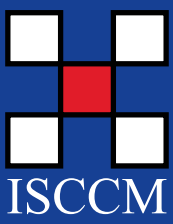
ICU Protocols

A Step-wise Approach, Vol II

Rajesh Chawla
Subhash Todi
Editors

Second Edition



Springer

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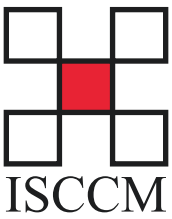

An endeavour of Indian College of Critical Care Medicine under the auspices of Indian Society of Critical Care Medicine (ISCCM).

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To my parents, wife Renu, and children Ankit, Aakanksha and Aakriti for their unconditional love and support. Special thanks to Dr. Sudha Kansal, Dr. Roseleen Bali, my students, residents, fellows, and colleagues who inspire and educate me.

—Rajesh Chawla

To my mother, my wife Shailja, and daughter Suchira for their understanding, tolerance, and patience shown during the gestational period of this manual.

—Subhash Todi

Preface

It gives us immense pleasure to present to you the second edition of *ICU Protocols: A Stepwise Approach*, an official publication of the Indian Society of Critical Care Medicine (ISCCM).

The first edition was published in 2012 under the same editorship. Concepts and evidence-based bedside practices in critical care medicine have further evolved since the first edition, and it was thought that modification and updating of the book was needed. The basic tenet of the ICU protocol book remains the same, i.e. to provide residents, fellows, critical care practitioners and allied health care professionals with a current and comprehensive stepwise approach for bedside diagnosis and management of the most frequently encountered problems in the intensive care unit (ICU). To prevent the manual from becoming voluminous, we have not gone into the details of the epidemiology and pathophysiology of each condition and restricted ourselves to practice points helpful to clinicians. The format of the book consists of introductory case scenario, bullet points, stepwise approach, flow charts, ample number of tables and figures for easy readability in each chapter. We have received positive feedback on the content and presentation of the chapters from our readers over the last 5 years. We have also collected feedback and suggestions from them on modifications, which are incorporated in the present edition.

There are some major changes that have been incorporated in the second edition. This edition is published in two volumes for increasing portability and allowing space for new chapters. Five new chapters have been added, namely High Flow Nasal Cannula, Antibiotic Pearls, CRBSI, Posttracheostomy Care in ICU and Research Methodology. Addition of these chapters became necessary due to the advancement of medical technology and increasing importance of research knowledge need for clinicians. Every chapter from the first edition have been incorporated with an updated version. For this multiauthor book, authors were carefully chosen for their expertise in the subject matter. In keeping with the multidisciplinary nature of our speciality, authorship also included non-intensivists like infectious disease specialists and gastroenterologists. Every chapter has been thoroughly discussed by both the editors, especially those referring to newer practices from Uptodate reference manual. Specifically, "Suggested Reading" sections with annotations have been updated with new references over the past 5 years, and current websites on the subject are added. Chapters on "Procedures" have also been revised to ensure correctness. The "Appendix" section has been thoroughly revised with special

emphasis on "Dosing" section in which doses of newer drugs like antibiotics have been added. A new appendix on "Glossary of Statistical Terms" has been added to make the reader familiar with ever increasing and sometimes confusing statistical terms. Formulae and equations have been updated wherever needed.

We sincerely hope that the second edition will give a new flavour to the much appreciated first edition and will serve its objective of improving bedside patient care by updating critical care practitioners. At the same time, we also realise that the field of critical care, like everything else, is not static but changes constantly and further modifications of this book will be needed in future.

ISCCM has been in the forefront of critical care education in India. This is an important educational venture of ISCCM, and we hope the book will be read not only in India but also regionally and internationally. Last but not least, we sincerely hope that this manual will be used by residents, wherever they are, for better bedside care of critically ill patients.

New Delhi, Delhi, India — Rajesh Chawla
Kolkata, West Bengal, India — Subhash Todi

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We would like to sincerely thank all the chapter authors who contributed their name and expertise in this endeavour. It would not have been possible to produce this manual without the hard work and support received from all of them. A special thanks to them for allowing editors the liberty to edit the chapters freely in order to maintain uniformity throughout the book. We would like to thank the Executive Committee of ISCCM for their unconditional support and patience during the long gestational period of this book. We would like to thank the experts who took the time and trouble to review the chapters and provide us with their inputs. We would like to acknowledge the hard work of all the fellows at Indraprastha Apollo Hospitals (Delhi) and AMRI Hospitals (Kolkata), who read all chapters and gave their inputs from the end users' perspective.

Special thanks to editorial team of Springer who have supported this medical project. We particularly thank Dr. Naren Aggarwal for multiple helpful suggestions and support throughout the process of finalisation of this book.

Also, we would like to give our special thanks to Mr. Vijay Prakash, Mr. Tapas Kayal, Mr. Bhagwan Dass, and Ms. Rajni for their assistance in the office work and completing the manuscript.

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Part I

Endocrine and Metabolic System

Hyponatremia

1

Rajesh Chawla, Subhash Todi,
and Devendra Kumar Agarwal

A 67-year-old chronic male smoker, a known case of small cell carcinoma, was admitted to hospital with altered sensorium, nausea, and dizziness. His vital signs were stable. Liver function tests, urea, and creatinine were normal. Serum sodium was 118 mEq/L and serum potassium was 3.0 mEq/L.

Hyponatremia is a very common condition encountered in the ICU as the primary admitting reason or as a complication of underlying medical illness. Hyponatremia is defined as serum sodium less than 135 mEq/L. It is considered severe if serum sodium is less than 120 mEq/L. It represents a relative excess of water in relation to sodium. Total body sodium may be normal, low or high. Hyponatremia can be induced by increased water intake and/or impaired water excretion. Too rapid correction can result in neurological complications. If the hyponatremia has developed over a period of less than 48 h, it is called acute hyponatremia. If it is known that hyponatremia has been present for more than 48 h, or if the duration is unclear, it is called chronic hyponatremia.

Step 1: Initiate Resuscitation (Refer to Chap. 23, Vol. 2)

- Assess and secure the airway in a patient with severe hyponatremia who cannot maintain airway.
- The patient may require assisted ventilatory support.

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- Insert a peripheral line and resuscitate with suitable fluids as deemed necessary.
- In a patient with concurrent hypovolemia and hypoosmolality, correction of volume deficit should take precedence over osmolality correction.
- In the hyponatremia patient, initial fluid resuscitation should be done cautiously.

Step 2: Take Focused History and Perform Physical Examination

- This should be done to assess severity of hyponatremia and urgency of correction.
- Pay immediate attention to neurological symptoms such as headache, lethargy, obtundation, disorientation, drowsiness, impaired consciousness, or seizures irrespective of duration of hyponatremia.
- Remember symptoms of hyponatremia depict neurologic dysfunction induced by cerebral edema. Cerebral edema occurs due to a decrease in serum osmolality which causes water movement into cells.
- Give attention to other symptoms of hyponatremia like anorexia, nausea, dizziness, and lack of balance.
- Examine previous records of serum sodium to assess chronicity.
- In chronic hyponatremia due to cerebral adaptation, neurologic symptoms are much less severe.
- Chronic hyponatremia patients may appear to be asymptomatic despite a serum sodium concentration that is persistently below 120 mEq/L.
- Symptoms in chronic hyponatremia that may occur include nausea, fatigue, lethargy, dizziness, gait disturbances, forgetfulness, confusion, and muscle cramps.
- Seizures and coma are not seen usually seen in chronic hyponatremia and often reflect an acute deterioration of the hyponatremia.
- Ask for a history of electrolyte-rich fluid loss (to vomiting, diarrhea, or diuretic therapy) that may point to hypovolemia.
- Ask for history of excessive water intake.
- Elicit history of low protein intake and/or high fluid intake.
- Look for history of use of medications which cause hyponatremia, such as thiazide and thiazide-type diuretics, mannitol, desmopressin (dDAVP), intravenous immune globulin and medications acting on the central nervous system including some antidepressants, antiepileptics, and antipsychotics.
- Inquire and look for any symptoms and signs of adrenal deficiency or hypothyroidism.
- A previous history of hyponatremia.
- Look for history consistent with malignancy, HIV, hepatic failure or plasma cell dyscrasia or renal failure.
- Look for, signs of extracellular volume depletion, such as decreased skin turgor, a low jugular venous pressure, or orthostatic / persistent hypotension which may be due to hypovolemia.
- Look for features of fluid overload such as pedal edema, ascites, and pleural effusion which can be due to heart failure, cirrhosis, or renal failure.

- Determine the severity of symptoms-mild, moderate or severe.
- Determine the need for hospitalization—patient who develop acute symptoms with severe hyponatremia require admission to the hospital.

Step 3: Identify Etiology

- Assess volume status, measure serum and urine osmolality, and measure spot urine sodium (see Table 1.1 and Fig. 1.2).
- Whenever hyperglycemia is present, correct the serum sodium concentration for the effect of glucose to identify correct sodium level and exclude hypertonic hyponatremia. Remember the sodium concentration will decrease by approximately 2 mEq/L for each 100 mg/100 mL (5.5 mmol/L) increase in glucose concentration.
- Patients with lipemic serum, severe obstructive jaundice, or a known plasma cell dyscrasia may have pseudohyponatremia. This laboratory artifact occurs when sodium is measured with flame photometry.
- Look for if patient had recent surgery utilizing large volumes of electrolyte-poor irrigation fluid (e.g., prostate or intrauterine procedures) or treatment with mannitol, glycerol, or intravenous immunoglobulin which cause isoosmolar or hyperosmolar hyponatremia.
- Estimate serum creatinine concentration for GFR. Both severely reduced GFR and thiazide (or thiazide-type) diuretics are important causes of hypotonic hyponatremia.
- Patients with hyponatremia due to heart failure or cirrhosis will have clinically apparent peripheral edema and/or ascites.
- Nonedematous patients with hypotonic hyponatremia are either euvolemic or hypovolemic.
- Most patients with hypovolemic hyponatremia can have obvious signs of volume depletion; however, some hypovolemic patients may have more subtle signs and are mistakenly judged to be euvolemic.
- Calculate serum osmolality:

$$2\times\left[\mathrm{Na}\right]+\left[\text{glucose mg / dL}\right]/18+\left[\text{BUN mg / dL}\right]/2.8.$$

Table 1.1 Risk factors of neurological complications in hyponatremia

Acute cerebral edema	Osmotic demyelination syndrome
Postoperative patients and young females	Too rapid correction of sodium Serum sodium less than 105 mEq/L Concurrent hypokalemia
Children	Malnourished patients
Psychiatric polydipsia patients	Alcoholics
	Burn patients
	Elderly women taking thiazides

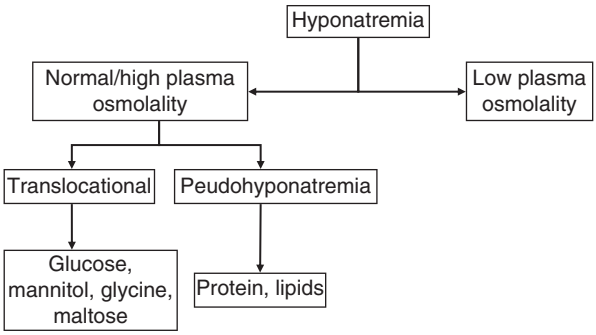

Fig. 1.1 Diagnostic approach to hyponatremia

- Normal: 275–290 mOsm/kg.
- Serum osmolarity should always be measured rather than calculated to differentiate hypo-, hyper-, and iso-osmolar types of hyponatremia (Fig. 1.1).
- Serum tonicity (effective serum osmolality), is the parameter sensed by osmoreceptors; serum tonicity controls the transcellular distribution of water. Water can freely cross almost all cell membranes and moves from lower tonicity area (higher water content) to an area of higher tonicity (lower water content).
- The main difference between tonicity and osmolality is that tonicity depicts the concentration of solutes that do not easily cross cell membranes (mostly sodium salts with a small contribution from glucose) therefore controls the movement of water between cells and the extracellular fluid.
- On the other hand osmolality also includes the osmotic contributions of urea and (if present) ethanol or other alcohols or glycols, which are considered "ineffective" osmoles since they can pass freely and equilibrate across the cell membrane and therefore have little effect on water movement.

$$\text{Tonicity} = \text{Measured serum osmolality} - \left(\frac{\text{BUN}}{2.8}\right)$$

$$\text{Tonicity} = \text{Measured serum osmolality} - \text{blood urea concentration}$$

- A patient with true hyponatremia will have low serum osmolality.
- Urine osmolality of less than 100 mOsm/kg: with low serum osmolarity: suggests excess water intake.
- Urine osmolality of more than 100 mOsm/kg: reflects impaired renal excretion of water (e.g. CCF, cirrhosis of liver, prerenal renal failure) or salt (e.g. salt loosing nephropathy) or SIADH.
- Urine osmolality may be calculated by the last two digits of urine specific gravity × 30.
- Measure spot urine sodium: less than 20 mEq/L or more than 20 mEq/L.
- Measurement of spot urinary sodium and assessment of the volume status can help to know the etiology (Fig. 1.2).
- These parameters are not applicable in patient receiving diuretics or have intrinsic renal disease.

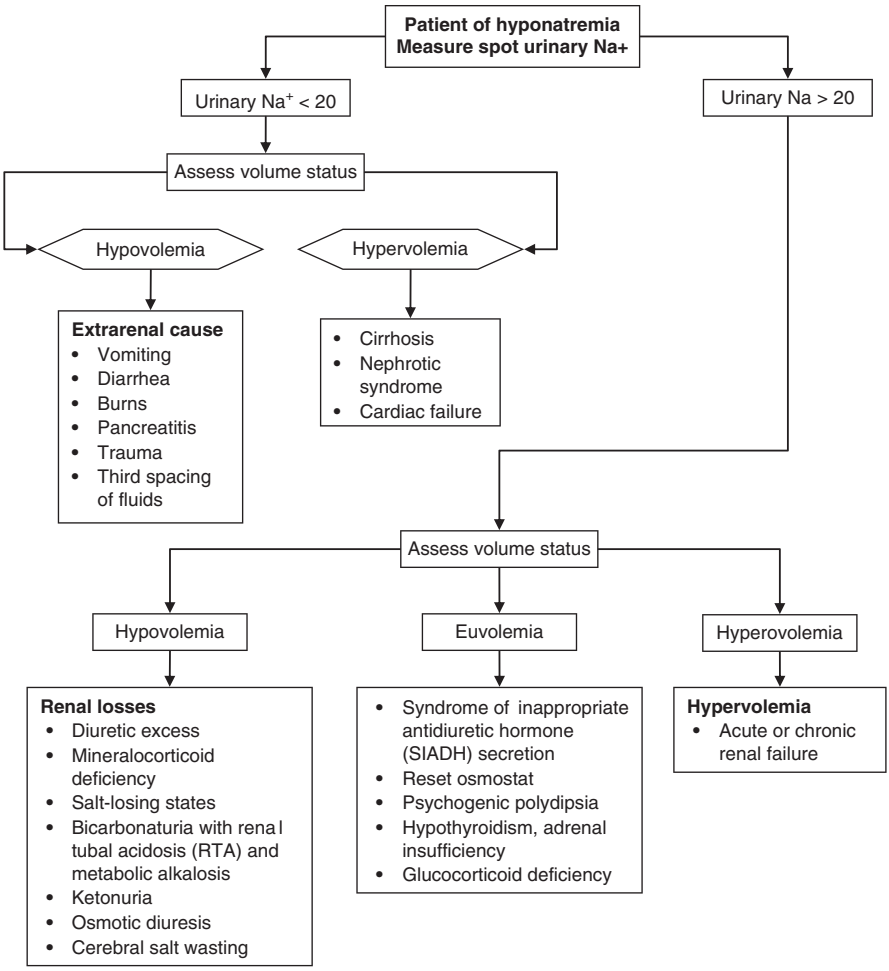

Fig. 1.2 Diagnostic approach to hyponatremia—measure urinary sodium and assess volume status

Step 4: Assess Severity of Hyponatremia

- Mild hyponatremia—130–134 mmol/L
- Moderate hyponatremia—120–129 mmol/L
- Severe hyponatremia—less than 120 mmol/L

Step 5: Send Further Investigations

In addition to serum osmolality, urine osmolality, and urinary sodium, send further investigations to ascertain the cause and severity of hyponatremia.

- Serum K, Cl, bicarbonate
- Serum glucose, urea, creatinine, total proteins, triglycerides, uric acid
- Arterial blood gases
- Serum TSH, cortisol
- Urine—creatinine, uric acid
- Fractionated excretion of sodium (FE Na) = (U Na × P Cr)/(P Na × U Cr) × 100

Step 6: Correct Serum Sodium

- The treatment of hyponatremia in hospitalized patients has four objectives.
  - To prevent further decrease in the serum sodium concentration,
  - To decrease intracranial pressure in patients at risk for developing brain herniation,
  - To alleviate symptoms of hyponatremia,
  - To avoid excessive correction of hyponatremia.
- Treatment of hyponatremia must be individualized.
- Factors to be considered are as follows:
  - Severity
  - Duration
  - Symptoms
- The risk of complications is greater in acute hyponatremia and it needs aggressive therapy.
- Chronic hyponatremia with lower serum sodium concentration also has the greater risk of complications from overaggressive therapy and it needs close monitoring to avoid overcorrection.
- Patients with acute severe (i.e., serum sodium less than 120 mEq/L) symptomatic hyponatremia, should be treated in hospital.
- Risks of treatment (osmotic demyelination) should be balanced against benefit (see Table 1.1). Too rapid correction of sodium is the most important risk factor for the development of osmotic demyelination syndrome.

Step 7: Determine the Rate of Correction of Sodium

- The goal of initial therapy in severe hyponatremia is to raise the serum sodium concentration by 4–6 mEq/L in a 24 h period. So in symptomatic patient achieve this in 6 h or less and rest of the time just maintain to avoid overcorrection. In symptomatic patients, sodium may be corrected at the rate of 1–2 mEq/L for an initial few hours or till seizure subsides.

- In asymptomatic patients, the rate of correction should not be more than 0.5–1.00 mEq/L/h and less than 8 mEq over the first 24 h. A correction of 4–6 mEq/L appears to be sufficient to avoid rapid correction.
- Avoid overcorrection of serum sodium concentration.
- Avoid isotonic saline in symptomatic hyponatremia except in hypovolemic states.
- It is the daily change rather than hourly rise of serum sodium that is associated with osmotic demyelination syndrome (ODS). In patient requiring emergency treatment, sodium can be corrected rapidly in first few hours of the 24 h period.

Step 8: Calculate Sodium Deficit and Rate of Rise of Sodium

- Sodium deficit = total body water (TBW) × (desired serum Na − measured serum Na).
- TBW = body weight (kg) × Y.

Y =	Children	Adult men	Adult women	Elderly men	Elderly women
	0.6	0.6	0.5	0.5	0.45

- The main use of this formula is in the volume depletion state and in SIADH to estimate initial rate of fluid administration.
- For example, in a 60-kg woman with a serum sodium of 115 mEq/L with a goal of increasing sodium by 8 mEq/L in first 24 h,

$$\text{Sodium deficit} = (60 \times 0.5) \times (123 - 115) = 240 \text{ mEq.}$$

- Three percent hypertonic saline contains approximately 500 mEq of sodium per liter or 1 mEq per 2 mL. So, 480 mL (240 mEq of sodium) of hypertonic saline given over 24 h or 20 mL/h will raise serum sodium by 8 mEq (from 115 mEq/L to 123 mEq/L in 24 h or 0.25 mEq/h).
- This should be confirmed by frequent serial measurements of serum sodium.
- Increase in serum sodium by any fluid = (infusate sodium − serum sodium)/TBW + 1.
- In cases when potassium is added to intravenous fluid, increase in serum sodium = [(infusate sodium + potassium) − (serum sodium)]/TBW + 1.
  For example, in a 60-kg woman with a serum sodium of 110 mEq/L, if 1 L of isotonic saline (containing 154 mEq/L of sodium) is administered, the estimated rise of serum sodium will be

$$(154 - 110) / (30 + 1) = 1.4 \text{ mEq / L.}$$

- That is, serum sodium will be 111.4 mEq/L after giving 1 L of normal saline.
- *Rule of thumb*
  - For hypertonic (3%) saline
  - Infusion rate = weight (kg) × desired rate of correction

  For example, to correct at 1 mEq/L/h in a 50-kg person,
  - Infusion rate = 50 × 1 = 50 mL/h.

To correct at 0.5 mEq/L/h in a 70-kg person,
  - Infusion rate = 70 × 0.5 = 35 mL/h.
- For isotonic (0.9%) saline,
  - 0.9 NaCl corrects at 1–2 mEq/L for every 1 L of NaCl.
- Remember that these formulas are just an approximation as they do not take into account translocation of water, correction of underlying cause, or ongoing water loss.
- Rise of sodium should always be verified by repeated sodium measurement.
- If infusate fluid osmolality is less than urine osmolality paradoxically serum sodium may fall after fluid infusion.

Step 9: Euvolemic, Hypoosmolar, Hyponatremia

Consider SIADH

- Clinical euvolumia.
- SIADH is the most common cause of hyponatremia in euvolemic patients with a high urine osmolality,
- It is diagnosed after other etiologies are excluded.
- The rate of sodium excretion is determined by sodium intake, as it is in normal individuals.
- SIADH is frequently associated with hypouricemia (serum uric acid concentration that is less than 4 mg/dL) due to increased urinary uric acid excretion, and low blood urea nitrogen due to increased urea clearance.
- Serum sodium less than 134 mEq/L
- Urine osmolality is more than 300 mOsm/kg H_2O
- Urinary sodium concentration more than 40 mmol/L
- Normal renal, hepatic, adrenal, and thyroid function
- Serum osmolality less than 275 mOsm/kg H_2O
- In severely symptomatic patients:
  - Give 3% hypertonic saline
  - Check serum sodium frequently
  - Patients with confusion and lethargy, initial administration of hypertonic saline therapy to raise the serum sodium.
  - The goal is to raise the serum sodium 1 mEq/L per hour for 3–4 h.
  - The serum sodium should be measured at 2–3 h and the subsequent infusion rate should be adjusted to achieve a rate of correction of no more than 6–8 mEq/L in any 24-h period.
- In asymptomatic and mildly symptomatic patients:
  - Fluid restriction is the mainstay of the treatment of most patients with SIADH, with a suggested intake of less than 800 mL/day; do not restrict fluid in subarachnoid hemorrhage since fluid restriction may promote cerebral vasospasm in these patients.

  - Fluid restriction is defined as intake of fluid less than urinary output.
  - Administer oral salt tablets (1 g NaCl = 17 mEq).
  - Use intravenous saline like hypertonic saline, the electrolyte concentration of which must be greater than the electrolyte concentration of the urine.
  - Isotonic saline is infrequently effective and often leads to further lowering of the serum sodium.
  - Potassium is as osmotically active as sodium. So, giving potassium (usually for concurrent hypokalemia) can raise the serum sodium concentration and osmolality in hyponatremic patients. Intracellular sodium moves into the extracellular fluid in exchange for potassium and also extracellular chloride moves into the cells with potassium so the increase in cell osmolality promotes free water entry into the cells and raise sodium.
- Loop diuretics may be added if urine output is very low and urine osmolality more than twice the plasma osmolality (typically more than 550). Loop diuretic like furosemide inhibit sodium chloride reabsorption in the thick ascending limb of the loop of Henle and interferes with the countercurrent mechanism and induces a state of antidiuretic hormone (ADH) resistance, resulting in the excretion of a less-concentrated urine and increased water loss.
- Consider vasopressin antagonist (vaptans) if no contraindications.
  - There are multiple receptors for the ADH vasopressin: the V1a, V1b, and V2 receptors.
  - The V2 receptors primarily mediate the antidiuretic response, while V1a and V1b receptors principally cause vasoconstriction and mediate adrenocorticotropic hormone (ACTH) release, respectively.
  - Some oral formulations, such as tolvaptan, mozavaptan, satavaptan, and lixivaptan, are selective for the V2 receptor,
  - Conivaptan, blocks both the V2 and V1a receptors.
  - The vasopressin receptor antagonists produce a selective water diuresis (also called aquaresis) without affecting sodium and potassium excretion.
  - The free water loss will tend to correct the hyponatremia.
  - Thirst increases significantly with these agents, which may limit the rise in serum sodium
  - Oral tolvaptan is available and recommended for use in these patients with hyponatremia due to SIADH. Dose 15 mg once daily to a maximum of 60 mg daily
  - Tolvaptan should not be used for longer than 1 month and should not be given to patients with liver disease (including cirrhosis).
  - Conivaptan, V1a receptor blockade might worsen renal function in patients with cirrhosis since terlipressin, a V1a receptor agonist, has been used to treat hepatorenal syndrome.
- Demeclocycline can also be given in SIADH 600–1200 mg/day.
- In all cases of SIADH, correct the underlying cause and withdraw any offending drug.

- Other causes of euvolemic, hypo-osmolar hyponatremia such as hypothyroid, adrenal insufficiency, renal disease, and psychogenic polydipsia should be managed by water restriction, hormone replacement, and treatment of the underlying disease.
- Hyponatremia with a reset osmostat pattern is a variant of the SIADH and should be suspected in any patient with mild to moderate hyponatremia (usually between 125 and 135 mEq/L) that is stable over time despite variations in sodium and water intake. The recommendations for SIADH do not apply to patients with reset osmostat. Treatment should be primarily directed at the underlying disease.

Step 10: Hypervolemic, Hypoosmolar, Hyponatremia

- Consider edematous states such as cirrhosis, nephrotic syndrome, cardiac failure, and renal failure.
- Patients with hyponatremia due to heart failure or cirrhosis typically have advanced disease and present with clinically apparent peripheral edema and/or ascites along with a previous diagnosis of heart or liver failure.
- There is no evidence so far that correction of hyponatremia improves the hemodynamic abnormalities associated with the severe underlying chronic heart failure or that it improves clinical outcomes.
- The main indications for specific therapy to correct hyponatremia are a serum sodium concentration below 120 mEq/L (severe hyponatremia) and/or the presence of symptoms that might be due to hyponatremia
- These should be managed by the following in cardiac failure with hyponatremia
  - Fluid restriction
  - Loop diuretics
  - Angiotensin inhibition with an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin II receptor blocker (ARB) and a loop diuretic maybe added to raise the serum sodium concentration.
  - Tolvaptan may have a role in the management of hyponatremia in patients with chronic heart failure when other management options have failed to increase the serum sodium above 120 mEq/L and/or ameliorate symptoms of hyponatremia.
  - Treating the underlying disease
  - Avoiding extra sodium

Cirrhosis with Hyponatremia

- Withdraw beta blockers, alpha blockers, diuretics (particularly thiazide diuretics),
- Correcting hypokalemia
- Treating patients who have persistent hypotension. Midodrine is the agent typically used to increase blood pressure in cirrhotic patients.

- In severe symptomatic patient attempt to raise the serum sodium with infusion of albumin or hypertonic saline.
- Hemodialysis in advanced renal dysfunctions.

Step 11: Hypovolemic, Hypoosmolar, Hyponatremia

- Consider the volume-depleted state (renal or extrarenal).
- These should be managed by the following:
  - Volume replacement
  - Treating the underlying disease
  - Low urine sodium (<20 mEq/L)—The urine sodium is less than 20 mEq/L in patients with hypovolemia caused by gastrointestinal fluid losses (e.g., diarrhea), by movement of fluid into the "third space" (e.g., pancreatitis).
  - High urine sodium (>40 mEq/L) with low urine chloride (<20 mEq/L)—In hypovolemic hyponatremic patients who have metabolic alkalosis caused by vomiting, the urine sodium concentration may be greater than 20 mEq/L, but the urine chloride concentration will be low (less than 20 mEq/L).
  - This is due to contraction metabolic alkalosis in volume depletion and subsequent loss of bicarbonate in urine which negates the use of urine sodium as a marker of hypovolemia.
  - High urine sodium and chloride (>40 mEq/L)—the sodium and chloride concentrations are usually above 40 mEq/L in hypovolemic hyponatremic patients with renal salt losses.

Diuretic-Induced Hyponatremia

- This may mimic SIADH, as it may be clinically euvolemic.
- Occurs predominantly with thiazide diuretics.
- May occur within a few days of starting diuretics.
- Elderly patients with low body mass are more vulnerable.
- May be associated with increased water intake.
- Managed by stopping diuretics, isotonic or hypertonic saline, in symptomatic patients.
- At high risk of rapid correction after stopping diuretics.
- Careful monitoring is required to avoid osmotic demyelination.
- Hyponatremic patients who present with clinical symptoms and signs of hypovolemia may have extrarenal fluid losses or renal fluid losses.
- Measurement of the urine sodium and chloride concentrations can often distinguish between these.
- Nonedematous patients with hypotonic hyponatremia are either euvolemic or hypovolemic.
- Sometimes both SIADH and thiazide induced hyponatremia may be present, due to underlying disease and diuretic used respectively.

Cerebral Salt Wasting (CSW)

- This may mimic SIADH as laboratory findings are similar.
- Hyponatremia with a low plasma osmolality.
- An inappropriately elevated urine osmolality (>100 mOsm/kg and usually >300 mOsm/kg).
- A urine sodium concentration above 40 mEq/L.
- Much less common than SIADH.
- Occurs with acute CNS disease, mainly subarachnoid hemorrhage.
- Clinically hypovolemic.
- Normal serum uric acid.
- Increased fractional excretion of urate.
- This can be differentiated from SIADH as mentioned in Table 1.2.

Management

- Treat the underlying causes of CSW like subarachnoid hemorrhage.
- Put the central line to assess volume status.
- Volume replacement—match urine loss.
- Amount of sodium required = sodium deficit × total body water (see Sect. 8).
- Blood product if anemia is present.

Step 12: Hyperosmolar Hyponatremia

- Consider hypertonic mannitol, glycine or other osmotic agents and hyperglycemia.

Table 1.2 Differentiating SIADH from CSW

	CSW	SIADH
Plasma volume	Decreased	Normal or increased
Salt balance	Negative	Normal
H_2O balance	Negative	Increased or no change
Signs of dehydration	Present	Absent
Weight	Decreased	Increased or no change
PCWP and CVP	Decreased	Increased or normal
Hematocrit	Increased	Increased or normal
BUN/creatinine ratio	Increased	Normal
Serum protein concentration	Increased	Normal
Serum K concentration	Increased or no change	Decreased or no change
Serum uric acid concentration	Normal	Decreased

PCWP pulmonary capillary wedge pressure, *CVP* central venous pressure, *BUN* blood urea nitrogen

- Patients with recent prostate or uterine surgery. The absorption of nonconductive glycine, sorbitol, or mannitol irrigation solutions during TURP of the prostate or bladder or during hysteroscopy or laparoscopic surgery can lower the serum sodium by escalating the extracellular fluid volume along with these sodium-free solutions.
- Treatment
  - Stop infusion.
  - Hyperglycemia—stop or decrease glucose administration.
  - Give insulin and fluids.
  - Target a drop in glucose concentration of 75–100 mg/dL/h.

Step 13: Iso-osmolar Hyponatremia

- Consider pseudohyponatremia (drip arm sample, hyperlipidemia, paraproteinemia, plasma cell dyscrasia and patients with obstructive jaundice)
- Usually asymptomatic
- No treatment is required.

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Hypernatremia

2

Rajesh Chawla and Sudha Kansal

A 75-year-old male patient, a case of chronic obstructive pulmonary disease (COPD), was transferred from another hospital with complaints of fever, increased breathlessness for 5 days, and altered sensorium since 1 day. He also had an episode of seizure 1 day. He was being managed on the lines of acute exacerbation of COPD with cor pulmonale with pneumonia. He received antibiotics and diuretic therapy in the previous hospital. On evaluation, his laboratory values showed hemoglobin 13 g/dL, packed cell volume of 38.5%, serum sodium 160 mEq/L, serum potassium 3.0 mEq/L, serum urea 146 mg/dL, and serum creatinine of 1 mg/dL.

Hypernatremia is a common problem characterized by a rise in serum sodium above 145 mEq/L. This is a hyperosmolar condition caused by a decrease in total body water relative to the sodium content. Hypernatremia is caused by impaired thirst and restricted water intake which is often exacerbated by conditions leading to increased fluid loss. The goal of management involves identification of hypernatremia and correction of volume disturbances and hypertonicity.

Step 1: Initiate Resuscitation (Refer to Chap. 23, Vol. 2)

- Assess and secure the airway and provide ventilatory support when required.
- Differentiate between Hypovolemia which is due to water and sodium loss and dehydration which is predominantly due to water loss.
- Infuse isotonic sodium chloride in hypovolemic patients.

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Step 2: Take History and Do Physical Examination

- This should be done to assess the etiology of hypernatremia and severity of the problem.
- Look for symptoms suggestive of hypernatremia (Table 2.1). These are nonspecific and may even mimic rapid fall of serum sodium.
- History should be taken focusing on of the following problems:
  - Extrarenal fluid losses (e.g., burns, vomiting, diarrhea, fever, high minute ventilation in mechanically ventilated patients)
  - Decreased fluid intake
  - Polyuria (i.e., signs of diabetes insipidus [DI] or osmotic diuresis)
  - Review drug chart (drugs causing DI, osmotic diuretics, osmotic laxatives)
  - Review previous sodium levels to assess chronicity
  - Hypertonic solution infusion (sodium bicarbonate, hypertonic saline, total parenteral nutrition)
  - Hypertonic feed (high-protein formula, concentrated formula)

Step 3: Assess Volume Status

- This is important to understand the underlying pathophysiology of hypernatremia (Table 2.2) and plan the treatment strategy.
- Volume status can be assessed by clinical means, hemodynamic monitoring, and urine biochemistry (Table 2.3).

Step 4: Send Investigations

- Arterial blood gases and serum electrolytes
- Blood glucose, blood urea, and serum creatinine
- Serum uric acid
- Hematocrit
- Serum osmolality and urine osmolality
- Urinary sodium and chloride
- If indicated do imaging studies: Head CT scan or MRI

Table 2.1 Clinical features suggestive of hypernatremia

Central nervous system			
Anorexia	Restlessness	Confusion	Weakness
Lethargy	Seizure	Respiratory failure	Coma
Musculoskeletal symptoms			
Twitching	Hyperreflexia	Ataxia	Tremor

Table 2.2 Pathophysiology of hypernatremia

Hypovolemic (i.e., water deficit > sodium deficit)
Extrarenal losses—diarrhea, vomiting, fistulas, significant burns
Renal losses
Osmotic diuretics
Diuretics
Postobstructive diuresis
Intrinsic renal disease(renal tubular disease)
Adipsic hypernatremia is secondary to decreased thirst
Damaged hypothalamic thirst centers
Hypervolemic (i.e., sodium gain > water gain)
Hypertonic saline
Sodium bicarbonate administration
Accidental salt ingestion (e.g., error in preparation of infant formula)
Mineralocorticoid excess (Cushing's syndrome)
Euvolemic
Extrarenal losses—increased insensible loss (e.g., hyperventilation)
Renal losses—central DI, nephrogenic DI
Mostly free water loss is from intracellular and interstitial spaces

Table 2.3 Assessment of low volume status

A. Clinical
Increasing thirst
Dry tongue, sunken eyes, reduced skin turgor on forehead and sternal skin
Orthostatic tachycardia (>20/min rise of pulse rate)
Orthostatic hypotension (>20 mmHg fall in systolic BP or >10 mmHg fall in diastolic BP)
Resting tachycardia and hypotension
Low urine output, concentrated urine (extrarenal loss)
B. Hemodynamic
Low central venous pressure
Arterial pressure variation (in ventilated patients)
Rising arterial pressure on passive leg raising (spontaneously breathing patients)
C. Biochemistry
Rising hematocrit
Rising albumin
Raised urea in proportion to serum creatinine
High serum uric acid
High urine osmolarity
Low urine sodium (extrarenal loss)
Low urine chloride (metabolic alkalosis)

Step 5: Make a Diagnosis

- Serum osmolality is always increased in patients with hypernatremia.
- Urine osmolality of less than 300 mOsmol/kg with high serum osmolality or, urine osmolality <100 mOsmol/kg with normal serum osmolality may be due to DI (central or nephrogenic), which can be distinguished by response to vasopressin.
- Urine osmolality of more than 600 mOsmol/kg could be due to unreplaced gastrointestinal or insensible loss (urine sodium <20 mEq/L) or excess sodium administration by enteral or parenteral route (urine sodium >40 mEq/L).
- Urine osmolality of 300–600 mOsmol/kg may be due to osmotic diuresis (check for glycosuria), partial central or nephrogenic DI.
- Calculate total solute excretion (urine osmolality × urine volume); if more than 1000 mOsmol per day—osmotic diuresis.

Step 6: Treatment

- Aim for symptom resolution, 10–15% improvement in sodium levels in first 24 h.
- Correction in chronic (>48 h) settings:
  - Total less than 10–12 mEq/24 h
- Rapid correction will cause rapid shift of water inside the brain causing cerebral edema and seizures.

