, as surgical preparation solutions may otherwise enter and damage the eye.

Blood loss can be substantial and difficult to estimate during nasal surgery. Deliberate hypotension is a strategy that may be employed to reducing surgical bleeding, with an attempt made to decrease systolic blood pressure to 90 mmHg or lower. Conditions such as chronic hypertension, cardiovascular

disease, or cerebrovascular disease may pose contraindications to deliberate hypotension. Decreased blood pressure is frequently obtained by deepening the plane of anesthesia with inhalational agent or hypnotic infusions or by the addition of short-acting opioid infusions such as remifentanil. Intermediate-acting vasodilators such as labetalol or hydralazine may also be of use. Finally, placing the patient in a backup or reverse Trendelenburg position can also help to lower systolic blood pressure and reduce bleeding. Placement of a throat pack is important to reduce drainage of blood into the stomach. All members of the operating team should be notified both of the pack's placement and its removal since retention of throat packs can result in postoperative airway obstruction.

Several issues present themselves as patients emerge from anesthesia following nasal surgery: coughing and valsalva on emergence and extubation should be avoided since elevated central venous pressure can be transmitted to nasal venous plexuses and result in significant postoperative bleeding. Extubating the trachea while the patient is still under a deep plane of anesthesia is a method sometimes used to prevent coughing. Blood often drains into the stomach during surgery despite attempts to occlude the esophagus with a throat pack. Passage of an orogastric tube or soft suction catheter into the stomach to evacuate any swallowed blood prior to extubation may be helpful to reduce the incidence of PONV.

Finally, adequate, spontaneous ventilation should be assured prior to extubation of the trachea, as positive pressure mask ventilation with a full-face mask may be both painful and detrimental to surgical repair. If mask ventilation should be required, a pediatric face mask may be rotated 90° and placed over the patient's mouth. Surgical packs in the nose should prevent leakage via the nares. For transport to the postanesthesia care unit, supplemental oxygen may be supplied via face tent, "blow-by," or by a standard facemask that has been custom-cut to exclude the nose.

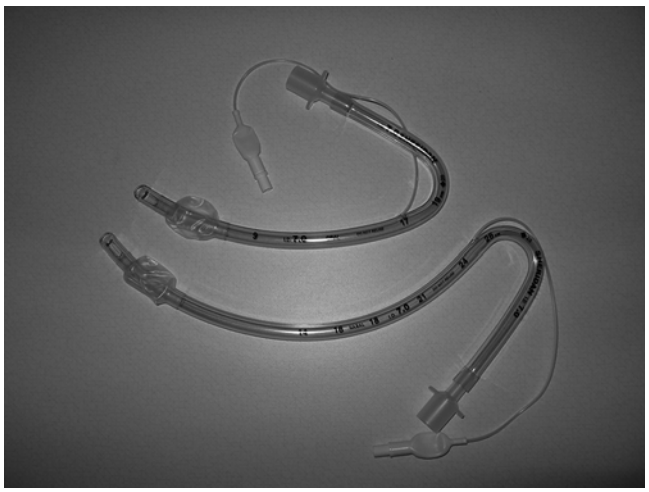

Fig. 37.1 An oral (*top*) and a nasal (*bottom*) RAE tube

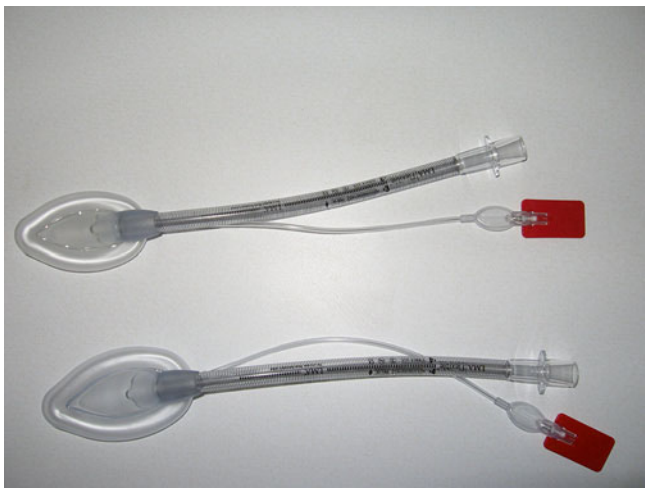

Fig. 37.2 Flexible laryngeal (LMA) mask airways

Tonsillectomy and Adenoidectomy

Tonsillectomy, one of the most common performed airway procedures in children, is performed for the treatment of chronic or recurrent tonsillitis or obstructive tonsillar hyperplasia. Children with adenotonsillar hypertrophy can present with nasal obstruction, recurrent infections, obstructive sleep apnea, otitis media, and deafness due to Eustachian tube dysfunction. Preoperative assessment should focus on airway considerations including history of recent URI, history of obstructive sleep apnea (OSA), presence of loose teeth, as well as assessment for presence of bleeding disorders. Patients with a recent upper respiratory tract infection are at increased risk for airway reactivity and laryngospasm, while patients with OSA are often obese and may pose difficulties with airway management.

Children often receive an inhalational induction followed by IV placement. Continuous positive end-expiratory pressure during induction may be beneficial in reducing airway obstruction. Placement of a cuffed endotracheal tube (ETT) will reduce the risk of aspiration of blood during the surgical procedure. Oral RAE tubes (Fig. 37.1) may provide better visualization of the surgical field and be less prone to kinking with placement of retractors. Some centers commonly use a flexible LMA for performing this procedure (Fig. 37.2). In addition, supraglottic packing may be inserted to limit drainage of blood during the procedure. At the end of the procedure, the throat pack should be removed, the stomach emptied with an oro- or nasogastric tube, and the oropharynx suctioned. Prophylactic antiemetics should be administered to decrease the high incidence of PONV. Tracheal extubation should be performed when the patient is awake and able to protect his airway.

Hemorrhage from a bleeding tonsil in the postoperative period is a recognized complication of tonsillectomy and is a surgical emergency. Post-tonsillectomy hemorrhage most commonly occurs with 24 h of surgery (primary hemorrhage) but can occur anytime thereafter. The anesthetic risks in a patient with a bleeding tonsil include hypovolemia, risk of pulmonary aspiration of blood, and potential risk of a difficult intubation due to the presence of ongoing bleeding. Appropriate intravenous access and fluid resuscitation are needed before reoperation since induction in a hypovolemic child can precipitate cardiovascular collapse. Hemoglobin, coagulation studies, and the availability of blood products should be ascertained, and transfusion should occur as needed. Preoxygenation and rapid sequence induction should be performed to ensure rapid control of the airway. Slight head-down position during induction may protect against pulmonary aspiration of blood or stomach contents. Prior to extubation a nasogastric tube should be used to empty the stomach. Extubation should be performed with the patient fully awake and able to protect his airway. Postoperatively, the patient should be closely monitored for the occurrence of rebleeding.

Tracheostomy

Tracheostomy is an operative procedure which creates a surgical airway in the cervical trachea. Tracheostomy is most commonly performed in patients who cannot be liberated from mechanical ventilation and who have suffered severe trauma or neurologic insult and need ongoing pulmonary toilet or in order to bypass the upper airway in cases of head and neck cancers. Advantages of tracheostomy over endotracheal intubation include improved patient comfort, decreased requirements for sedation, more effective pulmonary toilet, and increased airway security. There are two types of tracheostomy placement: surgical and percutaneous dilatational. While surgical tracheostomy is generally performed in the operating room, percutaneous dilatational tracheostomy lends itself to being performed at the bedside in the intensive care unit.

Anesthetic Considerations

Tracheostomy requires close coordination between the anesthesiologist and operator. The majority of patients undergoing tracheostomy are already being ventilated via an endotracheal tube. General anesthesia with muscle relaxation is generally provided to blunt the stimulating effects of the airway surgery and prevent patient movement. One hundred percent oxygen is delivered to maximize tissue oxygenation prior to periods of decreased ventilation which occur during the procedure. The surgeon begins the procedure with dissection down to the trachea. Before the surgeon cuts into the tracheal rings the endotracheal tube cuff is deflated and withdrawn into the upper trachea to avoid cuff perforation. Electrocautery should not be used to enter the trachea since ignition of the oxygen-rich environment in the trachea can lead to airway fire. After the tracheal wall is transected, the tracheostomy tube is inserted. The tracheostomy tube is then connected to the breathing circuit, and the tube position is confirmed by capnography and chest rise. The ETT remains in place within the upper trachea until the tracheostomy tube placement is confirmed and secured.

Tracheostomy is associated with both early and late complications, some of which may be life-threatening. Early complications include bleeding, pneumothorax, development of subcutaneous emphysema, tube obstruction from blood, clot or mucus, and tube dislodgement. Tube dislodgement early after tracheostomy is a particularly life-threatening complication since the tracheal stoma is immature and attempts to replace the tracheostomy can lead to false passage. Late complications include tracheal stenosis, tracheal necrosis, tracheoesophageal fistula, and tracheo-innominate fistula formation. Tracheo-innominate fistula formation can result in massive bleeding into the airway and is often fatal.

Head and Neck Surgery

Head and neck surgery for cancer composes a diverse group of procedures that may include laryngectomy, pharyngectomy, hemimandibulectomy, parotidectomy, or radical neck dissection. A variety of macrosurgical and microsurgical techniques involving soft tissue and bone may be used and tissue flap reconstruction may be required. These cases can be complex and lengthy. A thorough preoperative assessment is important since patients scheduled for head and neck surgery are often elderly and have a variety of comorbidities including hypertension, coronary artery disease, and chronic obstructive pulmonary disease from smoking and heavy alcohol use. In addition, they are often debilitated and suffer from malnutrition resulting from the effects of cancer.

Primary anesthetic concerns include establishing and maintaining a secure airway, preparation for bleeding, and nerve monitoring. Distortion of the oropharyngeal and/or laryngeal structures may result from tumor, prior surgery, or radiation treatment. In addition, radiation may lead to complications such as tissue friability and fibrosis or spondylosis of the temporomandibular joint, resulting in limited mouth opening or neck mobility. A well thought-out plan for airway management is essential; this might require an awake fiberoptic intubation or that an elective tracheostomy is performed under local anesthesia. In cases with potential for airway difficulty, the surgeon should be present and be prepared to perform an emergent surgical airway if needed. Given the proximity of the surgery to the airway, a wire reinforced (“armored”)

endotracheal tube may be beneficial to prevent kinking during the surgical procedure. The anesthesiologist must be vigilant to detect instances of unintended extubation.

In cases of flap reconstructive surgery, attention must be paid to providing adequate perfusion to the flap both during harvest and after implantation through maintenance of normothermia and ensuring adequate hydration. Minimizing the use of vasoconstrictors may also be desirable, although recent data indicate that vasopressor use during flap creation does not significantly increase the rate of graft failure or complications. Close communication with the surgical team will help to provide appropriate care in each case.

Larger head and neck reconstructive procedures can be notable for their length and potential for blood loss. The anesthesiologist should consider placement of large-bore intravenous access and intra-arterial blood pressure monitoring (especially as dictated by comorbidities) and ensure blood product availability. During surgical dissection, traction or pressure on the carotid sinus or stellate ganglion can cause wide fluctuations in blood pressure and dysrhythmias including bradycardia and asystole. The treatment is immediate cessation of the stimulus. Infiltration of the carotid sheath with local anesthetic may mitigate such effects. Neck dissection entails risk of injury to a number of nerves. Accordingly, peripheral nerve monitoring is frequently employed, posing a contraindication to long-acting neuromuscular blockade.

Postoperatively, the anesthesiologist should be aware of the potential for nerve injury and the presence of laryngeal edema following surgical manipulation. If airway compromise is anticipated postoperatively, then the patient should be left intubated and an elective tracheostomy may need to be performed. Injury to the recurrent laryngeal nerve can cause vocal cord dysfunction, with bilateral injury causing airway obstruction. Phrenic nerve injury can result in hemidiaphragmatic paralysis. Hematoma formation in the neck can rapidly result in airway compromise. Following laryngectomy, all caretakers should be aware that there no longer exists a conduit between the oropharynx and the trachea. Mask ventilation and intubation from above will be impossible; these may only be accomplished via the tracheostomy.

Laryngeal Surgery

Patients with laryngeal pathology are potentially difficult to ventilate and intubate. Patient symptoms and physical examination findings provide indicators of potential airway difficulty. Symptoms such as hoarseness or stridor may be indicators of vocal cord involvement, while dyspnea and shortness of breath may occur as a result of mass effect or cord fixation. Prior surgery and radiation can cause anatomic distortion and dysfunction and may increase the risk of aspiration and hemorrhage. During the basic physical examination, the neck should be palpated for evidence of masses, tracheal deviation, and tissue plasticity. Recent results of imaging studies can be useful in assessing the extent of airway compromise. If potential problems with a patient's airway are identified, an approach should be devised for establishing adequate airway control. Both the patient and the surgical team should be informed of the options discussed, including elective tracheostomy. Plans may need to include having a surgeon and instruments on hand for an emergency tracheostomy.

Surgery on the larynx and glottic structures commonly utilizes suspension microlaryngoscopy, a suspension laryngoscope in conjunction with an operating microscope. Using a supportive apparatus, the patient's head and neck are suspended from the bed, permitting visualization and bimanual access to the surgical field. Microlaryngoscopy is widely used for diagnosis of laryngeal lesions, biopsy, and resection of vocal cord tumors. Anesthetic technique must provide a secure airway, adequate ventilation, immobile vocal cords, and no risk of combustion, without time limitation for operative intervention.

Maxillofacial Reconstruction

Maxillofacial reconstruction is performed to repair facial trauma or correct facial deformity. Fractures of the midface are described by the plane of injury according to the Le Fort classification (Fig. 37.3). A type 1 Le Fort fracture is a horizontal maxillary fracture, separating the teeth from the upper face. The fracture line passes through the alveolar ridge, lateral nose, and inferior wall of the maxillary sinus. A type 2 Le Fort fracture is a pyramidal fracture, with the teeth at the pyramid base and nasofrontal suture at its apex. The fracture arch passes through the posterior alveolar ridge, lateral walls of the maxillary sinuses, inferior orbital rim, and nasal bones. In a type 3 Le Fort fracture, the fracture line passes through the nasofrontal suture, maxillo-frontal suture, orbital wall, and zygomatic arch resulting in complete craniofacial separation. Le Fort fractures are created for certain types of cosmetic surgery. Although nasotracheal intubation facilitates better access for repair of facial fractures, orotracheal intubation is necessary when intranasal damage is present. Nasal intubations are contraindicated in Le Fort type 2 and type 3 fractures.

Special Considerations for ENT Surgery

Laser Surgery

The laser has become an important tool for surgeons in many specialized areas especially for the otorhinolaryngologic surgeon performing laryngeal or tracheobronchial surgery.

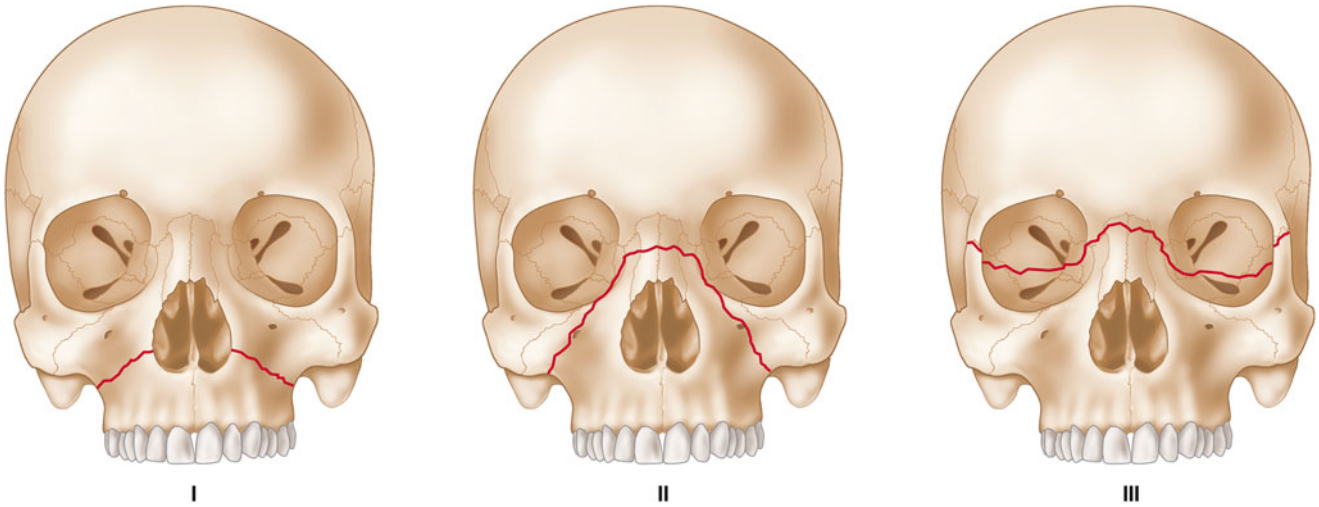

Fig. 37.3 Le Fort classification of facial fractures

The word laser is an acronym for "light amplification by stimulated emission of radiation." A laser allows delivery of high intensity light energy into a small area, allowing precise resection of tissue and hemostasis. Different types of lasers have differing energy properties including different wavelengths, tissue penetrations, and thermal effects. Advantages of using the laser over conventional surgical techniques are the precision of the technique, easier control of bleeding, removal of tissue by vaporization, and the ability to reach distant pathology without compromising the airway. Lasers may be used in conjunction with rigid bronchoscopy, laryngoscopy with jet ventilation, or traditional endotracheal intubation.

The various laser types that are employed include those based on gas media (e.g., CO_2, argon) and solid media (e.g., potassium-titanyl-phosphate [KTP], neodymium:yttrium-aluminum-garnet [Nd:YAG]). The CO_2 laser emits an infrared beam of wavelength 10,600 nm that is not directly visible so a low-energy red targeting laser usually accompanies the beam. Tissue is vaporized by the energy of the beam, and because of its long wavelength, there is little absorption of energy by deeper tissues. The CO_2 laser can be focused to very fine limits which allow it to be used as a precision cutting instrument or as a tissue vaporizer. The KTP laser is green colored at a 532 nm wavelength which can be transmitted fiberoptically. The beam is absorbed by hemoglobin leading to good hemostasis but also potentially resulting in deeper thermal burn and greater tissue damage. The laser is often used for very vascular areas such as the tongue, nose, and deep in the trachea.

Laser surgery requires special preparation and safety precautions because of the potential of tissue damage, combustion, and exposure to the laser plume. Operating personnel must be familiar with laser safety. OR doors must be closed, windows covered, and warning signs in place to identify that a laser is in use. The patient's eyes should be protected and all tissues adjacent to the surgical area protected with moist gauze. OR personnel should wear protective eyewear specific for the laser wavelength as well as an appropriate mask to protect from exposure to the potentially toxic or infectious aerosolized particles resulting from the laser plume. The procedure should utilize special endotracheal tubes (e.g., laser-tubus or laser-flex tubes; Fig. 37.4) and surgical instruments that are noncombustible. The endotracheal tube cuff may be inflated with saline dyed with methylene blue (to indicate rupture) instead of air.

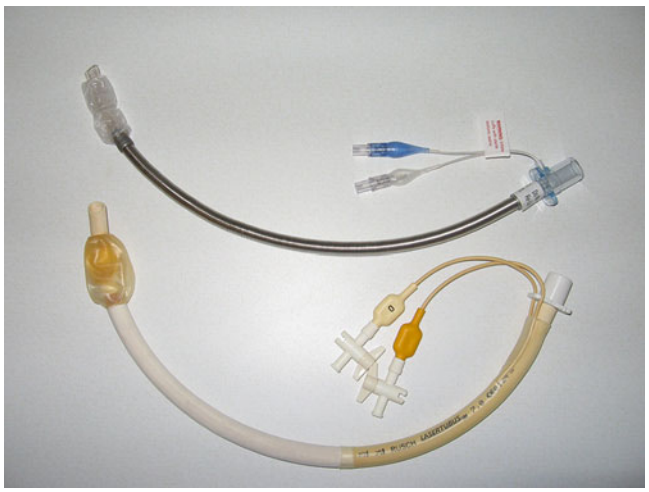

Fig. 37.4 Specialized endotracheal laser tubes

Jet Ventilation

Jet ventilation (JV) involves the delivery of gas under high pressure through an unblocked catheter into the airway that is open to ambient air. Jet ventilation takes advantage of the

Table 37.2 Advantages and disadvantages of high-frequency jet ventilation

Advantages
• Improved visibility and surgical access
• Less hemodynamic effects than regular positive pressure ventilation
• Useful in emergency transtracheal jet ventilation
Disadvantages
• Risk of barotrauma
• Less efficient gas exchange
• High required gas flow
• Humidification of delivered gas is difficult
• Not possible to use inhalational volatile agents

Table 37.3 Complications of jet ventilation

• Barotrauma—Pneumothorax, subcutaneous emphysema, pneumoperitoneum, pneumomediastinum
• Catheter malposition—Gastric distention or rupture, dysrhythmias
• Inadequate gas exchange—hypoxemia, hypercapnia

Table 37.4 Steps for management of an airway fire

1. Remove the endotracheal tube
2. Stop the flow of oxygen and other gases
3. Remove sponges, drapes, and any flammable material
4. Pour saline into the airway
5. Reestablish ventilation
6. Bronchoscopy by surgeon

Venturi effect to entrain room air, resulting in convective ventilation of the distal airways. Jet ventilation can be delivered via supraglottic, infra-glottic, or transtracheal catheters. While insufflation of gas into the airway is an active process, exhalation is passive. Parameters that can be altered include the inspired oxygen concentration, driving pressure of the gas, frequency of ventilation, and inspiratory time.

Jet ventilation is useful in situations where access to the airway is hindered by the presence of airway equipment such as an endotracheal tube or when the airway equipment might be adversely affected (kinked, dislodged, ignited). JV either does not require an ETT or only requires a narrow catheter resistant to ignition by laser beams. General anesthesia must be maintained by intravenous agents when jet ventilation is used. Disadvantages of JV include lack of airway protection by cuffed ETT, inability to monitor CO_2 concentration, and risk of barotrauma. Difficulties in maintaining oxygenation or ventilation with JV can be encountered in certain patients including those with morbid obesity, stiff chests, and restrictive or obstructive lung diseases and patients with reduced alveolar capillary diffusion capacity. A comparison of the advantages and disadvantages of JV as well as potential complications is summarized in Tables 37.2 and 37.3.

Airway Fire

Otolaryngologic surgeries that use an ignition source such as an electrosurgery unit (ESU) or laser pose a significant and potentially deadly complication risk of airway fire. When an endotracheal tube filled with oxygen and/or nitrous oxide is ignited, it can act as a blowtorch, sending heat and flames down the trachea to burn tissues throughout the airway. Traditional endotracheal tubes made of polyvinylchloride can be ignited with oxygen concentrations as low as 26 %, making them unsuitable for surgery with ESU or laser in proximity to the airway. Specialized endotracheal tubes which incorporate flexible metals into the tubes render them laser resistant. For airway surgery involving a laser, the FiO_2 should be limited to 30 % or less when possible and nitrous oxide should be avoided. An ESU should not be used to enter the trachea. Soaked gauze should be placed within and around the airway to reduce ignition risk.

If an airway fire occurs, immediate action is needed (Table 37.4): the ETT should be removed, flow of airway gases should be discontinued, sponges and flammable materials should be removed from the airway, and saline should be poured into the airway. If the fire is not extinguished using this approach, then a CO_2 fire extinguisher should be used. Once the fire is extinguished, ventilation can be reestablished with avoidance of an oxygen-enriched environment and the airway should be evaluated by bronchoscopy to remove fragments if present and assess injury. All operating room staff should be prepared for an airway fire.

Angioedema

Angioedema is the acute onset of nonpitting edema of skin, mucosa, and subcutaneous tissues which may be hereditary or nonhereditary in etiology. Hereditary angioedema is a rare, autosomal dominant disorder characterized by recurrent attacks resulting from a deficiency of C1 esterase inhibitor enzyme. The etiology of nonhereditary angioedema can be: acquired C1 esterase inhibitor deficiency; idiopathic allergic reaction to food, drugs, and various inhalants; or immune complex diseases. Angiotensin-converting enzyme inhibitors are one of the most common causes of nonhereditary angioedema, accounting for more than 25 % of cases. Other drugs which have been reported to precipitate angioedema include aspirin, nonsteroidal anti-inflammatory drugs, radiocontrast media, angiotensin II receptor antagonists, and certain antibiotics. Attacks of angioedema can vary in severity from mild facial edema to fatal airway obstruction. Areas commonly affected include face, lips, tongue, pharynx, and supraglottic and subglottic structures, although it can also affect hands and feet, mucus membranes, and genitalia. Patients with angioedema present with dyspnea, dysphagia,

stridor, and dysphonia with rapid progression to life-threatening airway obstruction.

Immediate treatment is focused on airway management. Endotracheal intubation should be strongly considered early in the management of angioedema. An airway compromised by swelling of the tongue and pharyngeal and laryngeal tissues can render intubation difficult or impossible. Increased oral secretions and distorted airway anatomy may further complicate airway management. There are reports of blind nasotracheal intubation succeeding in cases where use of the fiberoptic bronchoscope failed. Finally, should airway compromise be imminent and attempts at oro- or nasotracheal intubation prove unsuccessful, cricothyrotomy should be performed. Steroids, antihistamines, and epinephrine are often part of treatment for angioedema, although there is limited data demonstrating their efficacy. Fresh frozen plasma (FFP) has been used as a treatment option for patients with hereditary angioedema and with angiotensin-converting enzyme inhibitor-associated angioedema. The benefit of FFP for treatment of hereditary angioedema may result from the presence of Cl esterase inhibitor, while for patients with angiotensin-converting enzyme inhibitor-associated angioedema, the benefit of fresh frozen plasma may be due to the effect of kininase II in breaking down accumulated bradykinin.

Infections of the Neck and Airway

Patients with infections of the neck and airway may present with the need for emergency airway management that can be clinically challenging. An overview of some of the more common infections is described along with strategies for airway management.

Epiglottitis

Epiglottitis is an inflammation of the supraglottic structures that is more prevalent in young children (peak incidence 1–3 years) but can occur at any age. Traditionally, epiglottitis has been associated with *Haemophilus influenza* infection, and the incidence of this condition has been decreasing in the face of vaccination against *Haemophilus influenza* type B vaccination. The classic presentation is a child that is anxious, drooling, and adopting a characteristic sniffing position sitting forward with the head extended. Epiglottitis in adults typically has a slower onset of symptoms with dysphagia and sore throat preceding stridor, a more diffuse anatomic involvement and decreased incidence of need for airway intervention.

In a nontoxic patient without respiratory compromise, imaging either with CT or lateral neck radiographs may be undertaken to confirm the diagnosis. A lateral radiograph of the neck may show the characteristic "thumb sign" of a severely swollen epiglottis. Stridor is a late feature and imaging should not delay securing the airway with confirmation of diagnosis at laryngoscopy.

Management of acute epiglottitis is directed at first securing the airway, followed by medical treatment with antibiotics. Principles of airway management in children with epiglottitis include keeping the child as calm as feasibly possible and avoiding any airway manipulation until the patient is transported to the operating room. An inhalational induction of anesthesia is often performed with the patient in the sitting position in order to maintain airway patency and spontaneous ventilation. Once an adequate depth of anesthesia has been obtained, endotracheal intubation may be accomplished by direct laryngoscopy, with either an oro- or nasotracheal tube. Emergency airway equipment including a fiberoptic bronchoscope should be on hand, as well as the capability to perform a surgical airway. The diameter of the endotracheal tube used will frequently need to be downsized.

Retropharyngeal Abscess and Ludwig's Angina

Retropharyngeal abscess most commonly occurs due to a bacterial infection of the retropharyngeal spaces which results from tonsillar or dental infections. Other causes of retropharyngeal abscess include trauma from esophageal instrumentation, foreign bodies, and spread of infection from communicating spaces. Symptoms include odynophagia, dysphagia, dyspnea, and stiff neck. Respiratory distress and airway compromise can result from inflammation and anterior displacement of the pharyngeal wall and supraglottic structures. Contact with the abscess during laryngoscopy and intubation should be minimized since abscess rupture can lead to tracheal spillage.

Ludwig's angina is a diffuse infection of the submandibular and sublingual spaces that is normally associated with dental caries, sickle-cell disease, immunodeficiency, or trauma. Symptoms include fever, pain, and dysphagia with swelling that can lead to airway compromise.

Establishment and maintenance of a safe and secure airway remains the most important immediate goal for patients with infections of the neck and airway. Mortality occurs most often because of hypoxia rather than by overwhelming sepsis. When airway compromise seems imminent, early intubation or tracheostomy avoids the need for emergent attempts at airway control. Conventional endotracheal intubation is often difficult in these patients. The challenge faced in these situations is how to induce anesthesia and achieve intubation without loss of the airway.

Options for managing the difficult airway include inhalational induction, followed by laryngoscopy and intubation, awake fiberoptic intubation, and awake tracheostomy. Blind nasal intubation has been advocated by some but carries a considerable risk of damage to the swollen and fragile mucosa with bleeding, abscess perforation, and complete obstruction. An inhalational induction with sevoflurane allows rapid control of anesthetic depth while maintaining spontaneous

breathing. However, an inhalational induction does not protect the airway which is often swollen. Awake fiberoptic intubation provides advantages of maintaining airway patency and spontaneous ventilation. Positioning the patient in the sitting position prevents the tongue and pharynx from collapsing backwards and obstructing the view and prevents secretions from pooling in the back of the oropharynx. However, awake fiberoptic intubation is not without limitations or risks. Edema, secretions, blood, or pus may impair visualization, which may result in airway trauma. Furthermore, the technique may not be tolerated in some patients.

Performing a tracheostomy under local anesthesia can be a challenge because patients are often anxious and hypoxic and may develop worsening stridor on lying supine with the neck extended. Furthermore, normally palpable landmarks may be distorted due to the presence of inflammation from infection. Regardless of the strategy chosen for airway management, an experienced surgeon should be present and prepared to perform emergency tracheostomy if needed.

Supraglottic Airways in ENT Surgery

Although use of an endotracheal tube remains customary for airway management for most otorhinolaryngologic procedures, the use of a LMA and other supraglottic airways has been described. Otorhinolaryngologic procedures in which supraglottic airways have been successfully used include adenotonsillectomy, percutaneous tracheostomy, thyroidectomy, and laryngoscopic procedures. Advantages of supraglottic airways include the lack of tracheal stimulation and decreased incidence of coughing on emergence as compared to an endotracheal tube. Another advantage is the ability to insert the device without the use of neuromuscular blocking agents, which may aid in nerve monitoring. In addition the supraglottic airway can provide a conduit for surgical access to the glottis and trachea and provide a means to isolate the glottis from bleeding from pharyngeal sources.

Obstructive Sleep Apnea

Obstructive sleep apnea (OSA) is a common sleep disorder caused by repetitive partial or complete obstruction of the upper airway, resulting in cessation of breathing during sleep for periods of time. OSA is present in a significant proportion of the population, but the majority of patients go undiagnosed. OSA is associated with other medical conditions such as obesity, hypertension, coronary artery disease, and diabetes. Patients with undiagnosed OSA may have increased perioperative complications. Appropriate screening to detect undiagnosed OSA may reduce the perioperative risk associated with this condition. The gold standard for diagnosis is an overnight sleep study, or polysomnography, which is both expensive and resource intensive. The results of polysomnography are reported as the apnea/hypopnea index (AHI). The AHI is calculated by dividing the total number of episodes of apnea and hypopnea by the total sleep time. The American Academy of Sleep Medicine classifies the disease as follows: mild OSA=AHI of 5–15 events per hour, moderate OSA=AHI of 15–30 events per hour, and severe OSA=AHI of greater than 30 events per hour. Several screening tools have been validated to quickly identify risk for OSA in surgical patients. Chung et al. developed a "STOP BANG" questionnaire for screening for obstructive sleep apnea. Patients are asked/assessed the following questions. If they answer yes to more than three questions, they have an increased risk of OSA, while a yes to less than three questions indicates a low risk of OSA.

STOP: snore (S), feel tired (T), observed (O) by somebody to stop breathing during sleep, or have high blood pressure (P).
BANG: BMI (B) > 35, age (A) > 50 years, neck (N) circumference > 40 cm, or male gender (G)

In the early postoperative period, OSA-associated complications may be attributable to the lingering effects of opioids and sedatives. Later in the postoperative period, an increase in the amount of REM sleep due to chronic sleep deprivation known as "REM rebound" has been implicated in complications. Episodes of apnea and hypopnea increase during REM sleep so the risk of hypoxemia increases.

In 2006, the ASA published guidelines for the perioperative management of patients with OSA. For patients with a diagnosis of OSA or who are clinically determined to be at high risk, close attention to airway management is required. Extubation should be performed only when the patient is fully awake. Regional anesthesia should be used whenever possible. Postoperative pain management in patients with suspected or confirmed OSA should minimize the use of opioids and other sedatives. Such patients should also undergo close monitoring with pulse oximetry in a step-down unit after surgery and receive continuous positive airway pressure (CPAP) therapy as soon as possible. In addition to standard outpatient discharge criteria, the guidelines recommend that patients with OSA should be monitored for a median of 3 h longer than non-OSA patients before discharge, and monitoring of patients should continue even longer if an episode of airway obstruction or hypoxemia occurred.

Laryngospasm

Laryngospasm is a prolonged exaggeration of the glottic closure reflex due to stimulation of the superior laryngeal nerve and is associated with significant morbidity and mortality if not rapidly diagnosed and treated. Children are more prone to laryngospasm than adults, although it can occur in patients of all age ranges. Clinical signs include stridor or absent

Table 37.5 Treatment of laryngospasm

1.	Identification and removal of the noxious stimulus (blood, secretions)
2.	Chin lift and jaw thrust
3.	Positive airway pressure with 100 % oxygen
4.	Intravenous succinylcholine (0.5–1 mg/kg) or intramuscular (1–4 mg/kg) if no IV access
5.	Deepen anesthesia with propofol or inhalational agent
6.	Endotracheal intubation if required

breath sounds associated with ventilatory obstruction. Common stimuli that may elicit laryngospasm include secretions, blood, inhalation of irritating volatile anesthetics, light anesthesia, or mechanical instrumentation of the airway. Resultant hypoxia, hypercarbia, and acidosis can rapidly deteriorate into hypotension, bradycardia, and cardiac arrest unless airway patency is rapidly restored. Treatment includes removing the noxious stimulus (e.g., by suction), deepening the anesthetic level, and administering 100 % oxygen with positive pressure ventilation (Table 37.5). If these maneuvers are not successful, administration of 10–20 mg IV succinylcholine may be beneficial in breaking the laryngospasm. Laryngospasm can result in the development of negative pressure pulmonary edema, which may require treatment after the laryngospasm has resolved.

Airway Foreign Body

Asphyxiation from an aspirated foreign body is a leading cause of death for children under 4 years of age. Complications of foreign body aspiration can be divided into those related to the actual obstruction and those related to surgical retrieval. These include laryngeal edema, pneumothorax, mediastinal perforation, hypoxic brain injury, and cardiac arrest.

The presenting symptoms of foreign body aspiration may range from none to severe airway obstruction. Relevant data regarding the foreign body including the size and shape of the object, location and extent of the obstruction, and stability of the object are often unknown. A normal radiograph and a nonagitated child do not necessarily exclude the presence of foreign body aspiration, which may rapidly progress to airway obstruction and respiratory compromise.

Bronchoscopy is used to confirm the diagnosis and retrieve the object. Occasionally a cooperative mature patient can be examined under local anesthesia with fiberoptic bronchoscopy; however, general anesthesia is typically required. An anesthetic induction that maintains spontaneous ventilation is commonly performed to avoid converting a partial obstruction in to a full obstruction although controlled ventilation combined with IV anesthetics provides optimal conditions for rigid bronchoscopy. The surgeon should be prepared to perform an emergency tracheostomy or cricothyrotomy should total airway obstruction occur during bronchoscopy. Prompt management and close communication between the anesthesiologist and surgeon are essential for optimal outcomes. Postoperatively, patients should be observed for signs of airway edema and respiratory compromise.

Clinical Review

1. The following anesthetic agent may be best avoided during tympanoplasty
   A. Desflurane
   B. Ketamine
   C. Nitrous oxide
   D. Etomidate
2. A 4-year-old patient underwent tonsillectomy and is discharged home. Eight hours later the patient is brought to the emergency room with bright red blood oozing from the mouth. The patient is taken to the operating room. Your induction plan would be
   A. Inhalation induction with sevoflurane
   B. Premedicate the child followed by intravenous induction
   C. Rapid sequence intravenous induction
   D. Order type and cross, premedicate, followed by intravenous induction
3. The following laser is most commonly used to vaporize superficial tissues
   A. CO_2
   B. KTP
   C. Nd:YAG
   D. STP
4. First step in managing a case of an airway fire in the operating room would be to
   A. Stop the oxygen flow
   B. Call for help
   C. Pour saline down the airway
   D. Remove the endotracheal tube
5. Laryngospasm occurs due to spasm of the
   A. Recurrent laryngeal nerve
   B. Superior laryngeal nerve
   C. Glossopharyngeal nerve
   D. Hypoglossal nerve
6. A 6-year-old patient is extubated in the operating room after undergoing tonsillectomy. Immediately after extubation the oxygen saturation starts to fall, the patient is very difficult to ventilate, and positive pressure with 100 % oxygen does not relieve the airway obstruction. The next step would be to
   A. Ventilate the child with oxygen and sevoflurane
   B. Intubate the child
   C. Administer rocuronium
   D. Administer succinylcholine

Answers: 1. C, 2. C, 3. A, 4. D, 5. B, 6. D

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Obstetric Anesthesia

38

Manasi Badve and Manuel C. Vallejo

Most women who have had vaginal births will admit that the pain of childbirth is the worst pain that they have experienced in their lifetime. It induces feelings of apprehension, anxiety, and fear in the mother. Therefore, it is important to know the physiology of labor and pain mechanisms, and associated diseases in order to provide effective analgesia/anesthesia for labor and delivery. This chapter describes the physiologic changes occurring in the pregnant patient, the physiology of labor, techniques for labor analgesia, anesthesia for cesarean section, and common diseases associated with pregnancy and their management.

Physiologic Adaptations During Pregnancy

Numerous physiologic changes affecting major organ systems occur in a parturient to facilitate adaptation of the body to increased metabolic needs of the mother as well as the growing fetus. These maternal physiologic changes have significant implications for perioperative management, nonoperative or operative.

Changes in the Airway

Vascular engorgement of the mucosa affects the pharynx, larynx, and trachea resulting in airway edema which may be exacerbated in presence of preeclampsia and respiratory tract infections. Mucous membranes become friable and bleed easily. There is an increase in Mallampati scores and the risk of failed intubation is eight times higher in obstetric population than in general surgical patients. Therefore, need for a thorough airway assessment before any anesthetic intervention cannot be overemphasized. Smaller sized cuffed endotracheal tubes (6.0, 6.5, 7.0 mm-ID) should be readily available on the labor and delivery floor considering the possibility of airway edema. Airway manipulation and instrumentation can cause bleeding from the friable mucosa.

Respiratory System

Oxygen consumption, tidal volume, and minute ventilation (MV) increase during pregnancy and remain elevated for 6–8 weeks postpartum (Table 38.1). As the enlarging uterus causes elevation of diaphragm, the functional residual capacity (FRC) begins to fall and reaches 80 % of the prepregnancy value by term. The residual volume and the expiratory reserve volume tend to decrease whereas the inspiratory capacity increases as compared to the nonpregnant state. Vital capacity remains unchanged.

Progesterone acts as a direct stimulant of the respiratory center and increases the respiratory drive. Pregnancy is a state of mild respiratory alkalosis with a slight decline in $PaCO_2$ to 30 mmHg. Metabolic compensation by the kidneys results in a fall in serum bicarbonate concentration to 20 meq/L. The increased work of breathing is perceived by many pregnant women as shortness of breath. All the changes described above are further exacerbated during labor and delivery.

Pregnant women tend to desaturate rapidly during periods of apnea as compared to their nonpregnant counterparts because of higher oxygen consumption and reduced FRC. This occurs more so in the supine position as during induction of general anesthesia. Therefore, the parturient should be adequately pre-oxygenated with 100 % oxygen before induction of general anesthesia.

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Table 38.1 Respiratory physiologic changes at term pregnancy

Parameter	Change
Tidal volume	↑ 45 %
Residual volume	↓ 15 %
Respiratory rate	No change
Functional residual capacity	↓ 20 %
Minute ventilation	↑ 45 %

Table 38.2 Cardiovascular physiologic changes at term pregnancy

Parameter	Change
Cardiac output	↑ 50 %
Stroke volume	↑ 25 %
Heart rate	↑ 25 %
Ejection fraction	Increased
Systemic vascular resistance	↓ 20 %

The minimum alveolar concentration (MAC) for volatile anesthetic agents decreases up to 40 % during pregnancy. This, in conjunction with the rise in MV leads to rapid uptake and elimination of volatile anesthetics resulting in faster induction and emergence from anesthesia, respectively.

Cardiovascular System

Cardiac output increases early in pregnancy and by the end of second trimester, it is about 50 % higher than nonpregnant women and then remains stable in the third trimester (Table 38.2). During labor, the cardiac output increases by 40 % during the second stage above the prelabor values. It may be as high as 75 % above the predelivery values in the postpartum period. Women with limited cardiac reserve may not tolerate the increased cardiovascular demands of pregnancy. The rise in cardiac output can be attributed to an increase in both stroke volume and heart rate by 25 % each. Uterine perfusion increases from 50 ml/min to 700–900 ml/min at term. Extremities tend to be warm because of increased cutaneous blood flow and pregnant women may report nasal congestion as a result of enhanced mucosal blood flow. Mammary blood flow also increases leading to a continuous flow murmur called mammary souffle. Cardiac output falls to prelabor values about 24–72 h after delivery and returns to pre-pregnant levels 6–8 weeks postpartum.

The systemic vascular resistance (SVR) begins to fall early reaching its peak around 20th week of gestation. It increases slightly during later part of pregnancy but still remaining about 20 % below the nonpregnant level at term. The fall in SVR is explained by the vasodilatation caused by progesterone, estrogen, and prostacyclins and development of the low-resistance uterine vascular bed. The systolic, diastolic, and mean arterial pressures decrease during mid-pregnancy reflecting the alterations in SVR and return to baseline by term.

The cardiac muscle undergoes eccentric hypertrophy secondary to both an increase in the blood volume and the stretch and force of contraction of heart in the gravid state. As the gravid uterus enlarges, it causes elevation of diaphragm, in turn shifting the heart anteriorly and to the left. Due to these changes, some examination findings considered abnormal in the nonpregnant population no longer remain pathological in pregnancy. They include:

- Loud first heart sound and wide splitting of the second heart sound.
- A grade II ejection systolic flow murmur heard along the left sternal border.
- A third and a fourth heart sound during the third trimester.
- Displacement of the point of maximal cardiac impulse to the left of mid-clavicular line and cephalad in the fourth intercostal space.
- ECG changes such as tachycardia, axis shifts, shortening of PR and uncorrected QT intervals, depressed ST-segment, and isoelectric T waves.

Aortocaval Compression

When pregnant women assume supine position, the gravid uterus compresses the aorta and the inferior vena cava. The overall effect is a reduction in maternal systemic arterial pressure (due to reduced venous return) and uterine blood flow (because of aortic compression) leading to a fall in uteroplacental perfusion. Aortocaval compression in the supine position causing profound maternal hypotension and bradycardia is termed *supine hypotension syndrome.* Hence, pregnant women should be encouraged to lie on her left side after 16–20 weeks of gestation. The same effect can be achieved by placing a wedge under the right hip to maintain left uterine displacement (Fig. 38.1). This gains importance during the provision neuraxial anesthesia for labor and delivery.

Hematologic System

Both plasma and red blood cell volume increase during pregnancy. However the rise in plasma volume (55 % at term) relative to the red blood cell volume (30 % at term) is more and this leads to *physiologic anemia of pregnancy*. Blood volume returns to normal about 8 weeks after delivery. Physiologic advantages of this hypervolemia and hemodilution include:

- Improved delivery of nutrients to the fetus.
- Prevents maternal hypotension in presence of reduced vascular tone.
- Compensates for hemorrhage anticipated to occur during delivery. A healthy parturient loses around 600 ml of blood during a vaginal delivery and 1,000 ml during a cesarean section.

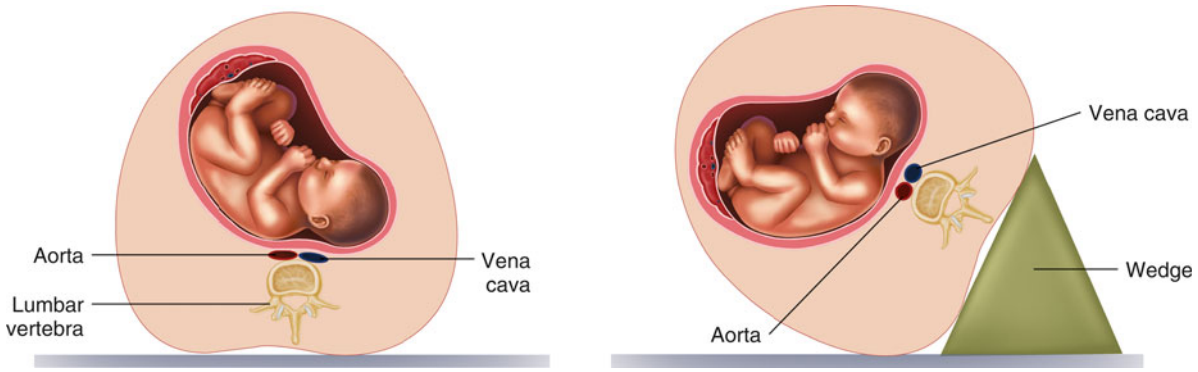

Fig. 38.1 Aortocaval compression, and its relief by placing a wedge under the right hip (left uterine displacement)

Pregnancy is a hypercoagulable state. The concentration of most of the clotting factors increases during pregnancy except factors XI, XIII which decrease and prothrombin and factor V which remain unchanged. *Gestational thrombocytopenia* is seen in about 7–8 % of otherwise normal pregnancies, where the platelet count falls below 150,000/mm^3 and in some this fall can be profound. It is the most common cause of thrombocytopenia in pregnancy and usually does not require treatment.

The plasma cholinesterase levels fall by about 25 % during pregnancy but are not usually associated with clinically significant prolongation of the effects of succinylcholine. The plasma albumin concentration as well as the albumin: globulin ratio fall, and the colloid oncotic pressure decreases by approximately 5 mmHg. The polymorphonuclear cell function is depressed and this is reflected by higher risk of infections and remission of the symptoms of autoimmune disease in pregnant women.

Gastrointestinal System

The stomach assumes a more horizontal position than normal and the lower esophageal sphincter tone decreases. This is attributed to progesterone as well as the rising intraabdominal pressure during the latter months of gestation. Almost 30–50 % of women experience gastroesophageal reflux, with a gastric pH under 2.5. Gastric emptying is unaltered during pregnancy but esophageal peristalsis and intestinal motility slow down under the inhibitory effects of progesterone. However, the gastric emptying is slowed in labor and more so in women who receive bolus doses of opioids for labor analgesia.

Giving importance to these considerations, pregnant women in labor are always considered "full stomach" regardless of their fasting status. In view of the potential for a difficult airway and the risk of regurgitation of stomach contents followed by pulmonary aspiration, regional anesthesia is preferred in this group of patients. If general anesthesia is required, rapid sequence induction with cricoid pressure should be carried out and the airway protected using a cuffed endotracheal tube.

Renal System

Both renal plasma flow and glomerular filtration rate increase by 75 % and 50 %, respectively, thus leading to a rise in creatinine clearance. Blood urea nitrogen and serum creatinine (decrease to 0.5–0.6 mg/dl) levels fall owing to enhanced clearance of nitrogenous metabolites from the blood. Sodium retention due to increased renin and aldosterone secretion along with elevated protein excretion promotes tissue edema. In response to alveolar hyperventilation and respiratory acidosis, the kidneys increase excretion of bicarbonates in an attempt to maintain the acid–base balance.

Endocrine System

Pregnancy induces a diabetogenic state. Human placental lactogen reduces tissue sensitivity to insulin and leads to hyperglycemia. The thyroid gland shows follicular hyperplasia and increased vascularity to support metabolism during pregnancy. However, free T_3 and T_4 levels remain normal. Adrenal secretion of corticosteroids is also elevated.

Musculoskeletal System

Almost 50 % parturients report back pain at term. It is proposed that the enlarging uterus increases the lumbar lordosis and the hormone relaxin (secreted by placenta) causes remodeling of the pelvic connective tissue and collagen.

The lumbar lordosis also changes the center of gravity of the body. Other musculoskeletal changes occurring during pregnancy include a higher incidence of carpal tunnel syndrome, meralgia parasthetica, and increased mobility of the pelvic joints to allow passage of the fetus.

Nervous System

The MAC of volatile anesthetic agents is decreased and is likely related to elevated levels of progesterone, endorphins, and enkephalins. The local anesthetic requirement during regional anesthesia is also reduced during pregnancy due to altered nerve tissue sensitivity, compression of the dural sac, and reduction in cerebrospinal fluid volume.

Uteroplacental Blood Flow

The spiral arteries are the main source of blood supply to the uteroplacental unit. They are derived from the uterine artery (branch of the internal iliac artery). The spiral arteries lose smooth muscle in their walls during trophoblastic invasion and create a low resistance placental vascular bed. A limited ability to autoregulate in response to noxious stimuli is an important characteristic of this circulation. Uterine blood flow is directly related to the uterine perfusion pressure and inversely to the uterine vascular resistance. The following equation expresses this relationship:

$$\text{Uterine Blood Flow} = \frac{\text{Uterine arterial pressure} - \text{Uterine venous pressure}}{\text{Uterine vascular resistance}}$$

Uterine blood flow is affected by hypotension (aortocaval compression, hemorrhage, sympathectomy), factors which raise uterine venous pressure (vena caval compression, uterine contractions), and those which raise uterine vascular resistance (catecholamines, stress).

Placental Function and Transfer of Drugs

The placenta produces enzymes and hormones like human chorionic gonadotropin and placental lactogen. It also acts as a permeable membrane between the mother and the developing fetus. Passive diffusion, active and facilitated transport, and pinocytosis are all involved in the transfer of substances across the placenta.

Lipid solubility, protein binding, pH, pK_a, and blood flow affect drug movement across the placenta in humans. Most of the anesthetic agents like benzodiazepines, induction agents (thiopental, propofol, ketamine), inhalational agents, opioids, and local anesthetics readily cross the placenta. Among the anticholinergic drugs, atropine and scopolamine readily traverse the placental barrier, while glycopyrrolate is poorly transported. Muscle relaxants, being ionized quarternary ammonium compounds, do not readily reach the fetal circulation. Heparin does not cross the placenta; low molecular weight heparin has limited ability, whereas warfarin easily enters the fetal circulation and is associated with fetal congenital anomalies. Anti-cholinesterase agents (neostigmine, pyridostigmine) have limited potential to cross the placenta.

Fetal Monitoring

Antepartum Assessment

The goal of antepartum surveillance is to accurately determine the gestational age and evaluate fetal growth and development. Information from the history and physical examination (last menstrual period, perception of quickening, fundal height) can be used to date the pregnancy. Ultrasonography (USG) is used to calculate the expected date of delivery and identify fetal anomalies. Other parameters used to assess fetal well-being include listening to the fetal heart rate (FHR), kick count, and abdominal palpation. USG in conjunction with a triple or quadruple screen can be used to screen for trisomies in advanced maternal age. Finally, chorionic villus sampling, amniocentesis, and cordocentesis are invasive tests for fetal karyotype and definitive diagnosis of chromosomal anomalies. The non-stress test and biophysical profile are used in the later part of pregnancy to ensure continuing fetal well-being.

Intrapartum Assessment

FHR can be monitored by a simple stethoscope, Doppler ultrasound, or fetal electrocardiography. FHR tracings in conjunction with uterine contraction patterns (using tocodynamometry or intrauterine pressure catheter) provide an indirect assessment of the uteroplacental unit and fetal well-being. FHR tracing is usually described in terms of the following parameters:

1. *Baseline heart rate*: The normal FHR ranges from 120 to 160 beats per minute (bpm). Bradycardia is less than 120 bpm and tachycardia is greater than 160 bpm. Changes in FHR are caused by fetal (cardiac pathology, hypoxia) as well as maternal (fever, infection, medications) factors.
2. *Variability*: It is the fluctuation in the baseline FHR of two cycles or more per minute. The presence of variability indicates integrity of neural pathways. Normal variability ranges from 6 to 25 bpm. Causes of decreased variability include fetal sleep state, hypoxia, neural pathology, and maternal administration of drugs like opioids.

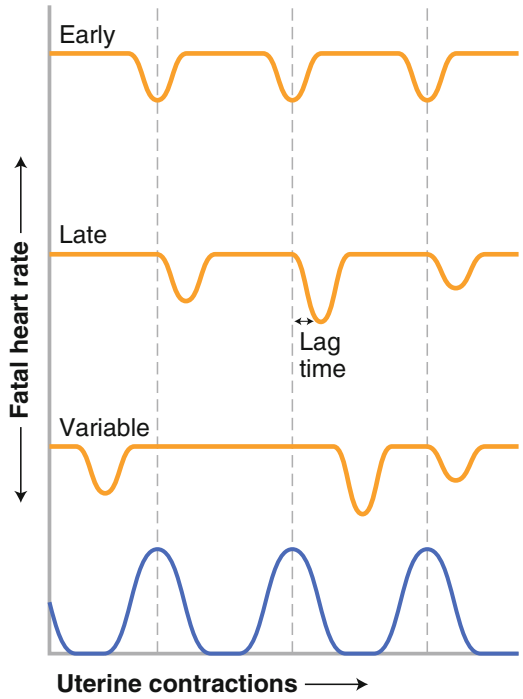

Fig. 38.2 Fetal decelerations (early, late, and variable)

3. *Periodic changes*: These include accelerations and decelerations. The presence of accelerations rules out fetal metabolic acidosis. However, their exact significance is unclear. *Decelerations (Fig.38.2) can be*
   (a) *Early*: They coincide with uterine contractions and are not considered harmful. They reflect vagal activity due to mild hypoxia or fetal head compression.
   (b) *Late*: These begin 10–30s after the onset of uterine contraction and last for 10–30s after the end of contraction. They occur in response to fetal hypoxia and are considered ominous if present with decreased or absent variability.
   (c) *Variable*: They are variable in onset and depth in relation to the uterine contractions. They indicate umbilical cord or fetal head compression in the second stage of labor. Intervention is indicated if they are severe (less than 60 bpm) and persistent (or prolonged >30s).

Categorization of tracing patterns: To improve the utility of electronic FHR monitoring, tracing patterns have been categorized as:

- *Category I (normal)*: Strongly predictive of normal fetal acid–base status.
- *Category II (indeterminate)*: Lack of adequate evidence to be classified as normal or abnormal and does not indicate a deranged fetal acid–base profile.
- *Category III (abnormal)*: Predictive of abnormal fetal acid–base status and needs prompt evaluation.

An older invasive technique of detecting fetal acidosis is sampling fetal scalp blood to determine its pH. It is indicated in cases of a persistently abnormal FHR tracing. A less invasive form of the test is to simply stimulate the fetal scalp and watch for acceleration of FHR as a response. *ST waveform analysis* (STAN) of fetal electrocardiogram (ECG) is a newer technique used in combination with cardiotocography for intrapartum fetal surveillance. It is based on the rationale that fetal hypoxia causes changes in the morphology of the ST segment and T wave of the fetal ECG.

Intrapartum Fetal Resuscitation

Some of the common causes of intrapartum fetal distress include maternal hypotension, fever, uteroplacental insufficiency, uterine hypertonus, umbilical cord compression, and oligohydramnios. Initial measures taken to improve fetal oxygenation include:

- Maternal repositioning to prevent aortocaval compression.
- Intravenous fluids, vasopressors to treat hypotension.
- Administration of supplemental oxygen via a face mask.
- Discontinuation or step down of oxytocin infusion, tocolysis (terbutaline) for uterine hypertonus.
- Saline amnio-infusion for oligohydramnios as a result of umbilical cord compression.

Physiology of Labor

Stages of Labor and Pain Pathways

Labor includes a series of events that are required for successful passage of the fetus through the birth canal into the external world. Mechanics of labor are described in terms of *powers* (force generated by uterine contractions), *fetal characteristics* (size, lie, presentation, station), and the *bony pelvis and soft tissues* of birth canal that the fetus has to traverse. Labor is divided into four stages:

Stage 1: Begins with onset of regular uterine contractions and ends with full dilatation of cervix (10 cm). It is subdivided into latent and active phases. The average duration is about 14 h in primigravidas and 7 h in parous women (sensory T_{10}–L_1).

Stage 2: This is the interval between full cervical dilatation and delivery of the baby. Cardinal events include descent of the presenting part though the maternal pelvis and requires more active participation from the parturient. The second stage prolonged if the baby is not delivered within 2 h in primiparous, and 1 h in multiparous women after complete dilatation of cervix without epidural analgesia (sensory T_{10}–S_4).

Stage 3: This lasts from delivery of the baby to expulsion of the placenta and the membranes, which takes about 30 min.

Stage 4: Some authorities describe the first 60 min after placental delivery as the fourth stage and recommend close monitoring of the parturient for signs of postpartum hemorrhage (PPH).

The discomfort associated with first stage of labor is described as "visceral pain" because of its diffuse nature and origin due to cervical dilation and stretching of the lower uterine segment. It is transmitted by C and A-delta nerve fibers to the dorsal horn of spinal cord at T_{10} to L_1 segments.

During the second stage, the afferents that innervate the vaginal portion of cervix, vagina, and perineum are also involved in addition to those described in stage 1. These afferents are carried by the pudendal nerve to the S_{2-4} dorsal root ganglia. This pain can be localized to the perineum and is described as "somatic." Successful labor analgesia using regional anesthesia techniques requires blockade of T_{10}–L_1 segments during the first stage with extension to cover the lower sacral nerve roots after complete dilatation of the cervix.

Effects of Labor Pain

Severe pain during uterine contractions causes a marked increase in MV and oxygen consumption. Hyperventilation causes respiratory alkalosis and a leftward shift of the oxygen hemoglobin dissociation curve in the mother. Compensatory hypoventilation between the contractions results in transient maternal and fetal hypoxia. The end result is diminished oxygen supply to the fetus.

The activation of the sympathetic nervous system due to pain and stress of labor leads to an increase in the levels of circulating catecholamines, cardiac output, systemic vascular resistance, and fall in uterine blood flow. Neuraxial analgesia reduces catecholamine surges. Uterine contractions cause autotransfusion of blood from uterus into the circulation. While normal parturients tolerate this increase in blood volume and cardiac work, it may be deleterious in mothers with limited cardiac reserve. As the uteroplacental unit is perfused only during uterine diastole, the decrease in uterine blood flow during contractions that occurs against a background of uteroplacental insufficiency may not be tolerated by the fetus. Therefore, effective pain relief may contribute to better outcomes in these situations.

Besides physiologic effects, a painful labor can interfere with maternal–neonatal bonding, affect future sexual relationships, and cause postpartum depression. Also, effective communication should exist between obstetricians, anesthesiologists, and the nursing personnel to identify potential high-risk patients (difficult airway, severe preeclampsia, cardiac disease). An anesthetic evaluation early in labor may be warranted in such cases so as to provide the best possible option for labor analgesia.

Labor Analgesia

Non-pharmacologic

Antenatal childbirth education, emotional support (provided by family or doula), massage, audio-therapy, and acupuncture have been used to mitigate pain and anxiety during childbirth. *Transcutaneous electrical nerve stimulation (TENS)* is the application of low-intensity, high-frequency electrical impulses to the lower back and is widely used in the UK and Scandinavian countries for labor analgesia. *Hydrotherapy* is the immersion of the parturient in warm water to cover the abdomen only during labor. *Intradermal water injection* consists of the injection of sterile water on the lower back and is supposed to relieve the back pain during labor. *Hypnosis* during childbirth is a labor intensive technique and requires prenatal training of the mother and her partner.

Systemic Labor Analgesia

This can be provided by using *inhalational agents* or *systemic opioid administration*. Systemic analgesia is used widely in institutions around the world which lack facilities for provision of safe neuraxial analgesia. It is useful in women who refuse regional anesthesia or have contraindications (coagulopathy) for provision of neuraxial blocks.

Inhalational analgesia is available in the UK as Entonox (50 % nitrous oxide+50 % oxygen). Special scavenging equipment is necessary to prevent contamination of the environment. The mother has to be taught the technique of use so that the peak brain concentrations of nitrous oxide coincide with the peak of contraction pain. The risk of hypoxemia exists with concomitant use of parenteral opioids and faulty equipment. Recently, there has been an interest in use of volatile anesthetic agents for labor analgesia due to availability of agents with low blood–gas solubility (sevoflurane, desflurane). However, these agents can cause maternal sedation and affect uterine tone.

Parenteral opioids can be used for providing analgesia during childbirth as intermittent bolus doses. Patient controlled analgesia (PCA) is rarely used for labor analgesia in the USA**.** Systemic opioids should be administered in the smallest dose possible, as they cause maternal sedation and respiratory depression both in the mother and the fetus (as they cross the placenta). Opioids blunt the pain but do not provide complete analgesia, and cannot substitute analgesia provided by neuraxial techniques. Trained personnel to care for the newborn in the immediate postpartum period should be available and made aware about the risk of neonatal respiratory depression due to maternally administered opioids. Commonly used parenteral opioids used as boluses are meperidine, fentanyl, butorphanol, nalbuphine, and remifentanil (Table 38.3).

Table 38.3 Parenteral opioids for intermittent bolus use during labor

Opioid	IV Dose	IM Dose	Onset of action (min)	Duration (h)
Meperidine	25–50 mg	50–100 mg	5–10 IV; 40–45 IM	2–3
Fentanyl	25–50 mcg	100 mcg	2–3 IV; 10 IM	0.5–1
Butorphanol	1–2 mg	1–2 mg	5–10 IV; 10–30 IM	3–4
Nalbuphine	10–20 mg	10–20 mg	2–3 IV; 15 IM	3–6
Morphine	2–5 mg	5–10 mg	3–5 IV; 20–40 IM	3–4

IV intravenous, *IM* intramuscular

Remifentanil is an ultrashort-acting synthetic opioid with rapid onset (blood–brain equilibration time 1.2–1.4 min) and short duration of action (metabolized by plasma and tissue esterases). The analgesic half-life of remifentanil is 6 min. It is given in a dose of 0.25 mcg/kg, up to 0.5 mcg/kg with a lockout interval of 2–3 min. It has the potential to become a popular agent for use in labor PCA. As with all other opioids, careful patient monitoring is required to avoid excessive sedation and respiratory depression. General advantages of PCA are better pain relief with lower drug doses, lesser side effects, and higher patient satisfaction as the mother can self-adjust the administration of opioid as per her individual needs. Besides respiratory depression, other side effects of opioids include nausea, vomiting, delayed gastric emptying, dysphoria, and drowsiness.

Neuraxial Anesthesia

Neuraxial anesthesia for labor and delivery includes continuous epidural, combined spinal epidural (CSE), and continuous spinal and caudal blocks. Caudal blocks are infrequently used in present day obstetric anesthesia. Continuous spinal analgesia may be used in cases of an unintentional dural puncture but is not practical in most parturients. Due to the long and unpredictable nature of labor, single shot techniques are not typically useful.

Advantages of Neuraxial Labor Analgesia

- Complete analgesia that prevents pain and stress induced maternal catecholamine surge and hyperventilation.
- Maternal participation in the process of childbirth due to lack of sedation.
- No neonatal sedation or respiratory depression.
- Continuous analgesia with catheter techniques can be used to provide surgical anesthesia in eventuality of an emergency cesarean section avoiding the need for general anesthesia.

Disadvantages

- Requires a skilled anesthesia provider.
- May prolong the second stage of labor increasing the chances of an instrumental vaginal delivery.
- Associated sympathectomy causes maternal hypotension, reduces placental circulation, and causes FHR changes.
- Possibility of a patchy or failed block.

Contraindications

- *Absolute*: Patient refusal, maternal coagulopathy, infection at puncture site, allergy to local anesthetic (LA) agents.
- *Relative*: Maternal hypovolemia, lumbar spine pathology, untreated systemic infection. Most obstetric anesthesiologists will perform regional anesthesia in a febrile parturient with possible chorioamnionitis, provided she has received preemptive antibiotics and is not in sepsis.

Initiation of neuraxial labor anesthesia should begin with a preanesthesia evaluation along with informed consent about the benefits and complications of the procedure. The caregiver must confirm availability of the resuscitation equipment and drugs. Basic monitoring should include noninvasive blood pressure measurement (NIBP), pulse oximetry, and continuous FHR record. Non-reassuring FHR patterns are associated with neuraxial blocks due to the hypotension following sympathectomy and intrathecal opioid administration. The American Society of Anesthesiologists (ASA) Task Force on Obstetric Anesthesia recommends monitoring of FHR before and after initiation of regional analgesia for labor pain management. Intravenous access should be established and maternal hydration started with a non-dextrose containing balanced salt solution (lactated ringer's). While some providers give a fluid bolus (1,000 ml) during initiation of regional block, the ASA Task Force does not recommend a fixed volume to be infused. Aseptic precautions must be maintained during block placement.

Lumbar Epidural Block

A lumbar epidural block is usually placed by the anesthesiologist when the parturient is having active labor contractions, with cervical dilation of 4–6 cm, and absence of fetal distress. The lumbar epidural space (usually $L_{3–4}/L_{4–5}$) is identified using a 17 or 18G Tuohy needle with the mother in the sitting (commonly) or lateral position (Table 38.4). A 19 or 20G flexible catheter is passed into the epidural space (2–4 cm) to provide continuous labor analgesia. An epidural test dose is given to recognize unintentional intravascular or subarachnoid placement. A typical test dose consists of epidural injection of lidocaine 1.5 % with epinephrine 5 mcg/ml (1:200,000) to a total volume of 3 ml.

One should avoid test dose administration during an active maternal contraction. An increase in the maternal heart rate by 20 bpm within 1 min and motor blockade in 3–5 min may indicate intravascular or intrathecal placement.

Table 38.4 Conduct of epidural analgesia for labor

Monitors	On
Position of patient	Sitting (usually)/lateral
Back skin preparation	Betadine × 3 times
Lumbar space	L_{3-4}/L_{2-3}
Local skin infiltration	1–2 ml of 1 % lidocaine
Needle	17G Tuohy
Technique	Loss of resistance to air/saline
(If wet tap)	Remove needle and go one space above/insert catheter into the subarachnoid space
Epidural catheter insertion	2–4 cm into epidural space
Aspiration of catheter	Negative for heme and CSF
Test dose	3 ml of 1.5 % lidocaine with 1:200,000 epinephrine
Agent	0.25 % bupivacaine/ropivacaine 5–10 ml
Desirable level of anesthesia	T_{10}
PCEA	Start

CSF cerebrospinal fluid

After ruling out a malpositioned catheter, epidural analgesia is initiated using a bolus injection of anesthetic agents (5–10 ml of 0.25 % bupivacaine or 0.25 % ropivacaine ± an opioid) and maintained with a continuous infusion (for example, 0.125 % bupivacaine plus 2 mcg/ml fentanyl, 10 ml/h, demand bolus 3–5 ml every 6–10 min, 4 h limit of 80 ml). The desired segmental anesthetic level is T_{10}. The epidural catheter is removed (tip intact) after delivery when the parturient is stable to be sent to the postpartum unit.

Combined Spinal Epidural Block

This is usually performed as a needle-through-needle technique. After the lumbar epidural space is identified as described above, a long 25 or 27G spinal needle is introduced through the Tuohy needle. An intrathecal agent is injected after dural puncture (CSF flow) and the spinal needle is withdrawn. A catheter is then threaded into the epidural space, fixed to skin, and used for continuous analgesia.

Advantages

- Faster onset of analgesia as compared to epidural block alone.
- Intrathecal injection of an opioid alone without local LA agent in early labor allows good pain relief without motor blockade. A combination of opioid with LA in advanced, rapidly progressing labor provides good sacral analgesia within minutes.
- Lower dose of opioid is required as compared to systemic or epidural dose.

Disadvantages

- Higher incidence of maternal pruritis and FHR changes noted after intrathecal administration of opioids.
- Dural puncture is required though the incidence of post-dural puncture headache (PDPH) is not any higher as compared to epidural analgesia.
- After initiation of CSE, it is difficult to evaluate functioning of the epidural catheter for 1–2 h until the effect of intrathecally administered drugs wears off. It may not be a practical option when an adequately functioning epidural catheter has to be ensured (difficult airway, FHR changes with high possibility of an urgent cesarean section).

Choice of Drugs

A combination of long-acting amide LA and lipid soluble opioid is commonly used for labor epidural analgesia. Advantages of using a combination are:

- Lower doses of both agents act synergistically to provide superior analgesia.
- Lesser incidence of unwanted effects (motor blockade by LA or pruritis due to opioids).
- Faster onset and duration of analgesia.
- Reduced shivering.

Local Anesthetic Agents

Traditionally, bupivacaine has been used in varying concentrations to provide epidural labor analgesia. Peak effect is seen at 20 min and analgesia lasts up to 90 min. It is highly protein bound limiting placental transfer. Ropivacaine and levobupivacaine (not available in the USA) are newer LAs similar to bupivacaine as far as the pharmacokinetic and pharmacodynamic properties are concerned. However, they are associated with less motor blockade and cardiotoxicity as compared to bupivacaine. All three provide adequate labor analgesia without affecting mode of delivery, labor duration, and neonatal outcome. Lidocaine is not commonly used for initiation of labor epidural analgesia because of its short duration of action. Chloroprocaine is used to provide surgical anesthesia for cesarean section or instrumental vaginal delivery due to its short onset of action. An initial epidural volume of 5–20 ml is usually required at initiation followed by 8–15 ml/h continuous infusion to maintain analgesia (Table 38.5).

Opioids

Lipid soluble opioids fentanyl and sufentanil are used in combination with low concentration of LAs for neuraxial labor analgesia. Morphine is not very popular for this purpose because of its slower onset and long duration of action with undesirable side effects (pruritus, nausea, vomiting). For maintenance of analgesia, a low concentration solution of a LA with an opioid is administered either as a continuous infusion or patient controlled technique. For CSE, intrathecal lipid soluble opioid along with a low dose of LA or opioid alone is used to initiate analgesia when a CSE is performed and epidural infusion is then started for maintenance.

Table 38.5 Drugs for initiation and maintenance of neuraxial labor analgesia

Drugs	Initiation of epidural analgesia	Initiation of spinal analgesia	Maintenance of epidural analgesia (continuous infusion/PCEA)
Local anesthetics			
Bupivacaine	0.0625–0.125 %	1.25–2.5 mg	0.0625 %–0.125 %
Ropivacaine	0.1–0.2 %	2.5–4.5 mg	0.1 %–0.2 %
Levobupivacaine	0.0625–0.125 %	2.5–4.5 mg	–
Opioid			
Fentanyl	50–100 mcg	15–25 mcg	1.5–3 mcg/ml
Sufentanil	5–10 mcg	1.5–5 mcg	0.2–0.33 mcg/ml

Adjuvants

Additives like epinephrine, clonidine, and neostigmine can be added to epidural or intrathecal solutions to prolong the duration of analgesia. However, they may cause severe hypotension and other side effects and, therefore, must be used with caution. Currently, clonidine is not recommended or approved for intrathecal use in obstetric patients.

Patient Controlled Epidural Analgesia

Patient Controlled Epidural Analgesia (PCEA) uses a programmable pump to deliver anesthetic agents into the epidural space for maintaining analgesia. PCEA parameters that can be adjusted include rate of background infusion, patient controlled bolus doses, lock-out interval, and maximum dose per hour. Typical PCEA settings are a background infusion rate of 6–12 ml/h, a patient controlled bolus dose of 3–5 ml with a lockout interval of 6–15 min using a combination of dilute LA solution and opioid. When a background infusion is not used, bolus dose is adjusted at 8–12 ml with lockout interval of 10–20 min.

Advantages of PCEA

- Reduced incidence of unscheduled clinician intervention for breakthrough pain.
- Reduced total anesthetic consumption and lower extremity motor blockade.
- Maternal satisfaction is equal or better than the continuous infusion techniques.

Newer Advances

Computer-integrated PCEA is a delivery system that automatically adjusts the background infusion rate based on the number of PCEA demands. A disposable PCEA device has been compared with a standard electronic PCEA device. Disposable devices are less bulky, which may facilitate ambulation during labor. However, they lack programmability and are associated with increased costs.

Ambulatory Analgesia

Popularly known as "walking epidural," it refers to the ability of a parturient to ambulate safely after initiation of neuraxial analgesia. It typically consists of low dose of anesthetic agents (usually an opioid) that provides pain relief without causing motor blockade. Regular epidural analgesia is initiated once active labor starts. Although the ability to ambulate may not affect labor outcome, excessive motor blockade does prolong the second stage of labor and increases the chances of having an operative vaginal delivery.

Side Effects of Neuraxial Analgesia

1. *Hypotension* **:** Sympathetic blockade following neuraxial analgesia causes peripheral vasodilation and hypotension in 10 % of parturients. Prolonged severe hypotension affects uteroplacental perfusion and causes fetal acidosis. Preventive strategies employed include avoiding aortocaval compression and preloading/co-loading with intravenous fluids. Hypotension is treated with additional intravenous fluids, oxygen, and vasopressors like ephedrine (5–10 mg iv) or phenylephrine (40–100 mcg iv) as bolus doses.
2. *Pruritis:* This is an opioid related side effect. Nalbuphine (2.5–5 mg iv) is popularly used to treat opioid induced pruritis.
3. *Nausea, vomiting*: This may be related to the labor itself, as a side effect of neuraxial opioids or due to hypotension following institution of neuraxial block. Hypotension should be treated as above, and antiemetics (ondansetron) administered as needed.
4. *Urinary retention*: Occurs due to blockade of sacral nerve roots that supply the urinary bladder and opioid induced suppression of detrusor contractility. A Foley's catheter is usually inserted after initiation of neuraxial analgesia.
5. *Delayed gastric emptying*: Labor as well as bolus opioid administration prolongs gastric emptying time. However, low dose epidural infusion with fentanyl and bupivacaine does not affect gastric emptying.
6. *Shivering*: A common occurrence in labor with loss of heat due to sympathetcomy. Warming blankets should readily be provided.

Complications of Neuraxial Analgesia

1. *Failed analgesia*: This refers to no neuroblockade, inadequate density, and unilateral block or missed segments. This is usually managed by additional doses of LA (testing to see whether an epidural is working), or repeating the epidural procedure.

2. *Accidental dural puncture and postdural puncture headache (PDPH)*: PDPH can occur after an intentional dural puncture during spinal anesthesia or an unintentional dural puncture with an epidural needle. The risk of developing a headache after accidental dural puncture with an epidural needle is about 52 %. The headache is described as fronto-occipital, radiating to the neck, worsening in upright position, and relieved on lying down in bed. It may be accompanied with nausea, photophobia, neck stiffness, and tinnitus. The headache usually appears within 48 h after dural puncture and disappears within a week in 95 % of cases without intervention. Diagnosis is clinical but brain imaging may be indicated in the presence of atypical symptoms to rule out other causes of postpartum headache (pseudotumor cerebri, pneumocephalus, posterior reversible encephalopathy syndrome, subdural hematoma).

Management strategies described include maintaining adequate hydration, caffeine, sumatriptan, epidural blood patch (prophylactic/therapeutic), epidural morphine, and intrathecal catheters. An epidural catheter placed intrathecally during an accidental dural puncture with an epidural needle and left in situ for 24 h reduces the incidence and severity of PDPH. The catheter can be used to provide analgesia during labor and surgical anesthesia for abdominal delivery if needed. For an epidural blood patch, up to 20 ml of the patient's blood is collected aseptically after the epidural needle is in place, and then injected slowly via the epidural needle (Table 38.6). Patients may feel significant pressure in the back during the injection. Relief of headache is almost immediate, and patients are discharged home.

3. *High/total spinal anesthesia*: This can result either due to accidental intrathecal injection or epidural overdose of LA. Care is supportive, which includes hemodynamic support (vasopressors), airway management (intubation may be required), and hydration.
4. *Respiratory depression*: This can occur due to a high level of LA or opioids directly causing respiratory depression.
5. *Intravascular injection of LA and systemic toxicity*: This manifests as dizziness, tinnitus, seizures, and ventricular fibrillation. Pregnant women are often difficult to resuscitate and intravascular placement of an epidural catheter should always be ruled out before LA injection. Treatment includes supportive and hemodynamic care, and administration of intravenous intralipid may be required.
6. *Excessive motor blockade*: This usually occurs because of repeated bolus doses or after prolonged continuous infusion of LA. It can adversely affect maternal expulsive efforts in the second stage of labor.
7. *Neurological complications*: These include trauma to the nerves or spinal cord during insertion of spinal needle or epidural catheter, neuraxial infections, epidural or subdural hematomas.

A *paracervical block, pudendal nerve block, and perineal LA infiltration* can be administered when neuraxial block is contraindicated or is inadequate. Infiltration of paracervical ganglia provides analgesia in the *first stage* of labor without somatic or motor block. However, the duration of analgesia is limited and discomfort due to distention of pelvic floor is present. Fetal bradycardia is frequently seen following the procedure. *Lumbar paravertebral block* may be useful in patients with previous back surgery and provides first stage analgesia similar to paracervical block without the risk of fetal bradycardia. Bilateral pudendal nerve blocks provide vulvovaginal and perineal analgesia and may be useful for a spontaneous vaginal delivery or outlet forceps application. Perineal infiltration with LA is most commonly done before an episiotomy for spontaneous vaginal delivery or for its repair.

Table 38.6 Conduct of an epidural blood patch

Monitors	On
Patient position	Usually sitting/lateral
Lumbar space	Same or near the first dural puncture site
Back skin preparation	Betadine × 3 times, local 1–2 ml of 1 % lidocaine
Needle	17G Tuohy
Loss of resistance	Air/saline
Autologous blood collection 15–20 ml	By assistant with full aseptic precautions (betadine skin preparation, sterile gloves, and syringe)
Blood injection	Via epidural needle
Patient position	Prone for about an hour

Anesthesia for Cesarean Section

Due to differences in practice and resources, the rates for cesarean section vary widely among different countries. In the USA, it is more than 30 % of all births. It may be a planned procedure (malpresentation, abnormal placentation, previous cesarean section) or in an emergency setting (fetal distress, placental abruption, cord prolapse, severe preeclampsia with maternal deterioration, arrest of labor, uterine rupture). The anesthesia technique used depends on factors like urgency of the situation, presence of a preexisting labor epidural catheter, and maternal–fetal status.

High-risk parturients should ideally be evaluated in a preanesthesia clinic in the late second or early third trimester even if a vaginal delivery is planned. Any woman admitted to the labor and delivery floor has the potential go to the operating room either for an abdominal delivery or for management of postpartum complications (retained placenta, repair of lacerations) and may require anesthesia in an emergency situation.

The ASA task force on obstetric anesthesia recommends insertion of a spinal or epidural catheter in high risk patients even before they request labor analgesia. Induction of anesthesia should be preceded by a focused preanesthesia evaluation with informed consent. Intravenous access should be secured and availability of necessary equipment and drugs including emergency supplies confirmed. Monitoring should include NIBP, ECG, pulse oximetry, end-tidal carbon dioxide ($EtCO_2$), and temperature, with additional monitoring decided on a case-by-case basis. Left uterine displacement should be maintained whenever the parturient assumes the supine position.

Fasting Guidelines and Aspiration Prophylaxis

Practice guidelines for obstetric anesthesia state an uncomplicated laboring patient may be allowed modest amounts of clear oral liquids (water, fruit juices without pulp, carbonated beverages, clear tea, black coffee, sports drink). Similarly, an uncomplicated parturient undergoing an elective cesarean section may have modest quantities of clear fluids up to 2 h before induction of anesthesia. Solid foods should be avoided in laboring patients. Parturients undergoing a planned cesarean delivery or postpartum tubal ligation should follow a fasting period of 6–8 h for solids.

Pharmacological aspiration prophylaxis, which helps to reduce gastric acidity and volume, should be provided in parturients undergoing cesarean section or tubal ligation. Sodium citrate (30 ml of 0.3 M orally), a non-particulate antacid, reduces gastric pH without affecting gastric volume. Other drugs that can be given are ranitidine (50 mg IV), famotidine (20 mg IV), and metoclopramide (10 mg IV).

Anesthesia Techniques

Cesarean section is usually performed under neuraxial anesthesia. Regional anesthesia allows the mother to be awake to experience childbirth, avoiding the need for general anesthesia, limiting the placental transfer of drugs, and can be used reliably to provide surgical anesthesia for operative delivery. General anesthesia is only done in an emergent situation, or when there is a contraindication to regional anesthesia.

Spinal Anesthesia

Spinal anesthesia is associated with faster onset of a dense block, technical ease, minimal maternal systemic drug absorption, low failure rate, and in experienced hands is almost as fast as general anesthesia. Therefore, it is suitable for both elective and emergency cases (as time permits). Disadvantages include faster onset of hypotension, limited time frame of action, risk of PDPH, and nerve root injury. Due consideration must be given to maternal hemodynamic and coagulation status. Intravenous fluid hydration should be started during institution of the block. Spinal anesthesia is usually performed as a "single-shot" technique at the L_{3-4} interspace, with the mother in the sitting (commonly), or lateral position using a pencil-point, non-cutting 25G spinal needle (whitacre), inserted using an introducer (Table 38.7). Longer spinal needles may be required for obese patients.