Step 7: Calculate Water Deficit

$$\text{Water deficit}\left(\text{L}\right) = \text{total body water}\left(\text{TBW}\right) \times \left[\left(\text{measured Na} / 140\right) - 1\right]$$

$$\text{TBW} = \text{body weight}\left(\text{kg}\right) \times \text{"}\ \text{Y}''$$

Y = children	Adult men	Adult women	Elderly men	Elderly women
0.6	0.6	0.5	0.5	0.45

(Y= This is percentage of water of the total body weight.)
For example:

- 60 kg adult woman with serum sodium of 160 mEq/L.
- Free water deficit = [(0.5 × 60)] × [(160/140) − 1] = 4.2 L.
- This can be given as 5% dextrose or free water by the nasogastric tube or orally.
- Free water deficit = 4.2 L (see above).
- Thus, 4.2-L positive water balance must be achieved to get serum sodium down from 160 to 140 mEq/L or by 20 mEq.
- Rate of correction = 0.5 mEq/h.

- 4.2 L of free water to be given over 40 h at a rate of approx.100 mL/h.
- Insensible water loss (30 mL/h) should be added.
- Thus, 130 mL/h of free water needs to be replaced for 40 h.
- This can be done with IV 5% dextrose, 0.45% saline or water by the nasogastric tube or orally.
- Large volume of 5% dextrose will lead to hyperglycemia, and if needed, insulin should be given to prevent glycosuria, otherwise osmolar diuresis can worsen hypernatremia.
- Sodium and/or potassium can be added to the intravenous fluid as necessary to treat concurrent volume depletion and/or hypokalemia (e.g., due to diarrhea).
- The addition of solutes decreases the amount of free water that is given.
- If potassium is also added, then even less free water is present and a further adjustment to the rate must be made.
- Repeat sodium level and entire calculation every 12 h and replan infusion rate. (This is because the urinary free water loss is not taken into account and it keeps on changing.)
- In general a net positive balance of 3 mL of electrolyte free water per kg body wt will decrease serum sodium by 1 mEq/L.
- Initially 5% dextrose at the rate of 3–5 mL/kg/h should be infused which should be reduced to 1 mL/kg/h once serum sodium normalises.
- These calculations are only approximations and frequent sodium and glucose measurement very 4–6 h should be performed till serum sodium is 146 mEq/L.

Step 8: Manage Specific Hypernatremic States

Hypovolemic hypernatremia	Volume deficit always takes precedence over correcting water deficit
	Correct volume deficit initially by isotonic saline until improvement of orthostasis, tachycardia, and urine output
	Calculate and correct water deficit
	Treat the etiology of volume loss
	After correction of volume deficit, administer 0.45% saline, 5% dextrose, or oral water, replacing deficit and ongoing losses
Euvolemic hypernatremia	Correct water deficit
	Administer 0.45% saline, 5% dextrose, or oral water, replacing deficit and ongoing losses
	Follow serum [Na] carefully to avoid water intoxication
	Central DI—treat underlying disease, long-term nasal pitressin
	Nephrogenic DI—correct calcium, potassium; remove offending drugs; low-sodium diet
Hypervolemic hypernatremia	Remove the source of extra sodium
	Correct the cause
	Loop diuretics alone can worsen hypernatremia. Thus combining with metolazone or thiazide diuretics will be a better choice
	Hemodialysis may be performed in renal failure

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Hypokalemia and Hyperkalemia

3

Subhash Todi and Rajesh Chawla

A 50-year-old male patient was admitted with generalized weakness and abdominal distension. On examination, he was found to be alert and hemodynamically stable. Neurological examination revealed quadriparesis. Abdominal examination revealed distension with sluggish bowel sounds. His serum potassium level was 2 mEq/L.

Disorder of potassium balance—both hypo- and hyperkalemia—is a common finding in the ICU. These abnormalities might be subtle requiring minimal intervention or life-threatening requiring urgent measures. A methodological approach is warranted to manage this problem.

Step 1: Initial Resuscitation

- Patients should be resuscitated, as mentioned in Chap. 23, Vol. 2.
- Patients with severe muscle weakness due to hypokalaemia need to be assessed for airway protection and if needed should be intubated or ventilated.
- Circulatory status needs to be maintained with intravenous fluids as hypokalemic patients are usually volume depleted.

Step 2: Assess Severity of Hypokalemia

- After initial resuscitation, the patient should be assessed for urgency of correction of hypokalemia.

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Table 3.1 ECG changes in hypokalemia

ST segment depression
Decrease in amplitude of T waves
Increase in amplitude of U wave (occurring at the end of T)
Premature atrial or ventricular ectopics
Sinus bradycardia
Paroxysmal atrial or junctional tachycardia
Atrioventricular block
Ventricular tachycardia (torsade de pointes)
Ventricular fibrillation

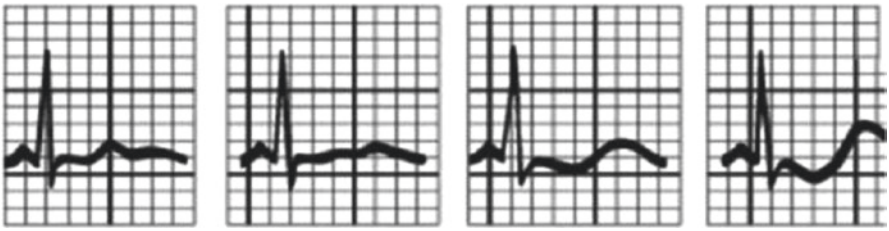

Fig. 3.1 Hypokalemia

- Urgent intravenous correction is needed in the following conditions:
  - ECG changes in hypokalemia (see Table 3.1 and Fig. 3.1)
  - Cardiac arrhythmia
  - Severely impaired neuromuscular function
  - Diaphragmatic weakness and respiratory failure
  - Patients on digoxin or antiarrhythmic therapy
  - Old age
  - Organic heart disease
  - Serum potassium of less than 3.0 mEq/L
  - Diabetic ketoacidosis
  - Hyperosmolar nonketotic diabetes

Step 3: Estimate Potassium Deficit

- Approximately 200 mEq potassium deficit is required to decrease serum potassium by 1 mEq/L in the chronic hypokalemic state.
- In acute situations, the serum potassium concentration falls by approximately 0.27 mEq/L for every 100 mEq reduction in total body potassium stores.
- These are only an approximation, and careful monitoring of serum potassium is required.
- These approximation only takes into consideration potassium deficit but does not account for ongoing losses or intracellular shifts and daily maintenance requirement of potassium.
- Daily requirement of potassium is 40–120 mEq/day

Step 4: Replace Intravenous Potassium Chloride (Table 3.2)

Step 5: Replace Intravenous Magnesium

- Hypomagnesemia is usually concurrently present with hypokalemia and needs to be corrected.

Step 6: Ascertain the Cause of Hypokalemia and Manage Specifically (Table 3.3)

- Detailed history and physical examination should be performed to look for systemic causes of hypokalemia.
- History of increased urinary or gastrointestinal loss of fluid (vomiting, diarrhea, polyuria) should be taken.
- Detailed drug history to rule out drug-induced hypokalemia should also be taken.
- Urinary potassium level of more than 30 mEq/day is a feature of loss of potassium in the urine.
- This can be calculated by the following
  - 24 h urine collection and measuring potassium concentration
  - Spot urinary potassium: less than 15 mEq/L suggest non urinary cause of hypokalemia

Table 3.2 Replacement of potassium chloride by intravenous route (Table 3.2)

Peripheral route
It is safe
One ampoule (50 mL) of potassium chloride contains 20 mEq of potassium
It is used in mild-to-moderate hypokalemia (3–3.5 mEq/L)
20–40 mEq/L of KCl is added to each liter of fluid given over 4–6 h
A saline rather than dextrose solution should be used. Half-strength saline with 20 mEq of KCl makes the solution isotonic and suitable for peripheral use
Do not use high concentrations over 60 mEq/L; it can lead to pain and sclerosis of peripheral vein
Volume overload is a potential risk in susceptible subjects
Central route (it is used in severe hypokalemia 2.5–3 mEq/L)
Prepare 20 mEq KCl in 100 mL normal or half-strength saline
5–20 mEq/h (through syringe pump) can be safely given by central route (preferably femoral vein)
Life-threatening arrhythmias
Up to 40 mEq/h of KCl can be given for few hours
No other infusion should be going through the same catheter
Avoid blood sampling and flushing the catheter
Frequently monitor potassium till 3–3.5 mEq/L
Continuous ECG monitoring is required

Table 3.3 Causes of hypokalemia

Increased entry into cells (redistributive hypokalemia)
Metabolic alkalosis
DKA after insulin replacement
Elevated β-adrenergic activity—stress or administration of β-agonists
Hypokalemic periodic paralysis
Refeeding syndrome
Hypothermia
Chloroquine intoxication
(increase loss: *gastro intestinal)*
Vomiting
Diarrhea
Nasogastric tube drainage
Laxative abuse
(increase loss: urinary)
Diuretics
Primary mineralocorticoid excess
Hypomagnesemia
Amphotericin B
Salt-wasting nephropathies—including Bartter's or Gitelman's syndrome
Renal tubular acidosis, polyuria
Other
Dialysis
Plasmapheresis
Increased sweating
Decreased potassium intake (rare)

  - Sending a spot sample of potassium in urine and multiplying it by 24 h urine output (e.g. if spot sample is 10 mEq/L and 24 h urine is 1 L, then 24 h urinary potassium loss is 10 mEq and denotes that hypokalemia is not due to urinary loss but due to a intracellular shift or non urinary loss).
- Spot Urine potassium to creatinine ratio: if more than 13 mEq/g (1.5 mEq/mmol) of creatinine indicates inappropriate urinary loss.
- Asses acid base status:
  - Metabolic acidosis with low urinary excretion of potassium is due to lower gastrointestinal loss like diarrhea.
  - Metabolic acidosis with high urinary potassium excretion is due to diabetic ketoacidosis or Type 1 Renal tubular acidosis
  - Metabolic alkalosis with low urinary excretion of potassium is due to upper gastrointestinal loss like vomiting or previous diuretic use
  - Metabolic Alkalosis with high potassium urinary loss is due to recent diuretic use or primary hyperldosteronism

Step 7: Send Investigation

- Complete blood count
- Na, K, Ca, Mg, PO_4, HCO_3
- Urea, creatinine
- Creatine phosphokinase (CPK) (To exclude hypokalemia induced rhabdomyolysis)
- Arterial blood gas analysis
- ECG
- Urine for K, Creatinine
- Urinalysis

Step 8: Replace Potassium Orally

- Once serum potassium has been raised to a safe limit of above 3 mEq/L, the rest of the replacement may be done slowly by oral route. This could be achieved by adding potassium-rich diet, potassium salt, or potassium chloride suspension.
- Treatment is usually started with 10–20 mEq of potassium chloride given two to four times per day (20–80 mEq/day).

Step 9: Reduce the Loss of Potassium

- In patients with hypokalemia due to increased urinary losses, potassium-sparing diuretics such as spironolactone, amiloride, or eplerenone may be tried.
- Oral/IV potassium should be used with caution in these situations specially in patients with impaired renal function and on concomitant use of ACE inhibitors or ARBs.

Hyperkalemia

A 60-year-old diabetic male patient, hypertensive and on angiotensin-converting enzyme (ACE) inhibitors, was admitted with dizzy spells. On admission, his pulse was 60/min, BP was 110/70 mmHg, and sensorium was normal. His blood biochemistry showed urea 90 mg/dL, creatinine 2.0 mg/dL, Na 130 mEq/L, and K 6.5 mEq/L.

Step 1: Initiate Resuscitation

- Patients with severe hyperkalemia need an urgent intravenous access and continuous ECG monitoring.

- They can have sudden bradycardic arrest. ACLS protocol should be followed in these situations (see Chap. 19, Vol. 1).
- Intravenous Calcium Gluconate/Chloride should be immediately given in cardiac arrest situations when hyperkalemia is suspected, even before potassium results are available.
- Avoid succinylcholine in suspected hyperkalaemia during rapid sequence intubation
- Avoid potassium containing resuscitation fluid like Ringers lactate and Balanced salt solution during resuscitation

Step 2: Assess Severity of Hyperkalemia and Urgency of Correction

- Hyperkalemia should be urgently managed in the following circumstances:
  - ECG changes (see Table 3.4 and Fig. 3.2)
  - The progression and severity of ECG changes do not always correlate well with serum potassium.
  - Muscle weakness or paralysis
  - Rhabdomyolysis
  - Crush injury
  - Tumor lysis syndrome
  - Serum potassium of more than 7.0 mEq/L
  - Rapidly rising potassium above 5 mEq/L

Table 3.4 ECG changes in hyperkalemia

Tall, peaked T waves with a shortened QT interval
Progressive lengthening of the PR interval and QRS duration
Disappearance of P waves
QRS widening and a sine wave pattern
Asystole and a flat ECG
Other conduction abnormalities: right bundle branch block, left bundle branch block, bifascicular block and advanced atrio ventricular block

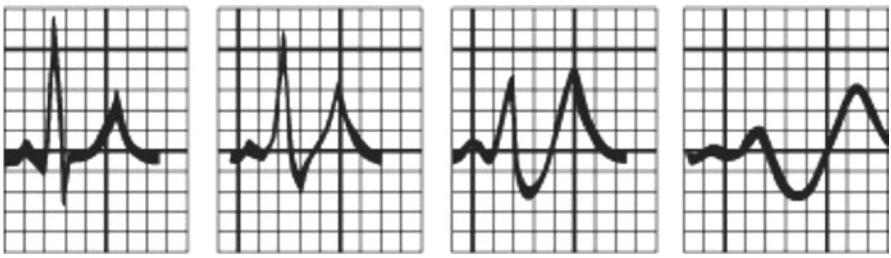

Fig. 3.2 Hyperkalemia

Step 3: Rapidly Correct Severe Hyperkalemia

- *Intravenous calcium*
  - Give calcium gluconate or calcium chloride—10 mL of 10% solution over 2 min under continuous ECG monitoring.
  - Intravenous calcium works within minutes, but effect is short-lasting (30–60 min).
  - Calcium acts by directly antagonizing the membrane action of hyperkalemia and does not cause lowering of serum potassium.
  - Calcium chloride contains three times more elemental calcium compared to calcium gluconate (13.6 vs. 4.6 mEq in 10 mL of 10% solution) and is the preferred drug.
  - Intravenous calcium can be repeated after 5 min, if ECG abnormalities persist.
  - Concentrated calcium solution is tissue-irritant and should be given in a large peripheral vein or central vein.
  - Calcium should not be given in a bicarbonate-containing solution to avoid precipitation of calcium carbonate.

    Calcium should be given cautiously as a slow infusion in patients on digitalis.
- *Insulin with glucose*
  - Give 10 units of regular bolus insulin intravenously along with 50 mL of 50% dextrose.
  - Monitor blood glucose every 30 min.
  - In patients with baseline hyperglycemia above 250 mg/dL, only insulin can be given.
  - The effect of insulin begins within 10 min and lasts for 4–6 h.
  - Insulin and glucose lowers serum potassium by driving potassium inside the cells.
  - It decreases serum potassium by 0.5–1.2 mEq/L.
  - Beware of hypoglycemia in renal failure.
- *Salbutamol (albuterol) nebulizer*
  - 10 mg in 4 mL of saline to be nebulized over 10 min (four times the usual bronchodilator dose) is given.
  - Its effect is seen within 90 min of nebulization.
  - Serum potassium usually decreases by 0.5–1.2 mEq/L.
  - It works by driving potassium inside the cell.
- *Sodium bicarbonate*
  - It should be given cautiously in selected cases of hyperkalemia associated with severe metabolic acidosis.
  - Usual dose is 25 mEq (25 mL of 8.4%) infused over 5 min.
  - Intravenous loop diuretics: In patients with normal or mildly impaired renal function

Step 4: Assess the Cause of Hyperkalemia

- Detailed history and physical examination should be performed to look for features of diseases associated with hyperkalemia such as renal failure and adrenal disease.
- History of renal disease or previous potassium levels should be looked for to assess sudden deterioration of renal function.
- Drug history should be taken to exclude drugs such as angiotensin-receptor blockers, ACE inhibitors, nonsteroidal anti-inflammatory drugs, aldosterone antagonist, and potassium-containing drugs that can cause hyperkalemia specially in renally impaired patients.

Step 5: Send Investigations

- Serum potassium should be monitored frequently.
- Blood urea, creatinine.
- Sodium, calcium, magnesium, phosphate.
- Arterial blood gases.
- Complete hemogram.
- Blood glucose.
- CPK.
- Lactate dehydrogenase.
- Measurement of urinary potassium excretion and transtubular estimation of potassium gradient (TTKG) is of limited use in deciding the cause of hyperkalemia

Step 6: Stop the Intake of Potassium

- Start potassium-free diet.
- Avoid the use of drugs containing potassium.
- Avoid drugs that can cause hyperkalemia.

Step 7: Remove Potassium

- *Diuretics*: A trial of loop diuretics in patients with preserved renal function and volume overload state may be done.
- *Cation exchange resin*: Sodium polystyrene sulfonate.
  - In the gut, sodium polystyrene sulfonate takes up potassium (and calcium and magnesium to lesser degrees) and releases sodium (1 g binds to 1 mEq of potassium).
  - It is usually given orally three times daily but may be given rectally.
  - Oral dose is usually 20 g given with 100 mL of a 20% sorbitol solution to prevent constipation.

  - A major concern with sodium polystyrene sulfonate in sorbitol is the development of intestinal necrosis, usually involving the colon and the ileum.
    - The serum potassium falls by at least 0.4 mEq/L in the first 24 h.
    - Patiromer is a recently approved gastrointestinal potassium exchanger
- *Dialysis*
  - It is indicated if hyperkalemia persists in spite of above measures or patients have any other indication of dialysis. Hemodialysis can remove 25–50 mEq of potassium per hour, with variability based on the initial serum potassium concentration, the type and surface area of the dialyzer used, the blood flow rate, the dialysate flow rate, the duration of dialysis, and the potassium concentration of the dialysate.
  - Beware of rebound hyperkalemia after dialysis.

Step 8: Ascertain the Cause of Hyperkalemia and Manage Specifically (See Table 3.5)

Table 3.5 Causes of hyperkalemia

Increased potassium release from cells
Pseudohyperkalemia (hemolytic sample, marked leukocytosis, thrombocytosis, vigorous fist clenching during phlebotomy): suspect when no ECG changes in patients with moderate to severe hyperkalemia
Metabolic acidosis
Insulin deficiency, hyperglycemia, and hyperosmolality (diabetic ketoacidosis (DKA), Hyperglycemic Hyperosmolar State (HHS), octreotide infusion)
Increased tissue catabolism
β-adrenergic blockade
Rhabdomyolysis
Digitalis overdose
Hyperkalemic periodic paralysis
Succinylcholine
Tumor lysis syndrome
Severe exercise
Reduced urinary potassium excretion
Renal failure
Hypoaldosteronism (drugs (spironolactone,eplerenone, propranolol, Labetalol, ARB, ACEI,NSAIDs), diabetes, adrenal insufficiency)
Hyperkalemic type 4 renal tubular acidosis
Ureterojejunostomy
Increased potassium intake (oral or intravenous specially in patients with renal failure)

Suggested Reading

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Skogestad J, Aronsen JM. Hypokalemia-induced arrhythmias and heart failure: new insights and implications for therapy. Front Physiol. 2018;9:1500. *This article review the current hypokalemia-induced arrhythmias mechanism and discuss how molecular changes in heart failure might lower the threshold for these arrhythmias. They also discuss how hypokalemia-induced arrhythmias could have implications for future antiarrhythmic treatment strategies*

Website

http://www.education.science-thi.org/edu_ecg/ecginclinicalpractice/abnormalecg/potassium.html

Arterial Blood Gases

4

Rahul Pandit and Gurudas Sadanand Pundpal

A 45-year-old alcoholic male patient was admitted to hospital for 2 weeks. He was being treated for pyogenic lung abscess. He seemed to be improving, but became unwell again. A blood gas analysis showed pH 7.31, $PaCO_2$ 30 mmHg, PaO_2 106 mmHg (0.3 FiO_2), HCO_3^- 14 mmol/L, standard base excess (SBE) 15 mmol/L, Na^+ 131 mmol/L, K^+ 5 mmol/L, Cl^- 96 mmol/L, osmolar gap 8 mmol/kg, lactate 2 mmol/L, and albumin 3 g/dL.

Arterial blood gas analysis is an essential component of diagnosing and managing critically ill patients in the ICU. The proper understanding and application of the concepts of acid base balance will help the clinician to follow the progress of the patient and also to evaluate the effectiveness of the treatment provided to them.

Step 1: Take an Arterial Blood Sample

- If possible take an arterial blood gas (ABG) sample at room air and start oxygen supplementation immediately.
- The radial artery is preferred for collecting the sample.
- Prefer to use 22-gauge needle.
- Avoid air bubbles.
- Cool the sample immediately (if transport is necessary for analysis).

1. Potential sampling error
   (a) Air contamination—spurious increase in PO_2
   (b) Duration of exposure is more important than volume of air bubbles
   (c) Expel air immediately
   (d) Discard the sample if froth is present

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R. Chawla, S. Todi (eds.), *ICU Protocols*, https://doi.org/10.1007/978-981-15-0902-5_4

2. Venous sample—absence of flash of blood on entry into the vessel, absence of pulsations during syringe filling and absence of autofilling of the syringe.
   (a) Cross-check with pulse oximetry and clinical status.
3. Anticoagulant effects: Dilution error—drop in PCO_2 and PO_2. pH usually remains unchanged if nonacidic (lithium) heparin is used
4. Metabolism: If analysed late and kept at room temperature, blood cells consume O_2; produce CO_2, and lower pH.

Step 2: Take Detailed History and Do Proper Clinical Examination

- Very often it is the presenting symptom or signs which are a clue to the interpretation of the acid–base status.
- For example in a patient with vomiting, the primary acid–base problem could be metabolic alkalosis (due to loss of hydrochloric acid) as opposed to someone with diarrhea, whose primary problem could be metabolic acidosis (due to loss of bicarbonate ions).
- The important aspect to remember is that it is the underlying disorder of the patient which determines the acid–base status and not just the pH of the blood.
- A stepwise approach helps to interpret ABG correctly.
- Interpretation of serum electrolytes is also important for an accurate estimation of mixed acid–base disorders.

Step 3: Know the Normal Values

	Normal range	For calculation
pH	7.34–7.45	7.4
PCO_2	35–45	40
HCO_3	22–26	24
PO_2	>80	>95

Step 4: Do Validity Check of ABG Report to Authenticate the Report

1. A: $H^+ = 24 \times PCO_2/HCO_3$
   Place the value of PCO_2 and HCO_3 and calculate H^+.
   Calculate H^+ from pH as seen on ABG:
2. B: Rule of thumb
   (a) At pH of 7.4, H^+ concentration is 40.
   For every 0.1 ↓ in pH, multiply H^+ concentration sequentially by 1.25.
   For every 0.1 ↑ in pH, multiply H^+ concentration sequentially by 0.8.
   (b) 80-Last two digits of pH after decimal = H^+ (e.g. if pH 7.35, $H^+ = 80-35 = 45$)

3. Match the H^+ concentration by two methods: A and B.
   If it is matching, ABG is valid.
   If it is not matching, recheck the ABG.

Step 5: Assess Oxygenation

- Look at oxygenation (PaO_2 and SaO_2).
- Look at the PaO_2/FiO_2 ratio.
  - Normally the ratio is around 400 to 500 given the fact that at 0.21 FiO_2 the PaO_2 is approximately 100 mmHg
  - Less than 400—suggestive of V-Q mismatch or diffusion defect or intracardiac shunt
  - Less than 300 with bilateral lung infiltrate in chest skiagram—ARDS mild
  - Less than 200 with bilateral lung infiltrate in chest skiagram—ARDS Moderate
  - Less than 100—ARDS severe
  - Expected normal Oxygen On room Air: 100-1/3 (age)
  - Expected normal Oxygen on Supplemental oxygen: FiO_2 (in decimals) × 500
  - FiO_2 increases by approximately 4% for each litre increase in supplemental oxygen above room air (0.21)
- A-a gradient
- A-a gradient = $PAO_2 - PaO_2$

Here, PAO_2 is alveolar PO_2 (calculated from the alveolar gas equation) and PaO_2 is arterial PO_2 (measured in arterial blood A-a gradient).

- In general, the A-a gradient can be calculated by:

A-a gradient = $[FiO_2 \times (P_{atm}\text{-}P_{H2O})\text{-}(PaCO_2/0.8)] - PaO_2$.

- On room air and at sea level, the FiO_2 is 0.21, the $P_{atm.}$ is 760 mmHg, and P_{H_2O} is 47 mmHg.
  - On room air, PAO_2 can be calculated by:
    $150 - PaCO_2/0.8$
- Normal A-a gradient in a 20-year-old person is 5 mmHg, which increases to 10 mmHg in a 35-year-old person. If A-a gradient is 20 mmHg at any age it is abnormal.
- Rule of Thumb: A-a gradient (on room air) = 2.5 + 0.21 × age in years

Step 6: Assess Acid–Base Disorder

1. Look at the pH—is there acidemia or alkalemia?
   A normal pH would suggest a mixed disorder or a normal acid–base status.
2. Check CO_2 and HCO_3^- to determine whether the primary problem is metabolic or respiratory in origin.

3. If the primary disorder is respiratory, determine whether it is an acute disorder or a chronic disorder.
4. Apply the rules of compensation to know if it is a simple or a mixed disorder.
5. Mind the gaps—anion gap, delta gap, and osmolar gap.

1. **Look at the pH**
   The pH is actually the −log [H^+]. By altering either the PCO_2 or the HCO_3^-, [H^+] will change, and so will pH.
   (a) An acidemia (low pH) can result from either a low HCO_3^- or a high CO_2.
   (b) An alkalemia (high pH) can result from either a high HCO_3^- or a low CO_2.
2. **Look at the CO_2 and HCO_3^- to determine if the primary problem is metabolic or respiratory in origin**
   The primary acid–base disturbances include the following:
   (a) Low pH: Low HCO_3^-—metabolic acidosis
   (b) High pH: High HCO_3^-—metabolic alkalosis
   (c) Low pH: High PCO_2—respiratory acidosis
   (d) High pH: Low PCO_2—respiratory alkalosis
   - **Metabolic acidosis**
     – Metabolic acidosis results from a primary decrease in plasma [HCO_3^-]
     – It is due to either an excretion of bicarbonate-containing fluids or by utilization of bicarbonate.
     – It is very important to calculate the anion gap (AG) if the primary disorder is metabolic acidosis.
     – AG = $Na^+ - (Cl^- + HCO_3)$; the normal AG is 12 ± 2 mEq/L.
     – In non-AG metabolic acidosis, the bicarbonate losses are accompanied by cation loss, hence no change in AG (Table 4.1).
     – A higher gap usually denotes the presence of unmeasured anions in the body (Table 4.2).
     – Remember to correct AG for hypoalbuminemia, which is very common in ICU patients. For this for every 1 g% drop in albumin below 4 g%, add 2–3 to the calculated gap.
     – Check urinary AG in non-AG metabolic acidosis (U Na + U K−U Cl)
       Normal—zero or negative
       Non-renal loss of bicarbonate (diarrhea)—negative
       Renal loss of bicarbonate or decrease H^+ excretion (renal tubular acidosis)—positive

Table 4.1 Causes of a non-AG metabolic acidosis (HARDUP)

H	⇒	Hyperalimentation/hyperchloremia
A	⇒	Acetazolamide
R	⇒	Renal tubular acidosis
D	⇒	Diarrhea
U	⇒	Uremia-acute
P	⇒	Postintubation hypocapnia

Table 4.2 Causes of a raised AG metabolic acidosis (MUDPILERS)

M	⇒	Methanol
U	⇒	Uremia-chronic
D	⇒	Diabetic ketoacidosis
P	⇒	Paraldehyde
I	⇒	Isoniazid, iron
L	⇒	Lactate
E	⇒	Ethanol, ethylene glycol
R	⇒	Rhabdomylosis/renal failure
S	⇒	Salicylate

Table 4.3 Urine Cl^- more than 20 mEq/L (usually saline unresponsive)

• Primary hyperaldosteronism
• Cushing's syndrome, ectopic ACTH
• Exogenous steroids, licorice ingestion, tobacco chewing
• Adrenal 11 or 17 OH defects
• Liddle's syndrome
• Bartter's syndrome
• K+ and Mg^{2+} deficiency
• Milk-alkali syndrome

Table 4.4 Urine Cl^- less than 20 mEq/L (usually saline responsive)

• Vomiting, nasogastric suctioning
• Chloride-wasting diarrhea
• Villous adenoma of colon
• Posthypercapnia
• Diuretic therapy

- **Metabolic alkalosis (high HCO_3)**
  - Metabolic alkalosis reflects an increase in plasma [HCO_3^-].
  - It is due to either gain of HCO_3^- or extracellular volume contraction.
  - It can be classified into saline responsive or nonresponsive. For this spot urinary chloride can be checked.
  - More than 20 mEq/L urinary chloride is saline unresponsive (Table 4.3) and less than 20 mEq/L urinary chloride is saline responsive (Table 4.4)
- **Respiratory acidosis (high PCO_2)**
  - Respiratory acidosis is due to a primary rise in CO_2.
  - Hypercapnia almost always results from alveolar hypoventilation due to one of the following causes:
    Respiratory center depression
    Neuromuscular disorders
    Upper airway obstruction
    Pulmonary disease
- **Respiratory alkalosis (low PCO_2)**
  - A respiratory alkalosis is due to decrease in PCO_2.
  - It results from hyperventilation leading to decrease in CO_2.

- **Causes of respiratory alkalosis**
  - Hypoxemia from any cause
  - Respiratory center stimulation
  - Mechanical hyperventilation
  - Sepsis, pain

3. **If the primary disorder is respiratory, determine whether it is an acute disorder or a chronic disorder**
   You must also take into consideration the patient's history while interpreting ABG. However, following formulae helps in this.
   (a) Normal pH is 7.4
   - Calculate the change in pH (from 7.4)
     - In acute respiratory disorder (acidosis or alkalosis)
       Change in pH = 0.008 × ($PaCO_2$−40)
       Expected pH = 7.4 ± change in pH
     - In chronic respiratory disorder (acidosis or alkalosis)
       Change in pH = 0.003 × ($PaCO_2$−40)
       Expected pH = 7.4 ± change in pH
   - **Compare the pH on ABG**
     - If pH on ABG is close to A, it is an acute disorder
     - If pH on ABG is close to B, it is a chronic disorder

4. **CO_2 and HCO_3^- compensatory mechanism** (Table 4.5)
5. **Mind the gaps**
   (a) Calculate AG in case of metabolic acidosis.
   High denotes raised AG metabolic acidosis, and normal or narrow denotes non-AG acidosis.
   (b) Calculate adjusted AG.
   Adjusted AG = calculated AG + 2.5 × (4−serum albumin in g%)
   (c) In less obvious cases, the coexistence of two metabolic acid–base disorders may be apparent by calculating the difference between the change in AG (delta AG) and the change in serum HCO_3^- (delta CO_2). This calculation is called the bicarbonate gap or the delta gap:
   - Bicarbonate (delta) gap = delta AG−delta HCO_3^-
   - Where delta AG = patient's AG−12 mEq/L{normal AG};
   - Delta HCO_3^- = 24 mEq/L{normal HCO_3^-}−patient's HCO_3^-.
     - Normally the delta gap is zero if there is only AG acidosis. A positive raised delta gap or a decreased delta gap denotes presence of mixed lesion.
     - A positive delta gap of more than 6 mEq/L is suggestive of presence of metabolic alkalosis and/or HCO_3^- retention.
     - The delta gap of less than 6 mEq/L is suggestive of presence of hyperchloremic acidosis and/or HCO_3^- excretion.

   Urinary Anion Gap
   - Urinary anion gap is measured to determine the source of HCO_3 loss.
   - UAG = Urinary Na^+ + Urinary K^+ − Urinary Cl^-

Table 4.5 CO_2 and HCO_3^- compensation

Primary disorder	Initial chemical change	Compensatory response	Compensatory mechanism	Expected level of compensation
Metabolic acidosis	↓ HCO_3^-	↓ PCO_2	Hyperventilation	$PCO_2 = (1.5 \times [HCO_3^-]) + 8 \pm 2$ PCO_2 = last two digits of pH
Metabolic alkalosis	↑ HCO_3^-	↑ PCO_2	Hypoventilation	$PCO_2 = (0.7 \times [HCO_3^-]) + 21 \pm 2$ PCO_2 = last two digits of PH
Respiratory acidosis	↑ PCO_2	↑ HCO_3^-		
Acute			Buffering—rule of 1	↑ $[HCO_3^-]$ = 1 mEq/L for every 10 mmHg delta PCO_2
Chronic			Generation of new HCO_3^-—rule of 4	↑ $[HCO_3^-]$ = 4 mEq/L for every 10 mmHg delta PCO_2
Respiratory alkalosis	↓ PCO_2	↓ HCO_3		
Acute			Buffering—rule of 2	↓ $[HCO_3^-]$ = 2 mEq/L for every 10 mmHg delta PCO_2
Chronic			Decreased reabsorption of HCO_3^-—rule of 4	↓ $[HCO_3^-]$ = 4 mEq/L for every 10 mmHg delta PCO_2

- Normally UAG is zero or slightly negative. During Normal AG metabolic acidosis, kidney increases ammonia excretion in the form of NH_4Cl, leading to more negative UAG, usually ranging from −20 to −50 mEq/L. This is observed in cases of HCO_3 loss due to non renal causes like severe diarrhea. In case of metabolic acidosis due to impaired renal function such as CKD or distal RTA, UAG remains positive.

(d) **Osmolar gap**

The difference between calculated plasma osmolality and the measured osmolality is called the osmolar gap. Normally the gap is less than 20 mOsmo/kg H_2O. If it is raised then it denotes presence of unaccounted ions.

Causes of increased osmolar gap

- Ethanol
- Isopropyl alcohol (no anion gap)
- Methanol, glycine, glycerol
- Ethylene glycol

Step 7: Look for Alerts to Mixed Acid–Base Disturbances

- Absence of compensation
- Longstanding pulmonary or renal disease
- Excessive compensation
- Respiratory assistance

- Temporal inconsistencies
- Settings conducive to mixed disturbances

Stewart Approach of ABG Interpretation

Why Stewart approach?
Limitations of traditional approach of ABG interpretation

1. It considers HCO_3 as an independent component, but HCO_3 concentration can be affected by respiratory (CO_2) or metabolic (H^+) components, so it's not a specific marker of either

$$H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

   The relationship between metabolic acidosis and HCO_3 is neither consistent nor linear
2. It does not quantify metabolic component, it is indirectly calculated.
3. It does not consider contribution of weak acids.
   Stewart approach puts water dissociation at the centre of acid base status of body fluids and is modified by PCO_2 and other weak acids and certain electrolytes.
   Principles of Stewart Approach

1. Electrochemical dissociation of water determines PH

$$H_2O \rightarrow H^+ + OH^-$$

2. Law of mass conservation

$$\left[H^+\right] \times \left[OH^-\right] = \text{Constant}$$

3. Principle of electro neutrality

$$\left[\text{cation}\right] = \left[\text{Anions}\right]$$

   Three independent variables determine the dissociation of water and consequently the hydrogen ion concentration to maintain electrical neutrality

1. SID (Strong Ion Difference)
   is the difference between strong cations and strong anions, and indicates the net ionic charge of weak anions.
   Apparent SID (SIDa) is the difference between measured strong cations and strong anions.

$$\text{SIDa} = \left\{\left[\text{Na}\right] + \left[\text{K}\right] + \left[\text{Ca}\right] + \left[\text{Mg}\right]\right\} - \left[\text{Cl}\right]$$

   SID calculated for electro neutrality is viewed as effective SIDe, and is calculated as the sum of bicarbonate and weak acids [A], albumin and phosphate.

$SID_e = [HCO_3] + [Alb] + [Pi]$.
[Alb] = 2.8 × Alb g/dL
[Pi] = 0.6 × Phosphate mg/dL
Normal range = 39 ± 1.
SIG or Unmeasured Anions: By law of electro neutrality SIDa and SIDe should be equal, but inability to measure all strong and weak ions in body leads to gap between both of them.

$$SIG = SIDa - SIDe$$

Is gap between unmeasured anions and unmeasured cations, normal range is 8 ± 2.

2. Weak acid total concentration (A_{tot})
   It represents all non bicarbonate buffers, i.e.; total plasma concentration of weak non volatile acids, mainly serum albumin and Phosphate. Increase in A_{tot} is suggestive of metabolic Acidosis and decrease is suggestive of metabolic alkalosis.
3. PCO_2
   So, by law of electro neutrality;

$$\{[Na]+[K]+[Ca]+[Mg]\} = \{[Cl]+[HCO3]+[Alb]+[Pi]+SIG\}$$

Change in acid base status occurs by either respiratory or metabolic mechanisms.
Respiratory: Change in PCO_2 produce s change sin PH

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO_3 + H$$

Metabolic or non respiratory
Metabolic acid base disturbances cannot be viewed as a consequence of change in HCO_3, as HCO_3 is dependent variable. Metabolic acid base disorders occur due to disturbance in either SID or Atot.

(a) **Changes in SID (Strong Ion Difference)**
Changes in SID occur by two different mechanisms.

- Change in concentration
  Change in status of hydration alters PH. Normal body PH is alkalotic, so dehydration leads to increased concentration of alkali; more alkalinity; contraction alkalosis and increase in SID; on the other hand over hydration leads to dilution of state of alkalinity; dilutional acidosis and decrease in SID.
- Change in strong ion concentration
  even with normal Na concentration changes in other strong ion concentration leads to alteration in SID.
  - Inorganic Acids: only strong ion capable of bringing significant change in PH is Chloride. Increase in Cl concentration leads to decrease in SID and thus acidosis and vice versa. Because Cl is measured it leads to non anion gap metabolic acidosis.
  - Organic Acids: increase in concentration of one of the organic acids like lactate or keto acids leads to metabolic acidosis with high anion gap, because of presence of 'unmeasured' organic acids. Chloride concentration remains normal.

(b) **Change in A_{tot}**

A_{tot} represents non volatile weak acids like Phosphate, albumin, other plasma proteins. Albumin can bring significant change in acid base status. Albumin being weak acid hypoalbuminemia leads to base excess.

Phosphate levels are normally too low to bring change in acid base status, but in the setting of renal failure high phosphate levels leads to acidosis.

Classification of acid–base disorders

	Acidosis	Alkalosis
Respiratory	High PCO_2	Low PCO_2
Metabolic		
Abnormal SID		
Water excess/deficit	Low SID	High SID,
	Low Na	High Na
Imbalance of strong anions		
Cl excess/deficit	Low SID	High SID
	High Cl	Low Cl
Unidentified anion excess	Low SID	High XA/SIG
Non volatile weak acids		
Serum albumin	High Alb	Low Alb
Phosphate	High Pi	Low Pi

Stewart's Algorithm of Interpretation of Acid Base Disorder

- Check history and determine expected acid base disorder
- Collect following data
  - Na, K, Cl, Alb, PCO_2, HCO_3
- Calculate corrected Cl, for assessment of volume status

$$\textbf{Corrected Cl} = \textbf{Observed Cl} \times \left(\textbf{Normal Na} / \textbf{Observed Na}\right)$$

  - Normal Na = 142,
  - Normal range of corrected Cl = 106 ± 2
- Calculate SIDa

$$\textbf{SIDa} = \left[\textbf{Na} + \textbf{K} + \textbf{6}\right] - \textbf{Cl};$$

  - (6 = value for presentation of Ca and Mg, provided they are normal)
- Calculate SIDe

$$\textbf{SIDe} = \textbf{HCO}_3 + \textbf{2.8} \times \textbf{Alb in g} / \textbf{dL} + \textbf{2}$$

  - (2 = substitute for Pi)
- Calculate SIG or Unmeasured anions (XA)
  SIG = SIDa − SIDe
- Make comparison for calculated data to its reference range.

Suggested Reading

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Websites

www.acidbase.org
www.lakesidepress.com
www.merck.com
www.uchc.edu

Diabetic Emergencies

5

Sandhya Talekar and Urvi Shukla

Diabetic emergencies consist of hyperglycemic conditions such as diabetic ketoacidosis (DKA), hyperglycemic hyperosmolar state (HHS) and hypoglycemic emergencies.

Insulin deficiency, increased insulin counter-regulatory hormones (cortisol, glucagon, growth hormone, and catecholamines), and peripheral insulin resistance leading to hyperglycemia, dehydration, ketosis, and electrolyte imbalance underlie the pathophysiology of DKA. DKA usually occurs in young patients with type 1 diabetes who are insulin dependent, and HHS usually occurs in the elderly with type 2 diabetes on either oral hypoglycemic agents or on insulin. The basic pathophysiological difference is absence of circulating insulin in DKA and presence of some residual insulin function in HHS, which prevents lipolysis, and ketosis.

Hyperglycemic Emergencies

DKA and HHS (Table 5.1)

A 18-year-old female patient presents to the emergency department with high grade fever, tachypnoea and altered mentation. She had diarrhoea for 3 days that was watery and large in volume. On examination, she was found to be febrile with a temperature of 101 °F. Her pulse rate was 130/min regular, and blood pressure was 90/70 mmHg. She had a Glasgow coma score of 9. Her random plasma glucose on arrival was 480 mg/100 mL. She was not known to have diabetes.

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Table 5.1 Differences between DKA and HHS

	Diabetic ketoacidosis	Hyperglycemic hyperosmolar syndrome
Ketoacidosis	Profound	Minimal or none
Glucose	~250–600 mg/dL	Often >900 mg/dL
HCO_3	<15 mEq/L	>15 mEq/L
Osmolarity	300–325 mOsm	Often >350 mOsm
Age	Young	Elderly
Onset	Acute; over hours to days	Chronic; over days to weeks
Associated diseases	Uncommon	Common
Seizures	Very rare	Common
Coma	Rare	Common
Insulin levels	Very low to none	May be normal
Mortality	0–10% (depends on underlying conditions)	20–40%
Dehydration	Severe	Profound

Step 1: Start Initial Resuscitation (Refer to Chap. 23, Vol. 2)

- Urgently insert two wide-bore intravenous peripheral catheters for volume resuscitation.
- Blood samples for a complete metabolic profile and other relevant tests are drawn.
- A central line should be inserted in the presence of severe hypotension, lack of peripheral access, need for multiple infusions, severe acidosis, and impaired cardiorespiratory or renal parameters.
- Infuse 1 L of 0.9% NS over 1 h.
- Serum potassium should be >3 mEq/L before Insulin therapy is started.

Step 2: Take Focused History and Perform Physical Examination

- History of insulin omission in a diabetic patient is common and often points toward a diagnosis of DKA or HHS. The table below points to general differences between the two syndromes.
- DKA could also be the first presentation in young individuals.
- A thorough physical examination helps in finding the precipitating cause/or possible focus of infection, which is often a trigger for the hyperglycemic crisis.
- History of SGLT2 inhibitors (Capaglifozin, Empaglifozin or Dapaglifozin) any of these may lead to euglycaemic diabetic ketoacidosis due to continuous renal elimination of glucose in ketotic state leading to euglycaemia.

Step 3: Send Essential Investigations

- Metabolic panel to include electrolytes along with Serum Magnesium and Phosphates.
- Blood urea nitrogen and plasma creatinine (may be spuriously high due to chemical analysis interference with ketones).
- Arterial blood gas with Anion Gap.
- Complete blood count with differential count.
- Urinalysis and urine ketones by dipstick.
- Serum ketones.
- Electrocardiogram, Chest X-ray.
- Screening for a possible infective cause as a trigger for the hyperglycemic crisis.

Management

1. Fluid resuscitation and correction of electrolyte disturbances.
2. IV Insulin therapy.
3. Watch for complications.
4. Treat precipitating cause.

Step 4: Fluid Therapy

- Patients with DKA and HHS usually have severe hypovolemia due to absolute or relative deficiency of insulin leading to osmotic diuresis.
- Average fluid loss in DKA and HHS is 8–10 L. HHS may result in fluid losses exceeding 10 L sometimes. The goal is to replace the total volume loss within 24–36 h with 50% of resuscitation fluid being administered during the first 8–12 h.
- In hypotensive patients, use crystalloids to restore circulating volume.
- Crystalloids are initial fluids of choice irrespective of sodium levels. Fluid resuscitation is initiated with 15–20 mL/kg/h of 0.9% NS for the first couple of hours.
- After initial bolus, fluid replacement rates can be reduced to 4–14 mL/kg/h. Type of fluid will be decided by hemodynamic stability, sodium levels and urine output.
- One-half isotonic saline (0.45%) at a rate of approximately 250–500 mL/h if the serum sodium is normal or elevated.
- Isotonic saline is continued at a rate of 250–500 mL/h if hyponatremia is present.
- In patients with HHS, comorbidities like renal and cardiac dysfunctions warrant more close monitoring of hemodynamics.
- Rapid correction of sodium and osmolality may risk cerebral edema.

- Large volumes of 0.9% NS can cause non anion gap metabolic acidosis which may confuse the clinical picture.
- Hypotonic (0.45%) saline infusion may be appropriate after volume correction in hemodynamically stable and hypernatremic patients (after correcting for high blood glucose) as hypotonic saline does not correct hypovolemia rapidly. This might also be appropriate in patients with concomitant potassium infusion to maintain isotonicity of infusion fluid. Calculate free water deficit to assist fluid replacement in patients with hypernatremia (see Chap. 56, Vol. 1) and replace with dextrose or enteral water.
- Volume resuscitation will enable renal losses of glucose and enhance peripheral action of insulin.
- Replace total body water losses slowly with 5% glucose solution (50–200 mL/h) once circulating volume and serum sodium are restored (usually when the blood glucose falls to <200 mg/dL). This is in order to avoid sudden osmolarity changes, which may lead to cerebral edema and convulsions, seen more frequently in the pediatric age group.

Step 5: Correct Electrolyte Abnormalities

Hyperglycemia may cause dilutional hyponatremia, so measured serum sodium is corrected by adding 1.6 mEq/L (1.6 mmol/L) for each 100 mg/dL (5.6 mmol/L) elevation of serum glucose over 100 mg/dL (5.6 mmol/L). On average, patients with DKA/HHS may have the following deficit of water and key electrolytes per kg of body weight: free water 100 mL/kg; sodium 7–10 mEq/kg; potassium 3–5 mEq/kg; chloride 3–5 mmol/kg; and phosphorus 1 mmol/kg.

- Replacement of serum potassium should begin early in the management of DKA as serum potassium concentration does not reflect total body potassium accurately.
- Potassium replacement should begin as soon as serum potassium concentration is less than 5.5 mEq/L. Target potassium concentration is 4–5 mEq/L.
- Ensure adequate urine output before replacing intravenous potassium.
- Guideline for replacing potassium is as follows:
  - If S. potassium is less than 3.5 mEq/L, give potassium at 20–40 mEq/h as a controlled infusion, through central venous line with continuous cardiac monitoring.
    - Start insulin infusion only after potassium replacement is started.
  - If S. potassium is 3.5–5.0 mEq/L, give potassium at 20 mEq/h.
  - If S. potassium is more than 5.0 or patient is anuric, no supplements are required.
- Potassium should be added to 0.45% saline instead of 0.9% saline to avoid hypertonicity of infused fluid. Correction of hypovolaemia and insulin treatment lead to intracellular shift in potassium.

- Hypomagnesemia occurs early in the course of DKA and requires correction. Monitor serum magnesium levels.
- Phosphorous depletion is common in DKA. Replacement is advised when it is severely depressed (<1 mg/dL) and in patients with respiratory failure, cardiac failure and hemolytic anemia.
- Sodium bicarbonate infusion: metabolic acidosis improves with restoration of intravascular volume and tissue perfusion. There is a limited role of bicarbonate therapy as it has not been shown to improve outcome in DKA. Moreover, bicarbonate therapy is associated with adverse effects such as increased paradoxical intracellular and cerebrospinal fluid acidosis, increased CO_2 production, adverse effect on tissue oxygenation, and post resuscitation metabolic alkalosis.
- Bicarbonate therapy may be considered in the following situations:
  - When pH is persistently less than 7.0 after 2–3 h of treatment.
  - When hypotensive shock is unresponsive to rapid fluid replacement and persistent severe metabolic acidosis exists.
  - In the presence of severe hyperkalemia.
- Even in these circumstances, bicarbonate can only "buy time" until other treatment corrects acidosis.
- Bicarbonate may be given as an infusion of 100 mEq over 4 h in sterile water till pH > 7.1.

Step 6: Start Intravenous Insulin Infusion

- Insulin therapy should be started only after fluid and electrolyte resuscitation is underway.
- Use regular (rapid acting) insulin at 0.1 U/kg body weight as a bolus dose and then 0.1 U/kg/h as a continuous infusion or 0.14 U/kg body weight as a continuous infusion without a bolus dose.
- When plasma glucose reaches 200–250 mg/dL, the insulin rate can be decreased by 50% or to the rate of 0.02–0.05 U/kg/h. If the blood glucose level does not decrease by 50–75 mg/dL/h, the rate of insulin infusion should be doubled.
- Rate of reduction of blood glucose should be less than 50–75 mg/dL/h.
- Rapid correction of blood glucose levels could lead to cellular edema seen mainly in pediatric population, which can lead to convulsion and electrolyte disturbances (hypokalemia, hypomagnesemia, and hypophosphatemia).

Step 7: Monitor Effectiveness of Therapy Clinically and Biochemically

- The following features indicate clinical improvement:
  - Increased sense of well-being, reduced tachycardia and tachypnoea.
  - Improved mental status, able to eat orally.

- The following biochemical parameters suggest resolution of DKA/HHS:
  - Serum glucose below 200 mg/dL in DKA and below 250–300 mg/dL in HHS.
  - Serum bicarbonate more than 18 mEq/L.
  - Venous pH more than 7.30.
  - Serum anion gap less than 12 mEq/L.
  - Decreasing urine sugar.
  - Urine or serum ketones by nitroprusside test are not reliable parameters to follow as this test predominantly measures acetoacetate and acetone, whereas β-hydroxybutyrate is the predominant ketone in severe DKA, which is not measured usually in the laboratory. There may be a paradoxical rise of serum or urinary ketones as patients improve due to conversion of beta-hydroxybutyrate to acetone and acetoacetic acid.
  - Direct estimation of beta hydroxybutyrate.
  - Plasma effective osmolality (exclude urea in osmolality calculation) below 315 mOsmol/kg.
  - Delta Anion Gap/Delta Bicarbonate: to detect combined metabolic disorders like anion gap and non anion gap metabolic acidosis and metabolic alkalosis.

Step 8: Switch to Subcutaneous Insulin When Stable

- Maintain IV insulin until biochemically stable and the patient has taken at least two meals.
- Switch to subcutaneous regular insulin with half dose of total intravenous insulin requirement either as a fixed dose or sliding scale insulin as per protocol (see Chap. 2, Vol. 2).
- IV infusion should be stopped 2 h after the first dose of subcutaneous insulin.

Step 9: Identify Precipitating Factors

- Precipitating factors should be sought and treated. Common precipitants include the following:
  - Missed insulin therapy.
  - Infections—pneumonia, sepsis, urinary tract infection.
  - Trauma.
  - Pancreatitis.
  - Myocardial infarction.
  - Pregnancy.
  - Stroke.
  - Steroid use.

Step 10: Continue Supportive Care

- The urinary catheter: Consider in persistent hypotension, renal failure, anuria, and impaired consciousness. Maintain strict asepsis during catheterization.
- Measure hemodynamics: static indices like CVP or dynamic indices of volume status should be monitored in patients who present with shock. Also consider in the elderly with concomitant illness, cardiac failure, or renal failure even in the absence of hypotension.
- Thromboembolic complications are common, and DVT prophylaxis should be initiated (see Chap. 21, Vol. 2).
- The nasogastric tube: If consciousness is impaired, insert a NGT to avoid aspiration of gastric contents.
- Start appropriate antibiotics if infection is a possible trigger.

Hypoglycemia

A 70-year-old male patient, with type 2 diabetes mellitus, was brought to the emergency department with history of feeling unwell, nausea, vomiting for 2 days, sudden onset of giddiness, sweating, palpitations, and altered sensorium. Blood glucose on a glucometer was 42 mg/dL.

Impaired consciousness in diabetic patients is most commonly due to hypoglycemia that is most often drug-induced. Symptoms of hypoglycemia are nonspecific, and this can masquerade as cardiorespiratory, neurological, and even psychiatric problems. A low threshold for checking blood sugar in all diabetic patients to exclude hypoglycemia is warranted as it is an imminently treatable condition and if left unattended leads to severe morbidity and mortality.

Step 1: Promptly Identify Clinical Features of Hypoglycemia

- Features of hypoglycemia could be autonomic such as diaphoresis, tremor, anxiety, palpitation, hunger, paraesthesia, and tachycardia caused by sympathetic stimulation.
- These may be absent in patients with autonomic neuropathy or on β-blockers.
- In some patients, neuroglycopenic features such as drowsiness, behavioral abnormalities, coma, and seizures predominate.

Step 2: Check Blood Glucose Immediately

- Urgent capillary sugar should be checked with the bedside glucometer. If possible, a simultaneous venous sample should be sent to the laboratory for glucose analysis. Point of care glucometers generally overestimate glucose values in the

lower range. Whenever hypoglycemia is suspected, always send blood for glucose estimation by glucose analyzer.
- Administration of dextrose should not be delayed if blood glucose checking cannot be done immediately.
- If the blood glucose level is less than 70 mg/dL and symptoms improve with glucose administration, then patient symptomatology may be attributed to hypoglycemia.

Step 3: Give Intravenous Dextrose

- Reverse hypoglycemia rapidly with 50 mL of 25–50% glucose given intravenously.
- Check blood glucose after dextrose infusion and repeat the injection till the glucose is above 70 mg/dL for at least two consecutive readings and the patient is asymptomatic.
- Start intravenous dextrose infusion 6-h with frequent blood glucose monitoring in patients on long-acting insulin, oral hypoglycemic drugs, or renal impairment as they are prone to recurrent hypoglycemia.

Step 4: Consider Alternative Agents in Specific Circumstances

- Injection glucagon may be given in a dose of 1 mg intramuscularly or subcutaneously if venous access is not possible.
- Injection octreotide 25–50 mcg may be given subcutaneously or as an intravenous infusion in patients with resistant hypoglycemia, sulfonylurea-induced hypoglycemia, or hypoglycemia induced by drugs like quinine or quinidine.

Step 5: Consider Precipitating Factors of Hypoglycemia in Diabetic Patients

- Missed meals/inadequate food intake.
- Insulin overdose.
- Change of therapy/dosage of hypoglycemic drugs or insulin.
- Concomitant ingestion of drugs causing hypoglycemia.
- Presence of hepatic or renal failure.

Step 6: Consider Disorders and Drugs Associated with Hypoglycemia (See Tables 5.2 and 5.3)

- In an intensive care unit, certain disorders are associated with hypoglycemia, and frequent blood glucose monitoring should be done in these patients.
- Hypoglycemia is more common if there is intolerance to enteral feeding and the patient is not started on parenteral nutrition.

Table 5.2 Common causes of hypoglycemia in the ICU

Insulin
Oral hypoglycemic agents
Sepsis (including malaria)
Hepatic failure
Alcohol
Adrenal crisis (including steroid withdrawal)
Drugs

Table 5.3 Drugs associated with hypoglycemia

Insulin
Oral hypoglycemic agents
Gatifloxacin
Quinine
Artesunate derivatives
Pentamidine
Lithium
Propoxyphene

- Many patients in the ICU have altered mental state and/or are under sedation, and hypoglycemic episode may remain unnoticed in these patients, and so, frequent blood glucose monitoring is essential in these groups of patients.
- Many patients in ICUs are on intravenous insulin infusion. Discontinuation or intolerance to enteral feeding and stopping parenteral nutrition without simultaneously stopping insulin lead to hypoglycemia.
- At lower glucose range and in low perfusion states, bed side glucometer lose their accuracy.
- Continuous blood glucose monitoring if available will help to detect hypoglycemia early.

Suggested Reading

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Glycemic Control in the ICU

6

Rajesh Chawla and Subhash Todi

A 45-year-old male patient was admitted to hospital with cough, breathlessness, dizziness, and fever for the past 5 days. He was hypoxemic (SpO_2 88% on a nonrebreathing mask) and hypotensive (blood pressure 82/34 mmHg after 2 L of IV fluid). He was intubated and started on mechanical ventilation. His blood glucose was 350 mg/dL on the glucometer.

Hyperglycemia is commonly seen in both diabetic and nondiabetic patients in ICUs. Hyperglycemia is also an independent risk factor for mortality and morbidity in medical and surgical ICU patients. Various factors contribute to hyperglycemia in the ICU. These include increased counterregulatory hormones (glucagon and cortisol), hepatic insulin resistance, glucocorticoid therapy, dextrose-containing solutions, and high-calorie enteral and parenteral nutrition.

Step 1: Check Blood Glucose

- Check Capillary glucose by point of care properly calibrated glucometer
- Caution is required in interpreting results of point-of-care glucose meters in patients with anemia, polycythemia, hypoperfusion, or use of medications that can interfere with glucose measurements.
- Arterial glucose (in patients with arterial line) or venous glucose measured in laboratory glucose analyser may be more accurate in patients with shock on vasopressors or hypoxia or anaemia.
- Treatment for the underlying disease should not be withheld while one is waiting for a laboratory glucose value.

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Step 2: Assess Glycemic Risk

- Patients should be asked about history of diabetes, current treatment and recent blood sugar levels
- Check for HbA1c to assess control of blood glucose.
- Check comorbidities such as hypertension, renal disease, liver disease, pancreatitis, chronic obstructive airway disease (COAD), obesity, and coronary artery disease.
- Enquire about medication history causing hyperglycemia—corticosteroids, octreotide, β-blockers, thiazide diuretics, niacin, protease inhibitors, and antipsychotic agents.

Step 3: Decide on Frequency of Blood Glucose Measurement

- All hemodynamically unstable patients, especially those on intravenous insulin infusion, should have blood glucose checked every hour or even more frequently.
- As the condition stabilizes or in less sick patients, this interval may be prolonged.
- With any change in patients' condition or nutrition delivery regimen, initiate more frequent glucose monitoring.

Step 4: Decide on the Target Blood Glucose Level

- The present recommendation in general medical/surgical ICU patients is to keep blood glucose between 140 and 180 mg/dL.
- Patients with expected length of stay for more than 3 days in ICU will benefit from this control.
- For patients with shorter stay may have a more liberal target sugar control.
- A more liberal blood sugar control is also advised in patients who are diabetic,

Step 5: Decide on Insulin Delivery Route

- All oral hypoglycemic agents and long-acting insulin should be discontinued during initial days of instability.
- Intravenous infusion of short acting regular insulin is the treatment of choice in critically ill patients.
- The following groups of patients may be candidates for periodic subcutaneous insulin:
  - Step-down therapy from intravenous insulin
  - Less sick patients on oral diet

Step 6: Decide on Insulin Delivery Protocol (Tables 6.1 and 6.2)

- Insulin protocol should be institution specific and nurse driven.
- All efforts should be made to educate nurses and residents and ensure compliance by periodic audits.
- Dynamic insulin protocols, ideally computerized, which can monitor trend of rise or fall of blood glucose and adjust insulin doses, tend to keep blood glucose at a more desirable range.
- Use insulin delivery protocol as per Table 6.1 e.g. A diabetic patient with admission blood sugar of 250 mg/dL should get 5 U regular insulin bolus followed by 3 U/h of insulin infusion. Next blood sugar after 1 h is 270 mg/dL, another bolus of 5 U regular insulin and increase insulin infusion to 4 U/h.
- Another insulin delivery protocol which can be used is described in Table 6.2 e.g. A diabetic patient with admission blood sugar of 250 mg/dL and normal renal function may be started on scale 2 at 4 U/h. Patient with impaired renal function could be started on scale 1 and non diabetic patient on scale 3 or 4. Next blood sugar check after 1 h is 270 mg/dL, the scale should shift vertically down (range 251–300) and infusion increased to 6 U/h. Next blood sugar is 264 (target 140–180 mg/dL) the scale should shift horizontally to the right to infusion rate of 9 U/h.

Table 6.1 An example of algorithm of IV insulin therapy in a critically ill patient

	Initiation		Maintenance	
Random blood sugar (RBS) (mg/dL)	Bolus (U)	Infusion (U/h)	At 1–5 U/h	At >5 U/h
151–199	0	2	Increase 1 U/h	Incr 2 U/h
200–249	3	2	Bolus 3 U + incr 1 U/h	Bolus 3 U + incr 2 U/h
250–299	5	3	Bolus 5 U + incr 1 U/h	Bolus 5 U + incr 2 U/h
300–349	8	3	Bolus 8 U + incr 1 U/h	Bolus 8 U + incr 2 U/h
350–399	10	4	Bolus 10 U + incr 2 U/h	Bolus 10 U + incr 3 U/h
400–449	10	5	Bolus 10 U + incr 3 U/h	Bolus 10 U + incr 4 U/h
>450	10	6	Bolus 10 U + incr 4 U/h	Bolus10 U + incr 4 U/h

Target RBS: 140–180 mg/dL

Table 6.2 Another example of algorithm of IV insulin therapy in a critically ill patient

RBS (mg/dL)	Scale 1 (IV—U/h)	Scale 2 (IV—U/h)	Scale 3 (IV—U/h)	Scale 4 (IV—U/h)
<64	Treat as hypoglycemia	Do	Do	Do
64–140	Nil	Nil	Nil	Nil
141–200	1	2	3	4
201–250	2	4	6	8
251–300	3	6	9	12
301–350	4	8	12	16
351–400	5	10	15	20
>400	10	15	20	25

The patient should be started on a particular scale depending on initial sugar and clinical scenario. In this scale, in order to arrive at a target glucose level of 140–180 mg/dL, insulin infusion rate should be shifted horizontally to the next or previous scale in the same row if sugar remains within the range for that row. If sugar increases or decreases to the other range, the infusion rate should be shifted vertically for that range in the same scale
Target RBS: 140–180 mg/dL

Step 7: Avoid Hypoglycemia (Blood Glucose <70 mg/dL)

- Rigorous blood glucose control (80–110 mg/dL) leads to hypoglycemic episodes in a mixed medical/surgical ICU, which may be detrimental to their outcome.
- The following groups of patients are more prone to hypoglycemia:
  - Renal failure
  - Dialysis
  - Liver failure
  - Malnourished
  - Adrenal insufficiency
  - Intolerance to enteral feed
- Stop insulin infusion immediately and give 50 mL of 25% dextrose intravenously and repeat this till blood glucose is more than 90 mg/dL and the patient is asymptomatic.
- Check blood glucose every 15 min and then decrease frequency depending on clinical response.
- Ensure adequacy of carbohydrate calorie intake either enterally or parenterally and avoid abrupt discontinuation.

Step 8: Avoid Large Variations in Glucose Concentrations in ICUs

- Glycemic variability is expressed as the standard deviation of each patient's blood glucose levels.
- Glycemic variability is an independent predictor of mortality in a heterogeneous population of ICU patients.

- The efficacy of continuous or near-continuous glucose monitoring and/or new algorithms targeted more specifically to reduce glycemic variability as well as mean blood glucose requires further clinical studies in ICU patients before the final recommendation is made.

Step 9: Avoid Under or Overtreatment and Safety Issues

- Overtreatment and undertreatment of hyperglycemia represent major safety concerns.
- Education of ICU staff is essential in engaging the support of those involved in the care of inpatients with hyperglycemia.
- Regular audit and process measures should be undertaken to assess compliance with insulin regimens and attainment of target glucose range, avoidance of hypoglycemia and minimising glycemic variability.

Step 10: Change to Intermittent Treatment Once Stable

- Switch over to subcutaneous insulin.
- Long-acting insulin should overlap discontinuation of insulin infusion to prevent hyperglycemia.
- Intermittent short acting insulin (either a fixed dose or based on sliding scale) pre meals or six hourly should be instituted
- Calculate the dosage taking into account the history of diabetes, type of diabetes, previous insulin dose, stress level, steroid use, risk of hypoglycemia, and general clinical status.

Suggested Reading

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The conclusion was that tight computerized glucose control with the computerised algorithm did not significantly change 90-day mortality and was associated with more frequent severe hypoglycemia episodes in comparison with conventional glucose control

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Part II

Oncology

Transfusion Practices and Complications

7

Nayana Amin and Vijaya Patil

Blood transfusion is a common practice in the ICU with an estimate of 40% patients receiving transfusion. It is generally safe but occasionally may lead to minor or life-threatening consequences if attention to details and protocols are not met during transfusion.

Step 1: Resuscitate

- Secure two large-bore (14G/16G) IV cannulae.
- Send blood for grouping, cross-matching, complete blood count (CBC), coagulation profile, and other appropriate investigations.
- Proper coordination with blood bank is mandatory in these situations for early and proper acquisition of blood products.

Step 2: Transfuse Packed RBCs or Blood Components (Tables 7.1 and 7.2)

- If the patient is bleeding profusely and hemodynamically unstable, use group-specific uncross-matched blood or O Rh-negative packed cells while waiting for cross-matched blood.
- In hemodynamically stable patient use group specific cross matched blood. There is no advantage of using fresh blood over old blood
- In the presence of active bleeding, transfuse blood rapidly over 30 min (if available, use the rapid infusion pump, which can give fluids at a faster rate).
- 4 mL/kg of packed RBCs (usually one unit) increases the hemoglobin by 1 g/dL and hematocrit by 3% in absence of active bleeding.

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R. Chawla, S. Todi (eds.), *ICU Protocols*, https://doi.org/10.1007/978-981-15-0902-5_7

Table 7.1 Alternative red blood cell products

Technique	Purpose	Indications	Comments
Leukoreduction	Minimize the risk of cytomegalovirus transmission Reduces Febrile nonhemolytic transfusion reactions (FNHTR) and alloimmunization	High-risk immunocompromised patients, patients needing multiple transfusions, patients who have had FNHTR	Does not prevent TA-GVHD (transfusion-associated graft vs. host disease)
Separate type of filters to allow for RBC and platelet passage only, ideally should be used during collection but may be used during transfusion			
Washed RBCs	Prevent allergic reaction Reduce risk of hyperkalemia Anti-IgA antibody	Recurrent severe allergic reactions in spite of premedication, IgA-deficient patients, patients at risk of hyperkalemia	Not equivalent to leukoreduction, 15–20% loss of RBCs
RBCs washed with saline to remove >98% of plasma proteins, antibodies, leukocytes, and electrolytes			
Gamma irradiation to inactivate leukocytes	Prevents TA-GVHD	Premature infants, patients with malignancy, recipients of allogenic hemopoietic transplants, transfusion to blood relatives	Does not reduce infectious risks or FNHTR
Frozen RBCs Whole blood Volume reduced red cells CMV negative RBC	For individuals with rare blood group Massive blood transfusion Reduces transfusion associated circulatory oerload (TACO) For immuno-suppressed patients at risk of CMV infection		

Table 7.2 Blood components and antifibrinolytics

Product	Content	Indications	Dose	Caution	Expected correction
FFP (fresh frozen plasma)	All coagulation factors in normal concentration and plasma proteins	Deficiencies and consumption of coagulation factors	15 mL/kg	Should be group specific	15 mL/kg of FFP will increase coagulation factor concentration by 25–30%, which is enough for adequate clotting
	Thawed plasma may be stored (1–6 °C) up to 5 days	Reversal of factor VI and factor V anticoagulants effect (warfarin)		Thawed plasma should be transfused within 24 h if kept at room temperature	
		Massive blood transfusion (>1 blood volume within several hours)		Use blood filters	
		Replacement in plasmapheresis			
		Raised INR and planned invasive procedure			
		Treatment of thrombotic thrombocytopenic purpura			
Cryoprecipitate	Fibrinogen VIII/vWF (von Willebrand's factor), factor XIII, and fibronectin	Decreased fibrinogen, liver disease, post-thrombolysis bleeding	1 unit/7–10 kg body weight	Should be transfused within 6 h of thawing	1 unit cryoprecipitate/10 kg body weight
				Use blood filters	Raises plasma fibrinogen concentration by ~50 mg/dL

(continued)

Table 7.2 (continued)

Product	Content	Indications	Dose	Caution	Expected correction
Platelet	Random donor platelets—approximately 8.0×10^{10} platelets with 50 mL plasma	Bleeding due to critically decreased circulating platelet counts or functionally abnormal platelets	Infused over 30–60 min	Should be group specific	Expect an adult platelet count increment of ~7000–10,000/mm^3 for each RDP (random donor platelet) given or 30,000–60,000/mm^3 for each SDP (single donor platelet) given
	Single donor platelets—$3.5–4.0 \times 10^{11}$ platelets with 250 mL plasma	Maintain platelet count >10,000/mm^3 in stable nonbleeding patients, >30,000/mm^3 in unstable nonbleeding patients, and >50,000/mm^3 in patients undergoing invasive procedures or actively bleeding >100,000/mm^3 or for CNS trauma		Do not refrigerate	In pediatrics, a dose of 5–10 mL/kg of platelets (RDP or SDP) should result in 50–100,000/mm^3 increment
Desmopressin	Stimulate the endothelial release of factor VIII and vWF into the plasma (V2 receptor-mediated effect), where they form a complex with platelets and enhance their ability to aggregate	Hemophilia A, von Willebrand's disease, uremic thrombocytopathy	0.3 mcg/kg repeated as clinically necessary at intervals of 12–24 h		Tachyphylaxis may occur after three or four doses
Antifibrinolytic drugs					
Epsilon-aminocaproic acid	Competitive inhibitor of plasminogen activation	Situations associated with hyperfibrinolysis such as operations requiring cardiopulmonary bypass, liver transplantation, and some urological and orthopedic operations	100 mg/kg as an IV bolus followed by an infusion of 15 mg/kg/h (max 24 g/day)		

Tranexamic acid	Competitive inhibitor of plasminogen activation		Bolus dose of 10–15 mg/kg IV followed by 1 mg/kg/h for 5–8 h		
Aprotinin	Powerful inhibitor of plasmin, trypsin, chymotrypsin, kallikrein, thrombin, and activated protein C	Cardiac surgery, major orthopedic surgeries, liver transplant	Loading dose of 2 million international unit followed by continuous infusion of 500,000 KIU/h		
Activated factor VIIa		Factor VIIa deficiency, retropubic prostatectomy, bleeding in trauma, orthotopic liver transplantation	30 up to 90 mcg/kg Repeat every 2–3 h till satisfactory hemostasis is achieved		Target trough activity of at least 10–15 IU% (10–15%) is needed
Prothrombin Complex concentrate					

- Blood should be transfused within 4 h except in emergency. Rate of transfusion can be adjusted as per need, that is, rapidly in hypovolemic patients and slowly in stable patients; however, once issued from blood bank, blood transfusion should get over within 4 h to prevent growth of organisms. If blood cannot be transfused fully within this time, it is advisable to discard it.
- Transfuse blood and blood products through the filter adequate to prevent passage of small clots that may form in stored blood.
- The filter with a pore size of 170–200 μm is recommended for routine transfusions of RBCs, platelets, fresh frozen plasma (FFP), and cryoprecipitate.
- Filters with smaller pore size are more efficient, but they would increase resistance and filter out platelet aggregates, reducing efficiency of transfused platelets.
- Microaggregate filters with 20–40 μm size are recommended during cardiopulmonary bypass only.
- Filters can slow down the rate of blood transfusion. So the standard recommendation is to use a new set for every transfusion. In case of rapid transfusion if filter does not look clogged, change the set every two transfusions.
- Use fluid warmer to transfuse blood in massive blood loss. This helps to prevent hypothermia, which can contribute to the coagulopathy by causing reversible platelet dysfunction, altering coagulation kinetics, and enhancing fibrinolysis.
- Hypothermia also causes ventricular dysrhythmias and citrate toxicity due to reduced citrate metabolism.
- Do not use unconventional and uncontrolled methods such as keeping near heat source or immersing the bag in hot water bath.

Step 3: Correct Coagulopathy

- Correct high INR with FFP/PCC or low platelets with platelet transfusions only in an actively bleeding patient.
- Do not correct raised INR prophylactically in a nonbleeding patient unless a surgical intervention is contemplated.
- Other coagulopathic abnormalities need to be corrected.
- Antifibrinolytic agents may be used to minimize bleeding in situation like trauma.
- Correct hypothermia.
- Normalize calcium.
- Consider activated factor VII in some specific situations.
- Use Thromboelastography (TEG) or Rotational thromboelastometry (ROTEM) if available to further guide transfusion strategy.

Step 4: Control the Source of Bleeding

- Investigate to find out the source of bleeding and consider options available for controlling the bleeding (interventional radiology or surgery).
- Urgent consultation is required if needed with these specialities.

Step 5: Assess the Severity of Bleeding

- Massive blood loss may be defined as:
  - Loss of one blood volume within a 24-h period
  - Loss of blood equivalent to 7% of lean body weight in an adult (5 L) and 8–9% in a child
  - Loss of 50% of blood volume within 3 h
  - Loss of blood at a rate in excess of 150 mL/min

Step 6: Manage Massive Blood Loss

- Institute continuous invasive pressure monitoring for fluid management if the patient continues to remain hypotensive due to ongoing bleeding.
- Serial CBC (Hb and platelets) and coagulation tests (prothrombin time, APTT, and fibrinogen), blood gas analysis, serum electrolytes (Na, K, Mg, ionized calcium), and serum lactate should be done.
- These should be repeated frequently in ongoing bleeding and after every component therapy.
- Transfusion of platelets, FFPs, and cryoprecipitate should be guided by laboratory results.
- FFP administration should begin after loss of one blood volume and platelets after loss of 1.5 times the blood volume.
- 1:1:2 ratio should be maintained for packed RBCs, FFP, and random donor platelets to prevent dilutional coagulopathy and dilutional thrombocytopenia due to massive blood transfusion, which results in a vicious cycle of bleeding diathesis.
- Administer cryoprecipitate if fibrinogen is less than 100 mg/dL or there is a fear of volume overload by use of FFP.
- If patients with A or B blood group have received multiple units of O Rh-positive whole blood, then they can be switched back to their inherent group-specific blood only after subsequent testing by the blood bank indicates it is safe to do so.