Table 38.7 Conduct of spinal anesthesia for cesarean section

Antibiotics/aspiration prophylaxis	Preoperatively
Monitors	On (BP measurement every 2 min after spinal administration for 15–20 min)
Patient position	Sitting preferably
Back skin preparation	Betadine × 3 times
Lumbar space	L_{3-4}/L_{2-3}
Local skin infiltration	1–2 ml of 1 % lidocaine
Needle	25G whitacre or smaller gauge (need a introducer)
CSF flow	Four quadrant free flow, typically no heme or paresthesia
Agent	10–12 mg of hyperbaric (8.25 % dextrose) bupivacaine (0.75 %)
Additives	Fentanyl 10–25 mcg/Morphine 0.2–0.3 mg
Desirable level of anesthesia	T_4
Patient position	Supine (plus left uterine displacement once adequate level is achieved—turn table towards left and/or wedge under right hip)
Oxygen supplementation	Nasal cannula/face mask
If hypotension	Ephedrine 10–15 mg, phenylephrine 40 mcg (watch for bradycardia), or epinephrine if life threatening, fluid supplementation, left uterine tilt
If nausea	Check BP (usually due to impending hypotension), metoclopramide, ondansetron
After baby delivery	Pitocin 20–30 U in 1 L IV bag
Ketorolac supplementation	Check with surgeon at end of procedure, 30 mg IV slowly

BP blood pressure, *CSF* cerebrospinal fluid

Table 38.8 Drugs for spinal anesthesia for cesarean section

Drug	Dose	Duration (min)
Local anesthetics		
Bupivacaine	7.5–15 mg	60–120
Lidocaine	60–80 mg	45–75
Opioids		
Morphine	0.1–0.2 mg	720–1,440
Fentanyl	10–25 mcg	180–240
Sufentanil	2.5–5 mcg	180–240

Table 38.9 Conduct of epidural anesthesia—with an epidural catheter in situ—for cesarean section

Antibiotics/aspiration prophylaxis	Preoperatively
Monitors	On
Patient position	Supine (plus left uterine displacement once adequate level is achieved)
Level check	Typically T_{10}
Aspiration of epidural catheter (gentle)	Negative for heme and CSF
Agent	2 % lidocaine 5 ml × 4 times = 20 ml, as necessary
Alternative and/or agents	3 % chloroprocaine or 0.25 % bupivacaine
Additives	Sodium bicarbonate 1 ml for each 10 ml of lidocaine or 0.1 ml for each 10 ml of bupivacaine (may cause precipitation)
Desirable level of anesthesia	T_4
After baby delivery	3 mg Epidural morphine and pitocin, with ketorolac at end of surgery
Epidural catheter	Removed intact at end of surgery

Hyperbaric bupivacaine with a lipophilic opioid (preservative free) is widely used as the drug of choice (Table 38.8). Due to smaller CSF volume and greater nerve fiber sensitivity, pregnant patients require smaller doses of LA. Other drugs that can be used include levobupivacaine and ropivacaine and adjuvants like meperidine, neostigmine, and epinephrine. A T_4 sensory level is desired for cesarean section. Hypotension following spinal anesthesia is usually treated with ephedrine (5–10 mg), as it causes minimal alpha vasoconstricting uterine arterial effects, which can limit uteroplacental blood flow. Phenylephrine (40–100 mcg) is still a good choice, but besides uterine arterial vasoconstriction can cause bradycardia. For severe refractory hypotension intravenous epinephrine is used.

Epidural Anesthesia

Due to widespread use of lumbar epidurals, it has become a common practice to supplement the preexisting epidural analgesia to provide surgical anesthesia for a cesarean delivery (Table 38.9). Advantages of epidural anesthesia include gradual onset of hypotension (if it occurs), ability to titrate the level and duration of block, and use for postoperative analgesia. Due to a longer onset of action, the drug should be injected as early as possible (at least half the dose in the delivery room) so that the transport time to operating room allows for an acceptable surgical level to develop. Solutions containing 2 % lidocaine with epinephrine (1:200,000) or 3 % chloroprocaine are commonly used as epidural top-ups due to their rapid onset of action. Adjuvants like morphine, fentanyl, sufentanil, clonidine, and neostigmine can be added to improve the quality of analgesia and for postoperative pain relief. Epinephrine causes vasoconstriction, reduces systemic absorption of the LA drug, and increases the density and duration of the block. Usually a total volume of 15–25 ml of LA is required depending on the preexisting extent of the block. Opioids, commonly preservative free morphine, are generally administered epidurally after the baby is delivered (Table 38.10).

Table 38.10 Drugs for epidural anesthesia for cesarean delivery

Drug	Dose	Duration (min)
Local anesthetic		
2 % Lidocaine ± epinephrine (5 mcg/ml)	300–500 mg	75–100
3 % 2-Chloroprocaine	450–750 mg	40–50
0.5 % Ropivacaine	75–125 mg	120–180
Opioids		
Morphine	3–4 mg	720–1,440
Fentanyl	50–100 mcg	120–240
Sufentanil	10–20 mcg	120–240

Epidural anesthesia is also used for cesarean section as a part of a CSE technique. Advantages include faster, predictable spinal block with ability to augment the surgical level and duration using additional LA through the epidural catheter. In *sequential CSE*, a low dose of intrathecal bupivacaine is followed by incremental doses of LA through the epidural catheter. In *low-dose sequential CSE with epidural volume expansion*, 0.9 % saline is injected epidurally instead of a LA to allow cephalad spread of the intrathecal administered drug. These techniques are useful in high risk cardiac patients but cannot be used in emergency situations due to greater latency to onset.

Finally, caregivers should keep in mind that epidural catheters placed for labor may not be reliable for use in surgical anesthesia. Failed epidural catheters should be replaced as soon as they are recognized to avoid repeating a regional technique or general anesthesia in an emergency situation. If epidural catheter failure is identified in the operating room, the choice of anesthesia depends on the urgency of the situation, whether the surgery has started, and maternal wishes. In case of a failed epidural block for cesarean section, the epidural catheter may be discontinued and spinal anesthesia performed. Caution must be taken, as spinal anesthesia after a failed epidural may cause a high level block (?see page of previously epidurally administered LA into the subarachnoid

space). Therefore, a reduced dosage of LA for spinal anesthesia may be used in these patients. Some parturients may have a patchy epidural. A patchy epidural may be supplemented with intravenous ketamine (10–20 mg prn, up to 1 mg/kg).

General Anesthesia

Although, regional anesthesia is preferred for cesarean section, general anesthesia may be required in urgent situations with fetal distress, maternal coagulopathy, and hemodynamic compromise. Concerns associated with providing general anesthesia in an obstetric patient is the risk of encountering a potentially difficult airway with "cannot ventilate cannot intubate" situation, pulmonary aspiration, and awareness. Inability to control the airway and pulmonary aspiration of gastric contents are leading causes of anesthesia related maternal mortality. Aspiration prophylaxis should be considered in all patients and left uterine displacement maintained using a wedge under the right hip (Table 38.11). Parturients with an anticipated difficult airway should be considered for an awake fiberoptic intubation.

The abdomen is prepared and draped before anesthesia induction to minimize fetal exposure to drugs. This time can be utilized by the anesthesiologist for preoxygenation with 100 % oxygen for 3 min or 4 vital capacity breaths over 30 s. Rapid sequence induction with application of cricoid pressure followed by endotracheal intubation should be performed in all patients. If intubation is not possible and there is no fetal distress, the patient should be woken up for an awake fiberoptic intubation. However, in the presence of fetal distress, every attempt should be made to deliver the baby, and ventilation maintained spontaneously or with positive pressure, with cricoid pressure. An LMA may have to be used. The life of the mother always takes precedent over the life of the fetus.

Thiopental (4–5 mg/kg) or propofol (2 mg/kg) can be used as induction agents. Ketamine (1–1.5 mg/kg) or etomidate (0.3 mg/kg) are preferred in case of hemodynamic instability. Succinylcholine (1–1.5 mg/kg) is used to provide muscle relaxation. Alternatively, rocuronium (0.6–1 mg/kg) can be used when succinylcholine use is contraindicated. Tracheal intubation is performed with a cuffed endotracheal tube and correct placement confirmed by auscultation as well as detection of $ETCO_2$. The obstetrician then immediately proceeds with the skin incision. The endotracheal tube is secured and depth of anesthesia maintained using 0.75–1 % MAC of a volatile anesthetic agent (with or without nitrous oxide up to 50 %). After delivery, the concentration of volatile agent can be reduced to 0.5-0.75 % MAC to avoid uterine relaxation and nitrous oxide can be increased up to 70 %. At this time midazolam and an opioid can also be administered to prevent awareness and pain, respectively. At the conclusion of surgery, the trachea is extubated when the patient is awake, responds to commands, and protective airway reflexes are present.

Parturient with Coexisting Diseases

Pathophysiology of frequently encountered medical conditions in pregnancy and their anesthetic implications are discussed in this section.

Hypertensive Disorders in Pregnancy

Hypertension affects 6–8 % of pregnant women and is the commonest medical disorder complicating pregnancy. The Working Group on High Blood Pressure in Pregnancy (year 2000) from the National High Blood Pressure Education Program categorized hypertension in pregnancy as:

- *Chronic hypertension*: Defined as a blood pressure measurement of 140/90 mmHg or more on two occasions before 20 weeks of gestation and persisting beyond 12 weeks postpartum.

Table 38.11 Conduct of general anesthesia for cesarean section

Antibiotics/Aspiration prophylaxis	Sodium citrate 30 ml, 30 min before induction, if possible Metoclopramide 10 mg IV, preferably in a liter of IV infusion bag
Position	Supine with left uterine displacement
Monitors	On
Preoxygenation	3 min/4–8 deep breaths of oxygen
Induction	Rapid sequence with cricoid pressure, propofol 2 mg/kg, succinylcholine 1–2 mg/kg
Incision	If emergent C-section—as soon as patient is asleep
Intubation	Usually a smaller size endotracheal tube (6–6.5 mm diameter), orogastric tube
Maintenance	Oxygen, inhalational agent (low concentration), may add nitrous oxide up to 50 %
After baby delivery	Pitocin and opioids (fentanyl), with ketorolac at end of surgery
Reversal of muscle paralysis (neostigmine and glycopyrrolate)	If nondepolarizing muscle relaxants used
Extubation	Awake

- *Gestational hypertension*: This is a provisional diagnosis for women who develop new onset hypertension without proteinuria after 20 weeks of gestation and resolving by 12 weeks postpartum. 50 % of women in this subset eventually develop preeclampsia.
- *Preeclampsia*: It is diagnosed with development of hypertension (>140/90 mmHg or more on two occasions 6 h apart) after 20 weeks of gestation with proteinuria (>300 mg/24 h).
- *Preeclampsia superimposed on chronic hypertension*: Development of preeclampsia in a parturient with chronic hypertension.

Preeclampsia

Around 3–5 % of all pregnancies worldwide are complicated by preeclampsia and it is a leading cause of maternal morbidity and mortality. Risk factors include chronic hypertension, diabetes mellitus, obesity, multiple gestation, and preeclampsia in previous pregnancies. Theories proposed for pathogenesis are abnormal placental angiogenesis and angiogenic factors, endothelial dysfunction, immunological intolerance between fetoplacental and maternal tissues. One or more of these factors leads to platelet activation, vasoconstriction, and hypertension leading to end organ damage.

Severe preeclampsia is said to be present if blood pressure is more than 160/110 mmHg on two or more occasions 6 h apart during bed rest, proteinuria >5 g in a 24-h urine sample, or +3 or greater in two random urine samples collected 4 h apart with features suggestive of organ involvement as described below.

Clinical Manifestations: These occur due to vascular endothelial damage and involve major organs.

Central Nervous System Severe preeclampsia can evolve into eclamptic seizures. The hypotheses proposed for cerebral edema and hemorrhage are loss of cerebral autoregulation and vasospasm leading to ischemia and edema. Severe headache and visual symptoms suggest impending eclampsia.

Airway Airway edema is exaggerated in presence of preeclampsia. This can obscure the usual landmarks at laryngoscopy, cause airway obstruction, and make airway management more challenging.

Pulmonary Pulmonary edema is seen in 3 % of women with severe preeclampsia and presents with tachypnea, worsening dyspnea, hypoxemia, and rales on auscultation. Management consists of supplemental oxygen, fluid restriction, and diuretics.

Cardiovascular Vasospasm, hypertension, and exaggerated sensitivity to circulating catecholamines are seen in preeclampsia. Most women have hyperdynamic left ventricular function and elevated systemic vascular resistance. In severe cases, left ventricular function may be depressed and vascular volume reduced.

Hematologic Thrombocytopenia is seen in 15–20 % of preeclamptic parturients. Platelet counts less than 100,000/mm^3 are seen in severe cases and HELLP syndrome. The platelet function is impaired.

Hepatic Epigastric or right upper quadrant abdominal pain suggests involvement of liver in the pathologic process. Elevated serum transaminase levels, hepatic subcapsular hemorrhage, and rarely capsular rupture resulting in life threatening bleeding are seen.

Renal Proteinuria and hyperuricemia are laboratory manifestations of preeclampsia. Presence of oliguria (urine output <400 ml in 24 h) suggests severe disease. Acute renal failure is rare.

Obstetric Complications are uteroplacental insufficiency, IUGR, placental abruption, and fetal demise.

HELLP syndrome It consists of *hemolysis, elevated liver enzymes, and low platelet count* and is seen in 20 % of women with severe preeclampsia. It is associated with increased maternal as well as perinatal morbidity and mortality. Clinical presentation is usually with epigastric or right upper quadrant abdominal pain, headache, nausea, vomiting, hypertension, and proteinuria. However, hypertension and proteinuria may not be present in all patients. Laboratory diagnosis includes:

- Evidence of hemolysis (abnormal peripheral smear, serum bilirubin >1.2 mg/dl, lactate dehydrogenase >600 IU/L)
- Elevated serum transaminase levels >70 IU/L
- Thrombocytopenia <100,000/mm^3

Eclampsia Eclampsia is onset of seizures in a parturient with severe preeclampsia and without prior neurological disorder. Risk factors include young nullipara, multiple gestations, prior history of severe preeclampsia or eclampsia, and hypertension. Eclamptic seizures are seen in 0.2–0.5 % of all pregnancies and are more likely to occur in the antepartum period. The seizure typically lasts for 60–90s and may be followed by a post-ictal phase characterized by confusion and agitation.

Complications of preeclampsia include disseminated intravascular coagulation (DIC), pulmonary edema, acute renal failure, hepatic subcapsular hematoma rupture, cerebral edema, and sepsis. The mainstay of management is the need for immediate delivery. Maternal corticosteroids may be administered for fetal lung maturity. Close maternal

and fetal monitoring in a high risk obstetric care unit is essential. Magnesium sulfate for seizure prophylaxis and antihypertensive agents to control the blood pressure should be started.

Serial laboratory assessment of platelet count and renal and liver functions is indicated. Coagulation parameters must be evaluated before placement of a neuraxial block for labor and delivery. Since preeclamptic patients are intravascularly depleted, they are more prone to hypotension after a neuraxial block. Women with significant bleeding, platelet count <20,000/mm^3, and those scheduled for cesarean section with a platelet count <40,000/mm^3 are candidates for platelet transfusion.

Management of Preeclampsia

Prophylaxis Calcium and antioxidants have been investigated for prevention of preeclampsia but have not shown definite benefits. Low dose aspirin is recommended by some investigators on the basis that thromboxane levels are increased in preeclampsia leading to a thromboxane–prostacyclin imbalance. Aspirin inhibits platelet synthesis of thromboxane and inhibits platelet aggregation.

Antihypertensive Therapy Maternal blood pressure should be controlled to prevent morbidity. However, any reduction in maternal blood pressure should be gradual to preserve uteroplacental circulation. The antihypertensive medications should be titrated to lower the blood pressure by 15–25 % to achieve a diastolic reading of 100–105 mmHg. Intravenous hydralazine (5 mg IV every 20 min; maximum 20 mg) and labetalol (20 mg IV every 10 min; maximum 220 mg) can be titrated for acute reduction of blood pressure.

Seizure Prophylaxis Magnesium sulfate is used for seizure prevention in severe preeclampsia. It is usually started as an intravenous loading dose of 4–6 g over 20–30 min and followed by a continuous infusion of 1–2 g/h. The infusion is continued 24–48 h postpartum. The therapeutic drug range for magnesium lies between 4 and 6 meq/L and this can be dangerously elevated in renal insufficiency. Side effects of magnesium administration include chest tightness, palpitations, flushing, nausea, vomiting, hypotension, and respiratory depression. A theoretical concern associated with magnesium sulfate therapy is that it prolongs the effect of non-depolarizing muscle relaxants. Patellar reflex, respiratory rate, and urine output should be monitored in patients receiving magnesium sulfate. Serial measurement of magnesium levels is important in women with compromised renal function. Magnesium toxicity is treated with discontinuation of infusion and administration of calcium gluconate (1 g over 10 min intravenously).

Management of Eclamptic Seizure This involves placing the parturient on her left side to protect the airway and minimize aspiration, oropharyngeal suction, and administration of supplemental oxygen. Intravenous access should be secured. Magnesium sulfate and antihypertensive agents should be started to control the blood pressure. Maternal monitoring using ECG, blood pressure measurements, and pulse oximetry should be carried out. FHR should be monitored. Soft padding and side rails prevent trauma during violent seizure activity. Plans for expedited delivery should be made after the initial supportive management.

Fluid Management Intravenous fluids should be restricted to 75–100 ml/h to prevent cardiopulmonary and cerebral overload. Urine output should be maintained at least 30–40 ml/h, and accurate intake-output charts should be maintained. A Foley catheter is indicated in severe cases.

Laboratory Workup This includes a urine dipstick sample for protein on admission as well as a 24 h urine collection to quantitate the proteinuria. Blood work includes a complete blood count, peripheral smear, and renal and liver function tests. A complete coagulation profile in addition to serial platelet counts should be obtained in severe cases especially before neuraxial anesthesia.

Route and Timing of Delivery The only definite cure for preeclampsia and eclampsia is delivery of the products of conception. Both maternal and fetal factors influence delivery decisions with due importance given to maternal well-being. Expectant management with careful maternal and fetal monitoring may be carried out in mild cases with gestational age less than 37 weeks. This involves balancing the risks of worsening of maternal status against birth of a premature neonate. Patients with severe disease and those with worsening maternal or fetal condition are immediately delivered irrespective of gestational age or fetal lung maturity. Vaginal delivery is preferred in preeclamptic parturients (even severe cases), unless cesarean section is needed for obstetric indications or maternal–fetal status warrants immediate delivery.

Anesthesia Considerations

Platelet count and serial trend should be considered before placement of neuraxial block. Traditionally, a platelet count of 100,000/mm^3 is considered safe for provision of neuraxial analgesia. Most anesthesia providers do not hesitate to place a neuraxial block at platelet counts of 75,000–80,000/mm^3. A neuraxial block is definitely contraindicated when a platelet count is less than 50,000/mm^3. Platelet counts between 50,000 and 75,000/mm^3 require individual discretion and assessment of risks and benefits. If the platelet count has been stable, it may be prudent to repeat the platelet count every 6 h. However, if the trend shows declining values, platelet counts obtained within the last 1–3 h should be

considered to minimize the risk of neuraxial hematoma. Further, in patients at risk for coagulopathy (abruption, HELLP), other coagulation parameters (international normalized ratio, prothrombin time, partial thromboplastin time, fibrinogen) should also be obtained. Normal coagulation profile should be confirmed not only during placement of the block but also during subsequent removal of the epidural catheter. Some centers use *thromboelastography* to assess functional coagulation status in case of low platelet counts.

Neuraxial analgesia (continuous epidural, CSE) is preferred during labor and delivery in preeclampsia whenever coagulation status permits. Due to superior quality of analgesia, stress related release of catecholamines is inhibited and uteroplacental circulation improves secondary to enhanced intervillous blood flow. The level of segmental analgesia can be extended to provide anesthesia in case of an emergency cesarean section.

Early institution of an epidural catheter during labor is recommended in a preeclamptic parturient in the setting of a declining platelet count. The choice of local anesthetic agent and dosage regimes is similar to those used in parturients without preeclampsia. Intravenous fluid overload should be avoided. Hypotension is treated with small incremental doses of ephedrine (2.5–5 mg IV) or phenylephrine (25–50 mcg IV) keeping in mind the increased sensitivity to vasopressors in preeclampsia. Epidural block is also a reasonable option for labor and delivery in women with eclampsia provided the seizures are controlled and there is no evidence of raised intracranial pressure.

General anesthesia is associated with an exaggerated hypertensive response during laryngoscopy and tracheal intubation. Although, this may be well tolerated by a healthy parturient, it increases the risk of intracranial hemorrhage in preeclampsia. Also, tracheal intubation may be difficult in the presence of airway edema. For these reasons, neuraxial anesthesia is preferred for abdominal delivery in a preeclamptic parturient. Epidural analgesia provides relatively stable hemodynamic parameters due to its gradual onset and ease of titration. Despite concerns of causing profound hypotension, spinal anesthesia is preferred over general anesthesia because of the risks associated with the later.

However, general anesthesia remains the technique of choice in presence of maternal coagulopathy, severe ongoing hemorrhage, eclampsia with ongoing seizures, or sustained fetal bradycardia requiring an urgent abdominal delivery. Anesthetic considerations for general anesthesia in such cases include:

- A careful airway assessment and availability of difficult airway equipment should be confirmed. Additional intravenous access should be established. Blood samples should be sent to the blood bank for type, screen, and cross-match.
- Invasive hemodynamic monitoring in addition to routine monitors may be indicated in severe preeclamptic cases.
- Agents like labetalol, esmolol, or remifentanil may be used to blunt the hypertensive response to laryngoscopy and intubation.
- The effect of magnesium sulfate in prolonging the effects of non-depolarizing muscle relaxants should be kept in mind. In addition, magnesium has tocolytic effects on uterine smooth muscle and hence the risk for postpartum uterine atony.
- Uterotonic agents (oxytocin, prostaglandins) should be readily available. Methyl ergonovine should not be used because of its vasoconstrictive effect on vascular smooth muscle and risk for hypertension.

Postpartum Care

Monitoring of vital parameters and coagulation profile should continue after delivery. As fluids are mobilized, patients may develop pulmonary edema. The platelet count reaches its nadir at 24–48 h postdelivery and should begin to rise by 72 h postpartum. The parturient is still at a risk of developing seizures up to 48 h postpartum, and magnesium sulfate is often continued during this period.

Asthma

Asthma is a chronic inflammatory disease of the airways characterized by bronchial hypersensitivity, bronchoconstriction, and edema leading to airway obstruction. It is the commonest respiratory disease seen in pregnancy and affects about 4 % of parturients. Typical symptoms are cough, wheezing, chest tightness, and shortness of breath. Pulmonary function tests are used to establish the reversibility of bronchoconstriction and severity of asthma. These are forced vital capacity (FVC) (reduced in asthma) and forced expiratory volume in 1 s (FEV_1). FEV_1/FVC ratio is less than 0.75 in asthma.

Effect of Pregnancy on Asthma Like most other chronic diseases during pregnancy, asthma follows the rule of thirds. It exacerbates in one-third of the parturients, shows no change in one-third, whereas one-third women show improvement. An increased circulating level of progesterone, prostaglandins, and cortisol during pregnancy leading to bronchial smooth muscle relaxation is the proposed mechanism for improvement.

Effect of Asthma on Pregnancy Severe asthma can lead to adverse maternal and neonatal outcomes due to associated hypoxemia. Maternal complications include pneumothorax, pneumomediastinum, and cor pulmonale. Maternal mortality is associated with status asthmaticus and approaches around 40 % when a parturient requires mechanical ventilation for worsening respiratory function.

Management

The medical management of asthma involves using bronchodilators and anti-inflammatory agents. Home monitoring of peak expiratory flow rate should be done in women with moderate to severe asthma. The risks and benefits of using these drugs in pregnancy should be weighed against the effects of asthma exacerbation on both mother and the fetus. Beta-adrenergic agonists (salbutamol, terbutaline) are used for acute exacerbation of symptoms. Aerosol administration is preferred as the drug can be directly delivered to the site of action with minimal systemic absorption. Use of methylxanthines (aminophylline, theophylline) is limited owing to side effects like tachycardia and nervousness. Sustained release preparations may be useful in patients with nocturnal symptoms.

Cromolyn sodium and nedocromil are mast cell stabilizers and anti-inflammatory agents used as aerosols. Inhaled glucocorticoids reduce airway sensitivity by inhibiting mediator release and cellular infiltration and limit fetal exposure to steroids. Careful monitoring for glucose intolerance is indicated in parturients who receive corticosteroids and beta-adrenergic agonist agents for asthma.

Prostaglandins can cause bronchospasm as a side effect and should be used with caution in asthmatic parturients or alternative methods are employed for induction of labor. For a similar reason, 15-methyl prostaglandin F2α is relatively contraindicated for treatment of PPH in these patients. Oxytocin does not affect the airway smooth muscles and can be used instead.

Anesthetic Considerations During Labor and Delivery

The scheduled maintenance medications are continued during labor and delivery stay. Inhaled beta-adrenergic agonists can be used to treat parturients experiencing wheezing and peak flow measurements (using a bedside Wright peak flow meter) can be used to guide the therapy.

Continuous lumbar epidural analgesia using a local anesthetic agent and a non-histamine releasing opioid like fentanyl provides effective labor analgesia and abolishes maternal hyperventilation in response to pain. The sensory analgesia level should be maintained at T_{10} dermatome to avoid respiratory insufficiency. It can be extended to provide anesthesia in case of a cesarean delivery. Use of high doses of opioids should be avoided to decrease the risk of maternal and neonatal respiratory depression. Paracervical and pudendal nerve blocks can be used in first and second stages of labor as these provide analgesia without risk of respiratory depression in asthmatic parturients.

Neuraxial anesthesia (spinal or epidural) is also the preferred choice for cesarean section in asthmatics with well controlled symptoms as tracheal intubation in a patient with airway hypersensitivity can trigger severe bronchospasm. However, a high thoracic block can impair the ventilatory drive in an actively wheezing patient using accessory respiratory muscles.

Obesity

Obesity affects more than a billion people worldwide and can lead to severe complications. The prevalence of obesity in pregnancy ranges from 6 to 28 % and is associated with an increased risk of hypertensive complications, Gestational DM, post-datism, urinary tract infection, prolonged labor, cesarean section, PPH, neonatal trauma and intensive care admission, and an overall increase in length of hospital stay. Obesity is usually classified on the basis of body mass index (BMI). Normal BMI ranges from 18.5 to 24.9 kg/m^2. A BMI of more than 25 kg/m^2 is considered overweight, >30 kg/m^2 obese, and >40 kg/m^2 morbidly obese.

Physiologic Changes in an Obese Parturient The changes seen in a normal pregnancy are exaggerated in an obese parturient. Breast enlargement and adipose tissue deposition in the upper torso increases the risk of a difficult laryngoscopy. There is a greater reduction in FRC, so that the closing capacity exceeds FRC during normal tidal breathing leading to reduced oxygen reserves. As the energy expenditure increases due to increased body mass, both oxygen consumption and minute ventilation rise to keep up with the demands.

An obese parturient experiences a greater increase in cardiac output and blood volume. Hypertension and diabetes occur more frequently among obese women. The parturient is at a greater risk of hypotension when she assumes supine position due to aortocaval compression. Hypercoagulable state of pregnancy along with immobility due to obesity predisposes to a higher incidence of thromboembolic complications.

Gastrointestinal changes including relaxation of lower esophageal sphincter tone, increased intraabdominal pressure, and hiatal hernia are exaggerated in this group of women. Increased neural tissue sensitivity lowers the therapeutic and toxic thresholds of local anesthetics by 30 %. Neuraxial injection of local anesthetics causes a more extensive spread and higher sympathetic blockade. Anesthetic drugs should be administered carefully using the ideal body weight to avoid prolonged effects.

Effects of Labor and Delivery Higher incidence of malpresentation, fetal macrosomia, prolonged labor, as well as medical comorbidities may place the parturient at an increased risk of cesarean section.

Anesthesia Considerations

Intravenous access may be difficult due to fat deposition. Landmarks are poorly appreciated and initial placement of

neuraxial block may be difficult. A higher initial epidural failure rate of 42 % has been noted in obese parturients as against 6 % in their non-obese counterparts. The need for longer spinal and epidural needles should be anticipated. There is a higher epidural catheter replacement rate and chances of accidental dural puncture. However, these women are less likely to develop a postdural puncture headache.

Equipment to deal with a difficult airway should be available anticipating the need for general anesthesia. Adequate preoxygenation should be carried out before anesthetic induction. Placing folded blankets under the head and chest to give a "ramped" position improves the laryngoscopic view in obese parturients. Left uterine displacement should always be maintained.

Diabetes Mellitus

Glucose intolerance first occurring during pregnancy is called gestational diabetes (GDM) and these women are at a risk of developing diabetes mellitus (DM) in the future. Glucose intolerance complicates around 7 % pregnancies. Preexisting DM can be either type 1 (absolute insulin deficiency) or type 2 (inadequate insulin secretion and/or target tissue resistance to insulin). Long-standing DM is associated with complications like accelerated atherosclerosis, microvascular damage (retinopathy, nephropathy), and autonomic neuropathy. Acute metabolic complications include diabetic ketoacidosis, hyperglycemic non-ketotic state, and hypoglycemia.

GDM is diagnosed using an oral glucose tolerance test usually performed at 24–28 weeks of pregnancy. The screening test consists of a 50 g glucose load followed by measurement of plasma glucose level after 1 h. A value of 140 mg/dl or more is considered abnormal and an indication for performing a 3 h diagnostic 100 g oral glucose tolerance test. It is performed after a fast of at least 8 h, and GDM is diagnosed if the fasting value is >99 mg/dl or if any two of the hourly post-glucose values exceed 180, 155, and 140 mg/dl, respectively. Risk factors for GDM include obesity, advanced maternal age, previous history of GDM or a family history of type 2 DM, polycystic ovarian syndrome, and prior history of stillbirth, fetal macrosomia, or congenital malformations.

Effect of Pregnancy on Glucose Tolerance

An increase in counter regulatory hormones (placental lactogen, growth hormone) causes peripheral resistance to the effects of insulin, especially in second and third trimesters of pregnancy. Pregnancy may accelerate development and progression of retinopathy and neuropathy. Diabetic ketoacidosis is usually seen in the last two trimesters and triggering factors include infection, emesis, insulin pump failure, poor compliance with treatment, and use of corticosteroids.

Obstetric Implications of Diabetes Mellitus

Maternal

There is an increased risk for infection such as pyelonephritis and vaginitis in pregnancies complicated by DM. Obesity and chronic hypertension are common comorbidities and both are risk factors for development of preeclampsia. Cesarean delivery rates are increased in women with DM.

Fetal

Women with overt DM are at a risk of stillbirth, macrosomia, and congenital malformations. Vaginal delivery of an overgrown baby carries the risk of shoulder dystocia where the fetal shoulder gets impacted on the maternal pelvis causing obstructed labor. It is suggested that maternal hyperglycemia causes fetal hyperglycemia and hyperinsulinemia which in turn leads to macrosomia. A difficult vaginal birth of a macrosomic neonate puts the mother at risk of having perineal lacerations.

Poor glycemic control during embryogenesis is associated with fetal congenital anomalies. The incidence of major anomalies is 5 times higher in women with pregestational diabetes as compared to nondiabetics. The proposed theory is generation of free radicals and deficient expression of Pax3 gene by an embryo in presence of hyperglycemia. Common malformations seen are neural tube defects, renal anomalies, caudal regression, and cardiac septal and abdominal ventral wall defects. Neonatal hypoglycemia and hyperbilirubinemia are other morbidities seen in babies born to women with DM.

Management (Glycemic Control)

Women diagnosed with GDM are initially started on diet and exercise as a means to control the blood glucose. Insulin is started if fasting blood sugar values exceed 80–105 mg/dl. Strict glycemic control during the preconceptional period is the key to prevent fetal anomalies in women with pregestational diabetes. Insulin requirements usually rise during the second and third trimesters of pregnancy and regular blood glucose measurements at home by the patient help to guide the diet and insulin therapy. Several insulin preparations with varying absorption rates and duration of action (regular, NPH) and insulin analogues (glargine, lispro, aspart) are available. These are administered either as intermittent subcutaneous injections or using a continuous programmable pump. Oral hypoglycemic agents like glyburide, glypizide, and metformin are also used in women with GDM.

As insulin requirements decrease at delivery, women on insulin should be instructed to avoid long-acting insulin preparations on the day of labor induction or scheduled cesarean section. Capillary blood glucose should be monitored regularly during labor and regular insulin used to keep blood glucose levels less than 110 mg/dl. Hyperglycemia should be avoided in the peripartum period to prevent neonatal hypoglycemia after birth.

Timing and Route of Delivery The obstetrician needs to balance the risks of having a stillborn baby against performing an iatrogenic preterm delivery in these patients. In women with pregestational diabetes, regular antepartum fetal surveillance is carried out starting at 32 weeks of gestation. If the test results are non-reassuring and fetal lung maturity is confirmed, immediate delivery is indicated. It is difficult to make a decision about timing of the delivery in presence of non-reassuring fetal condition and immaturity of fetal lungs as determined by amniotic fluid lecithin–sphingomyelin ratio. Pregnancy can be continued up to 38 weeks of gestation in presence of reassuring fetal testing.

The method of delivery depends on the estimated fetal weight, past obstetric history, fetal status, and condition of the cervix. In general, if the fetal weight is estimated to be at least 4,500 g, the caregiver may choose to perform an elective cesarean section to avoid a difficult vaginal delivery. In women with diabetes and estimated fetal weight between 4,000 and 4,500 g, performing an elective abdominal delivery is controversial while those with fetal weight less than 4,000 g should not be subjected to operative delivery only on the basis of fetal size. Due importance should be given to other factors like maternal pelvis, progress of labor, and prior delivery history.

Anesthesia Considerations

Labor epidural analgesia for vaginal delivery effectively controls pain and stress response, which if uncontrolled predispose to hyperglycemia. In long-standing DM, presence of autonomic neuropathy and potential for exaggerated hypotension following sympathectomy should be kept in mind. Frequent blood pressure monitoring and vigorous intravenous hydration may be indicated in these patients during neuraxial anesthesia. A non-dextrose containing balanced salt solution should be used for volume expansion to prevent peripartum maternal hyperglycemia.

Both spinal and epidural anesthesia are suitable for cesarean section and any resulting hypotension should be aggressively treated to prevent neonatal acidosis. In patients with long-standing type I diabetes, glycosylation of tissue proteins leads to *stiff joint syndrome*. When this affects the atlanto-occipital joint, limited mobility can lead to difficult laryngoscopy and subsequent intubation.

Cardiac Disease

The incidence of cardiac disease in pregnancy ranges from 0.2 to 3 % in the developed countries. Due to the differences in the pathophysiology of specific cardiac diseases, the anesthetic management during labor and delivery has to be individualized according to the maternal cardiovascular status and physiology of the lesion. Echocardiography is used for evaluation of cardiorespiratory symptoms in the peripartum period. Patients with valvular lesions are at risk of developing infective endocarditis and require antibiotic prophylaxis in the perioperative period. Also, many of these parturients receive anticoagulants and require due consideration while instituting regional anesthesia.

Neuraxial Blockade and Cardiovascular Changes

Sympathectomy is associated with a reduction in preload and hence cardiac output. Arteriolar dilatation reduces SVR and causes reflex tachycardia. Tachycardia is poorly tolerated by patients with stenotic valve lesions as well as coronary artery disease. Low SVR can cause reversal of blood flow across a left-to-right shunt and fall in pulmonary circulation. These changes are more sudden with a single shot spinal anesthetic as compared to more gradual onset epidural block. However, carefully conducted neuraxial techniques are advantageous for labor analgesia and cesarean section in most of the parturients with cardiac pathology. Neuraxial blockade with fixed doses of LAs should be avoided. An incremental dosing technique with epidural or CSE block avoids hemodynamic fluctuations. Hypotension should be treated with judicious use of vasopressors and fluid overload avoided.

Acquired Heart Disease

Ischemic heart disease is estimated to occur in 1 in 10,000 deliveries and mortality is as high as 45 % if myocardial infarction occurs within 2 weeks of delivery. Patients present with ischemic chest pain, abnormal ECG, and elevated cardiac enzymes. Ergometrine can cause coronary vasospasm and is avoided in these patients. Epidural block is an appropriate choice for vaginal as well as surgical delivery. Invasive monitoring is recommended depending on the functional cardiac status.

Primary pulmonary hypertension is characterized by markedly elevated pulmonary artery pressures in absence of intracardiac or aortopulmonary shunt. Severity of the disease is variable and depends on responsiveness of the pulmonary vasculature to vasodilators and right ventricular function. The maternal mortality is around 50 %. If neuraxial anesthesia is used for labor analgesia or abdominal delivery, carefully titrated segmental epidural should be used as sudden fall in SVR can cause decompensation. Hypotension should be treated with fluids initially and vasopressors should be used with caution. During general anesthesia, myocardial depression, hypoxia, hypercarbia, and acidosis should be avoided to prevent exacerbation of pulmonary hypertension.

Peripartum cardiomyopathy is defined clinically as the onset of cardiac failure with no identifiable cause in the last month of pregnancy or within 5 months after delivery, in the absence of heart disease. Viral myocarditis and abnormal immune response to pregnancy have been implicated as

etiological factors. Patients present with dyspnea, chest pain, cough, jugular venous distension, and pulmonary crackles and are evaluated with echocardiography. Medical management involves salt restriction, diuretics, and vasodilators. Anticoagulation is indicated due to risk of thromboembolic complications. The mode of delivery is usually based on obstetric indications but vaginal delivery is preferred. Effective pain management is essential to avoid fluctuations in hemodynamic parameters. General anesthesia as well as regional anesthetic techniques have been used in these patients. Regional anesthesia has the advantages of reducing the preload and afterload but is contraindicated in anticoagulated patients.

Valvular heart disease can be acquired (rheumatic heart disease) or congenital (bicuspid aortic valve). Parturients tend to tolerate regurgitant lesions better than stenotic lesions, because stenotic valves create a fixed cardiac output state and do not allow any further increase during pregnancy. *Mitral stenosis (MS)* is the commonest valvular heart lesion seen in pregnancy and is almost always due to rheumatic heart disease (RHD). In MS, a gradient develops across mitral valve, the magnitude of which depends on the severity of stenosis. While the normal surface area of mitral valve is 4–5 cm^2, <1 cm^2 is classified as severe stenosis, and symptoms usually develop when the size of the orifice is 2 cm^2 or less. Pregnant women with severe stenosis are at a risk of developing pulmonary edema due to the expanded blood volume and inability to increase the cardiac output.

Management of MS includes bed rest, diuretics, oxygen therapy, beta-adrenergic blockade, and balloon mitral valvuloplasty as a palliative procedure in severe cases. Most parturients can undergo vaginal delivery unless dictated otherwise by obstetric indications. Invasive hemodynamic monitoring is recommended in symptomatic patients. Epidural analgesia is extremely useful to prevent pain induced tachycardia and can also be used for a cesarean section. Maternal expulsive efforts and valsalva maneuver should be avoided in the second stage of labor and the obstetrician may perform a forceps or vacuum assisted delivery. If general anesthesia is required, a beta-blocker like esmolol and small dose of opioid can be used to control the heart rate during induction of anesthesia. Regardless of the technique of anesthesia used, these women are at risk of pulmonary congestion in the postpartum period due to autotransfusion of blood into central circulation as the uterus contracts and requires careful monitoring.

Aortic stenosis during pregnancy is usually caused by a bicuspid aortic valve and less commonly as sequelae of RHD. Women with severe stenosis (valve area <0.5 cm^2; gradient >60 mmHg) do not tolerate blood loss, sympathectomy, and tachycardia well. It is critical to maintain intravascular volume, uterine displacement, and sinus rhythm. Vaginal delivery with assisted second stage of labor is preferred. Though, single shot spinal anesthesia is contraindicated in moderate to severe disease, carefully titrated continuous epidural or spinal anesthesia has been successfully used for vaginal delivery as well as cesarean section in patients with less severe disease. Invasive hemodynamic monitoring is indicated as necessary. A combination of etomidate and opioid (small dose) can be used for induction in case of general anesthesia. Anesthesia induced myocardial depression, tachycardia, and vasodilatation should be avoided.

Mitral regurgitation (MR) during pregnancy is usually caused by mitral valve prolapse or RHD. Even severe MR is well tolerated during pregnancy because the expanded blood volume and lower SVR promote forward flow across the diseased valve reducing the regurgitant volume. Maintaining a normal or slightly increased heart rate is beneficial. Continuous epidural anesthesia is indicated for vaginal as well as cesarean delivery. If general anesthesia is required, ketamine may be used for induction because of its beneficial effect on the heart rate.

Aortic regurgitation is seen more commonly in pregnancy than aortic stenosis. It is associated with left ventricular volume overload ultimately leading to left ventricular hypertrophy and dysfunction. These patients are at a risk of myocardial ischemia due to increased oxygen demands and reduced myocardial perfusion. Pregnancy is usually well tolerated in patients having aortic insufficiency without left ventricular dysfunction. Principles of management during labor and delivery are similar to those for MR and consist of maintaining a normal to slightly elevated heart rate, uterine displacement, preventing myocardial depression during general anesthesia, and avoidance of increase in SVR. Continuous epidural anesthesia is a reasonable choice for vaginal as well as abdominal delivery.

Congenital Heart Disease

More women in child bearing age group are presenting with congenital heart disease (surgically corrected/uncorrected) due to advances in diagnoses and treatment. *Left-to-right shunts* include atrial septal defect (ASD), ventricular septal defect (VSD), patent ductus arteriosus (PDA), and these are well tolerated during pregnancy. Mode of delivery is determined by obstetric indications. Early institution of epidural labor analgesia and slow incremental dosing prevent catecholamine surges and sudden fall in SVR. This is important to prevent reversal of the shunt. Other considerations are avoiding intravenous infusion of air bubbles, hypercarbia, acidosis, hypoxia, and use of saline instead of air to locate the epidural space.

Tetralogy of Fallot (VSD, right ventricular hypertrophy, pulmonic stenosis, overriding aorta) is the most common congenital heart disease presenting as a right-to-left shunt. Though most pregnant women have had corrective surgery, it is also the commonest uncorrected cyanotic heart lesion seen in pregnant women. Women with corrected lesions may

exhibit cardiac arrhythmias prompting a 12-lead ECG and continuous monitoring of ECG during labor. A sudden fall in SVR should be avoided to prevent worsening of right-to-left shunt and so single shot spinal anesthesia may not be a reasonable choice. Early administration of neuraxial labor analgesia prevents increases in pulmonary vascular resistance and right-to-left shunting.

Eisenmenger's Syndrome consists of right ventricular hypertrophy, elevated pulmonary artery pressures, and right ventricular dysfunction due to a long-standing uncorrected left-to-right shunt (large VSD, PDA, ASD). These patients are unable to respond to increased demands for oxygen during pregnancy due to fixed pulmonary vascular resistance. There is high incidence of IUGR due to reduced oxygen delivery to the fetus. Thromboembolic phenomenon is common and maternal mortality is 30–50 %. Medical management during pregnancy consists of bed rest, supplemental oxygen, selective vasodilators like nitric oxide, and anticoagulation. Epidural labor analgesia with intrathecal opioids provides effective pain relief for labor and avoids hemodynamic consequences of pain. Instrumental vaginal delivery may be indicated to minimize maternal expulsive efforts. Slow incremental epidural dosing and careful watch on hemodynamic parameters is suitable for cesarean section. General anesthesia is avoided due to chances of myocardial depression, fall in cardiac output with positive pressure ventilation, and hemodynamic fluctuations.

Maternal Cardiac Arrest

Major causes of cardiac arrest in pregnancy are preexisting heart disease, amniotic fluid embolism (AFE), venous thromboembolism, severe hemorrhage, anesthesia complications, and drug allergy. Additional considerations have been suggested in the standard basic life support (BLS) and advanced cardiac life support (ACLS) protocols during cardiopulmonary resuscitation of pregnant women.

Modification of BLS Protocols Continuous cricoid pressure should be applied during positive pressure ventilation in any unconscious pregnant patient to prevent regurgitation of gastric contents. Chest compressions should be performed slightly above the center of the sternum. Defibrillation is performed as per the standard guidelines. Uterine and fetal monitors are removed before delivering electric shocks. Left uterine displacement must be maintained after 20 weeks of gestation to minimize aortocaval compression.

Modification of ACLS Protocols The trachea should be intubated promptly to facilitate oxygenation and ventilation and to protect the airway from pulmonary aspiration. Standard ACLS drug protocols for nonpregnant women should be followed for pregnant women. Femoral or other lower extremity veins should be avoided for administration of drugs before the baby is delivered as they may not reach maternal heart.

Perimortem Cesarean Section According to American Heart Association, the best survival chance for infants >24 weeks gestation is when delivery is performed within 5 min of the onset of maternal cardiac arrest. To accomplish this, emergency hysterotomy should be started within 4 min after cardiac arrest. Delivery of the baby also improves maternal oxygenation and ventilation by increasing the venous return and thoracic compliance.

Maternal Hemorrhage

Obstetric hemorrhage accounts for 25–30 % of maternal deaths worldwide and includes antepartum, intrapartum, and postpartum causes. It is also responsible for maternal morbidity arising from adult respiratory distress syndrome, coagulopathy, shock, loss of fertility, and pituitary necrosis. Blood loss leading to hypovolemic shock is the end result whatever be the cause of hemorrhage. Clinical signs and symptoms depend on the amount and duration over which the blood loss occurs, with cardiovascular collapse seen at losses of 35–45 % of the total blood volume. Accordingly the patient may present with sweating, cold clammy extremities, mental status changes, diminished urine output, tachycardia, tachypnea, and hypotension.

Antepartum Hemorrhage

This is defined as bleeding from the genital tract after 24 weeks of gestation and complicates 2–5 % of all pregnancies. Causes include cervicitis, uterine rupture, placenta previa, and abruption.

Placental abruption is premature separation of a normally situated placenta and complicates 1 % of pregnancies. Most of the women present with vaginal bleeding, FHR abnormalities, uterine tenderness, and contractions. However, in about 20 % of the women the bleeding is concealed. Diagnosis is clinical and confirmed by USG. Risks factors of abruption are hypertension, preeclampsia, cocaine and tobacco use, abdominal trauma, advanced maternal age, and multiparity. Complications include hypovolemic shock, renal failure, DIC, fetal prematurity, and demise. Maternal hypovolemia may be underestimated in cases of concealed abruption. Placental abruption is the commonest cause of DIC in pregnancy. Management of abruption depends on the maternal and fetal status, gestational age, and presentation. Epidural analgesia can be offered provided maternal volume and coagulation status are reassuring. However, general anesthesia with rapid sequence induction and endotracheal intubation is preferred when urgent abdominal delivery is required for placental abruption with non-reassuring fetal tracing.

Uterine rupture is the tearing of uterine wall during pregnancy or labor and is associated with high maternal and perinatal mortality and morbidity. Risk factors include prior uterine scar, trauma, uterine anomalies, dystocia, use of uterotonic drugs, and abnormal placentation. The parturient may present with severe localized abdominal pain, vaginal bleeding, hypovolemic shock, and FHR abnormalities. Some women may present only with a scar dehiscence without excessive bleeding or FHR changes. Prompt diagnosis and surgical intervention prevent adverse outcomes. General anesthesia is required in most cases along with aggressive fluid resuscitation.

Placenta previa is abnormal insertion of placenta on the lower uterine segment (Fig. 38.3). Depending on the extent to which it covers the internal os of cervix, it can be classified as marginal (lies close to cervical os but does not cover it), partial (covers a part of cervical os), or complete (completely covers the cervical os). Risk factors include previous uterine scar, multiparity, advanced maternal age, or prior history of placenta previa. Patients typically present with painless uterine bleeding in second or third trimesters, with the diagnosis confirmed by USG. Timing of the delivery is dictated by the severity of bleeding, maternal status, and the gestational age. Prematurity and IUGR are the fetal risks associated with placenta previa. The route of delivery is by cesarean section. Higher than normal intraoperative blood loss is anticipated because the obstetrician has to cut through the placenta to reach the baby, with risk of placenta accreta and poor contractility of the lower uterine segment postdelivery.

Choice of anesthesia depends on the overall maternal volume status and the urgency for delivery. A single shot spinal anesthesia is a good option in patients without active bleeding and low risk of placenta accreta. In patients presenting with active bleeding and maternal hypovolemia, general anesthesia is preferred. Fluid resuscitation with a crystalloid or colloid should be carried out simultaneously. Regardless of the technique of anesthesia used, two large bore intravenous cannulae must be inserted before starting the procedure. Blood type and screen must be confirmed and depending on the situation and preference of the care provider packed red blood cells (PRBC) made available in the operating room.

Vasa previa is velamentous insertion of fetal vessels over the cervical os ahead of the fetal presenting part. As a result, rupture of membranes causes tearing of vessels and fetal blood loss. It is associated with 50–75 % fetal mortality. Immediate delivery of the fetus by abdominal route is indicated to prevent fetal exsanguination. Neonatal resuscitation team should be notified. General anesthesia is required in most of the cases due to urgency of the situation.

Postpartum Hemorrhage

PPH is excessive bleeding from the uterus, cervix, or lower genital tract after delivery of baby (blood loss of more than 500 ml after vaginal delivery or 1,000 ml after cesarean delivery, fall in hematocrit by 10 % from admission to postpartum period, need to administer PRBCs). It can be primary (during first 24 h) or secondary (24 h to 6 weeks after delivery) and complicates around 5 % of deliveries. Causes can be related to uterine tone, retained tissue, genital lacerations, and coagulopathy.

Uterine atony is the commonest cause of PPH seen in about 1 out of 20 deliveries. The uterus fails to contract and involute effectively during the third stage of labor. Risk factors include uterine over distension (multiple gestation, polyhydramnios, macrosomia), chorioamnionitis, prolonged labor, multiparity, effect of tocolytics, or general anesthesia. Physical findings include a soft, boggy uterus and vaginal bleeding. However, vaginal bleeding may be absent and an engorged uterus with an unrecognized intrauterine bleeding can result in maternal hypovolemia.

Prevention of PPH entails immediate administration of intravenous oxytocin infusion after delivery. Initial management includes bimanual compression, uterine massage, emptying the urinary bladder, discontinuation of inhalational anesthetics if in use, and use of additional ecbolic agents. Presence of adequate intravenous access should be confirmed and fluid resuscitation started along with supplemental oxygen. A blood sample should be collected for complete blood count, coagulation profile along with type and cross-match.

The uterotonic agents that are commonly used are oxytocin (20–60 U/L intravenous infusion), methylergonovine (0.2 mg intramuscular), 15-Methylprostaglandin (250 mcg intramuscular/intrauterine), and misoprostol (800–1,000 mcg rectally). Invasive treatment in cases where pharmacological options fail include intrauterine balloon tamponade, uterine compression sutures, angiographic arterial embolization, internal iliac artery ligation, and hysterectomy.

Abnormal placentation is abnormal attachment of placenta to the uterine wall (Fig. 38.3) and is classified as accreta (adherence to myometrium without invasion of uterine muscle), increta (invasion of myometrium), and percreta (invasion of uterine serosa). Abnormally adherent placenta fails to separate after delivery and results in severe hemorrhage along with uterine atony. Risk factors include presence of placenta previa and prior cesarean sections with the risk rising with increasing number of previous cesarean sections. Antenatal diagnosis can be made by USG or magnetic resonance imaging. Sometimes, the condition is first suspected when the obstetrician finds difficulty in separation of placenta and later confirmed at laparotomy. If the diagnosis is made or strongly suspected before labor and delivery, the American College of Obstetricians and Gynecologists (ACOG) have suggested the following measures to optimize the management of these parturients:

- Patient counseling about the need for hysterectomy, blood, and blood products.

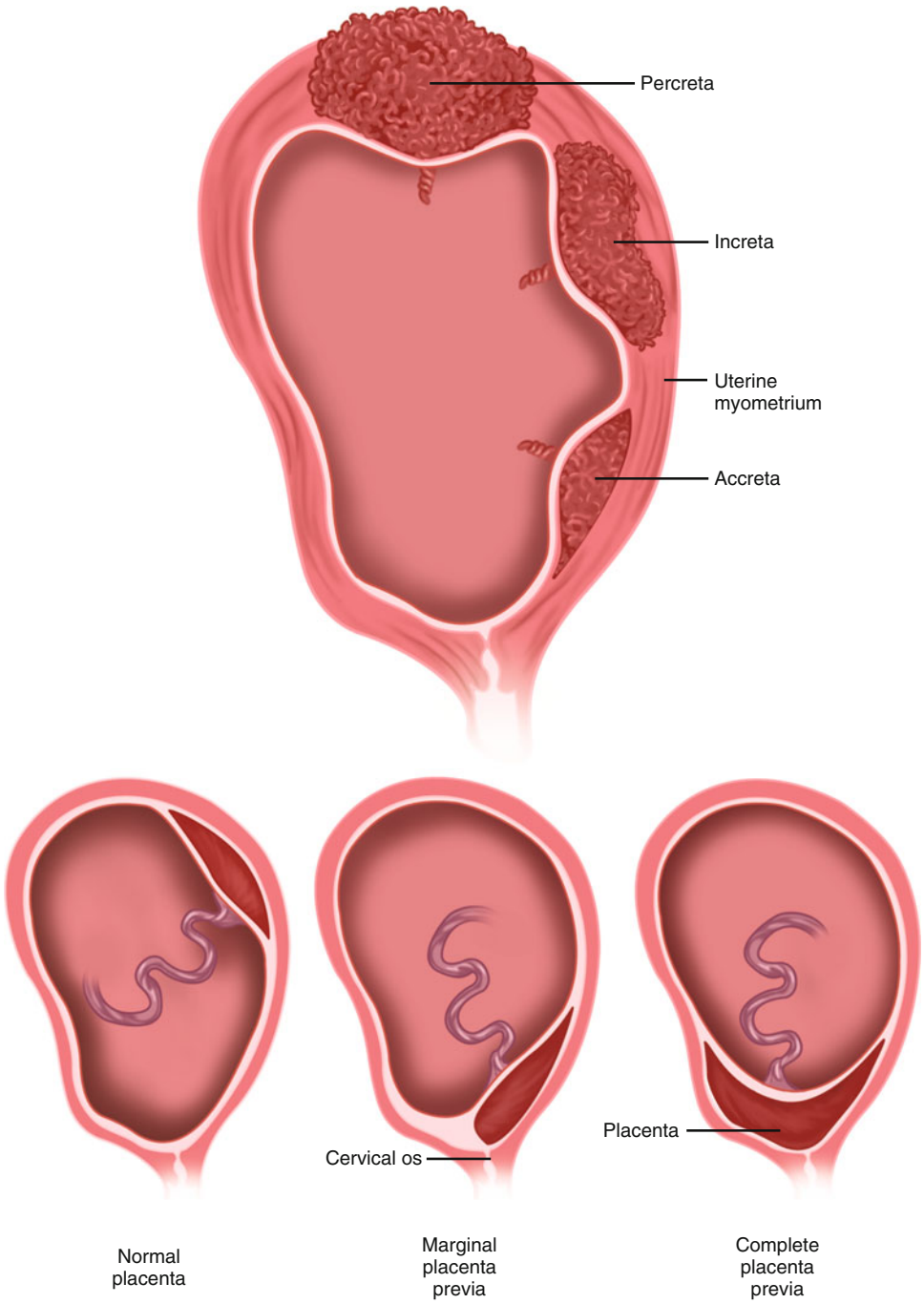

Fig. 38.3 Placental abnormalities

- Preoperative anesthesia consult.
- Availability of adequate personnel, blood and blood products, cell salvage.

Attempts to detach the placenta can result in severe catastrophic hemorrhage and most of the patients with abnormal placentation may need hysterectomy. If the diagnosis has been made before delivery, the obstetrician may proceed for an elective cesarean hysterectomy. Preoperative internal iliac balloon occlusion and embolization may decrease the blood loss and blood product requirement. Curettage and over-sewing have been described for selective cases of partial placenta accreta and avoids the need for a hysterectomy. General anesthesia is preferred in a bleeding patient for hysterectomy, whereas combined spinal epidural or general anesthesia may be provided for elective cases depending on the policy of the institution. Adequate large gauge intravenous access, cell salvage, and availability of blood and blood products should be confirmed.

Lacerations and hematomas of perineum, vagina, and cervix are the commonest childbirth injuries and can sometimes cause significant blood loss. Lacerations should be suspected in patients who have continuous vaginal bleeding in spite of a firm contracted uterus. Hematomas usually cause swelling and perineal pain. Conservative measures like pressure, ice application, and analgesics should be limited to small hematomas with no evidence of hemodynamic compromise. Large collections should be surgically explored, drained, and the vessels ligated preferable in the operating room. Anesthesia technique used depends on the maternal volume status, extent of surgical exploration, and urgency of the procedure.

Retained placenta refers to failure of delivery of fragments or whole of the placenta after delivery of the baby. Management usually involves manual removal of placenta under anesthesia. Patients who are hemodynamically stable can receive a neuraxial block (preexisting epidural or spinal). Other techniques described include 40–50 % nitrous oxide, small incremental doses of ketamine or fentanyl, taking care to preserve the protective airway reflexes. If uterine relaxation is deemed necessary, nitroglycerin can be given intravenous or general anesthesia with a volatile anesthetic can be administered. Inhalational agent should be switched off as soon as placental fragments are delivered.

Uterine inversion where the uterus turns inside out is a rare complication. Risk factors are improper fundal pressure, excessive umbilical cord traction, uterine atony, and anomalies. Treatment involves immediate replacement of the uterus and the anesthesia provider may require to provide uterine relaxation.

Coagulopathy as a cause of PPH is suspected in cases of unexplained and recurrent bleeding. Inherited bleeding disorders that can give rise to PPH include Von Willebrand disease and other clotting factor deficiencies (prothrombin, fibrinogen, factors V, VII, X, XI).

Whatever the cause of maternal hemorrhage, some general principles of management can be summarized as: multidisciplinary team approach, resuscitation using large bore access with fluid and blood, blood products, and coagulation factors to correct coagulation parameters, identification and treatment of the cause, and continuing evaluation of patient response using hemodynamic and laboratory parameters.

Amniotic Fluid Embolism

AFE is a dreaded complication of pregnancy with a reported incidence of 4–6/100,000 live births in the USA. It is often a diagnosis of exclusion and has high maternal morbidity and mortality. Initially it was thought that forceful passage of amniotic fluid during uterine contractions into the maternal pulmonary circulation gave rise to the clinical manifestations. However, it was seen that fetal squamous cells were found in the pulmonary vasculature of women with no evidence of the clinical syndrome and vice versa. Later, an immunologic etiology was proposed as the clinical manifestations of AFE are similar to those seen in an anaphylactic shock. Therefore, it has been suggested that AFE is an immunologic response to the presence of fetal tissue in the maternal intravascular compartment, and hence it should be designated as "*anaphylactoid syndrome of pregnancy*."

Clinical presentation is sudden with hypotension and fetal distress seen in almost all patients along with pulmonary edema, DIC, cardiac arrest, and sometimes seizures. Coagulopathy is a very prominent feature. Initially, there is pulmonary hypertension leading to right ventricular failure, hypoxia, and cardiac arrest. Pulmonary hypertension is replaced by left ventricular failure and pulmonary edema in the survivors. Differential diagnosis includes obstetric complications (abruption, eclampsia, uterine rupture), nonobstetric complications (pulmonary embolism, anaphylaxis, septic shock), and anesthetic complications (local anesthetic toxicity, total spinal).

Early diagnosis and prompt resuscitation can help improve the outcome for both mother and fetus. Airway must be secured with tracheal intubation and lungs ventilated with 100 % oxygen as hypoxia is always present. Several large bore intravenous lines must be secured and fluid resuscitation started. Arterial cannulation may be performed for hemodynamic monitoring and blood sampling and pulmonary artery catheterization may be considered. If the syndrome occurs intrapartum, obstetricians may expedite the delivery to improve the perinatal outcome and the quality of cardiopulmonary resuscitation for the mother. Circulation should be supported using vasopressors (phenylephrine) and inotropes (norepinephrine, epinephrine, dopamine, milrinone). The blood bank should be notified, and blood and blood products should be administered early to correct the coagulopathy. Echocardiography, when available, can be used to evaluate cardiac function and intravascular volume status but resuscitation measures should receive priority. These parturients usually require prolonged intensive care admission following successful resuscitation.

Newer advances reported for treatment of AFE include inhaled nitric oxide for pulmonary hypertension, cardiopulmonary bypass, and placement of intraaortic balloon pump with extracorporeal membrane oxygenation and right ventricular assist device with administration of recombinant factor VIIa.

Anesthesia for Nonobstetric Surgery During Pregnancy

Pregnant women may be exposed to anesthetic agents (>80,000 anesthetics/year in USA) during surgeries performed for maternal as well as fetal indications. The number

is ever increasing with the advances in the area of fetal surgery. Some commonly encountered maternal indications include incompetent cervix, ovarian cyst, appendicitis, trauma, and malignancy. Many times, pregnancy is not even confirmed at the time of surgery, unless a pregnancy test is performed. Physiologic changes of pregnancy need to be considered during anesthesia care.

Reduced oxygen reserves warrant adequate preoxygenation before induction of general anesthesia. The risk of encountering a difficult airway is not only present during cesarean section but also in early pregnancy. Induction with inhalational agents is faster in pregnant population and lower doses of local anesthetic agents are required to produce similar degree of neuraxial blockade. Left uterine displacement should be maintained during any surgery performed after 20 weeks of gestation. The hypercoagulable state in pregnancy combined with immobility in postoperative period increases the risk of thromboembolic complications. All pregnant women after early second trimester are considered "full stomach" irrespective of the timing of last meal and at risk pulmonary aspiration under anesthesia.

Fetal considerations include teratogenicity, intraoperative changes in the uteroplacental perfusion, and risk of abortion and/or preterm delivery. Manifestations of teratogenicity are death (abortion, stillbirth, fetal demise), structural abnormality, growth restriction, and functional impairment. The risk of drug teratogenicity in the fetus depends on the inherent drug toxicity, dosage, duration, and gestational age at the time of fetal exposure. Major congenital malformations are likely to occur if drug exposure occurs during the period of organogenesis, while functional deficiencies and minor morphological changes are seen when drug exposure occurs during late pregnancy. Also, though a drug may be harmful after single use of a high dose or long-term administration of a low dose, it may not incur a similar risk after a short exposure such as that occurs during surgical anesthesia.

As far as the anesthetic agents are concerned, teratogenicity is not usually seen with the commonly used induction agents (barbiturates, propofol, ketamine), opioids, benzodiazepines, local anesthetics, muscle relaxants, and inhalational agents for the doses used during anesthesia. However, due to experimental animal studies describing anesthesia induced neurotoxic effects on the developing brain and the need for more research in human, clinicians should avoid prolong and repeated anesthetic exposure in pregnant women and neonates. Although, surgery and anesthesia are associated with an increased risk of spontaneous abortion and fetal growth restriction, these effects are related to the procedure itself and/or underlying maternal condition and may not be due to anesthesia. Hypoxia, hypercapnia, temperature abnormalities, stress, and hypoglycemia during anesthesia and surgery can themselves have teratogenic potential. Maternal hypotension regardless of the cause can affect uteroplacental blood flow and hence the fetus.

Any elective surgery should be postponed until the second trimester (lowest risk of preterm labor) or preferably postpartum if possible. Surgery and anesthesia should be avoided in first trimester, especially during the period of organogenesis. Continuous intraoperative fetal monitoring may be carried out whenever feasible depending on case-by-case basis. Preoperative assessment and counseling about anesthetic risks and safety should be provided. Aspiration prophylaxis and endotracheal intubation should be performed during general anesthesia. No outcome difference is shown in the anesthetic technique used (regional vs. general) and regardless of the technique used every effort must be made to maintain maternal oxygenation, blood pressure, and acid–base status within normal limits. FHR and uterine activity must be monitored in the postoperative period.

Anesthesia for Fetal Surgery

Fetal surgery includes open surgical procedures (involve hysterotomy for the mother), minimally invasive techniques (endoscopic/percutaneous), and EXIT (Ex-utero intrapartum treatment). EXIT procedures are performed at cesarean delivery usually for neonatal airway obstruction due to large neck masses, where the airway is secured by tracheal intubation (or tracheostomy), while placental circulation is maintained. The goal of fetal surgical procedures is to improve neonatal outcome taking advantage of the fact that intrauterine environment supports rapid wound healing and the umbilical circulation takes care of nutritional and respiratory needs. Maternal complications include blood loss, preterm labor, and placental abruption. Fetal risks are nervous system injuries, prematurity, amniotic fluid leaks, and fetal demise. The basic anesthetic principles are same as those for non-obstetric surgery during pregnancy, except that during fetal surgery, the anesthesiologist also has to provide analgesia, amnesia, and immobility for the fetus. This can be achieved by direct fetal intravenous/intramuscular injection of drugs or placental transfer of maternally administered anesthetic agents. Depending on the procedure, the mother can receive local infiltration, intravenous sedation, and regional or general anesthesia. Uterine relaxation is important and needs to be continued in the postoperative period to prevent preterm labor.

Intrauterine Fetal Demise

Intrauterine fetal demise (IUFD) is death of the fetus after 20 weeks of gestation and before delivery. Causes can be maternal (preeclampsia, antiphospholipid antibody syndrome,

diabetes mellitus, isoimmunization), uteroplacental (abruption, placental previa, vasa previa, cord accident), or fetal (twin–twin transfusion syndrome, intrauterine infection, chromosomal and structural anomalies). Diagnosis is suspected when the fetal heart tones are not detected, and is confirmed by absence of fetal cardiac activity on USG. DIC develops in about 3 weeks in 20–25 % of women who retain a dead singleton fetus. Surgical dilatation and evacuation of uterus or induction of labor with prostaglandins or oxytocin should be carried out to deliver the fetus.

Clinical Review

1. The following respiratory parameter has the greatest change during pregnancy
   A. Tidal volume
   B. Respiratory rate
   C. Functional residual capacity
   D. Residual volume
2. In pregnancy, cardiac output increases the maximum during
   A. Second trimester
   B. Third trimester
   C. Labor
   D. Immediately after delivery of the baby
3. A 38 week pregnant women becomes bradycardic and hypotensive when she lies supine. Initial treatment consists of
   A. Administering ephedrine
   B. Intravenous fluids
   C. Oxygen and ephedrine
   D. Left uterine displacement
4. Analgesia should be provided for the following sensory level during the second stage of labor
   A. T8–S1
   B. T10–S1
   C. T8–S4
   D. T10–S4
5. A 32-year-pregnant patient is undergoing a cesarean section under spinal anesthesia. After administering the spinal anesthesia the patient is laid supine from the sitting position, and her blood pressure drops to 40/20 mmHg and the heart rate drops to 24 beats per minute. You would
   A. Administer ephedrine
   B. Administer phenylephrine
   C. Administer epinephrine
   D. Put the patient supine with left uterine displacement
6. Minimum recommended platelet count to perform a neuraxial block in a pregnant patient is (mm^3)
   A. 100,000
   B. 80,000
   C. 75,000
   D. 70,000
7. HELLP syndrome of preeclampsia is characterized by
   A. Hemolysis, elevated liver enzymes, low platelets
   B. Hemolysis, elevated liver enzymes, proteinuria
   C. Low hemoglobin, elevated liver enzymes, proteinuria
   D. Low hemoglobin, elevated liver enzymes, low platelets
8. Definite treatment of preeclampsia is
   A. Administer magnesium sulfate
   B. Delivery of the baby
   C. Keep the blood pressure below 140/90 mmHg
   D. Diuresis to prevent edema
9. All of the following may lead to maternal hemorrhage
   A. Placenta previa
   B. Placenta accreta
   C. Placenta increta
   D. All of the above

Answers: 1. A, 2. C, 3. D, 4. D, 5. C, 6. C, 7. A, 8. B, 9. D

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Pediatric Anesthesia

39

Terrance Allan Yemen and Christopher Stemland

The practice of pediatric anesthesia requires the understanding of maturational changes effecting growth and development that occur throughout the neonatal period and early infancy. Neonates are less than 30 days of age, while infants are 1–12 months of age. By 1 year rapid growth and development triples the child's birth weight. At 3 months of age, the respiratory system, cardiovascular system, and renal/fluid compartments begin to reflect the adult state. However, pediatric and neonatal physiology still differs significantly; hence pediatric patients are not simply "small adults." A thorough understanding of the physiologic and anatomical differences in children is essential for the anesthesiologist to provide optimal care for the pediatric patient.

Basic Pediatric and Neonatal Physiology

Respiratory

On a ml/kg basis, neonatal and young infant functional residual capacity (FRC) approach adult values (25–30 ml/kg); however, total volumes are smaller (Table 39.1). After birth, neonates take their first breath, define initial lung volumes, and hence establish functional residual capacity. Normal tidal breathing is 6 ml/kg as in adults; however, the rapid neonatal respiratory rate doubles the alveolar minute ventilation in neonates compared to adults. The increased alveolar ventilation allows for rapid uptake and distribution of volatile anesthetics.

Despite increased alveolar ventilation, neonates rapidly desaturate for two critical reasons. First, neonatal oxygen consumption is twice that of adults (6 ml/kg/min vs. 3 ml/kg/min), allowing for a high metabolic rate *relative* to FRC. This high metabolic rate in relation to the FRC leads to rapid desaturation in neonates and young infants. Secondly, infant closing volumes are high; hence small airways close during normal tidal breathing contributing to further desaturation.

Respiratory fatigue in neonates is a complex process that deserves further attention. Because the intercostal "accessory" muscles of respiration are not fully developed, respiratory work is primarily dependent upon the diaphragm. However, the neonatal diaphragm is comprised mostly of Type II fast-twitch *fatigable* fibers. In addition, neonates have noncompliant lungs but a very compliant chest wall, which make them prone to chest wall retractions, atelectasis, and increased work of breathing to maintain their functional residual capacity.

Adequate surfactant is critical for maintaining compliant lungs, open alveoli, and of FRC in compromised neonates at risk for respiratory fatigue/failure. Surfactant therapy can improve oxygenation and CO_2 elimination in critically ill pediatric patients. Inadequate oxygenation and/or CO_2 elimination, despite surfactant therapy, may require high-frequency oscillatory ventilation or even extracorporeal membrane oxygenation in select cases.

Cardiovascular

In utero, the high pulmonary vascular resistance allows for a parallel circulation, whereby both ventricles pump systemically with less than 10 % of the cardiac output entering the pulmonary system. To allow adequate placental oxygenated blood flow to the fetus, there are three shunts in utero: the ductus venosus, the foramen ovale, and the ductus arteriosus (Fig. 39.1). Oxygenated placental blood preferentially shunts across the foramen ovale because of relatively high right-sided heart pressures in utero (right to left shunt).

At birth, the pulmonary vascular resistance drops with the expansion of both lungs, thus promoting pulmonary blood

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flow and elevating the PO_2. As the left atrial pressure rises above right atrial pressure, the foramen ovale functionally closes; however, it still remains open in approximately 20 % of neonates. Upon exposure to higher PO_2, the ductus venosus almost immediately closes, while the ductus arteriosus musculature constricts leading to closure in a majority of term neonates (may remain open in some premature neonates).

The neonatal ventricle is rather noncompliant with a steep pressure-volume relationship that resembles the elderly population (fixed stroke volume). Therefore, inadequate preload leads to a stiff underfilled ventricle and hence low systemic pressures. Although hypotension after anesthetic induction usually responds to volume administration, practitioners must avoid overloading these patients. Volume overload can lead to pulmonary edema because the left ventricular myofibrils have decreased contractile mass. Moreover, the sarcoplasm sequesters Ca^{2+} (ineffective Ca^{2+} adenosine triphosphatase activity), thus impairing myocardial contractility. In addition, the neonatal ventricle tolerates afterload poorly because of relative noncompliance and poor contractility.

The underdeveloped neonatal sympathetic nervous system leads to a predominance of parasympathetic tone, and hence neonates are more prone to bradycardia under hypoxic conditions. Cardiac output in neonates/infants is heart rate "dependent" because of the fixed stroke volume. With a resting heart rate of 120–160 bpm (Table 39.2), bradycardia (<80 bpm) significantly impacts the cardiac output.

Table 39.1 Respiratory parameters in infants compared to adults

Parameter	Infant	Adult
Functional residual capacity	25–30 ml/kg	30 ml/kg
O_2 consumption	6 ml/kg/min	3 ml/kg/min
CO_2 production	6 ml/kg/min	3 ml/kg/min
Respiratory rate	35–50 breaths/min	12–20 breaths/min
Tidal volume	6 ml/kg	6 ml/kg
Alveolar ventilation	100–150 ml/kg/min	60 ml/kg/min
Vital capacity	35 ml/kg	60 ml/kg

Hematological

Circulating blood volume is highest for premature neonates (100 ml/kg), 85 ml/kg for term neonates, as compared with adults (70 ml/kg). Neonates have a hematocrit of about 60 %.

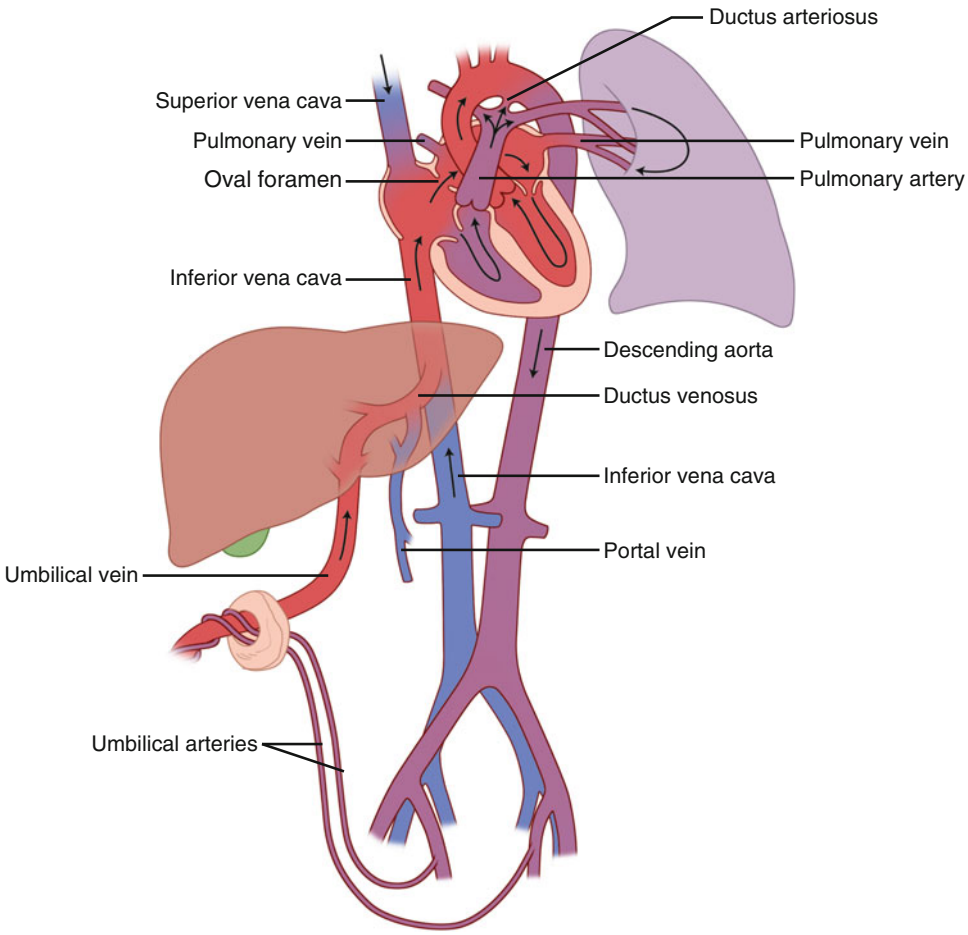

Fig. 39.1 Fetal circulation

Table 39.2 Cardiovascular parameters in children

Age	Blood volume (ml/kg)	Systolic BP (mmHg)	Heart rate (bpm)
Preterm neonate <37 weeks gestation	90–100	50	120
Term neonate <1 month	85	65	120
Infant (1–12 months)	80	75–95	120–160
Children > 1 year	75	75–95	80–100

The nadir in hematocrit occurs at about 6 months leading to a hemoglobin of 9 g/dl (hematocrit of 27 %). Because healthy neonates tolerate anemia better, blood transfusions may be deferred until the hemoglobin reaches 6–7 g/dl. However, the presence of congenital cyanotic heart disease or severe pulmonary disease has a higher trigger (Hb 10–13 g/dl) for blood transfusion. All neonates should receive irradiated blood to prevent graft-versus-host disease (where the donor lymphocytes attack the recipient's bone marrow). Lastly, the platelet count should be greater than 50,000/mm^3 to ensure the formation of an adequate primary hemostatic plug.

Renal

At birth, the GFR is 15–30 % of adult values (20–40 ml/min/1.73 m^2 compared to 120 ml/min/1.73 m^2) because of reduced nephron function, high renal vascular resistance, and low systemic perfusion pressures. In the 1st month, urine output is 1–2 ml/kg/h, but reduced GFR means large-volume administration can lead to hypervolemia and volume overload. Renally excreted drugs have a prolonged effect until the GFR approaches adult values at the end of 1 year. Because of decreased renal tubular function, neonates poorly concentrate urine as the medullary countercurrent exchange systems are immature. Both retention and excretion of sodium are impaired in neonates.

Neonates have proportionately a higher percentage of total body water (TBW) per kg body weight than adults, with fetuses having TBW of 90 %, preterm neonate 80 %, and full-term neonate 70 % of body weight. By 1 year, TBW decreases to the adult value of 60 % body weight. Initially, neonates have a predominance of extracellular fluid (ECF), which mobilizes as the GFR increases. Maintenance fluid requirements in neonates follow similar adult formulas; however, maintenance fluid should include sodium because of the reduced distal tubular reabsorption of sodium.

Temperature Regulation

Neonates and young infants have a large surface area to body weight ratio causing rapid heat loss in the operating room. The primary mechanisms for neonatal heat loss are conduction and radiation, with convection and evaporation playing a less significant role. Because neonates do not shiver, heat production occurs through non-shivering thermogenesis due to brown fat metabolism. Neonatal oxygen consumption is already elevated compared to adults (6 ml/kg/min vs. 3 ml/kg/min), and increased oxygen consumption due to cold stress may produce metabolic acidosis, cardiac irritability, or respiratory depression in compromised neonates. Heat loss can be prevented by using forced air-warming device, warm blankets, and warm intravenous fluids and most importantly by increasing the operating room temperature to 26 °C or higher. Heat lamp radiation is beneficial; however, it may produce mild burns when used too close to the skin.

Pediatric Airway

As compared to adults, the normal pediatric airway has a cephalad glottis (C4 vs. C6 in adults), large tongue, prominent occiput, long epiglottis, and short trachea and neck, with the narrowest part of the pediatric airway being the cricoid ring. Because neonates and infants <6 months are preferentially nasal breathers, bilateral choanal atresia can lead to complete airway obstruction. Airway management in healthy children is usually straightforward; however, airway management in craniofacial syndromes, such as Pierre Robin syndrome (micrognathia, retrognathia, and glossoptosis—large tongue in relation to oropharynx) or Treacher Collins syndrome (mandibular facial dysostosis with severe hypoplasia of the mandible and zygomatic arches), can be challenging.

Preterm Neonate

Neonates born of gestational age <37 weeks are labeled as preterm neonates. Preterm neonates have some unique differences than full-term neonates. Aberrant retinal vascular development leads to retinal tears and detachment and ultimately blindness, termed as retinopathy of prematurity (ROP). Risk factors for ROP include prematurity, low birth weight, and exposure to supplemental oxygen. Therefore, supplemental oxygen should be avoided, whenever possible, in neonates until 44 weeks of postgestational age and if given, should have a goal of maintaining oxygen saturation in the low 90 %.

Premature neonates are prone to the development of respiratory distress syndrome as the lungs mature after 34

weeks of gestation. Surfactant production begins at 26 weeks of gestation and enough is produced at 34 weeks of gestation for the alveoli to remain open. Neonates requiring supplemental oxygen at 36 weeks of gestation are said to have chronic lung disease. Premature neonates, because of reduced hepatobiliary function, are prone to hypoglycemia and hypocalcemia. Often they require dextrose-containing solutions for maintenance.

Preterm neonates are susceptible to apnea and thus require continous pulse oximetry monitoring in the post-operative period. Preterm neonates may have a hematocrit of 40 % as compared to 60 % for full term neonates, and this anemia further increases the risk of apnea. This predisposes a preterm infant to apnea. Moreover, preterm infants often have vitamin K deficiency and thrombocytopenia. Therefore, elective surgery should be deferred until 60 weeks postgestational age in preterm neonates. If surgery is performed before 60 weeks postgestational age, then these neonates are admitted postoperatively for observation for apneic episodes.

Pediatric Anesthetic Pharmacology

Inhalational Agents

The uptake and distribution of volatile anesthetics occur rapidly in pediatric patients. Firstly, high minute ventilation (high respiratory rate) to FRC ratio (5:1) causes a rapid increase in alveolar anesthetic concentration. Secondly, the distribution of high cardiac output to vessel-rich organs hastens the uptake of volatile anesthetics. The relatively insoluble sevoflurane (blood–gas solubility coefficient 0.62) has largely replaced halothane (blood–gas solubility coefficient 1.6) for inhalational induction. However, halothane's safety is well established despite sensitizing the myocardium to catecholamines and directly reducing cardiac output.

Nitrous oxide use can diminish sevoflurane's irritant properties and could hasten its uptake via the second gas effect; however, the clinical significance of this phenomenon is minimal. The cardiovascular effects of volatile agents include bradycardia and hypotension and could cause cardiac arrest in children less than 1 year of age and those with congenital heart defects. Cardiac arrests attributed to inhalational agents have declined since the decreased use of halothane.

The minimum alveolar concentration peaks in early infancy (2–3 months), remains elevated throughout childhood and adolescence, and then gradually declines with age. The MAC of sevoflurane peaks at 3.3 % for 3-month neonates, is 2.5 % for older children, and then declines to the 2 % value for adults. Intracardiac shunts (R>L shunt) may theoretically slow inhalational induction because greater blood flow bypasses the lungs. Conversely, L>R shunts would speed inhalation induction. The practical impact of shunt flow is negligible because the cardiac output drives anesthetic blood concentrations toward equilibrium.

Intravenous Induction Agents

Intravenous induction can be achieved with midazolam, ketamine, or propofol. Propofol is the commonly used intravenous agent for pediatric induction of anesthesia. Propofol doses of 2.5 mg/kg ablate eyelid reflexes within 50 s and increase mask acceptance. The maintenance of general anesthesia with intravenous propofol requires a continuous infusion of 200–300 mcg/kg/min. Prolonged infusion of propofol (in the ICU) may cause "propofol infusion syndrome" consisting of unexplained metabolic acidosis, heart failure, and even death.

Veno-irritation by propofol may be decreased by injection into a large antecubital vein and pretreatment or coadministration of lidocaine or opioids. In addition to causing profound apnea, propofol decreases both systemic vascular resistance and sympathetic outflow from the brain. While children experience mild reductions in blood pressure, preterm neonates with poorly developed sympathetics can become profoundly hypotensive with propofol.