Step 7: Identify and Manage Transfusion-Induced Complications (Table 7.3)

- Stop blood transfusion immediately if any acute hemolytic transfusion reaction is suspected.
- Hypotension may be due to acute ongoing hemorrhage, acute severe transfusion reaction, allergic reaction/anaphylaxis, or rarely due to septic shock (due to transfusion of blood with bacterial contamination).
- Check the identity of the recipient with the details on the bag and the cross-match form.

Table 7.3 Transfusion-related complications

Reaction	Cause	Clinical signs	Treatment
Febrile nonhemolytic transfusion reaction (FNHTR)	Reaction between the recipient's antibodies and transfused leukocytes	Fever, temperature rise	Give paracetamol and resume transfusion at a slow rate
	Pyrogenic cytokines released from the leukocytes in stored blood		
Allergic reaction	Reaction to soluble allergens in the donor's plasma	Urticaria, flushing, pruritus	Give 10 mg IV chlorpheniramine maleate and resume transfusion
Anaphylaxis	IgA-deficient individuals react to IgA in transfused units	Flushing, pruritus, laryngospasm, bronchospasm	Stop transfusion
			Supplement O_2
			SC/IV epinephrine, 100 mg IV hydrocortisone, 10 mg IV chlorpheniramine maleate
			Salbutamol nebulization
			IV fluids
			Send the blood back to the blood bank along with a sample of the patient's blood
			Use washed RBCs in future
Sepsis	Bacterial contamination of blood and blood products, Yersinia, bacteria, malaria	Fever, chills, hypotension	Stop transfusion
			Contact the blood bank and send the remaining blood to the blood bank
Acute hemolytic transfusion reaction (<24 h)	Immune-mediated—due to cytokines in transfused blood	Fever, chills, flushing, chest pain, back pain, vomiting, tachycardia, hypotension	Send blood for CBC, coagulation profile, direct Coombs' test, lactate dehydrogenase, haptoglobin, liver function tests for indirect bilirubinemia, peripheral smear for evidence of hemolysis
Delayed hemolytic transfusion reaction (24 h to 28 days)	Nonimmune-mediated—transfusion of damaged red cells		
			Gram staining and blood culture if bacterial contamination is suspected
			Send urine for hemoglobinuria O_2 supplementation, fluid resuscitation, and vasopressors to maintain mean arterial pressure >65 mmHg
			Broad-spectrum antibiotics if sepsis is suspected

Table 7.3 (continued)

Reaction	Cause	Clinical signs	Treatment
ABO (major blood group) incompatibility	Mismatched transfusion, IgM antibody against major RBC antigen, leading to intravascular hemolysis, renal failure, disseminated intravascular coagulation (DIC)	Fever, chills, flushing, chest pain or low back pain, hypotension, and dyspnea	Stop transfusion Reconfirm the patient's identity and blood group Inform the blood bank and return blood to the blood bank Infuse saline to maintain urine output of 100 mL/h Give diuretics if urine output falls Treat DIC with appropriate blood components
Transfusion-associated graft-versus-host disease (TA-GVHD) 2–30 days after transfusion	Donor lymphocytes initiate an immune attack against recipient's cells	Fever, skin rash, liver dysfunction, diarrhea, severe pancytopenia	No treatment Prevention by using gamma-irradiated blood products in high-risk patients
	Cause	*Presentation*	*Treatment*
TACO	Volume overload	Dyspnea, rales, hypertension, and desaturation, raised central venous pressure (CVP)	O_2 supplementation, diuretics, ventilatory support
TRALI	Antibodies in the donor's blood react with neutrophil antigen in the recipient	Dyspnea, rales, hypotension, and desaturation, normal or low CVP	Supportive management Ventilate according to acute respiratory distress syndrome network protocol Steroids not indicated

- Transfusion-associated circulatory overload (TACO) is circulatory overload following transfusion of blood or blood product.
- Transfusion-associated acute lung injury (TRALI) is defined as new acute lung injury (with hypoxemia and bilateral infiltrates on chest radiograph but no evidence of left atrial hypertension) occurring during or within 6 h after a transfusion, with a clear temporal relationship to the transfusion, and not explained by another acute lung injury (ALI) risk factor.
- Transfusion related hyperkalemia is increased in massive trauma, renal failure and in newborn/infants
- Increased risk of citrate toxicity in massive transfusion in patients with liver disease

Step 8: Use Less Allergenic Blood Products

- In patients with multiple blood transfusion and transfusion-related complications, alternatively processed blood products should be considered (Table 7.1).

Step 9: Consider Threshold for Blood Transfusion

- If the bleeding has stopped and there are no clinical signs of hypoperfusion, do not transfuse any more blood or blood products.
- In the absence of active bleeding, keep a transfusion threshold of less than 7.0 g/dL and 7–8 g/dL Hb in critically ill patients who are hemodynamically stable.
- In the presence of active bleeding, keep higher transfusion threshold of 9–10 g% and further guide by clinical needs.
- Adult critically ill medical and surgical patients suspected to have sepsis and septic shock, during the first 6 h of resuscitation one may consider higher transfusion threshold of 8–10 g/dL
- Transfusion threshold should be individualised depends on patients pre admission hemoglobin, age, hemodynamic stability, cardiac status and availability of group specific blood.
- RBC transfusion may be beneficial in anemic patients with acute coronary syndrome (keep Hb >9 g/dL).
- For patients undergoing cardiovascular surgery or orthopedic surgery blood transfusion to be given to maintain hemoglobin 7–8 g/dL
- All RBC transfusions in nonbleeding stable patients should be ordered as single units. Check posttransfusion Hb before ordering additional units.

Step 10: Use Blood Products Judiciously

- In the absence of bleeding, do not correct high INR with FFP.
- Patients having inadequate intake or on anticoagulants and broad-spectrum antibiotics are likely to have vitamin K deficiency, which can cause deranged INR.
- They will benefit from intravenous vitamin K supplementation.
- Consider judicious use of intravenous iron and erythropoietin where indicated to minimise need for blood transfusion

Step 11: Follow Blood Transfusion Protocol

- Take informed consent, patient identification, visual inspection of the blood transfused for feature of hemolysis
- Use only 0.9% normal saline or albumin, ABO compatible plasma through the same intravenous tubing

- Initial infusion rate 1–2 mL/min for the first 15 min to look for any features of hemolytic or allergic reaction
- Complete transfusion not exceeding 4 h
- If needed a post transfusion hemoglobin may be checked as soon as 15 min after transfusion.

48 year old female with prosthetic mitral valve on warfarin presents to emergency department with severe bleeding per vagina for last 12 h. She is pale with cold peripheries, rapid thready pulse and tachypnea. Her Hb is 5.0 g% and INR is 7.5.

Follow step 1 and step 2 similar to first case.

Step 3

- Give 5–10 mg Vit K IV over 15–20 min which will reverse the effect of warfarin in 4–6 h or use FFP/cryo/4 factor prothrombin complex concentrate (PCC) for uncontrolled bleeding. Monitor INR 6–8 h.
- For less severe bleeding one may consider Oral Vit K in the dose of 1–2.5 mg which will decrease the INR in 8–24 h.
- If there is life threatening bleeding or bleeding in critical areas (CNS, pericardium or airways) then temporarily stop the anticoagulant drug and correct coagulopathy with FFPs/cryoprecipitate or 4F-PCC.
- Consider supportive measures and give reversal agents whenever indicated. Use appropriate laboratory tests to determine the drug levels (Table 7.4)

Table 7.4 Various anticoagulant agents and their antidotes

Drug	Laboratory tests to determine drug levels	Treatment	
		Minor bleeding	Major bleeding
Unfractionated heparin	Activated partial thromboplastin time (aPTT)		IV Protamine 1 mg/100 units heparin
Low molecular weight heparin (LMWH)	Anti factor Xa levels		IV Protamin 1 mg/100 units dalteparin/tinzaparin or 1 mg protamine/1 mg enoxaparin dose received in previous 8 h Consider rFVIIa for critical bleeding

(continued)

Table 7.4 (continued)

Drug	Laboratory tests to determine drug levels	Treatment	
		Minor bleeding	Major bleeding
Vit K antagonist (Warfarin)	Prothrombin time (PT)/International normalized ratio (INR)	**If INR < 4.5** No bleeding—withhold warfarin till INR is in therapeutic range Reversal—give Vit K 2.5 mg PO **If INR 4.5–10** No bleeding—hold warfarin, Consider Vit K 2.5 mg PO Urgent reversal—give Vit K 2.5 mg oral or 1 mg IV **If INR >10** No bleeding—hold warfarin, Give Vit K 2.5 mg PO or 1–2 mg IV over 30 min. Repeat every 24 h Urgent reversal—give Vit K 1–2 mg IV over 30 min, repeat every 6–24 h	Discontinue oral anticoagulant (OAC) 5–10 mg IV Vit K 4F-Prothrombin complex concentrates (4F-PCC) **If INR 1.5-3.9**—give 25 units/kg 4F-PCC max of 2500 units **If INR 4-6**—give 35 units/kg 4F-PCC max of 3500 units **If INR > 6**—give 50 units/kg 4F-PCC max of 5000 units If 4F—PCC not available give FFP at 10–15 mL/kg Activated prothrombin complex concentrate (aPCC) is not indicated
Direct thrombin inhibitors Dabigatran	TT—dilute thrombin time ECT—Ecarin clotting time ECA—Ecarin chromogenic assay If above tests not available then thrombin time aPTT		IV Idarucizumab or IV 4 PCC/(aPCC) at 50 units/kg No role of FFP Anticoagulant discontinuation Antifibrinolytic agent (trenexemic acid) Consider activated charcoal if drug has been ingested within 2–4 h
Oral Factor Xa inhibitors Rivaroxaban, Epixaban, Endoxaban	Anti factor Xa levels Normal aPTT does not exclude significant drug levels Normal PT indicates complete clearance of Xa inhibitor PT and aPTT not sensitive for epixaban		Andexanet alfa if available IV 4 PCC/aPCC at 50 units/kg Anticoagulant discontinuation Antifibrinolytic agent (trenexemic acid) Consider activated charcoal if drug has been ingested within 2–4 h No role of FFP

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Disseminated Intravascular Coagulation and Thrombocytopenia

8

Vijaya Patil, Nayana Amin, Reshma Ambulkar, and Atul Kulkarni

A 40-year-old male patient was admitted with acute pancreatitis. He developed fever, tachycardia, hypotension, and respiratory distress on the 3rd day of admission. His abdomen was severely tender and distended. Next morning the nurse noticed excessive oozing from arterial and central line insertion site, and his abdomen was further distended.

Bleeding manifestation due to disseminated intravascular coagulation (DIC) occurs in 1% of hospital admission. Assessing and managing these patients require a systematic approach as DIC is a reflection of underlying systemic disease affecting the coagulation system, resulting in procoagulant activation, fibrinolytic activation, consumption coagulopathy, and end organ damage, which needs to be recognized and treated.

Step 1: Initial Resuscitation

- Special emphasis should be placed on stabilizing hemodynamics, and if needed, blood and blood product transfusion should be started.
- Care should be taken in establishing venous access in actively bleeding patients who may be coagulopathic.
- Peripheral access is preferable to central.
- Use ultrasound-guided venous cannulation if possible and preferably choose compressible sites like internal jugular or femoral vein.
- Avoid arterial punctures.

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Step 2: Take Relevant History and Perform Focused Physical Examination

- Take history of known systemic conditions associated with DIC and coagulation disorders (Table 8.1)
- Review the drug history, particularly the use of heparin and warfarin, and consumption of antiplatelet agents including nonsteroidal anti-inflammatory drugs.
- Look for bleeding manifestation, superficial like skin and mucosal (petechiae, purpura) or visceral and deep seated (gastrointestinal bleeding).
- Look for thrombotic manifestations like deep vein thrombosis (DVT) of lower limbs or venous or arterial thrombosis at any other site (e.g., cerebral).

Step 3: Investigate to Ascertain the Type and Cause of Bleeding (Table 8.2)

- Complete blood count, including platelet count and peripheral smear, for the presence of fragmented RBCs.

Table 8.1 Conditions associated with DIC

Infections	Bacterial—Gram-negative and Gram-positive sepsis
	Viral—cytomegalovirus, HIV, hepatitis, dengue
	Fungal
	Parasitic—malaria
Malignancy	Solid tumors
	Hematological—acute promyelocytic leukemia is commonly associated with DIC
Obstetric	Amniotic fluid embolism
	Placenta abruption
	Preeclampsia
	Intrauterine fetal death/retained products of conception
Toxic and immunological insults	Viper snake bites
	Massive transfusion
	ABO transfusion incompatibility
	Transplant rejection
Massive inflammation	Severe trauma
	Crush injuries
	Massive burns
	Fulminant liver failure
	Severe hypo-/hyperthermia
	Severe pancreatitis
Vascular disorders	Aortic aneurysms
	Giant hemangiomas

Table 8.2 Coagulation profile

Test	What does it monitor	Normal value	Inference
Prothrombin time	Factors that are in the extrinsic pathway and common pathway: factors VII, X, V, and II	11–13 s	Prolongation of the PT is most often a result of deficiencies in factor VII but can also be caused by any of the extrinsic and common pathway factors. Decreased fibrinogen, levels less than 100 mg/dL, will also prolong the PT
			Cholestatic jaundice
			Acute or chronic liver failure
			DIC
			Malabsorption
			Vitamin K deficiency
			Coumadin (warfarin) therapy
			Factors I, II,V, VII, X deficiency
Activated partial thromboplastin time	Factors that are designated in the intrinsic pathway: factors XII, XI, IX, VIII, X, V, II, and fibrinogen	28–34 s	Heparin therapy
			Factor deficiency
			Presence of an inhibitor like lupus anticoagulants
Platelet count	Quantifies platelet number	130–400 × 10^9/L	Decreased production (bone marrow disorder), increased destruction, idiopathic thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura, sequestration (hypersplenism)
Thrombin time	Evaluates the last step of coagulation (conversion of fibrinogen to fibrin)	13–15 s	Heparin therapy
			DIC
			Qualitative fibrinogen abnormalities or hypofibrinogenemia
			Elevated FDPs (fibrin degradation products)
Fibrinogen level		200–500 mg/dL	Congenital and acquired hypofibrinogenemia
			DIC
D-dimer	Cross-linked D fragments of the protein fibrinogen	500 ng/mL	Deep venous thrombosis, DIC, pulmonary embolism, thrombolytic treatment, postoperative
Antithrombin (AT), Protein C	Anticoagulant activity	65–135 IU/dL	Liver dysfunction, capillary leak syndrome
Plasmin-plasmin inhibitor complex	Antifibrinolysis	0.8 μg/dL	Venous thromboembolism, post surgery

- Prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin time (TT).
- Fibrinogen level, fibrin degradation product (FDP), D-dimer.
- Renal and liver function tests.
- The commonest laboratory abnormality is thrombocytopenia followed by elevated FDPs, prolonged PT, prolonged APTT, and a low fibrinogen.
- D-dimer, FDP, and antithrombin levels can be used for rapid and specific diagnosis of DIC, with antithrombin levels providing an indicator for severity and prognosis.
- Diagnosis of DIC is essentially confirmed by demonstrating increased thrombin generation (decreased fibrinogen) and increased fibrinolysis (elevated D-dimer or FDP).

Step 4: Ascertain Severity and Prognosticate Outcome

- Calculate the DIC score (Table 8.3) with the ISTH (International Society of Thrombosis and Haemostasis) scoring system which provides objective measurement of DIC and correlates with outcome.

Table 8.3 Scoring systems for DIC

	ISTH criteria	JMWH criteria	JAAM criteria
Clinical condition predisposing to DIC	Essential	1 point	Essential
The presence of clinical symptoms	Not used	Bleeding—1 point Organ failure—1 point	SIRS score ≥ 3—1 point
Platelet count ($\times 10^9$/L)	50–100—1 point <50—2 points	80–120—1 point 50–80—2 points <50—3 points	80–120 or >30% reduction—1 point <80 or >50% reduction—2 points
Fibrin-related marker	Moderate increase—2 points Marked increase—3 points	FDP (μg/mL) 10–20—1 point 20–40—2 points >40—3 points	FDP (μg/mL) 10–25—1 point >25—3 points
Fibrinogen	<1 g/L—1 point	1–1.5 g/L—1 point <1 g/L—2 points	
PT	Prolongation 3–6 s—1 point >6 s—2 points	PT ratio 1.25–1.67—1 point >1.67—2 points	PT ratio ≥1.2—1 point
DIC diagnosis	**≥5 points**	**≥7 points**	**≥4 points**

ISTH International Society of Thrombosis and Haemostasis, *JAAM* Japanese Association for Acute Medicine, *JMWH* Japanese Ministry of Health and Welfare

Step 5: Continue Resuscitation

- Continue resuscitation and maintain hemodynamic stability using crystalloids
- Avoid colloids, as they interfere with clotting.
- If colloids are used at all use, Gelatin or If you are using starches, use tetrastarch preferably, as they have less effect on the coagulation profile, but do not exceed maximum dose (50 mL/kg/day).

Step 6: Correct Coagulopathy

(See Table 8.2 in Chap. 7, Vol. 2)

- Repeat the coagulation profile and complete blood count frequently and replace blood and blood products.
- Rotation thromboelastometry (ROTEM) or Thromboelastography (TEG) can be used to guide blood product administration while managing DIC.
- In the presence of ongoing blood loss, try to normalize prothrombin time and APTT and aim to maintain platelet count of more than 50,000/mm^3.
- Do not use antifibrinolytic agents as they may aggravate thrombosis.
- Patients who have DIC with a primary hyperfibrinolytic state and who have severe bleeding can be treated with lysine analogues, such as tranexamic acid (e.g., 1 g every 8 h).
- There is no role of heparin in actively bleeding patients.
- It should be considered only where thrombosis predominates such as arterial or venous thromboembolism or severe purpura fulminans associated with vascular skin infarction.
- Use of Prothrombin complex concentrates (PCC) has shown to increase risk of thromboembolic complications especially with high or repeated doses. It should be only used in patients where FFP transfusion is not possible and patient is actively bleeding in critical areas

Step 7: Treat the Underlying Disorder

- Repeat the tests to monitor the dynamically changing scenario and continue treatment based on clinical observation and laboratory results.
- Once patient stops bleeding, do not try to correct laboratory abnormalities as transfusion of blood and blood products should be based on clinical condition and bleeding rather than laboratory values only.

Calculate Score

- More than 5 overt DIC: repeat score daily.
- Less than 5 suggestive for nonovert DIC: repeat for the next 1–2 days.

Thrombocytopenia

A 50-year-old male patient was admitted with acute pancreatitis. His blood investigations showed Hb 10.7 g%, WBC 12,000/mm^3, and platelets 110,000/mm^3. On the third day, he worsened clinically. His WBC count was 20,000/mm^{3}and platelets were 70,000/mm^3. However, the next day, he further deteriorated requiring inotropes and ventilatory support. His Hb dropped to 6.4 g%, WBC count rose to 28,000 mm^3, and platelets further dropped to 40,000/mm^3.

Step 1: Resuscitate

- Resuscitate, monitor, and stabilize in the ICU (refer to Chap. 23, Vol. 2). In patients with low platelets and coagulopathy, ultrasound-guided jugular venous catheter insertion for fluid resuscitation should be performed.
- Send blood for peripheral blood smear, grouping, cross-matching, coagulation profile, and biochemistry.

Step 2: Assess Severity of Thrombocytopenia

- Thrombocytopenia is defined as a platelet count less than 150×10^9/L.
- In critically ill patients, a threshold of less than100×10^9/L may be taken.
- The ability to form a hemostatic plug is retained until the platelet count drops to less than 100×10^9/L

Step 3: Assess Cause of Thrombocytopenia (Table 8.4)

- Careful history, physical examination, previous medical records, and current chart review usually reveal the cause of low platelet count.
- Ask about bleeding from other sites in past, for example, frequent nosebleeds, gum bleeds, melena, hemoptysis, and blood in stool or urine.
- History of previous platelet counts.
- History of previous blood or platelet transfusion.
- Medication history and review medication chart—particularly, use of heparin, warfarin, and antiplatelet agents including nonsteroidal anti-inflammatory drugs (Table 8.5).
- Heparin-induced thrombocytopenia (HIT) should be considered if the platelet count decreases by 50% and/or thrombosis occurs 5–14 days after starting heparin. 4Ts score for pretest probability of HIT (Table 8.6)

Table 8.4 Causes of thrombocytopenia

Pseudothrombocytopenia seen in asymptomatic patients	EDTA causes in vitro clumping of platelets. Presence of platelet clumps in the peripheral smear and a normal repeat platelet count in citrated blood confirm pseudothrombocytopenia. In some patients, automated blood reports show thrombocytopenia due to presence of giant platelets that are counted as RBCs in automated machines; however, manual platelet count is normal
Dilutional thrombocytopenia	Massive blood transfusion
Ambulatory patients	ITP
	Drug-induced—chemotherapy, miscellaneous drugs
	Infections—Epstein–Barr virus (EBV), HIV, others
	Connective tissue disorders—rheumatoid arthritis, systemic lupus erythematosus (SLE), antiphospholipid antibody syndrome
	Hypersplenism
	Primary marrow disorder
Acutely ill patients	Infection/sepsis
	DIC
	TTP-HUS
	Posttransfusion purpura
Pregnant patient	Gestational (platelet count >70 resolves after pregnancy)
	ITP
	HELLP—hemolysis, elevated liver enzymes, low platelets
Cardiac patients	HIT
	Cardiac bypass
	Dilutional
	Gp IIb/IIIa inhibitor-related
	TTP related to clopidogrel or ticlopidine
Patient with thrombosis	HIT
	Antiphospholipid antibody syndrome
	Paroxysmal nocturnal hemoglobinuria

Table 8.5 Drugs associated with thrombocytopenia

Mechanism	Drugs	
Drug-specific antibody	H_2 receptor blockers	Ranitidine, cimetidine
	Gp IIb/IIIa inhibitors	Abciximab
Drug-dependent antibody	Antibiotics	Vancomycin, rifampicin, chloroquine, amphotericin B, sulfonamides
	Salicylates/NSAIDs	Aspirin, diclofenac, ibuprofen
	Antiepileptics	Valproate, carbamazepine, phenytoin
	Antiarrhythmics	Amiodarone
	Miscellaneous	Quinine, furosemide, thiazide, morphine
Hapten-dependent antibody	Antibiotic	Penicillin, some cephalosporins

(continued)

Table 8.5 (continued)

Mechanism	Drugs	
Induction of autoantibodies	Antiarrhythmics	Procainamide
	Miscellaneous	Gold salts
Myelosuppression	Antibiotics	Linezolid
	Chemotherapeutic agents	
Unknown	Antibiotics	Fluconazole, daptomycin, ganciclovir, nitrofurantoin, piperacillin
	Miscellaneous	Digoxin, haloperidol
	Gp IIb/IIIa inhibitors	Eptifibatide
Immune complex with PF4	Heparins	Unfractionated and low-molecular-weight heparin
Interference with folate metabolism	Antibiotic	Meropenem
Thrombotic microangiopathy		Clopidogrel, ticlopidine
Preexisting antibodies		Abciximab

Table 8.6 4-T's score for pretest probability of HIT

Points	2	1	0
Thrombocytopenia (acute)	>50% fall in platelet count l	>30–50% fall platelet count	<30% fall in platelets
Timing of fall in platelet count	Onset within 5–10 days or, ≤1 day (if heparin exposure within 30 days)	After day 10, or timing unclear, or ≤1 day with recent heparin exposure within 31–100 day	Platelet count fall before day 4 (without recent heparin exposure)
Thrombosis	New thrombosis; skin necrosis or post–heparin bolus acute systemic reaction	Progressive or recurrent thrombosis; erythematous skin lesions; suspected thrombosis that has not been confirmed	None
Other cause of low platelet	No other cause of platelet count fall is evident	Possible other cause is evident	Definite other cause is present

Pretest probability score: 6–8 high; 4–5 intermediate; 0–3 low

- History of known systemic conditions associated with defects in platelets like alcoholism, cirrhosis, HIV infection, systemic lupus erythematosus (SLE), and uremia.
- Family history of excessive bleeding.
- Perform physical examination to look for:
  - Evidence of bleeding in skin, mucous membrane, joints, soft tissue
  - Lymphadenopathy
  - Splenomegaly

Step 4: Transfuse Platelets (Table 8.7)

- Three types of platelet products are commonly used in clinical practice:
  - Random-donor platelets (RDP)
  - Single-donor platelets (SDP)
  - HLA-matched platelets
- Platelet transfusions are contraindicated in thrombotic thrombocytopenic purpura (TTP), idiopathic thrombocytopenic purpura (ITP), and HIT unless the patient is bleeding.

Step 5: Assess Rise in Platelet Count After Platelet Transfusion (Table 8.8)

- Platelet counts should be measured 10–60 min after transfusion. Posttransfusion counts at 10–60 min are sensitive to immune platelet destruction. Posttransfusion counts at 24 h assess platelet survival, which is sensitive to nonimmune factors.
- The patient is considered refractory to platelet transfusions if two or three consecutive transfusions are ineffective.
- Alloimmunization is confirmed by demonstrating antibodies to specific human leukocyte antigen (HLA) or human platelet antigen (HPA).

Table 8.7 Platelet transfusion triggers

Transfusion indication	Threshold platelet count ($\times 10^9$/L)
Prophylactic transfusion of adult patients	**10**
Before central vein catheter placement	**20**
Urgent diagnostic lumbar puncture	**20**
Before elective diagnostic lumbar function	**50**
Before major elective surgery (excluding neurosurgery)	**50**
Neurosurgery/eye surgery	100

Table 8.8 Factors associated with platelet refractoriness

Nonimmune factors	Clinical factors	Splenomegaly, fever, infection, bleeding, disseminated intravascular coagulation
	Drugs	Amphotericin B, vancomycin, ciprofloxacin, heparin
	Patient factors	previous pregnancies, previous transfusions
Immune factors	Antibodies	HLA, platelet specific, erythrocyte
	Others	Length of time the platelets are stored

Step 6: Understand Strategies to Improve Response to Platelet Transfusions (Table 8.9)

- Treat underlying condition.
- Transfuse ABO identical platelets.
- Transfuse platelets less than 48 h in storage.
- Increase number of platelets transfused.
- Select compatible donor: HLA-matched, ABO compatible.

Table 8.9 Approach for management of thrombocytopenia

Etiology	Mechanism	Presentation	Treatment
ITP, after viral illness, may be associated with antiphospholipid antibody syndrome, may be initial presentation of connective tissue disease, lymphoploriferative malignancy	IgG antibodies against platelet antigens, platelet clearance by spleen, inadequate platelet production response	All ages, common in young adult females	Steroids, prednisolone 1 mg/kg/day for 1–2 weeks, taper
		Severe thrombocytopenia with normal RBC and WBC morphology and number	IVIG infusion 1 g/kg/day for 2 days
		Diagnosis by exclusion	Anti RhD antibodies 50–75 μ/kg IV (Rh +Ve patients with intact spleen)
TTP-HUS	-Inherited or acquired deficiency of von Willebrand factor cleaving protease (ADAMTS13)	Microangiopathic hemolytic anemia, thrombocytopenia, renal insufficiency, fever, and mental status changes	FFP transfusions until the patient is ready for plasma exchanges
	Idiopathic or secondary to *Escherichia coli* diarrhea, HIV infection, certain drugs (ticlopidine, clopidogrel, quinine, cyclosporine A, mitomycin A, cisplatin, etc.), pregnancy, bone marrow transplant, and metastatic carcinomas	Schistiocytes in peripheral smear, raised LDH, normal coagulation profile	Plasma exchanges
			Platelet transfusions only in life-threatening bleeding

Table 8.9 (continued)

Etiology	Mechanism	Presentation	Treatment
Drug-induced thrombocytopenia	Antiplatelet agents' and other drugs' immune mechanism	History—no other blood or coagulation abnormalities	Stop the offending drug
			Supportive care
	Chemotherapy and alcohol—directly inhibit megakaryocytes	Most chemotherapeutic drugs—nadir of blood counts in 7–10 days, recovers over 2–3 weeks Nitrosureas and mitomycin cause prolonged myelosuppression	Supportive care
	Heparin—antibodies against heparin–platelet factor 4 complex	Type I—modest transient thrombocytopenia in 2–3 days after heparin therapy	Spontaneous recovery
		Type II—less common, occurs 4–14 days after heparin therapy	Stop heparin
		ELISA assay for anti-PF 4 antibody, serotonin release assay, platelet aggregation studies	Doppler to rule out thrombosis
			Use direct thrombin inhibitors (argatroban, lepirudin) Fondaparinux should be used with caution
			LMWH and UFH should not be used

Step 7: Treat Underlying Cause

- Review and stop all offending medication.
- Evaluate the patient for evidence of secondary infection or DIC.

Suggested Reading

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Thachil J. Disseminated intravascular coagulation a practical approach. Anesthesiology. 2016;125:230–6. *A practitioner guide for the management of DIC*

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Website

http://www.bcshguidelines

Onco-emergencies

9

Atul Kulkarni and Vandana Agarwal

A 58-year-old male patient with metastatic renal cell carcinoma presented with lethargy, confusion, anorexia, nausea, and constipation. He was polyuric and polydipsic over the past few days.

Hypercalcemia

Oncological emergencies such as hypercalcemia, tumor lysis syndrome, superior vena cava syndrome, and spinal cord compression are occasionally seen as an intercurrent problem or presenting manifestation in certain cancers.

Step 1: Resuscitate

- Hydration is of utmost importance in these patients, and intravenous saline should be given rapidly once hypercalcemia is confirmed (refer to Chap. 23, Vol. 2). Intravenous normal saline enhances GFR and renal excretion of calcium (Ca) ions.

Step 2: Send Investigations

- Measure ionized serum calcium (arterial or venous).
- If total serum calcium is measured, correct for the albumin level. Corrected calcium = measured total calcium + [0.8 × (4.0 − albumin)].
- Assess severity of Hypercalcemia, Mild: <12 mg/dL, Moderate: 12–14 mg/dL and Severe: >14 mg/dL

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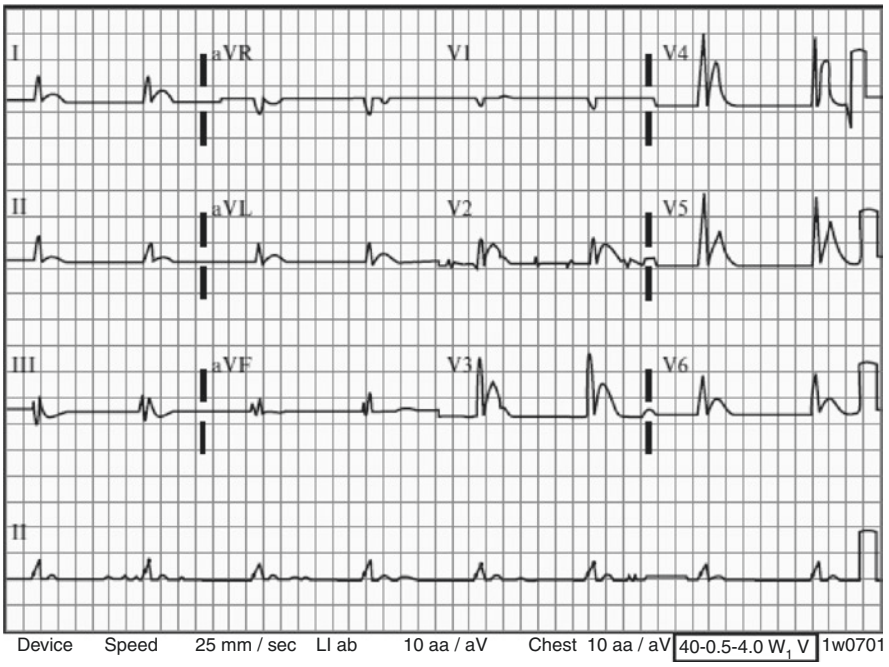

Fig. 9.1 ECG changes of hypercalcemia. The ECG shows a short QT interval with hardly any ST segment, characteristic of hypercalcemia. In this tracing, the QRS complexes are wide, indicative of an intraventricular conduction defect. No P waves are evident, and this is most likely a junctional escape rhythm

- Also, check serum creatinine, Phosphate, and alkaline phosphatase.
- A low serum chloride level (<100 mEq/L) suggests hypercalcemia of malignancy.

ECG Changes in Hypercalcemia (Fig. 9.1)

- ECG abnormalities reflect altered transmembrane potentials, affecting conduction such as QT interval shortening (common) and QRS interval lengthening (high levels). T waves may flatten or invert, and a variable degree of heart block may develop.

Step 3: Infuse Fluid

- Severe hypercalcemia is usually associated with marked hypovolemia.
- Give 500–1000 mL of normal saline in the first hour and continue at a rate of 200–300 mL/h until volume repletion is achieved and 100–150 mL/h urine output is established.
- In patients with impaired cardiorespiratory and renal function, aggressive fluid resuscitation should be done with close hemodynamic monitoring.

Step 4: Start Diuretics After Fluid Repletion

- Loop diuretics should not be routinely used.
- In patients with heart failure and/or renal failure judicious use of loop diuretics may be tried to prevent volume overload.
- Consider loop diuretics only when euvolemia is achieved, as hypovolemia causes renal hypoperfusion hampering calcium excretion. Frusemide inhibits Ca resorption in renal tubules.
- Diuretics are specifically useful if features of hypervolemia, secondary to aggressive fluid resuscitation, develop.

Step 5: Start Specific Therapy

- First line therapy
  - Bisphosphonates block osteoclastic bone resorption.
  - Use zoledronic acid with caution in patients with renal impairment, and adjust the dose according to creatinine clearance (Table 9.1).
  - Human monoclonal antibody—Denosumab binds to RANKL (soluble protein essential for the formation, function, and survival of osteoclasts) and

Table 9.1 Treatment for hypercalcemia

Intervention	Dosage	Comment
Normal saline	250–500 mL/h until euvolemic, thereafter 100–150 mL/h IV, may require 3–4 L Target urine output upto 100 mL/h	Fluids may be needed for 1–3 days depending on the patient's cardiovascular and renal function Caution in patients with congestive heart failure
Furosemide	20–40 mg IV	After volume correction
First line therapy		
Bisphosphonates	Pamidronate: 60–90 mg IV over 2–24 h in 50–200 mL normal saline (NS) Allow at least 7 days before retreatment Zoledronic acid: 4 mg IV over 15 min in 50 mL of NS	Caution in renal impairment Can cause flu like symptoms with fever, chills, and headache
Denosumab	120 mg subcutaneous every 4 weeks; administer additional 120 mg on days 8 and 15 during the first month	Hypertension, fatigue, nausea, arthralgia, and hypocalcemia
Second line therapy		
Glucocorticoids	Prednisolone: 20–40 mg/day PO for 10 days Hydrocortisone: 100 mg IV every 6 h for 3 days	Hyperglycemia, immunosuppression
Calcitonin	4–8 IU/kg SC or IM every 12 h	Rapid onset but short lived

inhibits osteoclast activity. Denosumab does not depend on kidneys for excretion and therefore is safe in patients with renal impairment.

- Second line therapy
  - Glucocorticoids inhibits conversion of vitamin D to calcitriol. In some patients with lymphomas, particularly Hodgkin's disease, hypercalcemia is caused by elevated levels of vitamin D ($1,25(OH)_2D$); glucocorticoids are particularly effective.
  - Calcitonin inhibits the bone resorption. It can be used in patients with heart failure or moderate to severe renal impairment as an alternative to normal saline. The efficacy is limited to first 48 h due to the development of tachyphylaxis.

Step 6: Decrease Intake

- Eliminate dietary sources of calcium.
- Discontinue medications such as thiazide diuretics (increase the reabsorption of calcium) and vitamin D that increase the calcium level.

Step 7: Consider Dialysis

- Dialysis should be considered for patients with renal failure and/or congestive heart failure when aggressive hydration and bisphosphonates cannot be used safely.

Step 8: Treat the Cause

- Treat the malignancy with chemotherapy and radiation to control the hypercalcemia if possible.

Step 9: Evaluate Prognosis

- In patients with advanced malignancy, hypercalcemia may commonly occur.
- In such circumstances, it may be appropriate, ethical, and humane to institute only comfort measures if no effective treatment for malignancy exists

Tumor Lysis Syndrome (TLS)

A 26-year-old patient with Burkitt's lymphoma recently started on chemotherapy presented with anorexia, lethargy, disorientation, vomiting, muscle cramps, tachypnea, and decreased urine output.

Step 1: Resuscitate

- These patients are usually dehydrated and will benefit with intravenous fluids (refer to Chap. 23, Vol. 2).

Step 2: Make a Diagnosis

- Investigations may show hyperuricemia, hyperkalemia, hyperphosphatemia, hypocalcemia, uremia, and raised lactate dehydrogenase levels.
- Obtain electrocardiogram to rule out serious arrhythmias and conduction abnormalities.
- Tumor lysis is associated with malignancies like acute lymphoblastic leukemia or Burkitt's lymphoma with high tumor burden and these tumors respond rapidly to chemotherapy.
- It usually follows chemotherapy, but may occur after radiation, corticosteroid therapy, or chemoembolization and rarely spontaneously.
- Check urine output and renal function.
- Tumor related and patient related factors can be used to estimate the risk of TLS in an individual patient.

Step 3: Start Hydration

This strategy is useful both as a preventive measure in patients at high risk of TLS and in patients with established TLS.

- A high infusion rate of fluids is appropriate.
- Patients with high risk of tumor lysis syndrome should have aggressive volume replacement as a preventive measure prior to chemotherapy.
- Infuse isotonic fluid at a rate of 200–300 mL/h.

- Volume should be adapted for the patient's age, cardiac function, and urine output.
- Increasing the urinary flow rate is the most effective strategy for preventing urate-induced obstructive uropathy.
- Urine output should be maintained within a range of 80–100 mL/m^2/h (4–6 mL/kg/h)
- Urine-specific gravity should be maintained at $\leq$1.010.

Step 4: Use Diuretics Cautiously

- Maintain adequate urine output.
- It is contraindicated if hypovolemia or obstructive uropathy exists.

Step 5: Alkalinization of the Urine

- Currently not recommended specially in patients with elevated phosphate.
- It can lead to the formation of urinary xanthine crystals which may cause obstruction of renal tubules if allopurinol is used concurrently.
- Alkalinization of urine is not recommended in TLS prophylaxis and therapy anymore.

Step 6: Start Allopurinol

This should be considered in patients with intermediate risk of TLS and pretretment uric acid level < 8 mg/dL.

- Purine catabolism results in the production of hypoxanthine and xanthine, which are metabolized to uric acid via the enzymatic action of xanthine oxidase.
- This pathway can be blocked by the use of allopurinol, a hypoxanthine analog that competitively inhibits xanthine oxidase.
- Start allopurinol PO at 600 mg/day if uric acid is less than 8 mg/dL.
- Allopurinol should be started at least 24 h prior to chemotherapy.
- After about 2–3 days, allopurinol therapy results in increased excretion of both hypoxanthine, which is more soluble than uric acid, and xanthine, which is less soluble than uric acid.
- A marked increase in xanthine excretion can occur when allopurinol is given for prevention of tumor lysis syndrome and may lead to acute renal failure or xanthine stones.

- It should be used cautiously in patients with renal impairment. It has many drug interactions and may cause skin hypersensitivity reactions.
- Allopurinol should be restricted to patients considered at low or intermediate risk for TLS. In established TLS, additional treatment options should be considered.
- Febuxostat may be used if the patient is hypersensitive to allopurinol.

Step 7: Consider Rasburicase (Recombinant Urate Oxidase)

This should be considered in patients with high risk of TLS and in patients with impaired cardiac or renal function and pretretment uric acid level > 8 mg/dL

- Urate oxidase—present in most mammals, but not in humans—oxidizes preformed uric acid to allantoin, which is five to ten times more soluble than uric acid in acid urine.
- When exogenous urate oxidase (uricase, rasburicase) is administered, serum and urinary uric acid levels decrease markedly within approximately 4 h.
- This should be used especially if the uric acid level is above 8 mg/dL.
- Uric acid levels should be monitored regularly to adjust dosing.
- Rasburicase degrades uric acid within the blood samples at room temperature, thus interfering with accurate measurement.
- Therefore, samples should immediately be placed on ice until the completion of assay.
- Rasburicase should not be given to patients with G6PD deficiency due to the risk of severe hemolysis.
- If administration of Rasburicase is needed in an emergent situation and results of G6PD is not available urgently, it can be given at a low dose of 0.02–0.05 mg/kg with provision of urgent dialysis in cases of hemolysis.

Step 8: Treat Associated Electrolyte Disorders

- Hyperkalemia—hemodialysis may be needed if renal insufficiency or volume overload is present.
- Hypocalcemia—if asymptomatic, no therapy is required.
- Hyperphosphatemia—restrict phosphate intake and increase loss with phosphate binders such as aluminum hydroxide or calcium carbonate, sevelamer hydroxide, and lanthanum carbonate.

Step 9: Consider Hemodialysis

- This modality should be considered in specific situation such as:
- Volume overload
- Uric acid of more than 10 mg/dL despite rasburicase
- Uncontrolled hyperkalemia and hyperphosphatemia
- A calcium X phosphate product >70
- Renal failure (Table 9.2)

Superior Vena Cava Syndrome

A 19-year-old patient with lymphoma presented with dyspnea, swelling of the head and the neck, and upper limbs, and distended veins on the neck and the upper chest.

SVC syndrome results from obstruction of blood flow in the SVC. The majority of cases are due to lung cancer or Non Hodgkins Lymphoma.

Step 1: Resuscitate

Resuscitation (refer to Chap. 23, Vol. 2).

Compression of the tracheobronchial tree causing airway compromise is an airway emergency, needing intubation (with a small size endotracheal tube) and ventilation till definitive treatment is initiated. Propped up position to help venous drainage. Do not give intravenous or intramuscular injections in upper extremity.

Step 2: Do Imaging

- Computed tomography (CT) scan of chest with or without venography is diagnostic
- These patients may not be able to lie supine for CT chest
- They have to be intubated prior to CT or empirical therapy needs to be started
- Upper extremity venogram or duplex ultrasound for patients with a central venous catheter in upper extremity to exclude venous thrombus.

Table 9.2 Treatment for tumor lysis syndrome

Intervention	Dosage	Comment
Fluids	3 L/m^2/day (200 mL/kg/day if ≤10 kg)	Exercise caution if congestive heart failure
Allopurinol	Oral dose: 50–100 mg/m^2 every 8 h orally (maximum 300 mg/m^2/day) or 10 mg/kg/day divided every 8 h (maximum 800 mg/day)	Drug interactions with 6-Mercaptopurine, azathioprine, thiazide diuretics, amoxicillin, cyclophosphamide, and methotrexate require dose reduction
	IV: 200–400 mg/m^2/day in 1–3 divided doses (maximum 600 mg/day)	Renal impairment—50% dose reduction
		Drug interaction with thiazide diuretics, ampicillin/amoxicillin
Febuxostat	60 mg/day PO	Can be considered in patients with hypersensitivity to allopurinol or those at intermediate risk of TLS
Rasburicase	IV infusion 0.1–0.2 mg/kg/day in 50 mL normal saline over 30 min, for 5 days	Contraindicated in glucose-6-phosphate dehydrogenase deficiency
		Adverse reactions—anaphylaxis, rash, hemolysis, and methemoglobinemia
Hyperkalemia	Calcium gluconate: 10 mL of 10% solution or calcium chloride (5–10 mL of 10% solution) by slow IV infusion for life-threatening arrhythmias	ECG monitoring
	Salbutamol nebulizer	
	Regular insulin: 0.1 U/kg IV + 25% D (2 mL/kg) IV	
	Sodium bicarbonate: 1–2 mEq/kg IV, push only if pH <7.2	Sodium bicarbonate and calcium not to be administered through the same line
	Sodium polystyrene sulfonate: 1 g/kg/day in 1–4 doses with 50% sorbitol PO/PR	Avoid PR route in neutropenics
	Dialysis: if severe	
Hypocalcemia	Calcium gluconate: 10 mL of 10% solution IV administered slowly or calcium chloride	ECG monitoring
Hyperphosphatemia	Hydration	Limit aluminum hydroxide use to 1–2 days to avoid cumulative aluminum toxicity
	Aluminum hydroxide: 50–150 mg/kg/day in divided doses PO or nasogastrically every 6 h	
	Dialysis: if severe	

Step 3: Confirm Diagnosis

- Obtain biopsies before instituting therapy if diagnosis is uncertain. Proper hemostatic measures should be taken while performing invasive procedures
- Current management guidelines stress the importance of accurate histologic diagnosis prior to starting therapy

Step 4: Chemotherapy and Corticosteroids

- These can be used, especially in tumors that are chemosensitive/steroid sensitive.

Step 5: Radiotherapy

- This is a standard treatment modality for sensitive tumors but may take a few weeks to show effect. Steroids are commonly used to prevent post-radiation swelling especially if there is pre-existing laryngeal edema.
- Emergency RT is no longer considered necessary on presentation in most cases

Step 6: Stenting of the Superior Vena Cava

- It has been shown to be effective and feasible in relieving the symptoms of superior vena cava syndrome
- Current guidelines recommend upfront use of an endovascular approach, in severely symptomatic patient. (Stridor due to central airway obstruction, laryngeal edema, coma due to cerebral edema)

Step 7: Thrombolysis and Long Term Anticoagulation

- Endovascular methods serve as a “bail-out” strategy in patients with life threatening symptoms such as cerebral edema, laryngeal edema or hemodynamic compromise. These usually obviate surgical interventions in patients with limited life expectancy.
- Patients with extensive thrombosis or stenotic SVC obstruction lesion may be considered for local catheter-directed thrombolysis or mechanical endovascular thrombectomy.

Step 8: Surgical Treatment

- Should be considered in patients with malignant thymoma, thymic carcinoma and selected patients of non-small-cell lung cancer along with other adjuvant therapy.

Malignant Spinal Cord Compression

A 68-year-old patient with carcinoma of prostrate developed worsening back pain progressively with radiating pain down the right leg associated with weakness and difficulty in walking and loss of bladder and bowel function.

Step 1: Resuscitate (See Chap. 23, Vol. 2)

(a) Pain relief with adequate analgesics is a priority in these patients.
(b) Urgent neurosurgical, radiotherapy, oncology consultation for limb salvage is necessary.
(c) Special precaution needs to be taken while transporting these patients.

Step 2: Do Imaging

- In patient with high index of suspicion and symptoms suggestive of metastatic bone disease, magnetic resonance imaging is gold standard for diagnosis.
- Alternative is CT scan of spine.
- It is important to image the entire spine as more than one area of compression may be present.

Step 3: Start Glucocorticoids

(a) Dexamethasone is indicated in patients with motor deficits or radiologic evidence of neural compression.
(b) It is given as an initial intravenous dose of 10–16 mg followed by 4 mg every 4 h.
(c) Ideally within 12-h of onset of symptoms. Definitive therapy with RT or surgery should be implemented and steroids promptly weaned usually over 10–12 days.
(d) Use proton pump inhibitors or H_2 blockers along with high dose of corticosteroids.

Step 4: Consider Surgery

- It is indicated in most cases, especially in patients with a good performance status. Indications are the following:
  - Gross instability of the spine
  - Rapidly progressive symptoms
  - Progressive symptoms during radiation therapy
  - When tissue for diagnosis is needed
  - Radio-resistant tumors
- Aggressive surgical treatment and post-operative RT should be considered for those with a more favorable prognosis, or who are expected to have a higher potential neurological recovery.

Step 5: Consider Radiation Therapy

- This has been the mainstay of the treatment in patients with and without motor deficit.
- This is usually combined with surgery for spine stabilization.

Step 6: Consider Chemo-Hormonal Therapy

- Hormonal chemotherapy and zoledronic acid should be considered in sensitive tumors such as prostate cancer, testicular tumor, or lymphoma.

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Part III

Trauma and Burn

General Management of Trauma

10

Deepak Govil and G. Praveen Kumar

A 40-year-old male patient hit by a car about 3 hours ago presented in the hospital. He had a labored breathing; his respiratory rate was 30/min with O_2 saturation of 95%. His heart rate was 132/min, blood pressure was 105/80 mmHg, and Glasgow coma score (GCS) was 8/15. After initial stabilization, the secondary survey revealed multiple rib injuries on the left side of the chest and fracture of the left femur.

Trauma is a major cause of death and disability in the first four decades of life. Improvement and organization of trauma care services are a cost-effective way of improving patient outcome. Proper organization of these systems reduces the time between injury and the definitive care, thereby reducing the morbidity and mortality.

Step 1: Preparation

- Alert the trauma team about the arrival of the injured patients and number of causalities so that rapid resuscitation can be initiated
- Trauma team includes the general/trauma surgeon, the emergency physician, the orthopedic surgeon and the critical care/anaesthesia specialist on call, and at least two trained nurses and two paramedics
- Besides the surgeon, the trauma team can also be led by an emergency medicine or critical care/anaesthesia specialist who is skilled in airway management
- Alert the imaging, laboratory services, blood bank and operating room personnel about arrival of a polytrauma patient
- Airway cart, crash cart, suction, monitors and IV cannula, warm IV fluids, and other equipment should be rechecked
- The team members should be ready with universal precautions by putting on mask, splash-resistant and lead gowns, eye protection, and gloves

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Step 2: Triage

- Triage is a process of determining the priority of treatment based on the patient's airway (A), breathing (B), and circulation (C) as well as availability of resources
- Injured patients can be categorized into five categories
  - The injured patient with compromised ABC who needs immediate treatment (red)
  - The injured patient with stable ABC whose treatment can wait (yellow)
  - Those with minor injuries (walking wounded), who need help less urgently(green)
  - The unsalvageable patients who are beyond help (blue or gray)
  - The injured patients who are already dead (black)
- A simple tool, which can be used for triage, is START (simple triage and rapid treatment) (Fig. 10.1)

Step 3: Primary Survey and Resuscitation

- The "ABCDE" of primary survey is, in essence, to identify injuries with immediate threat to life and institution of life-preserving therapies
- The management is concurrent with the assessment, resuscitation, and stabilization
- A 10 s assessment tool can rapidly assess patients ABCD. Ask the patient to identify himself and narrate the incident. A patient with normal and clear speech and normal level of consciousness, is unlikely to have a major compromise in ABCD, and unlikely to have a major event immediately
- Take history from the accompanying person about the following:
  - Mechanism of injury
  - Injuries suspected
  - Vital signs
  - Treatment en route to hospital
- Detailed history shouldn't interfere with primary survey, identification and treatment of life threatening injuries

ABCDE
Airway maintenance with cervical spine control
Breathing and ventilation
Circulation/hemorrhage control
Disability/neurological status
Exposure/environmental control

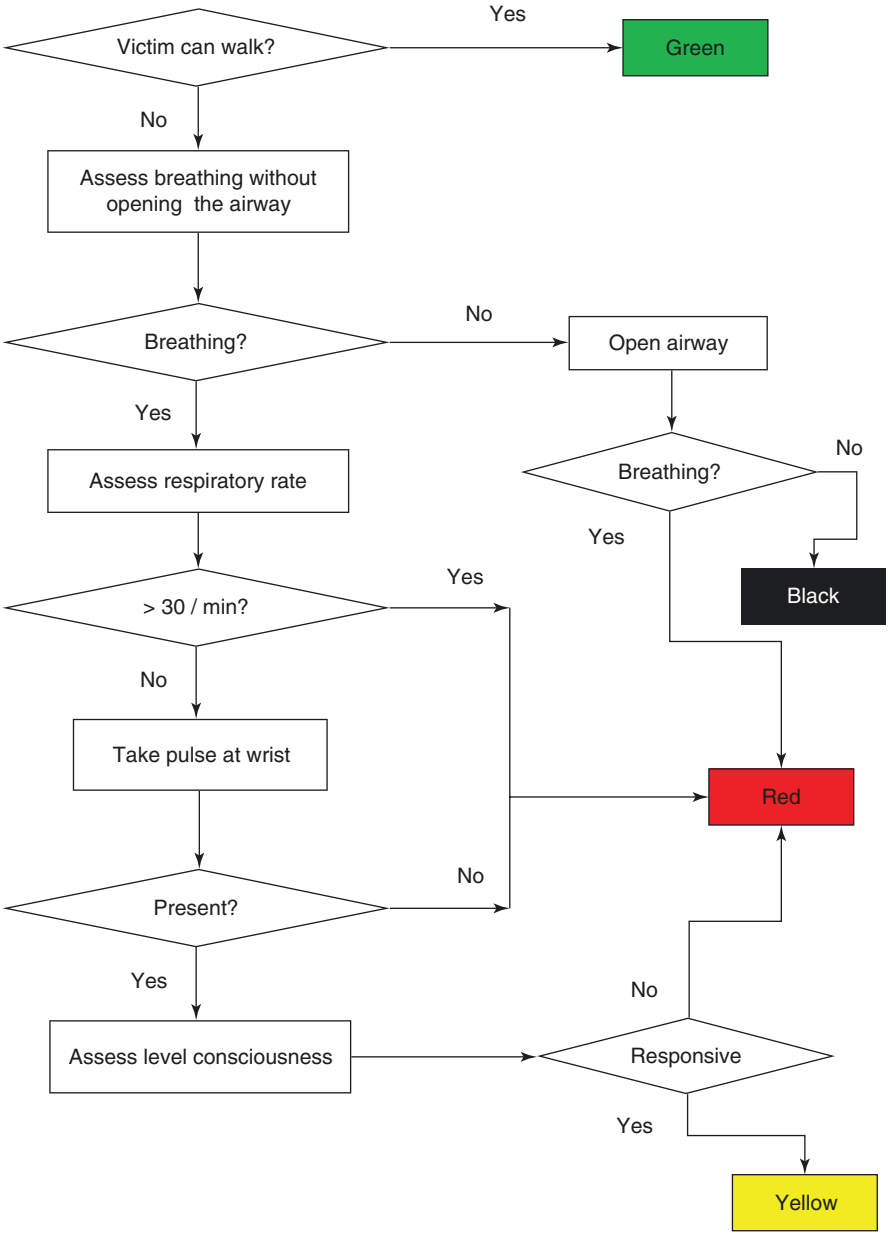

Fig. 10.1 Simple triage and rapid treatment

Airway with Cervical Spine Control

- Airway is assessed immediately for patency, protective reflexes, foreign body, secretions, and injury and burns
- The patency of the airway should be assessed with special attention to foreign body or maxillofacial fractures and laryngeal injuries that may result in airway obstruction
- Absence of response, stridor, confusion, or a hoarse reply may indicate airway compromise
- Chin-lift or jaw-thrust maneuver may be used to achieve airway patency, simultaneously protecting the cervical spine, either by a cervical collar or by manual restriction by team member
- Head tilt maneuver should be avoided in an injured patient while managing airway
- A definitive airway is required in the following conditions*:*
  - Inadequate ventilation and oxygenation
  - Impending or actual airway obstruction secondary to injury
  - Brain injury with a GCS of less than 8
  - Inability to adequately protect the airway from aspiration
  - Severe multisystem injury or hemodynamic instability
  - Facial burns or inhalation injury
  - Inability to closely monitor during ongoing resuscitation and investigation (e.g., angiography and CT scanning)
  - Uncooperative or combative behaviour
  - An infant or a child unable to cooperate with investigations
- Cervical spine protection (by application of cervical collar or manual restriction) during airway maneuvers should be done in all trauma patients unless specifically cleared for cervical spine injury preferably by a neurosurgeon.
- Three person intubation technique should be followed in all trauma patients
- Drug assisted intubation protocol should be followed in all trauma patients for securing airway
- Ketamine 1–2 mg/kg or Etomidate 0.2–0.3 mg/kg along with 1–2 mg/kg succinylcholine is used, depending on the hemodynamic stability
- Succinylcholine should be used with utmost caution in patients with pre-existing neuromuscular diseases, paralysis, renal failure, and in patients with major crush injuries, burns and electrical injuries as this can worsen potassium levels.
- Difficult or failed intubations
  - Call senior anesthesiologist or a more experienced person
  - Anticipate airway problems with the following:
    Injury to cervical spine
    Maxillofacial and neck trauma
    Facial and inhalational burns
    Obesity
    Variations in anatomy

- *Airway—management options with cervical spine control treatment include:*
  - Oxygen administration
  - Basic airway maneuvers: chin lift and jaw thrust (no head tilt)
  - Oropharyngeal or nasopharyngeal airway, with caution in bleeding and conscious patient
  - Adjuvants: Laryngeal mask airway, laryngeal tube airway and intubating LMA
  - Endotracheal intubation
  - Surgical airway, that is, cricothyroidotomy/tracheostomy
- Percutaneous tracheostomy is not recommended in emergency trauma situations

Breathing and Ventilation

- Chest wall mechanics are altered due to rib fractures and pulmonary contusions and cervical cord injury
- Breathing is assessed by determining the patient's respiratory rate and by subjectively quantifying the depth and effort of inspiration
- The patient's chest should be exposed to adequately assess chest wall excursion
- Identify injuries that hampers ventilation by rapid but thorough physical examination.
  - Flail Chest
  - Tension pneumothorax (hyper resonance on percussion with midline shift)
  - Hemothorax (dullness on percussion)
  - Tracheo-bronchial injuries (crepitus on palpation)
  - Open pneumothorax (sucking chest wound)
  - Cardiac tamponade (muffled heart sounds, Kussmaul's breathing)
- If tension pneumothorax is identified, immediate needle decompression in fifth intercostal space in mid axillary line should be performed, followed by intercostal tube drainage
- Needle decompression in second intercostal space in no longer recommended as a first choice
- Rapid respiratory effort, use of accessory muscles of respiration, hypoxia, hypercapnia, asymmetric chest wall excursions, and diminished or absent breath sounds will require treatment before proceeding further
- *Breathing—treatment options include:*
  - Endotracheal intubation and ventilation
  - Needle decompression
  - Intercostal tube drain
  - Pericardial drainage
  - Thoracotomy
  - Adequate analgesia

Circulation with Hemorrhage Control

- Hypotension in a trauma patient is always assumed to result from significant hemorrhage (>30% blood loss), once tension pneumothorax is ruled out
- Rapid and accurate assessment of the patient's hemodynamic status and identification of the site of hemorrhage is therefore essential
- It is critical to establish two large-bore short-length intravenous cannulas(16G or bigger) in a trauma patient, preferably in the upper extremities, and resuscitation should be started with warm crystalloids
- All patients with significant haemorrhage should receive Tranexemic acid within 3 h of trauma (1 g as a bolus followed by 1 g over 8 h)
- Blood and blood products transfusion should be done in patients with ongoing hemodynamic instability after initial fluid boluses, preferably in the ratio of 1:1:1 (PRBC:FFP:Platelets)
- Colloids should not be used in hemorrhagic shock
- All patients requiring massive transfusion should be identified early by using simple scores like Trauma Associated Severe Hemorrhage (TASH) and ABC score
- Point of care assessment for coagulopathy by thromboelastography (TEG) or other viscoelastic test should be done
- All steps to prevent hypothermia, acidosis and coagulopathy should be initiated
- Look for blood in five places: chest, abdomen, pelvis, long bones and floor (for missed bleeding source)
- Chest and pelvic radiographs and an extended focused assessment by sonography in trauma (eFAST) should be done in all trauma patients. Diagnostic peritoneal lavage (DPL) can be considered in select patients
- Diagnostic peritoneal lavage should not be considered in patients with morbid obesity, previous abdominal surgeries, coagulopathy and advanced liver cirrhosis
- Hemorrhage control by direct application of external pressure and/or careful application of tourniquet may be done in all patients. Tourniquets should be left in place till the bleeding is controlled surgically, but the time should be limited
- Pelvic ring should be closed using pelvic binders if the bleeding is suspected from an unstable pelvis
- Fractured long bones should be reduced, and traction splint applied if they are possible source of bleeding to decrease ongoing blood loss and pain as well as to prevent further local injury
- Damage control resuscitation should be considered in all hemodynamically unstable trauma patients due to hemorrhagic shock
- Repeated reassessment should be carried out to identify initial responders who would eventually become non responder
- *Circulation and hemorrhage control—treatment options include:*
  - Two large bore iv cannulas (16G or bigger)
  - Warm fluids (crystalloids)

- Warm blood and blood products
- Early use of tranexamic acid
- eFAST for early identification of source
- Arrest bleeding by direct local pressure and tourniquets
- Arrest bleeding by splinting pelvis and long bones
- Urinary catheter
- Surgery—laparotomy, thoracotomy, and/or pelvic fracture fixation should be undertaken to control bleeding
- Repeated assessments

Disability/Neurological Status

- A rapid neurological evaluation is carried out at the end of primary survey only after the resuscitation and stabilization have been achieved as mentioned above
- This assesses the patient's level of consciousness, pupillary size and reaction, and focal neurological deficit
- The level of consciousness may be described in terms of the GCS
- The GCS is used as a baseline determination of neurological function, and frequent reassessment is required to detect an early or previously missed injury
- Hypoglycemia, drug and alcohol intoxication should be considered for altered consciousness, but all trauma patients with altered GCS have brain injury unless proved otherwise
- A complete neurological examination is not appropriate at this time and should be performed during secondary survey
- *Disability—treatment options include:*
  - O_2 administration
  - Intubation (to ensure normal PO_2 and PCO_2)
  - Avoid hypotension and hypoxia to prevent secondary brain damage
  - Inotropes/vasopressors (to ensure adequate cerebral perfusion)
  - Head up, ensure venous drainage
  - Emergency imaging of the brain or spine
  - Early neurosurgical consultation

Exposure/Environmental Control

- The patient should be completely undressed to facilitate thorough examination and assessment in front and back
- At the same time, care should be taken to prevent hypothermia
- Remove wet or blood-soaked clothes, and use warm IV fluids (39 °C)
- Use blood warmers for transfusing and external warming (warmed blankets to all patients and forced, heated air, or radiant warmers as needed) to prevent hypothermia

Step 4: Adjuncts to Primary Survey and Resuscitation

(a) *ECG monitoring*
- The appearance of dysrhythmias may indicate blunt cardiac injury
- Pulseless electrical activity, the presence of cardiac rhythm without peripheral pulse, may indicate cardiac tamponade, tension pneumothorax, or profound hypovolemia
- Extreme hypothermia can also be the cause of cardiac rhythm disturbances

(b) *Urinary catheter*
- Urine output is a sensitive indicator of the volume status of the patient and reflects renal perfusion
- All trauma victims should be catheterized to enable monitoring of the urine output and to plan intravenous fluid therapy
- Transurethral catheterization is contraindicated in patients whom urethral transaction is suspected (presence of blood in meatus or perineal ecchymosis)

(c) *Gastric catheter*
- A nasogastric tube is indicated to reduce stomach distension and decrease the risk of aspiration. An orogastric is preferred in patients with skull base fracture.

(d) *X-rays and diagnostic studies*
- The chest and pelvis X-rays help in the assessment of a trauma patient
- The blood should be sent for crossmatching and arranging for packed cells, and important diagnostic parameters such as hemoglobin, coagulation profile, renal parameters, electrolytes, random blood sugar, and arterial blood gas (ABG) should be checked
- Pulse oximetry is a valuable adjunct for monitoring oxygenation and adequacy of peripheral circulation in injured patients

(e) *eFAST (extended focused assessment with sonography for trauma)*
- The FAST is a rapid, bedside, ultrasound examination performed to identify intraperitoneal hemorrhage or pericardial tamponade. FAST examines four areas for free fluid: perihepatic and hepatorenal space, perisplenic, pelvis, and pericardium
- eFAST helps in identifying pneumothorax and hemothorax

Step 5: Consideration for Interhospital Transfer

- Identify the early, potential need for transfer of the polytrauma patient to an institution where definitive care can be undertaken
- Transfer decision should be on the basis of known injuries and patterns of injury
- An effective communication including the condition of the patient, treatment given, and anticipated requirements during transfer should be made to the receiving hospital

Step 6: Admit in ICU

- Airway protection and mechanical ventilation
- Cardiovascular resuscitation
- Severe head injury
- Organ support
- Correct coagulopathy
- Invasive monitoring
- Active rewarming of hypothermic patients

Step 7: Secondary Survey

- Once the primary survey is accomplished—life-threatening conditions are managed and resuscitative efforts are underway—secondary survey is carried out
- This is a head-to-toe evaluation of the trauma patient, which includes a complete history and physical examination and reassessment of all the vital signs
- History includes the following:
  - A—Allergies
  - M—Medications currently taken
  - P—Past illness/pregnancy
  - L—Last meal
  - E—Events/environment related to the injury
- Each region of the body is completely examined
- The care should be continued with regular reevaluation of the patient for any deterioration and new findings so that appropriate measures can be taken

Reevaluation

- After the completion of the secondary survey, the patient should be reevaluated beginning with the ABCs and thorough physical examination and examined for any missed injury (tertiary survey) such as fractures
- Constant monitoring of the severely injured patient is required and may necessitate rapid transfer to the surgical intensive care unit, operating room, or to another centre having better specialized facilities
- Appropriate referral for specialists should be sent
- Adequate pain relief, tetanus prophylaxis, and antibiotic should be given
- Specific care should be taken to examine the possible missed injuries on the following:
  - Back of the head and the scalp
  - The neck, beneath semirigid collar
  - Back, buttocks, and flanks
  - Groin creases, perineum, and genitalia

Step 8: Sending Investigations

- Hemoglobin
- ABG
- Hematocrit
- Renal function tests and electrolytes
- Blood sugar
- Total leukocyte count
- Platelet count
- Liver function tests and coagulation tests
- Blood grouping and cross matching
- Urine pregnancy test (14–45 years)
- ECG
- Breath/blood alcohol

Radiological

- Plain radiographs
- CT scanning
- Contrast studies
- Angiography
- Ultrasound (including plain sonography echocardiography and color-flow Doppler)
- Endoscopy

Step 9: Tertiary Survey

- Tertiary survey consists of a repeat of the primary and secondary survey examinations, reassessment of the functions of all tubes and catheters, and review of all X-rays
- It is routinely performed in the morning after the patient's admission to detect any injuries not picked up earlier and to minimize the missed injuries

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Traumatic Brain and Spinal Injury

11

Kapil Zirpe and Balkrishna Nimavat

A 25 year old adult had alleged history of bike skid. On arrival to the emergency department, he was found to be unconscious with bleeding from the scalp. Patient had history of vomiting twice. His pulse rate was 60/min and blood pressure was 140/80 mmHg. The pupillary size showed asymmetry and his breathing was laboured.

Traumatic brain injury (TBI) is the leading cause of mortality and morbidity in children and young adults in both developed and developing nations worldwide. The aims and objectives of its management are prompt management of intracranial hypertension and secondary brain injury, maintenance of cerebral perfusion pressure, and ensuring adequate oxygen delivery to injured brain tissue.

Step 1: Initial Assessment/Components of Primary Survey

Airway Control and Ventilation

Airway, breathing and circulation takes precedence in spite of obvious head injury.

- Secure cervical spine with a cervical collar: The unstable cervical spine injury can occur in 5–6% cases of the TBI. Risk factors include a motor vehicle collisions, assaults, falls and a GCS less than 8.
- In suspected cervical spine injury, orotracheal intubation and ventilation with 100% oxygen along with manual in—line cervical immobilization with cervical

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collar off to reduce the chance of worsening a neurological injury until radiological clearance is obtained.
- Prevent hypoxemia: Avoid PaO_2 less than 60 mmHg or O_2 saturation below 90%.
- Consider Rapid Sequence Intubation. Succinylcholine or rocuronium may be used as muscle relaxant. Although succinylcholine may produce a small increase in ICP, this has not proven to be clinically significant. To facilitate intubation an opiate such as fentanyl (1 μg/kg) may be used, there is no evidence to support the use of lidocaine during intubation.
- Adequate sedation and muscle relaxation tends to reduce the cerebral metabolic oxygen requirement ($CMRO_2$), optimize ventilation and prevent coughing or straining.
- Choice of sedative agent: Anaesthetic drugs that allow for rapid control of the airway while avoiding an increase in intracranial pressure (ICP) and providing hemodynamic stability are preferred. Propofol and thiopental are the most commonly used drugs, but they may cause hypotension. Etomidate has advantages in terms of cardiovascular stability, but the possibility of adrenal suppression exists. Ketamine is popular in trauma patients and recent evidence suggests that its effect on ICP may be limited
- Ventilator strategy:
  - Hypoventilation should be avoided, as increased PCO_2 levels may lead to cerebral hyperemia with an increase in blood volume and ICP.
  - Hyperventilation, on the other hand, results in an increased risk of vasoconstriction and increased tissue hypoxia, especially in the penumbra zone, so it is best avoided. CO_2 level should be kept in low normal zone by the use of End Tidal CO_2 monitor in most intubated patient. Ventilator should be adjusted to achieve a PaO_2 of ~60 mmHg, which can oxygenate the penumbra zone. High PaO_2 should be avoided considering the risk of hyperoxic cerebral vasoconstriction. PEEP of 5–10 cmH_2O may be administered to prevent atelectasis and has been proven to be safe in these patients
  - Hyperventilation up to a $PaCO_2$ between 32 and 36 mmHg for the purpose of reducing ICP is recommended for a brief period of time to avoid brain herniation.

Blood Pressure and Cerebral Perfusion

Pressure (CPP)

- Maintain systolic blood pressure >100 mmHg in patients with 50–69 years old, and >110 mm Hg in patients 15–49 years or >70 years old.
- In a hypotensive TBI patient, hypovolemia resulting from non cranial hemorrhage should be ruled out.
- Choice of fluid: Hypotonic solutions like 5% dextrose should be avoided. Isotonic normal saline is the most common crystalloid used in TBI patients, but Ringer's

lactate or other balanced crystalloids are an alternative and result in less acute kidney injury. Infusion of large volumes of normal saline results in adverse hyperchloremic metabolic acidosis that is detrimental in TBI. On the other hand balanced crystalloids are relatively hypotonic and may exacerbate cerebral edema.

- Colloids appear to provide no further benefit.
- Saline is preferable to albumin resuscitation as the later has been found to increase mortality in TBI patients
- The recommended target CPP (MAP-ICP) value for survival and favourable outcomes is between 60 and 70 mmHg.
- Vasopressors are commonly used to augment CPP in the setting of TBI but avoid aggressive attempts to maintain CPP above 70 mmHg with fluids and pressors.
- Labetolol is the drug of choice for control of hypertensive emergency in TBI.

Step 2: Secondary Survey/Neurological Assessment

Neurological Assessment

- Glasgow coma scale (GCS) has been the most widely used method of recording the level of consciousness in patients at presentation and at subsequent assessment. A score of ≥13 correlates with a mild brain injury, 9–12 is a moderate injury, and ≤8 a severe brain injury.
- Patients with a Glasgow Coma Scale ≤13 and moderate to severe extracranial anatomical injuries should be rapidly transferred to the higher level of care.
- TBI can be classified based on severity and morphology (Table 11.1)

Table 11.1 Classification of TBI

Based on severity (GCS)	Mild	13–15	
	Moderate	9–12	
	Severe	<9	
Based on morphology	Skull fractures	Vault	Linear vs. stellate/compound
			Depressed/nondepressed
		Basilar	With/without CSF leak
			With/without cranial nerve palsy
	Intracranial lesions	Focal	EDH, SDH Intracerebral
		Diffuse	Hypoxic/ischemic injury Diffuse axonal injury Multiple contusion Concussion

Step 3: Do Imaging—CT Scan

Indications of CT in TBI

- CT scan brain should be carried out in all moderate to severe TBI.
- For mild TBI CT scan indications are:
  - Open or depressed skull fracture
  - Sign of basilar skull fracture
  - Vomiting more than 2 episodes
  - Age >65 years
  - Anticoagulant use
  - Seizure

Step 4: Monitoring of ICP and Measures to Reduce ICP

ICP Monitoring and Management

- ICP monitoring is important, but it does not replace careful neurological and radiological examination. ICP should be monitored in patient with GCS of 3–8.
- ICP should also be monitored in patient with severe traumatic head injury with normal CT scan if patient is above 40 years, unilateral or bilateral motor posturing, or systolic pressure less than 90 mmHg
- Patients with elevated ICP have been shown to have worse outcomes and are at a higher risk of mortality.
- Management of severe TBI patients based on ICP monitoring may reduce in hospital and 2-week post-injury mortality;
- Clinical judgement should be used to initiate intracranial monitoring in patients who are at a high risk of clinical deterioration.
- It is recommended to treat ICP > 22 mmHg to reduce mortality.

Initial measures of raised ICP include head of bed elevation, keeping neck in neutral position appropriate sedation and analgesia, osmotherapy and removal of CSF.

Sedation and Analgesia

- Sedatives and analgesics can affect outcomes in head-injured patients.
  - Adequate pain control and sedation can be used as initial measures to control raised ICP.
  - Short-acting agents such as fentanyl, midazolam, or propofol are preferred for frequent neurological assessments. (Table 11.2). High dose barbiturates are recommended to control ICP refractory to maximum standard surgical and medical treatments while ensuring hemodynamic stability.

Table 11.2 Drugs and doses of sedatives and analgesics

Commonly used sedatives	
Fentanyl	2 mcg/kg test dose, 2–5 mcg/kg/h continuous infusion
Midazolam	2 mg test dose, 2–4 mg/h continuous infusion
Sufentanil	10–30 mcg test bolus, 0.05–2 mcg/kg continuous infusion
Propofol	0.5 mg/kg test bolus, 20–75 mcg/kg/min continuous infusion (not to exceed 5 mg/kg/h)

Hemodynamic stability is essential before and during barbiturate therapy. Although propofol may be used for ICP control, it is not recommended for improvements in mortality or 6-month outcomes

- Care should be taken to maintain an adequate mean arterial pressure throughout the duration of sedation. Minimising sedation duration helps in decreasing Incidence of delirium and helps in early mobilization

Start Osmotherapy

- Osmotherapy with mannitol or hypertonic saline has been used since many years but controversy remains regarding which solution is the best agent and regarding the best method of administration.
- Mannitol is used more often as intermittent boluses (0.25–1 g/kg). It should be stopped if serum osmolality exceed 320 mOsm/L. It should be avoided in hypovolemia and renal failure patients. Hypertonic saline as intermittent boluses of 3% 250 mL over half an hour or 30 mL of 23.4% can also be used. It should be witheld if sodium exceeds 160 mEq/L. Serum sodium and osmolality must be assessed every 6 h.