The NMDA antagonist ketamine provides mild amnesia, profound analgesia, and produces general anesthesia at higher doses (1–2 mg/kg IV or 3–4 mg/kg IM). Although NMDA receptor blockade produces neuronal apoptosis and learning abnormalities in laboratory animals, ketamine's long-term neurobehavioral effects on children are unknown. The benefits of ketamine include maintenance of spontaneous ventilation (does not typically produce apnea unlike propofol), bronchodilation while preserving airway reflexes, and activation of the sympathetic nervous system. The propensity toward secretions and post-op nausea/vomiting with ketamine is prevented with anticholinergics (glycopyrrolate/atropine) and antiemetics, respectively. Dysphoria is prevented with the coadministration of benzodiazepines (midazolam).

Opioids

The use of an opioid at induction allows decreased dosage of induction agent, attenuates sympathetic response to laryngoscopy, and prevents veno-irritation from propofol. Typical dosages of opioids in children are fentanyl 0.5–1 mcg/kg, sufentanil 1 mcg/kg, morphine 0.1 mg/kg, methadone 0.2 mg/kg, hydromorphone 10–20 mcg/kg, and remifentanil 1–2 mcg/kg. Morphine and methadone should be used with caution in infants <6 months of age because of impaired clearance. The rapid administration of high dosage of an opioid

can cause chest wall rigidity making ventilation difficult. Chest wall rigidity is easily reversed by administering a non-depolarizing neuromuscular blocker or succinylcholine. The ultra-short-acting opioid remifentanil is ideal for procedural sedation, but its short duration of analgesia due to rapid non-specific esterase metabolism prevents its use for postoperative analgesia.

Succinylcholine

Succinylcholine provides rapid onset of neuromuscular blockade within 30 s of administration (2 mg/kg IV or 4 mg/kg IM), allowing for rapid sequence induction when pulmonary aspiration of gastric contents is a concern. Common indications of succinylcholine use are small bowel obstruction, pyloromyotomy, trauma-induced delayed gastric emptying, emergency surgery with recent solid food ingestion, and the treatment of life-threatening laryngospasm (0.1 mg/ kg).

Succinylcholine is used cautiously in pediatric patients because it can cause bradycardia (even with a single dose), rhabdomyolysis, and hyperkalemic cardiac arrest in children with undiagnosed myopathy (Duchenne muscular dystrophy) and is associated with malignant hyperthermia. These lethal reactions prompted the FDA's black box warning in the 1990s regarding the use of succinylcholine in at-risk pediatric populations. Other contraindications to succinylcholine include prolonged immobility, burn patients after 24 h, spinal cord injury after 24 h, myopathy, central core disease, and renal failure with hyperkalemia. Succinylcholine has been safely used in patients with cerebral palsy.

Non-depolarizing Neuromuscular Blocking Agents

Rocuronium (0.6–1 mg/kg—intubating dose) provides the onset of neuromuscular blockade within 1–2 min, and its paralytic effect is reversible in 30–45 min. Neuromuscular blocking agents have faster onset in children because of higher cardiac output and more rapid delivery to the neuromuscular junction. The ED-95 of a neuromuscular blocking agent is the dose providing 95 % single twitch depression. Multiple ED-95s (i.e., 2 mg/kg rocuronium) hasten the onset of laryngeal muscle relaxation by overwhelming the neuromuscular junction but at the expense of prolonged neuromuscular blockade. Rocuronium (with an ED-95 of 0.3 mg/kg) has a faster onset than vecuronium (ED-95 of 0.1 mg/kg). Both rocuronium and vecuronium are eliminated primarily in the hepatobiliary system (80 %), while the remainder of these drugs are excreted unchanged in the urine.

Pediatric Anesthesia Care

Preoperative Preparation

A parent signs the consent for anesthesia for children below 18 years of age. Children should be involved in the decision-making, as much as possible.

History and Physical

The preoperative history and physical should focus upon the birth history (prematurity or any complications), immunization status, any recent/current upper respiratory infection, and a pertinent review of systems (asthma, obstructive sleep apnea, cardiopulmonary symptoms). Unrepaired significant congenital heart disease, severe asthma, or moderate to severe obstructive sleep apnea likely precludes outpatient surgery and requires further evaluation.

Caution should be used for proceeding with elective surgery in healthy children recovering from a recent (2–4 weeks) upper respiratory infection (severe cough, high fever), understanding that these patients have a higher incidence of laryngospasm, bronchospasm, and oxygen desaturation. Risk factors for URI-related adverse events include airway surgery, history of prematurity, reactive airway disease, parental smoking, copious secretions, and nasal congestion.

Fasting

Pediatric fasting guidelines follow those for adults, namely, 6–8 h for solids, 6 h for formula, 4 h for breast milk, and 2 h for clear liquids. The incidence of pediatric aspiration is approximately 1:10,000 anesthetics, which is twice that reported in adults.

Preoperative Laboratory Tests

These are not routinely ordered for healthy patients undergoing minor surgical procedures. However, an electrolyte panel should be assessed in patients with renal disease and in patients with pyloric stenosis to determine the degree of resuscitation (chloride level > 95 meq/L). A preoperative CBC should be obtained for procedures involving significant blood loss, presence of coagulopathy, and presence of sickle cell anemia or if minor bleeding could be life-threatening.

Preoperative Sedation

The pediatric anesthesiologist plays a critical role in reducing both parental and patient preoperative anxiety on the day of surgery. Midazolam (0.25–0.5 mg/kg PO, maximum 20 mg) assists separation between the parent and the child, provides amnesia and anxiolysis, increases face mask acceptance, and smoothens the inhalational induction. Preoperative

anxiety is often linked to postoperative delirium and maladaptive behaviors. Although the effectiveness of midazolam is well established, anesthetic induction relies upon trust and rapport between the child and the anesthesiologist.

A majority of pediatric patients over the age of 6–8 years tolerate mask induction well without the aid of midazolam. Also, midazolam is usually not administered to infants and neonates. Other adjuvants that can be administered preoperatively include IM ketamine (3 mg/kg) for combative patients, oral ketamine 4–6 mg/kg, and oral clonidine 4 mcg/kg. Rectal administration of premedication is less common, but historically rectal methohexital and thiopental have been used.

Anesthetic Induction

The induction of anesthesia in pediatric patients is done via the inhalational route or intravenous route. Children over 10 years are usually cooperative for intravenous insertion. The procedure for inhalation induction is described in the chapter of "Inhalational anesthetics." If the patient is induced with an inhalational agent, an intravenous line is inserted once the patient is asleep (Table 39.3).

Intravenous access in children may be challenging. For awake IV insertions, applying EMLA skin cream (eutectic 5 % mixture of local anesthetics—lidocaine and prilocaine 2.5 % each) 45 min prior to insertion may be beneficial. Locations for blind intravenous access in children include the saphenous vein (anterosuperior to the medial malleolus), median cubital vein (antecubital fossa), and the dorsal hand vein (between 4th and 5th carpal bones). For emergency purposes, intraosseous access may be obtained by inserting an intraosseous or Tuohy needle in the proximal tibia, distal tibia, or distal femur.

Special Pediatric Problems

Recent Upper Respiratory Tract Infection

Because children experience frequent upper respiratory tract infections, they often present for elective surgery with rhinorrhea, cough, and nasal congestion. When proceeding with elective surgery, consideration includes the complexity of surgery, family circumstances that may prevent rescheduling, and any coexisting disease that may increase the risk of anesthesia complications. After an upper respiratory tract infection, airway hyperresponsiveness persists for at least 2–4 weeks, but healthy children could be anesthetized albeit with an increased risk of bronchospasm, laryngospasm, and oxygen desaturation. Risk factors for anesthetic complications include history of prematurity, reactive airway disease, endotracheal intubation, parental smoking, and copious secretions.

Down Syndrome/Trisomy 21

Trisomy 21 affects 1.5/1,000 live births and is commonly associated with advanced maternal age. The characteristic features include flat facies, oblique palpebral fissures, simian crease, large tongue, short neck, and associated mental retardation. The presence of both a narrower trachea and smaller subglottis may require the use of a smaller size endotracheal tube than predicted. Obesity is common, which can make IV access difficult. Patients may have overreactive vagal tone, hypotonia, and joint laxity. Trisomy 21 children also have a higher incidence of duodenal atresia and cervical ligamentous laxity contributing to radiographic atlantoaxial instability,

Table 39.3 Induction techniques in children

Inhalational induction	
Face mask	May add flavor smell
Induction	10 l flow of 100 % oxygen or 70/30 N_2O–O_2, plus sevoflurane 6–8 %
IV start	Once patient is asleep, no air bubbles in line
N_2O	Discontinued
Prior to LMA insertion/intubation	Administer fentanyl or small dose of propofol if desired, and if intubating a non-depolarizing muscle relaxant (rocuronium), avoid succinylcholine (some do not use any muscle relaxant)
Intravenous induction	
Preoxygenation if possible, give propofol (1.5–2 mg/kg) or muscle relaxant if needed (rocuronium—0.6–1 mg/kg)	
Endotracheal tube size and length	
Premature	2.5–3 mm tube
Neonates	3.0–3.5 mm tube
Children tube size (diameter) formula	4 + (age/4) in mm (correct size tube should have an air leak at 25 cm H_2O pressure, additional size tubes 0.5 mm larger and smaller should be available
Tube length formula	12 + (age/2) in cm, correct length should be confirmed by auscultation

clinically the cervical spine IS stable. Granted there is controversy here but most folks agree that the c spine is stable.

The incidence of congenital heart disease is high (43 %), most commonly involving partial or complete atrioventricular canal and ventricular septal defects. These children have a propensity toward obstructive sleep apnea, pulmonary hypertension, and pulmonary infections. Enlarged tonsils and small ear canals necessitate frequent otolaryngology procedures, including tonsillectomy and myringotomy. Patients may also present for repair of cleft lip/palate, cataracts, and strabismus surgery.

Epiglottitis vs. Croup

Epiglottitis presents in children aged 2–6 years with fever, dysphagia, drooling, inspiratory stridor, and sitting forward to promote clearing of secretions. Epiglottitis is a life-threatening bacterial infection caused by *Haemophilus influenzae* type B (HIb). Vaccination has significantly decreased the incidence of HIb infection in the developed world. Radiographic studies should not delay airway management. A lateral neck X-ray, if taken, shows a thumbprint sign, representing a swollen epiglottis.

Because epiglottitis can result in complete airway obstruction, awake manipulation of the mouth and oropharynx and even IV insertion should be avoided. Suspected patients are brought emergently to the operating room with the otolaryngologist or surgeon, anesthesiologist, and emergency tracheostomy/rigid bronchoscopy equipment readily available. Key management aspects include inhalational mask induction (sitting position), maintenance of spontaneous ventilation (O_2 and an inhalational agent), IV start, followed by laryngoscopy and intubation, avoidance of neuromuscular blockade for intubation, and availability of advanced airway equipment, including a pediatric glidescope and fiber-optic bronchoscope, plus tracheostomy equipment. Patients are adequately hydrated and antibiotics started as soon as possible.

Croup or laryngotracheobronchitis is caused usually by a viral infection. However, a more serious form of croup is caused by the bacteria *Staphylococcus aureus*. Croup commonly affects children aged 3 months to 3 years and is accompanied by low-grade fever, barking cough, and steeple sign on chest X-ray. Endotracheal intubation is rarely required. The treatment of croup is with humidified oxygen, racemic epinephrine, steroids, and brief mechanical ventilation for severe cases requiring active pulmonary suctioning.

Foreign Body Aspiration

Foreign body aspiration into the airway or esophagus is one of the most frequent pediatric surgical emergencies. It occurs commonly in children aged 18 months to 3 years and in the acute presentation is witnessed and accompanied by cough, dyspnea, stridor, unilateral decreased breath sounds, and frequently pulmonary hyperinflation from air trapping on chest film (alternatively atelectasis). A delayed presentation occurs when an aspiration episode is unwitnessed and the child develops unexplained respiratory symptoms including cough, wheezing, and respiratory tract infection. In both settings, definitive treatment is removal of the foreign body with rigid bronchoscopy and/or esophagoscopy, which discover about 70–90 % of the foreign bodies. These procedures carry a morbidity/mortality rate of up to 5 %.

Children are brought urgently to the operating room and anesthetized in the presence of an experienced otolaryngologist or pediatric surgeon. Although a majority of patients will have a functioning intravenous catheter, *inhalational* induction is usually performed, so as to permit spontaneous ventilation. Controversy exists regarding the maintenance of spontaneous ventilation versus administering neuromuscular blockade. While spontaneous ventilation can cause inadequate depth of anesthesia and lead to coughing, laryngospasm, and potentially bronchospasm, controlled positive pressure ventilation can further push down the foreign body into the bronchus.

Before introduction of the rigid bronchoscope, a deep level of anesthesia is best achieved by direct airway topicalization with 2 % lidocaine, intravenous propofol, and maintenance of spontaneous ventilation with sevoflurane. Oxygenation is provided through the rigid bronchoscope side port augmented by the child's spontaneous ventilation efforts.

Minor complications include postoperative nausea/vomiting, persistent coughing, and airway edema (all patients should receive low-dose dexamethasone—0.25–0.5 mg/kg). Major complications include stridor (treat with racemic epinephrine), hypoxia, hypercarbia, pulmonary atelectasis, and rarely inability to oxygenate/ventilate due to complete airway obstruction if the foreign body becomes trapped at the carina. The latter situation is treated by immediately removing the foreign body or pushing the object down one of the main stem bronchus.

Tonsillectomy and Adenoidectomy

Adenotonsillectomy is indicated for children with frequent throat infections or those with symptoms consistent with obstructive sleep apnea. The diagnosis of recurrent throat infections requires at least five infections in the preceding 2 years. Enlarged tonsils often cause obstructive sleep apnea, which can present as nighttime snoring, behavioral problems, and difficulty in learning.

Induction of anesthesia is done via the inhalational route, followed by an intravenous start and insertion of a *flexible*

LMA (wire reinforced) or endotracheal tube. The use of an oral RAE endotracheal tube in older children prevents kinking of the tube. The tube is taped preferably in the center of the mouth/chin. Pain control is achieved with opioids, and prophylaxis against nausea/vomiting is done by administering dexamethasone (0.25 mg/kg) and ondansetron (0.15 mg/kg). The surgeon empties the stomach (blood that goes down into the stomach) at the end of the case by inserting an orogastric tube. Presence on an LMA will prevent passage of an orogastric tube. The patient is extubated with return of airway reflexes and the head elevated to about 30°. The patient may then be placed in a lateral position to allow secretions to pool away from and out of the mouth.

Overnight observation should be considered for patients with moderate to severe obstructive sleep apnea. Patients with obstructive sleep apnea may develop post-obstructive pulmonary edema after relief of their chronic airway obstruction. Antiplatelet agents (NSAIDS) may be avoided for pain control, if bleeding is a concern.

Postoperative hemorrhage occurs commonly within 6 h after surgery but can occur up to 10–14 days after surgery. Post-tonsillectomy bleeding is a surgical emergency. Patients that are brought back to the operating room for hemorrhage should be considered full stomach (swallowed blood). Patients should be volume resuscitated, and in severe cases a type and crossmatch should be ordered. Adequate suction equipment should be readily available. The induction of anesthesia is always done via the intravenous route and rapid sequence with cricoid pressure. Titrated doses of propofol or ketamine may be used for the induction of anesthesia. After repair and achievement of hemostasis, the patient is extubated awake with return of airway reflexes.

Pediatric Scoliosis Correction

Idiopathic scoliosis affects between 2 and 4 % of children aged 10–16 years, but only 0.2–0.4 % of patients require surgical correction, the majority of which is performed for adolescent females. Scoliosis is usually idiopathic affecting healthy adolescents; however, secondary causes of scoliosis include congenital scoliosis, muscular dystrophy (frequently Duchenne), cerebral palsy, osteogenesis imperfecta, and connective tissue diseases (Marfan's syndrome and Ehlers–Danlos syndrome).

Spinal fusion is performed when the Cobb angle curvature exceeds 40–45°, so as to prevent disease progression and the onset of restrictive pulmonary disease. During the surgery, spinal column distraction (i.e., straightening) can cause spinal cord ischemia. Therefore, somatosensory-evoked potential monitoring (SSEP) and intermittent motor-evoked potentials (MEPs) monitoring are done to detect neurological injury. Volatile anesthetics (>1 MAC) decrease SSEP amplitude and increase SSEP latency. At concentrations of 0.5 MAC, volatile anesthetics depress SSEP signals to a much smaller degree, thus allowing for reasonable SSEP monitoring. However, small concentrations of volatile anesthetics profoundly diminish MEP signals and hence should be avoided while monitoring MEPs. Nitrous oxide decreases the amplitude but not the latency of SSEPs.

Blood loss during spinal column osteotomies may be significant, particularly for neuromuscular scoliosis. This warrants adequate monitoring (arterial and central venous catheters), insertion of a large-bore IV, and maintaining volume status, including the hematocrit/hemoglobin. The use of antifibrinolytic agents (tranexamic acid) may significantly reduce blood loss during scoliosis correction.

Urological Procedures

Common urologic pediatric procedures include circumcision, orchiopexy for undescended testicle, repair of hypospadias, and ureteral reimplantation for vesicoureteral reflux disease. A single-shot caudal epidural injection provides excellent analgesia even for day surgery cases. More complex procedures requiring overnight admission, such as ureteral reimplantation or repair of bladder extsrophy, benefit from caudal opioid additives, such as morphine (20–30 mcg/kg) and hydromorphone (15 mcg/kg), or a continuous lumbar epidural catheter. Morphine is associated with delayed respiratory depression requiring monitoring of ventilation and therefore, not appropriate for outpatient procedures.

PACU Complications

Vigilant monitoring in the postanesthesia care unit is required to detect acute airway obstruction, laryngospasm, bronchospasm, and hypoventilation. The incidence of laryngospasm varies from 1 % to 10 % depending upon the patient population, surgical procedure, and study methodology but remains consistently higher for procedures involving the airway such as adenotonsillectomy, direct laryngoscopy/rigid bronchoscopy, and removal of airway foreign body.

Post-intubation stridor, commonly due to airway edema, should be treated with oxygen supplementation, dexamethasone (0.5 mg/kg), and nebulized racemic epinephrine (0.5 ml of 2.25 % solution in 2.5 ml normal saline). The patient should be observed postoperatively for at least 4–6 h. Refractory stridor may warrant reintubation with a smaller-size endotracheal tube.

These airway procedures also have a higher incidence of both postoperative nausea/vomiting and emergence delirium, complications that require aggressive prophylaxis intraoperatively. A combination of dexamethasone (0.25 mg/kg) and

ondansetron (0.15 mg/kg) will prevent a majority of PONV, whereas the incidence of emergence delirium decreases with the use of opioids (adequate pain control), propofol-based anesthesia, and the α-2 agonist dexmedetomidine. Rescue treatment for postoperative nausea/vomiting is best done with promethazine (Phenergan) or droperidol 10–20 mcg/kg. Because of the FDA's black box warning regarding QT-interval prolongation with droperidol, most centers require 2 h of continuous ECG monitoring after droperidol administration.

Neonatal Emergencies

Necrotizing Enterocolitis

Necrotizing enterocolitis (NEC) is associated with prematurity and low birth weight (often <1.5 kg) and represents a true pediatric medical emergency that may require immediate surgical intervention in the presence of a dead bowel. It carries an overall mortality rate of 7 %. The clinical features are divided into three stages:

Stage 1—apnea, bradycardia, lethargy, abdominal distension, and vomiting
Stage 2—pneumatosis intestinalis (intestinal wall gas)
Stage 3—hypotension, acidosis, oliguria, and disseminated intravascular coagulation

These neonates may have lung disease, respiratory distress syndrome, and patent ductus arteriosus and may be susceptible to infections. Premature neonates with necrotizing enterocolitis have poor feeding, often distended tender abdomens, and associated hyperglycemia, hypotension, and characteristic "pneumatosis intestinalis" on abdominal films suggesting intestinal wall gas. Although free air under the diaphragm may suggest intestinal perforation, clinicians must suspect NEC in premature neonates having fever, unexplained hypotension, and a distended abdomen.

The management of NEC includes bowel rest, abdominal decompression, fluid resuscitation, broad-spectrum antibiotic therapy, and in some cases surgical treatment with either peritoneal drain placement or exploratory laparotomy with bowel resection, enterostomy, and stoma creation. Anesthetic management requires massive volume resuscitation, including administration of 5 % albumin, packed red blood cells to correct any anemia, and sometimes plasma to correct or prevent dilutional coagulopathy. To compensate for extensive third-space volume losses, fluid requirements may necessitate the administration of one blood volume of 5 % albumin (i.e., 100 ml/kg). Opioids are used to provide analgesia. Propofol and inhalational agents may cause profound vasodilatation and hypotension, especially in premature neonates, and therefore, should be used cautiously.

Tracheoesophageal Fistula

Esophageal atresia with distal tracheoesophageal fistula (TEF), Type C (distal TEF with proximal atretic esophageal pouch), accounts for 85 % of TEF lesions (Fig. 39.2). The overall incidence of TEF is 1/3,000 live births. TEF may be isolated or a component of the VATER syndrome that includes vertebral anomalies, imperforate anus, tracheoesophageal fistula, and renal abnormalities or VACTERL syndrome that also includes congenital heart disease and limb deformities.

TEF frequently presents with excessive oral secretions, poor feeding, respiratory distress with feedings (coughing and choking), and aspiration pneumonitis. The diagnosis is confirmed by failure to pass a nasogastric tube into the stomach, while confirmation is made with contrast radiographic studies. Definitive surgical treatment of TEF is delayed until the neonate is medically stable, has been assessed for coexisting congenital heart disease, and has adequate esophageal length for esophageal anastomosis.

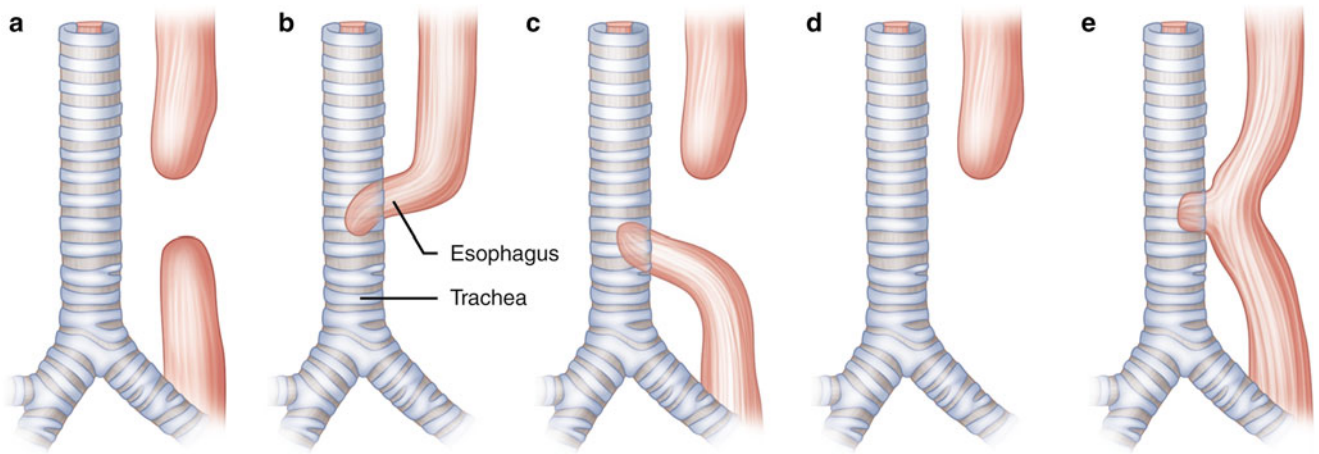

Fig. 39.2 Types of tracheoesophageal fistula (commonest is type C)

Although an awake intubation is feasible, the neonate usually undergoes inhalational induction followed by direct laryngoscopy and right endobronchial intubation. The endotracheal tube is then withdrawn until bilateral breath sounds are heard, thus placing the endotracheal tube tip distal to the fistula but above the carina. After confirming satisfactory endotracheal tube position, subsequent neuromuscular blockade prevents patient movement and endotracheal tube migration. Careful attention to airway management is critical because positive pressure ventilation (keep pressures <15 cm of H_2O) may result in excessive gastric distention through the fistula, making ventilation difficult, which may lead to cardiorespiratory arrest.

Anesthesia is maintained with 100 % oxygen, a volatile agent, opioids, and a muscle relaxant. Total intravenous anesthesia may have to be utilized because the leak of vapor may provide inadequate depth of anesthesia. If ventilation becomes inadequate or the end-tidal CO_2 tracing disappears, the anesthesiologist must consider endotracheal tube migration into the fistula prompting gentle retraction of the tube until ventilation improves.

Monitoring should include an arterial line, and blood should be available for transfusion. Surgical traction may compress the lungs, trachea, heart, great vessels, and vagus nerve (bradycardia). Most patients require postoperative mechanical ventilation with PEEP and lung reexpansion. Tachypnea and respiratory failure must be avoided to prevent reintubation and tracheal suture line disruption. Postoperative analgesia can be achieved with continuous caudal catheter local anesthetics.

Congenital Diaphragmatic Hernia

Congenital diaphragmatic hernia (CDH) results from incomplete closure of the pleuroperitoneal canal during embryological development and affects about 1/2,000–5,000 neonates. Either side of the body may be affected, but CDH usually involves the left posterolateral side, producing herniation of gastrointestinal contents into the thoracic cavity, which causes ipsilateral lung and pulmonary artery hypoplasia and pulmonary arterial hypertension (Fig. 39.3). The neonate has a scaphoid abdomen and radiographic evidence of bowel in the thorax. Approximately 20 % of CDH patients have coexisting congenital cardiac disease, which increases mortality by a factor of 2.9.

Surgical repair is performed after the patient is medically stabilized. Preoperatively, a nasogastric tube is placed to minimize gastric distension. The induction of anesthesia is by rapid sequence induction via the intravenous route or intubated awake without the use of muscle relaxants. One must avoid excessive positive pressure ventilation, thus limiting gastric distension and pulmonary compression on the ipsilateral side. Anesthesia is maintained with 100 % oxygen, a volatile agent, opioids, and a muscle relaxant. Nitrous oxide is avoided as it may cause bowel distension. Peak airway pressures are kept below 30 cm of H_2O. Excessive pulmonary pressures may indicate the development of a pneumothorax (ipsilateral or contralateral side), which may warrant the need to insert a chest tube.

Although surgical closure repairs the diaphragm, the hypoplastic ipsilateral lung often fails to expand, which can

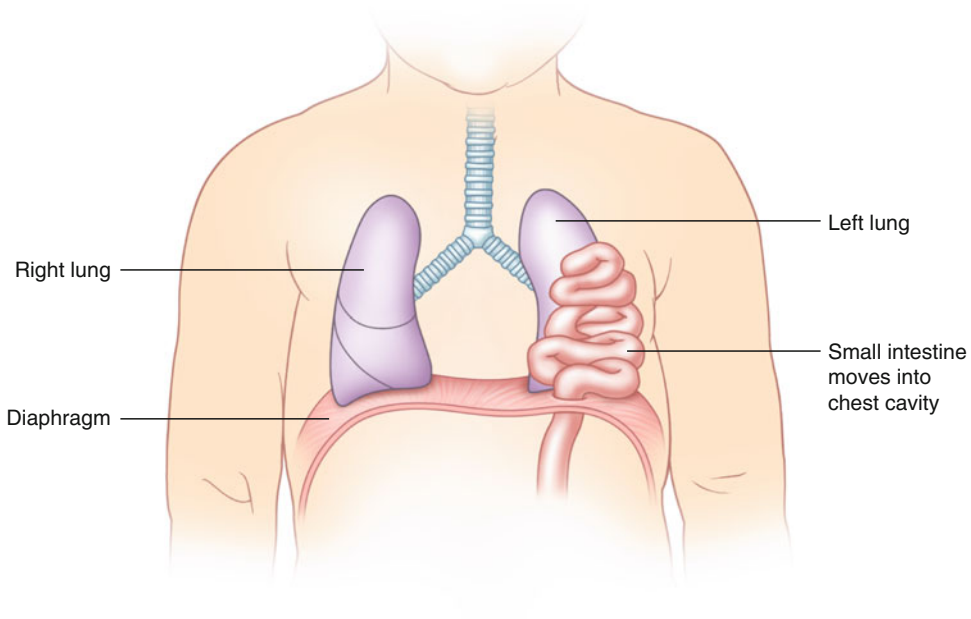

Fig. 39.3 Congenital diaphragmatic hernia

cause respiratory failure, hypoxia, and acidosis. Initially, respiratory distress is treated with endotracheal intubation, mechanical ventilation, and often mild permissive hypercapnia that avoids excessive barotrauma or volutrauma to the normal lung. The patient may, however, require high-frequency jet ventilation or brief extracorporeal membrane oxygenation (ECMO) for survival. The benefits of ECMO are unclear and mortality due to CDH remains between 10 and 30 % despite maximal medical and surgical therapy.

Omphalocele and Gastroschisis

Omphalocele and gastroschisis are both abdominal wall defects; however, they have different locations and developmental history, with omphalocele associated with other congenital malformations, while the more serious gastroschisis associated with an absent protective hernial sac (Fig. 39.4). During embryological development, the gut migrates from the yolk sac at about the 10th week of gestation. Failure of gut migration results in omphalocele with abdominal contents herniating through the midline abdominal wall. The herniated bowel is located within the umbilical cord and is covered with the amnion, which protects against fluid losses and infection. Omphalocele is associated with congenital cardiac disease and Beckwith–Wiedemann syndrome (macroglossia and hypoglycemia) and is found frequently with bladder exstrophy. The protective amniotic covering allows adequate time for preoperative fluid resuscitation and echocardiography to assess for congenital cardiac disease.

Although gastroschisis also results in abdominal contents herniating though the abdominal wall, the defect results from occlusion of the omphalomesenteric artery. The defect is off-midline and "periumbilical" and occurs without other associated congenital anomalies. However, as opposed to omphalocele, in gastroschisis the herniated bowel contents lack any protective covering, which leads to rapid insensible volume loss and susceptibility to infections.

Preoperatively, the presence of a nasogastric tube prevents gastric distension. Anesthesia is induced intravenously

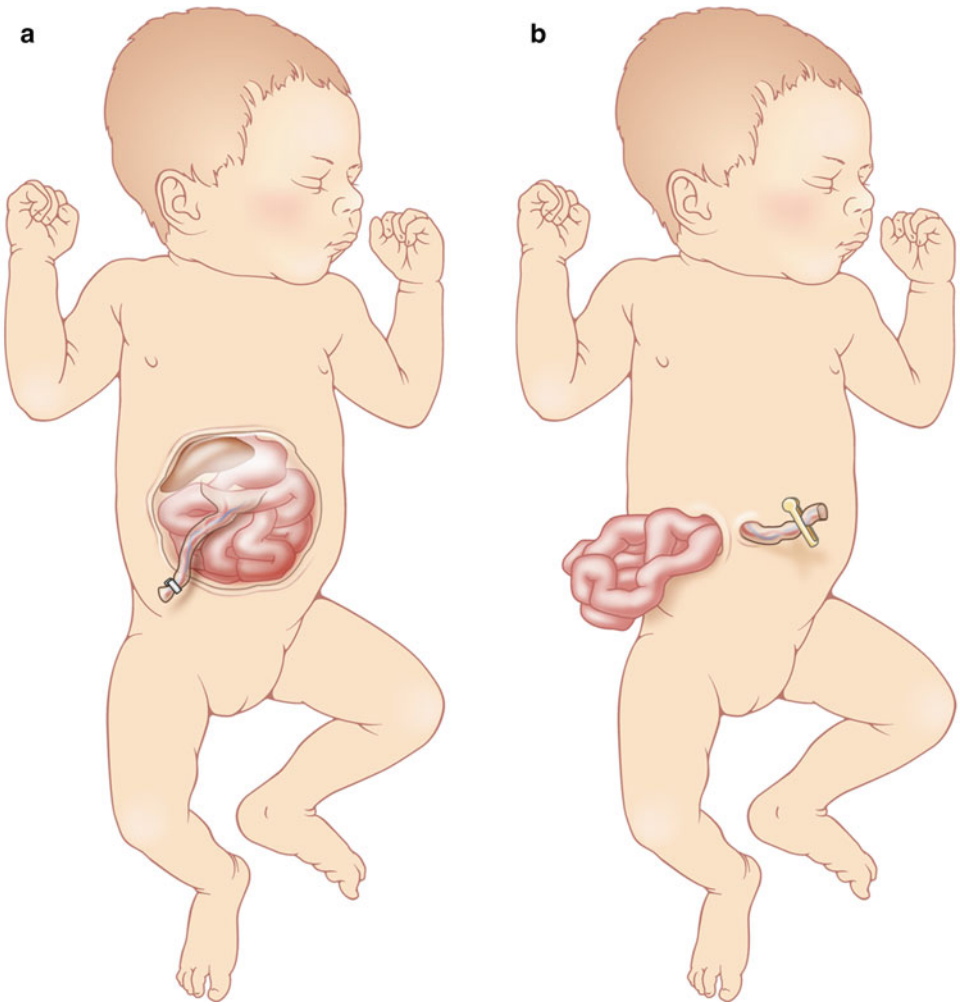

Fig. 39.4 (**a**) Omphalocele (bowel with membranous covering) and (**b**) gastroschisis (bowel without any covering)

or the patient is intubated awake without the use of muscle relaxants. Nitrous oxide is avoided to prevent bowel distension. Optimal hemodynamics can be achieved by using opioids for pain (fentanyl 10–20 mcg/kg), low-dose volatile agent, and replacing third-space fluid losses (10–20 ml/kg/h). Muscle relaxation is required so that the bowel can be replaced into the abdominal cavity.

Primary closure of the abdomen may result in excessive intra-abdominal pressures, high ventilation pressures, and abdominal compartment syndrome, thus providing the rationale for silo placement and staged closure. A central venous catheter may detect excessive intra-abdominal pressures if the CVP rises significantly during closure, providing evidence for a staged closure. Postoperatively, patients are kept intubated and weaned in the intensive care unit.

Pyloric Stenosis

Hypertrophic pyloric stenosis occurs in about 1/1,500 live births. There is a strong family history of pyloric stenosis, with the majority of patients being male. A hypertrophied pylorus (Fig. 39.5) results in a characteristic olive-shaped mass on abdominal examination, visible peristalsis, projectile vomiting, and dehydration. Vomiting and dehydration often lead to a hypochloremic, hypokalemic, and hyponatremic metabolic alkalosis.

Pyloric stenosis is a medical emergency and patients are resuscitated with 0.9 % sodium chloride to restore the circulating blood volume to ensure that plasma chloride exceeds 95 meq/L. In addition, the goal is to have a plasma bicarbonate level less than 29 meq/L, adequate urine output (0.5 ml/kg/h), and normal mental and activity level. Pyloromyotomy is undertaken once the patient is medically stable.

Prior to induction, the stomach is decompressed by nasogastric tube suctioning, which is followed by rapid sequence induction with propofol, succinylcholine, or an intubating dose of rocuronium to minimize the risk of aspiration. Mild cerebrospinal fluid alkalosis may cause an increased likelihood of apnea and respiratory depression in the postoperative period. Therefore, multimodal analgesia (acetaminophen, local anesthetics, ketorolac) should be used to minimize the use of opioid analgesics that may exaggerate postoperative respiratory depression.

Neural Tube Defects

Spina bifida occulta results from an incomplete closure of the embryonic neural tube, which causes incomplete vertebrae formation. The meninges and neural elements are still protected within the spinal canal. A more significant defect results in myelomeningocele (1/2,000 live births), where the unfused vertebrae (80 % lumbar/sacral) allow neural tissue to protrude, forming a meningeal sac that encases spinal elements (Fig. 39.6). Ninety percent of myelomeningoceles are associated with an Arnold–Chiari type II malformation resulting in downward displacement of the cerebellar vermis and the brain stem, frequently resulting in hydrocephalus. Folate deficiency is commonly associated with myelomeningocele.

Surgery, which usually includes the placement of ventriculoperitoneal shunt, is performed within 1–2 days of birth to minimize the risk of infection. To limit neuraxial pressure injury, careful positioning is done. Severe hydrocephalus enlarges the occiput making head positioning challenging during airway management. Myelomeningocele patients have a high incidence of latex allergy and health care providers must strictly adhere to latex precautions. Practitioners

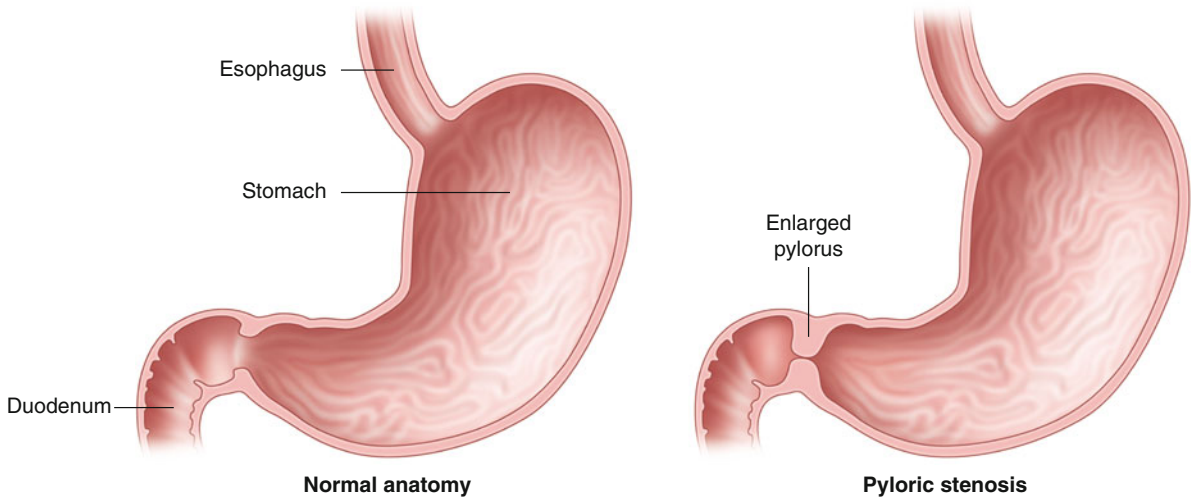

Fig. 39.5 Pyloric stenosis

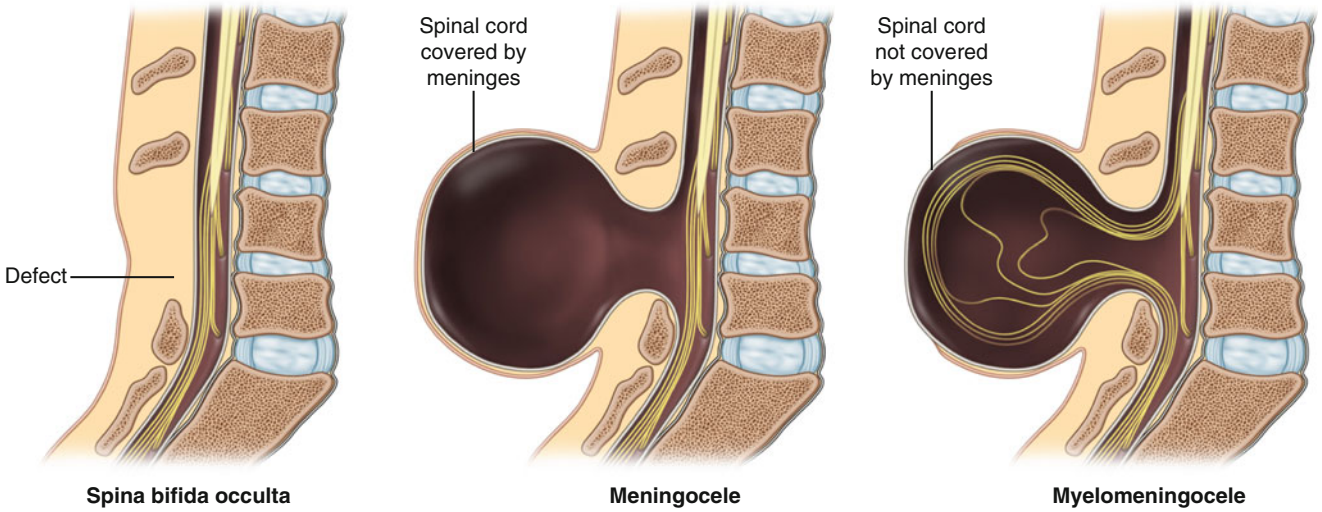

Fig. 39.6 Neural tube defects

should suspect latex anaphylaxis when confronted with unexplained hypotension under anesthesia that poorly responds to volume administration.

Pediatric Pain Management

Neonates experience both pain and physiological stress related to surgery and anesthesia, similar to adults. Opioids (for doses see above) adequately control neonatal and infant stress responses; however, they can contribute to postoperative respiratory depression, particularly in premature neonates and those with lung disease. Also, neonates have reduced hepatobiliary function and glomerular filtration rate leading to unpredictable pharmacokinetics and increased likelihood of drug-induced toxicity.

Acetaminophen doses exceeding 90 mg/kg/day in children and 60 mg/kg/day in infants may cause hepatotoxicity. Acetaminophen is given at a dose of up to 15–20 mg/kg PO q6h, while ibuprofen can be given at a dose of 10 mg/kg PO q6h. Ketorolac's association with mild platelet dysfunction limits its use in children undergoing surgeries associated with blood loss. These factors support the use of regional anesthesia procedures in children, which includes caudal blockade, lumbar and thoracic epidural catheter placement, and peripheral nerve blocks including ilioinguinal, penile, and fascia iliaca block among others.

Neuraxial Blockade

Because the benefits of regional anesthesia outweigh the risks, and children poorly tolerate regional anesthesia while awake, the practice of pediatric neuraxial anesthesia under general anesthesia is well accepted. However, one should be mindful of the complications of neuraxial anesthesia, including neurological injury, intravascular injection leading to cardiotoxicity and cardiac arrest, and intrathecal injection.

Caudal Epidural Anesthesia

The delayed fusion of the posterior sacral vertebra (S_5) until puberty allows caudal access to the epidural space via the sacrococcygeal membrane (Fig. 39.7). The practitioner inserts a blunt 22G needle at a cephalad 30–45° angle until obtaining a "pop." After negative aspiration, 0.25 % bupivacaine, 1 ml/kg of injected local anesthetic achieves a T_{10} sensory level, while 1.5 ml/kg provides sensory analgesia to a T_4 sensory level. Poorly developed epidural fat in children allows higher sensory levels for injected local anesthetics, for single-shot injections, or continuous epidural catheter-threaded cephalad from the caudal space. Until 3–6 months of age, caudal micro-catheters can be successfully inserted to the mid-thoracic region and provide effective postoperative analgesia after thoracoabdominal operations, including tracheoesophageal fistula repair. Clinicians must carefully measure the distance from the caudal insertion point or perform contrast studies to ensure accurate catheter tip location.

Epidural injectate solutions should always contain 1:200,000 concentration of epinephrine (5 mcg/ml) to allow early detection of intravascular injection of the local anesthetic. The most sensitive indicator of intravascular injection in children is a 25 % increase in T-wave amplitude, the increases in heart rate and blood pressure being much less sensitive. Neonates are susceptible to local anesthetic toxicity because of reduced α-1 acid glycoprotein levels, which is the protein that binds local anesthetic in the plasma, leading to an increased free fraction of the local anesthetic. Case reports of neonatal cardiac arrest after continuous caudal

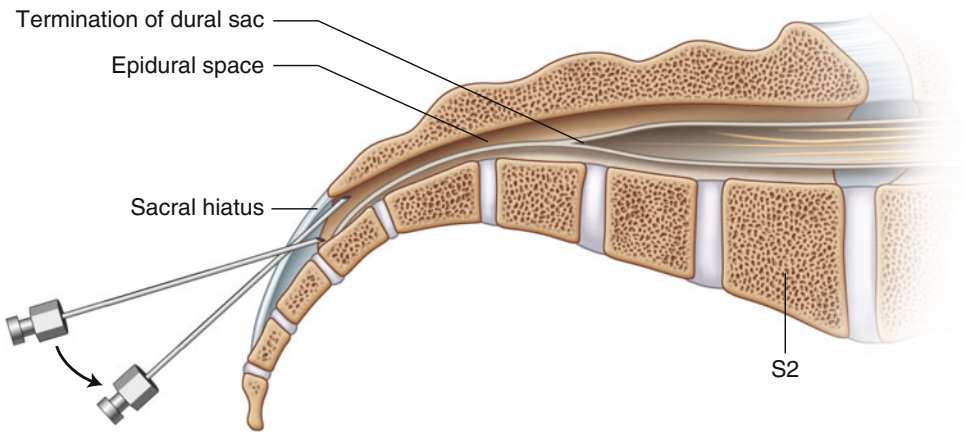

Fig. 39.7 Caudal epidural anesthesia

bupivacaine have led to the recommendation to limit bupivacaine to 0.4 mg/kg/h in neonates.

Spinal Anesthesia

Spinal anesthesia has been advocated for premature neonates and young infants with lung disease to avoid problems associated with mechanical ventilation. Successful implementation of spinal anesthesia requires experience, technical skill, and an efficient surgeon, because even the long-acting local anesthetics tetracaine or bupivacaine provide surgical anesthesia for only 60–90 min. Neonates have larger cerebrospinal fluid volumes and require higher doses of spinal bupivacaine (1 mg/kg), whereas young infants weighing 5–10 kg should best be dosed with 0.5 mg/kg spinal bupivacaine.

Although spinal anesthesia reduces postoperative apnea in premature neonates, the effect can be negated by the coadministration of sedatives during spinal anesthesia. A 25G spinal needle is inserted at L5/S1, CSF is gently aspirated, and the needle is withdrawn after slow injection of local anesthetic. Potential complications of spinal anesthesia include cardiac or respiratory arrest, infection (meningitis), and neurological injury from incorrect spinal injectate solution.

Peripheral Nerve Blocks

Common peripheral nerve blocks in children include femoral nerve block, sciatic nerve block, and penile nerve block (for circumcision). A penile block (Fig. 39.8), usually performed with 0.25 % bupivacaine without epinephrine (which can cause local ischemia), provides excellent analgesia for up to 18 h after circumcision. The fascia iliaca block is commonly performed in children and covers the femoral, obturator, and lateral femoral cutaneous nerve. A blunt needle is inserted through the anterior quadriceps area and advanced until feeling two "pops." This block provides effective analgesia for quadriceps and knee operations and can be performed without ultrasound guidance.

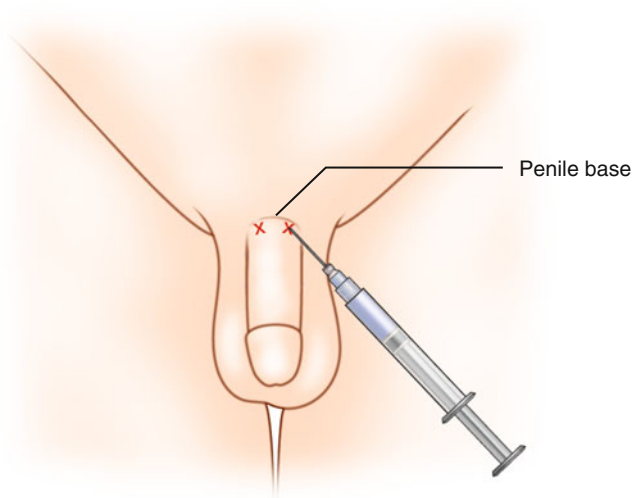

Fig. 39.8 Penile block

Ultrasound guidance should be used for sciatic, femoral, and axillary blocks. Most clinicians avoid interscalene blocks under general anesthesia given reports of permanent neurological injury in adults when performed under general anesthesia. For inguinal hernia repair or orchiopexy, an ilioinguinal block is performed just medial to the anterior-superior iliac spine (ASIS) on a line drawn between the ASIS and the umbilicus. Ultrasound guidance provides more precise deposition of local anesthetics.

Cardiopulmonary Resuscitation

Resuscitation in Children

A majority of in-hospital perioperative cardiac arrests in children occur from cardiovascular causes (41 %), the common causes being acute blood loss (12 %) or hyperkalemic cardiac arrest in the setting of massive blood transfusion

(5 %) or succinylcholine administration. Operations associated with acute blood loss (hypovolemia) include spinal fusion for scoliosis correction and neurosurgical procedures such as tumor resection or craniosynostosis repair. Because massive and rapid blood transfusion may cause a hyperkalemic cardiac arrest, clinicians should maintain a high index of suspicion and aggressively treat the hyperkalemia to promote cardiac membrane stability.

Respiratory events are the second most common cause of perioperative pediatric cardiac arrest (approximately 27 %) and most commonly occur subsequently to laryngospasm (6 %) either on induction, emergence, or during transportation after surgery. The pediatric anesthesiologist should always consider hypoxia as a potential cause of brady-dysrhythmias in children and promptly correct inadequate oxygenation and/or ventilation. Medication-related cardiac arrest is the third most common cause (18 %).

The American Heart Association has emphasized the importance of both early CPR and early defibrillation for pediatric resuscitation (Fig. 39.9). After an in-hospital cardiac arrest occurs, CPR is begun immediately and continued for 2 min, followed by rhythm check. External cardioversion is performed for ventricular fibrillation or ventricular tachycardia with 2–4 J/kg. CPR is performed by pushing hard with the heel of one hand and depressing one-third of the anterior-posterior depth of the chest at a rate of 100–120 bpm. Airway management includes ventilation with 8–10 breaths per minute to avoid hypoxia.

Appropriate drug therapy is administered every 3–5 min followed by rhythm checks. Peripheral intravenous access is adequate for initial cardiopulmonary resuscitation, and drug therapy should not be delayed for the insertion of a central venous line. Epinephrine may be administered endotracheally (100 mcg/kg), if required; however, current PALS algorithms emphasize intraosseous access for rapid administration of vasoactive drugs. Patients suffering refractory ventricular tachycardia or ventricular fibrillation should receive amiodarone 5 mg/kg in addition to epinephrine. For pulseless electrical activity or asystole, vasopressin may be substituted for epinephrine. Sodium bicarbonate may be administered to correct intracellular acidosis and promote responsiveness to inotropic and vasopressor agents. Acidosis depresses cardiac automaticity, predisposes to dysrhythmias including ventricular fibrillation, and reduces the inotropic state of the myocardium.

Extracorporeal membrane oxygenation (ECMO) has been used increasingly for in-hospital cardiac arrest with favorable survival rates (that approach 50 %) and good neurological outcomes. ECMO cannulation requires surgical expertise, specialized ECMO equipment, and effective CPR with rapid institution of ECMO perfusion within 30–45 min of cardiac arrest.

Resuscitation in Neonates

Is it important to know that an anesthesiologist can participate in neonatal resuscitation (NR) in the operating room during a cesarean section, only if the mother is in a stable condition. Like every other resuscitation protocol, NR should be initiated by assessing the ABCs. The APGAR score, taken at 1 and 5 min after birth, can be used to guide NR (Table 39.4). The presence of meconium, fetal congenital anomalies, and maternal complications is a risk factor that may predict the need for NR.

After initial assessment, the infant is provided with warmth and stimulation, and airway is cleared of any secretions. If the neonate is apneic, has a poor respiratory rate, or the heart rate is <100 bpm, bag mask ventilation is initiated. If the heart rate does not increase after 30–60 s, the neonate is intubated. The decision to do CPR is then made, and chest compressions are started. Epinephrine is administered to increase the heart rate above 100 bpm (10–30 mcg/kg).

Chest compressions are done at the rate of 100 bpm, with a breath given after every third compression (3:1 ratio). Chest compressions are done either by encircling the neonate with both hands and placing both thumbs on the lower sternum, or by placing two fingers perpendicular to the chest. Chest compressions should depress the sternum about 1/3 of the depth of the chest. Once the heart rate increases above 100 bpm, the CPR may be stopped.

Meconium is present in about 10 % of live births and can lead to respiratory failure and pulmonary infections. If meconium is present and the neonate has low APGAR scores, the neonate is intubated and the trachea is suctioned. Neonatal respiratory depression may occur if the mother received opioids within 4 h of delivery. The neonate should be assessed for adequate ventilation at birth, and if required naloxone may have to be administered.

Congenital Cardiac Disease

The care of children with complex congenital heart disease (CHD) requires anesthetic care in specialized pediatric centers. According to the POCA Registry (Pediatric Perioperative Cardiac Arrest Registry), patients with CHD have a high incidence of cardiac arrest while undergoing noncardiac surgery. Furthermore, these arrests occur more frequently in the general operating room (54 %), with half of the arrests occurring during the maintenance phase of anesthesia.

Subpopulations at most risk for cardiac arrest include patients with single-ventricle physiology, pulmonary hypertension, and severe cardiomyopathy. Congenital cardiac diseases are best described in terms of left to right shunt lesions, right-sided obstructive lesions (tetralogy of Fallot), and left-sided obstructive lesion. Workup for patients with CHD

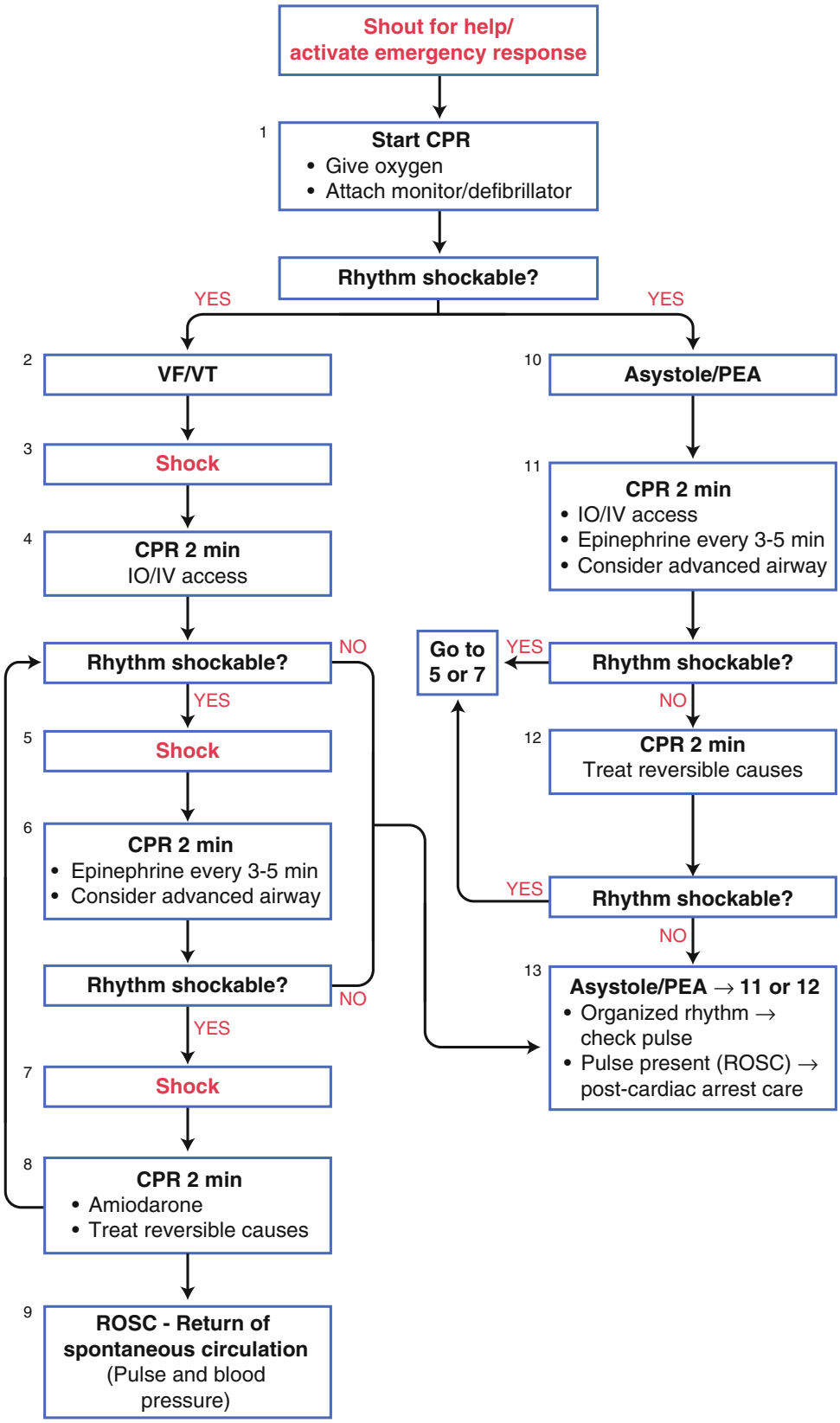

Fig. 39.9 Pediatric cardiac arrest algorithm

Table 39.4 APGAR score

Parameter	Score 0	Score 1	Score 2
*A*ppearance	Blue or pale all over	Body pink, blue extremities	Pink all over
*P*ulse rate (bpm)	Absent	<100	≥100
*G*rimace (reflex irritability)	No response to stimulation	Feeble cry/grimace on stimulation	Cry/pull away on stimulation
*A*ctivity	None	Some flexion	Flexed arms and legs that resist extension
*R*espiration	Absent	Weak, irregular	Strong cry

should include a thorough history and physical, baseline oxygen saturation, assessment of volume status, CBC, chemistry panel, coagulation profile, ECG, echocardiography, and cardiac catheterization.

Left to Right Shunt Lesions

Fifty percent of congenital cardiac lesions are primarily left to right shunt lesions, and these lesions most frequently are atrial septal defects (ASD), ventricular septal defects (VSD), and a patent ductus arteriosus (fetal connection between the pulmonary artery and the aorta). Rare left to right shunts are atrioventricular canal associated with trisomy 21 and partial or total anomalous venous return, whereby pulmonary venous blood is connected to the right atrium resulting in a large left to right shunt.

These lesions result in ventricular volume overload, congestive heart failure, and ultimately pulmonary overcirculation and pulmonary hypertension, if left untreated. ASDs are most commonly a defect in secundum (85 %), with primum defects accounting for about 7 %. Children are usually symptomatic, without any cyanosis. VSDs are most commonly perimembranous (70 %), muscular (20 %), inlet (5 %), or supracristal (5 %). VSD defects are acyanotic, until severe pulmonary hypertension develops, which causes a reversal of the shunt (Eisenmenger syndrome) producing cyanosis.

The degree of left to right shunting depends on the lesion size, the pressure gradient between the cardiac chambers or great vessels, and the ratio of pulmonary vascular resistance to systemic vascular resistance (PVR/SVR ratio). For example, flow through a patent ductus arteriosus (aortopulmonary connection) will be greatest when pulmonary vascular resistance is the least. Excessive pulmonary blood flow gradually leads to increased pulmonary vascular resistance, pulmonary hypertension, and potentially Eisenmenger syndrome resulting in shunt reversal to a right to left shunt. Shunt reversal occurs when right ventricular pressure exceeds left ventricular pressure. This leads to progressive hypoxia and even death.

A left to right shunt causes excessive pulmonary blood flow, which leads to systemic hypotension, lactic acidosis, and decreased urine output. Conversely, high pulmonary vascular resistance (PVR) leads to luxurious systemic flow at the expense of lower-oxygen saturations. PVR can be minimized

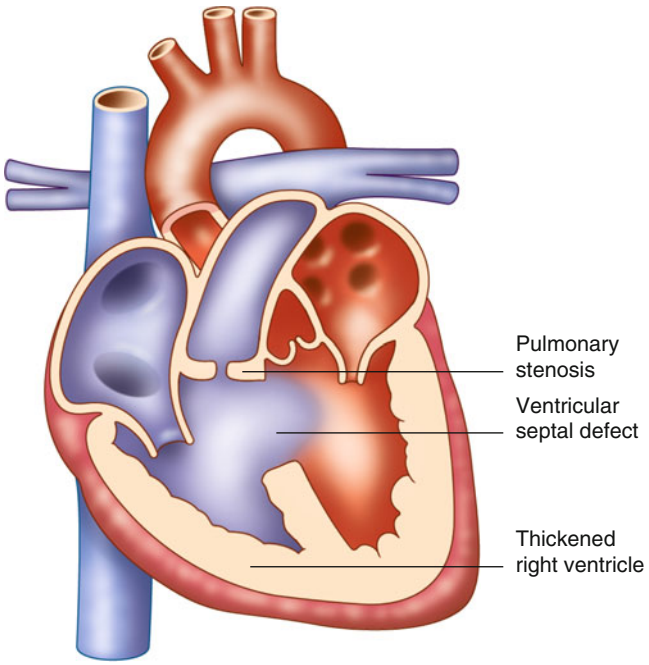

Fig. 39.10 Tetralogy of Fallot

with higher $P0_2$, hypocarbia, avoidance of high ventilator pressures, and use of pulmonary vasodilators, such as milrinone, inhaled nitric oxide, or sildenafil. Successful management of high PVR requires careful attention to oxygenation, ventilation, and PVR/SVR ratio and avoiding extreme vasodilation or vasoconstriction with anesthetic agents.

Right-Sided Obstructive Lesions

The most common right-sided obstructive lesion is tetralogy of Fallot (TOF), which has four components: (1) an overriding aorta; (2) right ventricular outflow obstruction (RVOTO)—can be sub-valvar, infundibular, valvar, or supravalvar; (3) compensatory right ventricular hypertrophy; and (4) a VSD (Fig. 39.10). Patients with TOF have "tet spells" which represent hypercyanotic spells occurring due to RVOT infundibular spasm. Tet spells may be "pink tets" (mild RVOTO) or "blue ets" (severe RVOTO) depending on the degree of right ventricular outflow tract obstruction, the size of the ventricular septal defect, and the ratio of PVR/

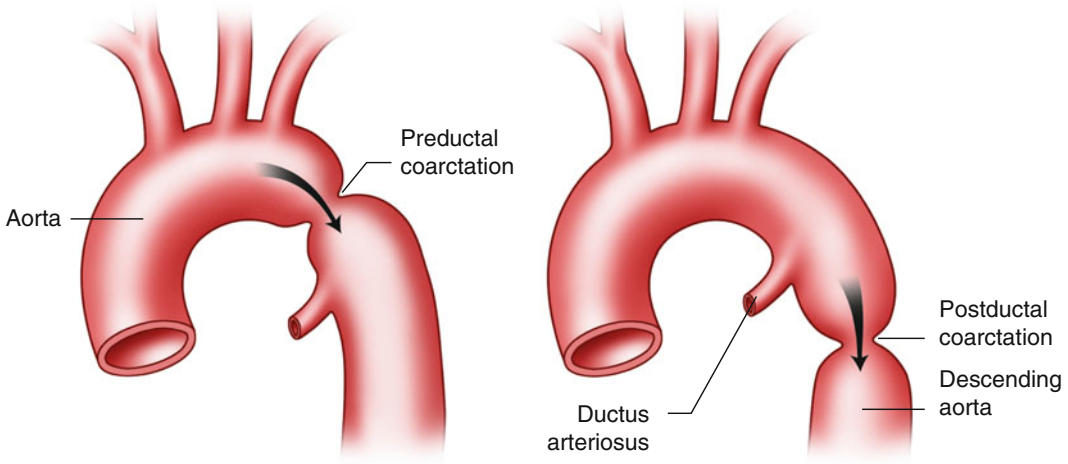

Fig. 39.11 Coarctation of aorta

SVR. The RVOT infundibular muscle spasm causes near-total RVOTO, shunting of deoxygenated blood through the ventricular septal defect, and profound arterial hypoxemia.

A tet spell is treated with fluids, beta-adrenergic blockade to mitigate infundibular spasm, phenylephrine to raise SVR, and squatting maneuvers that partially clamp the femoral arteries to raise SVR. After surgical repair of TOF, patients are predisposed to dysrhythmias, particularly junctional ectopic tachycardia, which can be treated with amiodarone. Ebstein's anomaly is a rare cause of right-sided obstruction that results in downward displacement of tricuspid valve leaflets, with a portion of the right ventricle resembling the right atrium.

Left-Sided Obstructive Lesions

Although hypoplastic left heart syndrome has many characteristics of left-sided obstruction (i.e., aortic atresia and hypoplastic left ventricle), it is actually a single-ventricle lesion. Left-sided obstructive lesions may be intracardiac (aortic stenosis, hypertrophic cardiomyopathy) or extracardiac (coarctation of the aorta). The most common left-sided obstructive lesion is coarctation of the aorta (8 % of CHD) (Fig. 39.11) that leads to narrowing of the descending aortic lumen between the distal left subclavian artery and the ductus arteriosus.

Critical coarctation can lead to acute increases in ventricular afterload, congestive heart failure, and cardiogenic shock. A coarctation often presents with diminished lower extremity pulses and upper extremity hypertension. A mild coarctation can initially go undetected. Repair is performed through a lateral thoracotomy with brief aortic cross-clamping, usually without cardiopulmonary bypass (ideally less than 20 min cross-clamp), with end-to-end anastomosis. Lower extremity pulses and blood pressure gradually improve; however, many patients have recurrent coarctation, adult-onset hypertension, and cardiovascular events (resultant stroke, coronary artery disease).

Clinical Review

1. Neonates desaturate more rapidly than adults because they have this:
   A. Higher metabolic rate
   B. Lower closing volumes
   C. Higher tidal volumes
   D. Lower functional residual capacity
2. In preterm neonates, elective surgery should be deferred until the following postgestational age:
   A. 40 weeks
   B. 45 weeks
   C. 50 weeks
   D. 60 weeks
3. Minimum alveolar concentration (MAC) of volatile anesthetics is highest for:
   A. Preterm neonate
   B. Full-term neonate
   C. Infant of 3 months age
   D. Infant of 12 months age
4. Airway should be rapidly secured in a patient with:
   A. Croup
   B. Epiglottitis
   C. Eaton–Lambert syndrome
   D. Stridor
5. This is the commonest metabolic abnormality in patients with pyloric stenosis:
   A. Hypochloremic metabolic acidosis
   B. Hypokalemic metabolic acidosis

C. Hypochloremic metabolic alkalosis
D. Hyperkalemic metabolic alkalosis

6. In a patient with tetralogy of Fallot, this is the volatile agent of choice for induction:
   A. Sevoflurane
   B. Isoflurane
   C. Halothane
   D. Desflurane
7. All of the following are used in the treatment of a tet spell in a patient with tetralogy of Fallot, except:
   A. Phenylephrine
   B. Propranolol
   C. Fluid administration
   D. Hydralazine

Answers: 1. A, 2. D, 3. C, 4. B, 5. C, 6. C, 7. D

Further Reading

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Critical Care

40

Paul K. Sikka

Critical care medicine is a multidisciplinary healthcare specialty that cares for patients with acute, life-threatening illness or injury. Many disease processes lead to critical illness, and these disease processes are commonly treated in an intensive care environment. Critically ill patients may be ill either due to medical or surgical causes, but the treatment of the illness is more or less the same. Table 40.1 lists the seven Cs of critical care.

Patients are admitted to intensive care unit usually with one or more of the following problems: cardiac problems (postsurgical or hemodynamic insufficiency), respiratory problems (postsurgical or failure), neurological issues (postsurgical neurotrauma), or abnormalities of fluid and electrolytes and sepsis.

A well-structured critical care unit is essential for providing care and treatment to critically ill patients. An intensive care unit is a place that has a very high nurse to patient ratio, where patients are usually invasively monitored, and life-sustaining therapies are utilized (mechanical and pharmacological). Therefore, proper functioning of a critical care unit consists of teamwork, evidence-based practice and cost-effectiveness, and very strong pharmacy and infectious disease backup. This chapter discusses various concepts of critical care medicine and care of critically ill patients.

Shock

Shock is defined as acute circulatory failure leading to inadequate tissue perfusion and end organ injury. There is a drop in blood pressure with accompanying hemodynamic changes. Blood pressure is a factor of cardiac output and systemic vascular resistance, and cardiac output, in turn, is a factor of heart rate and stroke volume. The three factors heart rate, stroke volume, and peripheral resistance exist in equilibrium. Normally, if there is disruption of one of them, then the other two components compensate. Therefore, hypotension is an indication of an abnormality of heart rate, stroke volume, or peripheral resistance and a failure of these to compensate each other.

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Progression of Shock

Shock typically progresses through four stages as described below. The pathophysiology of shock is depicted in Fig. 40.1.

Stage I (Initial)
Hypoperfusion of the tissues leads to hypoxia (lack of oxygen), which leads to anaerobic metabolism promoting the formation of lactic acid. Additionally, the lack of oxygen slows down the Krebs cycle causing more pyruvate to be available, which is converted to lactate by the cells.

Stage II (Compensatory)
In this stage the body tries to compensate the hypoxia and the acidosis through various physiological mechanisms. To rid the body of the excess CO_2 (acidosis), the person hyperventilates. The arterial baroreceptors sense the low blood pressure and cause increased sympathetic response and catecholamines to be released. The increased sympathetic response causes vasoconstriction and an increase in the heart rate, contractility, and cardiac output leading to an increase in the blood pressure. Blood is preferentially diverted to the arterial system and the vital organs (autotransfusion).

Additionally, because of reduced renal blood flow, the renin-angiotensin axis is activated causing release of the angiotensin, aldosterone, and antidiuretic hormone (ADH). These hormones act on the kidneys to conserve fluid (vasoconstriction, salt, and water retention). All these hormones preferentially act to divert blood to the

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heart, the lungs, and the brain. Conservation of fluid leads to a drop in the urine output.

Stage III (Progressive)

If the shock is not corrected, the compensatory mechanisms begin to fail, and the progressive stage ensues. As hypoperfusion and anaerobic metabolism continue, the acidosis worsens. Due to acidosis, the arteriolar smooth muscle dilates to cause pooling of blood in the capillaries. This increases local hydrostatic pressure causing exudation of fluid and protein into the surrounding tissues. Due to loss of fluid, the blood becomes more viscous causing sludging of the microcirculation and accumulation of toxic substances. The prolonged vasoconstriction also causes the vital organs to be compromised due to reduced perfusion.

Stage IV (Refractory)

Because of lack of oxygen, cellular ATP supply is irreversibly depleted. Adenosine perfuses out into the surrounding tissues and is not available to undergo phosphorylation into ATP. The vital organs begin to fail, and eventually cell death and brain damage ensues.

Table 40.1 Seven Cs of critical care

1.	Compassion
2.	Communication (with patient and family)
3.	Consideration (to patients, relatives, and colleagues) and avoidance of conflict
4.	Comfort: prevention of suffering
5.	Carefulness (avoidance of injury)
6.	Consistency
7.	Closure (ethics and withdrawal of care)

Causes and Classification of Shock (Fig. 40.2)

Shock can be classified as:

- Cardiogenic, malfunction of the pump (Fig. 40.3)
- Distributive or vasodilatory, malfunction of the vasculature (tubing)
- Hypovolemic, problems with loss of fluid

Cardiogenic shock results from failure of the cardiac muscle (ischemia, inflammation, fibrosis-myocarditis, and volume overload) and cardiac outflow obstruction (pulmonary embolism and aortic stenosis) or inflow obstruction (cardiac tamponade). Distributive shock occurs due to loss of sympathetic tone and release of vasoactive metabolites causing a decrease in peripheral vascular resistance, as in sepsis or anaphylaxis. The abnormal vasodilatation leads to a relative hypovolemia; the amount of fluid is the same, but the tubing becomes larger. There is redistribution of blood away from the vital organs to the periphery. Finally, hypovolemia shock may be due to dehydration, hemorrhage/exogenous fluid loss, or fluid redistribution (third space loss). Tables 40.2, 40.3, and 40.4 list the clinical signs of various types of shock.

Monitoring in Shock

The following monitoring modalities are used in patients with shock:

- Blood tests: CBC, chemistry, and crossmatch
- Standard monitors and arterial line
- Central venous line and pressure
- Arterial blood gas analysis
- Urine output measurements (Foley catheter)

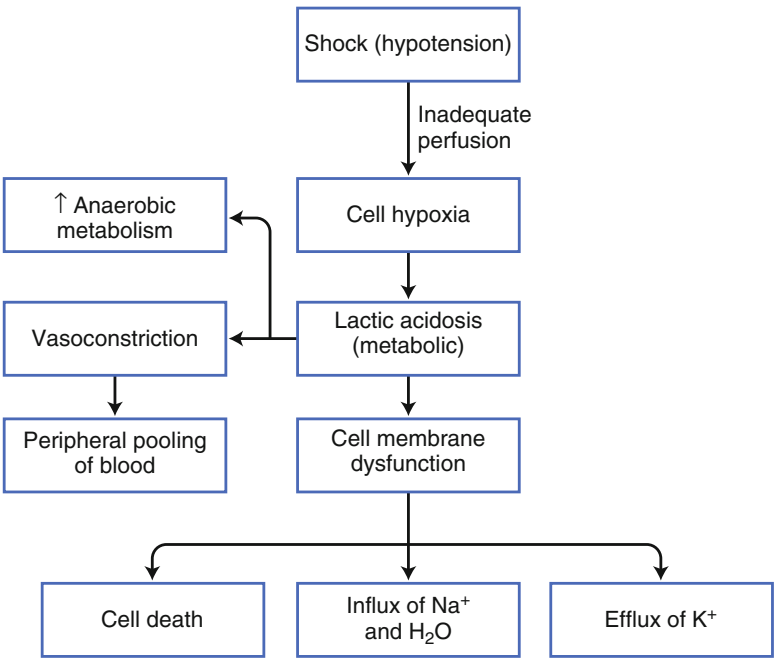

Fig. 40.1 Pathophysiology of shock

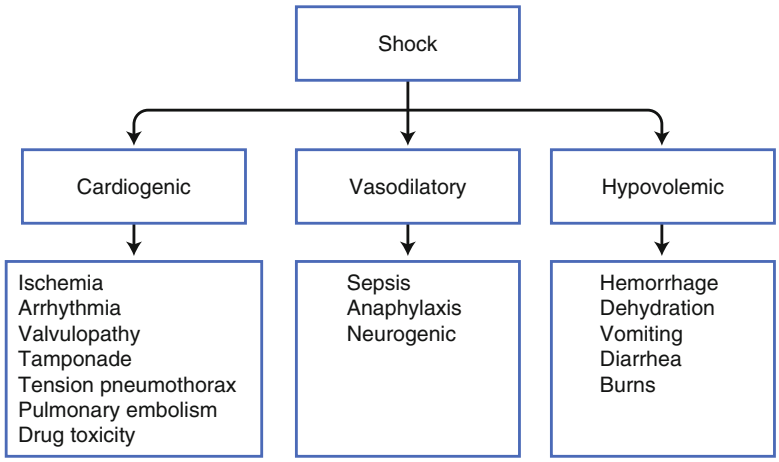

Fig. 40.2 Classification of shock

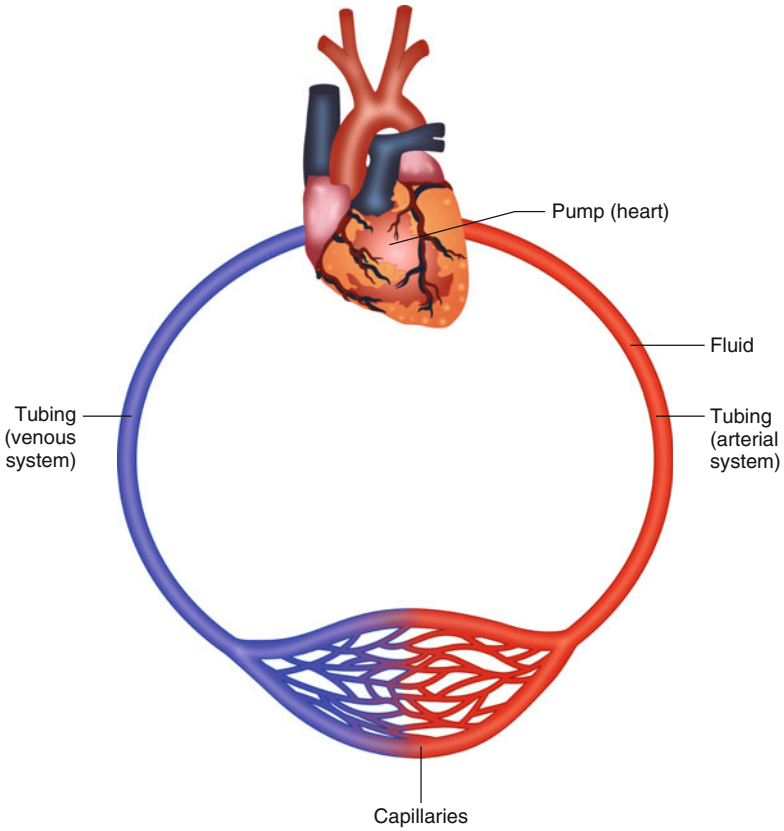

Fig. 40.3 Cardiovascular system showing the pump, the distribution system, and the fluid compartments

- Pulmonary artery catheter, if cardiac dysfunction
- Echocardiography

Central venous pressure (CVP), when measured, should be measured as a trend. The CVP measures right heart filling pressures, which are representative of systemic blood volume. It should be remembered that conditions such as complete heart block, atrial fibrillation, tricuspid stenosis, or regurgitation lead to an inaccurate CVP reading, which can be diagnosed by the CVP tracing itself. Hemodynamic parameters in various shock states are listed in Table 40.5.

Pulmonary artery catheters (PAC) are nowadays not commonly used to guide fluid resuscitation. If there is a strong suspicion that right-sided filling pressures are unrepresentative of left-sided pressures (refractory cardiogenic shock, myocardial contusion, myocardial ischemia due to sepsis), then a PAC may be inserted. A PAC measures the relationship between the pulmonary circulation and the left heart. When using a PAC, the wedge pressure, end diastolic volume, stroke volume, CVP, and mixed venous oxygen saturation measurements are used to guide fluid resuscitation.

Management of Shock

The first step is to confirm that the patient is in shock. Blood pressure should be measured with an adequate size cuff or commonly via an arterial line. Often the patient is sedated and would not be able to communicate fully, making mental status changes difficult to assess. If the patient is urinating adequately, it can be usually assumed that the tissues are being perfused adequately. However, if the patient is on diuretics, then measuring urine output is not a reliable sign for tissue perfusion. Presence of lactic acidosis (negative base excess) is another sign of tissue hypoperfusion.

The end point of management of shock is achieved by increasing the blood pressure (Fig. 40.4). Usually this end point is an awake patient with an adequate urine output. Fluid and vasopressors (Table 40.6) should always be targeted to the pressure that is normal for that particular patient. If there is concern about a patient's intravascular volume status, a central line is placed and the CVP is measured. Patients are then volume overloaded to a target CVP, which is usually a CVP of 8–10 mmHg in non-ventilated patients and 12–16 mmHg in patients on positive pressure ventilation.

If a cardiac abnormality/dysfunction is suspected, then ECG and echocardiography (ejection fraction, wall motion

Table 40.2 Clinical signs of cardiogenic shock

- BP—hypotension because of decreased cardiac output
- Heart rate—rapid, weak, thready pulse
- Respiratory rate—rapid and deep respirations (hyperventilation) due to sympathetic nervous system stimulation and acidosis
- Skin—cool, clammy, and mottled skin due to vasoconstriction and hypoperfusion
- Mental status—anxiety, restlessness, altered mental state due to decreased cerebral perfusion
- Urine output—oliguria due to insufficient renal perfusion
- Pulmonary edema—due to fluid backup in the lungs
- Jugular veins—distended, due to increased jugular venous pressure
- Hepatic congestion due to insufficient pumping of the heart

Table 40.3 Clinical signs of distributive (vasodilatory) shock

- Initial—BP normal, cardiac output maintained (by increasing stroke volume and heart rate)
- Late—metabolic acidosis and worsening myocardial perfusion cause a decrease in cardiac output leading to cardiac failure
- Heart rate—rapid
- Skin—initially warm, later cold and poorly perfused

Table 40.5 Hemodynamic parameters in various shock states

Type of shock	HR	SV and CO	CVP	PCWP	SVR
Cardiogenic					
Pump failure	↑	↓	↓	↓	↑
Volume overload	↑	↓	↑	↑	↑
Inflow/outflow obstruction	↑	↓	↑	↑	↑
Heart block	↓	↑ (CO ↓)	↑	↑	
Vasodilatory					
Sepsis	↑	↓ (CO ↑)	↓	↓	↓
Anaphylaxis and spinal shock	↑	N (CO ↑)	↓	↓	↓
Hypovolemic	↑	↓	↓	↓	↑

Table 40.4 Clinical signs of hypovolemic shock

Stage	Blood loss	Clinical signs
Stage I	15 % (750 ml)	• BP—maintained • Heart rate—normal • Respiratory rate—normal • Skin pallor—normal • Mental status—normal • Urine output—normal
Stage II	15–30 % (750–1,500 ml)	• BP—systolic maintained, diastolic increased (narrow pulse pressure) • Heart rate >100 bpm (tachycardia) • Respiratory rate—increased • Skin—pale, cold, clammy • Mental status—anxious, restless • Urine output—decreased (≤0.5 ml/kg/h)
Stage III	30–40 % (1,500–2,000 ml)	• BP—systolic BP falls to 100 mmHg or less • Heart rate >120 bpm (marked tachycardia) • Respiratory rate >30 bpm (marked tachypnea) • Skin—pale, cold, sweating • Mental status—confusion, anxiety, agitation • Urine output—decreased further (<0.5 ml/kg/h)
Stage IV	>40 % (>2,000 ml)	• BP—significantly decreased systolic blood pressure of 70 mmHg or less • Heart rate >140 bpm (extreme tachycardia), weak, thready pulse • Respiratory rate—marked tachypnea • Skin—extremely pale, cool, sweaty • Mental status—decreased level of consciousness, lethargy, coma • Urine output—negligible

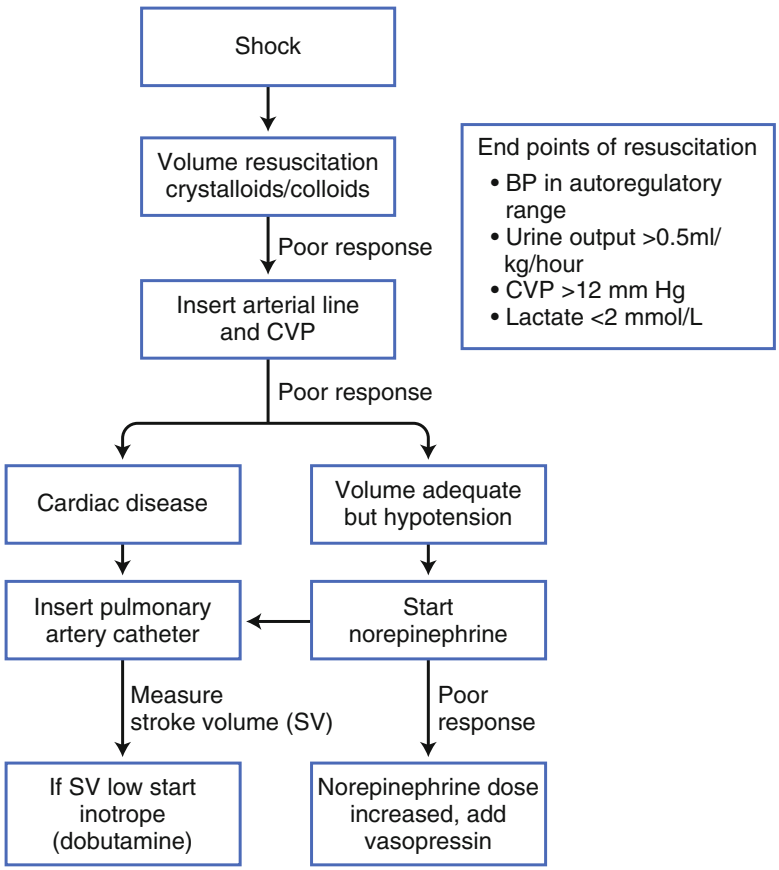

Fig. 40.4 Management strategies in shock

Table 40.6 Choice of vasopressor in shock

Cardiogenic shock—dobutamine, norepinephrine
Septic shock—norepinephrine
Anesthesia-related or spinal shock (with absence of bradycardia)—phenylephrine
Anaphylactic shock—epinephrine
Hypotension with bradycardia—epinephrine
Shock of unknown etiology—epinephrine or dopamine

abnormalities) are performed. If there is suspicion of significantly different muscle physiology/filling pressures between the right and left side of the heart, then a pulmonary artery catheter (PAC) may be placed. The PAC is used to measure stroke volume (cardiac output), left ventricular end-diastolic volume, wedge pressure, and mixed venous oxygen saturation.