Decompressive Craniectomy

- Decompressive craniectomy is a surgical procedure that involves removal of a large section of the skull. Craniectomy reduces ICP by giving extra space to the swollen brain, and it may quickly prevent brainstem herniation.
- Decompressive craniectomy may be a life-saving surgery, but it comes at the expense of higher chances of severe disability among survivors.
- Guidelines recommend a large frontotemporoparietal decompressive craniectomy, as opposed to a smaller one, to target reduced mortality and better neurological outcomes.

Step 5: Advance Multimodal Neuromonitoring (Tool to Monitor CPP if Resource Available)

- Identification of the range of autoregulation following TBI to provide individualized CPP therapy may be a means to improve outcome and is made possible by newer monitoring devices.

- Jugular venous oxygen saturation ($SjvO_2$): Used to estimate the balance between global cerebral oxygen delivery and uptake. Both reduction in $SjvO_2 < 50\%$ and $SjvO_2 > 75\%$ after TBI are associated with poor outcomes. Monitoring of $SjvO_2$ following TBI may lead to improved outcomes.
- Brain tissue oxygen tension: $PbrO_2$ represents the balance between oxygen delivery and cellular oxygen consumption. $PbrO_2$ provides a highly focal analysis of brain milieu and may be used to monitor the potentially salvageable penumbra following TBI. Normal values are between 35 and 50 mmHg. Following TBI, reduced levels of $PbrO_2$ (<5–10 mmHg) have been seen to be associated with poorer outcomes.
- Cerebral microdialysis: Increasingly used as a bed side tool to provide analysis of brain homeostasis in the intensive care setting. Severe ischemia is usually associated with significant increases in the lactate/pyruvate ratio (>20–25) and is associated with poor outcomes following TBI.

Step 6: Pharmacotherapy

Anticonvulsant Therapy

- Posttraumatic seizures are a major cause of secondary brain injury following TBI, and are associated with higher injury severity and worse outcomes. Seizures occur in up to 20% of patients with TBI. These seizures are usually nonconvulsive in nature and cannot be detected clinically and EEG monitoring (preferably continuous) is needed for this.
- This should be clinically suspected if consciousness impairment is disproportionate to the severity of injury
- Phenytoin or levetiracetam (500–1000 mg every 12 h) is effective in decreasing the rate of early posttraumatic seizures in the first 7 days of injury, but has no significant role in prevention of posttraumatic seizures after the first week of injury.
- Patients with TBI who develop any seizures will require prolonged antiseizure medications.

Role of Steroids

- No benefit in lowering ICP or improvement in patient outcome has been shown through the use of high-dose corticosteroids in acute TBI.
- The use of methylprednisolone in patients with moderate to severe TBI has been demonstrated to increase mortality and is contraindicated.

Antibiotic Therapy

- Since TBI patients are more likely to receive invasive monitoring and therapeutic treatments, including mechanical ventilation, they are also more likely to be at increased risk for the development of infections.
- Sources of potential infections need to be identified and appropriate therapy should be instituted. A common source of infection is invasive monitoring of ICP. The incidence of ICP device infection has been reported to range from 1% to 27%.
- The current guidelines suggest the use of antibiotic-impregnated catheters to reduce infection rates.
- Prophylactic antibiotic should be avoided

Role of Tracheostomy

- Early tracheostomy (preferably percutaneous) should be performed to reduce ventilation days in patients with anticipated prolonged ventilation and/or need for airway protection
- The goals of treatment including clinical, laboratory and monitoring parameters are summarized in Table 11.3

Table 11.3 Goals of treatment

Clinical	Systolic BP	≥100 mmHg, avoid hypotension
Laboratory	Temperature	36–38°, avoid hyperthermia
	Hb	≥7 g/dL
	Glucose	140–180 mg/dL
	INR	≤1.4
	pH	7.35–7.45
	$PaCO_2$	35–45, never less than 25 mmHg
	PaO_2	≥100 mmHg, avoid hypoxemia
	Na	135–145
	Platelet	≥75,000
Monitoring	CPP	≥60 mmHg, 60–70 mmHg
	ICP	<22, 5–15 mmHg
	$PbtO_2$	≥15
	SPO_2	≥95%

No role of prophylactic antibiotic and anticonvulsant. No role of steroid

Step 7: Supportive Care and ICU Bundle

Glycemic Control

- Prevention of hyper- and hypoglycemia Glucose-containing fluids should be avoided and blood sugar monitored to maintain levels between 140 and 180 mg/dL

Nutrition

- Early nutritional support is associated with better outcomes and early enteral feeding has been found to be beneficial.
- Calculated or measured caloric replacement (100–140% of basal expenditure) should be started early and full goal should be reached by 5–7 days
- Post pyloric feeding may also be used reduce the risk of ventilator associated pneumonia.
- Patients with severe TBI have gastric feeding intolerance, Prokinetic agents, such as metoclopramide, may improve feeding tolerance

Temperature Management

- Avoidance and aggressive treatment for fever should be instituted and normothermia should be maintained.
- Prevention of hyperthermia: In clinical practice, even mild hyperthermia has been associated with poorer outcomes and longer ICU stays, as it is may lead to increased brain edema and inflammation.
- Use of Therapeutic hypothermia is controversial.

Thromboprophylaxis

Intermittent pneumatic compression stockings should be used (except in lower limb injuries) and continued till the patient is ambulatory

- Low-molecular-weight heparin (e.g. enoxaparin 40 mg s.c) or low-dose unfractionated heparin (5000 s.c. 3 times a day) should be used in combination with mechanical prophylaxis when it is safe, preferably after 48–72 h of intracranial hemorrhage/craniotomy with close monitoring and repeat NCCT head to detect expansion of hematoma.

Coagulopathy Management

- Coagulation parameters and platelet count should be routinely monitored and if deranged should be corrected in patients with bleeding manifestation or requiring neurosurgery
- Rapid reversal is best attained with Activated prothrombin complex concentrate

- Antiplatelets and anticoagulants should be stopped and there effects reversed if clinically indicated
- **Stress ulcer prophylaxis**: early enteral nutrition, H_2 Blockers or PPI, physiotherapy, and Skin/Eye care.
- **Proper postdischarge care**

Step 8: Identify Complications of TBI

Complications of TBI

1. Trauma induced coagulopathy
2. ARDS/Negative pressure pulmonary oedema
3. Paroxysmal sympathetic hyperactivity/Stress cardiomyopathy
4. Hypothalamic-pituitary-adrenal dysfunction/SIADH/Cerebral salt wasting/DI
5. Hydrocephalus
6. Heterotopic ossification
7. Spasticity
8. Chronic traumatic encephalopathy/Post traumatic headache and depression/Cognitive impairment
9. GI and GU complications
10. Gastric ulceration and DVT

Step 9: Outcome Measures

- Three tools commonly used to measure outcome after TBI are Functional Independence Measure (FIM), Glasgow Outcome Scale (GOS) and Disability Rating Scale (DRS).

Step 10: Prognosis

- Very difficult and complex
- As a general rule patients with GCS < 8 have a 30% risk of mortality
- Patient who remain in vegetative state or minimally conscious state have a poor chance of meaningful recovery
- Recovery with functional independence or partial dependence may occur in >50% of severe TBI over a period of years, if initial aggressive management is pursued
- Individual risk factors for poor outcome are Low GCS score (specially GCS motor score), increasing age, bilaterally absent pupillary light reflex, associated injuries, abnormal CT scan, hypotension, hypoxemia, elevated ICP, reduced CPP, bleeding diathesis, pyrexia.
- CT findings associated with poor prognosis: Absence or compressed basal cisterns, tSAH, presence and degree of midline shift (CT severity) and presence of abnormalities in initial CT.

Traumatic Spine Injury

- Spine injury, with or without neurological deficits, must always be considered in patients with multiple injuries. Approximately 5% of patients with brain injury have an associated spinal injury, whereas 25% of patients with spinal injury have at least a mild brain injury and injury to limbs and viscera
- Approximately 55% of spinal injuries occur in the cervical region producing quadriparesis, 15% in the thoracic region, 15% at the thoracolumbar junction, and 15% in the lumbosacral area. Up to 10% of patients with a cervical spine fracture have a second, non-contiguous vertebral column fracture.
- Early management should incorporate a full Advanced Trauma Life Support (ATLS) assessment with the intent to avoid hypotension, bradycardia, and hypoxia

Manage Traumatic Spinal Injury Patient

1. Early intubation and mechanical ventilation is recommended for patients with high cervical injuries (C1–C5).
2. All trauma victims with suspected cervical spine injury should have cervical spine immobilised until an unstable fracture has been ruled out.
3. All patients with suspected cervical spine injury should have complete spinal imaging by X-ray or CT scan
4. Urgent neurosurgical consultation
5. Mean arterial pressure (MAP) augmentation with norepinephrine (if needed) is recommended for at least the first 72 h following injury to a maximum of 7 days. Goal MAP ≥85 mmHg for blunt/incomplete penetrating injury. Goal MAP ≥65 mmHg for complete penetrating injury
6. Use of high-dose methylprednisolone is not recommended routinely (not after 8 h of onset of injury). Even if it used, it should be within 8 h of onset of injury and in isolated non penetrating spinal cord injury as a 30 mg/kg IV bolus followed by an infusion of 5.4 mg/kg/h for 23 h
7. Early (definition of early not standardized ranging from <8 h to <72 h) neurosurgical decompression of acute spinal cord compression is recommended.
8. Venous thromboembolism prophylaxis should be initiated within first 72 h of injury.
9. Consider early (definition of early not standardized) tracheostomy in high cervical injury (C1–C5) patients.

Rehabilitation should be offered to all patients.

ICU Bundle Care

Nutrition, bowel care (as patient may develop neurogenic bladder and require urinary catheterization), skin care and bed sore prevention, psychological support, thromboprophylaxis, ulcer prophylaxis, treatment of spasticity and neuropathic pain are the supportive care required in spine injury patient.

Suggested Reading

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TorsoTrauma

12

Deepak Govil and G. Praveen Kumar

A 30-year-old male was hit by a motor vehicle about 3 h ago. At presentation, he had a threatened airway with labored breathing; his respiratory rate was 32/min with O_2 saturation of 85%. He had paradoxical chest movements and decreased air entry on the left side. His heart rate was 120/min, blood pressure was 100/80 mmHg, and Glasgow coma scale (GCS) score was 15/15. After initial stabilization and left-sided intercostal drainage (ICD), secondary survey revealed abdominal distention with tenderness over the left upper quadrant of the abdomen. A computed tomography (CT) scan of the chest and abdomen showed multiple rib fractures on the left side of the chest with underlying lung contusion and ICD in situ. It also revealed a shattered spleen and 3-cm laceration in segment 6 of the liver along with 1-cm laceration in the upper pole of the left-sided kidney and pneumoperitoneum suggesting both solid and hollow viscous injury. Exploratory laparotomy was performed. The liver and kidney were preserved, while the spleen was removed, primary repair of bowel segment was performed. The patient gradually recovered in intensive care unit (ICU).

Multiple life-threatening conditions can result from thoracic and abdominal trauma. Multiple factors including mechanism of injury, injured body region, hemodynamic status, and associated injuries determine the diagnostic approaches.

Step 1: Perform Primary and Secondary Survey

Primary Survey (A–E)

A. *Airway with cervical spine protection:* Evaluation of airways is the first priority during primary survey. All patients presenting with threatened airways and respiratory distress should have the airway secured.

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Cervical immobilization is maintained till the injury is excluded by radiological and/or clinical means.

B. *Breathing and ventilation:* Expose the chest to observe chest wall movement, breathing pattern, percuss for dullness/hyper resonance, auscultate breath sounds Monitor oxygenation.
   - Life threatening injuries that should be identified and treated during the primary survey are the following:
     - Tension pneumothorax—immediately a large size intravenous cannula or finger thoracostomy, followed by intercostal tube insertion
     - Massive hemothorax (more than 1500 mL blood or more than one-third patient's blood volume in thoracic cavity)—insertion of a large-bore (28–32 F) chest tube with volume replacement with surgical consult
     - Open pneumothorax—flutter valve dressing, taped on three sides, till ICD is placed; thereafter, closed dressing
     - Cardiac tamponade—pericardiocentesis as a temporary manouever followed by immediate thoracotomy or sternotomy
     - Flail chest with pulmonary contusion—analgesia and elective intubation and positive pressure ventilation
     - Tracheo bronchial disruption—guided intubation distal to the injury site, or unilateral ventilation and immediate surgical intervention

C. *Circulation with hemorrhage control:* The pulse rate, blood pressure, and level of consciousness determine the grade of shock. Circulation volume has to be maintained with isotonic fluids and blood transfusions. Identify the source of bleeding and control it. Urgent hemostatic laparotomy should be considered in all patients with hemodynamic instability and positive abdominal FAST.

D. *Disability (neurologic evaluation)*: Assess GCS and evaluate the pupillary size and reaction to light. Low GCS score may be due to decreased cerebral oxygenation or perfusion (shock) or direct cerebral injury.

E. *Exposure/environment control*: Completely undress the patient for thorough examination and assessment. Do not forget to examine the back. A warm environment should be maintained to avoid hypothermia.

Secondary Survey

- This involves detailed pertinent history, complete in-depth physical examination, relevant radiological, and laboratory investigations with reassessment of vital signs to identify all the injuries
- Injuries to be identified in secondary survey include the following:
  - Pulmonary and myocardial contusion
  - Aortic dissection
  - Traumatic diaphragmatic rupture
  - Tracheobronchial disruption (not identified in primary survey)
  - Esophageal disruption

Step 2: Triage for Surgery

Once the primary survey is concluded, the next step is to triage the nonresponders to emergency surgery—exploratory laparotomy or thoracotomy for damage control or definitive surgery as the clinical situation demands.

- Indications for urgent thoracotomy include:
  - ICD output: Blood more than 1500 mL immediately following insertion of drain or more than 200 mL/h for 2–4 h
  - Endobronchial blood loss
  - Massive pulmonary contusion leading to significant impairment of ventilation
  - Significant Tracheobronchial tree injury
  - Injury of the heart or great vessels leading to pericardial tamponade and hemorrhagic shock
  - Penetrating chest injury as a cause of hemodynamic instability
- Indications for urgent laparotomy include:
  - Hemodynamic instability with penetrating trauma or positive FAST examination in blunt trauma
  - Trans-peritoneal gunshot injury
  - Clinical signs suggesting peritonitis and evisceration
- The rest of the patients should undergo further necessary radiological investigations to identify and assess the exact anatomical injuries and their severity

A simplified approach for evaluation and management of blunt trauma of abdomen is discussed in Fig. 12.1.

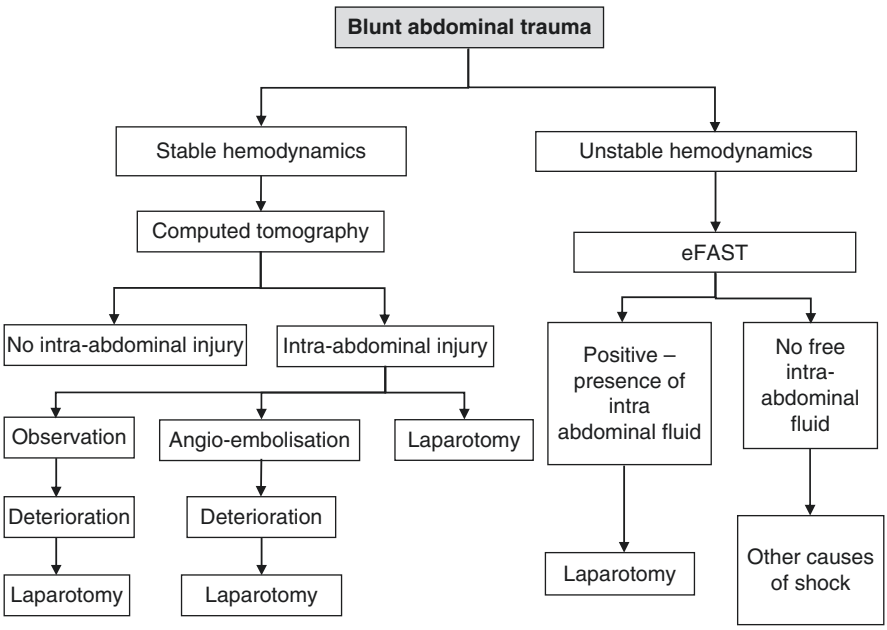

Fig. 12.1 Simplified approach to management of abdominal trauma and intrabdominal injury

Step 3: Triage the Patients to the ICU

- Triaging the patients to the ICU or to the floor (wards) is decided on the basis of the severity of the injury and the extent of surgery, requirement of the mechanical ventilator and inotropic support, age and comorbidities of the patient.

Step 4: Continue to Observe and Treat

While the need for complete and repeated clinical and eFAST examination in the ICU cannot be overemphasized, the following features will have to be focused during the daily examination of the patients:

1. *Ventilation and circulation assessment*
   - Lung protective ventilator strategies should be applied in all trauma patients
   - Pulse rate, blood pressure, urine output, hematocrit, and lactate levels indicate the degree of perfusion and the grade of volume deficit
   - Unstable or critically ill patients might warrant other invasive monitoring techniques such as intra-arterial pressure and cardiac output measurements. Echocardiography should be performed repeatedly for assessment of circulation.
   - Circulation is maintained with fluid and blood transfusion with or without inotropic support
2. *Management of the ICD tube*
   - Monitor volume and nature of the output daily, column movement, presence of air leak, and lung expansion clinically and radiologically.
     - Volume of the output

       Common causes for persistent high output:

       Ongoing Hemorrhage

       Thoracic duct injury

       Hypoproteinemia

       Sudden decrease in the volume of the output: Check for tube blockage or malpositioning. The tube should then be declotted (milking) or repositioned or changed to maintain the patency of the tube.

       Local thrombolytic agents may be used in exceptional cases to maintain tube patency
     - Nature of the output

       Sanguineous output—ongoing hemorrhage: Output of more than 200 mL/h of sanguineous fluid continuously for 4 h is an indication for thoracotomy.

       Turbid output with pyrexia - infective focus. Fluid should be sent for further microbiological analysis, and treatment should be started accordingly. Bacterial or Fungal growth from a drain which is >24 h old may reflect colonisation, a fresh sample with needle aspiration or sample from a new drain should be sent for culture.

Milky white, high-volume output - thoracic duct injury (chylothorax). Presence of chyle may be confirmed at the bedside by dissolving the drained fluid in equal amount of ether. If it gets dissolved, then it is chyle; otherwise, it is pus. Check the triglyceride level. Low output (<1000 mL/24 h) can be managed conservatively. High output usually requires surgical management.

- Wide swinging of column movement (>5 cm) is suspicious of poor lung expansion or lung collapse and should be investigated further with the chest X-ray and bronchoscopy if needed.
- Air leaks indicate the presence of tracheobronchial/parenchymal communication with the pleural cavity.

  Chest tube insertion sites should be checked for peritubal air entry due to loose sutures.

  Treatment of air leak: Minor air leaks usually heal with deep breathing exercises. Persistent air leaks, not settling down with chest physiotherapy alone, require application of negative pressure suction (usually 10 cm H_2O) to the underwater seal bottle. Massive air leaks causing oxygen desaturation will require insertion of a second ICD tube and usually thoracotomy.

  After stoppage of air leak, check the chest X-ray after clamping the tube for 24 h to look for lung collapse, and the ICD tube can be removed if the chest X-ray is normal.

  In case of subcutaneous emphysema, the extent should be marked and monitored daily for change in extent after insertion of the ICD tube. There is no role for skin incisions.
- In cases of clotted hemothorax, declotting is done with streptokinase. 1–1.5 million units of streptokinase is diluted in 100 mL and infused through the ICD tube under aseptic precautions. The tube is then clamped for 3–4 h; chest physiotherapy is done and then the tube is opened. This may be repeated once a day for 3–4 days till clots are evacuated. This procedure is not indicated in patients with coagulopathy or patients on systemic anticoagulation therapy like warfarin.
- Fever, productive cough, and infiltrates in the chest X-ray indicate pulmonary infections. Broad-spectrum antibiotics should be started empirically and changed to specific antibiotics depending on the sensitivity pattern.
- Radiological investigations

  Chest X-rays should be done to monitor the lung expansion and after the removal of the ICD tube to look for pneumothorax.

  Ultrasonography and CT scans should be done for suspected loculated effusions and pneumothorax and to guide its drainage percutaneously.

  The following conditions should be fulfilled before the removal of the ICD tube:

  Less than 50–100 mL output and serous in nature.

  Less than 5 cm swinging of air column with normal breathing.

  Full lung expansion.
- Chest tube insertion sites must be inspected every day for infections and air or fluid leakage with regular care of the wound site.

3. *Tracheostomy site and surgical wound sites:* Inspect for surgical site infection
4. *Regular active and passive chest physiotherapy.* This is required to prevent atelectasis and pneumonia.
5. *Pain control*

   Control pain through nonsteroidal anti-inflammatory drugs, opioids, epidural analgesia, and patient-controlled analgesia devices.
6. *Nutrition*

   Nutrition is maintained with enteral nutrition in most of the cases.

Abdominal injuries

Solid organ injuries are managed either nonoperatively or operatively depending on the severity of the injury and the hemodynamic stability of the patient. Hollow viscous injuries are usually managed operatively.

Whenever applicable damage control surgery along with hemostatic resuscitation should be considered as a first line strategy to prevent triad of death.

Step 5: Nonoperative Management of Solid Organs (Spleen, Liver, and Kidney)

- Nonoperative management should be practiced only in highly specialized trauma centers that have 24-h availability of trauma surgeons and interventional radiologists.
- Initial clinical examination and hemodynamic status dictate the decision rather than the grade of solid organ injury or the degree of hemoperitoneum.
- Daily clinical examination of the abdomen with hemodynamic status assessment is based on pulse rate, blood pressure, urine output, abdominal girth, intraabdominal pressure, and fall in hemoglobin and hematocrit levels.
- No antibiotic coverage is needed in cases of nonoperative management of solid organ injury alone.
- Ultrasound examination of the abdomen is done, if clinical situation demands, to look for significant increase in the intra-abdominal collection.
- Abdominal distention, development of peritoneal signs, and decrease in urine output indicate ongoing hemorrhage and need for operative management.
- Progressive drop in hematocrit with hemodynamic instability should also indicate the consideration for operative management.
- In case of liver injuries, biliary peritonitis may present the clinical picture of intestinal perforations. Clinical and radiological examinations should be performed to rule out missed intestinal injuries, and in their absence, percutaneous drainage of the bile collection can be done, avoiding laparotomy.

Step 6: ICU Care After Operative Management of Abdominal Injuries

- Repeated complete physical examinations should be performed every day.
- In case the abdominal closure seems to be difficult during the primary surgery (due to bowel edema/retroperitoneal collection, etc.), it is prudent to leave it

open as forceful closure would lead to increase in intra-abdominal pressure resulting in the abdominal compartment syndrome.
- Enteral nutrition is started at the earliest and gradually advanced to regular diet as tolerated.
- Immediate enteral feeding is beneficial (in comparison to parenteral) in a critically ill patient regardless of the patient's premorbid nutritional status.
- Care of the feeding jejunostomy tube should be taken properly.
- Conditions suggesting the need for parenteral nutrition are as follows:
  - Oral intake less than 50% of the energy needs
  - Unable to tolerate nasogastric or nasojejunal feed for more than 7 days in previously well-nourished patient.
  - Nonfunctioning gastrointestinal tract
- Inspection of the surgical sites is done for signs of inflammation and infection.
- Monitoring of the drain output and nature of fluid should be done.
- In case the drains show persistent and/or purulent output, it can be indicative of deep surgical site infections or intestinal fistulae. If such is the case, rapid clinical/radiological examination followed by opening of laparotomy incision site and thorough lavage is indicated. If intestinal fistulae are present, it should be treated either surgically or nonoperatively depending on its location and output.
- Persistent high drain output in cases of pancreatic and splenic injury should raise suspicion of the pancreatic fistula.
- Drain amylase should be requested on or after the third postoperative day in cases of suspected pancreatic fistula in cases of pancreatic and splenic injury.
- Continuing with the drains, if necessary CT guided drainage, antibiotic coverage (if signs of infections present), serial radiological examinations, and drainage of collections is recommended for the treatment of pancreatic fistulae. Use of somatostatin or its analogue may be useful in such situations.

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Burn Management

13

Sushma Sagar, Kamal Kataria, and Maneesh Singhal

A 50-year-old male patient with history of alcohol abuse was admitted to the emergency department with burns while sleeping in a closed room. On arrival, he was conscious and oriented with cold, clammy extremities and feeble pulse. Blood pressure was 80/50 mmHg. He had 60% burns involving face, torso, and extremities. Over the right lower limb, there were circumferential burns and swelling with absent pulsations. There was hoarseness of voice with production of sooty sputum. Chest radiograph was normal.

The mortality and morbidity of burn patients have improved due to improvement in the care over the past few decades. Local burn wound care and long term systemic, social and psychological care need to be addressed. The removal of deep wounds and biological closure helps to attenuate the development of wound sepsis. The care of the burn patient requires very advanced critical care, preferably in the burn unit.

First Day

Step 1: Initial Assessment and Resuscitation

All burn patients should be approached as a polytrauma patient. All severe burn injury that is complicated by major trauma or inhalational injury, chemical burns, high-voltage electrical burns, and in adults deep burns covering more than 20% of body surface area should be managed in a dedicated burn unit.

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Airway

- The airway is assessed first by asking the name of the patient and listening to hoarseness, which signifies upper airway burn.
- One hundred percent oxygen is administered, and oxygen saturation is monitored using pulse oximetry. Beware of falsely high saturation due to high carboxyhemoglobin levels in cases of carbon monoxide intoxication due to inhalation injury. Confirm oxygenation by measuring true oxyhemoglobin in blood gas analysis with a CO-oximeter which also measures carboxyhemoglobin levels.
- Wheezing, tachypnea, stridor, and hoarseness indicate impending airway obstruction due to an inhalation injury or edema, and immediate treatment is required.
- If the patient is not breathing or has labored respiration or signs of obstruction, clear the airway by oral/nasal suction followed by orotracheal intubation with in-line stabilization of the neck if an injury to the cervical spine is a consideration.
- Risk of upper airway obstruction increases with the following:
  - Inhalation burns—carbonaceous sputum, singed nasal hairs
  - All patients with deep burns of more than 35–40% TBSA (total burn surface area)
  - Burns involving face, neck, and upper torso
- Intubate early if progressive airway edema is suspected in cases of extensive burns or if the patient has signs of airway obstruction.
- Early intubation is also performed if the patient requires prolonged transport. Properly securing airway is of utmost importance in these patients.
- Awake fiberoptic intubation should be performed in difficult cases.

Breathing

- Breathing problem may be due to smoke inhalation injury, deep circumferential chest burn, or associated chest injury.
- Carbon monoxide (CO) is a by-product of incomplete combustion. Its intoxication is diagnosed by carboxyhemoglobin levels:
  - Less than 10% is normal.
  - More than 40% is severe.
- Treatment for carbon monoxide intoxication is to remove source and give 100% oxygen. Hyperbaric oxygen is also used to treat this condition. Patients with smoke inhalation injury often present with hoarseness, wheezing, carbonaceous sputum, facial burns, and singed nasal vibrissae.
- We should also consider the possibility of cyanide toxicity and keep a low threshold for initiating treatment. It is diagnosed by depressed level of consciousness, which may also be caused by carbon monoxide, traumatic shock, or head injury, in addition to potential cyanide toxicity. A serum lactate measurement and $EtCO_2$

monitoring may provide useful information as cyanide toxicity may cause lactic acidosis and a compensatory drop in $EtCO_2$. Antidotal treatment of cyanide poisoning involves three strategies: binding of cyanide, induction of methemoglobinemia, and use of sulfur donors. The combination of sodium thiosulfate and hydroxocobalamin has provided successful treatment of severe poisoning. At some places, the Cyanide Antidote Kit is also used if hydroxocobalamin is not available. This kit includes amyl nitrite and sodium nitrite to induce methemoglobinemia, and sodium thiosulfate to act as a sulfur donor.

- Diagnosis of Inhalational injury is often established by the use of bronchoscopy, which reveals early inflammatory changes such as erythema, edema, ulceration, sloughing of mucosa, and prominent vasculature in addition to infraglottic soot. Management of inhalation injury is directed at maintaining open airways and maximizing gas exchange.
- Bronchodilators can be useful when bronchospasm is present. Corticosteroids, however, should be avoided as they are associated with an increased risk of bacterial infection.
- A patient who is able to cough with a patent airway can clear secretions very effectively, and efforts should be made to treat the patient without mechanical ventilation.
- If respiratory failure is imminent, intubation is instituted early, and frequent chest physiotherapy and suctioning are performed to maintain pulmonary hygiene.
- Frequent bronchoscopies may be needed to clear inspissated secretions.
- In addition to the preceding measures, adequate humidification and appropriate treatment for bronchospasm is indicated.
- These patients should be ventilated as per ARDSnet protocol with low tidal volume (6 mL/kg ideal body weight). Try to keep the plateau pressure below 30 cm H_2O. Deep circumferential chest burn may limit chest wall mobility, so a higher plateau pressure up to 40 cm H_2O may be tolerated.
- Frequent escharotomies may improve breathing and airway pressures.

Circulation

- Obtain IV access anywhere possible and start giving fluids:
  - Unburned areas are preferred.
  - Burned areas are acceptable.
  - Central access is obtained if expertise available.
  - Cutdowns.
- Perform resuscitation in burn shock (first 24 h):
  - Massive capillary leak occurs after major burns.
  - Fluids shift from intravascular space to interstitial space.
  - Fluid requirement increases with greater severity of burn (larger percent total body surface area(TBSA), increased depth, inhalation injury, associated injuries)

Table 13.1 Resuscitation formulae

Formula	Crystalloid volume	Colloid volume	5% dextrose or plain water by the nasogastric tube
Parkland	4 mL/kg/% TBSA burn	None	None
Brooke	1.5 mL/kg/% TBSA burn	0.5 mL/kg/% TBSA burn	2.0 L
Galveston (pediatric)	5000 mL/m^2 burned + 1500 mL/m^2 total	None	None

TBSA total body surface area

- IV fluid rate depends on physiologic response and goals:
  - Sensorium—comfortable, arousable.
  - Base deficit—less than 2.
  - Goal for adults—urine output of 0.5 mL/kg/h.
  - Goal for children—urine output of 1 mL/kg/h; if urine output is below these levels, increase fluid rate.
  - Preferred fluid—lactated Ringer's solution as it is isotonic, cheap, and easily stored.
  - Resuscitation formulae—resuscitation formulae are just a guide for initiating resuscitation (Table 13.1).

Parkland formula is most commonly used for fluid calculation:

- Give half of the calculated volume in the first 8 h (from the time of injury).
- Give the other half in the next 16 h.
- Warning: Despite the formula suggesting decrease the fluid rate to half at 8 h, the fluid rate should be gradually reduced throughout the resuscitation to maintain the targeted urine output.

Resuscitation Endpoint

When maintenance rate is reached (approximately 24 h), change fluids to D5/NS with 20 mEq KCl at the maintenance level:

- Maintenance fluid rate = basal requirements + evaporative losses
- Basal fluid rate
  - Adult basal fluid rate = 1500 mL × body surface area (BSA) (for 24 h)
  - Pediatric basal fluid rate (<20 kg) = 2000 mL × BSA (for 24 h)
- Evaporative fluid loss
  - Adult evaporative fluid loss (mL/h) = (25 + percent TBSA burn) × BSA
  - Pediatric evaporative fluid loss (<20 kg) (mL/h) = (35 + percent TBSA burn) × BSA

Role of Albumin

- There is generally a profound hypoproteinemia following the initial resuscitation, and addition of intravenous albumin generally favours recruitment of interstitial fluid. Overall, no improvement in mortality has been noticed with albumin administration although complications are lowered by albumin compared with crystalloid in burn patients.

Role of Blood Transfusion

- Hemoconcentration occurs during the first several hours immediately following a severe burn and transfusions are generally unnecessary. Thereafter, bone marrow function is depressed and transfusions may be needed. Although, blood transfusions in severe burn injuries is associated with increased mortality but transfusion of two units of packed red blood cells can be given if the hemoglobin falls below 8 g/dL provided no high risk of acute coronary syndrome. Threshold for transfusion should be 10 g/dL for patients at risk for acute coronary syndrome.

Step 2: Take Detailed History

- Allergy
- Medication
- Pregnancy/past illness
- Last meal taken
- Environment (associated injuries)

Step 3: Start Supportive Treatment

- The nasogastric tube (small bore) for gastric decompression and initiating early enteral nutrition
- IV analgesics
- Antacids
- Tetanus prophylaxis

Step 4: Assess Severity

Burn severity is dictated by percent TBSA involvement, depth of burn, age, and associated injuries:

- Burns of 20–25% TBSA require IV fluid resuscitation.
- Burns of 30–40% TBSA may be fatal without treatment.

- In adults, rule of "nines" is used as a rough indicator of percent TBSA (Table 13.2 and Fig. 13.1).
- In children, adjust percents because they have proportionally larger heads (up to 20%) and smaller legs (13% in infants) than adults.
- Lund–Browder diagrams improve the accuracy of the percent TBSA for children.
- Palmar surface of the hand is approximately 1% TBSA helps in estimating percent total body surface area in children affected by burns.
- *Depth of burn injury*

1. Superficial burns (first-degree and superficial second-degree burns):
   - First-degree burns

Table 13.2 Rule of nines for establishing extent of burnt body surface

Anatomic surface	Total body surface (%)
Head and neck	9
Anterior trunk	18
Posterior trunk	18
Arms, including hands	9% each
Legs, including feet	18% each
Genitalia	1

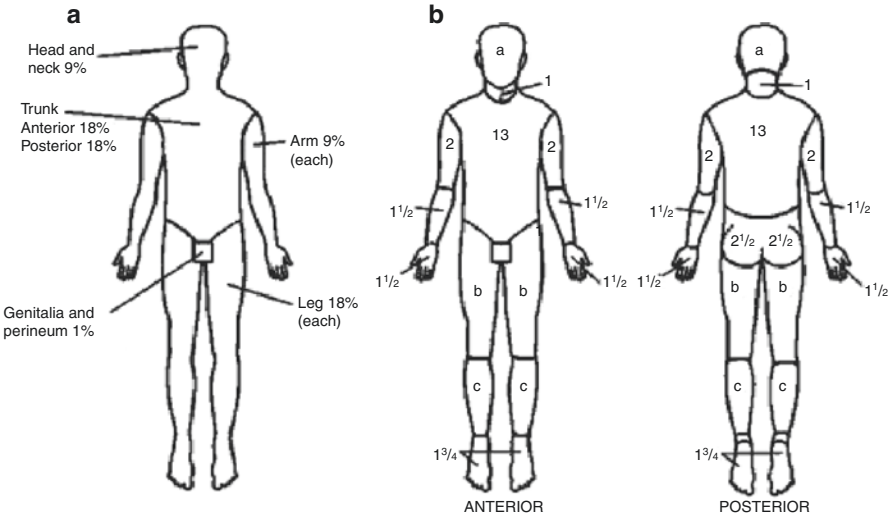

Fig. 13.1 (**a**) Rule of "nines" and (**b**) Lund–Browder diagram for estimating extent of burns (Adapted from Artz CP, Moncrief JA. The treatment of burns. 2nd ed. Philadelphia: WB Saunders Company; 1969)

  - Damage above the basal layer of epidermis.
  - Dry, red, painful ("sunburn").
- Second-degree burns
  - Damage into dermis.
  - Skin adnexa (hair follicles, oil glands, etc.) remain intact.
  - Heal by reepithelialization from skin adnexa.
  - The deeper the second-degree burn, the slower the healing (fewer adnexa for reepithelialization).
  - Moist, red, blanching, blisters, extremely painful.
  - Superficial burns heal by reepithelialization and usually do not scar if healed within 2 weeks.

2. Deep burns (deep second-degree to fourth-degree burns):
   - Deep second-degree burns (deep partial thickness)
     - Damage to deeper dermis
     - Less moist, less blanching, less pain
     - Heal by scar deposition, contraction, and limited reepithelialization
   - Third-degree burns (full thickness)
     - Entire thickness of skin destroyed (into fat)
     - Any color (white, black, red, brown), dry, less painful (dermal plexus of nerves destroyed)
     - Heal by contraction and scar deposition (no epithelium left in middle of wound)
   - Fourth-degree burns
     - Burn into muscle, tendon, and bone.
     - Need specialized care.
     - Deep burns usually need skin grafts to optimize results and lead to hypertrophic (raised) scars if not grafted.

Age

- Mortality for any given burn size increases with age.
- Children/young adults can survive massive burns.
- Children require more fluid per TBSA burns.
- The elderly may die from small (<15% TBSA) burns.

Associated injuries

- Other trauma increases severity of injury.

Use of alcohol or drugs

- It makes assessment of the patient more difficult.

Role of antibiotics

- It can be started later on when signs/symptoms of infection are present.

Step 5: Burn Wound Care and Control of Infection

Burn wound care: Current therapy for burn wounds can be divided into the following three stages: assessment, management, and rehabilitation:

- Once the extent and depth of the wounds have been assessed and the wounds are thoroughly cleaned and debrided, each wound should be dressed with an appropriate covering that serves three functions. First, it protects the damaged epithelium. Second, the dressing should be occlusive to reduce evaporative heat loss. Third, the dressing should provide comfort over the painful wound.
- The choice of dressing should be individualized based on the characteristics of the treated wound:
- First-degree wounds are minor with minimal loss of barrier function. These wounds require no dressing and are treated with topical agents to decrease pain and keep the skin moist.
- Second-degree wounds can be treated by daily dressing changes with an antibiotic ointment such as silver sulfadiazine covered with several layers of gauze under elastic wraps. Alternatively, the wounds can be covered with a temporary biologic or synthetic covering to close the wound. These coverings eventually slough as the wound reepithelializes underneath.
- Deep second- and third-degree burns will not heal in a timely fashion without autografting. These burned tissues serve as a nidus for inflammation and infection that can lead to death of the patient. Early excision and grafting of these wounds is preferred in terms of survival, less blood loss, and decreased length of hospitalization.
- Early excision should be reserved for third-degree wounds typically caused by flame. A deep second-degree burn can appear clinically to be a third-degree wound at 24–48 h after injury, particularly if it has been treated with topical antimicrobials that combine with wound drainage to form a pseudoeschar.
- Escharotomy: Excision and grafting is generally performed between 6 and 24 h after the injury. With circumferential deep second- and third-degree burns to an extremity, peripheral circulation to the limb can be compromised. The entire constricting eschar must be incised to relieve the obstruction to blood flow. Increased pressures in the underlying musculofascial compartments are treated with standard fasciotomies to avoid compartment syndrome.
- Control of infection: Decreasing invasive infections in the burn wound is due to early excision and closure and the timely and effective use of antimicrobials. The antimicrobials that are used can be divided into those given topically and those given systemically. Topical antibiotic includes 11% mafenide acetate, 1% silver sulfadiazine, polymyxin B, neomycin, bacitracin, and mupirocin:
  - Mafenide acetate has a broad spectrum of activity, particularly for Pseudomonas and Enterococcus species. Mafenide sulfate is typically reserved for small full-thickness injuries and ear burns to prevent chondritis.
  - Silver sulfadiazine, the most frequently used topical agent, has a broad spectrum of activity from its silver and sulphur moieties that cover Gram-positive

organisms, most Gram-negative organisms, and some fungi. It is painless upon application, has a high patient acceptance, and is easy to use.
- Petroleum-based antimicrobial ointments with polymyxin B, neomycin, and bacitracin are clear on application, are painless, and allow for observation of the wound. These agents are commonly used for the treatment of facial burns, graft sites, healing donor sites, and small partial-thickness burns.
- Mupirocin has improved activity against Gram-positive bacteria, particularly methicillin-resistant Staphylococcus aureus, and selected Gram-negative bacteria.
- Nystatin in the powder form can be applied to wounds to control fungal growth, and nystatin powder can be combined with topical agents such as polymyxin B to decrease colonization of both bacteria and fungi.
- Available agents for application as a soak include 0.5% silver nitrate solution, 0.5% sodium hypochlorite, 5% acetic acid, and 5% mafenide acetate solution.
- The use of perioperative systemic antimicrobials also has a role in decreasing sepsis in the burn wound until it is healed. Common organisms that must be considered when choosing a broad-spectrum perioperative regimen include S. aureus and Pseudomonas species, which are prevalent in wounds. After massive burns, gut flora are often found in the wounds mandating coverage of these species as well.

Step 6: Fluid of Choice on the Second Day

- Five percent dextrose in one-half isotonic saline (i.e., 0.45% sodium chloride). 20 mEq of potassium chloride should be added to each liter of fluid.

Step 7: Supportive Treatment—Nutrition

- Nutritional support is best accomplished by early enteral nutrition that can abate the hypermetabolic response to a burn. Therefore, duodenal or jejunal tube feeding should be commenced as early as within the first 6 h after burn if gastric feed is not possible due to ileus.
- The caloric and protein requirements are needed to gain weight and achieve nitrogen balance. It is estimated as 25 kcal/kg plus 40 kcal/% TBSA burn for 24 h (Table 13.3). Protein needs are approximately 2.5 g/kg. Estimation of 24-h urinary urea nitrogen for calculating nitrogen balance should be obtained (see Chap. 43, Vol. 1 on nutrition).

Table 13.3 Curreri formula for estimating caloric requirements for adult burn patients

Age	Formulas
6–60 years	25 kcal/kg/day + 40 kcal/% burn/day
>60 years	25 kcal/kg/day + 65 kcal/% burn/day

Table 13.4 Formulae for estimating caloric requirements for pediatric burn patients

Age	Formulas
0–1 years	2100 kcal/m^2 TBSA/day + 1000 kcal/m^2 TBSA burn/day
1–11 years	1800 kcal/m^2 TBSA/day + 1300 kcal/m^2 TBSA burn/day
12–18 years	1500 kcal/m^2 TBSA/day + 1500 kcal/m^2 TBSA burn/day

Shriners Hospitals for Children at Galveston, Texas

The pediatric formulae have been derived from retrospective analyses of dietary intake, which is associated with maintenance of average body weight over hospital stay (Table 13.4).

Ulcer prophylaxis and deep venous thrombosis prophylaxis should be started along with the rest of the management unless there are contraindications.

Step 8: Manage Complications

Successful management of burns involves management of predicted complications like Sepsis, ARDS and Renal failure.

Suggested Reading

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Part IV

Toxicology, Envenomation and Thermo Dysregulation

General Poisoning Management

14

Omender Singh, Prashant Nasa, and Deven Juneja

A 24-year-old lady was admitted to the hospital, with history of consumption of some liquid at home followed by vomiting, altered mental status, and labored breathing. She was brought to the triage in the comatose state with pinpoint pupils, frothy secretions from her mouth, heart rate 58/min, and blood pressure 90/48 mmHg.

High index of suspicion for intoxication is warranted in the practice of critical care medicine particularly for patients admitted with unexplained altered mental status, seizures, cardiac dysrrhythmias, and respiratory depression. Diagnosis may be complicated by the possibility of a multiple-drug ingestion. Supportive care during first few hours of admission may be lifesaving. Antidotes should be used early on suspicion of a particular poison to prevent organ dysfunction. Attempts to identify the toxin should be done by focused history, a directed physical examination, and commonly available laboratory tests.

Step 1: Initiate Resuscitation and Assessment

- Initiate resuscitation as mentioned in Chap. 23, Vol. 2

Airway

- Management of airways is very important in poisoning. Some toxins (acid or alkali ingestion) require extra care during airway management. When

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intubation is necessary, rapid sequence induction is indicated using short-acting paralytic agents.
- Urine toxicology screening should be obtained before any sedatives or hypnotics are administered.

Breathing

- A patient's oxygenation status can be monitored with a bedside pulse oximeter except toxins leading to dyshaemoglobenemias i.e. in carbon monoxide poisoning, pulse oximeter is unreliable in detecting carboxyhemoglobin. Similarly in methemglobinaemia due to cyanide poisoning pulse oximetry saturation is not reliable. In these cases true oxygen saturation can be measured by coximeter enabled blood gas analyser.
- Some newer generation pulse oximeters are capable of estimating carboxy and methemoglobin continuously by adding additional light emitting diodes of different wavelengths.
- Give oxygen by the nasal cannula or face mask to maintain SpO_2 more than 95%.
- When the patient is in respiratory distress and not able to maintain oxygenation or ventilation, assisted ventilation should be considered.

Circulation

- Monitor pulse and blood pressure. Do an ECG. Obtain a good peripheral line and start intravenous fluids.
- The "coma cocktail" of dextrose (50 ml D50W IV), naloxone (2 mg IV), flumazenil (0.2 mg IV), and thiamine (100 mg IV) can be considered in unknown poisoning with unconsciousness and coma but should be avoided in patients with history of benzodiazepines or opiates abuse as seizures or arrhythmias may be precipitated.

Step 2: Take Detailed History

- Detailed and targeted history from the family members and friends including the past medical treatment and occupational environment is important for making the diagnosis of poisoning.
- The history should include the type of toxin or toxins, time of exposure (acute versus chronic), amount taken, and route of administration (i.e., ingestion, intravenous, and inhalation).
- The patient should be asked about over-the-counter medications, vitamins, and herbal preparations.
- The patient or accompanying attendants should be asked about all drugs taken, including prescription drugs and empty bottles/containers, and the physician can also perform "pill count" to ascertain the number of consumed pills.

Table 14.1 Physiologic grading of the severity of poisoning—signs and symptoms

Severity	Stimulant poisoning	Depressant poisoning
Grade 1	Agitation, anxiety, diaphoresis, hyperreflexia, mydriasis, tremors	Ataxia, confusion, lethargy, weakness, able to follow verbal commands
Grade 2	Confusion, fever, hyperactivity, hypertension, tachycardia, tachypnea	Mild coma (nonverbal but responsive to pain); brainstem and deep tendon reflexes intact
Grade 3	Delirium, hallucinations, hyperpyrexia, tachyarrhythmias	Moderate coma (respiratory depression, unresponsive to pain); some but not all reflexes absent
Grade 4	Coma, cardiovascular collapse, seizures	Deep coma (apnea, cardiovascular depression); all reflexes absent

- Remember the history from the patient may not always be reliable.
- The clinical diagnosis of the type of poisoning can be identified by the clinical manifestations that may fit into a particular toxidrome. Toxic overdose can present with a wide array of symptoms, including abdominal pain, vomiting, tremor, altered mental status, seizures, cardiac dysrrhythmias, and respiratory depression, which may be the only clues to diagnosis (Table 14.1).
- Symptoms are often nonspecific (as in early acetaminophen poisoning) or masked by other conditions (e.g., myocardial ischemia in the setting of carbon monoxide poisoning).

Step 3: Perform Physical Examination

- The patient stabilization will take precedence over the detailed physical examination.
- Once the patient is stable, a more comprehensive physical and systemic examination should be performed.
- Serial examinations are even more important to assess dynamic change in clinical appearance. The systematic neurological evaluation is particularly important in patients with altered mental status. Alert/verbal/painful/unresponsive scale (AVPU) is a simple, rapid method of assessing consciousness in most poisoned patients.
- Focussed clinical examination e.g. characteristic odors of some poisoning (Garlic in OrganoPhosphorus [OP] poisoning), Pupillary findings, Movement disorders like seizures, skin findings (flushed or pale, dry or warm) Temperature alteration (hypo or hyperthermia), Respiratory alteration, etc. can help in differentiating types of poisoning
- Look for features of associated trauma or injury during intoxication

Step 4: Order Investigations

A basic metabolic panel should be obtained in all poisoned patients:

- Complete blood count
- Serum electrolytes
- Blood urea nitrogen and creatinine
- Blood glucose and bicarbonate level
- Liver functions test
- coagulation profile
- Arterial blood gases
- ECG
- If the patient is a female of child-bearing age, a pregnancy test is essential.
- The anion gap, serum osmolality, and osmolal gap should be measured in each patient as it can help in finding the cause (Table 14.2).
- Chest and plain abdominal X-ray should be done if high index of suspicion of radiopaque pills, drug- filled packets i.e. cocaine, enteric coated tablets, heavy metals etc.

Specific investigations:

- Sample for urine toxicology screening for common drugs must be taken before giving any sort of sedation to these patients.
- The cholinesterase level for organophosphorus poisoning: Specific levels of cholinesterase can guide treatment.
- Paracetamol, Salicylate and other drug levels where appropriate

Table 14.2 Common causes of abnormal anion gap

Elevated anion gap	Decreased anion gap	Increased osmolar gap
Lactic acidosis (type A)	Increased unmeasured cation	Methanol and ethylene glycol
Uremia	Hyperkalemia	Diabetic ketoacidosis
Sepsis	Hypercalcemia	Isopropyl alcohol (acetone)
Rhabdomyolysis	Hypermagnesemia	Ethanol
Ketoacidosis: diabetic, starvation, ethanol	Acute lithium intoxication	
	Elevated IgG (myeloma cationic paraprotein)	
	Unmeasured decreased anion	
	Hypoalbuminemia	
Toxic ingestions	Drugs	
Ethylene glycol	Bromide	
Methanol	Iodide	
Paraldehyde	Lithium	
Salicylate	Polymyxin B	
	Analytical artifact	
	Hypernatremia	
	Hyperlipidemia	

- Oxygen saturation gap (SaO_2–SpO_2): An oxygen saturation gap is present when there is more than a 5% difference between the measured **oxygen saturation** from a standard blood gas machine with cooximeter and the reading from a pulse oximeter. If it is greater than 5%, the patient's hemoglobin may be abnormal, representing carbon monoxide poisoning (carboxyhemoglobin), methemoglobinemia (Cyanide, Dapsone), or sulfhemoglobinemia (Hydrogen sulfide).

Step 5: Admit to the ICU

Admit in ICU if any of the following is present:

- Respiratory depression ($PaCO_2$ > 45 mmHg)
- Emergency intubation
- Seizures
- Cardiac arrhythmia (QT prolongation, preferably corrected QTc)
- QRS duration more than 0.12 s
- Second- or third-degree atrioventricular block
- Systolic BP less than 80 mmHg
- Unresponsiveness to verbal stimuli
- Glasgow coma scale score less than 12
- Need for emergency dialysis, hemoperfusion, or extracorporeal membrane oxygenation
- Increasing metabolic acidosis
- Pulmonary edema induced by toxins (including inhalation) or drugs
- Tricyclic or phenothiazine overdose manifesting anticholinergic signs, neurologic abnormalities, QRS duration more than 0.12 s, or QT more than 0.5 s
- Administration of pralidoxime in organophosphate toxicity
- Antivenom administration in envenomation
- Need for continuous infusion of naloxone

Step 6: Management

- The management of any clinically significant poisoning should begin with basic supportive measures. The first priority after airway, breathing, and circulation approach is to prevent and manage life-threatening complications.

Step 7: Decontamination

- The clothing should be removed in suspected or confirmed dermal exposures, and the skin should be copiously irrigated and washed with a mild soap and water in organophosphorus poisoning.

- The eye should be copiously irrigated with water in ocular exposure to acids and alkali.
- Gastric lavage: The place of gastric lavage in acute poisoning is debatable and is only of benefit in the hyperacute phase of poisoning (<1 h). Caution: Patients must be awake with a preserved gag reflex.
- Charcoal: Charcoal aspiration has a high morbidity and mortality. This should not be attempted in patients without a safe or protected airway.
- Administer 50-g charcoal as soon as possible and another 50 g every 4 h thereafter while indication persists. Coadministration with sorbitol has not been shown to increase efficacy.
- Charcoal administration is most effective when it is given within 1 h of ingestion.
- Contraindications to charcoal administration are as follows:
  - Elemental metals (lithium, iron)
  - Pesticides
  - Strong acids or alkalis
  - Cyanide
  - Late presentations (>4–6 h post-ingestion)

Step 8: Enhance Elimination

- Alkalinization of urine may help in excretion of drug in the urine in poisonings such as salicylates, phenobarbital, and chlorpropamide.
- Dialysis and charcoal hemoperfusion should be considered in severe poisoning if the toxin can be removed by dialysis (Table 14.3).
- Plasmapheresis has also been tried for removal of certain poisons (Table 14.3).
- Other therapies like extra corporeal membrane oxygenation (ECMO) for cardiac and pulmonary support has also been tried in several patients with acute poisoning (Table 14.3).

Table 14.3 Indication of Extracorporeal Support, dialysis and hemoperfusion

Hemodialysis	Hemoperfusion	Plasmapheresis	ECMO
Methanol	Theophylline	Tricyclic antidepressants	Amiodarone
Ethylene glycol	Phenobarbital	Thyroxine	Beta-blocker
Boric acid	Phenytoin	Heavy metals	Calcium channel blockers
Salicylates	Carbamazepine	Theophylline	Opioids
Lithium	Paraquat		Organophosphorous
	Glutethimide		Paraquat
			Tricyclic antidepressants

Table 14.4 Common poisons and their antidotes

Poison	Antidote
Acetaminophen	*N*-Acetylcysteine
Anticholinergics	Physostigmine
Anticoagulants (warfarin/coumadin, heparin)	Vitamin K, protamine respectively
Dabigatran	Idarucizumab (Praxbind)
Rivoroxaban, Apixaban	Andenaxet Alfa
Benzodiazepines	Supportive care, flumazenil[a]
Botulism	Botulinum antitoxin
β-Blockers	Glucagon
Calcium channel blockers	Calcium, glucagon
Cholinergics (i.e., organophosphorus)	Atropine, pralidoxime
Carbon monoxide	Oxygen, hyperbaric oxygen
Cyanide	Amyl nitrate, sodium nitrate, sodium thiosulfate, hydroxocobalamin (
Digoxin	Digoxin Fab antibodies
Iron	Deferrioxamine
Isoniazid	Pyridoxine
Lead	BAL, EDTA, DMSA
Methemoglobinemia	Methylene blue
Opioids	Naloxone
Toxic alcohols	Ethanol drip, dialysis Fomepizole
Tricyclic antidepressants	Sodium bicarbonate

[a]Use of flumazenil should be contraindicated in many situations including tricyclic overdose or in chronically habituated benzodiazepine users, as this may precipitate seizures

Step 9: Use Antidotes to Common Poisons

- Antidotes should be used early in the course in which the effects of poisoning can be counteracted (Table 14.4).

Step 10: Other Measures

Intravenous Fat Emulsion (IFE) has been suggested as a probably beneficial therapy in the management of local anesthetic overdose. e.g. Bupivacaine, mepivacaine, ropivacaine, levobupivacaine, prilocaine, lignocaine, lidocaine It has also been tried in several other poisoning, with varied results (Table 14.5). Although the exact mechanism of its action is unknown, it is postulated to mediate antidote activity or act by compartmentalization of the offending agent into lipid phase, and hence moving it away from its target receptors. As per the current dosing recommendations, a bolus of 1.5 mL/kg, followed by an intravenous infusion at the rate of 0.25 mL/kg/min should be initiated.

Table 14.5 Drugs which may benefit by use of intravenous fat emulsion

Probable benefit
All local anesthetics: Bupivacaine, mepivacaine, ropivacaine, levobupivacaine, prilocaine, lignocaine, lidocaine
Possible benefit
Anti-epileptics: Carbamazepine, lamotrigine
Anti-psychotics: Chlorpromazine, haloperidol, olanzapine, quetiapine
Anti-histamine: Diphenhydramine
Barbiturates: Pentobarbital, phenobarbital, thiopental
Beta-blockers: Atenolol, carvedilol, metoprolol, nevibilol, propranolol
Calcium channel blockers: Amlodipine, diltiazem, felodipine, nifedipine, verapamil
Disease-modifying anti-rheumatic drug: Hydroxychloroquine
Tricyclic antidepressants: Amitriptyline, clomipramine, dosulepin, dothiepin, doxepin, imipramine
Other anti-depressants: bupropion, venlafaxine
Others: Baclofen, cocaine, endosulfan, flecainide, propafenone

Step 11: Whenever in Doubt Seek Help from National Poison Information Centre (AIIMS)

Suggested Reading

American College of Medical Toxicology. ACMT position statement: interim guidance for the use of lipid resuscitation therapy. J Med Toxicol. 2011;7:81–2. *A statement on the use of lipids in poisionings*

Boyle JS, Bechtel LK, Holstege CP. Management of the critically poisoned patient. Scand J Trauma Resusc Emerg Med. 2009;17:29. If a poisoning is recognized early and appropriate testing and supportive care is initiated early, it will improve outcome. It is important to understand the indications and contraindications of antidotes prior to its use

Brooks DE, Levine M, O'Connor AD, French RN, Curry SC. Toxicology in the ICU: part 2: specific toxins. Chest. 2011;140(4):1072–85. *A review article on approach to poisioning in ICU*

Ghannoum M, Roberts DM, Hoffman RS, Ouellet G, Roy L, Decker BS, Bouchard J. A stepwise approach for the management of poisoning with extracorporeal treatments (ECTRs). Semin Dial. 2014;27:362–70. A detailed understanding of the capabilities and limitations of the different ECTRs can be useful to select the most appropriate ECTR for a given clinical situation

Lam SH, Majlesi N, Vilke GM. Use of intravenous fat emulsion in the emergency department for the critically ill poisoned patient. J Emerg Med. 2016;51(2):203–14. *Intravenous Fat Emulsion may be an effective antidote in poisonings from various xenobiotics*

Levine M, Brooks DE, Truitt CA, Wolk BJ, Boyer EW, Ruha AM. Toxicology in the ICU: part 1: general overview and approach to treatment. Chest. 2011;140(3):795–806. *A review article on approach to poisioning in ICU*

Levine M, Ruha AM, Graeme K, Brooks DE, Canning J, Curry SC. Toxicology in the ICU: part 3: natural toxins. Chest. 2011;140(5):1357–70. *A review article on approach to poisioning in ICU*

Ouellet G, Bouchard J, Ghannoum M, Decker BS. Available extracorporeal treatments for poisoning: overview and limitations. Semin Dial. 2014;27(4):342–9. *This articles discusses overview of extracorporeal treatments (ECTRs) like intermittent hemodialysis, sustained low-efficiency dialysis, intermittent hemofiltration and hemodiafiltration, continuous renal replacement therapy, hemoperfusion, therapeutic plasma exchange, exchange transfusion, peritoneal dialysis, albumin dialysis and cerebrospinal fluid exchange in poisionings*

Drug Abuse

15

Omender Singh, Prashant Nasa, and Deven Juneja

A 38-year-old male known alcohol abuser, chronic smoker, and IV drug abuser came to the emergency department in inebriated state. On examination, he was cachectic, stuporous with bilateral pin-point pupils. There were multiple black erythematous patches on forearm with multiple injection marks. His pulse rate was 46/min and blood pressure was 82/60 mmHg, and on auscultation, there were bilateral crepts.

Substance abuse may be persistent or sporadic, inconsistent with or unrelated to acceptable medical practice. This subset of patients may present to the hospital with acute intoxication, withdrawal, or infectious and other chronic complications related to drug abuse. They have overall better prognosis as compared to other critically ill patients, if diagnosed and managed timely. Narcotics, stimulants, and sedatives are the common prescription drugs of abuse. Patients may present with deliberate or accidental overdose.

Step 1: Initiate Resuscitation

- Initial resuscitation should be done as mentioned in Chap. 23, Vol. 2.
- In addition to routine investigations, CT Head should be done to rule out intracranial bleed in patients presenting as hypertension particularly with Stimulants abuse [i.e. Cocaine].
- Give IV naloxone if respiratory depression and opioid abuse is a possibility as it rapidly reverses the respiratory depression and intubation can be avoided. This

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should be avoided in patient with history of chronic abuse of these substances as it may precipitate seizures and arrhythmias.

Airway

- Management of airways is very important in poisoning. When intubation is necessary, rapid sequence induction is indicated using short-acting paralytic agents.
- Urine toxicology screening should be obtained before administering any sedatives or hypnotics.

Breathing

- A patient's oxygenation status can be monitored with a bedside pulse oximeter.
- Give oxygen by the nasal cannula or facemask to maintain SpO_2 more than 95%.
- The patient should be started on assisted ventilation if unable to maintain oxygenation or ventilation.

Circulation

- Monitor pulse and blood pressure and do ECG.
- Obtain a good peripheral line and start intravenous fluids.

Step 2: Initial Assessment

- This subset of patients may present to the hospital with acute intoxication, withdrawal, or infectious and other chronic complications related to drug abuse.
- The drugs of abuse can be classified into major groups (Table 15.1).

Table 15.1 Classification of drugs of abuse

Group	Commonly abused drugs
Cannabinoids	Hashish, ganja, marijuana
Opioids	Opium, heroin, morphine, fentanyl, codeine, oxycodone
Stimulants	Amphetamines, cocaine, MDMA (ecstasy), nicotine
Hallucinogens	Lysergic acid diethylamide, mescaline
Dissociative anesthetics	Ketamine, phencyclidine analogs
Depressants	Barbiturates, nonbarbiturates (benzodiazepines, gamma-hydroxybutyrate, antihistaminics)
Others	Alcohol, anabolic steroids, dextromethorphan

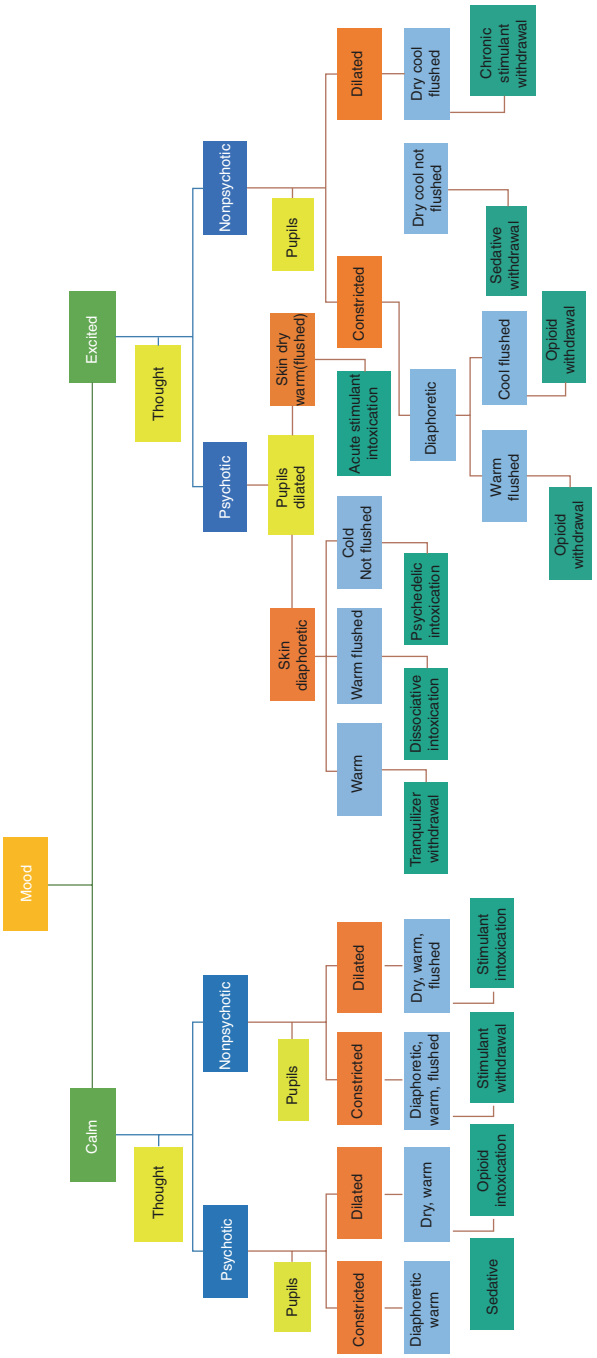

Fig. 15.1 Algorithm for the diagnosis of drug intoxication and withdrawal

The initial evaluation of these patients has multiple physical, social, emotional, and medicolegal issues that should be addressed.

- Complete and focused history should be taken from the patient, family, accompanying physician, or police, as mentioned in Chap. 14, Vol. 2.
- Do detailed examination (Fig. 15.1):
  - Once the patient is stable, a more comprehensive physical and systemic examination should be performed.
  - Serial examinations are even more important to assess dynamic change in clinical appearance.
  - The systematic neurological evaluation is particularly important, in patients with altered mental status. Alert/verbal/painful/unresponsive scale (AVPU) is a simple rapid method of assessing consciousness in most poisoned patients.

Step 3: Diagnosis by Toxidromic Approach

The signs and symptoms of drugs of abuse are organized around the activity of six neurotransmitters (Table 15.2), with this activity being sufficiently unique to permit rapid identification of the specific drug responsible for a given clinical situation.

- Based on history and examination, it may be possible to define a constellation of signs and symptoms or toxidromes, which may help in diagnosing the unknown poison and provide a specific antidote. Common toxidromes are listed in Chap. 14, Vol. 2.

Table 15.2 Specific treatment for intoxication, overdose, and withdrawal based on the affected neurotransmitter

Neurotransmitter involved in intoxication	Treatment
Acetylcholine	Physostigmine
β-Endorphin	Naloxone (Narcan)
Dopamine	Benzodiazepine
	Butyrophenone
GABA	Mechanical support
Norepinephrine	β-Blocker
	Benzodiazepine
Serotonin	Benzodiazepine
Withdrawal	
β-Endorphin	Methadone, clonidine
Dopamine	Bromocriptine
GABA	Barbiturate or benzodiazepine replacement
Norepinephrine	Desipramine
Serotonin	Fluoxetine

GABA gamma-aminobutyric acid

Step 4: Diagnose Common Drug Abuse

1. Alcohol
   - Acute effects:
     - CNS depressant.
     - In low doses, alcohol depresses inhibitory centers and resultant disinhibition (out-of-character activities).
     - At higher doses, alcohol inhibits excitatory centers.
   - Signs of chronic alcohol abuse:
     - Gastrointestinal—cirrhosis of the liver, peptic ulcer disease, gastritis, pancreatitis, and carcinoma
     - Cardiovascular—hypertension, cardiomyopathy, atrial fibrillation ("holiday heart syndrome")
     - Neurological—peripheral neuropathy leading to ataxia, Wernicke encephalopathy, Korsakoff psychosis, and structural changes in the brain leading to dementia
     - Immunologic—suppression of neutrophil function and cell-mediated immunity
     - Endocrine—in males, increase in estrogen and decrease in testosterone, leading to impotence, testicular atrophy, and gynecomastia
     - Psychiatric—depression or anxiety disorders
2. Opiates
   - Acute intoxication—decreased respiratory rate and pinpoint pupils, with complications including noncardiogenic pulmonary edema and respiratory failure.
   - Complications of chronic abuse are primarily infectious and include skin abscess at an injection site, cellulitis, mycotic aneurysms, endocarditis, talcosis, HIV, and hepatitis.
3. Cocaine

   Cocaine may be smoked, inhaled, used topically, or injected:
   - Acute cocaine intoxication may present with agitation, paranoia, tachycardia, tachypnea, hypertension, and diaphoresis.
   - Complications of acute and chronic use can include myocardial ischemia or infarction, stroke, pulmonary edema, and rhabdomyolysis.
4. Amphetamines

   Acute intoxication with amphetamines presents with signs of sympathetic nervous system stimulation, tachycardia, hypertension, anorexia, insomnia, and occasionally seizures.
5. Hallucinogens
   - Different hallucinogens present with a variety of organ system effects.
   - Phencyclidine (PCP) has been known to cause muscle rigidity, seizures, rhabdomyolysis, and coma.
   - Anticholinergics have been associated with delirium, supraventricular tachycardia, hypertension, and seizures.

     Other hallucinogens (e.g., lysergic acid diethylamide, peyote, marijuana, and nutmeg) rarely cause significant physical complications.

Step 5: Send Investigations

Patients:

- Complete blood count
- Serum electrolytes
- Blood urea nitrogen, creatinine
- Liver functions tests
- Blood glucose, bicarbonate level
- Arterial blood gases
- ECG
- Echocardiography

Special investigations:

- Urine toxicology screening: In the patient with acute intoxication, urine screening for substances of abuse and a blood or breath alcohol level may be considered, but these generally do not alter management. Urine toxicology screening is needed for the following:
  - Amphetamines
  - Barbiturates
  - Benzodiazepines
  - Cannabinoids
  - Cocaine
  - Opioids
  - Phencyclidine
- Caution: A single negative urine toxicology screening or urine immunoassay is not reliable, and repeat tests should be done after a few hours especially if clinical suspicion is high:
  - Blood toxicology profile—if available.
  - If the patient is a female of child-bearing age, a pregnancy test is essential.
  - Serum ethanol level, the anion gap, serum osmolality, and osmolal gap should be performed for alcohol intoxication.
  - A CT scan of the head is advised—if altered mental status is not explained or in the presence of new focal neurological deficit.

Step 6: General Management

- The general principle of management of patients with suspected drug overdose or withdrawal is supportive and includes standard resuscitative measures.
- Once the patient has been stabilized, the physician must consider how to minimize the bioavailability of toxin not yet absorbed, which antidotes (if any) to administer, and what other measures should be undertaken to enhance elimination.

- After initial resuscitation, use the specific antidote when available.
- The management of acute intoxication and withdrawal again will depend on the particular neurotransmitters involved (Table 15.2).

Step 7: Manage as per Specific Class

1. Dissociative drugs
   - *Acute intoxication*: Haloperidol, a presynaptic dopamine antagonist, is useful for blocking significant symptoms of dissociative intoxication.
   - *Dose*: 1 mg IV every 15–20 min up to maximum 10 mg. This can be given orally or intramuscularly, too.

     Alternative to haloperidol is risperidone.
   - *Chronic intoxication*: Desipramine for postwithdrawal depression.
2. Opiates
   - *Specific antidote* (naloxone, naltrexone, naltrefene): Naloxone, at a dose of 0.1–0.4 mg or 0.01 mg/kg IV, may have to be repeated every 1–2 min.
   - *Naloxone* should not be used in patients with chronic abuse as it can precipitate seizures or withdrawal.
   - *Withdrawal:* Methadone is the drug of choice, but not easily available. Clonidine orally/Ryle's tube 17 μg/kg/day in three to four doses can be used.
3. Hallucinogens
   - *Acute intoxication*: Benzodiazepines (midazolam, diazepam, alprazolam) are the drug of choice.
   - *Withdrawal*: Fluoxetine can be given orally.
4. Sedative–hypnotic drugs
   - *Acute intoxication*: For supportive management, flumazenil is the specific antidote for benzodiazepines but can precipitate seizures or withdrawal in patients with chronic abuse.
   - *Chronic intoxication/withdrawal:*

     Barbiturates: The equivalent dose of phenobarbitone for a period, which depends on the duration of action of the abused drug for withdrawal effect. Flumazenil can cause seizure in chronic intoxication of barbiturates.

     Benzodiazepines: Long-acting like chlordiazepoxide (Librium) orally/Ryle's tube maximum up to 25 mg, three to four times a day, or lorazepam 1–2 mg three to four times a day.

     Alcohol: Same as benzodiazepines. If chronic abuse give thiamine 200 mg.
5. Stimulant drugs
   - *Acute intoxication: Benzodiazepines (lorazepam) are the drug of choice.*
   - *Chronic abuse*: Bromocriptine and/or desipramine can be given orally.

Summary

- Patients with substance abuse may present to the hospital with acute intoxication, withdrawal, or infectious and other chronic complications related to drug abuse.
- Initial resuscitation should be done using the ABCDE approach.

- Based on detailed history and clinical examination, it may be possible to define a constellation of signs and symptoms or toxidromes, which may help in diagnosing the unknown poison.
- Specific investigations may be required to diagnose specific substance abuse.
- After initial resuscitation, use the specific antidote when available.

Suggested Reading

Betten DP, Vohra RB, Cook MD, Matteucci MJ, Clark RF. Antidote use in the critically ill poisoned patient. J Intensive Care Med. 2006;21(5):255–77. *The more commonly used antidotes that may be encountered in the intensive care unit (N-acetylcysteine, ethanol, fomepizole, physostigmine, naloxone, flumazenil, sodium bicarbonate, octreotide, pyridoxine, cyanide antidote kit, pralidoxime, atropine, digoxin immune Fab, glucagon, calcium gluconate and chloride, deferoxamine, phytonadione, botulism antitoxin, methylene blue, and Crotaline snake antivenom) are reviewed*

Chang G, Kosten TR. Detoxification. In: Lowinson JH, Ruiz P, Millman RB, Langrod JG, editors. Substance abuse: a comprehensive textbook. 4th ed. Baltimore: Lippincott, Williams & Wilkins; 2004. p. 579–86.

Holstege CP, Borek HA. Toxidromes. Crit Care Clin. 2012;28(4):479–98. *This article reviews the general approach to the poisoned patient, specifically focusing on the utility of the toxidrome. A toxidrome is a constellation of findings, either from the physical examination or from ancillary testing, which may result from any poison. There are numerous toxidromes defined in the medical literature. This article focuses on the more common toxidromes described in clinical toxicology*

Marraffa JM, Cohen V, Howland MA. Antidotes for toxicological emergencies: a practical review. Am J Health Syst Pharm. 2012;69(3):199–212. *This review highlights the role pharmacists can play a key role in reducing poisoning and overdose injuries and deaths by assisting in the early recognition of toxic exposures and guiding emergency personnel on the proper storage, selection, and use of antidotal therapies*

Moeller KE, Kissack JC, Atayee RS, Lee KC. Clinical interpretation of urine drug tests: what clinicians need to know about urine drug screens. Mayo Clin Proc. 2017;92:774–96. pii: S0025-6196(16)30825-4. *In this report, technical information related to detection methods of urine drug tests that are commonly used are provided, an overview of false-positive/false-negative data for commonly misused substances in the following categories: cannabinoids, central nervous system (CNS) depressants, CNS stimulants, hallucinogens, designer drugs, and herbal drugs of abuse are given . Brief discussions of alcohol and tricyclic antidepressants as related to urine drug tests is described . The goal of this review was to provide a useful tool for clinicians when interpreting urine drug test results and making appropriate clinical decisions on the basis of the information presented*

Snakebite

16

Dhruva Chaudhry, Sateesh Chandra Alavala, and Debraj Jash

Case 1: A 20-year-old male presented with history of diffuse abdominal pain, myalgias, difficulty in swallowing, and pooling of secretions. He also complained of difficulty in breathing and diplopia with acute onset drooping of eyes. He was conscious, oriented to time and space, with a respiratory rate of 12/min and a single breath count of 12. The power in all limbs was 4/5, but all reflexes were absent. He had ptosis, and the rest of the general and systemic examination was normal. He was absolutely normal the previous night, when he had slept on the floor.