The following interventions are carried out for a patient in shock:

- Large bore intravenous access.
- Oxygen supplementation and endotracheal intubation as necessary.
- Surgical repair of hemorrhagic sites.
- Fluid therapy: crystalloids, colloids, packed red blood cells, fresh frozen plasma, and platelets.
- Supportive care.
- Cardiogenic shock—goals are to increase cardiac output, decrease systemic vascular resistance, and decrease myocardial work and O_2 consumption. Cardiogenic shock is treated with fluid therapy and vasopressors, as needed. Dobutamine is preferred for inotropy as it increases contractility and heart rate and mildly decreases afterload. To decrease afterload effectively, other vasodilators (nitroglycerine, nitroprusside, nicardipine) may be used. Additional interventions in cardiogenic shock include diuretics (used cautiously), antiarrhythmic agents, angioplasty for an ischemic event, intra-aortic balloon pump to improve coronary circulation, or ventricular assist device for severe cardiac dysfunction.
- Distributive shock—fluids, vasopressors, anaphylaxis (epinephrine), and sepsis (see below).
- Hypovolemic shock—aggressive fluid therapy ± vasopressor support (dopamine, norepinephrine).

Other Causes of Hypotension in the ICU

Excessive Sedation

Many patients in the intensive care are sedated. Commonly used sedative agents include propofol, midazolam, and opioids (morphine, fentanyl). These agents, especially when used in combination, may lead to hypotension. Their effects may be decreased by decreasing their dose and/or treating with a vasoconstrictor (phenylephrine).

Bradycardia
The normal compensatory response to hypotension is tachycardia. Therefore, hypotension with bradycardia is pathological. Bradycardia may be due to excessive beta-blockade, which reverses after stopping the beta-blockers, or rhythm disturbances, which may require pacing.

Tachycardia
Sinus tachycardia, as mentioned above, occurs as part of the compensatory mechanism for low blood pressure in a vasodilated state. Treating the cause (hypovolemia, sepsis, pain) results in the resolution of the tachycardia. Therefore, no intervention to treat the tachycardia is required per se. However, in patients with cardiac disease, the increase in myocardial work due to the tachycardia may cause ischemia. Therefore, heart rate control may be achieved in such patients by using beta-blockers. Additionally, patients with hypotension due to tachyarrhythmias (atrial fibrillation or flutter) may have to be cardioverted, with correction of electrolyte disturbances (magnesium, potassium) and administrations of drugs (diltiazem, beta-blockers, or amiodarone).

Sepsis

In the United States, sepsis affects approximately 3/1,000 people, and severe sepsis contributes to more than 200,000 deaths per year. Sepsis causes millions of deaths globally each year. Sepsis occurs in 1–2 % of all hospitalizations and accounts for as much as 25 % of ICU bed utilization. Sepsis is characterized by a whole-body inflammation, usually in response to an infection. It consists of a systemic inflammatory response syndrome and can be defined as:

1. Infection: presence of infection leading to a systemic inflammatory response syndrome (SIRS) manifested by:
   - Temperature >38 °C or <36 °C
   - Heart rate >90 beats/min
   - Respiratory rate >20 breaths/min or $PaCO_2$ <32 mmHg
   - WBC count >12,000/mm^3, <4,000/mm^3, or >10 % immature (band) forms
2. Sepsis: infection confirmed or suspected, plus two of the above SIRS criteria
3. Severe sepsis: sepsis, plus one organ dysfunction
4. Septic shock: sepsis, plus hypotension despite fluid resuscitation

Pathophysiology

Sepsis is most commonly caused by bacteria, but can also be caused by fungi, viruses, and parasites in the blood, urinary tract, lungs, skin, or other tissues. No infective source is found in about one-third of the cases. Usually patients have an initial infection, called as the first hit. The inflammation may then persist, or the patient may have subsequent hits of infection. Persistent presence of inflammation then leads to the sepsis syndrome.

Unlike patients in cardiogenic shock, who are cold and hypotensive, septic patients are hot and hypotensive. This is because of the loss of sympathetic tone and vasodilation due to the accumulation of metabolites and increased amounts of nitric oxide. The vasodilation leads to a relative hypovolemia (normal amount of fluid but larger tubing). The stroke volume is reduced leading to myocardial ischemia and cardiac failure. Initially, the cardiac output may be increased due to an increase in heart rate. Eventually, due to persistent vasodilation of small blood vessels, there is widespread capillary leak and microcirculatory failure (Fig. 40.5). Additionally, the coagulation cascade is stimulated causing widespread deposition of fibrin and thrombi, which lead to stagnation of the microcirculation.

Common symptoms of sepsis include those related to a specific infection, accompanied by hypotension (decreased systemic vascular resistance); high fever or hypothermia; hot, flushed skin; tachycardia; hyperventilation; altered mental status; peripheral swelling; and disturbances in coagulation. Sepsis if not controlled leads to multiple organ dysfunction (MOD) and finally death (Table 40.7).

Management of Sepsis

Sepsis is usually managed as follows:

- Intravenous fluids: target CVP of 8–12 mmHg, urine output >0.5 ml/kg/h, mixed venous oxygen saturation >70 %.
- Antibiotics and antifungal medications.
- Vasopressors to maintain blood pressure (epinephrine, norepinephrine, vasopressin), systolic blood pressure >90 mmHg, or mean arterial pressure >65 mmHg.
- Mechanical ventilation.
- Dialysis to support kidney function.
- Central venous catheter, arterial catheter, or a pulmonary catheter may be placed to measure hemodynamic variables, such as cardiac output, mixed venous oxygen saturation, or stroke volume variation.
- Preventive measures for deep vein thrombosis.
- Prevention of stress ulcers and pressure ulcers.
- Control of blood sugar levels with insulin (targeting stress hyperglycemia), although hypoglycemia is seen with severe liver dysfunction.

Mechanical Ventilation

Many patients in the ICU are mechanically ventilated. Therefore, it is of utmost important to be familiar with the various modalities of mechanical ventilation in order to provide optimal care to patients. In addition, weaning off

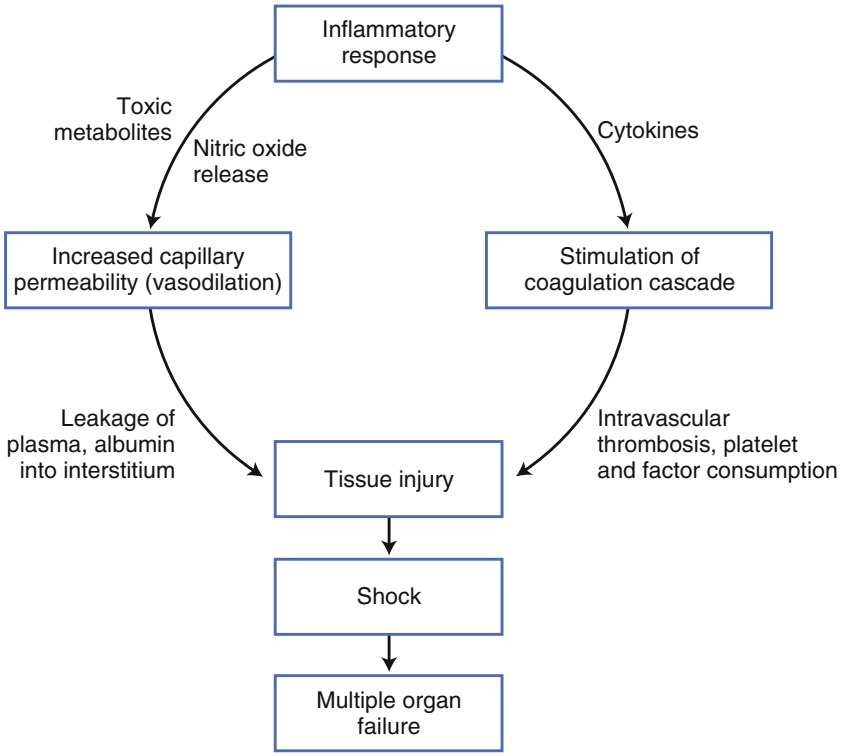

Fig. 40.5 Pathophysiology of sepsis

Table 40.7 End-organ dysfunction in sepsis

Lungs	Acute lung injury ($PaO_2/FiO_2 < 300$), ARDS ($PaO_2/FiO_2 < 200$)
Brain	Encephalopathy, delirium, ischemia, microabscess, microthrombi
Liver	Lactic acidosis, coagulopathy, disruption of metabolic processes, disruption of protein synthesis, elevation of bilirubin (jaundice) and liver enzymes, hypoglycemia
Kidney	Acute kidney injury, oliguria/anuria, electrolyte abnormalities, volume overload
Heart	Hypotension, heart failure, nonischemic troponin leak
Hematologic	Thrombocytopenia, elevation of PT and INR, disseminated intravascular coagulation, leukocytosis/leukopenia
GI tract	Stress ulcers
Adrenal	Cortisol deficiency, however, steroid therapy in sepsis is controversial

patients early from mechanical ventilation decreases the incidence of nosocomial infections. Mechanical ventilation is provided for three main reasons:

- Impaired oxygenation ($PaO_2 < 50$ mmHg)—reduced diffusion capacity of O_2 and V/Q mismatch (dead space ventilation or shunt). Examples—acute respiratory distress syndrome (ARDS), sepsis, pneumonia, pulmonary edema, pulmonary fibrosis, and cyanide or carbon monoxide poisoning
- Impaired CO_2 elimination ($PaCO_2 > 50$ mmHg)—neuromuscular disorders (myasthenia gravis), loss of ventilator drive (brain injury, stroke), spinal cord injury, bronchospasm, pneumothorax, airway foreign body, and COPD
- Airway protection—airway edema, loss of gag reflex, mental status changes (GCS <8), and inhalational burn injury

Noninvasive Positive Pressure Ventilation

Noninvasive positive pressure ventilation (NIPPV) is delivered without the use of an endotracheal tube. Positive pressure is delivered by a face mask covering the mouth and/or the nose. The face mask is held firmly in place by a tight fitting strap. Commonly used methods include continuous positive pressure airway (CPAP) and bi-level positive airway pressure (BiPAP).

CPAP

Continuous positive airway pressure is applied during both inspiration and expiration, in a spontaneously breathing patient. Oxygenation is improved due to recruitment of collapsed alveoli. In addition, CPAP helps to maintain the patency of the airway.

BiPAP

Continuous positive airway pressure is applied during both inspiration and expiration, but 2 airway pressure settings are used, higher pressure during inspiration and lower pressure during expiration.

Advantages and Uses

NIPPV allows ventilation for short periods, such as during sleep or immediately after discontinuation of endotracheal mechanical ventilation. Using NIPPV reduces complications with endotracheal ventilation; the patients remain awake, with reduced mortality and shorter ICU stays.

Disadvantages

These include lack of patient compliance, poorly fitting mask, and claustrophobia. Also, NIPPV offers no airway protection, and gastric distension can occur due to positive pressure and difficulty with oral feeding with the mask on.

Invasive Positive Pressure Ventilation

Invasive positive pressure ventilation is provided via an endotracheal tube (ETT) or tracheostomy. Once a patient is intubated for 2–3 weeks, it is prudent to change the ETT to a tracheostomy to prevent subglottic stenosis. The patient should be continuously monitored throughout (ECG, pulse oximetry, arterial blood pressure). A suction cannula should be readily available and put under the pillow before induction, plus a free flowing intravenous line should be available.

In unconscious patients, the ETT may be placed without sedation or muscle paralysis. After adequate preoxygenation, intubation may be facilitated with injection of drugs, such as midazolam, propofol, or etomidate, and succinylcholine. Ephedrine and phenylephrine should be available for hemodynamic support.

Using a small ETT may lead to high airway pressures; therefore, larger size ETTs should be used. Placement of the ETT is confirmed by auscultating the chest for breath sounds, using an $ETCO_2$ detector and later by a chest radiograph. All intubated patients should receive pulmonary toilet, that is, suctioning of secretions, aerosol mists to administer bronchodilators, mucolytic agents, chest percussion, vibration therapy, and postural drainage. The aim in all mechanically ventilated patients is to oxygenate adequately, while preventing O_2 toxicity.

Types of Ventilators

Ventilators are designed to give breaths which can be mandatory (controlled)—which is determined by the respiratory rate, assisted (as in assist control, synchronized intermittent mandatory ventilation (SIMV), pressure support), or spontaneous (no additional assistance in inspiration, as in CPAP). Ventilators can be generally classified as follows:

- Volume controlled—or volume limited/targeted/cycled and pressure variable
- Pressure controlled—or pressure limited/targeted/time cycled and volume variable
- Dual controlled—volume targeted (guaranteed) and pressure limited
- Flow cycled—such as in pressure support

Modes of Ventilation

Continuous Mandatory Ventilation

In continuous mandatory ventilation (CMV), the ventilator is programmed to a set tidal volume, respiratory rate, and I:E ratio (1:2) (Fig. 40.6). If the patient makes spontaneous ventilatory efforts between breaths, these are unsupported. For example, if the ventilator is set to deliver 10 bpm and the patient takes four spontaneous breaths/respiratory efforts per minute, the ventilator delivers the 10 set bpm, while the four patient breaths are unsupported.

Continuous mandatory ventilation (CMV) is most commonly used in the ICU in patients who are not breathing spontaneously. Usual ventilator settings are 10–12 breaths/min, tidal volume 6–10 ml/kg, desirable FiO_2, and positive end-expiratory pressure (PEEP) of 5 cm H_2O. With CMV, the patient receives the predicted minute ventilation, regardless of the patient's effort. Disadvantage of CMV is that the airway pressure is variable and can be undesirably high, which can cause barotrauma.

Assist Control Ventilation

In assist-control ventilation (AC), in addition to the set mandatory breaths, the patient's spontaneous efforts are fully supported by the ventilator, that is, each spontaneous effort by the patient leads to the delivery of a full ventilator-supported breath. For example, if the ventilator is set to deliver 10 bpm and the patient takes four spontaneous breaths/respiratory efforts per minute, the ventilator delivers a total of 14 bpm. The advantage of this mode is that the patient can breathe spontaneously without increasing the work of breathing.

Synchronized Intermittent Mandatory Ventilation

IMV is utilized in patients who are spontaneously breathing. The ventilator is set to deliver the desired tidal volume and respiratory rate, while the patient is allowed to breathe spontaneously in between the ventilator-delivered mandatory breaths. However, IMV can cause stacking of breaths, where the patient's spontaneous breath may be stacked upon the ventilator's mandatory breath (superimposing). To prevent the delivery of a large tidal volume breath and possibly barotrauma, SIMV is preferably used.

In SIMV, the ventilator synchronizes the delivery of mandatory breaths with the beginning of the patients' own spontaneous breaths. If the patient does not initiate a breath, then the ventilator delivers the set tidal volume as in CMV mode. For example, if the ventilator is set to deliver 10 bpm and the patient takes four spontaneous breaths/respiratory efforts per minute, then six breaths are delivered as CMV, while four breaths are delivered as AC. Now, if the ventilator is set at 10 bpm and the patient is breathing spontaneously at 14 bpm, then ten breaths are delivered as AC, while four breaths are unsupported. These four breaths may increase the work of breathing. Therefore, pressure support may be added to assist the spontaneous breaths (SIMV with pressure support ventilation).

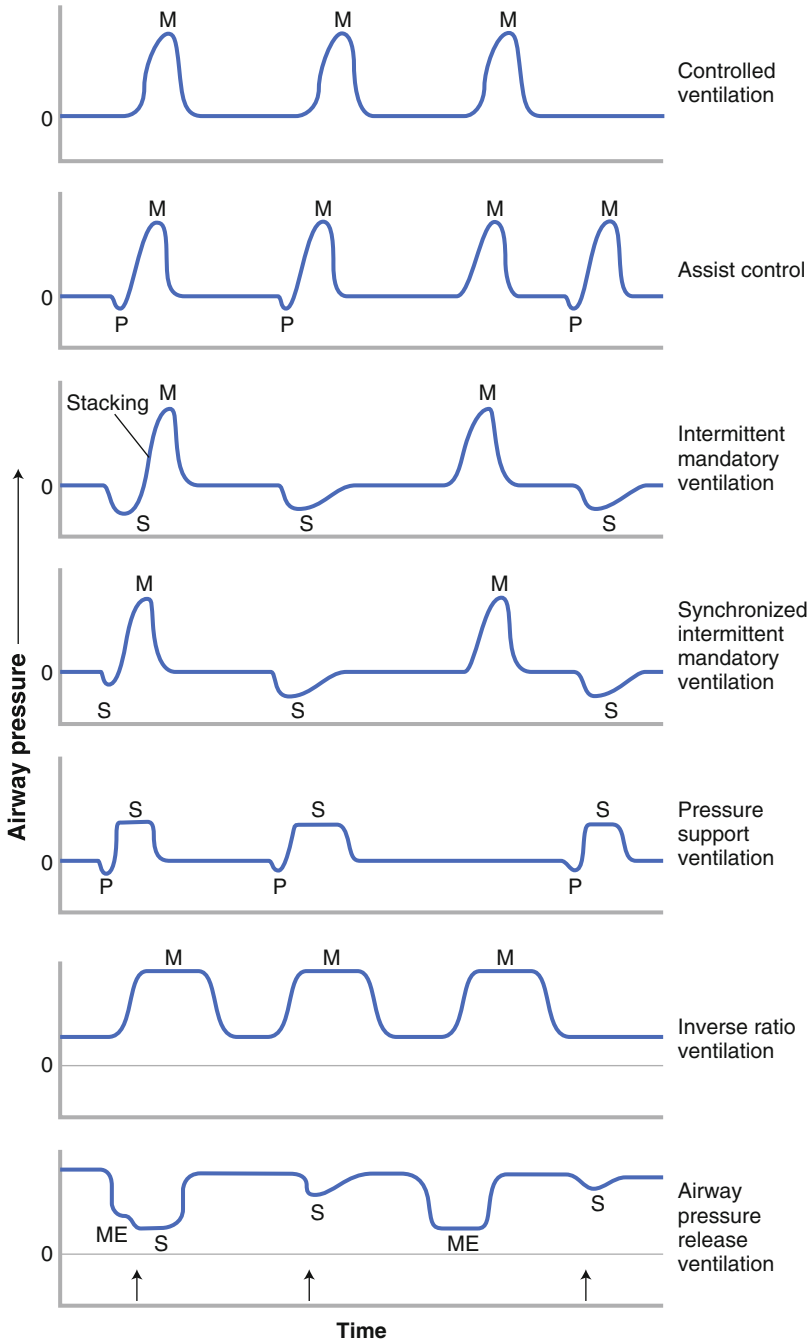

Fig. 40.6 Airway pressure wave forms in different modes of ventilation (*M* mechanical breath, *P* patient effort, *S* spontaneous breath, *ME* mechanical exhalation)

Pressure Control Ventilation

In pressure control ventilation (PCV), breaths are given to the patient at a set inspiratory pressure and respiratory rate. PCV may be used as assist control where both set and spontaneous patient breaths are delivered to the set pressure. Since PCV delivers breaths to a set and limited pressure, the risk of barotrauma is reduced. Disadvantage of PCV is that the delivered tidal volume is not guaranteed and requires more monitoring by the operator.

Pressure Support Ventilation

Pressure support ventilation (PSV) is used in spontaneously breathing patients, with no residual muscle paralysis. PSV decreases the work of breathing in spontaneously breathing patients (increases FRC). The patient determines the tidal volume and the respiratory rate. PSV differs from PCV, as only the inspiratory pressure is set and not the respiratory rate. When the patient initiates a breath, the ventilator delivers a preset inspiratory pressure to assist the patient in taking

an adequate breath. Pressure is set anywhere between 5 and 20 cm H_2O. Modern ventilators have a backup assist control, in case the patient's minute ventilation falls below the set threshold level.

Inverse Ratio Ventilation and Airway Pressure Release Ventilation

In inverse ratio ventilation (IRV), the I:E ratio is increased from typically 1:2 to 1:1. The patient is not allowed to breathe spontaneously and needs to be sedated with muscle paralysis. IRV leads to an increase in intrinsic PEEP, which leads to an increase in FRC, until an equilibrium is reached. IRV may be used in patients with acute respiratory distress syndrome (ARDS).

A newer mode of ventilation, especially used in patients with acute lung injury, is airway pressure release ventilation (APRV). APRV allows the patient to breathe spontaneously and, therefore, requires decreased levels of sedation, unlike IRV. In APRV, the ventilator cycles between two different set levels of CPAP, an upper and a lower pressure level. The baseline airway pressure is the upper CPAP level. Pressure is released intermittently to the lower CPAP level to release waste gas. Therefore, the two CPAP levels allow gas to move in and out of the lungs.

Positive End-Expiratory Pressure

PEEP is applied through the expiratory cycle in a mechanically ventilated patient. PEEP causes recruitment of alveoli and prevents atelectasis, but raises mean airway pressures. It increases FRC and improves pulmonary compliance and oxygenation. PEEP is usually set between 5 and 20 cm H_2O and always increases/decreases in increments. Optimal PEEP is one which leads to acceptable oxygenation ($PaO_2 > 60$ mmHg, O_2 saturation >94 %) with an FiO_2 of less than 50 %.

High PEEP can also be disadvantageous. High PEEP (>20 cm H_2O) may cause over distension of alveoli, increase dead space ventilation, reduce lung compliance, and cause excessive increase in intrathoracic pressure, which can cause barotrauma. High PEEP can reduce preload/venous return, decrease cardiac output and renal and hepatic blood flow, and increase central venous pressure leading to increased intracranial pressure. Pneumomediastinum, pneumothorax, pneumoperitoneum, and subcutaneous emphysema are all potential complications of applying PEEP.

When using PEEP, sufficient time should be allowed for exhalation to occur; otherwise the phenomenon of intrinsic or auto-PEEP may occur. Excessive development of auto-PEEP can lead to excessive end-expiratory pressures and hemodynamic effects.

Weaning Patients from Mechanical Ventilation

Patients should be weaned from the ventilator, ASAP, to decrease the risk of development of ventilator-associated pneumonia, barotrauma, airway trauma, and complications of prolonged sedation. It should always be remembered that premature discontinuation of mechanical ventilation can lead to loss of airway protection (aspiration), hypoxemia, muscle fatigue and acidosis, and cardiovascular effects. If reintubation is attempted, one may have to deal with an edematous airway. Factors that may prevent the patient from being weaned in the ICU include malnutrition, electrolyte abnormalities, prolonged sedation, and neuromuscular blocking agents.

Criteria for Weaning

To be weaned, the patient should have recovered from the original disease that leads to mechanical ventilation and should be hemodynamically stable, with minimal vasopressor support. The FiO_2 should be less than 50 %, which is chosen because this amount of FiO_2 can be delivered via a face mask. A requirement of an FiO_2 of more than 50 % means that significant V/Q mismatch is still present, and the underlying pulmonary process has not fully resolved. The PaO_2 should be >60 mmHg (adequate oxygenation), and $PaCO_2$ should be <50 mmHg (adequate ventilation), with near-normal pH (absence of acidosis). Other criteria of weaning are a negative inspiratory force of at least −20 cm H_2O and the patient's ability to inhale as forcibly as possible, enough to generate adequate tidal volume (vital capacity breath 10 ml/kg and tidal volume 5 ml/kg). The patient should not be tachypneic (respiratory rate <35 bpm) and should be able to protect the airway from aspiration (intact mental status—GCS >13, gag reflex, strong cough).

Weaning Trials

Weaning trials are done once daily. Weaning trials consist of spontaneous breathing with CPAP (adds physiological peep), or a T-piece (may cause atelectasis), and are protocol driven by respiratory therapists. Trials are initially carried out for 10–30 min and progressively increased by 5–10 min. Before the trials are begun, the mandatory ventilator settings are decreased slowly and guided by acceptable arterial oxygenation (pH, PaO_2, $PaCO_2$), as measured by arterial blood gas analysis. ABG analysis is usually done 15–30 min after any ventilator setting change. During the trial, the patient should be watched for fatigue, chest retractions, tachypnea, and hemodynamic instability, and if so, the trial should be terminated.

Hazards of Oxygen

Supplemental oxygen is used in various concentrations for patients in the ICU. One should be familiar with the undesirable effects (Fig. 40.7) of too much oxygen, an FiO_2 of 60–100 % for >24–48 h.

1. Hypoventilation—patients with COPD have chronic CO_2 retention, and their respiratory drive is dependent on a

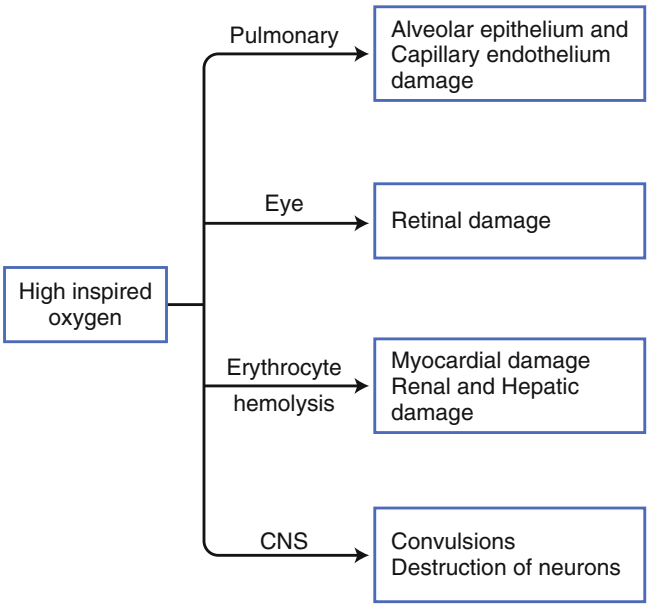

Fig. 40.7 Hazards of oxygen

relative hypoxemia. Therefore, raising the PaO_2 can depress their ventilatory drive. A high FiO_2 inhibits hypoxic pulmonary vasoconstriction causing increased blood flow to high V/Q ratios.

2. Absorption atelectasis—high FiO_2 leads to atelectasis in areas of low V/Q, causing absorption atelectasis and increased shunting (areas not ventilated but perfused).
3. Pulmonary toxicity—high FiO_2 (100 % for 24 h) causes increased production of free radicals (superoxide), which react with cellular DNA, proteins, and lipids, causing alveolar capillary leak mimicking ARDS.
4. Retinopathy of prematurity (ROP)—neonates, especially premature, when exposed to a high FiO_2 can develop retinopathy (ROP) of prematurity, as oxygen therapy can cause vascular proliferation, fibrosis, and retinal detachment.
5. Fire hazard—as oxygen is combustible.

Sedation in ICU

Sedation is commonly used in the ICU for multiple reasons. These reasons include providing analgesia, anxiolysis, amnesia, patient comfort, control of intracranial pressure, and prevention of dislodgement of ETT and lines. Excessive sedation has the risk of prolonging mechanical ventilation and development of ventilator-associated pneumonia and other infections.

Opioids provide excellent analgesia but little sedation or amnesia. Commonly used opioids are fentanyl (IV drip), morphine, and hydromorphone. Opioids have minimal effect on hemodynamics, but can cause significant respiratory depression if overdosed in a spontaneously breathing patient. Midazolam or lorazepam (benzodiazepines) provides anxiolysis and amnesia, but not analgesia. They can also be used to treat seizures and alcohol withdrawal syndrome.

Propofol also produces amnesia and anxiolysis, but not analgesia. It has a short elimination time, and its use facilitates the performance of wake-up tests by stopping the infusion. Excessive doses of propofol can cause hemodynamic instability (decreased myocardial contractility, systemic vascular resistance) and respiratory depression in spontaneously breathing patients. Propofol given at >4 mg/kg/h for >24 h can rarely cause propofol infusion syndrome (PIS). PIS is often fatal, causing cardiac failure, rhabdomyolysis, metabolic acidosis, renal failure, hyperkalemia, hypertriglyceridemia, and hepatomegaly. PIS is proposed to be caused by mitochondrial respiratory chain or fatty acid metabolism inhibition.

Dexmedetomidine, an alpha 2 receptor agonist, provides analgesia, sedation, and anxiolysis. However, excessive doses can lead to hypotension (decrease SVR) and bradycardia. Because it causes minimal depression of mentation and respiratory depression, it can be used for patient examination. Patients on mechanical ventilation, who buck or cough while being sedated, may have to be paralyzed with neuromuscular blocking drugs. This will prevent increases in intracranial pressure. However, long-term administration of muscle relaxants can lead to polymyoneuropathy.

Respiratory Failure

Pulmonary Edema

Pulmonary edema results when fluid transudes from the pulmonary capillaries into the interstitium and then into the alveoli. Pulmonary edema can be broadly classified as either cardiogenic or noncardiogenic. However, other causes of pulmonary edema include obstructive pulmonary edema (when a patient is trying to take a breath in the presence of an obstructed airway), high altitude, and neurogenic (marked increase in sympathetic tone causing severe pulmonary hypertension).

- Cardiogenic (CPE)—results from increased net hydrostatic pressure across the capillaries. The distinction between cardiogenic and noncardiogenic pulmonary edema can be made by measuring the pulmonary artery occlusion pressure, >18 mmHg means CPE. Additionally, the protein content will be lower in CPE edema because of increased permeability in NCPE.
  - Causes of CPE include left ventricular failure, mitral stenosis, left-right cardiac shunts, hypervolemia, severe anemia, and exercise. Management of CPE is aimed at decreasing the pressure across the capillaries,

which improves left ventricle function. Oxygen supplementation, diuretics, morphine, vasodilators (nitrates reduce preload), ACE inhibitors (reduce preload and afterload), and inotropic agents (dobutamine) are used to treat CPE.

- Noncardiogenic (NCPE)—results from increased permeability across the alveolar-capillary membranes. As mentioned above, the distinction between cardiogenic and noncardiogenic pulmonary edema can be made by measuring the pulmonary artery occlusion pressure, <18 mmHg means NCPE. Additionally, the protein content will be higher in NCPE because of increased permeability. Causes of NCPE include acute lung injury and ARDS.

Acute Respiratory Distress Syndrome

Increased permeability of the alveolar-capillary membrane leads to accumulation of fluid and protein (albumin) in the alveoli causing lung injury. Acute lung injury is said to occur when the PaO_2/FiO_2 ratio is <300. Acute lung injury with a PaO_2/FiO_2 ratio <200 is called as ARDS. The respiratory failure in ARDS is acute in onset, with the chest radiograph often showing bilateral infiltrates and a pulmonary artery occlusion pressure of <18 mmHg. Patients with ARDS are dyspneic, hypoxic (shunting), and often hyperventilate (low $PaCO_2$). Marked hypoxemia and respiratory muscle fatigue may mandate the patient to be mechanically ventilated.

Pathophysiology

Secondary to infection or trauma, an inflammatory response occurs (Fig. 40.8). This leads to the release of large amounts of inflammatory mediators, such as cytokines, free radicals, and proteases. These cause an increase in pulmonary capillary permeability causing diffuse alveolar damage (DAD), pulmonary vasoconstriction, and abolishment of hypoxic pulmonary vasoconstriction. DAD affects the function of type II pneumocytes causing decrease in surfactant production, which together with the edema leads to collapse of alveoli. Later in the inflammatory process, fibroproliferation occurs, which causes pulmonary fibrosis and reorganization of lung tissue.

Causes

ARDS can occur due to pulmonary and non-pulmonary causes. Pulmonary causes of ARDS include pneumonia, aspiration, pulmonary trauma, smoke inhalational injury, and embolism. Non-pulmonary causes of ARDS include sepsis (can be due to pneumonia), trauma in other parts of the body, acute pancreatitis, burns, near drowning, and blood transfusion related. Patients with ARDS have an increased tendency to develop renal failure (due to hypovolemia or nephrotoxins—renal failure with ARDS carries high mortality >50 %), gastrointestinal bleed (patients benefit from prophylaxis), and nosocomial infections.

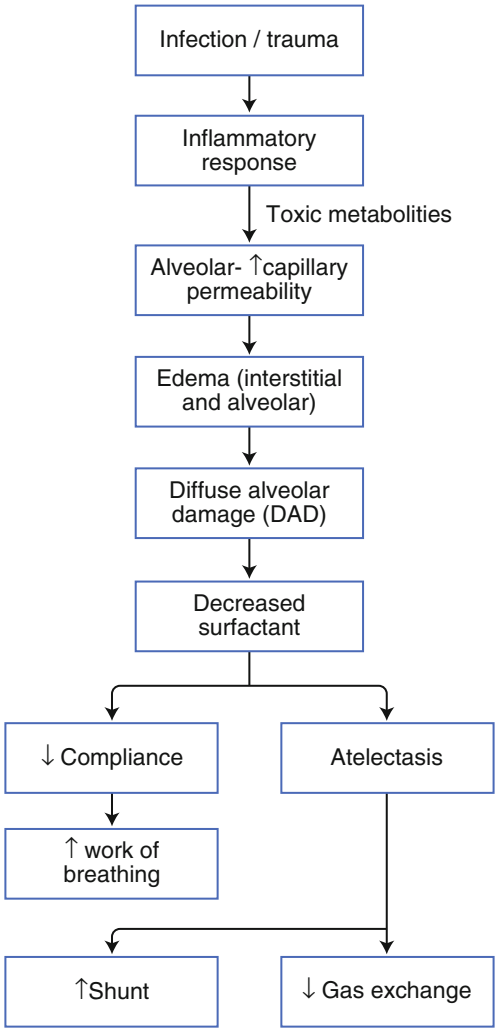

Fig. 40.8 Pathophysiology of acute respiratory distress syndrome

Management

Treatment of ARDS is supportive with providing adequate respiratory care (Table 40.8). If the original cause is known, therapy is directed toward the resolution of the cause. Antibiotics are started early in presence of confirmed or suspected infection. Patients with ARDS are often mechanically ventilated, preferably with low tidal volume breaths (6 ml/kg), an FiO_2 of less than 50 %, and adequate PEEP (for the recruitment of alveoli). PEEP can be optimized and adjusted by measuring the "stress index (aim for 1.0)" during constant-flow assist-control mechanical ventilation. Alternatively, patients can be mechanically ventilated with APRV, which is a pressure control mode of mechanical ventilation that utilizes an inverse ratio ventilation strategy (I:E ratio 1:1). APRV is an applied continuous positive airway pressure (CPAP) that at a set timed interval releases the applied pressure.

Low tidal volume has become the norm for ventilating patients with ARDS, so as to prevent over distention of the alveoli and prevent volutrauma. High tidal volumes (>10 ml/kg) can create high peak airway pressures and have been associated

Table 40.8 Therapeutic strategies in ARDS

Control of etiological factor	Sepsis, shock
Mechanical ventilation	• FiO_2 (preferably <50 %)—prevent O_2 toxicity • Low tidal volume (6 ml/kg)—prevents volutrauma • Adequate PEEP—prevent atelectasis • Inverse ratio ventilation (IRV)/airway pressure release ventilation (APRV) • Extracorporeal membrane oxygenation (ECMO)
Fluids	Restriction (as per CVP)
Drugs	Antibiotics, surfactant, nitric oxide, steroids
Position	Prone position
Patient comfort	Sedation, analgesia
Nutrition	Prevent malnutrition, may need enteral/parenteral feeding
Psychological support	For patient and family

Table 40.9 Differentiation between prerenal and intrinsic oliguria

Parameter	Prerenal	Acute tubular necrosis
Urine sodium (meq/L)	<20	>80
FENa (%)	<1	>3
U:P osmolality	>1.5:1	1:1
U:P creatinine	>50:1	<20:1
Creatinine clearance (ml/min)	15	<10
BUN/creatinine	>20	<10

with increased mortality. Patients ventilated with low tidal volumes will tend to have a lower PaO_2 and higher $PaCO_2$ (permissive hypercapnia), which can be offset by increasing the respiratory rate. Mechanical ventilation with high tidal volume is thought to be significantly more harmful in ARDS patients.

Other treatment modalities include putting the patient in a prone position (relieves atelectasis and improves perfusion), fluid restriction, diuresis, administration of methylprednisolone (decreases the inflammatory response) in low–moderate doses tapered over 2 weeks, and pulmonary vasodilator nitric oxide.

Acute Renal Failure

Acute renal failure (ARF) is an abrupt decrease in renal function, with urine output <0.5 ml/kg/h or 50 % increase in serum creatinine over 24 h. ARF carries a high mortality of up to 50 %. ARF can be due to prerenal, renal, or postrenal causes. The cause/type of renal failure can be diagnosed by measuring various parameters (Table 40.9). If the fractional excretion of sodium (FENa) is <1 %, renal failure is considered to be prerenal, and if it is >3 %, the renal failure is considered to be intrinsic (renal causes) in nature.

Prerenal ARF is due to decreased renal perfusion (hypotension, hypovolemia) and is treated with administration of fluids. Renal causes of ARF lead to acute tubular necrosis, which is caused by exposure to nephrotoxic drugs (NSAIDs), radiocontrast dye, aminoglycoside antibiotics, or prolonged hypotension (persistent prerenal causes). Postrenal ARF is due to obstructive causes (stones, tumor, BPH). Management of ARF is supportive, with dialysis required in most patients. Dialysis corrects volume overload, hyperkalemia, uremia, and other electrolyte abnormalities. Dialysis can be intermittent or continuous renal replacement (CRT) therapy. The benefit of CRT is that it removes fluid and solutes at a slow continuous rate and causes less hemodynamic instability (beneficial in hypotensive patients), but it is expensive to use.

Smoke Inhalation Injury

Gaseous injury can occur due to variety of gases, such as carbon monoxide (CO), hydrogen cyanide, hydrogen sulfide, ammonia, or chlorine gas. Smoke inhalation injury involves three modalities: heat injury to airways, exposure to toxic gases, and chemical deposition of carbonaceous particles in the lower airway. The inhalational injury leads to mucosal injury causing edema and inflammation. This can develop to acute lung injury and ARDS in a few days. Also, progressive edema can lead to hoarseness and stridor, a sign of impending airway obstruction.

CO poisoning can lead to greater than 15 % concentration of carboxyhemoglobin, the presence of which is detected by CO-oximeter measurements of blood, as the pulse oximeter cannot differentiate between oxyHb and carboxyHb. CO has 250 times the affinity for hemoglobin oxygen, and CO poisoning shifts the Hb-O_2 dissociation curve to the right, causing marked reduction in O_2-carrying capacity of blood and hypoxemia. Signs of CO poisoning include mental status changes and disorientation (neurological impairment) and peripheral vasodilation and shock. Fiberoptic bronchoscopy may be done to diagnose the inhalation injury. If airway edema is suspected (stridor/hoarseness), early intubation and even tracheostomy may be required. CO poisoning is treated with delivering high (100 %) FiO_2, and if no response, then hyperbaric O_2 therapy is instituted. Administering an FiO_2 of 100 % reduces the half life of carboxyHb from 3 h to 1 h.

Cyanide toxicity can occur from inhaling fumes from fires that burn synthetic material, such as polyurethane. Cyanide, when absorbed, binds to cytochrome enzyme

system and inhibits the production of ATP. Signs of cyanide toxicity include neurological impairment, lactic acidosis, and marked vasodilation. Cyanide toxicity is treated by administration of sodium nitrite, followed by sodium thiosulfate. Sodium nitrite converts Hb to cyan-methHb which has more affinity for cyanide than the cytochrome enzyme system. The rhodanese enzyme uses thiosulfate as a substrate to metabolize cyanide. Administration of exogenous sodium thiosulfate enhances this reaction. Other drugs that can be used to treat cyanide poisoning include hydroxocobalamin (a form of vitamin B_{12}) and 4-dimethylaminophenol (4-DMAP).

Nutrition in the ICU

Optimal nutrition prevents malnutrition and skeletal muscle weakness, reduces infectious complications, and enhances wound healing. Enteral nutrition should always be preferred over parenteral nutrition (TPN) in order to maintain the integrity of the gut and prevent gut atrophy. Enteral nutrition is cheaper, simpler, and associated with fewer complications than TPN. Enteral nutrition is given through a small bore nasogastric or gastrostomy tube. The most common complication of enteral feeding is diarrhea due to hyperosmolarity of the feeding solution.

If the GI tract cannot be used for enteral feeding, or if enteral absorption is inadequate, then parenteral nutrition is instituted. However, TPN is associated with multiple complications (Table 40.10). Hyperglycemia is the most common complication of TPN administration. To prevent hyperglycemia, insulin is added to parenteral solutions. Hypophosphatemia can be often missed in patients receiving TPN. Patients on TPN should have their blood chemistry checked daily and prealbumin weekly. Preoperatively, if TPN is stopped suddenly, the patient may develop hypoglycemia. However, the stress response to surgery may negate the development of hypoglycemia. Therefore, preoperatively, clinicians may continue, stop, or reduce TPN administration, but monitoring of serial blood glucose values is required.

Table 40.10 Complications of parenteral nutrition

Catheter related	Sepsis, thrombosis of insertion vein (jugular, subclavian), pneumothorax, hemothorax, air embolism
Electrolyte abnormalities	Hypophosphatemia, hyper/hypoglycemia, hyper/hypokalemia, hypernatremia, hypocalcemia
Refeeding syndrome	Hypokalemia, hypophosphatemia, hypomagnesemia
Ph	Metabolic acidosis or alkalosis
Liver	Hepatic dysfunction, cholestasis
Fat	Fat embolism, hyperlipidemia, pancreatitis
Anemia	Deficiency of iron, folic acid, vitamin B_{12}
Vitamin deficiency	D, K

Ethical Issues

Often in the ICU, decisions have to be made on withholding treatment or discontinuing life support. Continuing treatments in end-stage diseased patients places undue financial burden on the family and society. A competent patient may refuse treatment, but for minors and incompetent adults, the decisions are made by the next of kin or through the power of attorney. Sedation for end-stage diseased patients (morphine infusion) is only given for comfort measures and not to hasten death. Do not resuscitate/intubate (DNR/DNI) orders are usually suspended for the operating room and reinstated when the patient leaves the recovery room. However, the details of DNR orders should be discussed preoperatively, whenever possible.

Brain death is irreversible cessation of brain function. Criteria for brain death include coma, absent motor activity, absent brain stem reflexes (papillary, vestibuloocular, gag), and absent ventilator effort. These criteria are conclusive in the absence of hypothermia, hypotension, metabolic abnormalities, and negative toxic screen. Brain death is usually confirmed by more than one physician. Tests that are not required but confirmatory of brain death include an isoelectric EEG and absent cerebral perfusion by angiography, transcranial Doppler, or radioisotopic studies.

Myocardial Infarction

Acute myocardial infarction (MI) occurs because of disruption of blood supply to different parts of the heart due to blockage of one or more of the coronary arteries. MI carries a high mortality of about 25 %, with over half of the deaths occurring within one hour of MI due to arrhythmias, usually ventricular fibrillation.

MI can be caused by multiple precipitating factors, which include coronary plaque erosion, fissuring, or dissection, and factors which increase myocardial oxygen demand (heart rate; wall tension, preload/afterload; contractility) and decrease oxygen supply (heart rate/arrhythmias; coronary perfusion pressure, hypertension/hypotension; coronary artery spasm; anemia—arterial oxygen content).

Clinically, MI can be classified as an ST elevation MI (STEMI) versus a non-ST elevation MI (NSTEMI) based on ECG changes. ST segment elevations on an ECG are typically due to complete occlusion of a coronary artery, while in NSTEMIs there is a sudden narrowing of a coronary artery with preserved but diminished blood flow to the distal myocardium. Based on pathology, MI can be classified as:

- Transmural MI: this is associated with atherosclerosis, ultimately causing complete occlusion of a major coronary artery and can be subclassified based on location into anterior, posterior, inferior, lateral, or septal.
- Subendocardial MI: this involves a small area (particularly susceptible to ischemia) in the subendocardial wall of the left ventricle, ventricular septum, or papillary muscles.

Risk Factors

Risk factors for MI include smoking, age, male sex, diabetes mellitus, hypertension, dyslipidemia (hypercholesterolemia), family history of ischemic heart disease, obesity, lack of physical activity, psychosocial stress, chronic alcoholism, and hyperhomocysteinemia.

The classical symptom/sign of MI is chest pain/angina pectoris. Angina is a sensation of tightness, pressure, or squeezing over the center of the chest. The pain often radiates to the left arm, lower jaw, neck, right arm, back, and epigastrium (may mimic heartburn). Other symptoms include shortness of breath/dyspnea (with associated left ventricular failure), diaphoresis (excessive sweating), light-headedness, nausea, vomiting, and palpitations. The symptoms of MI can be explained by a massive surge of catecholamines from sympathetic nervous system stimulation caused by the intense pain and the hemodynamic abnormalities resulting from cardiac dysfunction. Also, inadequate cerebral perfusion can lead to loss of consciousness, while life-threatening arrhythmias can cause sudden death.

Diagnosis

About one-fourth of all MIs are silent, occurring without chest pain or other symptoms. These are more common in elderly and patients with diabetes mellitus, where differences in pain threshold and autonomic neuropathy lead to loss in experiencing the symptoms. Evidence of a silent MI can be later discovered on electrocardiograms.

The diagnosis of MI can be made from history and physical examination, serial ECG changes (site identification, ST elevation—Fig. 40.9—or ST depression), coronary angiography (visualization of narrow coronary arteries), levels of cardiac markers, new regional wall motion abnormalities on echocardiography, routine blood tests, and chest radiography.

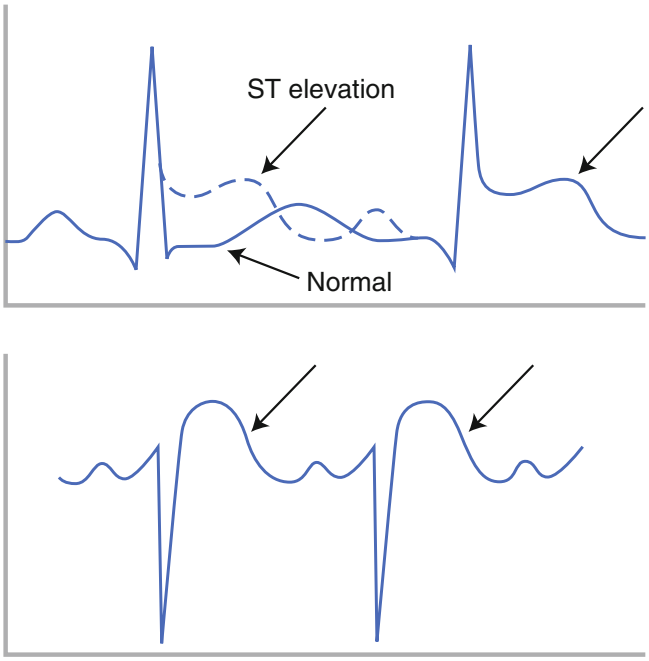

Fig. 40.9 Electrocardiogram showing ST elevation in myocardial infarction

Troponin T and I are very sensitive and specific for cardiac damage. Troponin is a contractile protein not found in the blood and released with myocardial damage. Troponin levels in the serum increase within 3–12 h from the onset of chest pain, peak at 24–48 h, and return to baseline over 5–10 days. The risk of death from an acute coronary syndrome (ACS) is directly related to troponin level. Patients with no detectable troponins have a good short-term prognosis. It should be remembered that elevated troponin levels can also occur in patients with congestive heart failure, sepsis, acute pulmonary embolism, chronic kidney disease, myocarditis, and aortic dissection.

Myocardial muscle creatine kinase (CK-MB) is found mainly in the heart. CK-MB levels increase within 3–12 h of onset of chest pain, reach peak values within 24 h, and return to baseline after 48–72 h. CK-MB is not as sensitive and specific as troponin.

Myoglobin is found in cardiac and skeletal muscle and is released more rapidly from infarcted myocardium than troponin and CK-MB. It may be detected (early detection of MI) as early as 2 h after MI. Myoglobin has high sensitivity but poor specificity.

Increase stretch of the myocardium, as in heart failure, can elevate levels of natriuretic peptides (B-type natriuretic peptide—BNP).

Management

"Time is muscle": MI management involves salvaging quickly as much myocardium as possible. Treatment of MI includes:

- Oxygen—used cautiously to prevent O_2 toxicity.
- Aspirin—given ASAP. Its antiplatelet effect inhibits formation of further thrombi.
- Nitroglycerin—given sublingually/IV to relieve angina, cause vasodilation, and decrease oxygen demand.
- Morphine—for pain (may increase mortality in NSTEMI).
- β-Blockers—(metoprolol) decrease the effect of the sympathetic nervous system on the heart and decrease the workload of the heart.
- Reperfusion—in patients with STEMI, immediate reperfusion is done with either thrombolytic therapy, percutaneous coronary intervention (PCI), or CABG. Thrombolytic therapy is contraindicated in patients with NSTEMI, as the etiology is usually coronary spasm.
- ACE inhibitor—in stable patients, an ACE inhibitor is started 24–48 h after an MI. They reduce mortality and development of heart failure.
- Aldosterone antagonist—spironolactone/eplerenone
- Control of risk factors—smoking and alcohol cessation, hypertension, diabetes, physical activity, and diet control (lipid). Statin therapy is used for LDL lowering and plaque stabilization effects.

Pulmonary Embolism

Patients who have a prior history of deep vein thrombosis (unilateral leg swelling—DVT) or those on prolonged bed rest are prone to pulmonary embolism (PE). These patients include those with fractures/surgery of the lower extremities, cancer, myocardial infarction postpartum, and hypercoagulability (protein C or S and antithrombin deficiency, factor V Leiden, estrogen-containing contraceptive pills).

In these patients, blood clots form in the venous system of lower extremities (commonly above the knees) or pelvic veins. These clots or fat cells (from bones), tumor cells, amniotic fluid, or talc (IV drug abusers) can travel to the pulmonary system via the right heart and can cause PE. PE causes a sudden increase in the pulmonary vascular resistance (acute pulmonary hypertension), causing vasoconstriction, shunting, V/Q mismatch, atelectasis, and hypoxemia.

Clinical signs of PE are often mild or absent and depend on the extent of the embolism. These signs may include tachypnea (respiratory alkalosis), chest pain on inspiration, dyspnea, wheezing, cyanosis, and even sudden death. Cardiovascular signs include tachycardia, wide fixed splitting of the second heart sound, hypotension, and elevated CVP. The latter 2 may be indicative of right ventricular failure. A chest radiograph is usually normal, but may show an area of radiolucency or atelectasis. An ECG (also to rule out MI) may show tachycardia, right axis deviation, and RBBB.

Diagnosis of PE can be confirmed with CT pulmonary angiography (noninvasive angiography done with radiocontrast and CT scanning) and ventilation-perfusion scans (showing areas of the lung which are ventilated but not perfused due to clots). Importantly, a negative D-dimer excludes the presence of thrombotic PE, but a positive D-dimer test warrants further work-up.

Management

One of the most important interventions is the prevention of PE. Patients should be ambulated as early as possible after surgery. In bedridden patients, subcutaneous heparin 5,000 U or low-molecular-weight heparin (LMWH) every 12 h is used for the prevention of PE/DVT. Elastic stockings or pneumatic boots can also be used. In patients with a high risk of developing PE, an inferior vena cava filter is inserted percutaneously under local anesthesia.

In patients with a confirmed PE/DVT, initial therapy is begun with LMWH and warfarin. LMWH is stopped once patient is therapeutic on warfarin (INR). Warfarin is continued for 3–6 months, when further testing is done to exclude PE/DVT. Massive PE is treated with thrombolytic therapy.

Regional anesthesia is said to decrease the incidence of PE, but is not used in anticoagulated patients. Intraoperatively, PE can be caused by air emboli, fat cells (during orthopedic procedures), or tumor cells. The patient may suddenly become hypotensive, hypoxic, and/or tachycardic, with a drop in $ETCO_2$ and a rise in CVP or wedge pressure (if available). Transesophageal echocardiography may be done to detect the presence of emboli or evaluate cardiac function. A CVP catheter may be used to aspirate the air out. Hemodynamic support is provided with fluids and inotropes.

Table 40.11 Cardiopulmonary resuscitation in adults and children

Parameter	Adult	Child > 1 year	Infant (<1 year)
Airway			
Patency of airway	• Maintain airway with head tilt and chin lift • Jaw thrust • Maintain neck stability (patient may have cervical spine injury)		
Breathing			
Initial breaths	Two breaths of 1 s each		
Breaths without advanced airway	10–12 bpm	12–20 bpm	
Breaths with advanced airway (ETTube)	8–10 bpm		
Circulation			
Circulation: pulse check	Carotid		Femoral/brachial
Chest compression site	Lower sternum/between nipples		Lower sternum/just below nipples
Compression technique	Heel of one hand with other hand on top	Heel of one hand or same as adults	With 2–3 fingers or with 2 thumbs and hands encircling the chest
Compression depth	1.5–2 inches	1/3–1/2 depth of chest	
Compression rate	≈100/min		
Compression/ventilation ratio	30:2	30:2 (1 rescuer) 15:2 (2 rescuers)	
Defibrillation	120–200 J (biphasic defibrillators), higher J with monophasic defibrillators	2 J/kg for 1st shock, then 4 J/kg	
For a foreign body	Abdominal thrusts		Back blows and chest thrusts

Cardiopulmonary Resuscitation

Cardiopulmonary resuscitation (CPR) consists of ABCD—maintaining a patent *a*irway, *b*reathing at a minimum rate; chest compressions and maintaining *c*irculation, and prompt *d*efibrillation (Table 40.11).

CPR begins with calling for help and placing the patient flat on a firm surface. The airway is made patent, which may require a head tilt-chin lift or a jaw thrust. A nasal/oral airway may have to be inserted to make the airway patent. Nasal airways should be avoided in patients suspected of basilar skull fracture. Also, manipulation of the cervical spine should be avoided in patients suspected of spine injury. If there are no signs of ventilation, then ventilation should be assisted.

Breathing can be assisted with mouth to mouth, mask to mouth, or bag to mouth ventilation. The patient should be ventilated normally and not hyperventilated. The airway is then secured with an endotracheal tube (ETT), the placement of which is confirmed with an $ETCO_2$ detector. In case of severe facial trauma, or when ETT placement is unsuccessful, a cricothyrotomy or tracheostomy is performed. For cricothyrotomy, a 12/14 gauge catheter is inserted through the cricothyroid membrane into the trachea and connected to a high-pressure oxygen source.

The circulation is checked next, usually the carotid pulse in adults. If no pulse is felt, CPR is begun. Drugs can be administered via a peripheral line, but a central line is preferred. The pharmacological effect of drugs administered via a peripheral line will be delayed for 1–2 min. Alternatively, if no intravenous access can be obtained, an 18G catheter can be inserted intraosseously, usually 2–3 cm below the tibial tuberosity at a 45° angle away from the epiphyseal plate. Placement is confirmed by aspirating bone marrow and a smooth flush of the IV catheter. Also, some drugs can be administered via the ETT (atropine, epinephrine, lidocaine, vasopressin).

If defibrillation is required, the pads should be positioned correctly. The survival rate after a ventricular fibrillation cardiac arrest decreases by 7–10 % with every passing minute. Defibrillators with biphasic waveform are more successful and use less energy (120–200 J) than defibrillators with monophasic waveform (360 J).

It is important to remember that the majority of heart rhythm dysfunctions are caused by the 5Hs and the 5Ts:

- H—hypovolemia, hypoxia, hydrogen ions (acidosis), hyper/hypokalemia, and hypothermia

- T—toxins, tamponade (cardiac), tension pneumothorax, thrombosis (coronary, pulmonary), and trauma

Various cardiac rhythms are summarized in Tables 40.12, 40.13, and 40.14 and depicted in Figs. 40.10, 40.11, and 40.12. Drugs commonly used during CPR are listed in Table 40.15. Figures 40.13, 40.14 and 40.15 depict algorithms for the management of adult cardiac arrest, symptomatic bradycardia, and symptomatic tachycardia, respectively.

Table 40.12 Abnormalities with cardiac rhythm

Type	Characteristics	Treatment/comments
Sinus bradycardia	Normal complexes with rate < 60/min	Occurs with increased vagal activity and beta-blockers, seen commonly in athletes
Sinus tachycardia	Normal complexes with rate > 100/min	Occurs with exercise, anxiety, pain, fever, caffeine, hypotension, increased sympathetic activity
Sinus arrhythmia	The longest PP or RR interval exceeds the smallest by 0.16 s, normal complexes with irregular rate, increased rate with inspiration, and decreased rate with expiration	Increased vagal activity, commonly and normally occurs in the young
Supraventricular tachycardia	Regular and rapid rate (160–220/min), P wave followed by QRS (1:1), T wave superimposed on P wave	Treatment includes vagal stimulation (Valsalva, carotid sinus massage) and same treatment as atrial fibrillation below
Junctional rhythm	Impulse originates in AV node rather than SA node, so p waves may not be seen, decreased SA node activity, heart rate is slow 45–50/min, normal QRS complex	Can occur due to volatile inhalation agents under anesthesia, no treatment or atropine/ephedrine to increase the heart rate
Atrial fibrillation (AF)	Irregular and rapid ventricular rate (100–200/min), no discernible P wave, variable RR interval	Causes include atherosclerosis, hyperthyroidism, etc.; patients have a fivefold higher risk of stroke and are on anticoagulants (warfarin) • Rate control with beta-blockers (esmolol, metoprolol) or calcium channel blockers (diltiazem) • Cardioversion, if hemodynamically unstable
Atrial flutter	Regular and rapid atrial rate (220–300/min), with ventricular wave on every 2nd or 3rd atrial impulse (2:1, 3:1 block), sawtooth wave pattern	Treatment same as atrial fibrillation

Table 40.13 Abnormalities with ventricular rhythm

Type	Characteristics	Treatment/comments
Premature ventricular contraction (PVC)	Wide QRS, bigeminy (every other beat), trigeminy (every 3rd beat), when R wave (ventricular depolarization) occurs during the repolarizing phase of the preceding beat (on T wave)—called as R on T phenomenon. The latter can result in VT/VF	Benign, but frequent premature contractions (>5/min), may indicate ischemia and electrolyte abnormalities, treated with removing the cause, lidocaine (1 mg/kg) and beta-blockers/calcium channel blockers
Ventricular tachycardia (VT)	Rapid and wide QRS complexes, regular/irregular	Due to myocardial ischemia/infarction, treated with cardioversion (if unstable), amiodarone when stable
Ventricular fibrillation (VF)	Irregular chaotic ventricular activity, no QRS complexes, impending death	Defibrillation, CPR, epinephrine q 3 min, vasopressin 40 U, amiodarone, lidocaine
Asystole/pulseless electrical activity	Causes—hypoxia, acidosis, electrolyte abnormalities, tension pneumothorax, tamponade, pulmonary embolism	CPR, no benefit from defibrillation, epinephrine q 3 min, vasopressin 40 U, atropine no longer recommended

Table 40.14 Types of AV (heart) block

Type	Characteristic	Treatment/comments
First degree	PR interval >0.2 s	Clinically insignificant
Second degree	• Mobitz type I (*Wenckebach*)—gradual lengthening of PR interval until a beat is dropped	Usually insignificant, may be seen with drug toxicity
	• Mobitz type II—intermittent dropped beats, can progress to third-degree AV block	Treat with atropine, isoproterenol, or pacing
Third degree	Disconnection between atrial and ventricular conduction	Pacing required

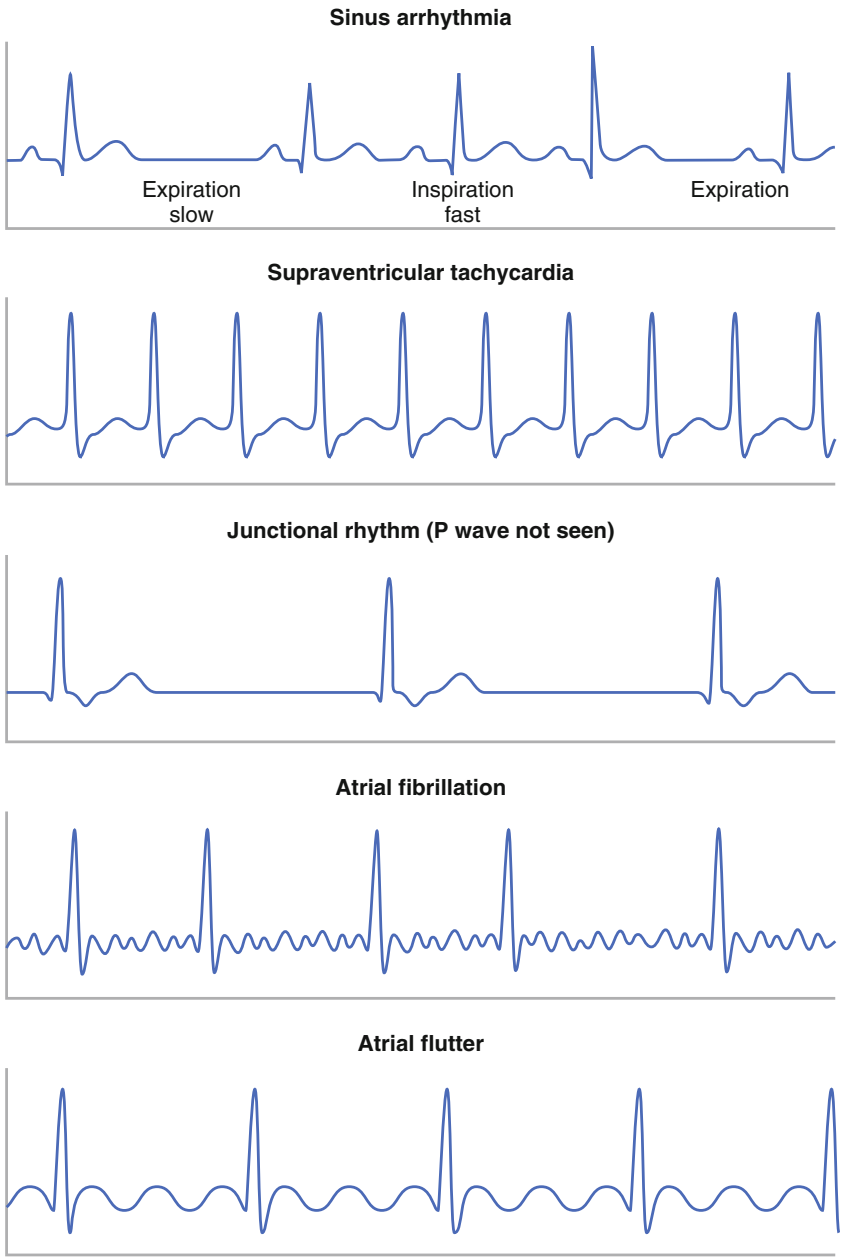

Fig. 40.10 Various types of supraventricular rhythms

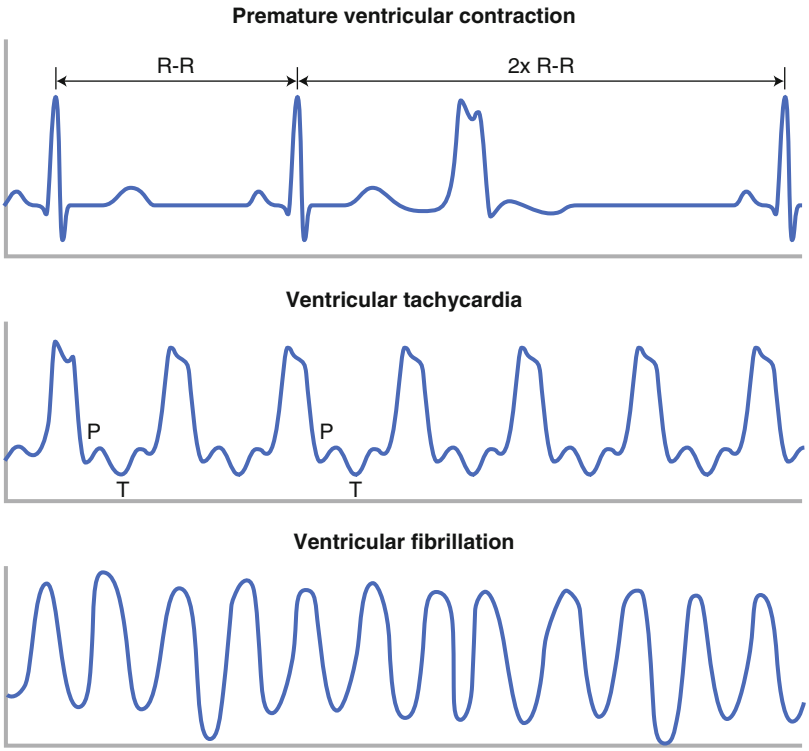

Fig. 40.11 Various types of ventricular rhythms

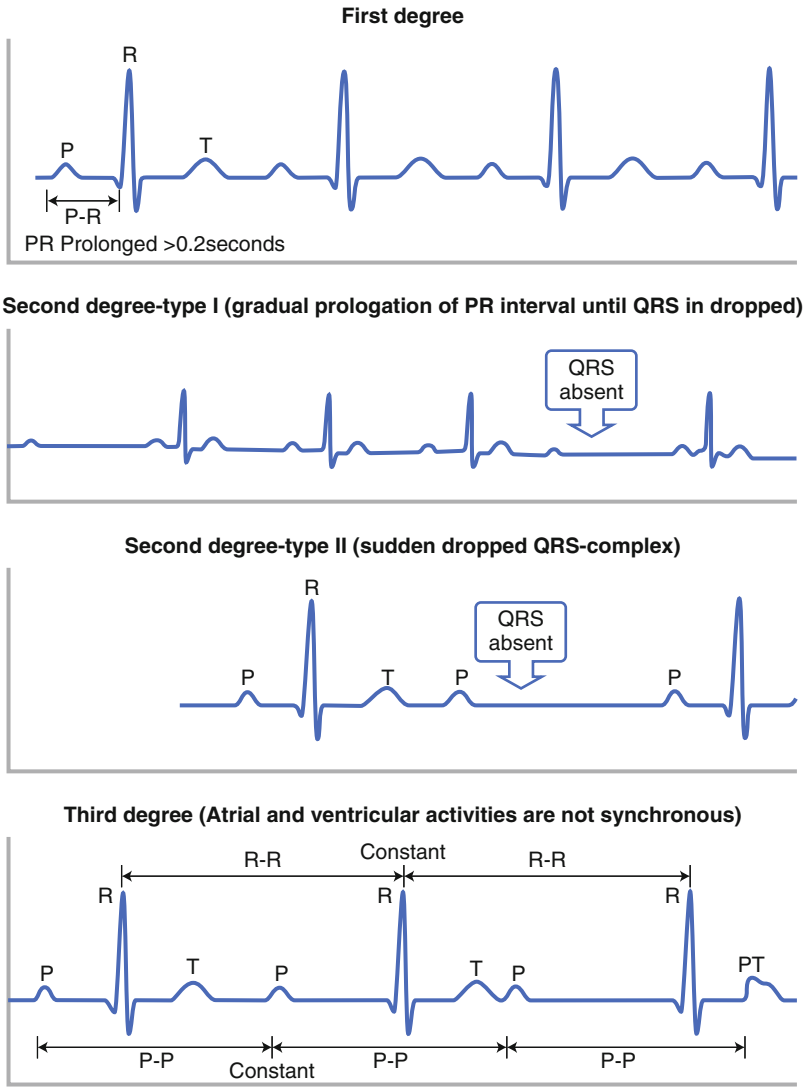

Fig. 40.12 Various types of heart (AV) blocks

Table 40.15 Drugs used during cardiopulmonary resuscitation

Drug	Indication	Dose
Adenosine	Narrow complex QRS tachycardia (SVT)	6 mg, may repeat 12 mg—IV push
Atropine	Bradycardia	0.5 mg IV push, up to 3 mg
Amiodarone	VT/VF	Loading dose of 150–300 mg
Diltiazem	Stable narrow complex QRS tachycardia—atrial fibrillation/flutter	0.25 mg/kg IV (10–20 mg), infusion 3–15 mg/h
Epinephrine	Pulseless cardiac arrest	1 mg IV, repeat q 3–5 min
Esmolol	Stable narrow complex QRS tachycardia—AF/flutter	Loading dose of 0.5 mg/kg, infusion 0.05 mg/kg/min
Lidocaine	VT/VF	1–1.5 mg/kg, up to 3 mg/kg
Metoprolol	Stable narrow complex QRS tachycardia—AF/flutter	3–5 mg IV, up to 15 mg
Vasopressin	To replace 2nd dose of epinephrine in VT/VF, asystole, PEA	40 U IV

PEA pulseless electrical activity, *AF* atrial fibrillation, *VT* ventricular tachycardia, *VF* ventricular fibrillation

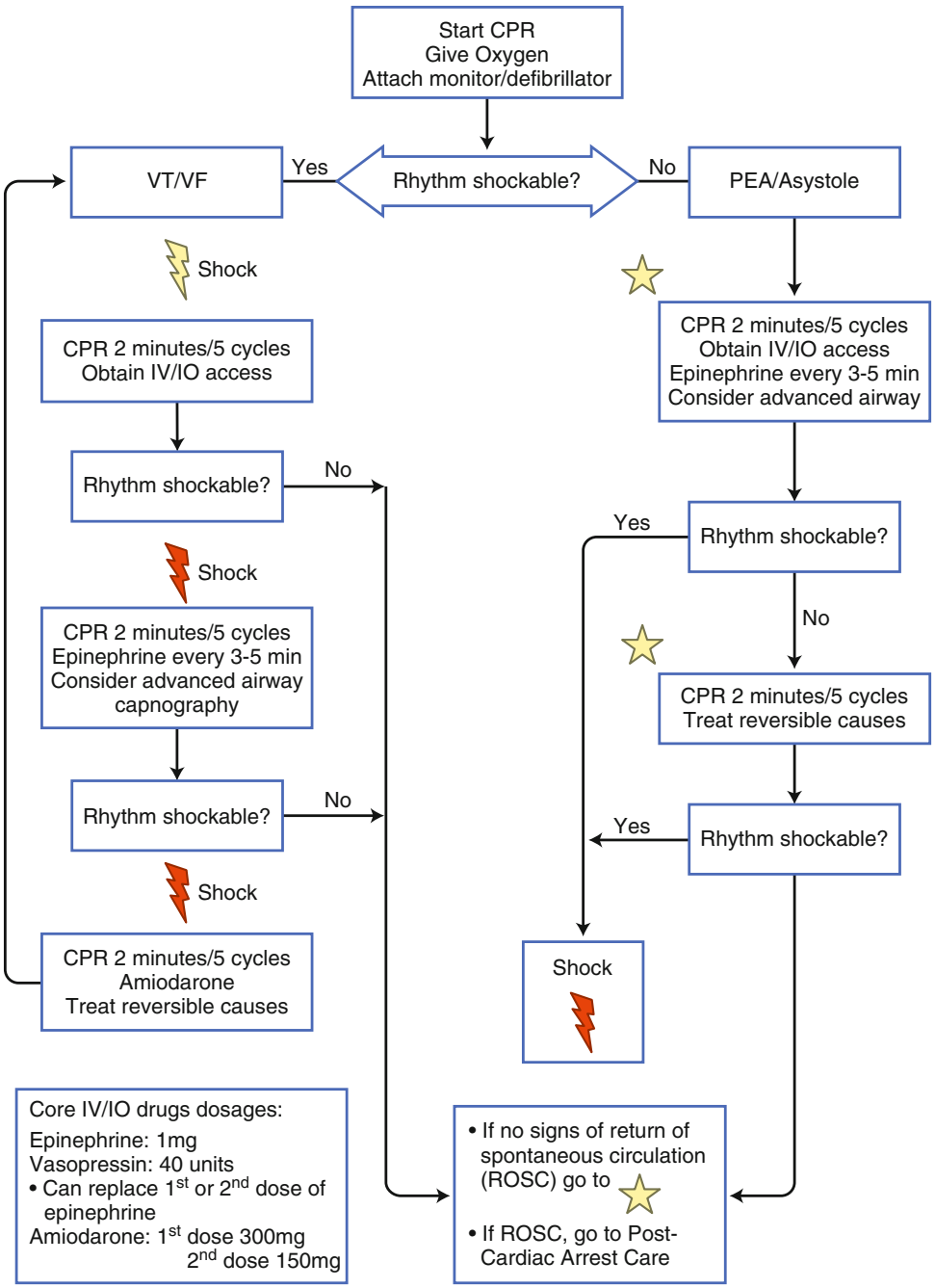

Fig. 40.13 Adult cardiac arrest algorithm

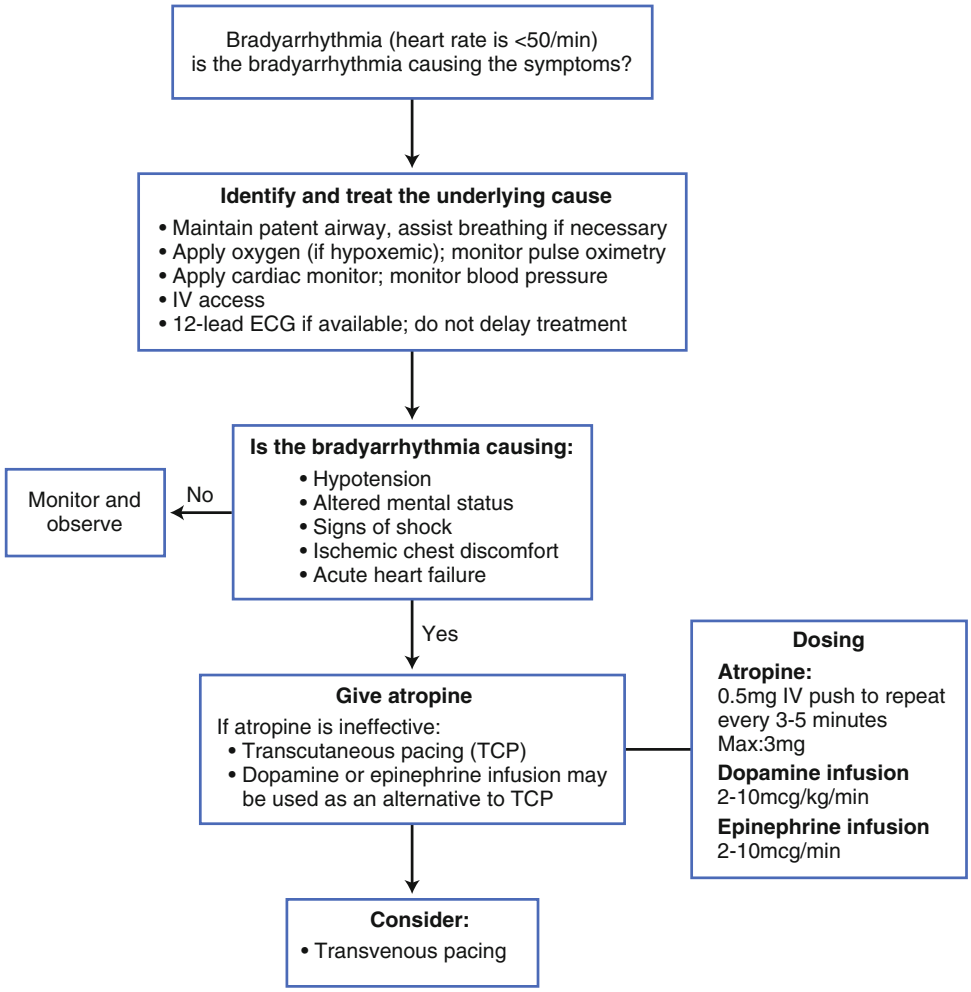

Fig. 40.14 Adult bradycardia algorithm

Post-Cardiac Arrest Care

Therapeutic Hypothermia

Therapeutic hypothermia induced to 32–34 °C (89.6–93.2 °F) when maintained for 12–24 h has been shown to improve neurological outcomes after cardiac arrest. The hypothermia should be induced soon after cardiac arrest, that is, as soon as spontaneous circulation returns. Hypothermia can be induced with rapid infusion of ice-cold (40 C) isotonic non-glucose-containing fluid to a volume of 30 ml/kg. The patient's temperature is monitored with an esophageal temperature probe or an in-place pulmonary artery catheter.

Ventilation

Patients after cardiac arrest should be ventilated with normocapnia. Hyperventilation leads to decreased $PaCO_2$, which can cause cerebral ischemia. Also, the FiO_2 should be ideally less than 50 % (to prevent O_2 toxicity), while maintaining a $PaO_2 > 60$ mmHg and an oxygen saturation >94 %. Positive pressure ventilation in the post-cardiac arrest patient can lead to high intrathoracic pressure, which can cause increased airway pressures, increased intracranial pressure, and detrimental hemodynamic effects.

Cardiovascular Status

The blood pressure and heart rate should be maintained within normal limits. Hypotension should be avoided and should be treated with fluids and vasopressors. The systolic pressure should be above 90 mmHg, or the mean arterial pressure should be maintained at >65 mmHg. Blood glucose should be maintained between 140 and 180 mg/dl to prevent both hyper- and hypoglycemia.

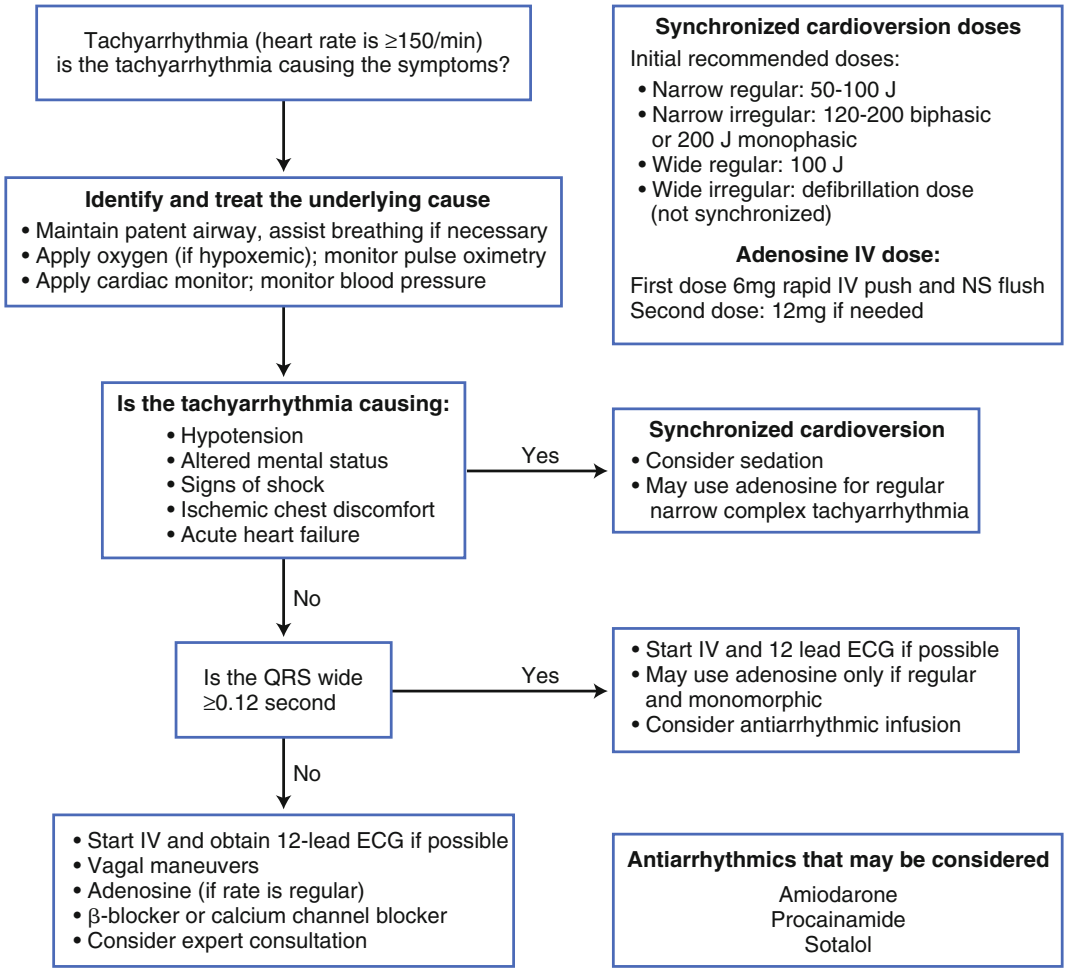

Fig. 40.15 Adult tachycardia algorithm

Burns

A burn is a type of injury caused to the skin or deeper structures by fire (heat), electricity, chemicals, or radiation. Large burns can be fatal; therefore, aggressive resuscitation measures are often required to improve outcomes. Burns are commonly classified as:

- First-degree burns—limited to the epithelium
- Second-degree burns—extend to the dermis
- Third-degree burns—involve the entire skin thickness (may not be painful due to loss of sensation)

Physiologic Changes

Burns induce a shift of fluid from the intravascular compartment to the interstitial space due to loss of capillary integrity. There is contraction of the intravascular compartment, which may cause the hematocrit to increase due to hemoconcentration. Loss of fluid causes the cardiac output to decrease significantly. After 24–48 h, capillary integrity starts returning to normal, resulting in an increase in the intravascular volume. The blood pressure (hypertension) and heart rate increase.

Inhalational injury leads to upper and lower airway edema and possible airway obstruction. Presence of stridor or hoarseness of voice may indicate impending airway obstruction. A decline in surfactant function leads to atelectasis and shunting. Major burns can lead to changes in pulmonary capillary function causing pulmonary edema, pneumonia, and ARDS. Smoke inhalational injury may lead to carbon monoxide poisoning.

Loss of fluid also leads to decreased renal blood flow, which can lead to the development of acute renal failure. ARF carries a high mortality. Also, an increase in ADH secretion leads to retention of sodium and water, with loss of potassium. There may be an initial hyperkalemia due to cell lysis, followed by hypokalemia due to renal and gastric wasting.

Burns can also cause a massive release of catecholamines. There may be increased consumption of clotting factors and

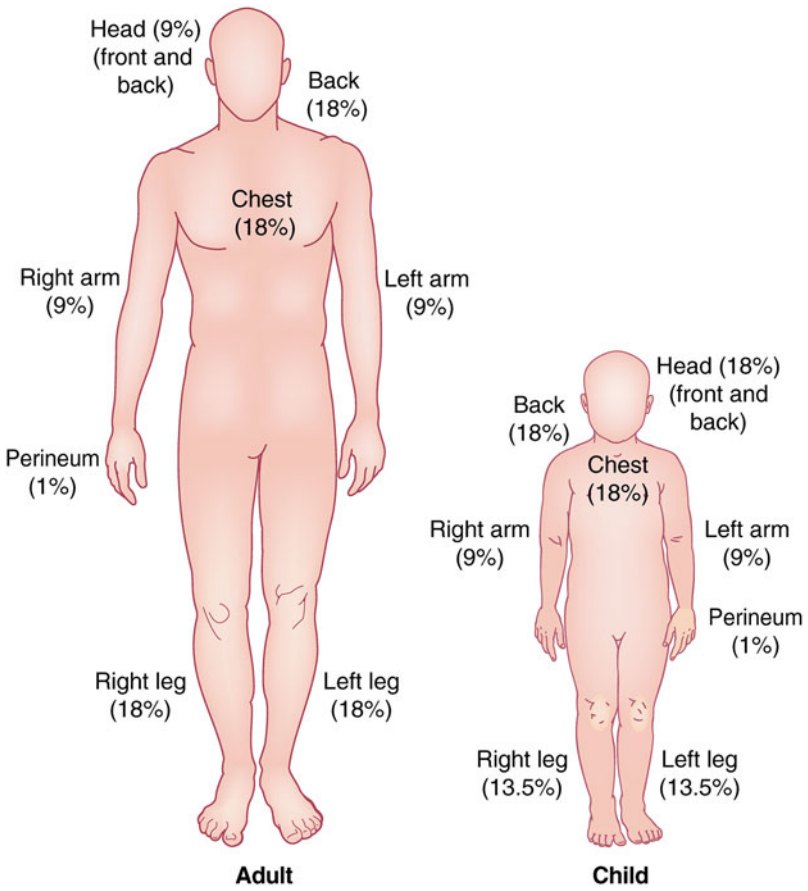

Fig. 40.16 Estimation of percentage of burns in an adult and child

thrombocytopenia. Burn patients are at an increased risk of infections and sepsis.

Anesthetic Considerations

Survival of a burned patient depends on the degree of the burn, the percentage of body surface burnt (Fig. 40.16), and the age of the patient. With electrical burns, the underlying skin may be damaged below a normal-looking superficial skin:

- Patient resuscitation begins with maintaining airway, breathing, and circulation (ABCs).
- Burnt patients may require O_2 supplementation or endotracheal intubation to maintain the airway. Severe facial burns or presence of airway edema may require an awake fiber-optic intubation, or a tracheostomy.
- Fluids can be administered by using the formula: 4 ml/kg/% of body surface burnt.
- Patients should have a large bore IV or a CVP catheter. Blood pressure may be measured via an arterial line, as a blood pressure cuff may be difficult to use on a burnt extremity.
- Blood pressure may be maintained by using a vasopressor, in addition to fluid administration.
- The urine output should be kept >0.5 ml/kg/h. Muscle damage may lead to myoglobinuria.
- Needle electrodes may be used for ECG as skin electrodes may not stick to the burnt chest surface.
- Patients with burns may have significant loss of sensory function in the burnt area.
- Burnt patients are prone to hypothermia due to heat loss from denuded skin. Patients can be warmed with a forced air warming device, heat lamps, increased in the OR temperature, use of humidified inspired gases, and warm intravenous fluids.

Burn patients may require early intubation due to the presence of airway edema. Induction can be performed with ketamine or etomidate. Ketamine is an excellent choice as it increases the blood pressure and provides analgesia. Additionally, opioids are used for pain control. Succinylcholine is contraindicated after the first 24 h to 6 months–2 years, as it may cause cardiac arrest due to sudden increase in potassium levels. Also, its action may be prolonged due to an increase in postjunctional acetylcholine receptors. Burnt patients require an increased dosage of nondepolarizing muscle relaxant due to an increase in extrajunctional acetylcholine receptors.

Clinical Review

1. Shock in sepsis is of the following type
   A. Cardiogenic
   B. Vasodilatory
   C. Toxic
   D. Hypovolemic
2. Nitric oxide is a pulmonary
   A. Vasoconstrictor
   B. Vasodilator
   C. Neither A nor B
   D. Artery pressure autoregulator
3. All of the following are end points in resuscitation of shock, except
   A. Systolic blood pressure of >90 mmHg
   B. Mean arterial pressure of ≥65 mmHg
   C. Urine output of >0.5 ml/kg/min
   D. Lactate of <6 mmol/L
4. Preferred type of ventilation in a patient with ARDS would be
   A. Intermittent mandatory
   B. Pressure support
   C. Airway pressure release
   D. PEEP
5. Administration of oxygen to neonates may most likely cause
   A. Retinal hemorrhage
   B. Corneal detachment
   C. Myopia
   D. Retinopathy
6. ARDS is characterized by
   A. Increased capillary permeability
   B. Increased capillary hydrostatic pressure
   C. Increased surfactant concentration
   D. PaO_2/FiO_2 ratio <400
7. A patient with atrial fibrillation, with HR 160/min and BP 84/54 mmHg, is treated with
   A. Esmolol
   B. Diltiazem
   C. Lidocaine
   D. Cardioversion
8. Gradual lengthening of the PR interval followed by a dropped beat is characteristic of
   A. 1st-degree AV block
   B. 2nd-degree type I AV block
   C. 2nd-degree type II AV block
   D. 3rd-degree AV block

Answers: 1. B, 2. B, 3. D, 4. C, 5. D, 6. A, 7. D, 8. B

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Postoperative Anesthesia Care

41

Maged Argalious

Anesthesia care has evolved over time. Considerable importance is now given to postoperative care, rather than just good pre/intraoperative care. As the number of operations is increasing, it has become important for patients to recover rapidly without side effects. This has lead to the development of newer anesthesia techniques and recovery protocols. Complications in the postanesthesia care unit (PACU) are frequent, and therefore, identification and timely management of these complications decreases patient morbidity and mortality. Standards of postoperative care are summarized below.

- All operative patients should receive postanesthesia care
- Every patient should be transported from the operating room to the PACU by a anesthesia personnel, who should provide continued care during the transport
- The patient is then handed over to the PACU nurse by giving a verbal report, which should include the patient's history, procedure performed, and intraoperative care. The amount of opioids/benzodiazepines administered, antiemetics, and fluids lost and administered should be communicated to the PACU nurse
- The patient's condition is continually evaluated in the PACU (Table 41.1)
- A physician then discharges the patient from the PACU

Postoperative Discharge and Bypass Criteria

Recovery of a patient begins from the end of intraoperative care, until the patient returns to the preoperative physiological state, that is, the resumption of normal daily activities. Patient recovery from anesthesia has traditionally been divided into three phases:

- Early recovery (phase I): awakening and recovery of vital reflexes
- Intermediate recovery (phase II): discharge from recovery room and home readiness
- Late recovery (phase III): full recovery including psychological recovery with resumption of normal daily activities

Several scoring criteria have been used to assess patients' early recovery, including the Aldrete scoring system and its modifications, the Mayo modified discharge score, and the standardized PACU Bypass/Discharge criteria. Table 41.2 lists a comprehensive PACU Discharge/Bypass scoring system that incorporates heart rate, pain, post operative nausea and vomitting (PONV), temperature, and surgical bleeding with the traditional discharge criteria.

Oral Intake and Voiding

The ASA Practice Guidelines for PACU Care specifically state that the requirement that patients drink clear fluids and urinate before discharge should *not* be part of a routine discharge protocol. Depending on the type of surgery, patients who are awake and free of nausea can have ice-chips, water, or clear juice (apple, cranberry). If the patients tolerate these fluids well, they can be offered crackers, jelly, or even a light sandwich.

Although patients need not void urine before discharge, they should be instructed to come back to the hospital if they do not void in about 8 h. Patients who have received long-acting neuraxial blockade or have undergone procedures that may interfere with urinary function, should be discharged from the PACU until they can void satisfactorily. Risks factors for postoperative urinary retention include the type of surgery (urinary tract, anorectal, pelvic surgery), old age, spinal or epidural anesthesia, and prolonged surgery.

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Table 41.1 Patient monitoring in PACU

• Respiratory—airway patency, respiratory rate, oxygen saturation
• Cardiovascular—heart rate, blood pressure, electrocardiogram
• Neuromuscular strength assessment
• Pain assessment
• Mental status assessment
• Presence of nausea/vomiting
• Temperature measurement
• Urine output measurement
• Examination of surgical site for any drainage/bleeding

Discharge Criteria After Regional Anesthesia

Regional anesthesia is being utilized with increasing frequency in the ambulatory setting as it offers improved pain control, decreased risk of nausea and vomiting, and faster discharge times. Discharge criteria after spinal/epidural anesthesia include

- Stable vital signs
- Adequate hydration
- Resolution of the block: normal perianal pinprick sensation ($S_{4\text{-}5}$), plantar flexion of the foot, and proprioception of the big toe. For spinal anesthesia which is not resolving after 6–8 h, an epidural hematoma should be ruled out (urgent surgical decompression)
- Peripheral nerve blocks: patients can be discharged before full resolution of the block, and instructed to take care of their insensate limb by using crutches to ambulate, elevate the limb to avoid swelling, and take analgesics as soon as the numbness starts to subside and a tingling sensation is felt in the limb

PACU Discharge Delay

Factors that can delay discharge from the PACU include

- Increasing age, obesity
- Long duration of surgery with general anesthesia
- Bleeding and surgical complications
- Presence of pain
- Nausea & vomiting (female sex, history of postoperative nausea, opioids, longer duration of surgery, laparoscopic surgery, middle-ear surgery)
- Sore throat (ETT > LMA, female sex, younger age, GYN surgery, use of succinylcholine)
- lack of escort
- Complications-cardiovascular, respiratory, or neurological

Table 41.2 Comprehensive PACU scoring criteria that can be used for both PACU phase I discharge and phase I bypass

A score ≥ 18 is required for PACU discharge/bypass with no category with a score of 0
• Physical activity (excludes extremity with peripheral nerve block)
A. For cases done using Monitored Anesthesia Care or General Anesthesia
2 = Able to move all extremities (or return to baseline motor function)
1 = Some weakness in movement of extremities
0 = No movement
B. For cases done using Central Neuraxial Anesthesia
2 = Gross motor movement of all four extremities (or return to baseline motor function) with return of sensory level to L5
1 = Two segment regression of central neuraxial anesthesia and return of sensory level to L1
0 ≤ two segment regression of central neuraxial anesthesia or sensory level above L1
• Level of consciousness 2 = Fully awake 1 = Arousable with verbal or tactile stimulation 0 = Unresponsive
• Blood pressure 2 = Systolic blood pressure ± 20 % of preanesthetic level 1 = Systolic blood pressure ± 21–30 % of preanesthetic level 0 = Systolic blood pressure ± > 30 % of preanesthetic level
• Heart rate 2 = 60–100 or if outside this range, ≤10 % change from baseline HR 1 = HR outside the range of 60–100 and the change from baseline is >10 % and ≤20 % 0 = HR outside the range of 60–100 and the change from baseline is >20 %
• Oxygen saturation 2 = SpO2 ≥ 92 % on room air or on supplemental oxygen with IV PCA 1 = SpO2 ≥ 92 % on supplemental oxygen not involving IV PCA 0 = SpO2 < 92 % on supplemental oxygen
• Respiration 2 = Able to breathe or cough freely 1 = Shallow breathing or coughing, maintains airway without support 0 = Apnea, dyspnea, tachypnea (RR > 24) or bradypnea (RR < 8), or requires airway support
• Pain 2 = No or mild pain with or without analgesics 1 = Moderate pain controlled with analgesics 0 = Persistent severe pain uncontrolled with analgesics
• Postoperative nausea/vomiting 2 = No or mild nausea with no active vomiting 1 = Moderate nausea or transient vomiting 0 = Persistent severe nausea or vomiting
• Temperature (tympanic) 2 = 36.0 °C to 38.0 °C 1 = 35.5 °C to 35.9 °C or 38.1 °C to 38.3 °C 0 = < 35.5 °C or > 38.3 °C
• Bleeding 2 = Dry dressing, no drainage or oozing 1 = Minimal oozing or drainage 0 = Active bleeding, blood soaked surgical dressing, surgical drains filling with blood

Table 41.3 Factors likely to increase PACU bypass eligibility for patients undergoing elective noncardiac surgery

- Identification and management of preoperative comorbidities of the patient
- Preoperative identification of patients for whom fast tracking is not suitable (fast-track ineligible)
- Use of evidence-based prophylactic therapies to reduce PONV (steroids, serotonin antagonists, transdermal scopolamine)
- Multidisciplinary service specific (e.g., orthopedic/plastics) pathways/protocols
- Continuous education for patients and the health care team: clear preoperative instructions for patients when and who to contact, helps sets expectations, reduces patient anxiety and increases their satisfaction
- Multimodal approach to acute pain management including local anesthetic infiltration, peripheral nerve blocks, acetaminophen, nonsteroidal anti-inflammatory agents, low dose ketamine, and parenteral and oral narcotics
- Utilization of anesthetic techniques that optimize surgical conditions while ensuring rapid recovery with minimal side effects
  (a) Monitored anesthesia care/general anesthesia:
    – Is endotracheal intubation necessary?
    – Is muscle relaxation required?
    – Use short acting agents:
      Benzodiazepines: midazolam
      Synthetic narcotics: fentanyl, alfentanil, remifentanil
      Anesthetic agents: Propofol, sevoflurane, desflurane
      Muscle relaxants: rocuronium, vecuronium, cisatracurium
  (b) Central neuraxial anesthesia:
    – Short acting local anesthetics: mepivacaine, lidocaine, or low dose
      bupivacaine
    – Hypobaric solutions for unilateral anesthesia
  (c) Peripheral nerve blocks: surgical anesthesia vs postoperative analgesia
- Checklist for fast-track eligibility utilized in the operating room by the anesthesia team after patient emergence

Fast-Tracking

With the rapid rise in ambulatory surgeries and the introduction of short acting anesthetics, it was recognized that criteria for early recovery from anesthesia were frequently met in the operating room, before patients were even transported to the PACUs. Therefore, criteria for bypassing (also called fast-tracking) phase I recovery were established to identify patient eligibility for PACU bypass, including the White and Song fast-tracking criteria and the Wake scoring criteria. These criteria if used by the anesthesia team after patient emergence can avoid unnecessary transfer of patients to the PACU if bypass criteria are met and have the following benefits:

- Reduce the "bottlenecks" that occur as a result of routine transfer of patients to phase I recovery areas
- Reduce PACU nursing staff workload (and the associated high nursing to patient ratio of 1:2)
- Avoid the delays that occur as a result of transfer of patients from phase I to phase II areas
- Improve patient satisfaction by reducing the number of postoperative "stations" before patient discharge
- Reduce the need for PACU recovery for patients undergoing inpatient surgeries with a disposition to monitored surgical floors.

PACU Bypass Protocols

Several studies have reported that the implementation and application of protocols for PACU bypass coupled with multidisciplinary education increases PACU bypass success. The lack of uniform PACU bypass/fast-track eligibility criteria across studies and the use of different outcomes measures to compare anesthetic techniques have complicated the interpretation of the results of these trials.

In addition to PACU bypass eligibility, other outcome measures have included mortality, morbidity (pain scores, PONV), time to discharge, unanticipated hospital admission, hospital readmission, and patient satisfaction. Table 41.3 lists a summary of the factors that are likely to increase PACU bypass eligibility.

Postoperative Complications and Their Management in the PACU

Airway Management

Airway management is often challenging in the PACU. Factors that contribute to these difficulties include surgery close to the airway (cervical spine), intraoperative airway instrumentation or manipulation, previous neck dissection or radiation, prolonged surgery in the prone position, large volumes of intraoperative fluids, and residual anesthetic effects. Even patients considered as having an "easy airway" in the operating room can pose airway challenges in the PACU.

Airway Obstruction and Hypoxemia

Promptly restoring airway patency reduces the likelihood of negative pressure pulmonary edema and, more importantly, prevents O_2 desaturation and hypoxemia. Oxygen supplementation during patient transfer to the PACU is reasonable for all patients. It is important to know that the hypoxic drive is inhibited by minimal residual concentrations of inhalational anesthetics.

The most common cause of postoperative airway obstruction is *pharyngeal obstruction* by the tongue. Simple interventions such as rousing the patient with gentle stimulation, jaw thrust, and, if necessary, insertion of a nasal or oral

Table 41.4 Causes of postoperative hypoxemia

Mechanism	Examples	Alveolar–arterial O_2 gradient	Response to 100 % O_2
Decreased partial pressure of inspired oxygen	Hypoxic gas mixture, high altitude	Normal	Increased Pao_2
Hypoventilation	Obesity–hypoventilation syndrome, neuromuscular disorders, sleep apnea	Normal	Increased Pao_2
Ventilation–perfusion mismatch	COPD, asthma, interstitial lung disease	Increased	Increased Pao_2
Shunt	Pulmonary edema, ARDS, atelectasis, pneumonia, pneumothorax	Increased	Minimal if any increase in Pao_2
Diffusion impairment	Pulmonary embolism	Increased	Increased Pao_2

ARDS Acute respiratory distress syndrome, *COPD* chronic obstructive pulmonary disease, *PaO2* Partial oxygen tension in arterial blood

airway may restore airway patency. Persistence of airway obstruction or signs of *laryngospasm* mandate the application of positive pressure ventilation with oxygen via a bag and mask. Small doses of succinylcholine (20–40 mg) may also be necessary to relieve laryngospasm.

Patients with *stridor* may require treatment with nebulized racemic epinephrine and may benefit from a helium/oxygen mixture (70 % helium, 30 % oxygen), which reduces airway resistance and work of breathing relative to oxygen or air. Quick recognition of problems is necessary because stridor may advance to total airway obstruction.

Persistent hypoxemia after restoration of airway patency requires evaluation of possible etiologies (Table 41.4). In negative-pressure pulmonary edema, inspiratory efforts against an obstructed airway can cause alveolar-capillary membrane injury. Such a capillary leak may lead to respiratory failure requiring mechanical ventilation with positive end-expiratory pressure. The most common cause of hypoxemia ($PaO_2 < 60$ mmHg) in the PACU is an increase in right to left shunting (most often from atelectasis). Other common etiologies include pulmonary aspiration and pulmonary edema. An unrecognized pneumothorax, perhaps caused by high inflation pressures during attempts to ventilate the patient, may lead to hemodynamic compromise and render resuscitation attempts difficult.

Hypoventilation

Postoperative hypoventilation and apnea can be caused by residual neuromuscular blockade, as a result of overdose, inadequate reversal dosing, hypothermia, or metabolic factors (hypokalemia, hypocalcemia), which are factors that interfere with adequate reversal.

Opioid-induced respiratory depression is also a frequent cause of postoperative hypoventilation. Opioids not only shift the carbon dioxide response curve to the right (i.e., raise the apneic threshold), but can also decrease the slope of the carbon dioxide response curve (i.e., reduce the minute volume response to a high $PaCO_2$) in anesthetized patients (the slope of the carbon dioxide response curve is unchanged by opioids in fully awake patients). *Splinting* resulting from incisional pain can also cause postoperative hypoventilation.

Airway Management After Cervical Spine Surgery

Patients undergoing surgery for cervical spine disease have a greater incidence of difficult intubation than do matched control subjects. Airway complications are common after anterior cervical spine surgery and range from acute airway obstruction (1.2 %) to chronic vocal cord dysfunction. Risk factors associated with airway obstruction after cervical spine surgery include

- Advanced age
- Obesity (weight >100 kg)
- Exposure of three or more vertebral bodies or exposure of C_2, C_3, or C_4
- Estimated blood loss greater than 300 ml
- Transfusion of four or more red cell units
- Operative time more than 10 h
- Combined anteroposterior cervical spine surgery
- Severe preoperative neurologic deficits

Airway complications may also occur after cervical spine surgery in the prone position, most commonly due to macroglossia and laryngeal edema. Decreased venous return from the face and upper neck is the likely etiology. A plan for reintubation should be in place before any extubation attempts. The presence of external stabilization devices complicates airway management. Removal of the anterior part of a cervical collar during reintubation attempts improves airway visualization, but should be accompanied by manual inline stabilization in patients with an unstable cervical spine. Manual inline stabilization reduces cervical spine motion during intubation attempts in patients with an unstable cervical spine.

Komatsu et al. reported a reasonable success rate of intubation with the use of an intubating laryngeal mask airway in patients with rigid neck collars. A recent study on postoperative patients after anterior cervical spine surgery showed a reduced incidence of airway complications with routine postoperative fiberoptic evaluation of the airway for evidence of airway edema. Patients' tracheas were only extubated if there was no reactive swelling or pharyngeal edema. Close communication among surgeons, anesthesiologists,

Table 41.5 Criteria for endotracheal extubation

Awake, cooperative patient
Hemodynamic stability on no or minimal vasopressors
Absence of surgical bleeding or coagulopathy
Temperature ≥ 36 °C
Mechanical criteria: Tidal volume ≥ 6 ml/kg Vital capacity ≥ 15 ml/kg Negative inspiratory force ≥ 30 cm H_2O Rapid shallow breathing index (Respiratory Rate/Tidal Volume) <100
Chemical criteria: pH ≥ 7.25 PaO_2/FIO_2 ratio >300 $PaO_2 \geq 65$ mmHg on $FiO_2 \geq 0.4$ Minimal PEEP of 5–8 cm H_2O Acceptable $PaCO_2$ ($PaCO_2 \leq 50$ mmHg) Stable metabolic status (serum $HCO_3 \geq 20$ mmHg)

and respiratory therapists helps in reducing emergency airway complications. Steps in extubating patients after complex cervical spine surgery include

- Adherence to evidence-based extubation criteria (Table 41.5)
- A preformulated plan for reintubation should extubation fail
- Established institutional protocols that guide extubation timing after complex spine surgery with close communication of the perioperative team (surgical, anesthesia, respiratory therapist, nursing)
- Consideration for routine fiberoptic evaluation prior to extubation for evidence of resolution of pharyngeal edema

Role of Airway Exchange Catheters

Although the presence of an airway exchange catheter (AEC) does not guarantee success at subsequent reintubation, a high success rate has been reported. In addition, oxygen insufflation through an AEC can maintain oxygenation until definitive measures are taken to secure the airway (e.g., tracheal intubation, cricothyroidotomy, tracheostomy).

Numerous AECs are available, but these devices must be used correctly because airway complications can develop (e.g., perforation of the tracheobronchial tree, failure to pass the endotracheal tube (ETT) over the AEC, barotrauma) when the wrong size, type, or technique is used. Suggestions for success include the following:

- AECs with a very small outer diameter should be avoided because they are prone to kinking, making railroading of the new ETT difficult
- Match the marking of the AEC with the centimeter markings on the ETT to avoid excessive advancement of the AEC, which can irritate the carina and cause bronchial trauma and bleeding
- Use an AEC with an inner hollow lumen that allows oxygen insufflation, whether by jet ventilation or a bag valve device. Two adapters Rapi-Fits adaptors (Cook Medical, Bloomington, IN) usually accompany the AEC for this purpose
- If resistance is encountered during the advancement of the ETT over the AEC, oral laryngoscopy (if feasible) can aid tube advancement. Rotation of the ETT in 90° increments also helps to pass the ETT tip past the arytenoids. ETTs with flexible tips (Parker Flex-Tip) serve the same purpose in that the tube tip is prevented from becoming caught against the arytenoids
- Avoid using force in advancing the AEC and the ETT because it may traumatize airway structures
- Applying a silicone-based spray or a lubricant gel on the outside of the AEC can facilitate ETT advancement
- The position of the new ETT should be confirmed before the AEC is withdrawn. This can be done by end-tidal capnography through a flexible bronchoscope adapter
- Longer AECs are available for double-lumen tubes and are used with the same precautions

Role of the Cuff Leak Test

A cuff leak test can be performed on a spontaneously breathing patient by deflating the ETT cuff, blocking the ETT opening, and listening for a leak around the cuff while the patient inspires. Because this method cannot quantify the volume of a leak, a cuff leak test is more effective in detecting postextubation stridor while a patient is being mechanically ventilated.

With the patient on controlled ventilation assist/control mode, an inspiratory tidal volume (VT) and six subsequent expiratory VT values are recorded after oropharyngeal suctioning and ETT cuff deflation. Six cycles are recorded because it was found that the exhaled VT values decreased decrementally during the first few breaths before reaching a plateau. The leak is measured as the difference between the preset inspiratory VT and the average of the three lowest of the subsequent six expiratory VT values.

A leak of less than 110 ml is considered a positive result of the cuff leak test and indicates that the patient is at risk for postextubation stridor secondary to laryngeal edema. Cuff leak tests have been criticized because of their poor sensitivity in detecting postextubation stridor and their low positive predictive value.

Expanding Neck Hematoma

In patients recovering from neck surgery who develop respiratory insufficiency, the possibility of an expanding the neck hematoma must be considered. In most instances, airway obstruction ensues quickly as a result of encroachment and distortion of the airway anatomy. If the neck hematoma is

Table 41.6 Management of postoperative neck hematoma

1. Apply pressure to the bleeding site
2. Notify surgery and anesthesia team (call for help)
3. Tight blood pressure control
Outcome:
A. No further hematoma expansion – Communication with surgical team – Mark the boundaries of the hematoma for early identification of further expansion – Close observation and extended (8–12 h) monitoring in a critical care environment
B. Continuous expansion of hematoma with no airway compromise – Endotracheal intubation, possibly awake fiberoptic intubation, either in the PACU or after immediate transfer to the operating room, followed by general anesthesia for exploration of the wound and drainage of neck hematoma – Assess neurologic status at the end of the case – Consider keeping the patient intubated postoperatively until resolution of reactionary airway edema
C. Expansion of neck hematoma with rapidly progressive airway compromise (dyspnea, stridor, airway obstruction) – Emergent intubation (ASA algorithm) – Cannot intubate Can Ventilate: use face mask, oral or nasal airways, laryngeal mask airway: Consider immediate surgical drainage of the neck hematoma followed by further attempts to secure the airway – Cannot intubate Cannot ventilate: Surgical airway (emergent cricothyroidotomy, percutaneous or surgical tracheostomy) Evacuation of hematoma and wound exploration Neurologic assessment Maintain secured airway postoperatively

visible but is not causing respiratory distress, applying pressure to the surgical site can avoid further hematoma expansion. If the airway needs to be maintained, then after notifying the surgeon, an awake fiberoptic intubation may be required to stabilize the patient's airway, before drainage of the hematoma.

In some cases, airway edema persists despite drainage of the hematoma. If emergent intubation attempts are unsuccessful, the decision to proceed with a surgical airway (emergency cricothyroidotomy or tracheostomy) depends on the ability (vs. inability) to ventilate the patient with a facemask or laryngeal mask airway. If ventilation is unsuccessful or becomes inadequate despite drainage of the neck hematoma, invasive airway access should be obtained. Table 41.6 identifies the steps in management of postoperative neck hematoma.

Hemodynamic Management

Acute Postoperative Hypertension

Despite advances in chronic hypertension management, acute postoperative hypertension (APH) occurs with a reported incidence of 4–35 %. APH may lead to serious neurologic (hemorrhagic stroke, cerebra ischemia, encephalopathy), cardiovascular (myocardial ischemia, cardiac arrhythmia, congestive heart failure, pulmonary edema), renal (acute kidney injury, acute tubular necrosis), and surgical site complications (bleeding, failure of vascular anastomosis) and, therefore, requires prompt intervention and management.

Table 41.7 Algorithm for management of acute postoperative hypertension (APH)

• Appropriate outpatient treatment of chronic hypertension before elective surgical procedures
• Avoid discontinuation of oral antihypertensive medications on the day of surgery
• Identify a baseline blood pressure preoperatively that acts as a reference point for postoperative management
• Exclude factors associated with APH (pain, anxiety, hypothermia, hypoxemia, hypercapnia, bladder distension, presence of an ETT on emergence from anesthesia, antihypertensive withdrawal, increased intracranial pressure, hypervolemia)
• Evaluate for APH and initiate therapy with intravenous short-acting antihypertensive agents after excluding other factors that can cause/exacerbate APH
• Short-acting intravenous agents are preferable for the initial management of APH (nitroglycerine, nitroprusside, nicardipine, fenoldopam) because their effect can be reversed by discontinuation of therapy. Esmolol may be appropriate for patients who will also benefit from beta-blockade
• Avoid abrupt reduction of blood pressure (greater than 20 %), especially in patients at no immediate risk (hypertensive urgencies)
• Resume oral antihypertensive therapy as soon as possible postoperatively to reduce the occurrence of rebound hypertension, especially in patients taking centrally acting alpha-2 agonists or beta-blockers

Although there is no precise quantification of APH in the literature, APH typically refers to stages I (systolic 140–159 or diastolic 90–99 mmHg) and II (systolic >160 or diastolic >100 mmHg) hypertension according to the Joint National Committee classification of hypertension. APH can also be defined as a 20 % or more increase in systolic blood pressure, diastolic blood pressure, or mean arterial pressure above baseline.

The final common pathway leading to hypertension seems to be the activation of the sympathetic nervous system as evidenced by increased plasma catecholamine concentrations in patients with APH. In addition to increasing the risk for end organ damage, APH is especially undesirable in patients where postoperative bleeding into a closed space (e.g. craniotomy, carotid endarterectomy) can have life-threatening consequences (airway obstruction, brain herniation).

In the nonoperative setting, hypertensive emergency has been differentiated from hypertensive urgency by the presence of end organ damage. In the postoperative setting, both clinical entities require prompt intervention to prevent the occurrence or progression of end organ damage and surgical site complications (Table 41.7). Identifying baseline blood pressure helps define a target blood pressure to avoid the

deleterious consequences of overaggressive treatment. Prospective studies showing clinical benefits of aggressive blood pressure control in the postoperative period are lacking. Whether to titrate to a target mean arterial pressure or systolic blood pressure is still controversial. There are, however, recent reports of the deleterious effects of pulse pressure hypertension on postoperative outcomes, supporting a focus on systolic blood pressure.

Postoperative Hypotension

Postoperative hypotension is defined as a decrease of 20 % from baseline preoperative blood pressure, a systolic blood pressure less than 80 mmHg, or a diastolic blood pressure less than 50 mmHg, whereas shock refers to multisystem organ hypoperfusion and inadequate oxygen delivery to tissues. Assessment of hypotension is commonly approached in terms of evaluation of cardiac rate, rhythm, contractility, peripheral resistance, and adequacy of intravascular volume.

Hypotension in the PACU is often a sign of hypovolemia and often responds to intravenous fluid boluses. In patients with persistent hypotension despite a fluid "challenge," additional fluids may precipitate acute pulmonary edema, especially in patients with reduced left ventricular function. Other causes of hypotension and shock are listed in Table 41.8.

Several studies have documented the value of early goal-directed therapy in patients with shock. Rapid diagnosis and intervention improve outcomes. Several simple tools are used in the initial management of shock, including chest radiography, electrocardiogram, serum chemistries, and blood gas analysis. Measurement of central venous pressure may be used to classify the mechanisms of shock (a low CVP in hypovolemic, a low normal CVP in distributive, and a high CVP in cardiogenic and mechanical shock), but multiple studies fail to show a good correlation between the so-called filling pressures and clinical reality. In addition, measurement of central venous oxygen saturation from a central vein may be useful in diagnosing and monitoring the impact of therapeutic interventions in patients with shock.

Volume Responsiveness in the PACU

One of the most frequently encountered management dilemmas in the PACU is the prediction of fluid responsiveness in postoperative patients with acute circulatory failure (Table 41.9). Most postoperative patients will have a positive fluid balance, and the presence of preload reserve in these patients is not guaranteed. The administration of a fluid challenge may result in acute pulmonary edema, especially in patients with increased capillary permeability.

Static markers of cardiac preload such as central venous pressure, pulmonary artery occlusion pressure, left ventricular

Table 41.8 Causes of hypotension and shock in the PACU

Hypovolemia:
Inadequate fluid replacement
Hemorrhage
External—surgical drain or incision site
Internal—concealed venous or arterial bleeding
Mechanical (obstructive):
Pneumothorax
Pericardial effusion
Abdominal tamponade
Excessive PEEP
Cardiogenic:
Chronic heart failure
Acute pulmonary edema
Acute myocardial infarction
Pulmonary embolism (venous air embolism, fat embolism)
Distributive (vasoplegia):
Anaphylaxis
Sepsis
Neurogenic with spinal cord transection

Table 41.9 Steps for assessment of fluid responsiveness

A.	Induce a change in cardiac preload
	1. Actual change: administer a fluid bolus
	2. Functional change
	– In mechanically ventilated patients, use existing respiratory variations in hemodynamic signals
	– In spontaneously breathing patients use "passive leg-raising" test
B.	Observe the change
	1. Change in arterial pulse pressure
	– Delta pulse pressure[a] A value of 13 % or higher predicts fluid responsiveness
	– Delta down[b] A value of 5 mmHg or higher predicts fluid responsiveness
	2. Stroke volume variation
	– Difference between maximal and minimal stroke volume divided by their mean during one respiratory cycle A value > 13 % change predicts fluid responsiveness
	3. Change in cardiac output A value > 13 % change predicts fluid responsiveness
C.	Use one of the following monitoring tools (varying sensitivities) capable of measuring changes in stroke volume or its surrogates
	1. Pulse oximetry plethysmography
	2. Invasive arterial monitoring with pulse contour analysis: uses data from the arterial pressure waveform for continuous monitoring of stroke volume and cardiac output. It relies on calculating the area under the systolic portion of the arterial pressure waveform, which, divided by aortic impedance, allows estimation of left ventricular stroke volume
	3. Esophageal Doppler measurements of descending aortic blood flow
	4. Transthoracic or transesophageal echocardiography measurement of variations in stroke volume, cardiac output, velocity time integral, mitral inflow velocities, superior/inferior vena caval diameter

[a]Difference between maximal and minimal pulse pressure during one respiratory cycle divided by their mean
[b]Systolic arterial pressure at the end of a 5-s respiratory pause and its minimal value during the course of one mechanical breath

end-diastolic volume, early/late diastolic wave ratio, even if available, do not identify fluid responders from nonresponders. While these static markers can identify whether a cardiac chamber is full or empty, they are not reliable in predicting the hemodynamic response to a subsequent fluid bolus administration.

The physiologic benefit of a fluid bolus is based on the Frank Starling relationship, whereby an increase in cardiac preload results in a higher stroke volume and subsequently a higher cardiac output. This concept assumes that a patient's preload is on the steep portion of the Frank Starling curve. However, there are several curves that rely on stroke volume and cardiac preload, depending on the ventricular function. A given value of cardiac preload can be associated with an increase in stroke volume in patients with good ventricular function (presence of preload reserve), while the same value of cardiac preload will not be associated with an increase in stroke volume in patients with poor ventricular function (no preload reserve). Thus, it is the actual interaction between the three parameters—preload, stroke volume, and cardiac contractility—that determine fluid responsiveness.

While inducing an actual change in cardiac preload can be simply and quickly accomplished by a fluid bolus, an alternative method to predicting volume responsiveness is to challenge the Frank Starling curve by inducing a functional change in cardiac preload and monitoring the response in stroke volume, cardiac output, or their surrogates.

Functional Change in Preload in Mechanically Ventilated Patients

In mechanically ventilated patients, this functional change in preload is already occurring as a result of mechanical ventilation-induced changes in cardiac preload, which can be monitored by observing the magnitude of change in hemodynamic signals in relation to cyclic changes in airway pressure. Arterial pressure rises during inspiration and falls during expiration due to changes in intrathoracic pressure secondary to positive pressure ventilation. In patients with preload reserve, mechanical ventilation will result in greater cyclic changes in right ventricle volume, and subsequently left ventricle stroke volume and therefore, mechanical ventilation can predict volume responsiveness. Respiratory variations affecting hemodynamic signals do not predict volume responsiveness in spontaneously breathing patients and in patients with cardiac arrhythmias and are inaccurate in patients with isolated RV dysfunction or pulmonary hypertension.

Functional Change in Preload in Spontaneously Breathing Patients

In spontaneously breathing patients, the functional change in preload is accomplished by the passive leg-raising test. It consists of lifting the legs passively 45° from the horizontal (supine) position and observing the change in hemodynamic effects (change in stroke volume, cardiac output, or arterial pulse pressure) occurring as a result of the gravitational transfer of blood from the lower extremities towards the intrathoracic compartment. The legs can be raised by utilizing the automatic bed control.

This test has the advantage of being simple, reversible, and applicable in spontaneously breathing patients (most patients in PACU). However, it is impractical to use the leg-raising test in patients with abdominal, pelvic, or lower extremity surgery, as surgical site pain can affect movement of the lower extremities.

Delayed Emergence

Delayed emergence requires a logical sequence to identify the underlying cause. Most commonly, anesthetics are the cause (inhalational anesthetics, intravenous anesthetics, narcotics, benzodiazepines, muscle relaxants). Metabolic causes can be ruled out by measuring blood glucose, serum electrolytes, blood urea nitrogen, creatinine, and hemoglobin concentrations. If an anesthetic cause of delayed emergence is ruled out by waiting for the predicted termination of anesthetic action, and by pharmacologic reversal of drug effects (naloxone, flumazenil, reversible anticholinesterase inhibitors), neurologic causes should be ruled out (brain edema, stroke), which may require a CT scan of the brain.

Management of Positioning Injuries

While most of the emphasis should be on the prevention of positioning-related injuries, identification and management of these injuries typically occurs in the postoperative period (recovery unit or nursing floor). It is important to note that it is common for symptoms of nerve injury (sensory and/or motor) to appear more than 48 h postoperatively, indicating that the etiology may also be related to events in the postanesthetic period. Guidelines for management of perioperative nerve injuries are listed in Table 41.10.

Nausea and Vomiting

PONV can affect up to 60 % of patients after general anesthesia. Risk factors for PONV include female gender, previous history of PONV, use of opioids, nitrous oxide, volatile anesthetics or neostigmine, nonsmokers, and type of surgery (intra-abdominal, laparoscopic, GYN, ENT, and strabismus surgery). Treatment of PONV includes adequate hydration, intravenous administration of a serotonin antagonist, phenothiazines, dexamethasone, or droperidol (monitor QT interval for 2–3 h). For patients who have received prophylactic

Table 41.10 Guidelines for management of perioperative nerve injuries

• Identify any preoperative motor or sensory deficits (history and physical examination)
• Consider awake positioning (even awake intubation) of patients with severe or unstable injuries with postpositioning neurologic examination prior to induction of anesthesia
• Careful positioning of patients and documentation of positioning details
• Frequent rechecking of position and assess pressure prone areas (eyes, ear, face, elbow, breasts, genitalia, sacrum, heels)
• Avoidance of hypotension, hypothermia and severe anemia
• Postoperative neurologic examination and documentation of preexisting and any new sensory or motor deficits
• Any suspected or confirmed newly diagnosed motor neuropathy requires a neurology consultation. Typically, electromyography is done to distinguish between acute and chronic motor deficits and to assess the location of any acute lesion
• Sensory deficits (tingling, numbness, paresthesias) are typically self limited and patients should be informed that most sensory deficits resolve within a few days. Follow up neurologic examination will identify persistent sensory neuropathy and warrant neurologic consultation

PONV treatment, rescue therapy should consist of drugs from classes other than those previously administered. A scopolamine patch (avoided in the elderly) is of limited value when applied postoperatively, but is highly effective in reducing rates of PONV when applied preoperatively.

Pain

Pain should be adequately treated in the PACU. Pain causes increased sympathetic discharge and can even cause nausea and vomiting. Analgesia should be started in the operating room and continued into the recovery room. Treatment of pain includes administration of opioids, patient-controlled analgesia for patients who require frequent boluses, NSAIDs/acetaminophen, and regional and peripheral sensory blockade.

Hypothermia

Hypothermia is associated with decreased platelet function and coagulopathy, electrolyte disorders, hypovolemia, arrhythmias, and delayed wound healing and infection (immunosuppression). Hypothermia, when accompanied by shivering, markedly increases oxygen consumption and lead to myocardial ischemia. Warm blankets may be sufficient for mild hypothermia, whereas forced-air warming devices are more efficient, if required. Shivering can be pharmacologically controlled with small doses of meperidine, clonidine, or doxapram.

Oliguria and Urinary Retention

Oliguria, urine output <0.5 ml/kg/h, can be due to prerenal or postrenal causes. Prerenal failure is usually due to reduced renal perfusion with no parenchymal damage and commonly caused by hypovolemia or hypotension. These patients usually receive an intravenous fluid bolus and may require further workup. Intrinsic renal causes of renal failure (acute tubular necrosis) include renal ischemia and exposure to nephrotoxins, such as aminoglycoside antibiotics or radiological contrast media. This may require a nephrologist consultation. Postrenal failure is caused by an obstruction to urine flow, which may be due to urinary catheter kinking or obstruction, or bilateral obstruction of the urinary tracts.

Myocardial Ischemia and Arrhythmias

Electrocardiographic (ECG) changes are common after surgical anesthesia, resulting from a variety of causes. Perioperative myocardial ischemia and infarction often occur within the first two days following surgery and can be difficult to diagnose in the PACU, as residual anesthesia and analgesia may mask chest pain, and pain perception may be altered due to the competing stimulus of surgical pain. A 12 lead electrocardiogram should be performed and serial markers of myocardial injury should be measured if myocardial ischemia is suspected. Oxygen administration, heart rate control, aspirin, and nitrates should be implemented immediately, and a cardiology consult called in.

Cardiac dysrhythmias commonly occur in patients with underlying structural heart disease and are precipitated by decreased cardiac output, hypotension, hypoxia, or electrolyte and acid-base abnormalities. Sinus tachycardia, the most common cardiac dysrhythmia in the immediate postoperative period, is, however, usually benign and resolves when its underlying etiology, such as pain, anxiety, anemia, hypovolemia, or hypoxia, is treated. Atrial fibrillation may require cardioversion for unstable patients and rate control in stable patients with beta-blockers, calcium channel blockers, or amiodarone.

Delirium

Postoperative delirium is the most commonly encountered mental disturbance in the PACU and presents as restlessness, hyperactivity, and agitation. Elderly patients and those with a history of organic brain disease or mental disorders are at particular risk. Physiologic causes of delirium include hypoxemia, hypotension, hypoglycemia, pain, bladder distension, electrolyte and acid–base disturbances, and medications (anticholinergics, benzodiazepines).

Treatment includes maintaining the ABC's, adequate restrain, and administration of physostigmine (to antagonize anticholinergic effects) or haloperidol.

Clinical Review

1. The most frequent cause of delayed emergence in the PACU is
   A. Hypotonia
   B. Hypoventilation
   C. Hypotension
   D. Hypothermia
2. Criteria for transporting a patient out of the operating room include all, except
   A. Patient with an LMA still in place
   B. TV of 300 ml/breath and respiratory rate of 25 breaths/min in a 65 kg patient
   C. Patient with a blood pressure of 84/32
   D. Oxygen saturation of 96 %
3. Extrapyramidal reactions are most likely to occur with the administration of
   A. Ondansetron
   B. Metoclopramide
   C. Droperidol
   D. Promethazine
4. A 35-year-old patient is brought to the PACU after undergoing an appendectomy. His anesthetics included propofol 140 mg, isoflurane 2.0 MAC, vecuronium 6 mg, and morphine 6 mg. In the PACU the patient's temperature is 33.5 C and is shivering. The most likely cause of his shivering is
   A. Use of isoflurane
   B. Presence of infection and dehydration
   C. Use of unwarmed fluids
   D. Use of morphine
5. A 47-year-old patient is brought to the PACU after drainage of a gluteal abscess under MAC anesthesia. The patient is not fully responsive and has labored and sonorous breathing. His BP is 136/82, HR is 89/min and O_2 saturation is 92 %. Your initial step in management would be to
   A. Change the nasal cannula to a non-rebreathing bag
   B. Increase the FiO_2
   C. Do a jaw thrust and head-tilt maneuver
   D. Use a ambu bag
6. A 29-year-old patient is undergoing a left knee hardware removal under general endotracheal anesthesia. At the end of the procedure the patient is extubated. A few moments later you hear high-pitched crowing noises from the patient's airway. The BP is 140/86, HR is 92/min and the O_2 saturation is 88 % and dropping. Your initial response would be to
   A. Insert an oral airway
   B. Suction the airway to remove secretions
   C. Give succinylcholine
   D. Positive airway pressure with a mask
7. The most common cause of postoperative hypoxemia following general anesthesia is a decrease in
   A. Functional residual capacity
   B. Tidal volume
   C. Residual volume
   D. Inspiratory capacity

Answers: 1. B, 2. C, 3. C, 4. A, 5. C, 6. D, 7. A

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Part V

Special Anesthesia Topics

Obesity

42

Ricky Harika and Cynthia Wells

Currently, one of the most pressing health crisis in the nation is the rise in obesity. Despite advancements in diet, nutrition, exercise, and health awareness in schools and professional settings, it has become one of the leading causes of health care costs. Approximately 34 % of adults and 17 % of children in the United States are obese. It has been clearly shown that these patients are at an increased risk of morbidity and mortality as well as reduced life expectancy. Obese patients clearly represent a unique challenge to the anesthesiologist. It is imperative that each anesthesia provider be knowledgeable of the pathophysiologic changes that occur with obesity and how to respond appropriately if a complication arises. With proper planning, preparation, and vigilance, they can be cared for in a safe manner.

Clinical Manifestations of Obesity

Obesity has a direct negative effect on each of the organ systems, increasing the risk of diseases such as diabetes mellitus, hyperlipidemia, hypertension, coronary artery disease, degenerative joint disease, obstructive sleep apnea (OSA), gallbladder disease, and venous thromboembolism (Table 42.1).

Classification of Obesity

As a physician, it is important to identify high risk patients. Two variables that help define obesity are metabolic syndrome and body mass index (BMI). The American Heart Association (AHA) and the National Heart, Lung, and Blood Institute (NHLBI) categorize patients as having metabolic syndrome if three or more of the following are met:

- Blood pressure $\geq$ 130/85
- Fasting blood glucose $\geq$ 100 mg/dL
- Waist circumference for men $\geq$ 40 inches, and for women $\geq$ 35 inches
- HDL cholesterol for men $<$ 40 mg/dL and for women $<$ 50 mg/dL
- Triglycerides $\geq$ 150 mg/dL

It is important to note that these criteria specifically point out waist circumference because central obesity, as compared to a more peripheral distribution, is associated with a higher risk of morbidity and mortality primarily related to cardiovascular disease. BMI is a calculated value used to determine amount of body fat and is commonly used to classify patients who are underweight, overweight, obese, and morbidly obese (Table 42.2).

$$\text{BMI} = \text{weight (kg)}/\text{height}^2 \text{ (meters)}$$

Pathophysiology of Obesity

Cardiovascular System

Numerous cardiovascular complications are associated with obesity. Clinically, all of these changes represent an increase in myocardial oxygen demand and carbon dioxide production as well as increased diastolic filling pressures and ventricular dysfunction.

- First, there is an increase in total blood volume, metabolic demand, and cardiac output which are secondary to an increase in complex capillary network in adipose tissue as well as increase in body mass.
- In the nonhypertensive patient, there is a decrease in total peripheral resistance, which is accompanied by an increased stroke volume. Over time this leads to an increase in ventricular wall stress, dilation and eccentric left ventricular hypertrophy.

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Table 42.1 Clinical manifestations of obesity

Organ system	Clinical manifestations
Neurologic	Cerebrovascular accident (stroke), idiopathic intracranial hypertension, dementia, depression
Cardiovascular	Coronary artery disease, chronic inflammation, obesity cardiomyopathy, congestive heart failure, hypertension, cor pulmonale, arrhythmias
Respiratory	Obstructive sleep apnea, obesity hypoventilation syndrome, atelectasis, ventilation/perfusion mismatch
Gastrointestinal	GERD, hiatal hernia
Metabolic	Diabetes mellitus, metabolic syndrome, dyslipidemia, gout, degenerative joint disease
Hepatic	Fatty liver (nonalcoholic), cholelithiasis
Renal	Chronic kidney disease, glomerulosclerosis, incontinence
Reproductive	Menstrual disorders, erectile dysfunction, hypogonadism, birth defects

Table 42.2 Classification of patients as per their BMI

Category	BMI
Underweight	16–18.5
Normal	18.5–25
Overweight	25–30
Obese Class I	30–35
Obese Class II	35–40
Obese Class III/morbid obesity	Over 40

- However, concomitant hypertension is often encountered with an elevated systemic resistance, which causes an increase in left ventricular afterload and concentric hypertrophy.
- Obese patients are also at risk of developing biventricular failure due to a high incidence of pulmonary hypertension and right ventricular dysfunction. Pulmonary hypertension most often occurs secondary to high left-sided pressures or underlying OSA.
- Obesity is an independent risk factor for the development of coronary artery disease, which occurs at an accelerated rate with a higher risk of myocardial infarction.
- A less known condition, cardiomyopathy of obesity, or Adipositas Cordis, has also been described. These patients demonstrate abnormal fatty infiltration of the myocardium as well as excessive epicardial fat deposition that leads to myocyte dysfunction and cardiac conduction defects.

Respiratory System

Obese patients experience several significant changes in pulmonary physiology.

- Decreased chest wall and lung compliance is secondary to increase in adipose tissue in the thorax and abdomen. This results in a significantly decreased vital capacity (VC), functional residual capacity (FRC), and expiratory reserve volume (ERV).
- The reduction in ERV is greatest in the supine position, at which point the FRC approximates the residual volume (RV), placing these patients at high risk of gas trapping, atelectasis, ventilation/perfusion (V/Q) mismatch, and rapid oxygen desaturation.

OSA is another condition commonly diagnosed in obese patients. OSA refers to a periodic, partial, or complete obstruction of the upper airway due to respiratory effort against a closed glottis when asleep. The cessation of airflow is for at least for 10 s or more. The airway is usually floppy, and profound muscle relaxation during anesthesia or sleep worsens the syndrome. A simple screening questionnaire includes questions about snoring, apneic events or arousals when sleeping, and daytime somnolence. These questions should be directed at both the patient and additional household members. The importance of diagnosing OSA is evident when considering the severe physiologic abnormalities that can result from interrupted breathing, including hypoxemia, hypercapnia, secondary polycythemia, pulmonary hypertension, and eventually cor pulmonale. A formal sleep study accurately diagnoses the disorder, at which time the patient can receive trials for continuous positive airway pressure (CPAP) therapy.

Obesity hypoventilation syndrome (OHS) is defined by extreme obesity and alveolar hypoventilation during wakefulness. Patients have hypersomnolence, dyspnea, and hypoxemia, with resulting cyanosis and polycythemia. These can result in pulmonary hypertension, leading to right ventricular failure and peripheral edema.

Gastrointestinal System

Obesity increases the risk for gastrointestinal disorders, including gastroesophageal reflux disorder (GERD), hiatal hernia, and delayed gastric emptying, which are largely due to increased abdominal mass compressing the stomach and possibly causing herniation of the gastroesophageal junction into the thorax. There is also an increased incidence of erosive gastritis that is related to the greater acidity and volume of gastric contents. When combined, these factors increase the risk of pulmonary aspiration. In addition, obese patients are at a higher risk of liver dysfunction due to fatty infiltration and gallbladder disease.

Endocrine System

Research has clearly shown that obesity is associated with an increased risk of impaired glucose tolerance and type II dia-

betes mellitus. While the mechanism is not completely understood, there appear to be genetic factors, which predispose patients to develop insulin resistance in the peripheral fatty tissue and pancreatic B-cell dysfunction. When combined with an increased caloric intake and sedentary lifestyle, patients develop a persistently elevated glucose. Perioperatively, exogenous insulin may be needed even for non-insulin-dependent diabetic patients.

Renal System

The initial effect of obesity on the kidneys is seen as an increase in renal blood flow, glomerular filtration rate, and renal hypertrophy. When combined with conditions that often accompany obesity such as hypertension, diabetes mellitus, hyperlipidemia, and atherosclerosis, the result is a thickening of the basement membrane, podocyte dysfunction, focal and segmental glomerulosclerosis, renal vascular injury, and proteinuria. If left untreated, these patients are at a high risk of developing chronic kidney disease.

Preoperative Assessment

Obesity has been shown to cause multiorgan dysfunction, which has a direct impact on anesthetic care. If time permits, each patient, especially the morbid obese, should be evaluated preoperatively in a multidisciplinary clinic that offers access to various subspecialties including cardiology and pulmonology, as well as imaging and laboratory services. Due to a sedentary lifestyle and limited mobility, obese patients often report being asymptomatic despite having significant underlying cardiopulmonary disease. For those patients who are not seen in a preoperative anesthesiology clinic, a thorough work up should be completed if time permits and the surgery is not deemed an emergency. All obese patients should be made aware of the potential for a difficult intubation, postoperative mechanical ventilation, or extubation to CPAP to ensure adequate ventilation and oxygenation. Goals of preoperative evaluation include

- Obtain pertinent data regarding the patient's medical or surgical history
- Obtain detailed list of medications, including any weight-reducing medications and herbal medications
- Obtain necessary laboratory data, including chest X-ray, pulmonary function tests, EKG, echocardiogram, and coagulation profile
- Optimize current physiologic functioning
- Determine an appropriate anesthetic care plan

Evaluation of the Cardiovascular System A thorough review of the cardiovascular system is important. Of particular concern are a history of hypertension, congestive heart failure, pulmonary hypertension, and ischemic heart disease, which may be present but not clearly defined. Detecting signs of compromised cardiac function may be challenging due to patient morphology; however, it is important to examine the patient for pulmonary congestion, elevated jugular venous pressure, hepatomegaly, and peripheral edema.

An EKG may reveal signs of ischemia, left or right ventricular hypertrophy, left atrial enlargement, and atrial fibrillation. A chest X-ray can show signs of pulmonary congestion and prominent pulmonary arteries as well as underlying lung disease. A transthoracic echocardiogram is a simple, noninvasive test, which demonstrates both systolic and diastolic function, the degree of ventricular hypertrophy and the presence of any valvular disease. Based on this information, a stress test may be considered. Lab tests should include electrolytes, blood glucose, and renal function studies, which may be compromised secondary to coexisting heart failure or diabetes mellitus.

Evaluation of the Respiratory System The evaluation should include a discussion of exercise tolerance, dyspnea, orthopnea, OSA and the use of CPAP/BiPAP, and a history of smoking. Coexisting obstructive or restrictive lung disease and the room air pulse oximeter value should be noted. Of particular importance is an assessment of the patient's ability to tolerate being in the supine position as this could lead to airway obstruction and profound desaturation. This information can be used as a screening tool to order further tests including spirometry, a sleep study evaluation or referral to a pulmonary specialist. However, it is important to note that multiple studies have shown that it is not cost effective to order pulmonary function tests in asymptomatic obese patients because obesity alone is not absolutely predictive of these changes in respiratory dynamics.

Evaluation of the Airway A history of difficult airway should be inquired and records be obtained, if possible. Given that many of these patients have difficulty lying supine, a thorough airway exam is imperative, as it will help guide the anesthetic plan. It should include mouth opening, dentition, Mallampati score, neck extension, neck circumference, and thyromental distance. Difficult mask ventilation has been defined by The ASA Task Force on Management of the Difficult Airway and occurs "when it is not possible for the unassisted anesthesiologist to maintain the oxygen saturation above 90 % using 100 % oxygen and positive pressure ventilation, or to prevent or reverse signs of inadequate ventilation." Independent risk factors for difficult mask ventilation include a BMI > 26 kg/m^2, history of snoring, presence of a beard, increased Mallampati grade, and lack of teeth.

The relative risk of difficult laryngoscopy and intubation in an obese patient is still controversial. Mashour et al argue

that since the Mallampati evaluation is done with the head in a neutral position, the degree of mouth opening is less than what can be achieved with craniocervical extension and can result in a false positive prediction of difficult laryngoscopy or intubation. Their study suggests that the Extended Mallampati Score (EMS) is superior to the standard Mallampati score in predicting difficult laryngoscopy in a morbidly obese patient. Neck circumference and an assessment of anterior neck soft tissue are also useful measurements when further assessing for a potential difficult airway. A patient with a Mallampati score > 3 and neck circumference greater than 50 cm may need an awake fiberoptic intubation.

Aspiration Prophylaxis Obese patients have an increased risk for regurgitation and pulmonary aspiration. They have greater gastric volumes, with increased prevalence of gastroesophageal reflux and hiatus hernia, predisposing them to esophagitis and pulmonary aspiration. Associated conditions that can cause delayed gastric emptying, such as diabetes mellitus and traumatic injury, further increase the risk of aspiration. Morbid obese patients can be considered as full stomach. Therefore, adequate aspiration prophylaxis should be given to obese patients preoperatively. This may include administration of H_2 blockers (ranitidine, famotidine), metoclopramide, and antiemetics (ondansetron, dexamethasone).

Anesthetic Plan The choice of anesthesia depends on patient preference, the procedure, the patient's comorbid conditions and body habitus. It is important to conduct a thorough history, physical, and airway examination to help guide the type of anesthetic. Similar to a normal weighing patient, anesthetic management of obese patients can include local or monitored anesthesia, general anesthesia, regional anesthesia (including peripheral nerve blocks), or a combination of techniques.

Regional anesthesia has many benefits in an obese patient including less airway manipulation and the use of a lower total dose of narcotic, which is important in a population that is at increased risk of respiratory complications. Nevertheless, there are unique challenges when performing a regional anesthetic in the obese population that requires an experienced anesthesiologist. It is technically more challenging to identify specific landmarks, correct positioning may be more difficult, specialized or longer needles may be required, and there is a higher risk of a failed block. Given this circumstance, one needs to be prepared for the possible conversion to a general anesthetic, or plan for a general anesthetic from the beginning, especially if the patient may have a difficult airway.

Several studies have evaluated different intubation techniques in obese patients. While an awake fiberoptic intubation remains the standard for patients with a class four airway, there are other methods, which have been evaluated for those patients with a lower grade score on their airway exam. The use of video laryngoscopes, such as the GlideScope, Storz V-Mac, and McGrath, has been shown to provide an equal or better view of the glottis with fewer intubation attempts compared to traditional direct laryngoscopy. Studies have also been conducted evaluating the intubating laryngeal mask airway (ILMA). This device has been shown to be safe when managing the airway of an obese patient. However, proper placement of the ILMA took slightly longer (11 s) in patients with high-grade laryngeal views when compared to lean patients.

Table 42.3 Appropriate blood pressure cuff size

Arm circumference (cm)	Cuff size (cm)
22–26	Small adult, 12 × 22
27–34	Adult, 16 × 30
35–44	Large adult, 16 × 36
45–52	Adult thigh, 16 × 42

Vascular Access Vascular access is another challenge that may present when caring for obese patients. If access appears to be difficult, it is recommended to use longer catheters and an ultrasound machine to visualize the veins. If this is not available and attempts remain unsuccessful, a central venous catheter may be necessary. However, given that anatomic landmarks are often obscured, extra caution is required because the use of blind cannulation is associated with an increased risk of complications due to multiple attempts.

Monitoring Accurate monitoring of blood pressure can be difficult in obese patients. It is important to remember that using a blood pressure cuff that is too large will underestimate the blood pressure and one that too small will overestimate values. The AHA has issued recommendations matching arm circumference to cuff size (Table 42.3). If proper cuff sizing on the upper arm is not possible, it can be placed on the forearm. This site may overestimate the blood pressure; however, data from various studies is inconclusive as to the extent and its significance. The blood pressure cuff can also be placed on the calf or thigh; however, there is still a question as to whether these sites are as precise as placing it on the upper arm. If an accurate cuff pressure cannot be obtained, this is an indication for intra-arterial line placement.

Special Equipment Special equipment may be required for obese patients, including stretchers and operating tables, in order to ensure their safety. Moreover, it is important to check that the operating room (OR) table is functioning properly and adequate padding is available to relieve pressure points and avoid nerve injury. If available, width extensions, straps, and footboards should be added to maintain proper positioning and avoid movement. Newer operating room tables can accommodate up to 600 pounds or more of patient weight.

Intraoperative Care

Positioning and Preoxygenation Changes in respiratory dynamics are most evident after a patient is placed in a supine position and sedative medications are administered. Therefore, it is crucial that obese patients be placed in a proper sniffing position to ensure optimal preoxygenation, mask ventilation, and visualization during direct laryngoscopy. This position may require the placement of a ramp under the upper body using such materials as folded blankets, pillows, and irrigation bags. There are several other devices that have been designed to achieve this position with greater ease including an inflatable ramp and a head support, which elevates the jaw. Another technique that helps achieve this head-up position is manipulation of the operating table by flexing at the trunk-thigh hinge and raising the back. It has been shown that preoxygenating a patient in a 25° head-up position, compared to laying flat, increases oxygen tension by 23 % by allowing for better diaphragmatic excursion.

Dosing of Medications After the patient is properly positioned and preoxygenated, one must be aware of appropriate dosing of medications for obese patients. Some of the physiologic changes which affect pharmacodynamics include an increased cardiac output, muscle mass, plasma volume, increased splanchnic and renal blood flow, and increased alpha$_1$ acid glycoprotein. Dosing recommendations for lean patients are generally based on total body weight (TBW), since it is similar to their ideal body weight (IBW). However, in obesity, these values are quite different, thus dosing based on TBW can result in an overdose. Most anesthetic medications should be dosed based on IBW or lean body mass (LBM).

Ideal Body Weight (IBW)
IBW (kg) = height (cm) – X
(where X = 100 for adult males, and 105 for adult females)

Lean Body Mass (LBM)
LBM = Body weight – (Body weight × Body fat %)
Male LBM = 1.1 (weight kg) – 128 (weight kg/100 × height m)^2
Female LBM = 1.07 (weight kg) – 148 (weight kg/100 × height m)^2

There are some dosing exceptions. For example, propofol induction doses are based on IBW while an infusion is based on TBW. Alterations in dosing are also recommended for reasons such as avoiding the respiratory depressant effects of sedative and narcotic-type medications. The use of short acting water-soluble anesthetics facilitate a smooth anesthetic induction, maintenance, and emergence from anesthesia.

Ventilation To improve oxygenation and FRC, obese patients can be ventilated using tidal volumes of 10–12 ml/kg. Additionally, positive end-expiratory pressure (PEEP) achieves an improvement in both FRC and arterial oxygen tension (but at the expense of cardiac output and oxygen delivery). For laparoscopic surgeries, the respiratory rate may be increased to 12–14 breaths/min. It is important to know that lengthy operations, and surgeries involving the abdomen, thorax, and spine, which include cephalad displacement of organs and surgical retraction, cause decreased alveolar ventilation, atelectasis, and pulmonary congestion, thereby, negatively influencing respiratory function.

Postoperative Care

The postoperative period can also present with additional challenges when caring for obese patients. Guidelines for care of an obsese patient are summarized in Table 42.4. Obese patients have a significantly higher risk of postoperative myocardial infarction, pulmonary complications, wound infection, peripheral nerve injury, and urinary tract infection.

Extubation Extubation after general anesthesia must be carefully planned given their preexisting comorbidities and physiologic changes that may have been further altered while under anesthesia. Applying PEEP throughout the case and positioning the patient in a reverse trendelenburg or head-up position prior to extubation improves oxygenation and lung mechanics. The presence of increased atelectasis in dependent lung zones causes abnormal gas exchange, and when coupled with other effects such as incomplete recovery from volatile anesthetics, residual muscle relaxant, and/or narcotic medications, these patients can experience critical oxygen desaturation immediately post-extubation. The patient must meet all extubation criteria, including maintaining an adequate tidal volume and saturation as well as demonstrate good grip strength or head lift prior to extubation. If there is

Table 42.4 Guidelines for anesthetic care for an obese patient

Thorough history and physical evaluation
Appropriate laboratory tests
Aspiration prophylaxis
Adequate vascular access
Adequate monitoring equipment
Preoxygenation and strict maintenance of airway
Proper positioning and padding
Optimal intraoperative oxygenation (tidal volumes, respiratory rate, peep)
Adequate use of muscle relaxants and avoidance of residual effects
Adequate volume replacement
Effective postoperative analgesia

any concern of possible respiratory decompensation and reintubation, it is important to be prepared. The difficult airway cart should be readily available, especially if the patient had been a difficult intubation at the start of the case. If the patient is on CPAP at home, it can be applied immediately after extubation to avoid the development of hypoxia and hypercarbia.

It is recommended that obese patients with a history of OSA and other comorbidities continue to be monitored postoperatively due to their higher risk of respiratory and cardiac complications. This may necessitate an overnight admission for patients who do not meet discharge criteria following ambulatory surgery or even an ICU admission for those patients who are not stable for a floor admission due to a high oxygen requirement or poor respiratory performance.

DVT Prophylaxis DVT prophylaxis must be considered in the postoperative period as obesity has been shown to be a strong risk factor for venous thromboembolism and pulmonary embolism. Studies have looked at various dosing regimens of heparin and enoxaparin (lovenox); however, the data remains inconclusive as it can vary for each type of surgery and the patient's other risk factors. Currently, it is recommended that for nonambulatory patients, subcutaneous heparin should be administered every 8 h postoperatively until the patient is ambulatory.

Clinical Review

1. BMI can be calculated by the following formula
   A. Weight (pounds)/height^2 (cm)
   B. Weight^2 (kg)/height (cm)
   C. Weight^2 (pounds)/height (m)
   D. Weight (kg)/height^2 (m)
2. Correct formula for measuring ideal body weight (kg) (IBW) is
   A. Height (cm)—100
   B. Height (m)—50
   C. Height (m)—15
   D. Height (cm)—50
3. A morbid obese patient has a BMI of
   A. 25–29
   B. 30–34
   C. 35–39
   D. Greater than 40
4. Drugs that are used in a morbidly obese patient should preferably be
   A. Highly lipophilic drugs
   B. Water-soluble drugs
   C. Metabolized in the liver
   D. Excreted by the kidneys

Answers: 1. D, 2. A, 3. D, 4. B

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The Elderly Patient

43

Preet Mohinder Singh and Ashish Sinha

In recent years anesthesiologists are increasingly becoming aware of "graying" of the patient population in the operating rooms. The United States 2011 census showed that 13.3 % of the total population is above the age of 65 years (the age which typically describes an elderly patient). As per the "Centers of Disease Control USA's 2009 report, of the 48 million inpatient surgical procedures that were performed, 37.1 % of these were performed on patients 65 years or older. With improving healthcare and increasing life expectancy, these proportions are likely to grow in the future.

The importance of understanding "anesthesia for the elderly" is not only substantiated by the above numbers, but also by the fact that these patients exhibit different drug pharmacokinetics compared to younger adults. Another unique aspect is the diversity and heterogeneity of functional status in this cohort population. A patient may be 75 years "young" or 55 years "old," highlighting the importance of "functional age" rather than merely the chronological age for the anesthesiologists' perspective. Increasing age tends to decrease the functional reserves of the body. For tailoring anesthesia techniques for the elderly, understanding the physiological changes is critical. Here we will describe such changes and their clinical implications.

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Physiologic Changes in the Elderly

Cardiovascular System

Since normal physiological activity, and thereby, metabolic demands decrease with age, cardiovascular disease in elderly may not present symptomatically in the preoperative period.

Changes in Cardiac Contraction System

Aging leads to progressive decline in the number of myocytes and increase in ventricular collagen content (left ventricular hypertrophy). The ventricular relaxation phase is maximally affected, leading to diastolic dysfunction. Maximal heart rate (increased vagal tone), peak exercise cardiac output, and peak ejection fraction tend to decrease with age (Table 43.1). Fluid management under anesthesia is critical as with relatively stiff ventricles, measures like CVP/End diastolic pressure may be spuriously elevated, decreasing their significance under anesthesia.

Changes in Cardiac Conduction System

The conduction system gradually undergoes fibrosis predisposing to atrial fibrillation, sick sinus syndrome, and heart block. Atrial fibrillation is the commonest clinically significant rhythm disorder affecting about 6 % of patients older than 65 years and 12 % of patients above 85 years in the United States. As the conduction defect is anatomical and the rhythm disorder is permanent, perioperatively rate control overscores the need of rhythm control in elderly patients.

Changes in Cardiac Autonomic Innervation

Autonomic tissue is progressively replaced with connective tissue producing a relative "hyposympathetic state," impairing cardiac ability to augment output via increased chronotropy and inotropy. Perioperatively these patients, thus primarily, depend upon adequate preload to raise their cardiac output whenever needed. The relative denervation leads to receptor upregulation and associated conduction system

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Table 43.1 Cardiovascular and pulmonary changes with age

Cardiovascular changes	
Arterial compliance	Loss of arterial compliance, increase in SVR, LVH, diastolic dysfunction, hypertension
Venous compliance	Loss of venous compliance
Cardiac output	Resting cardiac output-normal, diminished ability to increase stroke volume, preload important
Pacemaker cells	Decreased, conduction abnormalities
Beta-adrenergic response	Diminished response, decrease in maximal heart rate
Pulmonary changes	
No change	Functional residual capacity, $PaCO_2$
Increase	Residual volume, closing capacity, dead space, work of breathing, VQ mismatch
Decrease	PaO_2, FEV_1, HPV, thoracic wall compliance, alveolar elasticity, vital capacity, total lung capacity, maximum breathing capacity

SVR systemic vascular resistance, *LVH* left ventricular hypertrophy, *VQ* ventilation-perfusion, *FEV1* forced expiratory volume in 1 s, *HPV* hypoxic pulmonary vasoconstriction

defects, predisposing elderly patients to increased arrhythmogenic potential of autonomic drugs. Impaired autonomic efferents along with age-related arteriosclerosis impair adequate baroreceptor responses in elderly, increasing the propensity for uncompensated hypotension to induction agents and acute blood loss under anesthesia.

Changes in Vascular System

Aging of the vasculature results in increased arterial thickening and endothelial dysfunction. These changes cause increased systolic blood pressure (pressure > 180 mmHg) and pulse pressures, pulmonary hypertension, and present as risk factors for atherosclerosis, coronary artery disease, and stroke.

Respiratory System

Available evidence suggests that even after adjusting for comorbidities, aging remains a significant factor accounting for postoperative pulmonary complications in the elderly. Compared to patients younger than 60 years, patients between 60 and 69 years are twice and patients between 70 and 79 years are thrice as likely to develop postsurgical pulmonary complications.

Changes in Anatomy and Mechanics of Breathing System

Loss of laryngopharyngeal muscle mass and coordination predispose elderly patients to perioperative airway collapse and pulmonary aspiration, respectively. Decline in lung function is primarily contributed by loss of lung elasticity, increasing chest wall stiffness, and reduced inspiratory muscle strength (Table 43.1). Small airway collapsibility causes air trapping, which leads to "senile emphysema." However, this must be distinguished from actual emphysema in the preoperative evaluation, as the total lung capacity is decreased significantly in the latter.

Basal hyperinflation leads to flattening of the diaphragm, which accompanied by weaker chest muscles has major consequences. The vital capacity is decreased; hence '4-vital capacity breaths' for preoxygenation in an elderly patient may not be effective. The already compromised thoracic muscles are highly susceptible to postoperative residual weakness with the use of nondepolarizing neuromuscular blockers. A flattened diaphragm not only makes respiration abdominothoracic, but significantly increases the work of breathing, leading to difficult weaning and extubation of these patients. Other notable changes include fall of FEV_1 (6–8 % per decade), increased closing capacity, and residual volume. The closing capacity (volume of air in the lungs at which small airways begin to close) exceeds the functional residual capacity (volume of air remaining in the lungs at the end of a normal expiration) at age 45 years in the supine position, and at age 65 years in the sitting position.

Changes in Diffusion Properties

Uneven distribution of ventilation, increased closing capacity, and increased thickness of the interstitial barrier account for age-related fall in diffusion capacity. With age, arterial oxygen tension falls by 0.3–0.4 mmHg yearly; however, the partial pressure of CO_2 remains almost constant due to decreased production and much higher diffusion capacity of CO_2. This predisposes the elderly patient to desaturation under anesthesia. Positive pressure ventilation extends West's Zone I (see Chap. 28), which increases dead space ventilation.

Changes in Central Respiratory Drive and Sensitivity

As a result of decreased peripheral and central chemoreceptor sensitivity with age, the ventilatory drive in response to hypoxia and hypercarbia falls by about 50 % and 40 %, respectively. This becomes even more significant in the perioperative period, where drugs like opioids and benzodiazepines further suppress these ventilatory responses, preventing compensatory responses to desaturation, with resultant CO_2 retention.

Renal System

Postoperative renal failure accounts for up to 25–50 % of etiologies of acute renal failure in the elderly. This renal injury is often iatrogenic and preventable, and thus, is a significant modifiable factor in improving the outcome of surgery in the elderly.

Changes in Glomerular Function

Renal function is commonly determined by the glomerular filtration rate (GFR) and serum creatinine. The average age-related loss in GFR is 6–8 % per decade. By the age of 80

years, the number of glomeruli is reduced to half than that at age 30 years, causing increased rate of sclerosis of the residual hyperfunctioning nephrons. As the body muscle mass also decreases, the deteriorating renal function may not be reflected by measurements of serum creatinine (measuring creatinine clearance reflects renal function better). However, the decrease in GFR tends to prolong the half-life of the anesthetic drugs which are primarily dependent upon glomerular clearance. Newer tests with molecules like cystatin C, neutrophil gelatinase-associated lipocalin (NGAL), and kidney injury molecule 1 (KIM-1), which remain unaffected by age, may serve better in measuring perioperative renal function.

Changes in Tubular Function

The ability to conserve sodium and excrete H^+ decreases with aging, diminishing the ability to regulate fluids and acid-base balance. Decreased sensitivity to renin-angiotensin and ADH impairs renal ability to compensate for perioperative hypervolemia and extra renal fluid losses. The susceptibly to fluid overload also increases, due to the inability to excrete excess fluids as a result of decreased GFR.

Changes in the Urinary Tract

Urinary retention and catheter sensation are typically common problems in the elderly, which are aggravated by the use of opioids. Prostatic hyperplasia in elderly males and decreased estrogen levels in females alter urinary sphincter tone leading to urinary retention, thus promoting urinary tract infections and predisposing the patients to perioperative bacteremia.

Hepatobiliary and Gastrointestinal System

Anesthesia can be considered as a pharmacological interplay between the drugs metabolized by the liver, with age-related changes making significant alterations to both the pharmacokinetics and pharmacodynamics.

Changes in Hepatobiliary System

Liver blood flow and size both decrease by around 35 % in old age. Any hypotension causing a further decrease in hepatic blood flow can significantly prolong drug action. Phase I metabolic reactions (cytochrome p450 enzyme-based reactions) are prolonged, whereas phase II reactions (conjugation reactions) are well preserved, which may guide the anesthesiologists' choice to use drugs metabolized via phase II reactions in the elderly. Furthermore, there is a decreased production of albumin and plasma cholinesterase enzyme.

Changes in the Gastrointestinal System

Gastric emptying is prolonged and the gastric pH tends to rise. Age-related changes do not significantly alter anesthetic plan in these patients. Perioperative opioids, may however, aggravate constipation, which already has a higher incidence in the elderly.

Central Nervous System

Neurological complications are probably the most frequent complications seen in the elderly with postoperative delirium accounting for up to 53 % of the complications. Senile dementia, with an incidence up to 25 % at 85 years, is the strongest predictor of postoperative cognitive disorders. This indirectly adds to hidden morbidity in the elderly by increasing pulmonary complications (inability to cough/failing chest physiotherapy), inadequate analgesia (improper reporting, inability to use patient controlled analgesia), and failed early ambulation (increased incidence of deep vein thrombosis, muscle wasting).

The requirements of local and general anesthetics (minimum alveolar concentration-MAC) are reduced in the elderly. This is reflected by the decrease in cerebral blood flow, cerebral oxygen consumption, brain mass (30 % loss by 80 years of age), and decreased synthesis of neurotransmitters. Strong evidence exists in favor of multimodal analgesia in the elderly so as to decrease the use of long acting opioids. This may decrease the incidence of neurological complications in the elderly. Studies indicate the use of benzodiazepines to be associated with an increased incidence of delirium, and therefore, agents like dexmedetomidine are favorable for sedation purposes.

Pharmacology Changes in the Elderly

Pharmacokinetics

Biometric changes in body composition modify drug distributions in the elderly and cause changes in effect site concentrations. Lean muscle mass decreases by 40 %, with a decrease in the total body water. Subsequently, the volume of distribution of water-soluble drugs decreases, which increases the achieved effect site concentration. Conversely the proportion of body fat increases and, therefore, fat-soluble drugs undergo extensive redistribution, thereby, slowing their rate of elimination.

Centrally acting drugs may have a slower onset of action as a result of prolonged brain-arm circulation time. As hepatic and renal function decrease with age, drugs which are dependent on hepatic/renal clearance will have a prolonged duration of action. Lower serum albumin causes an increase in free plasma drug concentration, thus increasing the active form of the drug for the same dose. Initial boluses of drugs may need no dose modification (considering no change in drug sensitivity); however, subsequent doses need reduction or interval lengthening in view of slower elimination (Table 43.2).

Furthermore, MAC of volatile agents decreases by 5 %/decade after the age of 40 years. Decreased cardiac output will

Table 43.2 Effect of aging on pharmacology of common anesthesia drugs

Drug	Bolus/IV doses (for elderly >65 years)	Infusion	Adverse effects	Advantages	Comments
Sedatives and induction agents					
Midazolam (sedation only)	0.5 mg increments Age > 70—half dose Age > 90—quarter dose	Not recommended	Respiratory depression, rarely paradoxical reaction	Amnesia, anxiolysis, hemodynamic stability	Clearance same as in young, increased brain sensitivity
Propofol	Sedation 0.5–0.8 mg/kg Induction 40–60 % reduced dose	0.5–2 mg/kg/h (sedation)	Respiratory depression, hypotension	Rapid onset/offset, anti-emetic, clear headed recovery	Gradual doses cause less hypotension, decrease dose when used in combination with other drugs
Dexmedetomidine (FDA approval for sedation only)	Sedation 0.5 mcg/kg (over 10 min)	Sedation 0.2–0.7 mcg/kg/min	Hypotension, sympatholysis, bradycardia	No respiratory depression, decreased cognitive dysfunction, analgesia, decreases IOP	No pharmacokinetic changes with age
Etomidate (induction only)	0.15–0.2 mg/kg	Not recommended	Respiratory and adrenal suppression, myoclonus	Minimal hypotension, short acting	Reports of single dose prolonged adrenal suppression in elderly
Ketamine	Use lower dose ranges 1–4 mg/kg	Not recommended	Arrhythmia, hypertension, secretions	Minimal respiratory depression, no hypotension	Dissociative reactions, avoid in elderly
Inhalation agents					
Most preferred-sevoflurane and desflurane	MAC values decrease by 5 % each decade, elderly show 20–40 % lower MACs	Maintenance-20–40 % MAC reduction	Hypotension, post operative residual effects, increased PONV	Duration-affected minimally with age as pulmonary excretion is unaffected with age	Use low solubility agent (sevoflurane/desflurane), slower uptake with age, age related VQ mismatch
Opioids					
Remifentanil	Half of adult dose-12.5–25 mcg	One-third adult dose (0.025–0.05 mcg/kg/min)	Respiratory depression, chest wall rigidity, bradycardia, Not for postoperative analgesia	Rapid onset/offset, no change with hepatic renal comorbidities	No pharmacokinetic changes with age, increased brain sensitivity
Fentanyl	10–25 mcg	0.5 mcg/kg/h (up to 40 mcg)-titrate to effect	Sedation, respiratory depression, slow awakening	Respiratory depression is of shorter duration than morphine	Increased brain sensitivity
Tramadol	50–75 mg		PONV, low analgesic efficacy, agitation	Minimal respiratory depression, long duration of action	Avoid in patients taking SSRIs antidepressants
Morphine	25–50 % reduction of dose, titrate to effect	25–50 % reduction of dose	Sedation, respiratory depression, slow awakening	Longer analgesia duration	Smaller volume of distribution with age, higher maximum plasma concentrations
Neuromuscular blockers					
Depolarizing (succinylcholine)	Same as younger population	Not recommended	Fasciculation and myalgia (lesser in elderly), Increased IOP, ICP	Rapid onset/offset, good relaxation	Plasma cholinesterase activity decreases with age, but half life of succinylcholine not significantly prolonged
Non depolarizing—shorter acting preferred	Same as younger population- about 10 % increase in re-dosing interval	Same as younger population	Concern of postoperative residual paralysis, leading to postoperative pulmonary complications	Cisatracurium—minimal age related effect on duration, No effect of comorbidities	Onset of action may be delayed, minimal increase in ED95, slight increased half life, decreased clearance (clinically insignificant)

tend to hasten the onset of action, while increased body fat will tend to prolong elimination and hence the recovery. Elderly patients have lower dose requirements for anesthesia induction agents (propofol), opioids, and benzodiazepines. Lower plasma cholinesterase enzyme concentrations in the elderly may cause prolongation of the effects of succinylcholine. Slow muscle blood flow and decreased hepatic/renal clearance may prolong the effects of nondepolarizing muscle relaxants.

Pharmacodynamics

Most anesthetic drugs act on the CNS, and various mechanisms of increased sensitivity in the elderly have been proposed. Recent research attributes this alteration to synaptic level modifications. Decrease in presynaptic GABA release upregulates the GABA receptors and enhances responses to sedatives and induction agents. NMDA receptors show enhanced binding to antagonists, thus increasing activity of N_2O, ketamine, etc. However, the quantification of these changes is difficult with current technology, and therefore, the exact dosing criterion in the elderly is difficult to predict.

Operative Risk Stratification in Elderly

Complications in the elderly often lead to a cascade, causing disability and deterioration of the quality of life. Most preoperative assessment scores used in younger population have limitations for the elderly, as the body reserves decrease with age. However, no test can quantify this decrease. Evidence-based medicine has shown the "Frailty Syndrome" as a reliable predictor of decreased function, with significant correlation to perioperative complications. Frailty may be defined as a free-standing syndrome marked by loss of function, strength, physiologic reserve, and increased vulnerability to sickness/death.

The criteria included in Frailty grading are listed in Table 43.3. Each positive in the table carries a score of 1. Patients with a score of 3 or more are labeled as Frail and have about two to six times higher risk of perioperative complications.

Table 43.3 Frailty grading

Test	Features
Weight loss	Unintentional weight loss greater than 10 pounds in preceding year
Weakness	Decreased handgrip strength to 20 % or less, measured objectively via hand held dynamometer
Exhaustion	Self reported exhaustion, early fatigue on effort and activity
Decreased physical activity	Activity in terms of caloric expenditure falls to 20 % or less
Slowness	Adjudged by time to walk 15 feet, falls to 20 % or less

Patients with 1 or 2 positives (pre-Frail) have a risk of complications about twice the age-matched cohorts. Strategies that may reduce the frailty score and thus decrease perioperative risks include

- Adequate nutrition—diet with sufficient protein, vitamin and mineral intake
- Exercise in the elderly—encouragement to walk and perform daily activities has proven to improve muscle mass by about 100 % in 6 weeks time, and brings down the perioperative complication risk, significantly
- Hormone therapy—use of growth and sex hormones is an experimental approach that has shown promising results so far
- Prevention of infections—vaccines for influenza, pneumococcal, herpes zoster
- Regular monitoring of the individual—basic abilities, such as walking, equilibrium, and cognition
- Rapid reconditioning—after stressful events via renutrition and individually tailored physiotherapy

Various studies have attempted to quantify the risk associated with surgery. For example, Aust et al. proposed an objective scoring system with weighted scores for serum albumin, age, the ASA score, and whether the surgery is an emergency or oncologic surgery. In general, factors that are associated with increased postoperative mortality in the elderly include

- ASA score of 3 or 4
- Less than 4 MET, physical inactivity
- Poor nutritional status (serum albumin, anemia)
- Major or emergency surgery
- Comorbid diseases (cardiac, pulmonary, liver, kidney, hypertension, diabetes)

Perioperative Pain Management

Inadequately treated pain has been strongly associated with slower recovery and postoperative cognitive dysfunction. Whenever possible, objective pain scoring must be used to access and treat pain in elderly. Even cognitively impaired elderly patients may be able respond appropriately to simple numeric or visual analogue pain scales. It must be realized that pain-related agitation itself might further worsen the patient's cognitive ability and thus worsen communication. The nature and site of pain must be appropriately evaluated, as not uncommonly urinary catheter sensation especially in elderly males is wrongly treated as pain. Often catheter sensation presents as an uncomfortable patient rather than a patient in pain. The presence of pain in the elderly can have serious consequences on the already compromised cardiovascular system by precipitating tachycardia and increasing myocardial oxygen consumption. Pain precipitates lung

atelectasis and development of pneumonia by attenuating the patient's inspiratory efforts.

Route of analgesia is extremely important in the elderly. Intraoperative and postoperative epidurals/regional blocks using local anesthetics are effective in sparing opioids and providing analgesia without sedation or significant respiratory depression. Although the elderly are more susceptible to opioid-related respiratory depression, this should not lead to withholding of analgesia. Cautious use of titrated doses or using shorter acting agents may be the safe approach. Multimodal analgesia, whenever possible, should be preferred. In view of the higher incidence of gastrointestinal bleeding and renal compromise in the elderly, NSAIDS may need dose reduction or complete avoidance. Use of intravenous acetaminophen (paracetamol) seems to be an effective and safe adjuvant to opioids for pain relief in the elderly. In patients capable of following instructions, using patient-controlled analgesia (PCA) has shown to be associated with a steady level of analgesia with much higher satisfaction scores.

Regional Anesthesia VS General Anesthesia for Elderly

There is little evidence proving superiority of one technique over the other. Recent meta-analysis found that regional techniques decreased the incidence of DVT, pneumonia, and pulmonary embolism at 30 days after surgery; however, these differences could not be maintained at 6 months. General anesthesia often is a concern in elderly patients because of decreased cardiorespiratory reserves. In addition, a higher incidence of cognitive dysfunction has been noted after general anesthesia.

Regional techniques are often limited by improper positioning and lack of coordination due to decreased hearing or poor cognitive functions. Regional anesthesia may be associated with significant hypotension, postoperative urinary retention, and delayed ambulation. When sedation is used with regional anesthesia, the incidence of respiratory depression and hemodynamic instability may even surpass that with general anesthesia. Therefore, whichever technique is used, a patient-based modification is needed to make anesthesia safe and appropriate for the perioperative period in the elderly.

Perioperative Anesthetic Considerations Unique to Geriatric Anesthesia

Preoperative Examination

A thorough preoperative evaluation is essential for the safe administration of anesthesia to elderly patients. The goals of preoperative evaluation in elderly patients are to establish the baseline health and functional status of the patient, identify comorbid conditions, and determine if further evaluation and optimization is required. Important preoperative considerations in elderly patients are as follows.

- Early identification of patients requiring further investigations or with special issues may help with advance planning and room scheduling (obtain previous medical records)
- Elderly patients usually have a number of comorbid conditions, about 3–4 diseases. Optimizing these medical conditions is essential to prevent postoperative complications.
- Elderly patients are frequently on multiple medications (polypharmacy). A complete list of medications, including over the counter and alternative medications/treatments, should be inquired.
- A history of depression or alcohol abuse will increase the risk of delirium in the postoperative period.
- Chronic pain or dementia may prevent the patient from lying still for surgical procedures requiring sedation.
- Laboratory studies or further investigations should be directed by the history, physical examination, comorbidities of the patient, and the complexity of the surgical procedure. Elderly patients may not undergo laboratory testing just based on their age.
- Presence of abnormalities on the EKG is common, and if an EKG is done, it should be compared to previous EKGs. Similarly, a chest radiograph is done only in patients undergoing major surgery or who have significant cardiorespiratory disease.
- Frail elderly patients will frequently need assistance postoperatively. The plan for postoperative care should be discussed in advance with the patient and/or relatives or caretakers.

Functional Assessment

The crux of preoperative evaluation for risk stratification, as described by the "ASA," is "functional capacity." Energy requirements for various activities should be assessed (MET-metabolic equivalent). Limitation of ambulation in elderly may be as a result of arthritis or muscle weakness. This leads to a major limitation in quantifying the patient's activity, and thus the assessment of cardiopulmonary reserve. Investigations like pharmacological stress testing and cardiac ultrasound may be able to give information on latent cardiovascular compromise, but the cost-benefit ratio for minor procedures may not permit their routine use. Clinically, a well-explained Breath Holding Time (BHT) may hold a significant value. A bedside BHT value of 20 s or more can predict reasonably good cardiopulmonary reserve.

Venous Cannulation

Identification of veins is often not a problem in the elderly, but with loss of perivascular tissue support cannulation may be difficult (the veins tend to slip and slide away from the approaching needle). Even after successful establishment of an intravenous line, the soft tip of the cannula is capable of tearing through the vein and causing infiltration. Thus careful catheter fixation allowing minimal movement of the cannula tip is important to maintain a functioning line.

Preoperative Sedation

As discussed above, elderly patients are sensitive to preoperative sedative medications. Midazolam should be used sparingly, as it can add to the incidence of postoperative delirium. Preoperative opioids should be administered in titrated doses, and only in the presence of pain. Scopolamine patch, which is commonly applied in younger patients to prevent postoperative nausea and vomiting, should be avoided in the elderly as it may cause confusion postoperatively.

Central Neuraxial Blockade

Although intervertebral space identification is often easy in the elderly, procedural difficulties may limit the degree of success. These difficulties may be due to calcification of ligamentum flavum or age-related spine deformities (scoliosis, kyphosis, lordosis), which make needle guidance difficult. Elderly patients often require lower doses of local anesthetics and may have exaggerated cardiovascular responses to neuraxial procedures. Epidural analgesia may provide better pain control than do general anesthesia and reduce the incidence of pulmonary complications by providing better pain control, decreasing the incidence of atelectasis, and sparing of opioid use. The incidence of postdural puncture headache is very low in elderly patients.

Induction of Anesthesia

Elderly patients need more time to be adequately preoxygenated because of decreased cardiopulmonary reserves. Decreased doses of induction agents, especially propofol, are used for induction, as they may cause hypotension. Additionally, preoperative medications, such as beta-blockers or ACE inhibitors, may add to the degree of hypotension. The onset of drug action may be slower because of the increased brain-arm circulation time. Volatile inhalation agent onset of action may be, however, faster because of decreased cardiac output. Elderly patients may have comorbidities, which may warrant the need for closely monitoring the EKG for ischemia or arrhythmias (5-lead EKG), plus any invasive monitoring as needed.

Airway Maintenance

Due to loss of buccal fat, facial contours often do not fit conventional facemasks leading to significant air leaks, which make mask ventilation difficult. Furthermore, elderly patients may be partially or completely edentulous, which also makes mask ventilation difficult (though that makes intubation easier). Modifications in facemasks or mask holding techniques to establish a seal are helpful. The airway muscle tone is already compromised and on induction of anesthesia a tendency to airway obstruction may be seen. This may often warrant use of an oral airway in these patients, even in absence of other predictors of difficult mask ventilation.

Intraoperative Positioning

Elderly patients have loss of subcutaneous fat and atrophied skin, which predispose them to accidental injury from seemingly benign positions. Musculoskeletal changes like arthritis, deformities, and limited range of movements may make positioning during surgery difficult in elderly patients. These patients are also predisposed to pressure sores due to unequal weight distribution and positioning-related fractures with application of minimal stress due to loss of organic bone content. Therefore, the extremities should be appropriately padded and over stretching avoided.

Maintenance of Anesthesia

As discussed above, MAC of inhalational agents decreases with age. It may be prudent to use shorter acting inhalation agents, such as desflurane or sevoflurane. Elderly patients are sensitive to opioids and are prone to respiratory depression and other side effects. Hence opioids should be used in smaller doses in the elderly. In the presence of hepatic and or renal disease, muscle relaxants may have prolonged duration of action due to decreased metabolism or prolonged elimination. Intraoperative ventilation mechanics may be improved by using PEEP or pressure support ventilation. Fluids should be judiciously administered as elderly patients are prone to hypotension or volume overload.

Elderly patients are more prone to the effects of hypothermia, which occurs due to less heat production and more heat loss. Hypothermia, which slows the metabolism of drugs, causes platelet dysfunction, or prevents wound healing, should be prevented (forced air warming device, warm IV fluids, increasing ambient room temperature).

Emergence from Anesthesia

Criteria of extubation in elderly patients are similar to younger patients. However, elderly patients may be prone to delayed emergence from anesthesia. This may be due to opioids, muscle relaxants, volatile inhalational agents, hemodynamic instability, ventilation problems (hypoxemia, hypercarbia), metabolic derangements, or hypothermia.

Postoperative Care and Complications

Because of decreased cardiorespiratory reserves, elderly patients have an increased risk of postoperative complications, such as myocardial infarction (leading cause of death in patients above 80 years), aspiration pneumonia, deep vein thrombosis and pulmonary embolism, and stroke. Postoperative pain should be adequately treated as it may cause tachycardia and increase myocardial oxygen demand. Similarly, shivering also increases myocardial oxygen demand (at least by 25–38 % in elderly patients). As the metabolic rate is slower in the elderly, patients may have a longer stay in the recovery unit.

Postoperative Stroke

Postoperative stroke is a significant cause of altered mental status and morbidity following surgery. Conditions that are associated with an increase in the incidence of stroke include cerebral arteriosclerosis, carotid occlusion, hypertension, and diabetes, as well as intra/postoperative hemodynamic instability or hypoxemia. Compared to younger aged patients, the overall incidence of stroke is 1.5 times higher in individuals 65–74 years, 2 times in patients 75–84 years, and 3 times in patients aged 85 years or more. Perioperative stroke risk increases from 0.2 % in patients less than 65 years of age to 3.4 % in patients more than 85 years of age.

Postoperative Delirium

Postoperative delirium is a common occurrence in elderly patients. Elderly patients are predisposed to delirium due to the brain aging process (decreased cerebral mass or synthesis of neurotransmitters). Postoperative delirium is characterized by severe disturbances in attention, orientation, perception, arousal, and intellectual function. It is often associated with excitement and agitation (hyperactive delirium), which may be followed by periods of lethargy and unawareness (hypoactive delirium). Patients may require the use of restraints to prevent injury to themselves or care providers, and to prevent falls or pulling out lines and tubes.

Specific causes contributing to delirium and agitation, such as arterial hypoxemia or hypercapnia, presence of pain, preexisting dementia, bladder distention, alcohol and sedative withdrawal, dehydration and hypovolemia, sepsis, and metabolic disturbances (hyper- or hyponatremia), as well as possible pharmacological causes, should be ruled out. Tools for diagnosis of delirium include Confusion-Assessment Method (CAM-ICU), Mini Mental-State Examination (MMSE), or the memorial Delirium Assessment Scale.

Fortunately, most incidences of delirium are time limited and ultimately resolve. Delirium prevention should start in the operating room by maintaining hemodynamic stability, providing adequate oxygenation, maintaining hydration, optimizing the acid base status, minimizing electrolyte abnormalities, and administering appropriate drug dosages during the operation. Laboratory measurements of glucose and electrolytes and an arterial blood gas should be performed as necessary. Treatment of delirium should consist of maintaining the ABCs (airway, breathing, circulation). Pharmacological treatment of delirium includes administration of haloperidol 1–2 mg IV, which may be repeated every 15–20 min. Side effects of haloperidol include extrapyramidal effects (which may be confused with agitation) and prolonged QT interval. Delirium due to anticholinergics (for example, scopolamine), termed as "anticholinergic syndrome," is treated with physostigmine (10–30 mcg/kg, IV), whereas delirium due to sedatives and analgesics can be treated by using an alpha-2-agonist.

Clinical Review

1. Elderly patients, compared to younger patients, have a
   A. Normal resting cardiac output
   B. Similar maximal heart rate
   C. Decrease in SVR
   D. Similar beta-adrenergic response
2. Elderly patients, compared to younger patients, have a
   A. Similar FRC
   B. Increase in $PaCO_2$
   C. Similar PaO_2
   D. Similar total lung capacity
3. Incidence of post dural puncture headache in elderly patients, when compared to younger patients, is
   A. Similar
   B. Higher
   C. Lower
   D. Variable
4. Pharmacological treatment of postoperative delirium includes, mainly, the administration of
   A. Midazolam
   B. Clonidine
   C. Lorazepam
   D. Haloperidol

Answers: 1. A, 2. A, 3. C, 4. D

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Pulmonary Aspiration and Postoperative Nausea and Vomiting

44

Paul C. Anderson and Li Meng

Pulmonary aspiration and postoperative nausea and vomiting (PONV) are two critical issues in anesthesia that have received considerable attention over the past several years. Aspiration is a rare but serious complication that has the potential to result in devastating consequences for the patient. PONV, on the other hand, is extremely prevalent and is the most feared aspect of surgery and anesthesia for patients.

Pulmonary Aspiration

Pulmonary aspiration occurs when gastric contents are refluxed and then subsequently spill into the tracheobronchial tree and lung fields. In order for true aspiration to occur, the gastric contents must be of sufficient volume, and must move from the stomach into the esophagus (reflux), then into the pharynx, through the larynx, and finally down into the lungs. Acidic gastric matter within the pulmonary tree can then cause significant damage to the protective mucosal barrier, leading to subsequent edema and vulnerability to infection.

Fortunately, pulmonary aspiration is an extremely rare event, with incidence of about 1 in 6,000–8,000 general anesthetics. The majority of perioperative aspirations occur during induction of anesthesia. The effects of pulmonary aspiration are often very serious. Consequences may include significant morbidity, mortality (5 % of those who develop aspiration pneumonia), unplanned hospital admission, ICU admission, escalation of care, and case cancellations.

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Clinical Signs and Risk Factors

Clinical signs of pulmonary aspiration may include coughing, gagging, wheezing, rales and rhonchi, tachypnea, hypoxemia, cyanosis, pink/frothy sputum, and refractory laryngospasm. Signs appear within 1 h after aspiration in 90 % of patients, and within 2 h in nearly all patients. Radiographic findings may often include extensive, bilateral involvement of the lungs; however, these changes may not be evident until 6–24 h later and can often lag behind the patient's clinical changes.

There are a number of risk factors for aspiration, including emergency surgery (3–4*x* risk), recent oral intake, higher ASA score, pediatric and elderly ages, female gender, pregnancy, obesity, decreased consciousness, dysphagia, gastrointestinal and esophageal disease, and diabetes mellitus. Infants and children are at elevated risk, especially due to the higher incidence of gastroesophageal reflux disease (GERD) in neonates (50 %), the transient pharyngeal weakness of newborns, and the higher rates of swallowing dysfunction in pediatric populations. Increased gastric volume (often from recent oral intake) is a major risk factor for aspiration. It is recommended that healthy, fasting patients have gastric volumes no more than 1.6 ml/kg prior to elective surgery. However, assuming a gastric pH of <2.5, only one-fourth of this volume (about 0.4 ml/kg, or roughly 25 ml) is required to reach the trachea/airways before significant pulmonary injury occurs. Lower gastric pH, especially pH less than 2.5, is also a prominent risk factor for pneumonitis—as the pH of the gastric matter decreases, a smaller volume of aspirated material will cause significant damage to the lungs.

With regard to airway devices, it has been established that supraglottic airway devices, such as laryngeal mask airways (LMAs), do not offer an airtight laryngeal seal. They are, therefore, contraindicated if there is serious concern for regurgitation of gastric contents (for example, in trauma patients). However, a recent study showed that in selected patients, LMAs do not increase the risk of aspiration in comparison to endotracheal tubes. Anesthesia providers must be prudent in

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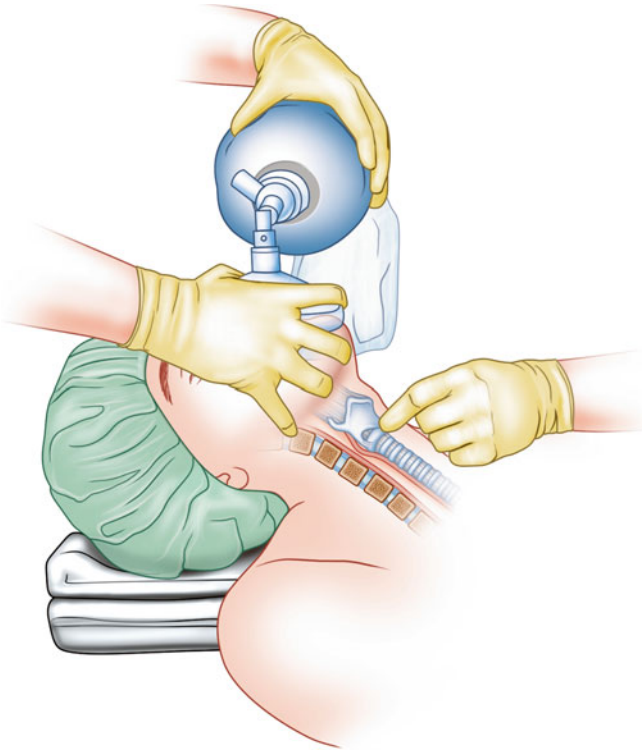

Fig. 44.1 An assistant applies cricoid pressure to prevent aspiration during rapid sequence intubation

deciding which patients are appropriate for alternative airway devices, such as LMAs, and it appears that the airway device alone does not increase the risk of aspiration.

Prevention

A great deal of research has been dedicated towards preventing aspiration from occurring. The American Society of Anesthesiologists Task Force on Preoperative Fasting has made several recommendations to help minimize the risk of clinically significant aspiration. Specifically, it recommends a thorough preoperative assessment (including review of medical records, history, and physical exam) to evaluate risks for regurgitation and aspiration. Additionally, except for patients undergoing emergent surgeries, patients should abide by the following fasting guidelines:

- No clear liquids for 2 h before surgery
- No breast milk for 4 h
- No infant formula or nonhuman milk for 6 h
- No eating for at least 6 h

The Task Force does not recommend routine preoperative use of antiemetics, gastric acid blockers, or gastrointestinal stimulants for patients without elevated risk for aspiration. For patients at elevated risk for aspiration, evidence for prophylaxis has been mixed. Most physicians seem to favor pharmacologic agents that decrease gastric pH and gastric acid production, such as antacids, H_2 blockers, and proton pump inhibitors. Metoclopramide, which increases gastric emptying and lower esophageal sphincter tone, is also sometimes used although it provides inconsistent benefits.

Among the most well-known methods for preventing aspiration is the rapid sequence intubation (RSI) technique. This sequence includes preinduction oxygenation, applying firm cricoid pressure during the intubation process (Sellick maneuver, Fig. 44.1), and securing the airway. Despite its common usage, this method has not actually been prospectively proven to decrease the frequency of aspiration, and many practitioners question its effectiveness.

Another means that could eventually screen for patients at high risk of aspiration is gastric sonography. Perlas et al. recently devised a simple, 3-point grading system (based upon two ultrasound views) that can predict a patient's gastric residual volume prior to intubation. This information may then be used to classify patients into risk groups based on their residuals. After applying their new method, they determined that approximately 43 % of preoperative, fasted patients truly had empty stomachs, 53.5 % had small residuals (still considered safe for surgery), while 3.5 % of patients had gastric residuals beyond the recommended safe limit. Work remains to be done in developing this method, but it certainly appears to have promise for evaluating a patient's risk of aspiration and guiding subsequent decisions.

Treatment

If pulmonary aspiration does occur, treatment includes suctioning the upper airway, considering use of a bronchoscope (if there is solid matter within the airways), and continuing to provide supportive respiration and oxygenation. Endotracheal intubation may be necessary to maintain gas exchange. Tracheal secretions should be cultured. Antibiotic decisions are often based on the culture results, and empiric antibiotics are only recommended if the patient has aspirated grossly contaminated matter. Steroids should probably not be used since they may potentiate the development of secondary pneumonia or sepsis. Additionally, neutralizing agents should not be administered.

Postoperative Nausea and Vomiting

Postoperative nausea and vomiting (PONV) is defined as nausea or vomiting occurring within 24 h after completion of surgery. The overall incidence of PONV in surgical patients who have not received prophylaxis is approximately 25–35 %, while up to 70–80 % of high-risk patients experience PONV. Postdischarge nausea and vomiting (PDNV), which

is particularly relevant to patients undergoing ambulatory surgery, refers to nausea and vomiting occurring within 72 h after surgery. The incidence of PDNV has been quoted at 20–50 %, including 17 % and 8 % of patients who experience nausea and vomiting after discharge, respectively.

Avoiding nausea and vomiting after surgery is an extremely important issue for patients. In fact, patients rated nausea/vomiting as their biggest fear during the perioperative period—even above concerns of death, perioperative pain, myocardial infarction, and stroke. In addition to patient dissatisfaction and discomfort, PONV can have grave effects on patient outcomes. It is among the leading causes of unanticipated hospital admission and can lead to delays in discharge, readmissions to the hospital, compromised mobility, respiratory problems (aspiration, pneumonia, pneumothoracies), wound dehiscence (tension on suture lines), surgical bleeding, subcutaneous emphysema, and esophageal rupture among other things. PONV also leads to hundreds of millions of dollars of added healthcare expenses each year.

Risk Factors

There are a number of risk factors which predispose a patient to PONV. Identified risks include female gender, nonsmoking status (1.5–2.5 times risk), age (5 % incidence in infants, 25 % in children <5 years old, 40–50 % in 5–15 year olds, and 20–40 % in adults), history of motion sickness, history of PONV, obesity, anxiety, history of migraines, duration of surgery, use of narcotics during surgery and/or postoperatively, intraoperative use of volatile anesthetics and/or nitrous oxide, decreased administration of fluids during surgery, hypotension, and use of anticholinesterases (>2.5 mg neostigmine). Surgeries that predispose patients to PONV include laparoscopic procedures (especially gynecological), intra-abdominal surgeries, head/neck surgeries, strabismus repair, neurosurgeries, shoulder procedures, dental surgeries, and varicose vein stripping.

Recently, models have been developed that incorporate these risk factors to predict the likelihood of a patient experiencing PONV. Among such models, the Apfel score is the best known and most widely used. This model assigns one point for each of the following patient characteristics: female gender, nonsmoker, history of motion sickness or PONV, and plan to use postoperative opioids. When 0, 1, 2, 3, or 4 of the risk factors are present for a given patient, his/her risk of experiencing PONV is approximately 10 %, 20 %, 40 %, 60 %, or 80 %, respectively. The Koivuranta score and the Eberhart score (specifically for pediatric patients) have also been developed as alternative risk models. All three models have gained popularity because they are very simple and easy to apply—they all use only 4–5 risk factors to calculate a prediction score, with each factor worth exactly one point.

The Apfel, Koivuranta, and Eberhart scores, among other risk models, were developed to minimize unnecessary administration of prophylactic antiemetics. Like all medications, antiemetics have costs, side effects, and variable efficacies. Proponents of the Apfel score and other risk prediction models argue these tools are useful for determining which patients should versus should not be given antiemetic prophylaxis. The Apfel score is often applied in conjunction with recommendations from the "Society for Ambulatory Anesthesia Guidelines for the Management of Postoperative Nausea and Vomiting," and the "Consensus Guidelines for Managing Postoperative Nausea and Vomiting." These documents recommend not providing prophylaxis to low-risk patients, giving one or two antiemetics to moderate-risk patients, and administering two or more antiemetics from different classes to those patients at highest risk of PONV. Propofol can also be used throughout the case for total intravenous anesthesia (TIVA), and this allows for one less antiemetic to be given. When applied to help guide decision making regarding prophylaxis, Apfel's model has been shown to be efficacious and efficient in decreasing PONV in adults.

Despite this evidence, many clinicians support a more liberal use of antiemetics for preventing PONV. They strongly emphasize the low cost, benign side effects, and impressive efficacy of the available antiemetic drugs. Given the essential need to avoid PONV, it is recommended that all surgical patients be treated with at least two antiemetics. The risk factors should certainly be considered and applied to help guide decision making, but physicians should not be restricted to risk models (with inherent limitations) to predetermine their actions.

Antiemetic Therapy

Nausea is a very complex phenomenon, and it can be triggered from multiple centers—the lateral reticular formation of the medulla, chemoreceptor trigger zone (CRTZ) in the area postrema, nucleus tractus solitarius (NTS), vestibular system, higher cortical regions, cerebellum, glossopharyngeal nerve, and vagal nerve (Fig. 44.2). There are multiple receptors that contribute to the sensation of nausea, including serotonin, histamine, acetylcholine, and dopamine. This explains why such a wide variety of pharmaceuticals have shown benefit in preventing and treating nausea and vomiting (Table 44.1). It is important to note that drugs from different classes work additively (but not synergistically), and they can be combined safely as they do not usually interact with one another.

Among the most widely used antiemetics are the 5-HT_3 antagonists (ondansetron). Other drugs in this class include dolasetron, granisetron, and palonosetron. These drugs are

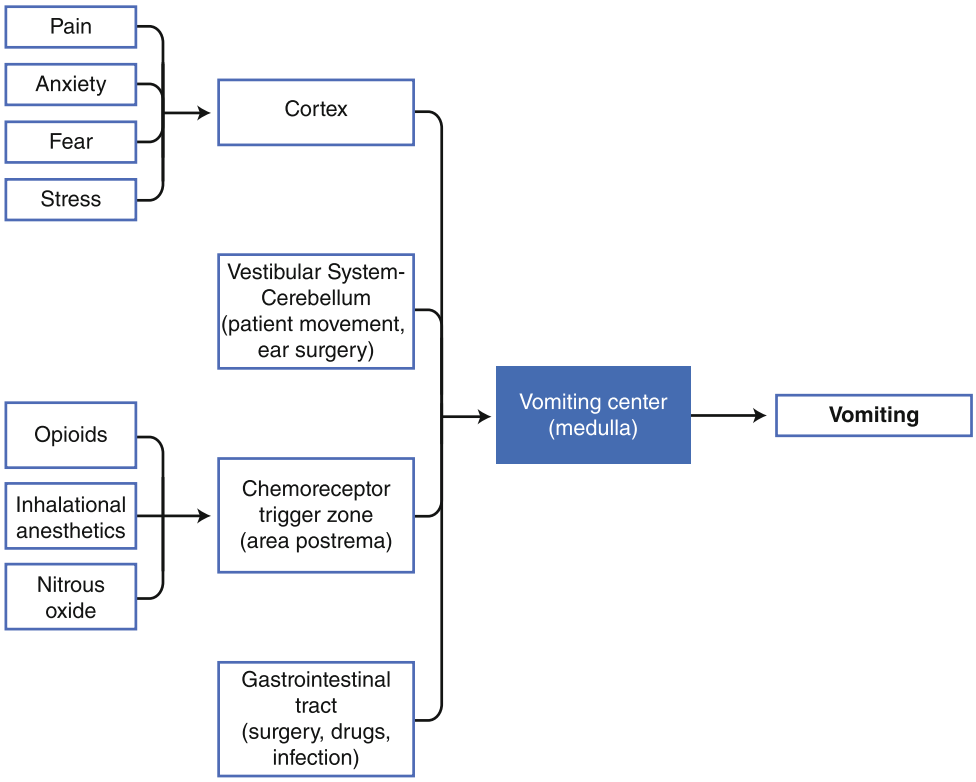

Fig. 44.2 Mechanism of nausea and vomiting

effective for both nausea and vomiting prophylaxis. They are equal in efficacy to dexamethasone and droperidol, and superior to promethazine, prochlorperazine, scopolamine, and propofol when used as single agents. They are also relatively inexpensive and have a very favorable safety profile, with headache and transient electrocardiogram (ECG) changes being the most common side effects. When given for prophylaxis, 5-HT_3 antagonists should preferably be administered within the last hour of surgery. Palonosetron, the newest drug within this class, has been shown to have a stronger affinity and significantly longer half-life (40 h) than the other 5-HT_3 antagonists. Unlike the other 5-HT_3 antagonists, it has not been shown to increase the QTc interval. It is not surprising that palonosetron is quickly becoming an attractive option for outpatient surgeries, where prolonged antiemetic effects are often desired.

Another popular antiemetic is dexamethasone, a glucocorticoid agent. When used for prophylaxis, it should be given at the time of induction or shortly afterwards since its effects require several hours. Dexamethasone is at least as effective as ondansetron and droperidol for preventing nausea and vomiting—each of the three agents reduces the relative risk of PONV by approximately 25 %. However, dexamethasone is not effective as a rescue agent for already established nausea/vomiting.

Many years ago, droperidol was among the most widely used antiemetics, and for good reason!—it is extremely cheap and very effective against both nausea and vomiting. However in 2001, several decades after droperidol was approved for use, the FDA issued a black-box warning due to droperidol's potential to cause QT prolongation and subsequent arrhythmias, including torsades de pointes. This essentially eliminated droperidol as a drug used for routine prophylaxis or treatment of PONV since it required a preoperative ECG as well as constant telemetry monitoring for 2–3 h after completion of surgery. It is now used as a last resort for refractory nausea and vomiting. Droperidol's black-box warning has been challenged by the anesthesia world, as many experts do not think the warning is appropriate for typical prophylaxis dosages.

Scopolamine, an anticholinergic drug, is another drug that can be used as prophylaxis against nausea and vomiting. It is constantly released over 72 h when applied via a transdermal patch, placed usually behind the ear. This makes it an attractive adjuvant option for outpatient surgeries, when prolonged antiemetic effects are desired. It provides additional prophylactic benefit when added to either intraoperative ondansetron or dexamethasone. Its side effects include vision changes, dry mouth, and dizziness.

There are a number of promising new antiemetics drugs, some of which are still being investigated. Among these drugs are the NK1-RAs, which include aprepitant (FDA approved), rolapitant, and casopitant (still being investigated). Aprepitant is nonsedating, does not cause QTc prolongation, and has a relatively long half-life. Furthermore, it has been shown to have greater antiemetic effect than any

Table 44.1 Antiemetics

Class/mechanism of action	Drug	Efficacy	Side effects	Comments
Serotonin ($5\text{-}HT_3$) antagonists	Ondansetron (Zofran), granisetron, dolasetron, tropisetron, palonosetron	All agents are equally effective • Ondansetron is equal to dexamethasone and droperidol in efficacy • Palonosetron has stronger affinity and longer half-life	• Minimal • Mild headache, constipation, dizziness • Asymptomatic QT prolongation, increased LFTs • Does not cause sedation	• Best when given near end of surgery for prophylaxis • Best agent for pediatric patients • Most effective when combined with other agents • Better antivomiting than antinausea effects
Glucocorticoids	Dexamethasone	• Very effective as prophylactic agent, but not as rescue treatment • Equal to ondansetron and droperidol in efficacy	• Usually no adverse effects if given as a single dose (2–10 mg) • Occasional insomnia, mood changes, anxiety, GI upset	• Best if given prior to induction
Butyrophenones	Droperidol, haloperidol	• Equal efficacy to ondansetron in prophylaxis and rescue treatment • Prevents PONausea and POVomiting equally well	• QT prolongation, sedation, hypotension, tachycardia	• Should be given at end of surgery • Has relatively short-lived effects
Anticholinergics	Transdermal scopolamine (TDS) patch	• More effective as a prophylactic agent • Helps prevent both nausea and vomiting • Requires 2–4 h to take effect	• Visual disturbances, dry mouth, dizziness, constipation, confusion	• Apply in evening before surgery, or 4 h prior to end of surgery
Antihistaminics	Diphenhydramine (Benadryl), Promethazine (Phenergan), Meclizine	• Insufficient quality data to support efficacious use for prophylaxis	• Sedation	
Dopamine antagonists	Prochlorperazine (Compazine)		• Extrapyramidal symptoms, dystonia • Hypotension • Sedation, lethargy	
Benzamides	Metoclopramide (Reglan)	• Less effective than ondansetron and droperidol • Not a first-line agent	• Extrapyramidal symptoms, dystonia, akathisia • CV effects • Sedation	• Not commonly used due to side effects • Increases rate of gastric emptying (useful for gastroparesis) • Contraindicated in Parkinson's disease
Neurokinin-1 antagonists	Aprepitant, Fosaprepitant	• Works for up to 24 h	• Headache, fatigue, dizziness • Elevated LFTs	• Work best when combined with $5\text{-}HT_3$ antagonists and dexamethasone

other drug when used alone. When compared to ondansetron, it was shown to have equal efficacy at preventing nausea, yet superior ability to prevent vomiting. The NK1-RAs may be especially useful for patients with very high risk of developing PONV as well as those who have not responded to other drug classes.

Aside from the plethora of medications used for PONV, there are also some nonpharmacologic therapies which have been shown to be effective. These include acupuncture, acupoint stimulation, acupressure, and transcutaneous electric nerve stimulation. These interventions are recommended as possible adjuvant therapies to pharma-ceuticals.

Recommendations

The "IMPACT" trial showed that ondansetron, dexamethasone, and droperidol are all equally effective, and they each reduce the risk of PONV by about 25–30 %. TIVA has also been shown to be nearly effective (19 % risk reduction). These treatments may be used in any combination, since they work independently of each other and have additive effects. Dexamethasone and ondansetron seem to be excellent first-line choices for prophylaxis of PONV since both drugs are relatively cheap, safe, and effective. For the high and highest risk patients, multimodal therapy such as dexamethasone, ondansetron, TIVA, aggressive administration of IV fluids, and minimizing use of volatile anesthetics, opioids, and nitrous oxide may be recommended. If patients do end up experiencing PONV (including those that failed prophylaxis), then rescue therapy should be provided. Administering repeated or increased doses of the same drug class usually provides no further benefit. Therefore, if a patient does get sick, he/she should be treated with an agent that has not yet been tried.

Clinical Review

1. Prominent risk factor for developing pneumonitis is a gastric pH of
   A. Less than 2.5
   B. 2.5–3.0
   C. 3.1–3.5
   D. Greater than 3.5
2. Correct statement about pulmonary aspiration is
   A. A chest radiograph taken immediately after aspiration is diagnostic of pulmonary aspiration
   B. Risk of pulmonary aspiration is higher in children than adults
   C. The ASA Task force recommends the routine use of metoclopramide or H_2 blockers to prevent the effects of pulmonary aspiration
   D. Patients with pulmonary aspiration should be routinely treated with antibiotics and steroids
3. All of the following are risk factors for developing PONV EXCEPT
   A. Anxiety
   B. Nonsmoker
   C. Female patient
   D. Laparoscopic surgery
4. A 46-year-old female patient underwent a laparoscopic surgery under general anesthesia. Intraoperatively, she received 8 mg of dexamethasone, 8 mg of ondansetron for prophylaxis against nausea and vomiting. Postoperatively, the patient is complaining of nausea. Your initial step in management would be to
   A. Give an additional 4 mg of dexamethasone
   B. Give an additional 4 mg of ondansetron
   C. Treat pain
   D. Give 20 mg of propofol
5. All of the following statements about PONV are correct, EXCEPT
   A. Treatment of PONV should consists of two or more drugs
   B. Adequate perioperative hydration can prevent nausea and vomiting
   C. Effective treatment of pain can prevent nausea and vomiting
   D. Dexamethasone is an effective *rescue* agent for the treatment of nausea and vomiting

Answers: 1. A, 2. B, 3. B, 4. C, 5. D

Further Reading

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Acid Base Balance

45

Kristi D. Langston and Jonathan H. Waters

Management of acute acid-base changes is a common part of the practice of anesthesiology. Historically, analysis of these changes focuses on the Henderson–Hasselbalch equation and the relationship among the three parameters—pH, PCO_2, and HCO_3^-. Respiratory changes are easily recognized and treated by changes in the partial pressure of CO_2. Metabolic changes are easily recognized by bicarbonate or base excess (BE) abnormality; however, the treatment is not simple because the bicarbonate or BE is only a reflection of the actual problem. For example, a lactic acidosis will cause a change in bicarbonate, and if only looking at the bicarbonate, this lactic acidosis cannot be differentiated from a hyperchloremic metabolic acidosis. Unlike PCO_2, HCO_3^- is not an independent determinant of pH. In other words, we know that by changing the ventilator setting we can change the PCO_2 and directly change the pH; however, a similar relationship between HCO_3^- and pH does not exist.

The clinician can gain further information as to the cause of a metabolic problem through use of the anion gap. The anion gap is based on the concept of electroneutrality, that is, the sum of the cations must equal the sum of the anions in solution. The classic acid-base theory focuses on electroneutrality and the Henderson–Hasselbalch equation, but unfortunately, reliance on these two concepts fails to identify the independent determinants of metabolic acid-base change.

In this chapter a brief overview of classic acid-base theory will be discussed, and a new approach, the "physicochemical" acid-base approach will be introduced. This approach incorporates the Henderson–Hasselbalch equation and electroneutrality but rearranges the importance of each in acid-base analysis. This new approach identifies the independent determinants of pH, and by determining these variables, a better understanding is gained of the impact that fluid and electrolyte management have on acid-base status.

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Classic Acid-Base Theory

Henderson–Hasselbalch Equation

Traditionally, assessment of $[H^+]$ or pH abnormalities has focused on the Henderson–Hasselbalch equation and its two primary components, PCO_2 and HCO_3^-.

$$\mathrm{pH} = \mathrm{p}K_a + \log\left[\mathrm{HCO_3^-}\right] / \left[\mathrm{CO_2}\right]$$

$$\left(\mathrm{pK_a\ is\ the\ negative\ log\ of\ the\ acid\ dissociation\ constant}\right)$$

From this equation, respiratory disorders are defined by changes in CO_2 and metabolic disorders result from changes in the HCO_3^-. Increases in CO_2 cause a respiratory acidosis while decreases in CO_2 cause a respiratory alkalosis. Similarly, an increase in HCO_3^- causes a metabolic alkalosis and a decrease causes a metabolic acidosis. From this it would appear that by this equation, $[H^+]$ is determined by two variables, CO_2 and HCO_3^-.

By reviewing the derivation of the Henderson–Hasselbalch equation we discover that these two variables are interdependent and not independent as these definitions would suggest. The Henderson–Hasselbalch equation is derived from the carbonic acid equilibrium and its associated equilibrium equation.

$$\mathrm{CO_2 + H_2O = H_2CO_3 = HCO_3^- + H^+}$$

$$\left(\mathrm{carbonic\ acid\ equilibrium}\right)$$

$$\mathrm{K\ (equilibrium\ constant) = [CO_2][H_2O]/[H^+][HCO_3^-]}$$

$$\mathrm{(equilibrium\ equation)}$$

From this equilibrium, it is seen that an increase in CO_2 results in hydration of the CO_2 and an increase in H_2CO_3. The

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H_2CO_3 will partially dissociate yielding equimolar quantities of H^+ and HCO_3^-. Both changes will be dictated by the equilibrium equation and its associated constant. As a result a change in CO_2 must be matched by a change in HCO_3^-. Thus, CO_2 and HCO_3^- are dependent on each other and not truly independent determinants of pH as is commonly implied.

Metabolic Indices

The CO_2–HCO_3^- relationship has resulted in the proposal of multiple metabolic indices. These indices are intended to circumvent the CO_2–HCO_3^- relationship. One of these indices is the standard bicarbonate concentration (SBC). The SBC attempts to correct for the interrelationship by standardization of the CO_2. By exposing a blood sample to CO_2 at a partial pressure of 40 mmHg, the sample will equilibrate to this standard CO_2 partial pressure. From this standardization, any deviation of the HCO_3^- from normal will be an indicator of a nonrespiratory problem. In 1960, Siggaard-Andersen proposed that the BE be the standard metabolic index.

Anion Gap

When using the SBC or the BE, the origin of a metabolic deviation is left unexplained. For instance, an abnormal BE would not tell a clinician whether a metabolic acidosis is a result of ketoacidosis, lactic acidosis, or hyperchloremia. For further understanding of a metabolic acidosis, the anion gap is utilized.

The anion gap is based on the concept of electroneutrality. The sum of the positive ions and the negative ions in a solution must be zero, (Σcations = Σanions). In other words, any body fluid will have no net charge. This charge balance means that the charge of Na^+, K^+, Mg^{2+}, Ca^{2+}, and H^+ must be balanced by an equal and opposite charge of Cl^-, SO_4^{2-}, PO_4^{3-}, CO_3^{2-}, HCO_3^-, OH^-, lactate, and the charges on the proteins. The anion gap can be defined as

$$\text{Anion gap} = \left[Na^+\right] - \left(\left[Cl^-\right] + \left[HCO_3^-\right]\right)$$

$$= \text{Unmeasured anions} - \text{Unmeasured cations}$$

By this definition K^+, Ca^{2+}, and Mg^{2+} have been relegated into a grouping of unmeasured cations. Likewise, SO_4^{2-}, PO_4^{3-}, lactate, and the proteins have been grouped into unmeasured anions. An increase in anion gap represents an increase in unmeasured anions or a decrease in unmeasured cations, and a decrease in anion gap can be caused by a decrease in unmeasured anions or an increase in unmeasured cations.

Traditional Approach of Arterial Blood gas Analysis

Arterial blood gases are routinely used to assess acid-base disturbances, which can be analyzed as follows (Fig. 45.1, Table 45.1):

1. pH—The normal pH is 7.35–7.45. A blood pH less than 7.35 is termed as acidosis, while a pH higher than 7.45 is termed as alkalosis.
2. $PaCO_2$—The normal $PaCO_2$ is 35–45 mmHg. A $PaCO_2$ less than 35 mmHg is termed as respiratory alkalosis, while a $PaCO_2$ more than 45 mmHg is termed as respiratory

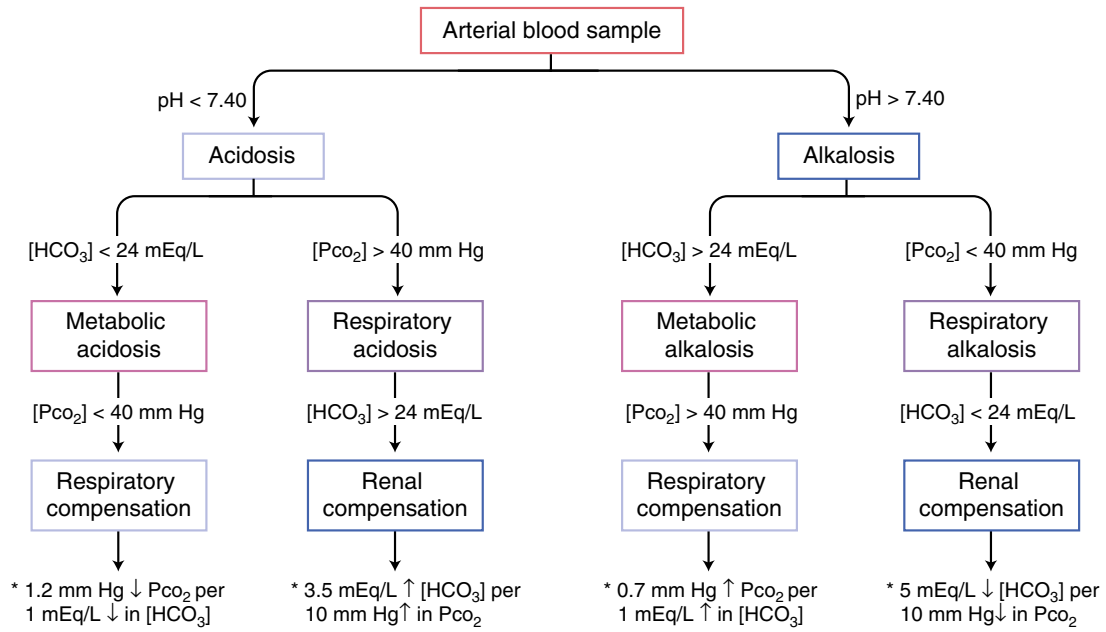

Fig. 45.1 Approach to determine acid-base disorder

acidosis. Adequacy of ventilation can be assessed by calculation of the dead space (V_D) to tidal volume (V_T) ratio, using the Bohr dead space equation:

$$V_D / V_T = \left(P_A CO_2 - ETCO_2\right) / PACO_2,$$

the normal ratio should be less than 0.3

3. PaO_2—Hypoxia is defined as a $PaO_2 < 60$ mmHg. Adequacy of ventilation can be assessed by measuring the
   (a) Alveolar-arterial gradient of oxygen: $PAO_2 - PaO_2$

$$PAO_2 = \left(\begin{array}{l}\text{atmospheric pressure} - \\ \text{water vapor pressure}\end{array}\right) \times FiO_2 - PaCO_2 / 0.8$$

   where 0.8 is the respiratory quotient and is the ratio of CO_2 produced to O_2 consumed. Normally, about 80 % of CO_2 is produced for 100 % O_2 consumed (200 ml CO_2:250 ml of O_2)
   (b) Ratio of PaO_2:FiO_2, the P/F ratio. The lower the ratio, the worse the oxygenation. A P/F ratio less than 300 denotes acute lung injury, whereas a P/F ratio less than 200 denotes ARDS.
4. HCO_3—The normal HCO_3 is 22–26 mmol/L. A HCO_3 less than 22 is termed as metabolic acidosis, while a HCO_3 more than 26 is termed as metabolic alkalosis.
5. Assess compensatory changes.

Regulation of pH in the Body

Regulation of pH or the hydrogen ion concentration in the human body occurs mainly via three processes: the buffer systems, central and peripheral chemoreceptors, and the renal system. Causes and compensatory mechanisms for acid base disturbances are summarized in Tables 45.2 and 45.3. Adverse effects of acid-base disturbances are summarized in Table 45.4.

Buffer Systems

Buffers are chemicals/substances which tend to maintain the pH of the body fluids at 7.4. The main buffer systems in the body are the bicarbonate and the hemoglobin buffer systems. Additionally, some proteins and phosphate also have buffering capabilities.

Table 45.1 Simplified approach to blood gas analysis (approximate equality)

pH, normal 7.4	Is there an acidosis or alkalosis
$PaCO_2$	Is the change in $PaCO_2$ consistent with respiratory component; if not, does the change in HCO_3 indicate a metabolic component
Acute respiratory acidosis	10 units increase in $PaCO_2$ = 1 unit increase in HCO_3
Chronic respiratory acidosis	10 units increase in $PaCO_2$ = 4 units increase in HCO_3
Acute respiratory alkalosis	10 units decrease in $PaCO_2$ = 2 units decrease in HCO_3
Chronic respiratory alkalosis	10 units decrease in $PaCO_2$ = 5 units decrease in HCO_3
Metabolic acidosis	1 unit decrease in HCO_3 = 1 unit decrease in $PaCO_2$
Metabolic alkalosis	10 units increase in HCO_3 = 7 units increase in $PaCO_2$

For example, a patient with a pH of 7.27, $PaCO_2$ 60, HCO_3 25, has respiratory acidosis. If the HCO_3 would have been 29, the patient would have chronic (compensated) respiratory acidosis

Table 45.2 Causes and compensation of respiratory acidosis and alkalosis

Respiratory acidosis—increased $PaCO_2$ causing an increase in carbonic acid and hydrogen ions		
Hypoventilation (decreased CO_2 elimination	COPD, asthma, sleep apnea, restrictive lung diseases (fibrosis, sarcoidosis), anesthetics, opioids, scoliosis, obesity, pneumothorax, pulmonary edema	Metabolic compensation • (Acute) Change in pH = 0.008 × change in $PaCO_2$ • (Chronic) Change in pH = 0.003 × change in $PaCO_2$ The kidneys increase H^+ ion secretion and bicarbonate reabsorption over the course of few days to bring the pH to near normal
Increased CO_2 production	Hyperthyroidism, exhausted soda lime CO_2 absorbent, pneumoperitoneum from laparoscopic surgery	
Respiratory alkalosis—decreased $PaCO_2$ relative to bicarbonate		
Hyperventilation (increased CO_2 elimination)	Pain, anxiety, pregnancy, hypoxemia, sepsis, hyperthermia, mechanical ventilation	Metabolic compensation • (Acute) Change in pH = 0.008 × change in $PaCO_2$ • (Chronic) Change in pH = 0.017 × change in $PaCO_2$ – The kidneys compensate by a decrease in bicarbonate reabsorption and an increase in H^+ excretion to bring the pH back to normal in a few days – Increased glycolysis leads to generation of lactic acid – Respiratory alkalosis can cause hypocalcemia and tetany, as plasma proteins bind more calcium in an alkaline pH
Decreased CO_2 production	Hypothyroidism, hypothermia	

Table 45.3 Causes and compensation of metabolic acidosis and alkalosis

Metabolic acidosis—serum anion gap (SAG) is calculated as Na^+-($Cl^- + HCO_3$)		
High anion gap acidosis (>12 meq/L)	Diabetic ketoacidosis, lactic acidosis, cirrhosis of liver, uremia or poisoning due to cyanide, ethanol and salicylates	*Ventilatory compensation* Expected $PaCO_2 = 1.5 \times HCO_3 + 8$ (±2). Increase H^+ ions stimulate the carotid bodies to increase alveolar ventilation, the kidneys increase the secretion of H^+ ions to bring the pH back to normal Measure serum albumin. Hypofibroginemia decreases the anion gap Severe acidosis can be temporarily treated with alkanizing agents, such as sodium bicarbonate, Carbicarb, or THAM
Normal anion gap acidosis (3–12 meq/L)	Excess saline administration, hyperparathyroidism, renal tubular acidosis (bicarbonate loss), diarrhea, pancreatic fistula, or drugs, such as spironolactone and acetazolamide	
Metabolic alkalosis	Loss of hydrogen, chloride and potassium ions, increased metabolism to bicarbonate ions (lactate, citrate, acetate), hypovolemia, hyperaldosteronism, hypercapnia	*Ventilatory compensation* Expected $PaCO_2 = 0.7 \times HCO_3 + 20$ (±1.5) Compensation with alveolar hypoventilation, increased renal tubule reabsorption and decreased secretion of H^+. Kidney needs sodium, potassium and chloride ions (infusions) to effectively excrete excess bicarbonate

Table 45.4 Deleterious effects of respiratory and metabolic acidosis/alkalosis

Respiratory and metabolic acidosis	Hyperkalemia CNS vasodilation, increased ICP Decrease in cardiac contractility, cardiac arrhythmias Increased sympathetic activity (tachycardia, vasoconstriction) Rightward shift of oxyhemoglobin dissociation curve
Respiratory and metabolic alkalosis	Hypokalemia, hypocalcemia Hypoxia Central nervous system excitation Decrease myocardial contractibility, cardiac arrhythmias Neuromuscular irritability Leftward shift of oxyhemoglobin dissociation curve

Bicarbonate: CO_2 combines with water to form carbonic acid; the reaction accelerated by the enzyme carbonic anhydrase. The carbonic acid then dissociates into hydrogen and bicarbonate ions. The bicarbonate reaches the lung, where an opposite reaction occurs. Hydrogen ions are added to the bicarbonate to form carbonic acid, which dissociated into CO_2 and water. The CO_2 is then exhaled.

$$CO_2 + H_2O \xleftarrow{\text{Carbonic anhydrase}} H_2CO_3$$
$$(\text{occurs in the tissues})$$

$$HCO_3^- + H^+ \rightarrow H_2CO_3 \rightarrow CO_2 + H_2O$$
$$(\text{occurs in the lungs and kidneys})$$

Hemoglobin: Hemoglobin also plays a role in buffering CO_2. A similar reaction, as above, takes place in erythrocytes. CO_2 diffuses freely into the erythrocytes, where it combines with water to form carbonic acid. The latter then dissociates into hydrogen and bicarbonate ions. The hydrogen ions are absorbed by the hemoglobin, and the bicarbonate ions are exchanged for chloride (Chloride shift) to maintain electroneutrality. A reverse reaction happens in the pulmonary capillaries, where bicarbonate combines with the hydrogen ions to form carbonic acid and ultimately CO_2, which is exhaled. Also hemoglobin, especially deoxyhemoglobin, can directly combine with CO_2 to form carbaminohemoglobin, which facilitates removal of CO_2 from peripheral tissues.

Chemoreceptors

CO_2 freely passes the plasma membrane of cells. In the brain it decreases the pH of CSF, thereby stimulating the central chemoreceptors causing an increase in minute ventilation. The increase in minute ventilation decreases the $PaCO_2$ and maintains the pH. In addition, the peripheral chemoreceptors, which are present in the carotid bodies and the aortic arch, sense a decrease in blood pH or a decrease in PaO_2 and stimulate the respiratory center in the brain to increase the minute ventilation.

Renal Buffering

Proximal tubule cells of the kidney absorb most of the bicarbonate from the glomerular filtrate and secrete hydrogen ions into the tubules. The kidneys thus regulate the pH by altering the absorption of bicarbonate and the secretion of hydrogen ions. Renal tubal acidosis results from wasting of bicarbonate ions due to a defect in the absorption of bicarbonate. The drug acetazolamide can cause a normal anion gap acidosis by inhibiting the reabsorption of bicarbonate ions in the renal proximal tubule.

The PhysicoChemical Approach

In 1981, Stewart proposed a change in the approach to acid-base problems. He recognized that multiple chemical interactions affect [H^+] and that the carbonic acid equilibrium was just one of these interactions (Fig. 45.2). The focus of

his approach is on the concept of electroneutrality, the basis of the anion gap. He incorporated the multiple chemical equilibria that affect [H^+], including the carbonic acid equilibrium, into a single electroneutrality equation.

From this mathematical development, he found that [H^+] is dependent on three independent variables: (1) the strong ion difference (SID) which is a modified anion gap, (2) the PCO_2, and (3) the total weak acid concentration [A_{tot}], which is primarily composed of protein and phosphate. For most purposes, the weak acid concentration does not change during a surgical procedure, so we can define the CO_2 as the respiratory component which drives pH and the SID as the metabolic component which changes pH.

For simplicity, the SID = [Na^+] + [K^+] − [Cl^-] − [lactate$^-$]

Remembering the law of electroneutrality, we can think of H^+ and OH^- as charge buffers. As the relationship of the strong ions changes, so does the H^+ and OH^- change, as reflected in Fig. 45.2. For instance, an increase in the negatively charged chloride will result in a decrease in the SID and an increase in H^+ to maintain electroneutrality, which results in acidosis. Because of the inverse relationship between H^+ and OH^-, it is sometimes easier to assess pH changes through changes in the basic OH^-. Increased OH^- leads to alkalosis, decreased OH^- results in acidosis.

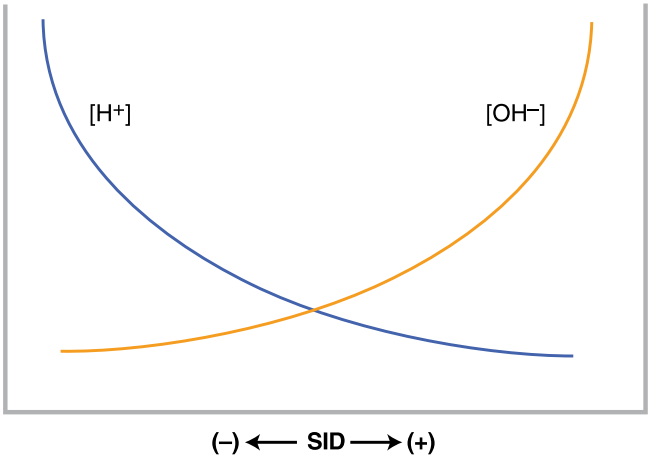

Fig. 45.2 Relationship of SID change and H^+ and OH^- change (SID-strong ion difference)

Specific Metabolic Abnormalities

From this general approach more specific metabolic problems can be addressed. There are three general mechanisms by which SID changes: changing the water content of plasma (contraction alkalosis and dilutional acidosis), changing the Cl^- (hyperchloremic acidosis and hypochloremic alkalosis), and increasing the concentration of unidentified anions (organic acidosis).

SID Free Water Change

Dilutional Acidosis

Development of a dilutional acidosis is best illustrated by an example. If a liter of water contains 140 mEq/L of sodium and 110 mEq/L of chloride then the SID of that solution is 30 mEq. This represents a positive charge excess which needs to be balanced by a negative charge of 30 mEq. Hydroxyl ions (OH^-) act as this charge equalizer. If we were to add another liter of water without adding any more electrolytes, the solution would contain 70 mEq/L of sodium and 55 mEq/L of chloride (Fig. 45.3). Now the SID is 15 mEq. Because we have decreased the positive charge contribution of the SID from 30 to 15 mEq, a fall in OH^- would occur and a "dilutional" acidosis would be seen. In the operating room, dilutional acidosis can theoretically occur as part of the Trans Urethral Resection of the Prostate (TURP) syndrome.

Contraction Alkalosis

Contraction alkalosis can be seen in the perioperative patient who has been fluid restricted or treated with diuretics. It can

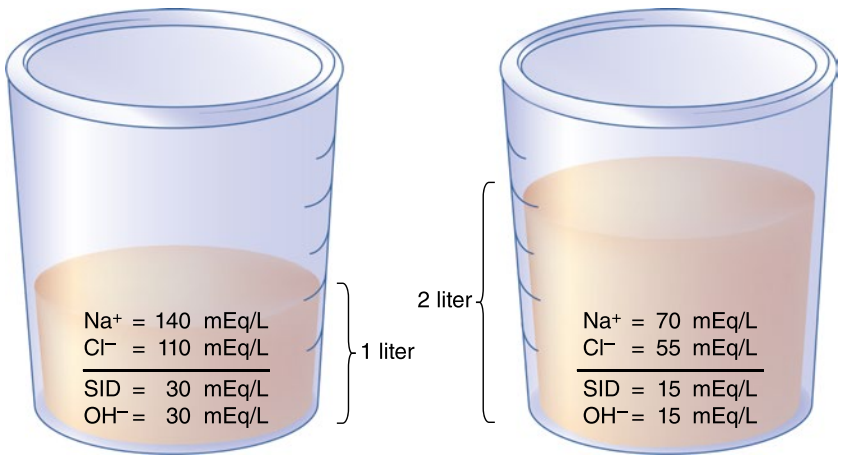

Fig. 45.3 Dilutional acidosis

also be seen intraoperatively if evaporative loss of free water is not replaced. Similar to dilutional acidosis, this problem arises from free water and SID changes. If we return to the original volume of water containing 140 mEq/L of sodium and 110 mEq/L of chloride (as above), and boil off half of the water, it would result in a sodium concentration of 280 mEq/L and a chloride concentration of 220 mEq/L. Now the SID is 60 mEq, and the OH^- "buffer" would increase so that the solution would remain electrically neutral.

Treatment of contraction alkalosis simply requires free water administration in the form of hypotonic solutions. Using the beaker model, treatment can be explained mechanistically. We would now add one liter of 0.45 % NaCl solution containing 77 mEq of Na^+ and 77 mEq of Cl^-. The final electrolyte concentration would contain 238 mEq of Na^+ and 198 mEq of Cl^-, and a SID of 40 mEq. By the use of this hypotonic fluid, we have changed the SID from 60 to 40 mEq resulting in a decrease in the OH^- and a correction of the alkalosis.

SID Chloride Change

Hypochloremia

Chloride shifts occur in relation to gastrointestinal abnormality. If the hyperchloremic gastric contents are lost through vomiting or through gastric tube suction then a hypochloremia can result. Hypochloremia leads to an increase in SID. The positive charge increase associated with the SID must be balanced by an increase OH^-. Treatment can be with normal saline administration. The treatment can be illustrated in the same fashion as free water changes. If we have a 1 L of water with 140 mEq/L of Na^+ and a "hypochloremic" 95 mEq/L of Cl^- then the SID is 45 mEq. If 1 L of normal saline is added, the beaker would then contain 147 mEq/L of Na^+ and 125 mEq/L of Cl^-, with the SID being 22 mEq/L. By shifting the SID, we have shifted the pH in the normal direction.

Hyperchloremia

Hyperchloremia results in an increase in H^+. Hyperchloremia typically results from aggressive normal saline administration. Treatment of the elevated Cl^- and decreased SID would be done by increasing the SID. This could be accomplished through sodium bicarbonate administration. Here, the Na^+ is the effector agent and not the HCO_3^-. The HCO_3^- is a dependent variable and is rapidly excreted as CO_2. Other ways of administering Na^+ with a metabolizable anion are through the use of the sodium salts of lactate, gluconate, acetate, or citrate.

SID Unidentified Anions

SID can also be affected by the presence of organic acids such as lactate or ketoacids. Again, because these negatively charged molecules lower the SID, they result in an acidosis. Treatment is usually focused on stopping the development of acid. Resolution of the abnormal H^+ can also be achieved by increasing the SID using $NaHCO_3$.

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Trauma

46

Phillip Adams and James G. Cain

Anesthesiologists play an integral role in the resuscitation and treatment of patients with traumatic injuries. This subset of patients presents particular challenges. For instance, information about the patient's comorbidities, identity, pertinent past medical, surgical, and social history, and current medications are often unobtainable upon their presentation to the trauma bay. Furthermore, anesthesiologists are removed from the comfort and familiarity of the operating rooms and are required to provide pertinent care in an unfamiliar environment during the early phases of patient resuscitation. Given the often lack of information available, it is important to be involved in the reporting process from the first responders to receive as much information as is possible. In particular, information of specific interest to the anesthesiologist such as airway management difficulties, hemodynamic status during transit, and medications such as paralytics, narcotics, benzodiazepines, and vasoactive medications. One should also have been to the trauma bay at some point prior to being called for a trauma with the opportunity locate and be comfortable with equipment and resources available in the emergency department, facilitating competent management of these acutely ill patients. Activation of operating room staff, transfusion service and the blood bank are also of critical importance.

Epidemiology

Trauma continues to be a leading cause of death throughout the world and is the most common cause of death and disability for those under the age of 35 in the United States. Gunshot wounds, traffic accidents, and falls are the leading causes of mortality associated with trauma. Mortality due to trauma is most often associated with central neurological injury, followed by exsanguination, and finally, multiorgan failure. The injury severity score (ISS) has been used to describe the severity of injury and ranges from 0 (no injury) to 75 (unsurvivable injury). Most published reports show that mortality is most often associated with a mean ISS of ~36–38. The ISS may prove useful in a mass casualty triage situation and in providing an expectation of outcomes to family members; however practically, it is not used to ration care or meter resources in the standard trauma paradigm.

Retrospective reviews have also shown that elderly trauma patients (≥65 years old) have worse outcomes, increased length of hospital stays, and higher mortality rates. Falls and motor vehicle accidents appear to be the largest contributors to geriatric trauma. Motor vehicle accidents of all sorts, including pedestrian and bicycle versus motor vehicle, are the leading cause of pediatric trauma as well, with approximately two-thirds of fatal automobile accidents being attributable to children being incorrectly restrained.

Initial Exam

Initial examination of trauma patients is often referred to as the A, B, C, D, Es of trauma care. This refers to the addition of evaluation of disability or neurological status and well as exposure to the ABC's of standard resuscitation protocols. Upon presentation to the trauma bay, patients initially undergo a primary survey to assess their airway, breathing, and circulatory status. Unstable patients or patients with altered mental status commonly are intubated at the scene. Upon arrival to the hospital, confirmation of correct endotracheal tube placement is vital. Hemodynamically unstable patients may require the immediate administration of crystalloids, colloids, blood products, or vasoactive medications.

A secondary survey then follows consisting of a head to toe examination to identify any and all injuries sustained.

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Table 46.1 Injury Severity Scale (ISS) calculation

Anatomic area	Abbreviated injury score	Square of top 3
Head and neck	1	
Face	1	
Chest	0	
Abdomen	4	16
Extremity	3	9
External	2	4
ISS		29

Table illustrating an example of how to calculate an injury severity scale. This particular patient has had traumatic injuries to his head and neck, face, abdomen, extremities, and skin. The three highest abbreviated injury scores and squared and added together to yield the ISS

Table 46.2 Glascow coma scale

Motor	Verbal	Eye opening
6. Spontaneous	5. Oriented	4. Spontaneous
5. Localizes to pain	4. Confused	3. Verbal stimuli
4. Withdraws to pain	3. Inappropriate	2. Painful stimuli
3. Decorticate posturing	2. Incoherent	1. No response
2. Decerebrate posturing	1. No verbalization (Intubated[a])	
1. No movement		

[a]Intubated patients are appointed a verbal score of 1 with a modifier "t" added to their score to indicate their intubated status [for example, a 6 t for a patient who is intubated (1-non verbal), does not open their eyes (1), and withdraws with painful stimuli (4)]

Several scales exist to quantify the severity of traumatic injuries. The abbreviated injury scale (AIS) looks at several anatomical areas and a score of 1–6 is assigned to the injuries in each area, with 1 being minor and 6 being unsurvivable. The anatomic areas include the head and neck, face, chest, abdomen, extremity, and external surfaces. The three highest scores are then squared and added together to yield the ISS (Table 46.1). The ISS ranges from 0 to 75. Any single score of 6 in the AIS automatically yields an ISS of 75.

Initial Resuscitation

Airway

If a patient is felt to be inadequately oxygenating or ventilating or is unable to appropriately protect their airway, rapid assessment of the patient's airway must occur with a proper plan to establish a controlled and definitive airway. Benumof describes an 11-step examination of the airway to help determine the possibility of difficult intubation. Many of the steps can be performed in the trauma patient.

The length of the upper incisors, presence of an overbite, ability to prognath the jaw, inter-incisor distance, visibility of the uvula, shape of the palate, mandibular space compliance, thyromental distance, and the length and thickness of the neck may be assessed in many trauma patients. The range of motion of the head and neck are usually unable to be evaluated due to cervical spine immobilization.

The American Society of Anesthesiology has modified the 2003 difficult airway algorithm to account for trauma patients. A stable patient with a recognized difficult airway would likely require an awake, fiber-optic intubation. Topicalization of the oropharynx and laryngopharynx with a local anesthetic should be considered as time permits to aid the intubation process, provide patient comfort, and decrease likelihood of coughing and "bucking" after intubation, which risks inadvertent extubation, undesired cervical spine movement, and potentially dangerous hemodynamic swings. The deviation from the traditional difficult airway algorithm is that if the patient is unable to be intubated in this manner, it is unlikely that their surgical procedure can be cancelled or postponed, and surgical acquisition of an airway (awake tracheostomy) would most likely be necessary. Likewise, if the patient is uncooperative, unstable, or unconscious, the ability to awaken them in the event of an unanticipated difficult airway is diminished and the likelihood of requiring a surgical airway is increased.

In the patient without a suspected difficult intubation, there is no evidence that any technique is better than anesthetized intubation with direct laryngoscopy and manual axial inline stabilization (MAIS). Stabilization of the cervical spine is part of the standard of care for trauma patients as approximately 2 % of all blunt trauma patients have a cervical spine injury. The risk of cervical spine injury is increased in patients with a Glascow Coma Score of <8 (Table 46.2). When the decision to intubate a trauma patient has been made, the procedure should be performed with MAIS and concurrent cricoid pressure. An assistant maintains the head and neck in a neutral position while the trachea is intubated to limit the degree of cervical spine motion. Also, trauma patients are treated as full-stomachs because they typically have an unknown last oral intake status, necessitating cricoid pressure and rapid sequence induction. Both MAIS and cricoid pressure have been shown to worsen glottic views with direct laryngoscopy. External laryngeal manipulation, in particular backwards, upwards, and rightwards pressure (BURP) of the thyroid cartilage, was found to improve glottic views. Once intubated, pressure control (PC) ventilation is most often utilized with inspiratory pressures adjusted to maintain tidal volumes of 5–10 cm^3/kg with positive end-expiratory pressure (PEEP) of 5–10 cm H_2O. Caution must be exercised upon initiation of positive pressure ventilation. In an under-resuscitated patient, hemodynamic collapse may occur as the positive ventilation pressures decrease venous return.

In addition to fiber-optic intubation, one has a number of options to facilitate intubation. Devices include Glidescope®, AirTraq® laryngoscope, Bullard, and/or a lighted stylette. Blind nasal intubation can also be performed but is often avoided if there is any suspicion of nasal, nasopharyngeal, or

skull base trauma because of the possibility of inadvertent insertion of the tube into the cranial vault via a fractured cribriform plate. A study performed using fluoroscopic imaging showed decreased cervical motion when the AirTraq® was used as the intubating device when compared to a standard Macintosh blade, which could be beneficial for patients with suspected cervical spine pathology. If blood or excess secretions are present around the glottic opening, visualization with fiber-optic devices such as a fiber-optic bronchoscope or Glidescope® could be greatly reduced. With the presence of blood in the laryngopharynx and the inability to insert a laryngoscope blade or blindly pass a nasotracheal tube due to maxillofacial and nasal trauma, a retrograde wire technique is a possible alternative in a stable patient.

When only partial glottic views are obtained with laryngoscopy, a gum elastic bougie can be used to assist tracheal intubation. Several studies have shown a high success rate when utilizing the gum elastic bougie in cases of difficult intubation. Also, supraglottic devices such as the laryngeal mask airway (LMA), King LT™, and combitube may be considered in the difficult intubation scenario. While not providing a "definitive" airway, they enable ventilation and oxygenation until a definitive airway is obtained. The intubating LMA allows for ventilation of the patient as well as facilitating blind or fiber-optically assisted passage of an endotracheal tube or bougie.

Should insertion of an endotracheal tube, either via laryngoscopy, blind nasal passage, or passage through a supraglottic device not be possible, acquisition of a surgical airway may be indicated prior to aspiration, hypoxemia, or significant hypoventilation. If intubation is unsuccessful and tracheostomy or cricothyrotomy cannot be immediately performed, the availability of a jet ventilator and transtracheal jet ventilation can provide life-sustaining oxygenation until a surgical airway can be obtained. Assurance of intratracheal catheter placement is imperative when performing transtracheal jet ventilation because the massive subcutaneous emphysema that could result from jet ventilation of subcutaneous tissues will only further impair attempts at surgical airway acquisition. One medical provider should be assigned the sole task maintaining the intratracheal position of the transtracheal catheter. Additionally, caution must be undertaken to ensure that there is not an obstruction upstream from the transtracheal catheter such that exhalation is impaired or impossible. Pulmonary hyperdistension can result in pulmonary volutrauma, tracheal injury, or hemodynamic collapse by dynamic hyperdistension.

Circulation

After the establishment of a secure airway and the confirmation of adequate oxygenation and ventilation, attention then turns to circulation. Second only to unsurvivable neurologic injury, exsanguination is a leading cause of death and is responsible for most trauma-related mortality in the early hours after presenting to the trauma bay. Mortality rates were >90 % in the 1970s when massive transfusions were necessitated. With advances in trauma care and transfusion medicine, mortality rates are now between 30 and 70 %.

Adequate venous access is vital to the resuscitation of a trauma patient. According to Poiseuille's Law, venous cannulas that are shorter in length and wider in diameter will allow higher flow rates. Two large bore peripheral intravenous catheters are preferable over smaller diameter access. The location of venous access should be supradiagphragmatic if at all possible so that if there is a need for caval clamping in the event of intra-abdominal trauma, one will still have venous access. Large bore central access, such as 7–9 French catheters allow for the administration of large volumes at high flow rates. If only smaller gauge (that is, 20 gauge) peripheral access can be obtained, a Rapid Infusion Catheter (RIC™) of 6–8.5 French may be considered and can be inserted via Seldinger technique. This is accomplished by inserting a guide-wire through the existing angiocatheter, removing the catheter, cutting the skin to allow passage of the sheath and the dilator, and then removing the dilator leaving only the sheath in the vein. Another option to consider is central venous access with the best option often being the subclavian vein. The subclavian vein is effectively stented open with fibrous interconnective tissue and may be accessed even when markedly hypovolemic. When selecting which side to obtain subclavian venous access, the best choice is to select whichever side might already have a chest tube in place. By doing so, if there is an inadvertent pleural puncture, there will not be the risk for a tension pneumothorax and the need for another chest tube.

If venous access cannot be obtained in a timely fashion, intraosseous (IO) access is another option. There are specific IO kits, but should they not be available, one can use a Tuohy needle. When in the IO space one should be able to withdraw marrow, which can be sent for all venous labs desired. If marrow is unable to be withdrawn, the IO access should be considered malpositioned. Additionally, in a fashion similar to that described with transtracheal catheter ventilation, the IO catheter must be securely fastened. Should it become malpositioned while providing large volumes of fluid, the patient is at significant risk of developing compartment syndrome.

Fluid resuscitation of trauma patients has long been debated. No absolute conclusions have yet been made as to what is the best resuscitative fluid therapy. Ringer's lactate solution (LR) had been the most widely studied isotonic fluid. Isotonic sodium chloride solution (NS) may also be used, but when given in large volumes it can cause hyperchloremic acidosis in patients already predisposed to acidosis. Recent interest in hypertonic saline (HTS) and hypertonic saline with dextrose (HTS-D) has led to several studies. The military utilizes hypertonic saline in the field largely for its

Table 46.3 General management of a patient with trauma

Types of trauma	Blunt, penetrating, chemical, thermal radiation
Evaluation	Triage—primary survey—resuscitation—secondary survey—further care
Patient preparation	Adequate personnel and readiness of the operating room, standard and invasive monitors, intravenous access
Airway management	If the patient is intubated confirm proper endotracheal tube placement, and if not intubated secure the airway. For full stomach a rapid sequence induction is done, and the patient is intubated with in-line neck stabilization. For difficult airway, awake intubation or a cricothyroidotomy/tracheostomy may be required
Patient management	Maintain ventilation and oxygenation, hemodynamics and organ perfusion, euthermia, prevent coagulation abnormalities
Fluids	Crystalloids (normal saline or lactated ringers), colloid (hespan or albumin) or blood products. Use of pressure bags, blood warmer, or a rapid infusion system may be necessary
End point of resuscitation	Normal vitals, urine output, cardiac output, blood pH, mixed venous oxygen saturation

ability to expand intravascular volume significantly more than the equivalent volumes of isotonic saline, thus allowing more effect with less cost in weight carried by medics. Albumin and hydroxyethyl starch at several different concentrations has also been studied. No one fluid has proven to be superior; however, according to one large retrospective study, resuscitation with L-isomer LR may be the least detrimental in terms of invoking less immune dysfunction and electrolyte abnormalities.

Large volume resuscitation has been associated with abdominal compartment syndrome, extremity compartment syndrome, pulmonary edema, and immune system dysfunction as well as other adverse outcomes. Therefore, goal-directed therapy, including fluid resuscitation and vasopressin (4 units IV), has been described to limit these effects. Hypotensive resuscitation by attempting to achieve mean arterial blood pressures between 40 and 60 mmHg has been associated with less blood loss, improved tissue oxygenation, and less acidemia and coagulopathy in patients able to be rapidly transported to Level 1 Trauma Centers to receive definitive care. However, prolonged hypotension (more than 90 min) was associated with increased organ damage. Additionally, all fluids should be warmed as they are infused to prevent hypothermia and worsening of coagulopathy. Significant hypothermia is an independent predictor of morbidity and mortality in trauma patients.

Traditionally, blood product transfusion is started if 2 l of LR or NS is insufficient to reverse the signs of shock. The Assessment of Blood Consumption (ABC) score has been developed and validated by a multicenter study as a predictor of massive transfusion. Massive transfusion has typically been described as transfusing ≥10 units of packed red blood cells (PRBC) within a 24-h period. The ABC score is based on four parameters, each receiving a score of either 0 (absent) or 1 (present). A score of ≥2 is considered positive for predicting massive transfusion. The parameters include a penetrating mechanism of injury, positive focused assessment with sonography for trauma (FAST) exam, heart rate ≥120, and systolic blood pressure ≤90 mmHg. Most trauma centers have developed their own massive transfusion protocol, which should be implemented immediately when massive transfusion is anticipated. This usually involves communicating with the laboratory and the transfusion service, as well as the immediate assessment of the prothrombin time (PT), partial thromboplastin time (PTT), platelets, fibrinogen, and hemoglobin levels. Thromboelastography also offers the ability for relatively rapid assessment of coagulation parameters when compared to the time required for traditional coagulation studies.

The exact ratio of how to administer various blood products is another area of debate. Recent literature, largely driven by studies from the military that have been replicated in civilian trials, has shown improved survival in massive transfusion when a 1:1:1, PRBC:plasma:platelet ratio is implemented. This differs from older ratios of 1:4 for plasma:PRBC and 1:10 for platelet:PRBC. This is due to the theory of trauma-induced coagulopathy, a secondary event felt to be due to consumption and dilution of coagulation factors, acidemia, and hypothermia. This 'lethal triad' is felt to contribute greatly to the morbidity and mortality associated with trauma.

Most recently, early trauma-induced coagulopathy (ETIC) has been introduced based on retrospective evidence of early, elevated PT in trauma patients. ETIC is felt to be due to elevation in tissue factor levels and a disseminated intravascular coagulation (DIC) type pattern and elevated protein C levels from tissue hypoperfusion leading to systemic anticoagulation. However, both the suggested reduced plasma:PRBC:platelet transfusion ratios and ETIC are based on retrospective studies and lack prospective randomized control trials. Nonetheless, the consensus remains that early and aggressive blood product transfusion has been shown to improve outcomes and can be recommended. General management of traumatic injuries is summarized in Table 46.3.

Anesthetic Considerations for Traumatic Injuries By Anatomic Area

Head, Neck, and Spine

The goal of caring for patients with traumatic brain injuries (TBI) is that of preserving cerebral oxygenation. About 50 % of patients succumbing to TBI had a lucid period after the primary brain injury. This indicates that secondary injury plays a significant role in the morbidity and mortality in TBI. Additionally, hypoxemia, hypercarbia, and hypotension have all been implicated in worsening the outcomes. Arterial blood oxygenation, cerebral blood flow (CBF), and cerebral metabolic rate of oxygen consumption ($CMRO_2$) are the three main variables affecting cerebral oxygenation. Cerebral perfusion pressure (CPP) is commonly used as a surrogate measure of CBF, and pulse oximetry can provide information about arterial oxygenation. $CMRO_2$ is not usually measured. When intracranial pressure (ICP) is greater than central venous pressure (CVP), the difference between the mean arterial pressure (MAP) and intracranial pressure (ICP) is the CPP. The optimal CPP has been debated; however, recent studies have shown that pressures $\geq$70 mmHg are associated with improved outcomes. Mannitol, cerebrospinal fluid drainage, and hyperventilation have been shown to optimize CPP in patients with TBI. However, due to the fact that most TBI patients already have lower than normal CBF, prophylactic hyperventilation to a $PaCO_2 \leq 25$ mmHg (as had been the prior cornerstone of treatment) has fallen out of favor, especially within the first 24 h of the insult. Phenytoin reduces the incidence of early posttraumatic seizures due to TBI. Steroids are not recommended for the treatment of TBI.

Patients who have sustained oral, maxillary, mandibular, or other forms of facial trauma present various challenges. First, airway management may be more difficult in this population due to traumatic alteration of their anatomy. Also, the surgical field may be in the area of airway instrumentation, making intraoperative assessment and any needed corrections more difficult. Nasotracheal intubation is sometimes warranted for oral surgery. However, in a patient with a potential skull base fracture, this technique carries the potential of passing the endotracheal tube into the cranial vault via a disrupted cribriform plate. Tracheostomy may be required when surgical access to both the nasal and oral cavities is necessary. An alternative to tracheostomy for these patients is submental intubation, where an oral endotracheal tube exits through the floor of the mouth through a submental incision. This allows for interdental occlusion and unobstructed oral and nasal surgical fields.

Spinal cord injury (SCI) presents challenges such as maintaining immobility and spinal alignment as well as airway challenges. SCIs are most common in the cervical region, followed by the thoracic region, and least common in the lumbar area. Complete SCI, central cord syndrome, and anterior cord syndrome were the most commonly encountered SCI. Surgical decompression of the spinal cord may be emergently indicated. High spinal injury can lead to neurogenic shock, which manifests as hypotension and bradycardia due to sympathectomy and unopposed vagal activity as well as respiratory failure due to lack of respiratory drive. Initial treatment is supportive with intravenous fluid administration, vasopressors, and chronotropes as well as elective intubation for respiratory support. Later treatment may include cardiac and/or diaphragmatic pacing.

Thorax

The goal of managing thoracic trauma is that of preserving oxygen delivery and transport. Critical thoracic structures such as the heart, lungs, and great vessels are all susceptible to injury from both penetrating and blunt trauma.

Pulmonary injuries may result from blunt force. Pulmonary contusions with resultant alveolar hemorrhage and edema may cause significant difficulties in oxygenation and ventilation. In the perioperative or critical care setting an initially easily ventilated and oxygenated patient may become increasingly difficult to oxygenate and ventilate as the effects of the contusion progress and the lungs become less compliant. Fractured ribs may lead to a pneumothorax or hemothorax from injury to vessels. Any compressive force on the lung, whether by air or blood within the pleural space, can lead to atelectasis and impaired gas exchange. Each hemithorax can hold greater than one half of the entire circulating blood volume before clinical signs become apparent. Tension pneumothoraces require immediate needle thoracotomy and placement of a chest thoracotomy tube before cardiovascular collapse occurs. For massive hemothoraces, emergent open thoracotomy may need to be performed in the emergency department. Emergency thoracotomy can allow for the release of pericardial tamponade, control of massive hemorrhaging, release of a massive air embolus, allow for descending aortic cross-clamping, and permit open cardiac massage. These maneuvers can aid in myocardial and cerebral perfusion and limit further bleeding while fluid and blood product resuscitation is delivered. Insertion of a double lumen tube to obtain lung isolation can provide a better surgical field for vascular and other tissue repair. If a double lumen tube is not accessible or able to be inserted, use of a bronchial blocker to isolate a lung or to prevent overspilling of blood or secretions from one lung to another can be extremely beneficial.

Injury to the heart and great vessels can result in decreased cardiac contractility due to myocardial contusion and exsanguination. Penetrating injuries usually cause direct trauma to

the structures that are contacted. Blunt forces usually result in shear stress at ligamentous attachment points of the heart and great vessels. Intraoperative transesophageal echocardiography (TEE) is valuable in these situations to assess volume status, left ventricular filling and function, and aortic integrity.

Abdomen

As in thoracic trauma, both blunt and penetrating abdominal trauma may be associated with massive blood loss. Damage to solid organs may be due to either penetrating or blunt trauma, whereas damage to hollow viscous organs, such as the bowel, is usually secondary to penetrating trauma. One exception to this is the injury associated with lap belts in motor vehicles. The shear force from the lap belt frequently causes catastrophic intestinal injuries. Damage to hollow viscous organs usually does not produce as much bleeding as damage to solid organs. However, a concurrent injury to a mesenteric vessel can lead to significant bleeding. Highly vascular, solid organs such as the liver, spleen, and kidneys can result in significant hemorrhaging if they or their vasculature is disrupted. In the vast majority of these injuries, solid organ injuries are now managed nonsurgically.

The focused assessment with sonography for trauma (FAST) exam is a quick exam performed in the emergency department to determine the presence of intra-abdominal fluid collections. Ultrasonography is used to determine if free fluid is present by investigating the right upper quadrant, the left upper quadrant, and the pelvic region. This exam is felt to be both specific and sensitive in blunt trauma; however, studies have shown that sensitivity is worse in patients with penetrating trauma and more severe, polytraumatic injuries. Therefore, a negative FAST exam should be followed by a more definitive exam such as computerized tomography or diagnostic peritoneal lavage.

For patients with evidence of severe intra-abdominal hemorrhage, damage control surgery is usually implemented. This is performed with the goal of minimizing the progression of the 'lethal triad' of coagulation impairment, acidemia, and hypothermia. Emergent laparotomy is performed with the goal of fixing larger injuries, packing the abdomen, and admitting the patient to the intensive care unit for further resuscitation. Early correction of the sources of large bleeding prevent further blood loss which improves oxygen carrying capacity and tissue oxygenation as indicated by decreased lactic acid formation. Ambient room temperature is increased and warm fluids are infused to prevent hypothermia. Once the patient is stabilized, further surgical correction of less urgent injuries may be performed in a staged manner.

Abdominal compartment syndrome becomes a risk due to edema of abdominal contents related to the injury and the volume necessary for resuscitation of these patients. Normal intra-abdominal pressure is <5–7 mmHg. Intra-abdominal pressures (measured by bladder manometry) >20 mmHg, abdominal perfusion pressure <60 mmHg, and evidence of organ dysfunction represents abdominal compartment syndrome. Compression on the abdominal vasculature decreases venous return to the heart and inhibits proper perfusion of the kidneys, liver, and brain. For this reason, the abdomen is often left open and packed after damage control surgery.

Extremities

Orthopedic trauma patients can present with injuries ranging from an isolated, single, long bone fracture that can be easily reduced, to multiple long bone, flat bone, and irregular bone fractures necessitating several surgical interventions. More than 1 l of unapparent blood loss can occur with a femur fracture. Pelvic bone fractures may also bleed extensively into the retroperitoneal space and can remain undetected for quite some time, especially if the patient is unconscious. Patients often require external fixation devices to maintain fractured osseous structures in their anatomical positions. Other common fractures in the trauma patient include burst fractures within the vertebral column, which may necessitate corpectomy with cage insertion or other instrumented fusion.

In the patient with long bone fractures, it is of high importance to assess the fractured limb's neurovascular status. A patient with a known fracture or extensive soft tissue injury who demonstrates distal pulselessness, pallor, paresthesias, pain out of proportion to the stimulus, and paresis of the extremity is likely to be developing compartment syndrome. Normal tissue pressures range from 0 to 10 mmHg. Capillary perfusion is diminished when compartment pressures exceed 20 mmHg. Muscle and nerve fibers are at risk for ischemia when intracompartmental pressures exceed 30–40 mmHg. Fasciotomy is typically performed when intracompartmental pressures exceed 30 mmHg, and compromised arterial flow through the compartment is present. If fasciotomy is performed within 12 h of onset, most deficits are prevented. If compartment syndrome persists untreated for more than 24 h, severe muscle ischemia may result, leading to myoglobinuria, renal failure, acidosis, permanent limb contractures, and/or loss of the limb.

Burns

Burn injuries are associated with significant morbidity and mortality. Burns are responsible for about 4,000 deaths annually. Immediately upon presentation, the patient's airway should be examined for evidence of inhalational injury as may be indicated by facial burns, stridor, or carbonaceous

sputum. If there is evidence of significant inhalational injury, intubation should be performed early and with a large diameter endotracheal tube, as sloughing of tracheal mucosal frequently clogs smaller diameter tubes. Even in the absence of facial burns or inhalational injuries, severely burned patients should be intubated early in anticipation of large volume fluid resuscitation with resultant pharyngeal edema. Frequent suctioning and bronchoscopy may be necessary. Saline lavage is relatively contraindicated as it may only push debris further down the respiratory tree.

Care should be taken to identify full thickness, circumferential burns as the eschars can produce a tourniquet effect. Circumferential burns around the chest produce a chest banding effect and may result in elevated peak airway pressures in patients already predisposed to respiratory complications. Circumferential abdominal burns may lead to abdominal compartment syndrome. Escharotomy should be performed to alleviate these effects.

Volume resuscitation is critical for burn patients. Burn resuscitation guidelines (BRG) recommend Ringer's lactate solution (LR) at 2 ml/kg/% total body surface area (TBSA) burned infused over 24 h. TBSA can be estimated based on the Lund-Browder chart, which is more specific than the traditional 'rule of 9's' method (see chapter on Critical Care). Hourly increases in fluid administration rate are made by 20–25 % to maintain a urine output of 30–50 ml/h. After 12 h of volume infusion and rate adjustments, the 24-h predicted requirement should be calculated. If this value exceeds 6 ml/kg/%TBSA, LR is discontinued and 5 % albumin is infused at rates corresponding to TBSA based on BRG. As per BRG, patients who are hypotensive and not producing at least 30 ml/h of urine output should be started 0.04 units/h of vasopressin and have their fluids titrated to a goal CVP of 8–10 mmHg. If a patient's CVP is at goal and they remain hypotensive, a norepinephrine infusion should be started.

Burn patients who survive the initial resuscitation continue to present several clinical problems, including acidosis, hyperkalemia, and increased susceptibility to infection. They also usually require frequent operations for wound debridements, vacuum-assisted closures (VAC), and skin grafting.

Clinical Review

1. The most common cause of mortality for people aged less than 35 years in the United States is
   A. Myocardial infarction
   B. Cancer
   C. Trauma
   D. Stroke
2. Three components of the Glascow Coma Scale are
   A. Motor response, verbal response, eye opening
   B. Motor response, verbal response, pain response
   C. Consciousness, motor response, verbal response
   D. Consciousness, motor response, eye opening
3. Most important concern for a malpositioned intraosseous catheter inserted for fluid resuscitation is the likely hood of
   A. Infection
   B. Bleeding
   C. Kinking of the catheter
   D. Compartment syndrome
4. Patients with traumatic injury at the following vertebral level will most likely to be intubated
   A. C-3, 4, 5
   B. C-6, 7, 8
   C. C-7, 8, T-1
   D. C-8, T-1, 2
5. A patient is brought to the emergency room with a contusion on the right chest. His blood pressure is 76/50 mmHg, heart rate is 112/min, oxygen saturation is 84 %, and the patient complains of dyspnea. In the next 5 min, the blood pressure drops further to 68/44 mmHg and the oxygen saturation to 78 %. You initial step in management would be to
   A. Administer epinephrine
   B. Administer albuterol
   C. Insert a needle into the right second intercostal space
   D. Administer fluids via a rapid infuser

Answers: 1. C, 2. A, 3. D, 4. A, 5. C

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Spine Surgery

47

Pulsar Li and Laura Ferguson

Spine surgery encompasses a broad range of procedures. The most commonly performed procedures involve nerve root or spinal cord decompression resulting from intervertebral disk herniation or osteophyte formation. Other procedures include spinal fusion surgery for scoliosis or trauma, tumor resection, vascular malformation resection, and abscess or hematoma drainage. In addition, patients presenting for spine surgery often have significant comorbidities and may have a challenging airway with cervical spine pathology. Spine surgery may also be associated with significant blood loss, anesthesia in the prone position, and complex pain management issues.

Spinal Cord Perfusion

The spinal cord receives its blood supply from a single anterior and two posterior spinal arteries. The single anterior spinal artery arises from the union of the vertebral arteries and supplies the anterior two-thirds of the spinal cord. The posterior spinal arteries arise from the posterior inferior cerebellar arteries (branch of vertebral artery) and supply the posterior one-third of the spinal cord. Radicular branches provide additional blood flow to the spinal cord along its course. The largest branch is the radicularis magna, also called the artery of Adamkiewicz, and originates from the aorta between T_9 and T_{12} providing the majority of blood supply to the lower two-thirds of the anterior spinal cord. During spine surgery, it is important to maintain spinal cord perfusion because even transient ischemia can cause irreversible neurologic damage. Neurologic monitoring is used to try to identify points in the surgery or anesthesia where the spinal cord is not receiving adequate perfusion.

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Preoperative Evaluation

A comprehensive preoperative assessment is essential before spine surgery. A thorough physical exam identifying preexisting neurologic deficits should be performed by the anesthesiologist and clearly documented on the anesthetic record. During surgery, it is common to refer to these preexisting deficits, especially if there are alterations in the neurophysiologic monitoring during the procedure.

Airway assessment should include previous intubation history, documentation, and a thorough airway examination including neck movements. The cervical spine should be assessed for pain, any neurologic deficits, and radiographically for instability (>3 mm horizontal displacement of vertebrae on a lateral radiograph or >10° rotation of the vertebrae).

The respiratory system should be assessed by obtaining a thorough history, smoking habits, and pulmonary function tests (PFTs) where required. Patients with scoliosis have a restrictive pattern on PFTs, which includes a reduced vital capacity and total lung capacity, with an unchanged residual volume and ventilation perfusion mismatch (increased shunting). The PFTs decline postoperatively and take up to 1 year to improve to preoperative values. Cardiac evaluation again includes a thorough history, tests (electrocardiogram, echocardiogram, or a stress test), and presence of cor pulmonale or pulmonary hypertension.

Arthritis

Osteoarthritis is common in the elderly and is characterized by degenerative changes in the joints. Patients have pain, stiffness, and limited movements of the joints. Obesity compounds the problem by putting additional weight on the joints. The knees and hands are commonly affected in osteoarthritis, while degenerative changes in the spine may lead to intervertebral disk herniation and nerve root compression.

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Table 47.1 Rheumatoid arthritis and ankylosing spondylitis

Factor	Rheumatoid arthritis	Ankylosing spondylitis
Pathophysiology	Autoimmune disease causing chronic inflammation and destruction of synovial membranes (flexible joints), morning stiffness of joints	Autoimmune disease, chronic inflammatory arthritis
Joints affected	Small- to medium-sized joints—hands, feet, cervical spine (limited range of motion), temporomandibular joint (mouth opening limitation), cricoarytenoid joint (hoarseness, stridor) involvement Instability of atlantoaxial joint may cause subluxation, which can cause spinal cord compression (cervical spine radiographs) leading to quadriplegia. Neck movement may cause syncope/dizziness	Affects the cervical spine causing fusion, bamboo spine on radiograph, sacroiliac joint, chest wall rigidity, severe limitation of neck motion, risk of neck fractures
Systemic manifestations	Cardiovascular involvement causing LV dysfunction (MI), conduction defects, valvular destruction, pericardial effusion, stroke, pulmonary fibrosis (restrictive lung disease), renal amyloidosis, anemia, effects of immunosuppressive drugs used for treatment (steroids, methotrexate)	Cardiomegaly, conduction defects, valvular defects, uveitis (inflammation of anterior chamber of eye)
Intubation	May be difficult, neck stabilization required during intubation	May require awake fiber-optic intubation
Labs	CBC (anemia), electrolytes, ECG, presence of autoantibodies to IgGFc, known as rheumatoid factors (RF), and antibodies to citrullinated peptides (ACPA)	CBC, electrolytes, ECG
Positioning	Careful positioning to prevent joint and nerve damage	Careful positioning

Osteoarthritis should be differentiated from other types of arthritis (Table 47.1). Cervical spine abnormalities and airway difficulties are usually not encountered in patients with osteoarthritis, as opposed to patients with rheumatoid arthritis and ankylosing spondylitis. All patients should receive a thorough history and physical examination, laboratory tests, radiographic studies, and medications being taken (NSAIDs, opioids, steroids, immunosuppressive agents).

Patient Positioning

Most spine surgery requires patients to be positioned prone on the operating table. Patients are anesthetized and intubated supine, typically on the transport stretcher or bed, and then rolled into the prone position on the operating table. It is the shared responsibility of the anesthesiologist and surgeon to safely turn the patient prone while maintaining a secure airway and attending to intravenous lines and other monitors ensuring they remain functional. In the prone position, the patient's arms are either fully adducted or abducted less than 90° at the shoulder and elbow joints and placed on arm boards with cushioning. The neck should also be in a neutral position neither flexed nor extended. Ulnar nerve compression and other brachial plexus injuries are recognized complications of prone positioning, and attention to proper alignment of the neck and arms is essential.

The head can rest on a pillow designed for prone positioning or be placed in Mayfield pins. Mayfield pins, commonly used for cervical spine procedures, are placed in the patient's scalp and then secured to the operating table to optimize surgical conditions. Movement by the patient must be prevented with the use of Mayfield pins, thus, requiring vigilance with regards to the depth of anesthesia and level of paralysis. If the head is placed in a prone positioning pillow, it is imperative that the patient's eyes, nose, ears, and chin are free from direct pressure by the pillow. There are several types of prone positioning pillows, and these are chosen by the anesthesiologist according to availability and personal preference.

There are a variety of operating tables and devices that are used to facilitate surgery in the prone position. The choice of operating table is determined by the surgeon and chosen based on surgical exposure and preservation or modification of the curvature of the spine. Both the Jackson table and the Wilson frame preserve the curvature of the spine and allow relief of pressure points at the chest and abdomen decreasing abdominal compression. With the Andrews frame, the patient is prone and kneeling which modifies the curvature of the spine allowing for better access to the lumbar spine.

Complications of Positioning

Abdominal compression in the prone position increases intra-abdominal pressure and leads to cardiopulmonary compromise due to elevated pulmonary pressures and decreased venous return. Abdominal compression can also lead to increased bleeding at the surgical site due to epidural venous plexus engorgement secondary to inferior vena cava compression and redistribution of blood flow to collateral veins.

Complications of prone positioning include peripheral nerve injuries, facial edema, endotracheal tube kinking or dislodgement, and blindness or other ophthalmologic injury. Peripheral nerve injuries can be minimized with attention to positioning of the arms and neck as stated above. Facial and airway edema is dependent on the length of the procedure and the amount of fluid administered. Endotracheal tube complications can be minimized with careful securing of the

tube prior to turning the patient prone. Ophthalmologic injuries include corneal abrasions, central retinal artery occlusion (CRAO), and ischemic optic neuropathies (ION).

Venous air embolism is a life-threatening complication that may also occur in the prone position. It is characterized by hypotension, tachycardia, and an increase in end-tidal nitrogen concentration. Treatment includes irrigating the surgical wound with saline, discontinuation of nitrous oxide, and treatment of hypotension with fluids and vasopressors.

Intraoperative Care and Monitoring

The anesthetic plan should provide anesthesia while, at the same time, permitting optimal conditions for neurologic monitoring. Anesthetic agents can alter evoked potential responses. Neuromuscular-blocking agents will have a dose-dependent effect on motor evoked potentials (MEPs) due to muscle paralysis. Most anesthetic agents alter somatosensory evoked potentials (SSEPs) in relation to spinal cord ischemia, and they must be adjusted to minimize this change. Volatile agents have the most effect on SSEPs of all anesthetic agents and should be kept at less than 1 MAC to minimize the anesthetic-induced changes. Muscle relaxants are not used when monitoring MEPs. Some anesthesiologists prefer to use a propofol-opioid-based anesthetic for maintenance of anesthesia instead of using volatile agents. A central venous line may be inserted for monitoring and vascular access, and an arterial line may be inserted for blood pressure monitoring, especially when controlled hypotension may be required by the surgeon. Also, it is of prime importance that hypothermia be prevented during the surgery.

Evoked potentials (EP) are a noninvasive way to measure neuronal pathway dysfunction by stimulating sensory and motor pathways and measuring the electrophysiologic response. Commonly used evoked potentials during spine surgery include somatosensory evoked potentials (SSEPs) and motor evoked potentials (MEPs). SSEPs are generated by stimulating subcutaneous electrodes along the radial, ulnar, or posterior tibial nerves. Electrodes placed on the scalp measure the response to the stimulation of these peripheral nerves and the adequacy of nerve transmission through the dorsal columns of the spinal cord. MEPs are obtained by stimulating the primary motor cortex directly or transcranially and measuring the transmission anywhere along the nerve pathway. MEPs monitor the anterior spinal cord for ischemia.

An intraoperative wake-up test is sometimes employed during spine surgery to test lower limb muscle strength when SSEP signal abnormalities cannot be explained or if the patient is at high risk of neurologic injury. This test is used less frequently today due to the combined use of SSEPs and MEPs. The use of a wake-up test requires preparation of the patient preoperatively to alleviate any emotional distress that might ensue.

Postoperative Care

Postoperatively, the patient should be assessed to meet the criteria for extubation. Mechanical ventilation may be needed if the surgery involved multiple vertebral levels, high spinal levels, prolonged surgery, excessive blood loss, or significant facial or airway edema. Adequate thromboembolic prophylaxis should be provided to prevent deep vein thrombosis and embolic complications.

Wake-Up Test

Postoperatively, spine surgeons want to assess their patients immediately following the surgical procedure. Often, a neurologic evaluation is performed in the operating room before transport to the recovery room. It is important to tailor the anesthetic to allow for a quick emergence and evaluation of the patient's ability to follow commands. This can include limiting certain drugs, like opioids, which might keep the patient sedated or sleeping longer into the postoperative period. Infusions of short-acting opioids are also commonly used and stopped prior to the end of the surgery to achieve a similar effect.

Postoperative Visual Loss

Postoperative visual loss (POVL) is an uncommon but serious risk of surgery in the prone position with an incidence less than 0.2 %. Most often, POVL is caused by ischemic optic neuropathies (ION), but the cause of this devastating complication has not been fully elucidated. Recent analysis of the American Society of Anesthesiologists POVL Registry using a case-control study identified independent risk factors for ION after spinal fusion surgery. These risk factors include male sex, obesity, Wilson frame use, longer anesthetic duration, greater estimated blood loss, and lower percent colloid administration. These findings are in agreement with the 2012 Practice Advisory for POVL Associated with Spine Surgery that identified prolonged operative duration (exceeding 6.5 h) and substantial blood loss (44.7 % of estimated blood volume) as risk factors for perioperative ION.

Spinal Cord Injury

Traumatic spinal cord injury (SCI) presents some unique challenges in the setting of spine surgery. Many patients with SCI present for stabilizing surgery to prevent further damage or injury. Emergent surgery is pursued if there is potentially reversible compression of the spinal cord. The patient will have neurologic deficits determined by the level of the injury.

The risk of succinylcholine-induced hyperkalemia should be taken into account in the SCI patient. It is presumed safe to use succinylcholine within the first 48 h after an SCI, but after this time, the depolarizing neuromuscular blocker should be avoided.

Spinal shock is a possibility in the setting of acute SCI and is characterized by the loss of sympathetic tone below the level of the lesion. Patients can be hypotensive and bradycardic and require significant fluid resuscitation and vasopressor support. Autonomic hyperreflexia is associated with a $T_{5–6}$ or above SCI but is not a problem during acute management (concern usually after 2–3 months of SCI). It is characterized by severe hypertension and is usually caused by stimulation, surgical or visceral, below the level of the SCI resulting in a reflexive sympathetic discharge. In the setting of a cervical spinal cord injury, the patient's airway is of utmost concern given the potential for apnea if $C_{3–5}$ is affected, and the risk of aspiration if coughing is impaired. Early intubation is often required. To prevent further injury, intubation should be performed with in-line neck stabilization, or an awake fiber-optic intubation should be performed if the situation allows.

Clinical Review

1. Blood supply to the lower 2/3rds of the anterior spinal cord is by the
   A. Vertebral artery
   B. Artery of Adamkiewicz
   C. Circle of Willis
   D. Basilar artery
2. Commonest cause of visual loss during spine surgery in the prone position is
   A. Corneal abrasion
   B. Central retinal artery occlusion
   C. Ischemic optic neuropathy
   D. Damage to the optic lens
3. The following agent has the greatest effect on somatosensory evoked potentials
   A. Propofol
   B. Vecuronium
   C. Nitrous oxide
   D. Isoflurane
4. Autonomic hyperreflexia following spinal cord injury is usually seen after
   A. 1 month
   B. 3 months
   C. 6 months
   D. 12 months

Answers: 1. B, 2. C, 3. D, 4. B

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Robotic Surgery

48

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The practice of surgery continues to evolve as physicians advance surgical techniques to improve patient outcomes and safety. Patients with significant medical comorbidities often present to the operating room, in whom anesthetic management and postoperative recovery are usually more complicated. Minimally invasive surgery is becoming the standard of care in these patients, and robotic-assisted surgery can be considered as an evolution of minimally invasive surgery. Robotic surgery has several anticipated benefits and disadvantages as listed in Table 48.1. As more surgeries evolve into robotic-assisted surgeries, anesthesiologists should have a basic knowledge of the procedures as well as the robotic devices in order to formulate an anesthetic plan and provide appropriate patient care.

History

The first minimally invasive surgery was a laparoscopic cholecystectomy that was performed in 1987. Since then, laparoscopy has gained widespread acceptance, and today it is used in a wide variety of procedures. The current technology behind robotic surgery was aided largely by the United States Army (Department of Defense). They desired a system that would allow surgeons to treat soldiers on the battlefield from a safe distance, that is, the concept of telerobotic surgery. The technologies of telerobotic surgery and laparoscopic surgery were eventually developed into two tele-manipulative robotic systems, the da Vinci Robotic Surgical System and the Zeus Robotic Surgical System. The two systems were developed in parallel until the manufacturer of the da Vinci system (Intuitive Surgical) acquired the rights to the Zeus robotic system. They continue to support existing Zeus robotic systems which are still used in Europe and other countries. The only full-scale robot system available and currently in use in the United States is the da Vinci system.

Today robotic assistance is being used in a wide variety of surgeries and specialties including urologic, cardiac, thoracic, otorhinolaryngologic, orthopedic, gynecologic, and pediatric surgery (Table 48.2). The first robotic-assisted surgery was performed by Kwoh et al., who used the PUMA 560 to perform neurosurgical biopsies. Internal mammary artery harvesting was successfully performed thoracoscopically by Nataf in 1997. The first reported endoscopic coronary artery bypass surgery was performed in 1998 by Loulmet. Since then, robotic-assisted cardiac surgery has expanded to include mitral valve repairs, patent ductus arteriosus ligations, and atrial septal defect closures. As of 2008, more than 80,000 robotic procedures have been performed.

The Robot

The da Vinci robot (Fig. 48.1) consists of three main parts: the master console, an optical tower, and the surgical cart. The control console is where the surgeon sits and controls the robot. It consists of a 3-D screen that projects an image from the intraoperative camera. The surgeon controls the robot using hand controls, three robotic arms, and foot pedals. The right and left hand controls control the right and left arms of the robot respectively, while the third arm controls the endoscopic camera. Foot pedals control electrocautery and ultrasonic instruments and adjust the camera.

The robotic system allows for ergonomic anatomic control of the instruments which mimic the movement of the human wrist. The instruments have seven degrees of motion

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Table 48.1 Advantages and disadvantages of minimally invasive/robotic surgery

Advantages	Disadvantages
Technical precision	Loss of force and tactile perception
Less pain	Decreased natural hand-eye coordination
Less blood loss	Fixed/immobile robot
Smaller incisions and better cosmetic results	Effects of CO_2 insufflation
Faster recovery and shorter hospital stay	Expensive and new technology
Less risk of infection	Large size of the system
Better postoperative immune function	

Table 48.2 Examples of robotic-assisted surgeries

General surgery	Cholecystectomy, gastric bypass, bowel resection
Urologic surgery	Radical prostatectomy, nephrectomy
Gynecology	Hysterectomy, tubal reanastomosis
Orthopedic surgery	Hip arthroplasty, knee and spine surgery
Neurosurgery	Image-guided surgery
Cardiothoracic surgery	Coronary artery bypass graft, mitral valve repair, mammary artery harvesting

versus four degrees of motion with the standard laparoscope. The robotic system has motion scaling that can be adjusted from 1:1 up to 5:1 that allows the system to be set up to compensate for surgeon's hand tremor and when required a larger movement by the surgeon for a smaller movement in the operating field. The optical tower projects the images from the field and displays it for the operating room and also has the capability to record. The surgical cart, or robot itself, has 3–4 arms and must be manually wheeled in close vicinity to the patient.

Anesthetic Considerations

Robotic surgery produces some unique challenges, and the anesthesiologist should be aware of these in order to provide the safest patient care. A few issues related to robotic surgery are patient positioning, hemodynamics, hypothermia, blood loss, and the effects of pneumoperitoneum.

Patient positioning is important in every case and is a task for which the anesthesiologist and surgeon are both responsible. This is all the more important when dealing with robotic-assisted procedures. Some robotic cases can be lengthy depending on the complexity of the case and the learning curve of the surgeon. Therefore, careful attention should be paid to padding position points as well as securing the patient to the bed. The patient's airway may be some distance from the anesthesiologist and should be secured accordingly. In certain cases, the patient may even be 180° from the anesthesiologist and the monitors.

The robot is large and must be docked in close vicinity to the patient, and *access* to the patient after it is docked can be very limited. Depending on the complexity of the case and the history of the patient, the anesthesiologist should consider additional intravenous (IV) access since obtaining additional IV access once the procedure has commenced may be extremely difficult. Most cases will require two IVs, and if an arterial line is required, it must be inserted at the start of the case. Once the patient is positioned, the anesthesiologist may not have access to the arms.

The *position of the robot* in relation to the position of the patient is just as important. The robot has 3–4 arms that move with some force in relation to the surgeon's movements. The surgeon has some tactile feel from the operative site but is not aware of how the arms move in relation to the patient, which is one aspect of robotic surgery that is different from other laparoscopic procedures. If a brisk movement of the arm was to contact the patient, it could injure the patient. Therefore, the patient, especially the face and arms, must be clear of the range of motion of the robot arms. Cameras and light sources should be monitored and never left in direct contact with the drapes or the patient for risk of fire and injury to the patient. The staff in the room must be trained on dismantling the robot and moving it in the quickest fashion in order to gain access to the patient in case of an emergency.

Once the robot is engaged and the surgical instruments are within the patient for the operation, *muscle paralysis* of the patient is of utmost importance, as patient movement can be detrimental both to the patient and the robot, which is fixed. Muscle relaxation with a non-depolarizing neuromuscular agent is critical to the anesthetic plan. Anesthesia can be maintained with an oxygen-air mixture and a volatile agent with or without the combination of an intravenous agent.

Carbon dioxide *insufflation* is routinely used intraoperatively, which can have many hemodynamic effects. It increases systemic vascular resistance, filling pressures, and mean arterial pressure. Central venous pressure and pulmonary capillary wedge pressure may rise during pneumoperitoneum. Pneumoperitoneum can cause a decrease of pulmonary compliance by 30–50 % secondary to diaphragmatic elevation. Also, an increase in minute ventilation may be necessary to compensate for the increase in $PaCO_2$.

Emergence and neuromuscular blockade reversal should be delayed until the robot is completely disengaged and removed from the patient. Pain medication requirement and intraoperative blood loss for robotic-assisted surgeries are generally decreased when compared to traditional open procedures.

Robotic surgery, although still in its infancy, is set to revolutionize surgery by improving laparoscopic procedures and

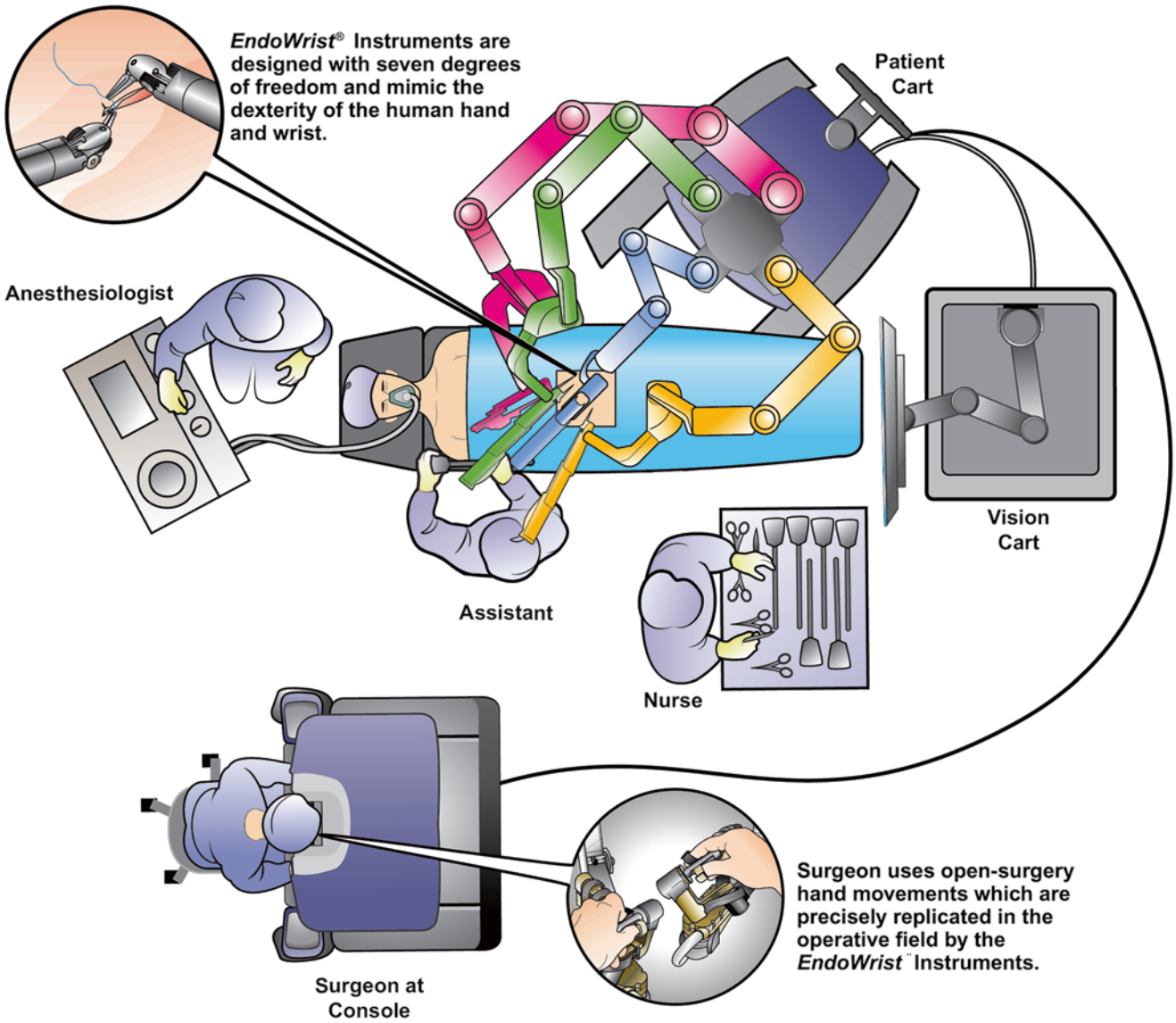

Fig. 48.1 General operating room setup of the da Vinci robotic system (courtesy Intuitive Surgical, Inc.)

bringing surgery into the digital age. Robotic surgery has the potential to advance surgical procedures beyond human capabilities, though high costs remain a significant hindrance factor. The anesthesiologist should be aware of the complex equipment as well as specific anesthetic considerations in order to formulate a plan for optimal patient health and safety. Patient positioning is extremely important, and specific attention should be made to padding pressure points. The position of the robot in respect to the patient should be noted, and securing the airway is of prime importance. Movement of the robotic arms should be clear of the patient, and therefore, patient paralysis is important to prevent unintentional harm to the patient. As technology and surgeon's learning curve improve in the area of robotic-assisted surgery, the anesthesiologist must stay current and adjust their anesthetic plan accordingly.

Clinical Review

1. Compared to traditional open surgeries, robotic-assisted surgeries have
   A. Similar blood loss
   B. Similar pain medication requirements
   C. Similar cosmetic results
   D. Faster recovery times
2. All of the following are true statements regarding robotic-assisted surgery, EXCEPT
   A. The robot is large and once in place is fixed in position.
   B. Air is used for intraoperative insufflation.
   C. The operating room size generally has to be bigger to accommodate the robot.
   D. The surgeon has loss of touch sensation while performing the surgery.

3. A 58-year-old patient is undergoing a robotic-assisted radical prostatectomy under general anesthesia. Anesthesia is best maintained by
   A. Oxygen, nitrous oxide, and an inhalational agent
   B. Oxygen, air, and an inhalational agent
   C. Oxygen, air, inhalational agent, and a muscle relaxant
   D. Oxygen, air, inhalational agent, and a propofol infusion

Answers: 1. D, 2. B, 3. C

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Patient Positioning and Common Nerve Injuries

49

Jonathan Estes and Ryan C. Romeo

The goal of positioning the anesthetized patient is to facilitate the performance of the surgical procedure by the surgeon while maintaining physiological position to safeguard the patient from potential complications. The position of the anesthetized patient may have unintended physiological effects, such as impaired venous return to the heart, ventilation-to-perfusion mismatching, hypotension, as well as nerve and eye injuries. It is imperative for clinicians to recognize the possible cardiovascular and respiratory physiological changes that occur in various positions of the anesthetized patients. The American Society of Anesthesiologist Closed Claims Database establishes that nerve damage is the second most common type of anesthetic complication and further illustrates the importance of positioning. Proper patient positioning is a critical responsibility requiring the participation of the anesthesiologist, surgeon, and nursing staff.

Peripheral Nerve and Eye Injuries

Peripheral nerve injuries are a significant perioperative complication. Studies of the ASA Closed Claims Database have found that the major injuries were death, nerve damage, and brain damage, in the order of frequency. Of the nerve injuries, ulnar neuropathies were the most frequent, followed by injuries to the brachial plexus, lumbosacral nerve root, and spinal cord (Table 49.1). Further findings showed that nerve damage claims were equal in males and females, and ulnar nerve injury is the most common after general anesthesia. Also, spinal cord and lumbosacral nerve root injuries were associated mainly with regional anesthesia. In 1999 and updated in 2011, the ASA Task Force on Prevention of Perioperative Peripheral Neuropathies released a practice advisory in recognition of the significant morbidity associated with perioperative peripheral neuropathies. A summary of the findings can be seen in Table 49.2. Eye complications represent 3 % of all claims in the ASA Closed Claims Database.

There are five in vivo mechanisms for perioperative peripheral neuropathies—stretch, compression, generalized ischemia, metabolic derangement, and surgical section. Observational studies have reported postoperative peripheral neuropathies occurring in patients with specific preexisting conditions, such as diabetes mellitus, vascular disease, extremes of body weight, and age.

Evaluation of Perioperative Nerve Injuries

A thorough preoperative history and physical examination is imperative for evaluation of perioperative nerve injuries. When a suspected perioperative nerve injury occurs, a neurologist should be consulted. Sensory neuropathies are more common than motor neuropathies. Also, sensory neuropathies tend to be transient, often less than 5 days, and patient reassurance is appropriate. Motor neuropathies can be evaluated by electromyogram (EMG) to establish the exact location of the injury and also help uncover if the neuropathy was present preoperatively (an EMG done postoperatively will show evidence of nerve injury weeks before the surgery).

Upper Extremity Nerve Injury

Ulnar Nerve Injury

Ulnar nerve injury is the most common perioperative nerve injury. The mechanism of ulnar neuropathy in the perioperative period is unclear. While external nerve compression or excessive stretch from positioning does cause neuropathy, other factors appear to play a role. As stated above, overall peripheral nerve neuropathies occur equally in men and women; however, ulnar nerve neuropathies occur more often

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in men (less fat, larger tubercle of the ulnar coronoid process in men). Other factors include extremes of body habitus and prolonged hospitalization of greater than 14 days. Also, multiple outcomes have shown that initial symptoms from ulnar neuropathies were noted more than 24 h after the procedure. With this information, there is a consensus that ulnar neuropathies are not always preventable even when taking all precautions. When they do occur, the possible results are decreased sensation along its innervation, a failure to abduct or oppose the fifth finger, and eventual atrophy of the intrinsic muscles of the fourth and fifth finger producing a "claw"-like hand.

Brachial Plexus Injury

Brachial plexus injury is the second most common injury and results from excessive stretching, direct trauma, and compression during surgery. Stretching can result when there is arm abduction greater than 90°. Displacement of the first rib during median sternotomies is a key source of brachial plexus injuries where up to 4.9 % of patients who underwent open heart surgery had this complication. Shoulder braces for steep Trendelenburg position are another risk for injury to the brachial plexus and should be avoided. The use of a nonsliding mattress should be used in place of braces. Further, attention is required when a patient is in steep Trendelenburg, as the patient is at risk of moving cephalad while the arms or shoulders are steadied in place causing stretching of the brachial plexus.

Table 49.1 Commonest peripheral nerve injuries

Nerve injury	Claims
Ulnar	
Brachial plexus	
Lumbosacral nerve root	
Spinal cord	
Sciatic	
Median	
Radial	
Femoral	

Radial and Median Nerve Injury

Radial and median nerve injuries are rare. The radial nerve can be injured as it wraps around the middle of the humerus laterally in the spiral groove. Injury results in wrist drop, weak thumb abduction, inability to extend the metacarpophalangeal joints, or a sensory deficit. Median nerve injury may be due to trauma while attempting to obtain intravenous access in the antecubital fossa. Another proposed mechanism for median nerve injury occurs in men who have hypertrophied biceps muscles. Under general anesthesia and muscle relaxation, there may be increased stretching at the elbow for these patients. Median nerve injury results in inability to oppose the first and fifth digits.

Lower Extremity Nerve Injury

The lithotomy position is responsible for the majority of lower nerve injuries. According to Warner et al., there are three risk factors associated with increased risk of developing a neuropathy in the lithotomy position, which include surgery time greater than 2 h, thin body habitus, and recent cigarette smoking. The most common lower nerve injury is to the common peroneal nerve. This can occur from the stirrups, which are used to position the patient in lithotomy, compressing the nerve at the head of the fibula. Injury produces foot drop, loss of dorsal extension of toes, and incapability to evert the foot. Sciatic nerve damage can ensue from excessive flexion of the hips or extension of the knees. Insult to this nerve may also cause foot drop and decreased sensation to the foot, except the medial aspect of the ankle and arch. Femoral and obturator nerve injury occur with lower abdominal surgery as a result of excessive retraction. Impairment of these nerves results in loss of hip flexion and knee extension and the inability to adduct the leg with diminished sensation over the medial thigh, respectively. Obturator nerve injury can also follow difficult forceps delivery.

Table 49.2 Prevention of perioperative peripheral nerve injuries

Preoperative history and physical examination	Ascertain if patients can comfortably tolerate the anticipated operative position
Upper extremity positioning	
• Arm abduction: in supine patients, it should be limited to 90°, while prone patients may comfortably tolerate arm abduction greater than 90° • Ulnar nerve: place forearm in supination/neutral position to decrease pressure on the postcondylar groove of the humerus (ulnar groove) • Radial nerve: avoid prolonged pressure in the spiral groove of the humerus • Median nerve: avoid excessive elbow extension • Arms tucked at sides: forearm should be in a neutral position	
Lower extremity positioning	
• Sciatic nerve: may be stretched by hamstring muscle stretch and by extensive flexion or extension at the hip or knee • Peroneal nerve: avoid prolonged pressure at the fibular head	
Protective padding	• Padded arm boards, chest rolls, elbow padding • Padding should be too tight • Avoid using shoulder braces for steep Trendelenburg position
Adequate documentation and postoperative assessment	

Eye Injury

Corneal abrasions are the most common eye injury. Pressure on the eyes should be avoided throughout the entire procedure using specific pillows or support for the head while in the prone position. Blindness is a devastating complication, most commonly found in anesthetized patients who undergo surgery while in the prone position. This has led to the development of the American Society of Anesthesiologists' Postoperative Visual Loss Registry. An ASA Task Force on Perioperative Blindness issued a practice advisory stating there are subsets of patients who undergo spine procedures in the prone position that have an increased risk for perioperative visual loss. They include those who undergo procedures that are prolonged, have substantial blood loss, or both. They further advise using colloids *with* crystalloids to replace intravascular volume in patients who have significant blood loss and also that high-risk patients should be positioned so that their heads are level with or higher than the heart.

A more recent study including patients from the registry supports the advisory recommendations. In addition to the advisories and findings, they identified that the use of Wilson surgical bed frame, which places the patient head down, obesity, decreased percentage of colloid administration, and male sex are associated with ischemic optic neuropathy. Several of the above findings support acute venous congestion of the optic canal as a possible etiology of ischemic optic neuropathy. Cardiopulmonary bypass also has an augmented possibility of perioperative visual loss. New evidence suggests that prolonged steep Trendelenburg may also be a risk for ischemic optic neuropathy.

Patient Positions

Supine Position

The supine position is the most commonly used position for surgical procedures. The patient lies on his/her back with the arms padded and beside the body or abducted less than 90° on padded arm boards (Fig. 49.1a). The patient's heels should be padded and legs must be uncrossed. The lawn chair position is a variation of the supine where the hips and knees are slightly flexed. This position may provide better comfort for the patient and can be implemented by placing a rolled towel, pillow, or blanket beneath the patient's knees.

Physiological effects of supine position:

- Functional residual capacity of the anesthetized patient decreases by approximately 500 ml in adults. This can be explained by an inward displacement of the rib cage along with the change in shape of the diaphragm, as the abdominal viscera push the diaphragm cephalad.
- Spontaneous ventilation is better in dependent lung areas, while controlled ventilation is better in nondependent lung areas.

Tissues which overlie bony prominences can be concerning for ischemic necrosis secondary to pressure unless proper padding is utilized. The regions that are most concerning involve the heels, elbows, and sacrum. Compartment syndrome has been described due to excessive force used to restrain the arm in a proper position. Also, pressure alopecia resulting from ischemic hair follicles has been described, which can be prevented by using a cushion and periodically rotating the head. Full hair regrowth is usually expected by 3 months. Backache is not uncommon in the supine position because of the loss of paraspinal musculature tone and ligamentous relaxation that occurs with anesthesia.

In the *Trendelenburg position*, the patient is supine with the head down, occasionally with the knees flexed to help preventing cephalad movement (Fig. 49.1b). Significant swelling of the face, eyelids, conjunctiva, and tongue has been observed. Additionally, one report describes postextubation respiratory distress requiring reintubation secondary to laryngeal edema where the patient was in an extreme Trendelenburg position for a prolonged time. This is noteworthy as robotic surgery becomes more prevalent especially for prostate surgery.

Physiological effects of Trendelenburg position:

- Increase in venous return and blood pressure
- Increased central venous, intracranial, and intraocular pressure
- Increased pulmonary venous pressure, decreased lung compliance, and reduced functional residual capacity, V/Q mismatch

Reverse Trendelenburg places the patient opposite of the Trendelenburg position (Fig. 49.1c). Reverse Trendelenburg may be particularly beneficial in obese patients, especially during induction and intubation. Patients in the reverse Trendelenburg position drop their SaO_2 the least during periods of apnea and recover the fastest.

Physiological effects of reverse Trendelenburg position:

- Decrease in venous return, cardiac output, and blood pressure
- Increase in the functional residual capacity and respiratory compliance while decreasing peak inspiratory pressures

Lithotomy Position

The lithotomy position is used commonly in gynecologic and urologic surgery. The legs are flexed at the hip approximately 90°, and the legs are abducted from the midline by 30° to 45°. The knees are flexed such that they are parallel to the torso (Fig. 49.1d). The legs are held in this position with various different support devices. Placing the patient in lithotomy requires coordination of two providers such that flexing the hips and knees occurs simultaneously to prevent torsion of the lumbar spine. Additionally, when the patient is to be returned to supine at the end of the procedure, this should be done by first bringing the knees and ankles together

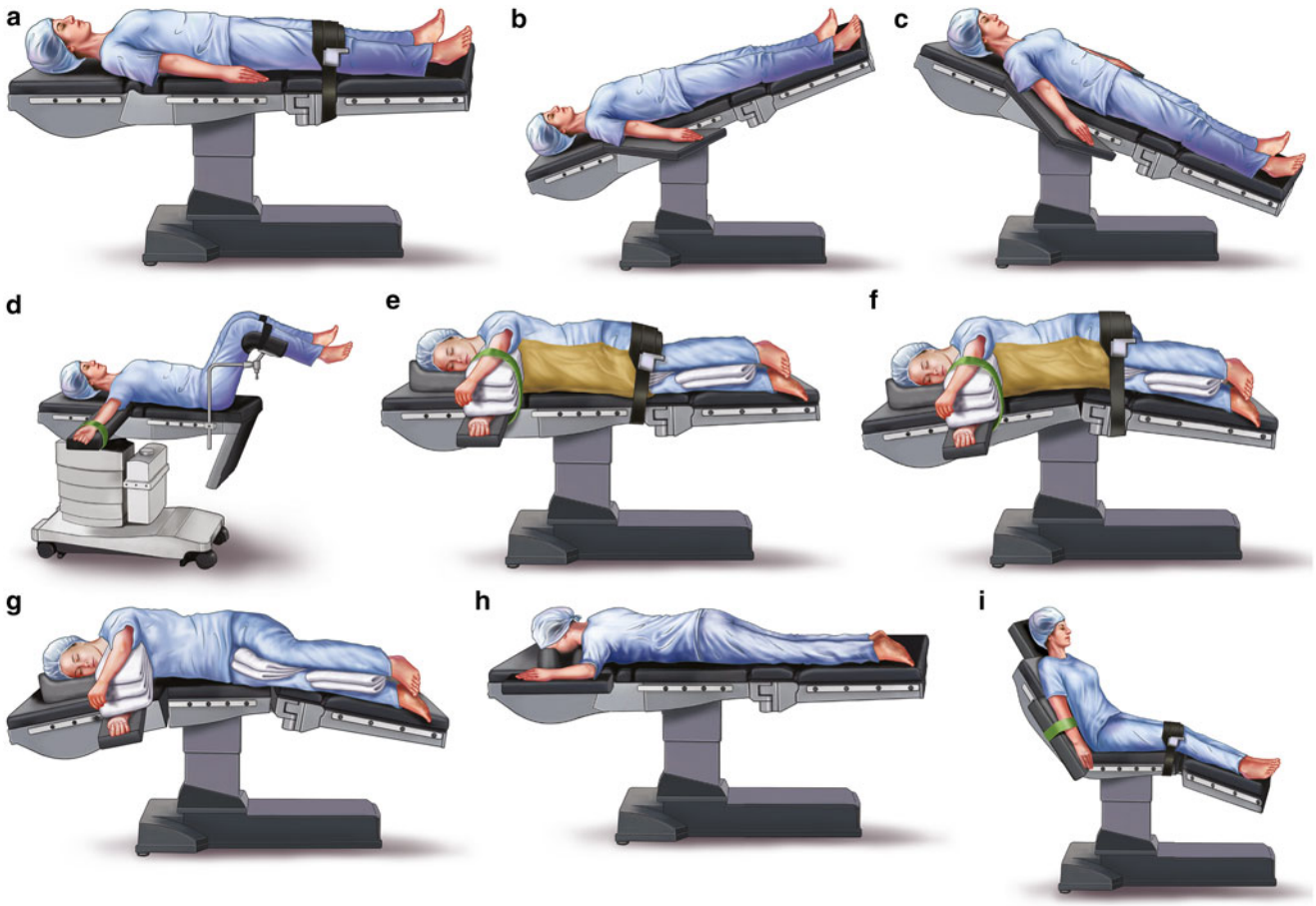

Fig. 49.1 Various patient positions during surgery. (**a**) supine, (**b**) Trendelenburg, (**c**) reverse Trendelenburg, (**d**) lithotomy, (**e**) lateral decubitus, (**f**) lateral jackknife, (**g**) lateral kidney, (**h**) prone, (**i**) sitting

before lowering the legs, again, to reduce stress on the lumbar spine.

Another consideration is elevation of the legs, which can cause pain secondary to the loss of the normal curvature of the lumbar spine. Lower extremity compartment syndrome is a consequence of inadequate perfusion which results in ischemia, edema, and rhabdomyolysis. Finally, to prevent crush injury, special attention is required to protect the fingers from getting caught between the break in the operating table. Common peroneal nerve injury is the commonest nerve injury following a lithotomy position.

Physiological effects of lithotomy position:

- Increase in venous return leading to a transient increase in cardiac output and intracranial pressure
- Decrease in tidal volume results when abdominal viscera displace the diaphragm cephalad

Lateral Decubitus Position

Patients for thoracotomy and total hip arthroplasty are usually placed in the lateral position. This position requires contribution from the entire operating room staff to ensure patient safety (Fig. 49.1e). A chest roll or an "axillary roll" is placed slightly caudad to the dependent axilla to reduce pressure on the axillary neurovascular bundle and prevent diminished blood flow to the extremity. The chest roll should not be placed in the axilla itself. The dependent arm is placed perpendicular to the torso on a padded arm board, with the nondependent arm resting on an armrest or suspended with foam padding. The dependent leg is flexed at the hip and knee avoiding pronounced flexion of the hip so that obstruction of venous return to the inferior vena cava does not occur. Padding, often a pillow, is placed between the legs for additional support. The head is supported with a headrest so that the head and spine are in neutral position.

Physiological effects of lateral decubitus position:

- Arterial blood pressure may decrease.
- Increased weight of the mediastinum and cephalad pressure of the abdominal contents on the dependent lung in anesthetized patients encourages increased ventilation of the nondependent lung. Further, gravity causes pulmonary blood flow to favor the dependent lung. This combination worsens the ventilation-to-perfusion mismatch.

Variations of the lateral decubitus position include the lateral jackknife and kidney positions (Fig. 49.1f, g, respectively). In the lateral jackknife position, the operating table is positioned so that the thighs are flexed on the trunk laterally. Once the patient is positioned, the thorax is made horizontal resulting in the legs significantly lower than the right atrium. This position helps stretch the upside flank and widens intercostal spaces, which is helpful for a thoracotomy incision. The kidney position is similar to the jackknife, but it includes a kidney rest under the downside iliac crest, which increases the amount of lateral flexion. This improves access to the upside kidney under the costal margin. Caution is needed to safeguard the dependent eye from external compression to avoid corneal abrasion and retinal artery thrombosis and confirm that the patient's eyelids are taped closed. It is important to check the downside ear to ensure it is in neutral position as well. The lateral jackknife position results in considerable pooling of the blood in the lower extremities. Use of this position should be limited due to the physiological stress created.

Prone Position

The prone position is commonly used for surgical access to the posterior fossa of the skull, the posterior spine, the buttocks, and lower extremities (Fig. 49.1h). Typically, the patient is intubated on a bed beside the OR table, after which the endotracheal tube is keenly secured in place. The patient is then turned prone with cooperation of the entire OR staff while being sure to keep the neck in neutral position during the rotation. The head is kept in the neutral position with a surgical pillow designed to support the forehead and facial prominences while avoiding placing pressure on the eyes, nose, and mouth. Also, horseshoe headrest or Mayfield pins can be used to facilitate a neutral head position.

The head may be turned to one side; however, this could lead to compromise to the cervical nerve root and carotid or vertebral artery blood flow, along with excessive pressure to the dependent eye or ear. In the prone position, the thorax is supported by rolls or bolsters to relieve abdominal compression by the operating table. The female breasts should be placed medial to the support to prevent tissue damage along with padding over the iliac crests to prevent pressure injury. The arms should not be abducted greater than 90°. Also, increased bleeding during back surgery could result in increased epidural pressure. This effect is secondary to the communication between the abdominal veins and the vertebral venous plexus.

Physiological effects of prone position:

- Pressure on the abdomen may cause compression on inferior vena cava and aorta decreasing venous return and cardiac output, respectively.
- Increased abdominal pressure can cause a decrease in functional residual capacity and pulmonary compliance and an increase in peak airway pressure. The use of rolls/bolsters helps prevent these unfavorable effects.

Sitting Position

In the sitting position, the patient is usually in a semi-reclining posture with the legs elevated to the level of the heart and the head flexed (Fig. 49.1i). The sitting position provides excellent surgical exposure for posterior fossa craniotomy and also shoulder surgery (where the patient is in a variation of the sitting position). This position also allows excellent access to the airway, reduces facial swelling, and decreases the amount of blood pooling in the operative field.

Head flexion should not be severe enough where the chin is against the suprasternal notch because this can hinder both arterial and venous blood flow, kink the endotracheal tube, and cause excessive pressure on the tongue and stroke. There should be two fingerbreadth distance between the chin and the sternum to prevent these problems. Adequate support is needed to prevent the weight of the arms from stretching the brachial plexus. Flexion of the knees is necessary to help avert sciatic nerve injury. The sitting position has an increased incidence of *venous air embolism* compared to other positions.

Physiological effects of sitting position:

- Pooling of the blood in the lower extremities resulting in decreased preload and hypotension
- Functional residual capacity increases
- Decrease in cerebral perfusion

Clinical Review

1. Commonest perioperative nerve injury is of the following nerve
   A. Ulnar
   B. Radial
   C. Common peroneal
   D. Sciatic
2. Commonest perioperative lower extremity nerve injury is of the following nerve
   A. Femoral
   B. Common peroneal
   C. Sciatic
   D. Deep peroneal
3. Signs of common peroneal nerve injury are
   A. Foot drop, loss of plantar flexion of toes, and incapability to evert the foot
   B. Foot drop, loss of dorsal extension of toes, and incapability to invert the foot
   C. Foot drop, loss of dorsal extension of toes, and incapability to evert the foot
   D. Loss of plantar flexion and dorsal extension of toes and incapability to invert the foot

4. Venous air embolism can most frequently occur with the following position:
   A. Prone
   B. Lateral decubitus
   C. Reverse Trendelenburg
   D. Sitting

Answers: 1. A, 2. B, 3. C, 4. D

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Substance Abuse

50

Daniel J. Ford and Thomas M. Chalifoux

Substance abuse and dependence may have major anesthetic implications. The physiologic and pathologic changes associated with acute toxicity, chronic use, and withdrawal may require changes in the perioperative plan. The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) defines substance *abuse* as a maladaptive pattern of substance use leading to clinically significant impairment or distress as manifested by one or more of the following: failure to fulfill major life obligations, repeated substance use in situations that are hazardous (such as driving), recurrent legal problems, or continued use despite social or interpersonal problems. Substance *dependence* has a similar pattern of substance use but is further defined by tolerance, withdrawal, and compulsive use. *Tolerance* is the need for increased amounts of the substance to achieve intoxication or the desired effect or markedly diminished effect with continued use of the same amount of the substance. *Withdrawal* is characterized by a typical syndrome after discontinuation of the substance.

General Considerations

Substance abuse occurs across the social spectrum. The preoperative assessment should include screening for substance abuse and, if necessary, a substance abuse history. Drug type, amount, route, and last use should be determined. In identified substance abusers, polysubstance abuse is common. Further history and physical exam should focus on the organ systems most affected by the identified substances. Acute intoxication may necessitate delaying elective procedures and complicate obtaining informed consent. Patients acutely intoxicated by CNS depressants are at risk for aspiration pneumonia and may need a chest X-ray. Postoperative planning should include monitoring for and treatment of withdrawal.

Central Nervous System Depressants

Alcohol (Ethanol)

Alcohol's effect is mainly as a CNS depressant, but virtually every organ system is affected. In many states, a blood alcohol level of 80 mg/dl is the legal driving limit. Table 50.1 summarizes important characteristics of commonly abused drugs.

Toxicity: Acute toxicity is mediated by agonism of γ-aminobutyric acid type A ($GABA_A$) receptors. Signs usually vary with blood alcohol level and are progressive, causing impaired judgment, psychomotor retardation, impaired balance, anterograde amnesia (blackout), coma, and respiratory failure. The effects of long-term ethanol use are profound and may include cognitive impairment, cerebellar degeneration, Wernicke–Korsakoff syndrome (from thiamine deficiency), peripheral neuropathy, dilated cardiomyopathy, dysrhythmias, hypertension, cirrhosis (including esophageal varices), gastritis, pancreatitis, malnutrition, hypoglycemia, hypoalbuminemia, electrolyte imbalances (hypomagnesemia, hypophosphatemia, hypocalcemia, and hypokalemia), ketoacidosis, anemia, thrombocytopenia, leukopenia, and myopathy.

Withdrawal: Alcohol withdrawal can be lethal. The signs and symptoms of alcohol withdrawal are the opposite of acute intoxication and are, therefore, adrenergic in nature. Anxiety, insomnia, tachycardia, hypertension, diaphoresis, nausea, and mild tremors can be seen as early as 6–8 h after

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Table 50.1 Characteristics of commonly abused drugs

Drug	Effect on MAC	Detection in urine	Effect on fetus
Alcohol	Acute, decrease; chronic, increase	Blood level measured	Fetal alcohol syndrome (FAS)
Opioids	Acute, decrease; chronic, increase	1–3 days	Neonatal abstinence syndrome (NAS)
Cocaine	Increase	2–3 days	Placental abruption, preterm labor, spontaneous abortion, IUGR
Tobacco	Not significantly affected	2–4 days	IUGR, low birth weight
Marijuana	Acute, decrease; chronic, increase	1–2 days	IUGR

FAS facial dysmorphia, neurological/developmental abnormalities, *NAS* withdrawal syndrome in neonates exposed to opioids in utero, *IUGR* intrauterine growth retardation

the last drink. Delirium tremens can occur 2–3 days later and is distinguished by completely altered sensorium, pronounced adrenergic signs, and, occasionally, fevers. The mainstay of treatment is benzodiazepines, treatment of electrolyte abnormalities, prevention of any seizure activity, airway maintenance if required, and supportive care.

Anesthetic Implications: A thorough preoperative evaluation to determine the extent of alcohol use is paramount. Further testing should focus on affected organ systems. EKG and echocardiography may reveal dysrhythmias and decreased cardiac function, respectively. Electrolytes should be measured and abnormalities corrected. If hypoglycemia is present, thiamine should be included with glucose administration, to prevent Wernicke–Korsakoff syndrome. Liver tests typically reveal an AST/ALT ratio greater than 2 and decreased albumin. CBC and coagulation testing are also important.

Acute intoxication decreases MAC due to GABA activation. In contrast, chronic alcohol use increases MAC, due to induction of the cytochrome P-450 system or cross-tolerance to anesthetics. Therefore, anesthetic plans need to be adjusted accordingly. Other manifestations of alcohol use can also affect the anesthetic plan. Hypoalbuminemia affects both oncotic pressure and pharmacokinetics, whereas anemia and coagulopathy may necessitate administration of blood products.

Opioids

Examples of opioids include: morphine, codeine, heroin, hydromorphone, oxycodone, meperidine, fentanyl, methadone, and buprenorphine. It is important to know that, besides street use, prescription opioid abuse is very common.

Toxicity: Opioid toxicity classically presents with a triad of sedation, hypoventilation, and miosis (though mydriasis may be present with hypoxia). Other effects include decreased gastric motility and constipation, urinary retention, sense of euphoria, hypotension, bradycardia, and, rarely, seizures. These effects however can vary, depending on the opioid type, route of administration, and with tolerance (however little tolerance develops for miosis and constipation). Acute toxicity is managed with ventilatory support and the opioid receptor antagonist naloxone, titrated to reverse ventilatory depression.

Withdrawal: Opioid withdrawal, while not life threatening in most adults, can be long and extremely unpleasant. Signs and symptoms include extreme pain, irritability, tachycardia, nausea, vomiting, diarrhea, rhinorrhea, lacrimation, diaphoresis, and cardiovascular collapse. Naloxone administration can cause acute withdrawal. Withdrawal is treated with long-acting opioids such as methadone and the μ-opioid receptor partial agonist buprenorphine.

Anesthetic Implications: In the preoperative assessment, the type, amount, frequency, and route of opioid use should be determined. Routes of administration include enteral (oral, rectal) and parenteral (intravenous, subcutaneous, transdermal, transmucosal, inhalational). Scabbing and/or scarring (track marks) particularly on the extremities may indicate intravenous abuse. Intravenous drug users are susceptible to infectious diseases such as HBV, HCV, HIV, and bacterial endocarditis. Vascular access can be difficult and, in addition, these patients may be malnourished. It is important to remember that chronic opioid use can cause secondary adrenal insufficiency. In the intraoperative phase, patients may exhibit tolerance to opioids and cross-tolerance to anesthetics. Special attention should be paid to patients on methadone, which may cause QT prolongation and precipitate cardiac dysrhythmias.

In general, these patients require higher doses of opioids for adequate analgesia and are also prone to hyperalgesia and allodynia. Perioperative management strategies include calculation and continuation of baseline methadone or buprenorphine requirements, increasing opioid doses to account for tolerance as well as maximizing other strategies such as peripheral nerve blocks and non-opioid medications.

Central Nervous System Stimulants

Cocaine and Amphetamine

Cocaine and amphetamines (α-methylphenethylamine or amfetamine) are sympathomimetics, as they cause CNS excitation. In general, these substances work by causing

release of epinephrine, norepinephrine, dopamine, and serotonin from nerve terminals, as well as inhibiting reuptake of these neurotransmitters, allowing them to remain within the synaptic cleft in greater concentration and for a longer duration. Cocaine is now rarely used as a local anesthetic. Amphetamines are used to treat narcolepsy, attention-deficit hyperactivity disorder, enuresis, and incontinence.

Toxicity: The clinical features of both cocaine and amphetamine toxicity and chronic abuse are similar. CNS effects include euphoria, mydriasis, stroke, and cerebral edema. Cardiac effects include hypertension, dysrhythmia, tachycardia, cardiomyopathy, and even death. Another important consequence of toxicity is coronary artery vasospasm, which, when combined with increased myocardial oxygen demand, can lead to cardiac ischemia. Cocaine-induced dysrhythmias arise from sodium and potassium channel blockade and subsequent prolongation of the QT interval. When smoked, cocaine can cause pulmonary problems, including cough, dyspnea, and pneumonitis. Other features of cocaine abuse include diaphoresis, hyperthermia, thrombocytopenia, and malnutrition. In the parturient, cocaine use can cause fetal abnormalities as well as preterm labor, premature rupture of membranes, and abruptio placentae.

Withdrawal: Withdrawal from stimulants is unpleasant and can be life threatening. Symptoms (sometimes referred to as "crashing") include anxiety, irritability, depression, fatigue, lethargy, malaise, and increased appetite.

Anesthetic Implications: Preoperative evaluation must include a thorough cardiac history and physical. EKG, chest X-ray, and other testing may be indicated. Patients who are acutely toxic should have elective procedures delayed. Cocaine abusers may have increased anesthetic requirements and increased MAC. Acute amphetamine toxicity can increase MAC, while chronic use can decrease MAC.

Ketamine should be avoided as it can cause sympathetic activation and potentiate effects of cocaine. Intraoperative concerns include extreme hemodynamic changes and myocardial ischemia with noxious stimulation or sympathomimetic administration. It is important to remember that beta blockade may result in unopposed alpha activation and worsen coronary vasoconstriction and is, therefore, contraindicated for treatment of cocaine-associated myocardial ischemia.

Nitroglycerine and calcium channel blockers are often considered better options for management of hypertension in these patients. For short-lived dysrhythmias, antiarrhythmics should be avoided, if possible, as these medications may synergistically act with cocaine to worsen cardiac contractile function. Supraventricular tachycardia (SVT) can be treated with adenosine or cardioversion. Cocaine decreases the seizure threshold and increases the possibility of seizures from local anesthetic toxicity. Also, sympathetic activation can mimic malignant hyperthermia.

Inhaled Substances-Tobacco and Marijuana

Tobacco (*Nicotiana tabacum L.*) smoking causes an array of diseases across multiple organ systems. Tobacco can be smoked, chewed, or sniffed. Though marijuana (*Cannabis sativa*) is primarily smoked, it can also be ingested causing a less potent yet more prolonged effect.

Toxicity: Nicotine, the addictive substance in tobacco, is mainly a stimulant and causes an increase in heart rate and blood pressure that may cause myocardial ischemia in compromised patients. Smoking causes accelerated atherosclerosis and thus coronary artery and peripheral vascular disease. Pulmonary effects of smoking include impairment of the mucociliary escalator, which causes accumulation of mucus, chronic inflammation, and destruction of alveoli. This results in an increase incidence of bronchitis and chronic obstructive pulmonary disease (COPD). Carbon monoxide in smoke binds hemoglobin, shifts the oxyhemoglobin curve to the left, and, therefore, decreases the amount of oxygen available to tissues (tissue hypoxia). Both blood glucose levels and insulin production increase. Children of smokers are at greater risk for asthma. Finally, smoking is associated with numerous forms of cancer, including lung, larynx, esophageal, stomach, and bladder cancers.

Marijuana's primary psychoactive component, tetrahydrocannabinol (THC), causes euphoria, distortion of time, and a heightened sense of awareness. Other effects include increased appetite, conjunctival infection, and drowsiness. Acute intoxication can cause vasodilation leading to hypotension and tachycardia. Marijuana smokers are at risk for many of the same airway complications as tobacco smokers, and they tend to develop lung and throat cancer at earlier ages.

Withdrawal: Nicotine withdrawal can cause anxiety, irritability, depression, fatigue, difficulty concentrating, sleep disorder, nightmares, headache, and hunger. Symptoms start 2–3 h following the last tobacco use and peak about 2–3 days later. Treatment may include nicotine (chewing gum, patch), bupropion, or varenicline. Marijuana withdrawal has been associated with anxiety and irritability, but the existence of marijuana withdrawal is controversial.

Anesthetic Implications: Preoperative evaluation must include complete cardiopulmonary history and physical. The optimal timing of smoking cessation prior to surgery is controversial, though it is generally advised to stop smoking about 8 weeks prior to surgery. Smoking cessation close to

the time of surgery decreases carboxyhemoglobin levels, which helps to improve oxygenation. Paradoxically, smoking cessation close to the time of surgery may make the airway more reactive, but this has not been shown to increase the risk of pulmonary complications. Smoking cessation interventions, such as counseling and nicotine replacement therapy, 4–8 weeks before surgery are associated with decreased postoperative complications. Marijuana users should be similarly counseled.

Marijuana use decreases MAC. Smokers are at higher risk for perioperative bronchospasm, especially during intubation and mechanical ventilation. Premedication with inhaled β-agonists and corticosteroids reduces the incidence of intubation-evoked bronchoconstriction. Mucus overproduction can cause mucus plugging. Prevention of postoperative atelectasis and pneumonia requires an adequate cough mechanism to clear mucus. Postoperative plans should ensure good pain control and include incentive spirometry. Chronic marijuana use may impair the patient's ability to follow postoperative instructions.

Other Substance Abuse Drugs

Following is a list of additional drugs which can be abused:

- Dissociative drugs—Ketamine, PCP and analogs (phencyclidine), dextromethorphan (found in cough medications)
- Hallucinogens—LSD (lysergic acid diethylamide), mescaline, psilocybin
- Club drugs—Ecstasy/MDMA (methylenedioxymethamphetamine), flunitrazepam
- Anabolic steroids
- Inhalants—Solvents (paint thinners, gasoline, glues), gases (butane, propane)

Substance Abuse in Anesthesiologists

Because of the easy availability of drugs, substance abuse is quite common in anesthesiologists. In addition, personal problems, a family history of substance abuse, presence of a psychiatric/personality disorder, and occupational stress make anesthesiologists more prone to substance abuse. Commonly abused drugs in anesthesiologists are opioids, benzodiazepines, nitrous oxide, and propofol (plus alcohol). Early identification of drug-abusing anesthesiologist, effective treatment and rehabilitation, and prevention of relapse are important management strategies.

Emergent Consultation

For emergent consultation with a medical toxicologist, one can call the US Poison Control Network at 1-800-222-1222 or access the World Health Organization's list of international poison centers (www.who.int/ipcs/poisons/centre/directory/en).

Clinical Review

1. Chronic alcohol abuse causes MAC of inhalational volatile agents to:
   A. Increase
   B. Decrease
   C. Remain the same
   D. Decrease or remain the same
2. Chronic opioid abuse does not cause tolerance to its following effect:
   A. Pruritus
   B. Sense of euphoria
   C. Respiratory depression
   D. Constipation
3. A 36-year-old patient presents to the operating room for an appendectomy under general anesthesia. He gives a history of cocaine abuse. His vitals are BP, 180/100 mmHg; heart rate, 120 beats/min; and oxygen saturation, 98 % on room air. Best drug among the following to manage his vitals is:
   A. Metoprolol
   B. Phentolamine
   C. Nitroglycerine
   D. Esmolol
4. It is recommended that smoking should be stopped before surgery for at least:
   A. 3 days
   B. 1 week
   C. 2 weeks
   D. 8 weeks
5. The most common drug abused by anesthesiologists is:
   A. Midazolam
   B. Fentanyl
   C. Propofol
   D. Nitrous oxide

Answers: 1. A, 2. D, 3. C, 4. D, 5. B

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Awareness Under Anesthesia

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Tiffany Lonchena and Cynthia Wells

One of the commonly accepted goals of general anesthesia is the achievement of decreased consciousness and the prevention of intraoperative awareness. Intraoperative awareness and recall can have serious psychological effects on the patient as well as legal consequences for the provider. As such, it is imperative to maintain vigilance in the operating room in order to avoid preventable anesthesia awareness, as well as to be prepared to address such events when they arise.

Incidence

The overall incidence of intraoperative awareness has been quoted at 0.18 % with NMBDs and 0.10 % without NMBDs. This correlates with approximately 30,000 surgical patients per year. High-risk surgical cases with a greater incidence of awareness include cardiac surgery (1.0–1.5 %), trauma surgery (11–43 %), and cesarean section under general anesthesia (0.4 %). This increased incidence is attributed to the intentional use of light anesthesia with the desire to minimize the negative hemodynamic effects of anesthetic agents.

Risk Factors

Factors that increase the incidence of intraoperative awareness include the absence of volatile agents or propofol during maintenance of anesthesia, total intravenous anesthesia (TIVA), NMBDs, and prolonged or difficult intubation. Patient-related risk factors include chronic alcohol use, chronic use of neurodepressant drugs (antiepileptic, opiate, and sedative), a history of awareness during general anesthesia, a limited cardiac reserve requiring light anesthesia, and ASA Classes IV–V.

Intraoperative awareness generally occurs secondary to either a decreased dose of anesthesia, often referred to as "light" anesthesia, or to a patient's decreased response, or resistance, to a seemingly appropriate dose of agent. For inhalation agents, the depth of anesthesia is estimated using minimum alveolar concentration (MAC). While MAC can be used as a general guideline, it is affected by numerous factors, including age, temperature, chronic drug exposure, acute drug exposure, and genetic factors. Furthermore, multimodal anesthesia (the mixture of inhalation and intravenous drugs of varying mechanisms of action) results in the unreliability of MAC as the only method of measuring anesthetic depth.

With the common addition of neuromuscular-blocking drugs (NMBD) to the anesthetic plan, the assessment of intraoperative consciousness becomes increasingly difficult. Movement, which could be indicative of light anesthesia, is now chemically prohibited. Furthermore, NMBDs allow for a decreased required volatile anesthetic dose and thus an at least theoretical greater probability of light anesthesia.

Characteristics

Intraoperative awareness can result in two types of memory formation, explicit and implicit. Explicit memory, or the recall of specific events, is more detrimental to both the practitioner and the patient. Implicit memory, which is characterized by changes in behavior without the recall of specific events, is often still traumatic for the patient but tends to have less legal consequence. The most common memories during cases of intraoperative awareness involve awake paralysis, feeling surgery with or without pain, panic, the process of tracheal intubation, and the recollection of conversations, sounds, or comments concerning body habitus. There have

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also been incidences of inadvertent paralysis due to residual neuromuscular-blocking drug in the intravenous tubing, both in the operating room as well as in the postoperative care area.

Prevention

Although not all cases of anesthesia awareness can be avoided, it is imperative that the anesthesia provider minimizes the preventable causes of anesthetic awareness. This requires a complete machine check daily, a thorough preoperative evaluation, and vigilant clinical monitoring.

Anesthesia Machine Check: One of the most preventable causes of intraoperative awareness is the failure to deliver an adequate dose of volatile anesthetic. This can be secondary to equipment malfunction, vaporizer complications, and breathing circuit failures. With a thorough machine check prior to the patient's arrival into the operating room, most complications can be prevented.

Preoperative Evaluation Patients at high risk for intraoperative awareness should be identified preoperatively and properly counseled regarding their increased risk. These patients should be asked about previous episodes of awareness and tolerance to sedatives and opioids and whether they have a known difficult airway or are having a surgical procedure with increased risk of awareness. Prior anesthesia records should be checked whether these patients received NMBDs during maintenance of anesthesia, reduced amount of inhalational agents, or total intravenous anesthesia. Patients can be given midazolam preoperatively, as prophylactic administration of midazolam has been shown to decrease the incidence of awareness. In the event of prolonged attempts at intubation after intravenous induction, additional intravenous anesthetic agent should be readily available to maintain unconsciousness.

Monitoring This includes monitoring for adequate depth of anesthesia (end-tidal concentration of inhalational agent, patient movement) and conventional monitoring (blood pressure and heart and respiratory rate). In the past, monitoring of intraoperative awareness was largely concentrated on clinical signs of awareness, including tachycardia, hypertension, sweating, tearing, mydriasis, and patient movement and reflexes. While these physiologic signs may be suggestive of awareness, they have been found to be unreliable markers. In a literature review of 271 cases of awareness, only 20 % of patients experienced intraoperative tachycardia, and 18 % experienced intraoperative hypertension. With this in mind, significant effort has been made toward the development of a more objective clinical tool for measuring anesthetic depth.

Although a number of devices have been used to measure the depth of anesthesia, the Bispectral Index, or *BIS monitor*, is currently the most widely utilized. The BIS monitor records and processes spontaneous cortical brain electrical activity and converts it into a mathematical form. This conversion results in a scaled score of 0–100, which correlates with a patient's progressive loss of consciousness (awake, sedated, light anesthesia, deep anesthesia, and EEG silence). The range of 40–60 is indicative of a low probability of consciousness and is considered to be the target score for general anesthesia maintenance. The aim of this machine is to minimize the given anesthetic dose while preventing anesthetic awareness.

While the BIS monitor may be helpful in monitoring a patient's level of consciousness, it does have limitations. Most importantly, the BIS is unresponsive to a number of anesthetic agents, including nitrous oxide, ketamine, opioids, and xenon. Thus, it is of limited use in a variety of anesthetic techniques. In addition, movement, electrocautery, and EMG activity may cause interference in the EEG signal.

The effectiveness of BIS in the prevention of awareness has been investigated in several large, randomized trials. There is conflicting evidence as to whether BIS-guided anesthesia significantly reduces the risk of awareness in high-risk populations. While some studies have shown decreased anesthetic drug consumption as well as reduced times to awakening, first response, and eye opening, others have not found such clear results. With the cost of approximately $16 dollars per use, the routine use of BIS monitoring has been brought into question. At this time, the Anesthesia Task Force does not recommend routine use of BIS monitoring for prevention of awareness or depth of anesthesia monitoring in non-high-risk patients undergoing general anesthesia. For the high-risk patient, BIS monitoring can be used as an adjunct to guide anesthetic dosing.

Approach to the Aware Patient

Once a case of intraoperative awareness has been detected, it must be addressed immediately. If such an event is suspected in the operating room, the practitioner should speak to and reassure the patient while addressing the anesthetic depth. Currently, there are no studies that support the administration of a benzodiazepine as a means of achieving retrograde amnesia once awareness is suspected. However, immediate benzodiazepine administration is still considered the standard of care if one suspects an acute episode of awareness in the operating room.

Postoperatively, the approach to intraoperative awareness includes full disclosure and a structured interview investigating the event, an apology regarding its occurrence, and an early psychological referral. A strong social support and acknowledgment of the event has been shown

to be the most important method of prevention against long-term psychological consequences and the development of PTSD. Psychological counseling is centered on exposure-based therapies, antidepressants (SSRI), and the use of sedative-hypnotics for insomnia. After a case of intraoperative awareness has been recognized, the anesthesia provider is responsible for completing a quality assurance report.

Psychological Consequences

Intraoperative awareness can have severe psychological consequences for the patient. In fact, up to twenty-two percent of patients who experienced intraoperative awareness have suffered significant psychological symptoms. Patients have been noted to be emotionally traumatized, may develop severe behavioral disturbances, and are at risk for the development of post-traumatic stress disorder (PTSD). With PTSD, patients may repeatedly re-experience the event, exhibit avoidance, have feelings of numbness, and may have increased arousal at triggering stimuli including smells (rubbing alcohol), colors (blue associated with scrubs), and hospitals. They have reported flashbacks of paralysis, pain, terror, and helplessness. Such feelings can disrupt sleep and instill fear concerning future anesthetics.

Legal Consequences

In a review of Closed Claims Analysis from 1961 to 1995, 79 of the 4,183 claims involved anesthesia awareness. Of these claims, 23 % cited awake paralysis, and 77 % described recall during general anesthesia. Nearly all of the claims involving awake paralysis (94 %) and almost half (43 %) of the claims of recall were found to be due to preventable errors in labeling and administration of NMBD.

Most legal claims involved women who were less than 60 years old, ASA Class I–II, or undergoing elective surgery utilizing an anesthetic technique involving high-dose opioids, NMBD, and/or no volatile anesthesia. There was an increasing incidence of claims as the years progressed, indicating that the legal consequence of such events is increasing. Interestingly, financial payments were made to a greater proportion of awake paralysis claims versus other awareness claims (78 % vs. 55 %). However, the payout for these cases was significantly less ($18,000 vs. $100,000). The legal and financial ramifications reinforce the serious nature of such events.

Clinical Review

1. Patients having the following surgery may have the highest risk of intraoperative awareness under anesthesia:
   A. Cesarean section under general anesthesia
   B. Trauma
   C. Cardiac surgery
   D. Neurosurgery
2. Increased incidence of intraoperative awareness under anesthesia is more likely to occur in all of the following patients, except
   A. Chronic alcoholic user
   B. Chronic drug abuser
   C. Chronic use of neurodepressant drugs
   D. Sevoflurane end-tidal concentration of 2.0
3. Target range of BIS number for general anesthesia should be
   A. 20–30
   B. 20–40
   C. 40–60
   D. 50–70

Answers: 1. B, 2. D, 3. C

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Infectious Diseases

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Seth R. Cohen and Kristin Ondecko Ligda

Infectious disease agents include viruses, bacteria, fungi, protozoa, parasites, and proteins called prions. Some patients are asymptomatic from their infection, whereas in other patients, clinical or subclinical illness affects the patient during the perioperative period. Transmission of the agents can occur through airborne inhalation, through contact with contaminated body fluids, via food, through physical contact, or through vector organisms. Additionally, patient-patient and patient-healthcare worker (HCW) transmission of infectious diseases remain a high concern. The perioperative period represents a unique challenge in the prevention of transmission. While diligent hand washing remains a staple in the standard of care, other measures must be implemented with certain infectious agents. Several of the major infectious diseases will be reviewed in this section, and universal precautions will be examined. Careful perioperative planning and situational awareness should be practiced by the healthcare worker taking care of patients with transmissible diseases.

Human Herpes Virus

The human herpes family viruses (HHV) consist of eight separate viruses, all with potential of causing human disease. The prevalence of *HSV-1* (*HHV-1*) *and HSV-2* (*HHV-2*) in the general population is 65 % and 29 %, respectively. HSV-1 is mostly transmitted through nonsexual contact and is most frequently associated with oral mucosal lesions, while HSV-2 is mostly transmitted through sexual contact and commonly infects urogenital mucosa. Shortly after primary infection, the virus can be found in a dormant state in sensory neurons. Reactivation may occur at a later time. Immunocompromised patients are at increased risk for reactivation with subsequent disseminated disease. HSV reactivation in posttransplant patients can cause pneumonia, hepatitis, encephalitis, and disseminated disease. Oral acyclovir has been shown to be an effective prophylactic and treatment agent for HSV-1 and HSV-2.

Varicella zoster virus (VZV, HHV-3) is responsible for chickenpox and shingles in the healthy, immunocompetent population. However, it may cause significant, life-threatening disease in the immunocompromised population, such as posttransplant patients. Primary infection (chickenpox) or reactivation (shingles) in healthy patients with intact immune systems will manifest with a vesicular rash in a dermatomal pattern. Shortly after primary infection, VZV remains dormant in neurons of dorsal root ganglia. However, reactivation in posttransplant patients may manifest with cutaneous infection, encephalitis, myelitis, and pneumonia. Many studies have documented the efficacy of acyclovir and ganciclovir for the prophylaxis of VZV. Vaccination is available for patients and their close contacts and has shown to be effective in preventing disease.

Epstein-Barr virus (EBV, HHV-4) is the causative virus associated with infectious mononucleosis and the more serious (but rare) Burkitt's lymphoma, nasopharyngeal carcinoma, and posttransplant lymphoproliferative disorder (PTLD). About 90 % of the general population has been found to be seropositive for EBV. While patients generally demonstrate flu-like symptoms, more significant symptoms may occur. These include encephalitis, optic neuritis, and hepatosplenomegaly with increased risk of splenic rupture. Like VZV, EBV is generally transmitted through respiratory secretions and saliva. Shortly after primary infection, EBV can be found in a dormant state in B cells of the immune

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system. No vaccination currently exists for EBV, although some studies have shown the effectiveness of antiviral medications for treatment.

Cytomegalovirus (CMV, HHV-5) is a common infection with a prolonged latency period. Estimates of seropositivity rates range from 40 % in young adults to above 90 % in the elderly population. While most infections occur asymptomatically in the healthy population, immunocompromised patients are at risk for disseminated disease. In particular, post-lung transplant patients are at risk for CMV pneumonitis, a common cause of bronchiolitis obliterans syndrome. Valganciclovir has been shown to be an effective prophylactic measure in these high-risk patients.

HHV-6, a common infection that occurs in over 90 % of the population, causes roseola infantum which is manifested by high fevers and a viral exanthem rash. After primary infection, it remains dormant in CD4 lymphocytes. Reactivation in immunocompromised patients may lead to neurologic symptoms, gastroenteritis, pneumonitis, hepatitis, and myelosuppression. While no vaccine currently exists, antiviral agents are an effective treatment.

HHV-8 gained attention as an opportunistic disease of AIDS patients, referred to as Kaposi sarcoma. In addition, HHV-8 is a causative agent in primary effusion lymphoma and multicentric Castleman disease in immunocompromised patients. While only 1.5 % of Americans are seropositive, up to 50 % of the sub-Saharan population is infected. Treatment of these diseases appears to be a reduction in the degree of immunosuppression, chemotherapy, radiation therapy and also resection of localized tumors, and treatment of other coinfections.

Paramyxovirus

Respiratory syncytial virus (RSV) and parainfluenza are part of the paramyxovirus family that is a frequent cause of both upper and lower respiratory tract infections in children. Peak seasonal appearance occurs in the winter, similar to influenza. Immunocompromised patients, such as posttransplant and lymphopenic patients, are more likely to have progression of the infection into the lower respiratory tract with significantly higher mortality rates. The paramyxoviruses have been associated with posttransplant complications, including post-viral obliterative bronchiolitis, a cause of chronic rejection. While vaccination is not available, RSV prophylaxis can be effectively managed with immunoglobulin and monoclonal antibodies. Treatment centers on the use of ribavirin, RSV antibodies, and supportive measures. In comparison, there are no proven preventative or treatment measures for parainfluenza.

Influenza Virus

Perhaps the one virus that has gained global notoriety in history for global epidemics has been the influenza virus. Despite widespread vaccination, the potential for antigenic shift and drift exists, a situation that could contribute to worldwide pandemics. Influenza A and B are RNA viruses that cause upper and lower respiratory tract disease. Like RSV, the progression to lower respiratory tract disease is more prevalent in immunocompromised patients and disease peaks in the winter. Neuraminidase inhibitors, such as oseltamivir and zanamivir, are effective treatments, especially when begun early in the viral course. These treatments are augmented by amantadine and rimantadine. Vaccination is available, but it may not cover all strains of the virus.

Blood-Borne Viruses

Blood-borne viruses are a major concern in the hospital for both the patient and healthcare providers. Virus transmission from an infected host during percutaneous or mucosal penetration is reported to be 0.3 % for human immunodeficiency virus (HIV), 3 % for hepatitis C, and 30 % for hepatitis B. In order to calculate risk of transmission from percutaneous or mucous membrane injury, several factors must be considered, including method of transmission (needle penetration versus blood splash to mucous membrane), needle type (hollow-bore needle such as an IV needle versus solid-bore needle such as suture needle), needle gauge, penetration of needle into patient and healthcare worker, presence of blood on needle, access of the needle to the patient's bloodstream, or whether the needle has passed through gloves or other barriers prior to entering the skin. Personal protective equipment and situational awareness remain the mainstays of prevention. Effective protection methods to minimize risk of transmission of blood-borne diseases include gloves, double gloving if needed, face shields or other eye protection, sleeve reinforcements, knee-high trauma boots, plastic aprons under surgical gowns, and avoidance of blind suturing techniques.

HIV is an RNA retrovirus that produces reverse transcriptase, which allows the creation of complimentary DNA that is substituted into the host cell. The virus attacks the host and causes cell lysis, with subsequent loss of helper CD4 T cells. Although mandatory preoperative HIV screening has been advocated by many, ethical concerns in addition to financial concerns are barriers to this screening. Furthermore, consent must be obtained before performing testing. Instead, a more accepted practice among many practitioners seems to be

testing either high-risk patients or those undergoing higher risk procedures. Regardless of the patient's infection status, universal precautions are standard practice. Upon receiving a percutaneous or mucosal injury from a patient with unknown HIV status, prophylactic treatment is begun and consent for HIV testing is obtained from the patient. If the host was determined to have asymptomatic disease, a two-drug regimen is recommended. However, if the patient was symptomatic at the time of exposure, a three-drug regimen is commenced for at least 4 weeks.

Hepatitis B is mainly transmitted through intravenous drug abuse, blood transfusions, and sexual contact. Viral replication of the virus occurs in hepatocytes. After exposure, 25 % of patients demonstrate clinical symptoms of hepatitis. About 95 % of patients exposed will have spontaneous clinical resolution, while 5 % will be antigen positive for life with potential for progression to chronic hepatitis, cirrhosis, portal hypertension, and hepatocellular carcinoma. The state of exposure for hepatitis can be determined through antibody testing. The presence of the core antibody indicates previous exposure, and the presence of core antigen indicates persistent disease. The presence of the "e" antigen indicates active viral replication, a marker of higher infectivity. If the surface antibody is the only antibody present, this signifies previous vaccination against hepatitis B. Despite the high transmission of hepatitis B through percutaneous injury, vaccination effectively eliminates transmission. However, those with unreactive antibody testing or no prior vaccination history are at risk and should receive postexposure prophylaxis. These individuals should receive the HBV immunoglobulin and either a booster dose of the vaccine or the full vaccination series.

Hepatitis C is estimated that over four million people in the United States have been exposed to hepatitis C. Transmission occurs through intravenous drug abuse, sexual contact, and transfusions. Like hepatitis B, about 25 % of people exposed demonstrate clinical symptoms. However, unlike hepatitis B, 50–80 % of those patients with hepatitis C will go on to develop chronic disease. About 20 % of those with chronic disease will progress to cirrhosis and hepatocellular carcinoma. Antibody testing after exposure may yield a positive result for up to a year. Unfortunately, no effective vaccination or prophylaxis after exposure is available at this time.

Nosocomial Infections

Infectious bacterial organisms are a major concern when considering infection control measures to prevent patient-patient transmission. Nosocomial infections are a major source of morbidity and mortality, including vancomycin-resistant *Enterococcus* (VRE), methicillin-resistant *Staphylococcus aureus* (MRSA), quinolone-resistant *Pseudomonas*, and *Clostridium difficile*. Many interventions have been proposed to eradicate or control the spread of nosocomial infections. Infection control measures include proper hand washing techniques, implementation of contact precautions, active surveillance cultures from patients, staff education, and effective environmental cleaning. All of these interventions, especially when combined, have been shown to reduce the incidence of multidrug-resistant organisms and its spread.

The duration of patient isolation is an area of high debate. Some advocate that once a patient is labeled as a carrier, they should always be isolated as if they were a carrier and that any testing indicating that they have been cleared of their infection is a result of poor culturing, poor sensitivity, or removal of antibiotic selection pressure. However, the Hospital Infection Control Practices Advisory Committee (HICPAC) recommends removal of isolation precaution after three negative cultures, at least 1 week apart. This duration of colonization of these antibiotic-resistant organisms is highly variable and currently unknown.

MRSA In addition to its nosocomial origin, MRSA is now being found in the community and is an important source of skin and soft tissue infections presenting in the outpatient setting. In the inpatient setting, it is a leading cause of pneumonia, surgical site infections, and disseminated infections. Risk factors for contracting MRSA include advanced age, prior antibiotic use, previous surgery, and extended hospitalization. MRSA colonization occurs in asymptomatic patients on normal skin flora and in the nares. Furthermore, colonization in the nares has been shown to be a risk factor for development of surgical site infections. For this reason, many advocate MRSA screening with eradication therapy through antiseptic decontamination prior to surgery. Screening of asymptomatic patients also allows for more effective prevention of cross-contamination of other patients through implementation of isolation and barrier precautions. Despite these measures, the Center for Disease Control (CDC) recommends against routine active surveillance screening of all patients.

VRE Up to 9 % of nosocomial-acquired bloodstream bacterial infections are attributed to *Enterococcus*, with a significant percentage as VRE. Unlike MRSA, VRE has a low rate of asymptomatic carriers. When colonization occurs, it is most likely on the skin and in the gastrointestinal tract. A higher prevalence of VRE has been found in intensive care, dialysis, and oncology units. The most common mechanism of transfer among patients appears to be ineffective hand hygiene among healthcare workers. Contact precautions typically are not implemented until after a diagnosis or history of VRE is known.

Clostridium difficile is considered a part of the normal intestinal flora in 1–3 % of healthy patients. When *C. difficile* overgrows and dominates the intestinal flora secondary to

eradication of the other normal gut flora, clinical symptoms can occur, which can range from mild diarrhea to the more severe pseudomembranous colitis and toxic megacolon. The toxins released from the bacteria are implicated in causing mucosal damage and inflammation. Measures to control the spread of this infection include proper hand washing to remove the *C. difficile* spores, disinfection of the physical environment, implementation of contact precautions, and proper selection of antibiotics when necessary. Some experts have recommended that contact precautions be maintained until 48 h after resolution of diarrhea. Environmental cleaning after physical exposure by an infected patient can be accomplished with chlorine-containing agents or hydrogen peroxide.

Airborne Disease

Droplet transmission is limited by distance spread from host to less than 1 m due to particle size. The size of the particle is a source of controversy, but the World Health Organization (WHO) employs a particle size of >5 μm. In comparison, particles that undergo airborne transmission are usually <5 μm, may remain suspended in air for an extended amount of time, and may be spread to greater distances. In addition, smaller infectious particles are more likely to penetrate the lower respiratory tract, while larger particles generally settle in the upper respiratory tract. Proper precautions should be followed in the operating room. Laminar airflow systems with HEPA filters are effective in removing the majority of airborne particles. These systems can be ceiling or wall mounted, with frequent air changes that limit colony-forming units. Other measures to prevent infection transmission in the operating room include sterile surgical gowns and drapes, face masks, antiseptic hand scrub, and the timing of opening surgical instruments prior to performing a procedure.

Tuberculosis (TB) is currently the eighth leading cause of death worldwide, and an estimated 1/3 of the world's population is infected. The highest concentration is focused in the less developed areas of sub-Saharan Africa, India, Southeast and Central Asia, Eastern Europe, and Micronesia. Tuberculosis is spread through respiratory droplets by individuals with active pulmonary disease. While most healthy patients exposed will have an asymptomatic and localized course, this infection may remain dormant in pulmonary tissue for years, referred to as latent tuberculosis infection. Reactivation may occur years later in normal healthy patients. However, reactivation is more likely to occur in immunocompromised patients, such as patients with malignancies, HIV, end-stage renal disease, diabetes, and patients on immunosuppressive medications.

Active tuberculosis is characterized by chest X-ray findings of infiltrates found in the apical-posterior segments of the upper lobes and may include cavitations. Symptoms most frequently associated with TB infection include the constitutional symptoms of fevers, night sweats, cough, and unintended weight loss. Diagnosis of latent TB infection is made by tuberculin skin testing (TST), with interpretation of test results based on prevalence and risk of the patient. Active disease is diagnosed through a combination of chest X-ray findings, culture results, and acid-fast bacilli detection from either sputum testing or bronchoalveolar lavage. Treatment is usually accomplished through direct observational therapy (DOT) with at least 6 months of treatment. While latent TB can be effectively treated with one agent, the danger of multidrug-resistant organisms necessitates the use of multiple medications. Patients found to have active tuberculosis infection should be kept in a negative-pressure isolation room with at least 6 air exchanges per hour until clinical resolution of symptoms is achieved with three consecutive negative results of sputum testing. Healthcare providers should wear N95 masks that have been individually fit-tested when caring for patients with active disease.

Severe Acute Respiratory Syndrome (*SARS*) In 2003, SARS, a form of *Coronavirus*, was responsible for a major pandemic that affected many healthcare providers. This virus was spread through respiratory droplets and was found to have a high level of infectivity. There has been some debate on whether this virus was also spread to greater distances from the host through airborne transmission. Flu-like symptoms were associated with mild acute infection and symptoms of serious infection included reactive hepatitis, a severe acute neurologic syndrome, and pulmonary involvement with pneumonia and acute respiratory distress syndrome (ARDS). Healthcare providers were found to be at significant risk for contraction of the virus, especially when caring for patients that required oxygen therapy, positive-pressure ventilation, and resuscitation. Recommendations for healthcare providers caring for these patients involve strict contact and droplet precautions. However, airborne precautions, such as the use of N95 fitted mask, must also be observed when performing procedures that may generate aerosols, such as bronchoscopy.

Prions

Creutzfeldt-Jakob disease (CJD), a family of neurodegenerative disorders, has become a surgical concern over the past couple decades. The infectious entity of this disease has been found to be mutated prions that are protease resistant. Mean incubation period until appearance of symptoms has averaged over 10 years with subacute progression of neurologic disease. However, average survival after the appearance of symptoms is only a few months. Diagnosis can only be made through biopsy of infected tissue.

Prion disease may be transmitted through familial, sporadic, or iatrogenic spread. In particular, the iatrogenic form is concerning for infection control precautions, as more than 400 patients have been exposed to prion-contaminated surgical equipment. Certain surgical operations such as ophthalmologic and neurosurgical procedures are considered high risk for prion transmission. Historically, EEG electrodes, human pituitary hormone, cornea transplant, and dura mater grafts have also been implicated. A few case reports have found transmission through blood transfusion from an infected donor. These mutated prions have been shown to be less susceptible to standard methods of sterilization. WHO has made specific recommendations regarding the sterilization of surgical instruments that have come into contact with tissues that carry a risk of high infectivity or patients with suspected or confirmed prion disease. Moreover, some experts recommend the use of disposable surgical instruments in these situations.

Clinical Review

1. Vaccinations exist for all of the following viruses, except:
   A. Influenza
   B. Varicella
   C. Hepatitis C
   D. Hepatitis B
2. Chronic liver disease is most likely to develop with infection with the following virus:
   A. Hepatitis C
   B. Hepatitis B
   C. Human immunodeficiency virus
   D. Herpes virus
3. Following is the most common cause of death due to infection:
   A. Tuberculosis
   B. Human immunodeficiency virus
   C. Hepatitis C
   D. Lower respiratory tract infections
4. Effective hand hygiene is important in preventing spread of infections:
   A. True.
   B. False.
   C. Is irrelevant.
   D. Double gloving has been shown superior to hand hygiene.

Answers: 1. C, 2. A, 3. D, 4. A

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Alternative Medicine and Anesthesia

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E. Gail Shaffer and Patricia L. Dalby

Complementary and alternative medicine (CAM) is gaining increasing popularity across the United States. A 2007 survey found that approximately 38 % of the general adult population uses some form of complementary and alternative therapies. Almost 58 % of surgical patients use some form of CAM, with over 20 % using herbal or vitamin supplements. With such a wide-spanning influence, it is easy to see why knowledge of CAM may be important to the anesthesiologist.

A comprehensive definition of CAM is difficult to ascertain, as it is continually evolving and changing. The National Center for Complementary and Alternative Medicine (NCCAM), part of the National Institutes of Health, defines CAM as "a group of diverse medical and health care systems, practices, and products that are not generally considered part of conventional medicine." There are no official guidelines regarding perioperative use and discontinuation of herbal supplements, but the American Society of Anesthesiologists suggests that many herbal medications should be stopped 2–3 weeks prior to surgery.

Commonly Used Herbal Medicines

Echinacea

Echinacea (coneflower, purple coneflower) is used for prevention or treatment of common viral and/or bacterial infections, specifically of the upper respiratory tract. It is postulated to work by an immunostimulatory effect. Allergic reactions after echinacea use have been reported, including documented anaphylaxis. Patients with asthma or allergic sequelae should avoid the use of echinacea. Echinacea may interact with immunosuppressive drugs (via inhibition of cytochrome P450 system) necessary for patients with organ transplant and, therefore, should be avoided in this patient population too.

Ephedra

Ephedra (ma huang) use is common in Chinese medicine. It is used as a weight loss adjunct, to increase energy, and to treat upper respiratory symptoms, asthma, flu, and headaches. It was banned by the Federal Drug Administration (FDA) in 2004, as a result of reports of cardiovascular complications and death. The main cardiovascular effects of ephedra are mediated by its most active compound ephedrine, a sympathomimetic compound with alpha-1, beta-1, and beta-2 activity. The effects of ephedrine are an increase in heart rate and blood pressure.

Use of ephedra preoperatively by patients may result in tachyphylaxis due to depletion of catecholamines. In this situation, the use of direct-acting vasopressors is necessary. In addition, the interaction of ephedra and monoamine oxidase inhibitors may lead to a life-threatening hypertensive reaction.

Garlic

Garlic has been extensively studied for its benefits in patients with atherosclerotic disease. A meta-analysis showed that garlic may reduce blood pressure (vasodilation) and cholesterol levels. In addition, garlic has effects on platelets, inhibiting platelet aggregation with possible irreversible effects. Due to this effect, it is recommended that patients taking garlic discontinue usage at least 7 days prior to surgery.

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Ginkgo

The leaf of the *Ginkgo biloba* tree has been used for thousands of years as a medicinal adjunct. Currently, interest in ginkgo to prevent/treat cognitive dysfunction is high. However, the Ginkgo Evaluation of Memory study found no improvement in cognitive decline and no change in the incidence of dementia and Alzheimer's disease in elderly patients taking ginkgo. Ginkgo has also been used for treating symptoms of intermittent claudication. Ginkgo appears to inhibit platelet-activating factor, and therefore, it may increase perioperative bleeding risk.

Ginseng

Ginseng is an herb that has a variety of physiologic effects that are incompletely understood. Both American ginseng and Asian ginseng are commonly marketed. The active chemical compounds are ginsengosides. Ginseng may lower blood glucose and has been used for this effect. In addition, ginsengosides may alter coagulation parameters, and therefore, it is recommended that ginseng be discontinued at least 7 days prior to surgery.

Kava Kava

Kava, an herb derived from the plant *Piper methysticum*, is used as a sedative-anxiolytic medication. Kava may exert its effects through GABA receptors. Because of the potential for interaction with other sedatives used perioperatively (potentiation of anesthetic action), it is recommended that it be discontinued at least 24 h prior to surgery. Hepatotoxicity is a major side effect of its use.

Melatonin

Melatonin, a naturally occurring hormone, is found in over-the-counter preparations used for treatment of insomnia, jet lag and as a sedative. Melatonin has been tested as a preoperative anxiolytic as well.

Saw Palmetto

Saw palmetto (SP) gained popularity among men as a treatment for benign prostatic hypertrophy. However, studies have shown that is it largely ineffective for this purpose. It has been proposed that SP inhibits 5-alpha reductase, but in vivo data does not consistently support this. SP does appear to have an effect on the cyclooxygenase pathway and may cause inhibition of platelet aggregation. For this reason, it should be discontinued in the perioperative period.

St. John's Wort

St. John's wort (*Hypericum perforatum*) is popular for the treatment for depression, but a large clinical trial has shown it to be ineffective. The mechanism of action of its active compounds is the inhibition of the reuptake of serotonin, dopamine, and norepinephrine. Serotonin syndrome can occur with concurrent use of other serotonin-blocking agents. St. John's wort also induces metabolism via the cytochrome P450 enzyme, which may increase the metabolism (decreased blood levels) of drugs (benzodiazepines, amitriptyline, theophyline, digoxin, warfarin) and antirejection medications (cyclosporine) for organ transplantation. Discontinuation of St. John's wort, perioperatively, may increase the blood level of these medications.

Valerian

Valerian is used for the treatment for insomnia, possibly acting on GABA receptors to produce hypnosis and sedation. The dose of valerian should be tapered preoperatively, if possible, as acute withdrawal may occur in patients taking valerian.

Non-herbal Supplements

Non-herbal supplements such as vitamins and minerals are commonly used by patients in the perioperative period. While generally safe, high doses of fat-soluble vitamins (A, D, E, and K) may lead to toxicity. Other supplements, such as creatine, glucosamine, and chondroitin may also have side effects.

Vitamin E

Vitamin E is a supplement that has been very popular for its antioxidant properties, especially for its ability to enhance wound healing, prevent the development of atherosclerotic vascular disease, and potentially retard aging. However, taken daily in doses greater than 400 IU, it has been associated with an increase in blood pressure.

Dietary supplementation with vitamin E, ginkgo, ginger, garlic, and feverfew has been associated with anticoagulant properties and prolonged surgical and postoperative bleeding. This effect is compounded if these substances are taken in conjunction with any other medication that has anti-clot forming ability such as aspirin or the NSAIDs. Generally, use is discontinued 2 weeks preoperatively.

Acupuncture

Acupuncture, the stimulation of various points on the body to enhance and promote health, has been practiced in various parts of the world for centuries. It is a part of Traditional

Chinese Medicine but is considered CAM in the United States. The interest in acupuncture is for pain relief and treatment of postoperative nausea and vomiting (PONV).

The basis of acupuncture for treatment of pain is the stimulation of small-diameter nerves that subsequently result in the release of endogenous opioids. Additional mechanisms of action may relate to immune system modulation and regulation of neuropeptides. The P6 acupressure point, located in the wrist, is the most commonly studied acupressure point for PONV. One large meta-analysis showed an absolute risk reduction of 20–25 %. Recommendations vary regarding the timing of stimulation of this acupressure point, and the studies differ in method of stimulation, unilateral versus bilateral, injection of solution, etc.

Other Therapies

There are other adjunctive CAM therapies that may have limited utility in the perioperative setting. *Music therapy* has been shown to reduce anxiety in perioperative settings. A recent review, however, showed inconclusive results regarding the ability of music therapy to lower blood pressure and heart rate in patients preoperatively. *Hypnosis* has been used to decrease postoperative pain, as well as being used as an adjunct to anesthesia in children for dental procedures. In addition, hypnosis has been used as an adjunct to conscious sedation in several patient populations.

Clinical Review

1. Most herbal supplements should be stopped before surgery for at least
   A. 3–7 days
   B. 7–14 days
   C. 14–28 days
   D. Continued preoperatively
2. The following herbal drug may increase the risk of perioperative bleeding
   A. Echinacea
   B. Ephedra
   C. Kava kava
   D. Ginkgo
3. The following herbal drug may potentiate anesthetic action
   A. Kava kava
   B. Garlic
   C. Saw palmetto
   D. Echinacea
4. Acupressure applied at the following site may reduce the risk of postoperative nausea and vomiting
   A. Knee
   B. Scalp
   C. Wrist
   D. Neck

Answers: 1. B, 2. D, 3. A, 4. C.

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Cosmetic Surgery

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Jessica O'Connor and Patricia L. Dalby

The American Society of Plastic Surgery recently reported that more than 11 million cosmetic procedures were performed in the United States per year. This number is expected to rise as plastic surgery procedures become more advanced and less invasive. With this continued increase, careful clinical decision making for the safe and effective administration of anesthesia for patients undergoing cosmetic surgery is imperative. Furthermore, many cosmetic procedures are performed in diverse environments, including traditional hospital operating rooms, outpatient surgery centers, and private offices, reinforcing the need to consider all factors that ensure patient safety.

Preanesthetic Assessment

The preanesthetic evaluation of the cosmetic patient is one of the most important functions for the anesthesiologist. In general, ASA physical status I and II indicate patients who are good candidates for these elective procedures. Usual preoperative concerns should be adhered to. The number of patients with a variety of severe medical conditions (ASA 3 and 4) undergoing cosmetic surgery, however, continues to increase. Specific considerations to focus upon include obesity, diabetes mellitus, immunocompromised states, advanced age, hypertension, hepatic disease, smoking, cardiovascular disease, obstructive sleep apnea, thyroid disease, coagulopathy, and psychiatric disease. In addition, the drugs with interactions that may affect the metabolism of lidocaine (those that inhibit cytochrome P450 isoenzyme system) must be evaluated during the preoperative assessment and possibly suspended.

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Intraoperative Management

Choice of Anesthetic Method

Anesthesia for patients undergoing cosmetic surgery must accomplish a number of important goals. These include anxiolysis, intraoperative and postoperative analgesia, and rapid recovery with the absence of postoperative side effects. Techniques most commonly used are intravenous anesthesia, regional anesthesia, and general inhalation anesthesia.

Total intravenous anesthesia (TIVA) using short-acting hypnotics and opioids has emerged as an attractive alternative to inhaled anesthesia in the setting of ambulatory cosmetic procedures. It allows for rapid control of intraoperative stresses in a variety of surgical procedures and for faster recovery with less toxicity, than when the individual drugs are used alone in higher doses. Several different combinations of hypnotic-analgesic agents have been used for TIVA, notably propofol-remifentanil-midazolam, propofol-ketamine-fentanyl-midazolam (PKFM), and dexmedetomidine with PKFM.

Regional anesthesia, which includes both central neuraxial techniques as well as peripheral nerve blocks, minimizes requirements for additional anesthetic, analgesic, or sedative agents, thereby reducing side effects such as postoperative nausea, vomiting, and sedation. Spinal anesthesia provides rapid-onset, bilateral surgical anesthesia for cosmetic procedures from the abdomen to the lower extremities. Epidural anesthesia provides similar advantages (thoracic epidurals for surgery involving the breast and thorax; thoracolumbar epidurals for lower body regions) with the addition of extended postoperative analgesia. Unfortunately, spinal and epidural anesthesia have a risk of post-dural puncture headache as a side effect, and intrathecal or epidural narcotics such as morphine require prolonged postoperative observation. Peripheral paravertebral nerve blocks can offer intraoperative anesthesia and prolonged postoperative analgesia with rare side effects.

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Local Anesthetic Toxicity

Lidocaine toxicity has accounted for a significant proportion of patient morbidity and mortality regarding cosmetic procedures. Surgeons and anesthesiologists attempt to calculate the "maximal safe dose" of lidocaine. Still prolonged surgical cases involving liposuction, rhinoplasty, and/or breast augmentation can create complex physiologic scenarios in which determination of the "cutoff" level of safe lidocaine dosing can be a difficult calculation.

Subcutaneous lidocaine injection has been limited to 4.5 mg/kg without epinephrine and 7.0 mg/kg with epinephrine. In addition to the dose, lidocaine absorption, and thus the plasma concentrations, depends upon the rate of administration, dilution, vascularity of the area injected, and coadministration of a vasoconstrictor. A lidocaine plasma level of 3–5 mcg/ml is associated with subjective signs of toxicity, whereas cardiopulmonary arrest occurs at levels above 20 mcg/ml. Systemic manifestations of toxicity may include headache, tinnitus, perioral and tongue paresthesias, restlessness, and, in advanced stages, convulsions and cardiopulmonary collapse. Treatment of acute local anesthesia toxicity includes stopping the local anesthetic injection, call for help, maintaining the ABCs (airway, breathing, circulation), treatment of seizures, treatment of arrhythmias, and administration of intralipid.

Specific Procedural Considerations

Liposuction

Liposuction is the second most commonly performed cosmetic procedure after breast augmentation and is performed primarily by plastic surgeons and dermatologists. It is accomplished by inserting hollow rods into small incisions in the skin and suctioning subcutaneous fat into an aspiration canister. Superwet and tumescent techniques use large volumes (1–4 l) of dilute local anesthetic and epinephrine (normal saline or Ringer's lactate solution with epinephrine 1:1,000,000 and lidocaine 0.025–0.1 %) for each cubic centimeter of fat to be removed. This is done to facilitate anesthesia and decrease blood loss. Blood loss is generally 1 % of the aspirate with these techniques. While the maximum dose of lidocaine with epinephrine is commonly cited as 7 mg/kg, the limit is dramatically increased to 35–55 mg/kg when used in tumescence fluid. The plasma levels remain below the toxic threshold of 5 mg/l because of immediate suctioning of the infiltrate as well as delayed absorption of the extremely dilute lidocaine tumescent solution. As the volume of tumescence and aspirate approaches 4–5 l, the large lidocaine dose puts the patient at risk for delayed toxicity. The peak serum levels of lidocaine occur 8–16 h after injection and decline over the subsequent 6–14 h.

Liposuction is not without significant risk. Complications include hypervolemia, hypovolemia, hypothermia, and local anesthetic toxicity. Causes of mortality include pulmonary embolism, abdominal viscous perforation, anesthesia "causes," fat embolism, infection, and hemorrhage. Risk factors include the use of multi-liter wetting solution infiltration, high-volume fat aspiration causing massive third spacing, multiple concurrent procedures, anesthetic sedative effects yielding hypoventilation, and permissive discharge policies. The management of the postoperative period, with attention to fluid and electrolyte balance and pain control, is critical to an optimal outcome after liposuction. The patient's fluid deficit, maintenance, intraoperative loss, and probable interstitial fluid sequestering should guide fluid management throughout the perioperative period.

Facial Aesthetic Procedures

One of the concerns of using supplemental oxygen in patients undergoing facial surgery is the increased likelihood of fire hazard. Any supplemental oxygen must be turned off during periods of laser or electrocautery use about the face, and this requires vigilance by the anesthesiologist who must be in constant communication with the surgeon. Methods for delivering supplemental oxygen to a patient having a facial procedure include nasal cannula or placement of oxygen tubing in an oral/nasal airway, in addition to suction of oxygen-enriched areas that may be draped. The use of airways usually requires a deeper level of sedation. The avoidance of supplemental oxygen when medically appropriate is ideal. Also if a general anesthetic is given for these procedures, avoidance of prolonged coughing or retching at extubation and in the postoperative period is important. Use of a laryngeal mask airway versus an endotracheal tube for airway management may aid with a smoother emergence from anesthesia.

Breast Surgery

A number of adjunctive analgesic regimens have been described to manage pain after breast surgery, which is significant in the first 48 h. Four methods highlighted in recent literature include bupivacaine administered through

Jackson-Pratt drains prior to wound closure, paravertebral blockade supplemented with IV sedation, and preoperative IV dexamethasone combined with a nonsteroidal anti-inflammatory drug, as well as use of intravenous acetaminophen perioperatively. The advantages of these techniques are decreased narcotic requirement, minimal nausea and vomiting, and shortened recovery.

Postoperative Nausea and Vomiting

Postoperative nausea and vomiting (PONV) is cited as one of the most unpleasant experiences following surgery. The overall incidence of postoperative nausea and vomiting within plastic surgery is estimated to be about 35 %. It has been associated with longer recovery periods, unintended hospital admissions, hematoma formation, suture and wound dehiscence, and aspiration.

Several risk factors have been identified that place patients at higher risk for the development of postoperative nausea and vomiting. These include female gender, nonsmoking status, a history of motion sickness, prior postoperative nausea and vomiting, a history of opioid-induced nausea and vomiting, use of general anesthesia, and use of parenteral opioids perioperatively. Proper risk assessment and prophylaxis performed on patients preoperatively have been shown to reduce the incidence of postoperative nausea and vomiting tenfold.

The cause of postoperative nausea and vomiting is a multifactorial process involving multiple neuroanatomic sites. Each site contains receptors specific for at least one of four neurotransmitters: acetylcholine, serotonin, dopamine, and histamine. Current antiemetic medications available target one of four of these systems; therefore, combination antiemetic therapy is recommended.

More recent preoperative medications available produce antiemetic effects through selective antagonism of human substance P/neurokinin-1 (NK1) receptors as opposed to targeting one of the aforementioned neurotransmitter systems. Two recent multicenter, randomized, double-blind trials of NK1 antagonists demonstrated superior efficacy in the prevention of postoperative and post-discharge nausea and vomiting.

Conclusion

With the continued increase in the number and variety of cosmetic procedures performed each year, careful clinical decision making for the safe and effective administration of anesthesia for patients undergoing cosmetic surgery is imperative. Risk reduction involves thorough perioperative evaluations. Special attention should be directed at reducing anxiety, optimizing medical conditions, establishing antiemesis, maintaining normothermia, acquiring hemostasis, providing adequate analgesia, and avoiding delayed local anesthetic toxicity. By focusing on these specific issues as well as general anesthetic concerns, creation of an anesthetic plan is important that provides both patient and surgeon satisfaction, enhances procedure safety, minimizes postoperative sequelae of anesthesia, and avoids prolonged hospital stay.

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Hazards of Working in the Operating Room

55

Faith J. Ross and Ibtesam I. Hilmi

The practice of anesthesiology is associated with exposure to many potential hazards, both physical and psychological. Operating room (OR) personnel are routinely exposed to low levels of anesthetic gases, radiation, and infectious disease and occasionally to high levels of psychological stress. Anesthesiologists should be aware of these potential hazards so that they can take steps to mitigate these risks by the application of proper safety precautions.

Exposure to Anesthetic Gases

Exposure to anesthetic gases has long been suggested as a potential cause of adverse effects in operating room personnel. The two types of anesthetic gases are nitrous oxide and the halogenated inhalational anesthetic agents (isoflurane, sevoflurane, desflurane, halothane). Studies in several animal species, though inconclusive in humans, have shown an association between exposure to surgical level anesthesia during the vulnerable period of early fetal neural development and long-term cognitive dysfunction. Neurodegenerative changes and the deterioration of cognitive functions in OR personnel due to daily exposure to trace amounts of inhalational agents have not been thoroughly studied, but a serious consideration should be applied in the milieu of the recent animal studies.

In vitro, high levels of nitrous oxide have been found to irreversibly oxidize the cobalt atom of vitamin B_{12} which inhibits methionine synthase, thus impairing DNA synthesis, myelin, and neurotransmitter production. High concentrations of nitrous oxide may therefore lead to anemia and neuropathy. Repeated and long-term exposure to halothane, especially in pediatric anesthesiologists, may cause halothane hepatitis. In addition, there may be an association between anesthetic gas exposure in OR personnel and the increased incidence of spontaneous abortion and congenital abnormalities in the offspring of female OR staff. However, these results are controversial and not supported by all studies on the subject.

In 2007, the National Institute for Occupational Safety and Health (NIOSH) developed safety criteria, which is summarized in Table 55.1.

Radiation Safety

The widespread use of fluoroscopic guidance techniques in modern surgical procedures has dramatically increased the level of radiation to which the OR personnel are exposed. Decreasing time of exposure, proper shielding, and increasing distance from the radiation source are three factors which help to limit the degree of exposure. Body shielding by wearing lead aprons, though effective in blocking radiation, does not protect all areas of the body. Therefore, a thyroid shield and eye protection should also be worn. As radiation intensity decreases proportionally with the inverse square of the distance from the source, maintaining a distance of at least 36 inches (3 feet) from the radiation source is one of the most effective methods of decreasing radiation exposure.

Radiation is carcinogenic at high levels. The US Nuclear Regulatory Commission (US-NRC) has set an annual radiation exposure limit of 5 rem/year (Table 55.2). As developing fetuses are particularly vulnerable to the adverse effects of radiation, the maximal dose should be <0.5 rem during the gestational period. Healthcare workers exposed to constant radiation should wear radiation monitoring badges, so that they are not exposed to excessive radiation above the annual radiation exposure limit.

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Table 55.1 NIOSH safety recommendations

• Exposure limit of 2 ppm of halogenated anesthetic used alone or 0.5 ppm of halogenated anesthetic combined with 25 ppm of nitrous oxide
• Proper functioning scavenging system
• Low pressure leaks of <100 ml/min at 30 cm water pressure
• High pressure leaks from gas cylinder or pipeline of <10 ml/min
• Anesthetic gas flows turned off when not in use
• Employee training on handling of hazardous chemicals
• Air sampling performed in all locations of possible exposure to chemicals
• Documentation of abnormal outcome of pregnancies of employees or spouses of employees

ppm parts per million

Table 55.2 NRC occupational radiation dose limits

Site	Limits (Rem/year)
Whole body	5
Any organ	50
Skin	50
Extremity	50
Lens of eye	15
Embryo/fetus	0.5
Member of public	0.1

NRC nuclear regulatory commission

Latex Sensitivity

Healthcare workers have an increased risk of allergic reactions to latex. The prevalence of sensitivity in anesthesiologists is reported to be about 15 % and in other healthcare workers to be about 8–12 %. These reactions generally manifest as irritant contact dermatitis, but anaphylaxis is also possible. People with spina bifida have increased risk of latex allergy, as well as people with allergies to certain foods, such as banana, tomato, potato, and kiwi fruit.

Infectious Diseases

Healthcare workers are routinely exposed to a variety of infectious agents including respiratory viruses (influenza and respiratory syncytial virus), measles, rubella, and, perhaps most concerning, hepatitis B and C and the human immunodeficiency viruses (HIV). The risk of contracting an infectious disease can be attenuated by rigorous adherence to universal and contact precautions. Serologic studies in the 1970s, prior to routine vaccination and postexposure prophylaxis, showed that healthcare workers had 10 times the prevalence of hepatitis B virus (HBV) infection compared to the general population. Routine HepB vaccination with verification of immunity by antibody titers is recommended for all healthcare providers who have direct contact with patients.

Acute HBV infection may be asymptomatic or may cause chronic hepatitis and rarely fulminant hepatitis. The degree of infectiousness of a patient is related to the presence of HBeAg (antigen) which is an indicator of active viral replication. The risk of transmission of hepatitis B after needlestick injury from a needle contaminated with blood from an HBV-positive patient is 1–6 % if the patient is HBeAg negative and 1–30 % if the patient is HBeAg positive. Acquisition of HBV by healthcare workers may be prevented by prophylactic vaccination or postexposure prophylaxis with HepB immune globulin. However, many healthcare workers with acquired HBV do not recall a percutaneous injury. HBV can survive in dried blood on environmental surfaces for up to 1 week, so it is possible that some healthcare workers may be infected by inoculation of the virus into cutaneous lesions or mucosal surfaces.

Hepatitis C virus (HCV) is much more likely than HBV to cause chronic infection and cirrhosis of liver. However, it is much less easily transmissible than HBV. The risk of transmission after percutaneous exposure to infected blood is ~1.8 %, with transmission from mucous membrane exposure being rare. Transmission through skin exposure has not been documented, and unlike HBV, HCV is thought to have a limited ability to survive in dried blood on environmental surfaces. In 1994 the Advisory Committee on Immunization Practices found that routine postexposure immunoglobulin administration for HCV was not supported by existing evidence. The use of postexposure antiviral agents is not currently recommended; however, there is some evidence that a short course of interferon early in the course of documented acute HCV infection may increase the rate of resolution of the infection.

Acquisition of HIV is perhaps one of the most feared complications of exposure to infected body fluids. The risk of transmission of HIV is 0.3 % after percutaneous exposure to blood and 0.09 % after mucous membrane exposure. Animal and human studies suggest that postexposure prophylaxis with antiretroviral agents is effective in decreasing the seroconversion rate after exposure to HIV. A two- or a three-drug regimen is recommended for postexposure prophylaxis depending on the level of risk from the particular exposure.

Fire Safety

Operating room fires, though rare, can be potentially disastrous. Oxygen and nitrous oxide can be ignited by ignition sources such as electrocautery and lasers, which cause flammable solutions, endotracheal tubes, sponges, etc. to burn. It is recommended that the ignition sources be as far as possi-

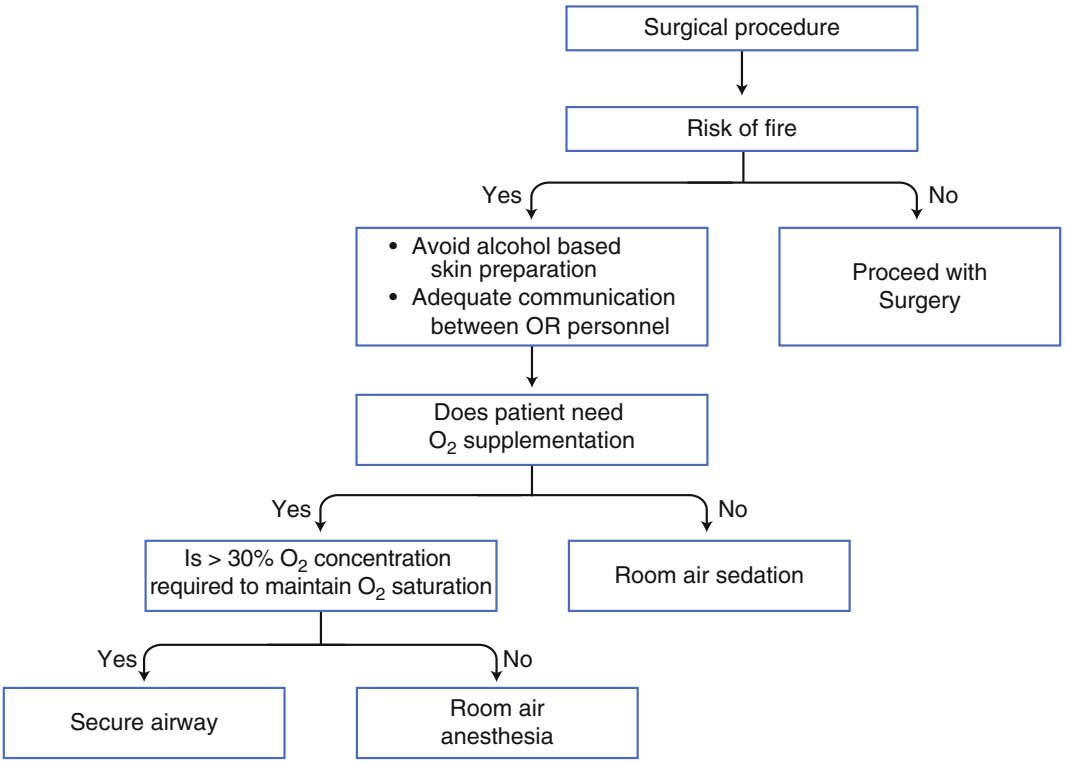

Fig. 55.1 Fire prevention algorithm

ble from flammable gases and drapes. In case of a fire, effective communication and a rapid response are vital. A fire prevention algorithm is summarized in Fig. 55.1.

The most common patient-related fires are airway fires, which can occur during procedures of the head and neck. In case of an airway fire, the surgeon should remove the source of ignition and immediately inform the anesthesiologist, who should stop ventilation (disconnect the circuit), and turn off the combustible gases. The patient should then be ventilated with 100 % oxygen via mask and the anesthesia should be continued. The surgeon should then assess the airway by direct laryngoscopy and bronchoscopy. The patient may need to be reintubated or a tracheostomy be performed.

Laser Safety

The term laser stands for "light amplification (by) stimulated emission (of) radiation." There are four types of laser currently in clinical use: CO_2 laser, argon laser, neodymium:yttrium-aluminum-garnet (Nd:YAG) laser, and potassium titanyl phosphate (KTP-green) laser. Each type of laser has its own wavelength, and the greater the wavelength, the less deep is the tissue penetration.

The CO_2 laser has a wavelength of 10,600 nm and produces tissue destruction to a depth of 100–200 μm (about half the thickness of the epidermis). The argon laser has a wavelength of 488 nm and 514 nm and emits a blue-green color. It is absorbed by pigmented tissue and hemoglobin and is used to coagulate blood vessels. The Nd:YAG laser has a wavelength of 1,064 nm and is used for eye and bladder surgeries. The KTP laser has a wavelength of 532 nm and emits a green color. It is used for prostate surgery.

Risks of laser surgery include eye injuries, thermal burns, fires, and explosions. Laser-specific protective eye wear should be worn by OR personnel. Thermal destruction of tissues by laser results in smoke plumes, which can be hazardous and cause ocular and upper respiratory tract irritation in OR personnel. These smoke plumes contain toxic vapors such as benzene, hydrogen cyanide, formaldehyde, plus cellular material, and viruses.

Psychological Stress

Psychological stress associated with poor patient outcomes is a frequently overlooked occupational hazard in anesthesiology. Despite the relative rarity of anesthesia-related operative mortality, anesthesiologists may experience an operative death at some point in their career. Many physicians feel a strong emotional response to the death of a patient even if they did not have a long relationship with the patient. It is common for physicians to feel guilty or partially responsible for intraoperative death of a patient, with junior physicians

more likely to be impacted emotionally. Nearly all physicians report the desire for additional support in coping with the emotional stress surrounding a patient's death; however, physician support groups are unfortunately not widespread currently. Exposure to emotionally stressful situations and inadequate support systems in anesthesiology may partially account for the higher incidence of chemical dependence and suicide in anesthesiologists compared to the general population and other medical specialties.

Chemical Dependency

There is a higher risk of drug abuse and dependence among anesthesiologists than other medical specialties. Factors responsible for drug abuse in anesthesiologists represent a combination of susceptible personality, job stress, and the availability of drugs with a high potential for abuse. Anesthesiologists may be particularly prone to developing drug addiction as they both prescribe and administer psychoactive medications, thus eliminating a large degree of oversight inherent in other specialties. Because of the powerful nature of the drugs commonly used in anesthesiology, fatal overdose is often the first recognized sign of abuse.

Whether a recovering addict should be allowed to return to the practice of anesthesiology is a contentious subject. Reentry into the field is associated with a high rate of relapse, often with disastrous consequences. One survey found 9 deaths in 100 anesthesiology residents who returned to training after treatment for drug abuse. Three factors have been found to be associated with increased risk of relapse: family history of drug abuse, abuse of a major opioid, and coexisting psychiatric disorder.

Membership in a support group such as Narcotics Anonymous or Alcoholics Anonymous may be helpful for physicians struggling with a history of chemical dependence. Also, most state medical societies have programs which provide assistance to physicians who voluntarily seek treatment. Physician self-reporting through state medical societies may mitigate the legal repercussions of their behavior and allow them to find effective treatment for their disease before it becomes more problematic.

Work Hours and Sleep Disturbance

In anesthesiology, as in other fields of medicine, long work hours and frequent disturbance of sleep-wake cycles are a source of potential errors, which can adversely affect patient outcomes as well as practitioner well-being. Surveys show that greater than 50 % of anesthesiologists report having made a medical error related to fatigue. In fact, continuous wakefulness for 24 h produces a level of impairment of psychomotor skills equivalent to a blood alcohol level of 0.1 % (over the legal limit for driving in most states). The decline in performance associated with fatigue is particularly pronounced in older anesthesiologists. Chronic partial sleep deprivation may be as detrimental as intermittent acute sleep deprivation. Long-term disruption of circadian cycles has also been shown to be an independent risk factor for the development of gastrointestinal and cardiovascular diseases, cancer, and adverse pregnancy outcomes.

The risks of sleep deprivation may be attenuated by alertness strategies such as planned naps, strategic caffeine use, and good sleep habits. Work hours reform has so far been controversial, as increased patient-care hand-offs also have the potential to adversely affect patient outcomes.

Clinical Review

1. Long-term exposure of operating room personnel to volatile inhalational anesthetic agents may lead to all, EXCEPT
   A. Cognitive dysfunction
   B. Neurodegenerative changes
   C. Hepatitis
   D. Anemia
2. As per the US Nuclear Regulatory Commission, the maximal annual radiation exposure should be the following rem/year
   A. 5
   B. 50
   C. 100
   D. 500
3. The following vaccine is strongly recommended for healthcare workers
   A. Hepatitis B
   B. Hepatitis C
   C. HIV
   D. Influenza
4. Following an airway fire, the first step the anesthesiologist should do is
   A. Stop the gas flows
   B. Stop the ventilation and disconnect the circuit
   C. Remove the endotracheal tube and reintubate
   D. Saline lavage down the endotracheal tube

Answers: 1. D, 2. A, 3. A, 4. B

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Operating Room Management

56

Sean M. DeChancie and Mark E. Hudson

The operating room (OR) is responsible for significant hospital and practitioner revenue in US hospitals. However, the OR is also well recognized as a high-cost, high-risk environment, whose resources are often perceived as poorly utilized. The goal of OR management is to create a safe, efficient, and structured environment at minimal cost. OR management is responsible for the coordination of the components of the surgical suite to optimize patient outcome and surgeon access and minimize patient delay while maximizing resource efficiency (personnel, equipment, and time) and maintaining an effective workplace for all personnel (surgical, nursing, and anesthesiology). Effective OR management has become vital for stability and success as hospitals struggle in a declining revenue environment.

Basic Principles of OR Management

The foundation for effective OR management is created by an engaged OR/Surgical Services Committee charged with decision-making authority for the OR. This committee is generally comprised of representation from surgery, OR nursing, anesthesiology, and the administration. Effective OR management requires integrated strategic (long-term), tactical (mid-term), and operational (short-term) decision-making. Operational decisions made the day of surgery are most effective when previous strategic and tactical decisions have been made with the goals of patient safety and OR utilization and efficiency within the OR suite. The OR manager must be armed with structured decision-making algorithms that prioritize decisions on the day of surgery with these same goals in mind. Confusion and conflict between the OR's components are best avoided when these decision-making algorithms have been delineated and understood by all parties prospectively.

Strategic decisions include the number of operating rooms or additions of operating rooms, size, structure, and location of preoperative holding areas and postanesthesia recovery areas, recruitment of surgical subspecialists, orientation of support areas (blood bank, pharmacy), and relative location of ICUs or offsite procedural areas that impact anesthesiology coverage (GI lab, cardiac catheterization lab). Strategic decisions are costly and must consider overall impact on operating room function.

Tactical decisions made months in advance include allocation of OR time and development of staffing schedules. Particular consideration to specialty equipment and provider staffing is essential to avoid costly equipment duplication and assure adequate specialty resource coverage.

Operational decisions deal with the day-to-day management within the OR and begin with final staffing assignments the day prior, with coordination of subspecialty staffing and equipment needs. Priority-based decisions made the day of surgery focus first on patient safety and quality of care delivery, followed by surgeon access, operating room efficiency, and reduction of patient wait times. Other priorities, including education and professional satisfaction, should also be considered. Recently, authors have modeled OR operational decisions utilizing gaming and queuing models or algorithms based on cost implications. This information allows the OR/Surgical Services Committee to develop informed algorithms used by the OR management team to effectively manage the dynamic environment of the OR to address overall daily surgical demand.

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Operating Room Performance Metrics

Typical OR performance metrics include on-time starts, turnover time, gap or idle time, OR utilization, and OR efficiency (Table 56.1). The relative value for improvement in each of these measures is institution specific. Efforts for improvement should evaluate each within a given site. On-time starts, idle time, and OR efficiency have the greatest value for improved performance and also pose the greatest challenges.

When comparing on-time starts between institutions, it is important to note that "start time" is often defined differently. Wheels-in time, prep/position time, and incision time each have been used as the defining event for a start time. However, a standard definition must be used for comparative metrics. Historically, the standard has been wheels-in time. However, this does not align with the primary purpose of an OR or capture periods of costly delays that often occur after the patient crosses the OR threshold. Incision time includes variables such as prep and positioning that are often difficult to account for in planning for a standard start time. Prep/position time is the time that all components of the OR converge: anesthesiology has completed induction, OR nursing is prepared, and the surgical team is ready. For this reason, prep/position time sets timing expectations for each component of the OR team.

OR efficiency relates to how well OR resources are utilized in completing the actual caseload and can be translated to costs using simple formulae. Underutilized time is the amount of allocated time not used to perform OR workload, while over-utilized time exists when OR workload exceeds allocated time, resulting in overtime or other premium costs. Over-utilized time costs between 1.5 and 2 times underutilized time. Therefore, a goal for the OR manager must be to reduce over-utilized time. The cost of these inefficiencies can be calculated as follows:

$$\text{Inefficiency}(\$) = \left[\begin{array}{c}(\text{cost per hour of under} - \text{utilized time})\times \\ (\text{hours of under} - \text{utilized time})\end{array}\right] + \left[\begin{array}{c}(\text{cost per hour of over} - \text{utilized time})\times \\ (\text{hours of over} - \text{utilized time})\end{array}\right]$$

An effective OR manager has the authority to manage these inefficiencies by shifting caseload into gaps that develop in the schedule. This idle time often represents the bulk of inefficiency in the OR with attempts to managed this time difficult due to conflict with surgeons from changes in anticipated surgical start times. However, in an environment of limited OR personnel resources, shifting caseload to reduce idle time can reduce over-utilized time and reduce the queues that can develop with restriction of resources later in the day.

Table 56.1 Basic definitions

Case duration	The time from when the patient enters the OR to when the patient exits the OR
Turnover time	The time from when a patient exits the OR to when the next scheduled patient enters
Idle time	Time where the OR is staffed and available but there is no surgery
OR workload	The total hours of surgical time, including turnover time
Utilization	Workload/available time—can be reported as block utilization, primary time utilization, or overall utilization
Underutilized OR time	The positive difference between allocated OR time and OR workload
Over-utilized OR time	The time that the OR runs past scheduled OR time. Many employees collect overtime pay
Inefficiency of use of OR time	Inefficiency of use of OR time ($) = (cost per hour of under-utilized OR time) × (hours of under-utilized OR time) + (cost per hour of over-utilized OR time) × (hours of over-utilized OR time)
OR efficacy	The value that is maximized by minimal inefficiency of OR time

Operating Room Information Systems

The OR manager relies on effective information management and communication governed by clearly defined rules and priorities in the dynamic OR environment. Informational management and communication can be complex and expensive, with RFID (radio frequency identification) tracking of patients, patient tracking boards, OR cameras, and automated notification systems. Also, simple vigilance, rounding, and effective direct communication by the OR manager can be equally effective as these newer modalities. Further, models for decision-making by the OR manager have been developed to make critical operational decisions to minimize over-utilization. Currently, priority-based algorithms are being developed for automated case management decisions. These tools may help the OR manager to more effectively manage the complex dynamic OR environment.

Challenges in OR Management

Allocation of OR Time

Currently, block scheduling is the most common methodology for allocation of OR time. However, the introduction of service-specific staffing has resulted in many institutions adopting this methodology or blending basic concepts of this

methodology into their OR allocation methods. The relative benefits of each allocation method are institution specific; however, service-specific staffing is becoming increasingly recognized for its benefit in personnel efficiency.

Block scheduling relies on the allocation of a set number of set-sized blocks determined by OR and anesthesiology staffing capabilities. Allocation of OR blocks is made to surgeons and services based on requests and hospital priorities. Maintaining the block generally depends on a defined level of utilization. Block scheduling attempts to shape the caseload to available overall resources distributed evenly throughout the week (e.g., within the five available ORs, five 10 h blocks are created each day for a total of twenty-five 10 h blocks per week).

Alternately, service-specific staffing approaches allocation of OR resources based on *expected* surgical case volume. Tactical planning by an OR allocation committee assigns first case starts by service or surgeon with the length of allocated time determined by historic caseload length. The resultant schedule is staffed to most efficiently manage its size and shape. While the number of rooms running and length of schedule may vary by day of the week, the resultant schedule is built to match expected caseload. When viewed from an efficiency standpoint (matching resources to actual caseload), with block scheduling, surgeons are responsible for efficiency by fully filling their "blocks," while with service-specific staffing, managers are responsible for efficiency by staffing to match service need.

Case Scheduling and Emergent Case Management

Effective scheduling within allocated time relies on accurate projection of case length and required resources (Fig. 56.1). Many institutions have computerized the scheduling systems to limit case duration bias and prevent overlap of cases requiring specific equipment or other resources. The impact of emergent or urgent caseload must be considered within the overall availability of OR resources. The most effective way to manage this caseload is dependent on individual hospitals and OR conditions. Emergent cases can be accommodated within the elective schedule by moving or "bumping" cases. Urgent cases can be performed after completion of the elective schedule. "Holes" can be built into the elective schedule based on expected urgent and emergent caseload. Finally, specific ORs can be designated solely for the anticipated urgent/emergent caseload. Determining the best methodology relies on utilizing priority-based queuing models with evaluation of expected case flow. Effective urgent/emergent case flow management can significantly improve overall OR efficiency and utilization by limiting the impact of these cases on the elective schedule and appropriate resource allocation for expected non-elective caseload.

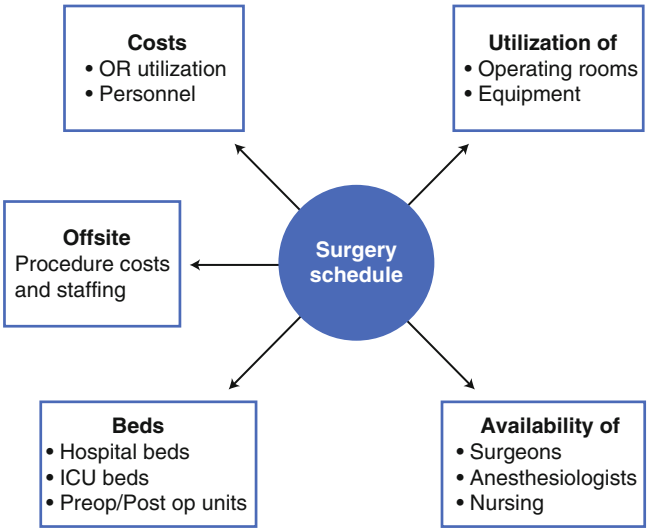

Fig. 56.1 Factors in scheduling

Constraints of Effective Operational Management

There are several constraints to effective operating room management that are common in the average US hospital. These include competing goals, incentives, priorities, and expectations of the OR's components (surgery, anesthesiology, and OR nursing). All components tend to focus on individual performance rather than the overall goals and priorities of the OR, and mismatched goals and incentives often lead to conflict. For example, prepaid or hourly workers gain control of the workday by maintaining inefficiencies. This may be reflected in the end of shift slowdowns or longer turnovers. Incentive workers (surgeons and anesthesiologists) gain control with greater efficiency, pushing for faster turnovers and more cases. This leads to conflict and disruption of teamwork within the OR. Further, while the OR manager concentrates on overall OR efficiency and effectiveness, surgeons may view efficiency as individuals, pushing for that second room, or otherwise willing to sacrifice the OR's overall efficiency for their own cause. These are common areas of conflict within the operating room, and the OR manager must be charged with the authority- and priority-based algorithms to prevent disruption of the OR by these conflicts.

Summary

Effective OR management requires an insightful and informed Surgical Services/OR decision-making team and an operational OR manager armed with effective information management and priority-based management algorithms and skilled in conflict mitigation. Anesthesiologists are positioned well to take the lead in this role. The success of an Anesthesiology

department is tied to the success of the operating room with incentives directly aligned with the hospital. Inefficient utilization of allocated surgical time impacts costs for both the hospital and anesthesiologists. An anesthesiology-led OR management environment focusing on patient care and surgical access, while improving OR efficiency and reducing costs, can change the perception of our specialty from that of a necessary cost to a partner in success.

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Residency Requirements and Guidelines

57

Joseph P. Resti and Shawn T. Beaman

A residency is the first step to becoming a board-certified anesthesiologist in the United States. This postgraduate training period is the essential period when the newly graduated medical student trains to be an independent practitioner and specifically focuses on specialty training. Although residency programs in the United States vary widely, they all share basic requirements and guidelines that are required by a governing body, the Accreditation Council for Graduate Medical Education (ACGME). It should be noted that ACGME requirements for anesthesiology residencies in the United States are ever changing and are subject to change at any moment.

ACGME Requirements

ACGME has shared requirements of all specialties, including anesthesiology. They define a residency as longitudinal learning experience in which the trainee develops the skills, knowledge, and attitude required to be proficient in the specialty of their choice. This is done by care of individual patients with supervision, assuring safe and effective patient care. Furthermore, there is graded and progressive responsibility, ensuring that by the end of their training, the trainee is able to enter the unsupervised practice of medicine. The ACGME has six core competencies in which residents are regularly evaluated upon: patient care, medical knowledge, practice-based learning and improvement, interpersonal and communication skills, professionalism, and system-based practice. These core competencies have specific applications to training in anesthesiology, and these will be discussed below:

- Patient care: Residents must be able to provide patient care that is compassionate, appropriate, and effective for the treatment of health problems and the promotion of health.
- Medical knowledge: Residents must demonstrate knowledge of established and evolving biomedical, clinical, epidemiological, and social behavioral sciences, as well as the application of this knowledge to patient care.
- Practice-based learning and improvement: Residents must demonstrate the ability to investigate and evaluate their care of patients, to appraise and assimilate scientific evidence, and to continuously improve patient care based on constant self-evaluation and lifelong learning.
- Interpersonal and communication skills: Residents must demonstrate interpersonal and communication skills that result in the effective exchange of information and collaboration with patients, their families, and health professionals.
- Professionalism: Residents must demonstrate a commitment to carrying out professional responsibilities and an adherence to ethical principles.
- System-based practice: Residents must demonstrate an awareness of and responsiveness to the larger context and system of health care, as well as the ability to call effectively on other resources in the system to provide optimal health care.

Duty Hour Requirements

Duty hour requirements have recently changed and have an impact on both the individual resident as well as the structure of the residency program. First, there is a restriction of an 80 h workweek, which applies to all residents. Currently, postgraduate year (PGY)-1 residents are restricted to duty periods of 16 h, while PGY-2 residents and above are restricted to 24 h. Because of concerns of effective transitions in care,

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residents are allowed to remain on site past these limits in the name of patient safety; however, this time is limited to 4 h. In between duty periods, residents must have 8 h free of duty, although 10 h is suggested. In between periods of 24 h duty, residents must have 14 h free before their next shift. Also, residents must be scheduled for a minimum of 1 day free of duty per week (when averaged over 4 weeks); home call cannot be counted as a free day. These duty hours were revised and were effective starting July 2011.

Moonlighting (voluntary, compensated medically related work) during residency is allowed by the ACGME, although whether or not residents can participate in it is up to each individual program. It is essential that moonlighting must not interfere with the resident's education (as well as patient's safe-being), and the ACGME states that all moonlighting shifts must be granted individually by program directors. Many programs have guidelines on top of the ACGME moonlighting guidelines, often ensuring the resident is in good academic standing. Furthermore, the hours that the resident moonlights must be counted to all of the work hour limits, including the 80 h maximum weekly limit.

Clinical Anesthesia Years

Currently, anesthesia training is 3 years long; these years are often called the clinical anesthesia (CA) years (Fig. 57.1). However, the ACGME requires that before beginning the clinical anesthesia training, trainees complete a 1-year internship for a total of 4 years of training. In the past, this intern year was almost always separate and in the fields of either surgery or medicine. However, more recently, the ACGME has encouraged anesthesiology residency programs to incorporate a clinical base year into the structure of the residency, to increase the continuity of education. Although this is not a requirement, the majority of available positions in the United States include the clinical base year (841 of the 1404 available positions in the 2011 match). Clearly, the trend of anesthesiology training is to incorporate this intern year into the continuum of the anesthesiology training.

Throughout the clinical anesthesia years, there are *mandatory rotations* residents must complete throughout their residency. These include mandatory rotations through surgical anesthesia, critical care medicine, and pain medicine. The

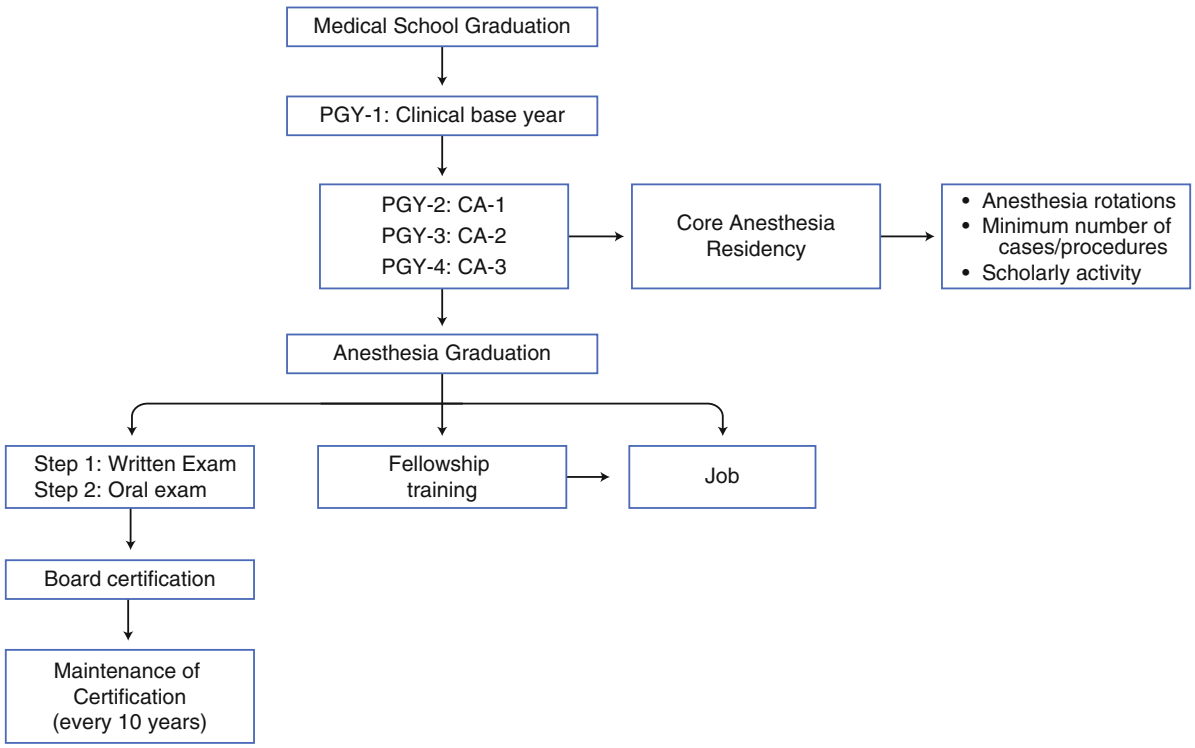

Fig. 57.1 Career pathway of an anesthesiologist. *PGY* postgraduate year, *CA* clinical anesthesia year

Table 57.1 Minimum case/procedure requirements during anesthesia residency

Case/procedure	Minimum number
Vaginal delivery	40
Cesarean sections	20
Cardiac surgery	20
Vascular	20
Intrathoracic (noncardiac)	20
Intracerebral	20
Epidurals	40
Spinals	40
Complex	20
PNBs	40
Pain evaluations	20
Age < 12 y/o	100
Age < 3 y/o	20
Age < 3 m/o	5

surgical subspecialty rotations must include rotations through obstetric anesthesia, neuroanesthesia, cardiothoracic anesthesia, and pediatric anesthesia. If the resident satisfactorily completes his or her rotation through a specialty, they can continue to do subspecialty rotations, although the cumulative time that can be spent in one subspecialty cannot be more than 6 months. Also, these subspecialty rotations must show increased responsibility and learning opportunities.

Residents must also rotate through other *perioperative rotations*, which include post-anesthesia care unit, pain management, and preoperative evaluation. Of the three mandatory months of pain management, 1 month may be spent in chronic pain, another month in regional pain management, and a last in acute perioperative pain management. Although the vast majority of these subspecialty rotations must be completed during the 36-month clinical anesthesia rotation, a total of 2 months of critical care and 1 month of pain medicine can be completed during the clinical base year.

Residents are also required to obtain *minimum number of certain cases* to ensure they see a variety of patients during their residency. These include both specific case types, as well as procedures (Table 57.1). There are stated case minimums for cardiac surgery, noncardiac thoracic surgery, vascular surgery, and intracranial surgery. Also, residents must show that they are involved with patients undergoing vaginal and cesarean deliveries (including high-risk obstetrics). A minimum number of spinal and epidural are required as well, as are a minimum number of peripheral nerve blocks performed. Also, there must be evidence of pain evaluations (separate from a nerve block) for patients who are suffering from either acute or chronic pain. It must be documented that patients with complex, life-threatening injuries, such as trauma or burn patients, must also be treated by anesthesiology residents during their training. Finally, to ensure that the resident has cared for an adequate number of pediatric patients, there are minimums based on patient's age.

Performance Evaluations

Continuous evaluation of *resident performance* is another requirement of residency, anesthesiology, as well as other specialties. The ACGME requires that the residency program provide objective assessments on resident performance in all six core competencies. This is done mainly through faculty evaluation but should include other evaluators, including patients, peers, and other professional staff. These evaluations do not only have to show adequate performance but also document progression in performance throughout the resident's training. Although evaluation is continually occurring throughout the residency, semiannual meetings with the program director are required in order to formally document performance to the resident and provide feedback.

There is also mandatory *evaluation for faculty and program* by the resident. This ensures that there is resident input on the quality of the teaching within the program. Evaluation is confidential, which ensures that residents can be honest about faculty performance. The evaluations should include not only teaching abilities but also professionalism, knowledge, and scholarly activities. The program also has an annual, formal assessment by their residents in the form of a survey. Again, this review is confidential and ensures that many of the ACGME guidelines for residencies are being followed.

Scholarly Activities

Another mandatory step to completing a residency is participation in *scholarly activity*. These academic projects must be supported by the program, including educational resources and ample opportunities for resident involvement in these projects. There are many different types of projects that can qualify, including book chapters, grand rounds presentations, or writing review articles. Also, clinical or laboratory research would also qualify as scholarly activity, and the resident is encouraged to present at meetings and publish results in peer-reviewed journals. Regardless of the type of activity chosen, a faculty supervisor must act as a mentor.

A structured *education program* is also provided during the residency. This includes a structured didactic program. The ACGME does not dictate how often didactics must occur, and because of this, there is a lot of variability in the structure and time commitment residencies give to their didactic programs. When choosing a residency, this is a very important factor to evaluate. The didactic programs include

lectures on the basics of anesthesia and all of specialties within its scope. Also, there should be lectures that focus on practice management, such as OR management, contract negotiations, billing, liability, and legislative issues.

Most residents are required to take the Step 1 computer-based annual in-training examination administered by the American Board of Anesthesiology (ABA). After graduating from residency, to become ABA certified, one has to pass the Step 1 examination and an oral clinical examination.

Fellowship Training

An extension of residency training is fellowship training. After completion of a residency, a newly graduated anesthesiologist may choose to continue their training by completing a fellowship in a subspecialty of anesthesia. Most fellowships are 12 months in length, although some that incorporate research may be longer. Almost all anesthesia subspecialties have available fellowships. However, there are only a few that are ACGME certified; these include pediatric anesthesiology, cardiothoracic anesthesiology, pain medicine, critical care medicine, and, most recently, obstetric anesthesiology. However, non-ACGME-approved fellowships are available in neurosurgical anesthesiology, regional/acute pain, ambulatory anesthesiology, thoracic anesthesiology, trauma anesthesiology, and transplant anesthesiology, among others. Regardless of the field chosen, this extra year strengthens a candidate in the job market, particularly if he or she is looking to work in the academic setting.

Overall, residency is a time when a physician truly learns medicine. When a candidate is selecting a residency program, he or she should match their own personality, learning styles, and career goals with a residency program. With 131 residency programs (and counting), there is sure to be a program that will suit each and every medical student preparing for a career in anesthesiology. However, the candidate must be aware of the structure and requirements of residency guidelines.

Clinical Review

1. All of the following are core competencies of the Accreditation Council for Graduate Medical Education (ACGME), *except*:
   A. Patient care
   B. Medical knowledge
   C. Communication skills
   D. Previous anesthesia training
2. Anesthesia residents are restricted to the following maximum number of work hours per week:
   A. 40
   B. 80
   C. 100
   D. 120
3. True statement regarding anesthesia residency is:
   A. Anesthesia residents can choose a specific clinical rotation any number of times.
   B. Anesthesia residents can choose specific clinical cases any number of times.
   C. Completing a scholarly activity is mandatory before graduating from anesthesia residency.
   D. Anesthesia residents have an absolute right to do moonlight duty if they choose to do so.

Answers: 1. D, 2. B, 3. C

Appendix of Management Algorithms For Certain Clinical Conditions

A1. Management of Local Anesthetic Toxicity

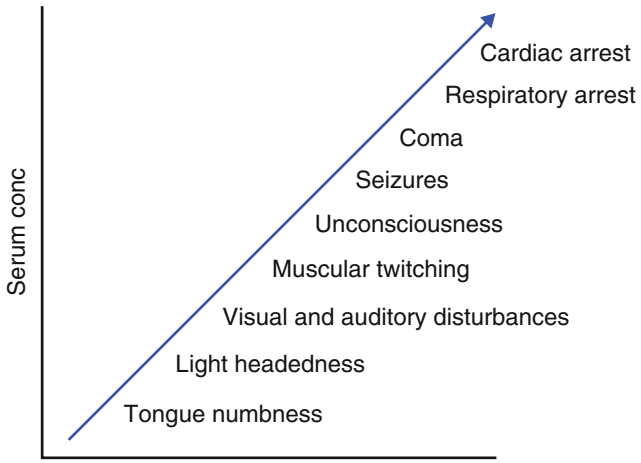

Fig. A.1 Signs of local anesthetic toxicity

Get Help and Code Cart Ready

Maintain ABCs

Airway management—100 % O_2, airway support with possible endotracheal intubation
Treatment of seizures—Benzodiazepines (midazolam 2–4 mg), or propofol (avoid if hypotension) 30–100 mg
Management of hypotension/cardiac arrhythmias/arrest—ACLS protocol, vasopressors

↓

Consider Intralipid (20 % lipid emulsion)

Indicated for severe toxicity (convulsions, unconsciousness, respiratory or cardiac arrest)
- Bolus of 1.5 ml/kg IV over 1 min
- Infusion of 0.25 ml/kg/min
- May repeat bolus up to 2 more times with an interval of 5 min
- May double the infusion rate if hypotension persists
- Total intralipid dose not to exceed 10 ml/kg in 30 min

↓

Refractory cases may need cardiopulmonary bypass
Patients with severe toxicity are monitored in the ICU

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A2. Management of High Spinal Anesthesia

Recognize signs and symptoms

Tingling of arms, slurred speech, difficulty in breathing, drowsiness

↓

Call for help

↓

Maintain ABCs
Airway, Breathing, Circulation

↓

100 % oxygen/airway support
Head-up patient position (reverse trendelenburg) as tolerated
If bradycardia—administer IV atropine/epinephrine
If hypotension—administer IV ephedrine/phenylephrine/epinephrine
Maintain hydration

↓

If patient is pregnant—left lateral uterine tilt
If baby is compromised—emergency cesarean section

A3. Management of Postdural Puncture Headache

- Establish diagnosis. Rule out other causes of headache such as tension headache, migraine, meningitis, subdural hematoma, subarachnoid hemorrhage, pneumoencephalus, benign intracranial hypertension (a neurological consult may be needed)

PDPH diagnosed
Commonly a female less than 40 years
Headache worse on sitting and standing (postural)
Can be associated with neck pain, nausea, visual disturbances

↓

Conservative management
Bed rest
Hydration
Caffeinated drinks or IV caffeine infusion
Analgesics
(Uncommonly used: sumatriptan, gabapentin,
occipital nerve block, sphenopalatine ganglion block)

↓

If no relief in 24 h
Consider Epidural blood patch (EBP)

↓

If headache still persists
May administer Cosyntropin 1 mg IV
May repeat EBP
Reevaluate

A4. Management of Anaphylactic Reaction

Establish diagnosis
Airway—swelling, stridor, hoarseness of voice
Breathing—tachypnea, wheezing, hypercarbia, low oxygen saturation
Circulation—hypotension, pale, drowsy

↓

Call for help

↓

Monitor pulse oximetry, ECG, blood pressure
Maintain ABCs—Airway, Breathing, Circulation

↓

Epinephrine IV
Adults 50 mcg, Child 1 mcg/kg

↓

Supportive management
IV hydration
IV hydrocortisone
IV diphenhydramine (antihistaminic)
Beta-2 agonist for bronchospasm

A5. Management of Intraoperative Bronchospasm

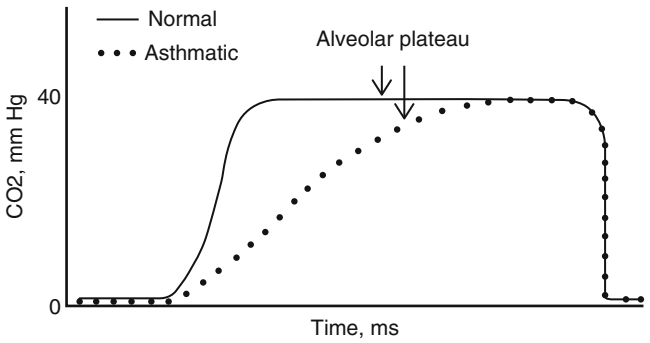

Fig. A.2 Capnograph in a normal and asthmatic patient

Diagnosis

Increased peak airway pressure
Wheezing on auscultation of lungs
Decrease in tidal volume
Increased $ETCO_2$ with up-sloping of waveform

↓

Inform Surgeon
Increase FiO_2 to 100 %

↓

Precipitating causes and management

- Light anesthesia—deepen anesthesia by increasing volatile anesthetic concentration and/or administering propofol
- Increased secretions—suction secretions, may administer glycopyrrolate
- Main stem intubation/kinking of endotracheal tube (ETT)—use fiberoptic bronchoscope to ascertain position of ETT
- Anaphylaxis causing bronchospasm—administer IV epinephrine
- Pneumothorax—chest tube insertion by surgeon. If tension pneumothorax, then place a 14/16G needle in the second intercostal space in the midclavicular line

↓

Treatment of bronchospasm

Increase FiO_2 to 100 %
Beta-2 agonist (albuterol puffs via endotracheal tube)
IV epinephrine for severe bronchospasm
IV ketamine 0.2–1 mg/kg

A6. Management of Myocardial Ischemia in the PACU

Think MONA: Morphine, Oxygen, Nitroglycerin, Aspirin

- Administer FiO_2 of 100 %
- Obtain a 12 lead ECG
- Call cardiology consult
- Administer metoprolol/esmolol to control heart rate
- Nitroglycerin patch/infusion for coronary vasodilation
- Morphine for pain
- Aspirin orally/rectally
- Labs: CBC, electrolytes, cardiac enzymes (troponin, CPK), arterial blood gas
- If hypotension—administer vasopressor/s
- If fluid overload—administer diuretics (furosemide)

A7. Management of Malignant Hyperthermia

- Early Signs—Increased $ETCO_2$ (hypercarbia), tachycardia, masseter muscle rigidity, generalized muscle rigidity, metabolic and respiratory acidosis
- Late Signs—hyperkalemia, cardiac arrhythmias, hyperthermia, myoglobinuria

Rule out

Light anesthesia (tachycardia, hypertension)
Hypoventilation (hypercarbia)
Malfunction of expiratory valve on anesthesia machine
Transfusion reaction
Drugs (cocaine, ecstasy)
Neuroleptic malignant syndrome (slow onset)
Thyroid storm (no muscle rigidity)

↓

Inform Surgeon
Stop surgical procedure
If surgical procedure cannot be stopped, then complete procedure ASAP under total intravenous anesthetic

↓

Treatment of established MH

- FiO_2 of 100 %
- Increase minute ventilation
- Discontinue triggering agents—succinylcholine, volatile inhalational anesthetic agent, avoid calcium channel blockers
- Administer Dantrolene IV—Dantrolene is prepared by diluting each 20 mg vial in 60 ml of sterile water. An IV bolus of 2.5 mg/kg is administered (up to 10 mg/kg). Then 1 mg/kg is given every 6 h for 24–48 h
- For severe acidosis—sodium bicarbonate 1–2 meq/kg may be given
- Hyperkalemia—is treated by administering glucose+insulin, sodium bicarbonate or calcium chloride
- Temperature—cool the patient with ice packs or cold saline lavage. Monitor core body temperature
- Cardiac arrhythmias—treat as per ACLS protocol
- Urine output and color—is measured by inserting a Foley catheter
- Monitor labs—ABG, creatine kinase, serum myoglobin, PT, PTT, lactic acid

A8. Management of Anterior Mediastinal Mass

The most common anterior mediastinal mass in adults is a thymoma, whereas in children it is a lymphoma. Patients may present with dyspnea, cough, hoarseness of voice, and superior vena cava (SVC) syndrome (dyspnea, cough, facial swelling, headache). General anesthesia carries the risk of airway and cardiovascular collapse.

- Tracheal diameter should be examined on a CT chest scan
- For patients with SVC syndrome, a large bore lower extremity IV/s is placed
- A biopsy could be performed under local anesthesia. For resection, general anesthesia is required
- If general anesthesia, then secure airway with possible awake fiberoptic bronchoscopy
- Maintain spontaneous ventilation
- Avoid muscle relaxants
- Patient is placed in semi-Fowler's position (supine with head 30° high), or position of greatest comfort
- Ability to change patient position, as needed (lateral/prone)
- Rigid bronchoscope should be available
- Cardiopulmonary bypass should be available for high-risk patients

A9. Management of Foreign Body Aspiration in the Airway

- Diagnosis is made by a careful history and physical examination
- Signs include choking and wheezing following a witnessed aspiration, cough, stridor, and unilateral decreased breath sounds
- Chest X-ray may be normal, or may show atelectasis or area of hyperinflation (obstruction causing distal hyperinflation from air trapping)
- Dexamethasone is administered to decrease airway edema, and glycopyrrolate as an antisialagogue
- Induction of general anesthesia is usually intravenous
- However, inhalational induction may be done in an emergency or in a distressed child
- Inhalational induction is carried out with 100 % O2 and sevoflurane
- Spontaneous ventilation is safest and is commonly used, as it will not push the foreign body more distally, but there is risk of coughing, laryngospasm, and patient movement
- Controlled ventilation provides better control of airway, and no patient movement; however, positive pressure breaths may push the foreign body more distally
- Rigid bronchoscopy for removal of foreign body: Surgeon instruments the airway in consultation with the anesthesiologist

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