Case 2: A 36 year-old male, farmer, presented to emergency department with swelling and bleeding from the left leg after he was bitten by a snake early in the morning when he was working in the farm. He also complained of bleeding from gums, hematuria and not passed urine since morning. He was conscious and oriented. His blood pressure was 90/60 mmHg. Neurological examination did not reveal any abnormality.

Snakebite is an injury caused by a bite from a snake which sometimes results in envenomation. Most of the snakes are nonvenomous. Some snakebites result in envenomation. The outcome of snakebite depends on numerous factors which include species of snake, the area of the body bitten, and the amount of venom injected.

Step 1: Initial Resuscitation and Assessment

Airway

- Management of airway is very important in neuroparalytic snakebite.

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- The patient should be assessed for any pooling of secretions, inability to open mouth or protrude tongue, weakness of neck flexors (broken neck sign). Patients with any of these signs or single breath count of <10 should be immediately intubated following the standard procedure of intubation.

Breathing

- The patient's oxygenation status can be monitored with a bedside pulse oximeter. Supplemental oxygen should be given in the presence of hypoxia.
- When the patient is in respiratory distress and not able to maintain oxygenation, he/she should be put on assisted ventilation.

Circulation

- Obtain a good peripheral line and start intravenous fluids. Start vasopressors if hypotension persists after adequate fluid resuscitation.
- Be careful while venipuncturing in patients with coagulopathy.

Step 2: Take Detailed History

- Detailed history should be taken such as the type of the snake (species), timing of bite, what was he/she doing at that time, location (in which part of the body the snake has bitten), and first-aid measures received.
- Patients with snakebite usually present with history of sudden onset of generalized weakness, abdominal pain and vomiting.
- Neurological symptoms include drooping of eyelids, blurred or double vision, difficulty in swallowing, pooling of secretions, difficulty in breathing. (Remember 4Ds-Diplopia, Dysphagia, Dysphonia, Dyspnea).
- Ask for local swelling or pain in the body and bleeding from any site (Table 16.1).

Step 3: Perform Physical Examination

- A comprehensive general physical and neurological examination should be performed in all patients with suspected snakebite.
- The examination may reveal generalized motor weakness with sluggish deep tendon reflexes.

Table 16.1 Syndromes associated with snake bite

Local effects	Vipers, Cobra, Sea snakes (usually absent in krait)
Coagulopathy	Vipers (Russell's Viper, Hump Nosed Viper, Saw scaled Viper)
Neurotoxicity	Cobra, Common krait, Sea snakes, Russell's viper (in some cases)
Renal toxicity	Russell's viper, Hump nosed viper
Myotoxicity	Sea snakes, some krait species

- There may be ptosis and both internal and external ophthalmoplegia giving a false impression of brain stem dysfunction. However, the patient responds to commands by using the frontalis muscle and orbicularis oculi.
- Usually, there are no local reactions in neuroparalytic snake envenomation (krait); however, in cobra bite, severe local reaction can be seen.
- The differential diagnosis of any patient presenting with sudden onset of neurological deficit with respiratory compromise is enumerated in Table 16.2.
- Examination of the bitten part: fang marks, extent of swelling, blisters, necrosis, infection, and abscess formation.
- Bleeding from the bite site may be the first manifestation of envenomation.
- Look for hematuria, epistaxis, bleeding from gums, hematemesis, and ecchymosis.
- Check blood pressure and carefully follow and monitor (Table 16.3).

Table 16.2 Differential diagnosis of acute neurological weakness

Acute inflammatory demyelinating polyradiculoneuropathy (AIDP, i.e., LGB syndrome)
Transverse myelitis
Periodic paralysis (hypokalemic, hyperkalemic, normokalemic)
Acute myasthenic crisis
Organophosphorus poisoning
Hypomagnesemia and hypophosphatemia
Hypoglycemia
Acute intermittent porphyrias
Polymyositis/dermatomyositis
Tick paralysis
Head/spinalcord injury

Table 16.3 Symptoms and signs of snake bite

Local	Fang marks, swelling, blisters, necrosis, bleeding from bite site, lymphnode enlargement, infection, abscess formation, compartmental syndrome
Neurological	Diplopia, ptosis, cranial nerve palsies, dysphagia, dysphonia, pooling of secretions, neck muscle weakness, respiratory muscle weakness, paradoxical breathing, descending paralysis, diminished or absent deep tendon reflexes
Coagulopathy	Bleeding from bite site, bleeding from gums, epistaxis, hemoptysis, hematemesis, retroperitoneal bleeding, intracranial bleeding resulting in various neurological manifestations
Renal	Loin pain, hematuria, hemoglobinuria, myoglobinuria, oliguria/anuria. Symptoms and signs of AKI
Cardiovascular	Visual disturbances, faintness, collapse, hypotension, shock, arrhythmias, myocardial damage. Generalized increase in vascular permeability resulting in facial, periorbital edema, conjunctival oedema, pleural and pericardial effusions, haemoconcentration and albuminuria
Skeletal muscle	Generalized pain, stiffness and tenderness of muscles, pain on passive stretching, trismus, myoglobinuria
Others	Fear, anxiety, nausea, vomiting, abdominal pain, weakness, and drowsiness. Stroke due to arterial thrombosis. Acute pituitary or adrenal insufficiency

Table 16.4 Severity of snakebite

Severity	Local findings	Systemic findings
Nonenvenomation (dry bite)	None or puncture wounds only	None
Mild	Puncture wounds, pain, soft tissue swelling confined to the bite site	None
Moderate	Swelling beyond bite site	Mild nausea, vomiting or fasciculations, paraesthesia, microscopic hematuria
Severe	Severe pain and swelling	Respiratory failure or hypotension or bleeding

Step 4: Severity of Snakebite

Once a diagnosis of snakebite is made, the patient should be assessed for the severity, as enumerated in Table 16.4.

Step 5: Order Investigations

- Complete hemogram with platelet counts, bleeding time (BT), coagulation time (CT), and 20 min whole blood clotting test (20WBCT).
- Urine examination—RBCs in the presence of gross hematuria.
- Prothrombin time, INR, PTTK, fibrinogen level, fibrin degradation product, D-dimer.
- If urine is smoky, dipstick positive for blood and RBCs absent, look for myoglobulin to rule out myoglobinuria.
- Blood urea and serum creatinine levels should be regularly monitored in patients with renal failure.
- Serum electrolytes and blood gas analysis.
- ECG for arrhythmias.
- Aminotransferases and muscle enzymes (creatine kinase and aldolase).

Step 6: Admit to the ICU

- Indications of ICU admission are mentioned in Table 16.5.

Step 7: General Management

- All the patients should receive antitetanus toxoid, and the local wound should be cleansed with soap and water.
- The limb with the bite mark should be immobilized; however, no tourniquet should be tied.

Table 16.5 Admission to the ICU

Circulatory shock, cardiac dysfunction, pulmonary edema
Hemorrhage, hypovolemia
Coagulopathy, disseminated intravascular coagulation
Coma, seizures, intracranial hemorrhage
Cranial nerve dysfunction
Rhabdomyolysis, renal failure, hyperkalemia
Gastrointestinal bleeding
Respiratory failure
Anaphylaxis (component of venom or antivenom)

- Keep the bitten limb lower than the heart as far as possible.
- Open the tourniquet, if applied outside, only when resuscitative measures are available.
- Patients with mild features should be observed for at least 24 h.
- Do not apply ice to the bite site. Avoid vigorous cleaning, incision, or suctioning to bite site.
- Routine use of antibiotics is not recommended.
- Measure intracompartmental pressure if compartmental syndrome is suspected.
- Monitor blood pressure, oxygenation, cardiac rhythm, and urinary output.

Step 8: Specific Management

Antisnake venom

- Antisnake venom (ASV) is prepared from horses' serum.
- It can be monovalent or polyvalent.
- One milliliter of reconstituted polyvalent antivenin neutralizes 0.6-mg venom of Indian cobra and Russell's viper and 0.45 mg of common krait and saw-scaled viper.
- ASV should not be administered locally at the bite site.
- The usual initial dose of ASV is 10 vials.
- ASV can be give either by slow injection (maximum 2 mL/min) or by intravenous infusion (diluted in normal saline or dextrose—5 mL/kg body weight) over 30–60 min.
- Repeat the initial dose of ASV if blood remains non coagulable after 6 h, or 1 h later if spontaneous bleeding persists, or neurotoxic or cardiovascular signs persists or deteriorates.
- Children should be given the same dose of ASV as adults since the amount of venom injected is same.
- ASV will not have a dramatic effect in neuroparalysis. Low-dose ASV is as effective as high dosage in neuroparalytic snake envenomation.
- ASV will however have dramatic effect in stopping bleeding and coagulation abnormalities.

Step 9: Watch for Reaction

- ASV is a foreign protein. Therefore, allergic reactions including anaphylaxis are not unknown.
- Skin test before injection is not recommended to predict infusion reactions.
- H_1 blockers, H_2 blockers, and hydrocortisone do not decrease the incidence of infusion reactions.
- Routine use of prophylactic adrenaline 0.25 mg (0.25 mL of 1% adrenaline given subcutaneously) is recommended to decrease the incidence of infusion reactions.
- An adrenaline syringe should always be kept ready before infusing ASV.
- In case the patient develops reaction to ASV during infusion, first stop the infusion of ASV.
- It should be followed by adrenaline—usual recommended dosage is 0.5 mg of 1:1000 dilutions intramuscularly.
- Additional dosages of H_1 (chlorpheniramine maleate) and H_2 (ranitidine) blockers with hydrocortisone 100 mg, though later will take 4–6 h to act, should be given simultaneously.
- If needed, adrenaline can be repeated up to two to three dosages or an infusion can be started in dilution of 1:50,000.
- Hypotension is treated with fluids. Inotropes may be required in patients who had overt myocardial dysfunction.

Step 10: ICU Management

- Initiate mechanical ventilation at appropriate time as it reduces the mortality significantly in neuroparalytic envenomation.
- Anticholinesterase drugs such as edrophonium and neostigmine have also been recommended for the treatment of neuroparalytic snake envenomation. They should be given with atropine to take care of their cholinergic effect.
- 10 mg of edrophonium (IV) or 0.5 mg of neostigmine (IM) should be given over 2–3 min with atropine pretreatment (0.6 mg). In case the patient improves, he/she should be managed with neostigmine/atropine over the next 24–48 h.
- General ICU management—propped up nursing, ulcer prophylaxis, DVT prophylaxis, glucose control and appropriate sedation, and analgesia.
- Majority of patients usually recover within 48 h.

Step 11: Manage Complications

- Patients who develop complications should be managed in the ICU till they are resolved (Table 16.5).
- Consider wound debridement if local swelling and necrosis is severe enough to threaten viability of the limb and life.

- Consider fasciotomy if there is clinical evidence of intracompartmental syndrome or when the intracompartmental pressure exceeds 40 mmHg (in adults)
- Rhabdomyolysis should be managed with adequate hydration, correction of acidosis with bicarbonate and promoting alkaline diuresis.

Step 12: Discharge from the ICU

The patient can be discharged from the ICU if the following conditions are present:

- Resolution of paralysis more than 24 h
- Fifty percent improvement in creatine phosphokinase and potassium
- Peak expiratory flow rate (PEFR) more than 100 L/min
- Normal oximetry and blood gas analysis on room air
- Normalization of BT, CT, CRT, and platelets more than 50,000
- Stable or improved urine output

Patient should be informed about late reactions (serum sickness) which can be treated with oral antihistamine or steroid.

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Heat Stroke and Hypothermia

17

Jagdish Dureja, Harpreet Singh, and Saru Singh

Heat Stroke

It was the month of July; a 35-year-old male laborer became unconscious at work. On examination, he was found to be obtunded with minimal response to painful stimulus. His skin was hot and flushed. He was tachypneic, tachycardiac, hypotensive and hyperthermic (core temperature 107 °F or 41.7 °C).

Normal temperature is a balance between heat production and dissipation. Evaporation, the principal mechanism of heat dissipation is less effective with high humidity. Convection and conduction and other mechanism of heat dissipation are ineffective when external temperature exceeds skin temperature. High fever can have serious consequences such as renal failure, disseminated intravascular coagulation and death. Prompt and appropriate management can improve the outcome in these patients.

Step 1: Initiate Resuscitation

- These patients should be resuscitated as mentioned in Chap. 23, Vol. 2.
- Administer IV fluids promptly as these patients are dehydrated. The type and amount of fluid should be guided by volume status, electrolytes, and cardiac functions.
- Use of Vasopressors (alpha agonists) is discouraged if possible to avoid peripheral vasoconsriction

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Step 2: Assess the Cause and Type of Hyperthermia by History and Examination

Hyperthermia may be caused by sepsis, CNS infection, tetanus, malaria and typhoid fever

- Severe Hyperthermia with core temperature greater than 104 °F or 40 °C is commonly seen due to failure of thermoregulation in heat stroke, malignant hyperthermia and neuroleptic malignant syndrome.
- Heat stroke is usually caused by prolonged exposure to excessive heat.
- Exertional heat stroke occurs in young, healthy individuals engaged in heavy exercise during periods of high ambient temperature and humidity.
- Nonexertional heat stroke is diagnosed with history of exposure to severe environmental heat, core temperature >40 °C, central nervous system dysfunction. It is precipitated by various medications, such as anticholinergic drugs, antihistaminics, diuretics, antipsychotics (e.g., MAO inhibitors and tricyclic antidepressants), neuroleptic agents and illicit drugs (amphetamines, cocaine, LSD, MDMA) as vasodilation, sweating, and other heat-loss mechanisms are reduced by these drugs.
- Brain hemorrhage, status epilepticus and damage to the hypothalamus can also cause severe hyperthermia.
- Thyrotoxicosis and pheochromocytoma cause hyperthermia by increasing heat production.
- Malignant hyperthermia is a rare complication of general anaesthetics such as succinylcholine and halothane and should be suspected if there is sudden rise of $EtCo_2$ in a patient undergoing surgery under general anesthesia.
- Signs and symptoms of heat stroke include altered mentation or seizures, possible hallucinations, delirium, dry skin, rapid pulse, tachypnea, rales due to noncardiogenic pulmonary edema, pupil dilation, muscle rigidity, hypotension, arrhythmias, rhabdomyolysis, dyselectrolytemia and coma. Disseminated intravascular coagulation and mixed respiratory and metabolic acidosis can accompany the elevated temperature.

Step 3: Send Investigations

- Haemogram
- Creatine phosphokinase—elevated levels suggest rhabdomyolysis
- Renal functions
- Urine for myoglobin
- When indicated, coagulation studies, toxicologic screening, CT head, and lumbar puncture should be carried out.
- Diagnosis of malignant hyperthermia is confirmed by in vitro muscle contracture test.

Step 4: General Management

- Advise the patient to rest, preferably in a cool place.
- If the patient is conscious, offer fluids but avoid alcohol and caffeine.
- Intravenous fluid should be titrated using vital signs, urine output and hemodynamic measurements to avoid pulmonary edema associated with fluid overload.
- Confirm the diagnosis with a calibrated thermometer to measure high temperature (40–47 °C).
- Encourage him/her to shower and bath, or sponge off with cool water.
- There is no role of antipyretics (acetaminophen/acetylsalicylic acid).
- Monitor core temperature continuously with a rectal or esophageal probe.
- In order to avoid iatrogenic hypothermia, stop cooling at 39.5 °C (103 °F).

Cooling measures: The biggest predictor of outcome is the degree and duration of hyperthermia, time to initiation of cooling measures and number of organ systems affected.

External cooling techniques are easier to implement, effective, well-tolerated, and include the following:

- Conductive cooling-direct application of sources such as hypothermic blanket, ice bath, or ice packs to neck, axillae and groins. Ice packs are effective but poorly tolerated by the awake patient. Avoid vasoconstriction and shivering as vasoconstriction impedes the heat loss and shivering creates heat. Shivering may be suppressed with IV benzodiazepines such as diazepam (5 mg) or lorazepam (1–2 mg).
- Convective techniques include removal of clothing and use of fans and air conditioners
- Evaporative cooling can be accelerated by removing clothing and using a fan in conjunction with misting the skin with tepid water or applying a single-layer wet sheet to bare skin.
  - Immersing the patient in ice water is the most effective method of rapid cooling specially for young patients presenting with exertional heatstroke; however, it complicates monitoring and access to the patient. Also, it is associated with poor outcome in elderly patients presenting with non exertional heatstroke.
- *Internal cooling techniques* such as ice water gastric or rectal lavage, thoracic lavage, peritoneal lavage and extracorporeal blood cooling are effective, but they are difficult to manage and are associated with complications. Cold peritoneal lavage results in rapid cooling but is an invasive technique contraindicated in pregnant patients or those with previous abdominal surgery. ECMO can also be done in severe cases.
- Cold humidified O_2, cold IV fluids are useful adjuncts.

Step 5: Specific Management: Malignant Hyperthermia and Neuroleptic Malignant Syndrome

- Dantrolene, a nonspecific skeletal muscle relaxant, is the mainstay of treatment. It acts by blocking the release of calcium from the sarcoplasmic reticulum, thereby decreasing the myoplasmic concentration of free calcium and diminishes the myocyte hypermetabolism that causes the symptoms.
- It is most effective if given early in the illness, when maximal calcium can be retained within the sarcoplasmic reticulum.
- There is associated risk of hepatotoxicity with dantrolene, so it should be avoided if liver function tests are abnormal (see Fig. 17.1 for detail).

Step 6: Manage Complications

- *Rhabdomyolysis*
  - Expand the intravascular volume with normal saline and administer mannitol and sodium bicarbonate.
  - Alkalinization of urine (to pH 7.5–8.0) prevents the precipitation of myoglobin in the renal tubules, treats acidosis and hyperkalemia. Maintain a urine output of 3 mL/kg/h.
  - The goal is to prevent myoglobin-induced renal injury by promoting renal blood flow, diuresis. Monitor serum electrolytes to prevent life-threatening arrhythmias.
- *Hypotension:* To sustain organ perfusion, hypotension refractory to fluid optimization should be managed by using vasopressors, isopreterenol or dobutamine to maintain MAP more than 65 mmHg.
- *Seizures* should be managed with EEG monitoring and IV benzodiazepines, Leviteracetam
- *Multiorgan failure*: Give supportive therapy until organ function recovers (see Chap. 32, Vol. 2).

Step 7: Prevention

- Hyperthermia, caused by physical exertion or hot environment, can be prevented by taking frequent rest breaks and staying hydrated.
- Genetic testing can be used to evaluate individual susceptibility in patients from families with a history of malignant hyperthermia.

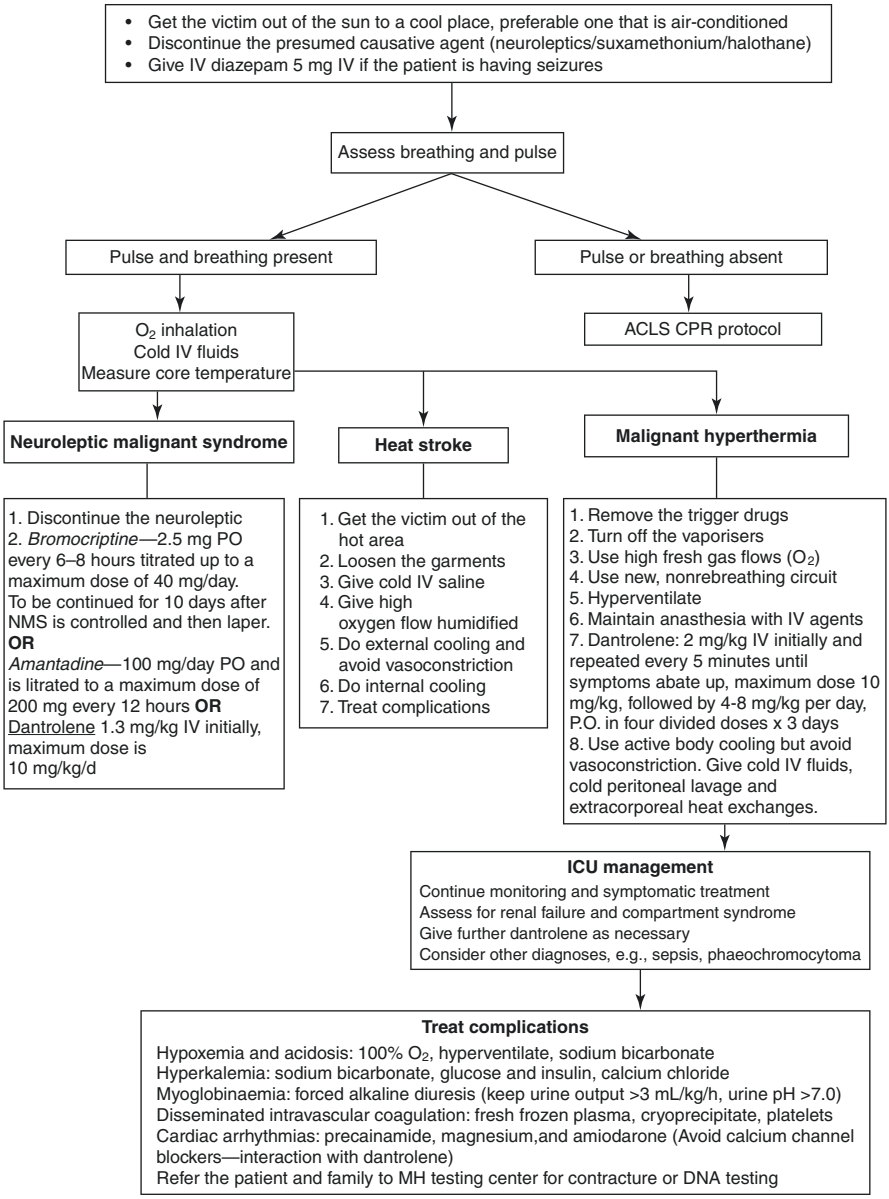

Fig. 17.1 Management of hyperthermia

Hypothermia

An 82-year-old man, a known case of Alzheimer's disease and hypothyroidism was found unresponsive on his backyard lawns. He had been taking aspirin, olanzapine, and levothyroxine for the past 3 years. Examination revealed femoral pulse 35/min, blood pressure (BP) unrecordable, Glasgow Coma Scale 3 and temperature 28 °C.

Hypothermia is defined as core temperature below 35 °C which should be measured by core temperature measuring probes.

Step 1: Initiate Resuscitation

Initiate resuscitation as mentioned in Chap. 23, Vol. 2.

- The management should start with removal of wet clothing if any and replacing it with warm, dry sheet.
- In severe hypothermia, if indicated, the patient is intubated gently and ventilated with warmed humidified O_2 while closely monitoring cardiac rhythm.
- One should be prepared to treat ventricular fibrillation with a single DC shock (200 J) and initiate cardiopulmonary resuscitation.
- In case the patient is found in unfavourable terrain and needs evacuation, cardiopulmonary resuscitation can be done with mechanical device.
- In case mechanical device is not available, continuous high quality CPR should be done if temperature is ≥28 °C.
- CPR can be done intermittently for 5 min alternated with ≤5 min without CPR (if temp <28 °C) and ≤10 min without CPR (if temp <20 °C) to assist evacuation.
- Continue CPR till the temp is above 32–35 °C at which point renewed attempts at defibrillation may be attempted
- Neuroprotective effects of low temperature may allow recovery following prolonged arrest
- Start IV line and infuse warm normal saline

Step 2: Diagnose Types and Severity of Hypothermia

Primary (Accidental Hypothermia)

- Normal thermoregulation
- Overwhelming cold exposure

Secondary

- Abnormal thermogenesis

Table 17.1 Severity of hypothermia

Mild (32–35 °C)	Shivering, amnesia/dysarthria, loss of coordination, tachycardia, tachypnea, normal BP
Moderate (28–32 °C)	Absent shivering, bradycardia/atrial fibrillation, ↓ BP, ↓ respiratory rate, and stupor
Severe (<28 °C)	Coma, absent corneal and oculocephalic reflexes, ↓↓ BP, ventricular fibrillation, apnea, areflexia, dilated and fixed pupils, flat EEG, asystole

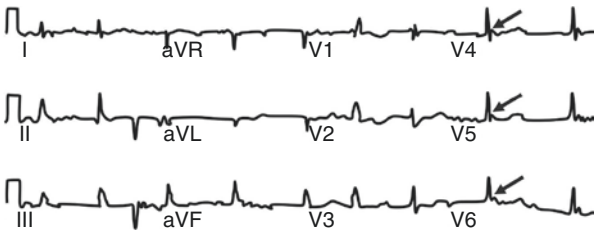

Fig. 17.2 Osborn (J) waves (marked with arrows)

- Multiple causes (hypothyroidism, burns, hypothalamic abnormalities, sepsis, ethanol abuse, sedative—hypnotic, oral hypoglycemics)
- Severity of hypothermia with presentation is described in Table 17.1.
- ECG may show Osborn (J) waves especially when temperature is less than 33 °C (Fig. 17.2).
- It is a positive deflection, and its amplitude is proportional to the degree of hypothermia, usually seen in leads V3–V6 at junction of QRS and ST segment.

Step 3: Manage Hypothermia

The patient should be warmed as soon as possible by the following rewarming methods**:** passive, active external, and active internal.

- *Passive rewarming:* It allows endogenous heat production to increase the core temperature, but heat conserving mechanisms must be intact (e.g., shivering, metabolic rate, and sympathetic nervous system).

  It also includes decreasing heat loss by removal from cold environment, removing wet clothes and providing the blanket. Passive warming increases body temperature by 0.5–2.0 °C/h. It is the rewarming method of choice for mild hypothermia and also adjuncts for moderate hypothermia.
- *Active external:* It transfers exogenous heat to the patient. It can be provided by heating blankets (fluid filled), air blankets, radiant warmers, immersion in hot bath, hot water bottles, and heating pads. It is less effective than internal rewarming if the patient is vasoconstricted.

The rewarming rate is 1–2.5 °C/h. Rewarming of the trunk should be undertaken before the extremities as active external warming of extremities can lead vasodilatation of the vessels in the extremities and shunts cold blood to the core, resulting in an overall further decrease in body temperature. This paradoxical drop in core temperature is known as the after-drop phenomenon. Circulatory problem may be decreased by applying rewarming devices to trunk only.

- *Active internal warming:* It is done by the following:
- Warm IV fluids
- Warm and humidified oxygen
- Peritoneal lavage
- Gastric/esophageal lavage
- Bladder/rectal lavage
- Pleural lavage
- Intermittent hemodialysis
- Atrial arrhythmias should be monitored without intervention, as the ventricular response is slow, and unless preexistent, most will convert spontaneously during rewarming. Preexisting ventricular ectopy may be suppressed by hypothermia and can reappear during rewarming. If available, bretylium tosylate, the class III ventricular antiarrhythmic, is the drug of choice.
- Electrolytes and thyroid profile should be assessed and corrected if required.

  Cardiopulmonary bypass and Extracorporeal life support is a method of choice used for rewarming patients with cardiac arrest and severe hypothermia and Hyperkalemia.
  - ECMO is useful when applied to a patient with core temp <30 °C. This strategy provides circulation, oxygenation, and ventilation while core body temperature is increased. If cardiopulmonary bypass facilities are not available, a combination of invasive rewarming methods should be used. Once spontaneous circulation is returned, passive or active external rewarming methods can be used. Basic life support should be continued until core temperature is more than 30 °C. Cardioactive drugs and further defibrillation should be withheld until this temperature is reached.

Stepwise management of hypothermia is shown in Fig. 17.3.

If core body temperature does not respond to warming efforts, underlying infection or endocrine derangements must be considered. Treatment with broad spectrum antibiotic and glucocorticoid may be instituted empirically. Look and treat for Myxedema and hypoglycemia.

Step 4: Manage Associated Complications Rhabdomyolysis, Bleeding Complication, Infection

After resuscitation pay close attention to hypotension during active rewarming, arrhythmias, hypokalemia, hypoglycemia, bleeding diathesis, and bladder atony.

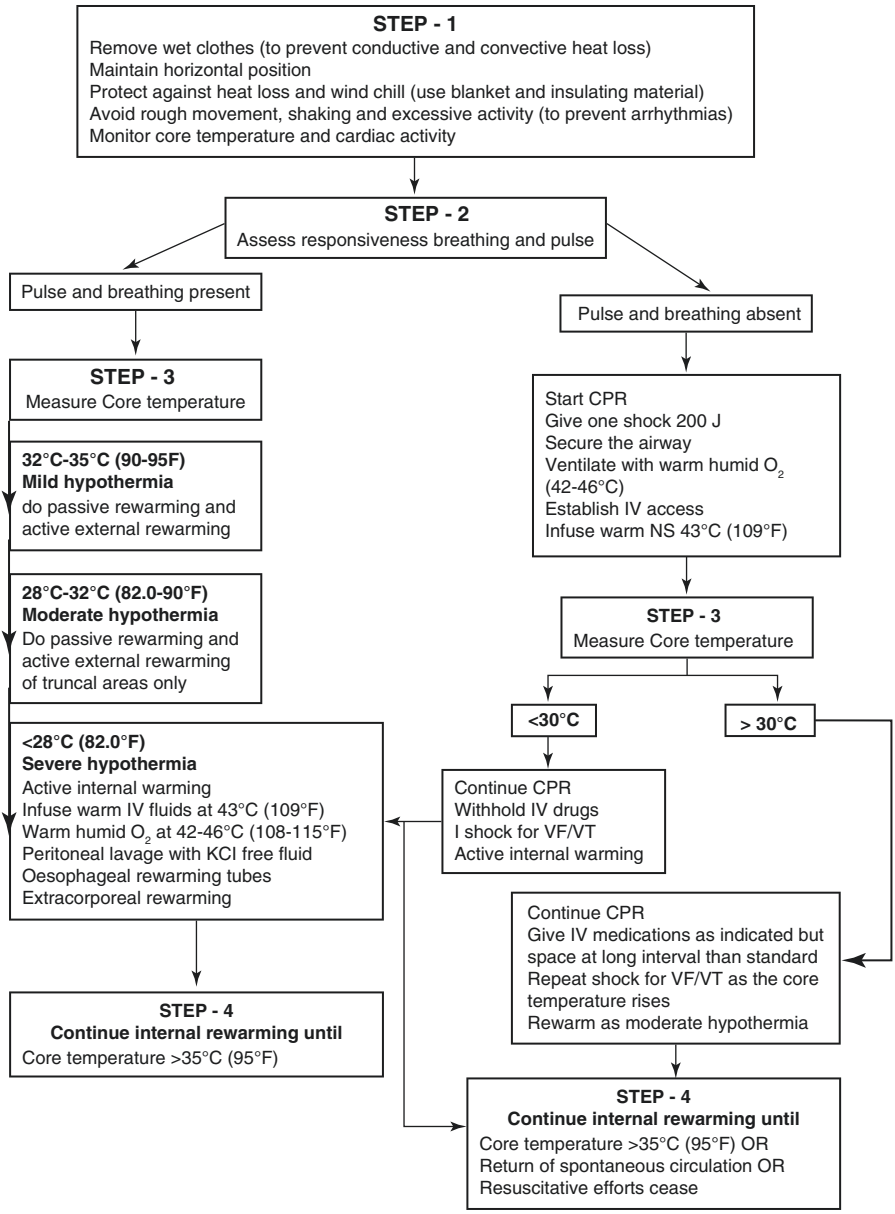

Fig. 17.3 Stepwise management of hypothermia

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Part V

Obstetrics

Jaundice in Pregnancy

18

Rajesh Chawla, Prashant Nasa, and Aakanksha Chawla Jain

A 25-year-old female primigravida at 35 weeks of pregnancy had been admitted to the hospital with jaundice for 3 days, decreased fetal movements, and decreased urine output for 8 h. Her antenatal status was fine, with no history of pregnancy-induced hypertension. HBsAg and HIV were negative. Her Blood pressure is 140/96 mmHg, icteric with SGOT-92, SGPT –110 IU/L, total bilirubin 9.3 mg/dL and direct (6.7 mg/dL), alkaline phosphatase 208, Albumin 2.5, INR 1.8.

Jaundice in pregnancy can occur due to pregnancy-related and unrelated diseases.

Pregnancy-related liver diseases are real threat to the survival of the fetus and the mother.

Rapid diagnosis is needed to manage them appropriately.

Step 1: Initiate Resuscitation

Airway intervention may be required in the following conditions:

- Altered mental status and seizures.
- Acute respiratory failure not responding to conservative measures.
- Cesarean section under general anesthesia.
- Shock—to reduce work of breathing.

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- Always anticipate difficult airway in pregnant patients.
- Endotracheal intubation should be performed sooner rather than later to protect the airway.
- Intubation must be performed by an experienced operator.
- Difficult airway equipment for airway management must be thoroughly checked before proceeding to intubation, and the alternative plan for definitive airway including surgical access should be identified.
- Raised intracranial pressure (ICP) in the jaundiced pregnant patient is a serious concern, and therefore, proper sedation should be ensured with minimal manipulation during intubation.
- Supplemental oxygen may be required in some patients depending on their oxygen saturation, target SpO_2 more than 95%.

Circulation

- Two large-bore intravenous cannulae (14G or 16G) should be placed to administer fluids.
- Be careful of associated coagulopathy.
- A Foley's catheter should be placed to monitor urine output.
- Use fluid administration judiciously to optimize preload and at the same time to avoid overload, which might increase ICP.
- Nurse in the left lateral position (30° wedge to the right hip) to prevent supine hypotension syndrome.

Disability (Neurological)

- Perform a brief neurological assessment including Glasgow coma score, pupil size, and reaction to light in case of altered mental status.

Step 2: Take History and Perform Physical Examination

Take detailed history that should cover the following:

- Details about pregnancy (trimester of pregnancy)
- Antenatal evaluation and immunization
- History of hypertension, pregnancy-induced hypertension during the previous pregnancy, complications and outcome of previous pregnancy, and family history of hypertension
- Duration of jaundice and pruritus, other constitutional symptoms such as malaise, nausea, anorexia, fever, weight loss or increased abdominal girth from ascites, and seizures
- History of abdominal surgery, medication history (amount and time of acetaminophen, herbal medications), and transfusion history

- History of alcohol consumption, HIV and hepatitis risk factors, intravenous drug abuse, exposure to travel, occupational, and recreational history
- History of hepatitis B or C in the spouse
- In physical examination, also look for the signs of acute liver failure:
- Altered mental status
- Icterus, anemia
- Ecchymotic patches/bleeding from gastrointestinal tract or urinary tract
- Epigastric or right upper quadrant abdominal tenderness
- Peripheral edema, hyperreflexia, or clonus
- Seizures
- Hypotension (hypovolemia, hemolysis, sepsis)
- Spider angioma and palmar erythema may be normal in pregnancy

Step 3: Assess the Severity of Hepatic Encephalopathy

One should assess the severity of hepatic encephalopathy to plan the appropriate treatment (Table 18.1).

Step 4: Send Investigations

- Complete blood cell count.
- Liver function tests—remember normal physiological changes in pregnancy (Table 18.2).
- Renal function tests and serum electrolytes.
- Arterial blood gas analysis and blood glucose.
- Hepatotropic virus profile (IgM anti-HEV, IgM anti-HAV, IgM anti-HCV, anti-HBc antibody, HBeAg, HBsAg).
- Coagulation profile (prothrombin time, activated partial thromboplastin time, fibrinogen, fibrin degradation product).
- Uric acid.
- The antinuclear factor—to exclude autoimmune hepatitis.

Table 18.1 Stages of hepatic encephalopathy

Stage	Mental status	Neuromuscular function
1	Impaired attention, irritability, depression	Tremor, incoordination, apraxia
2	Drowsiness, behavioral changes, memory impairment, sleep disturbances	Asterixis, slowed or slurred speech, ataxia
3	Confusion, disorientation, somnolence, amnesia	Hypoactive reflexes, nystagmus, clonus, muscular rigidity
4	Stupor and coma	Dilated pupils and decerebrate posturing, oculocephalic reflex

Table 18.2 Physiological changes in liver tests during normal pregnancy

Liver functions affected by pregnancy	
Albumin and total protein	Decrease from first trimester
Alkaline phosphatase levels	Increase in second and third trimester
Bilirubin levels	May decrease from first trimester
Gamma glutamyltransferase levels	Decrease in late pregnancy
Cholesterol levels	Increase by twofold
Fibrinogen levels	Increase by 50%
Tests remain unaffected by pregnancy	
Serum aminotransferase levels (ALT, AST)	
Prothrombin time	
Serum concentration of total bile acids (fasting state)	
Lactate dehydrogenase (LDH)	

Table 18.3 Classification of liver diseases in pregnancy

	Pregnancy-unrelated liver diseases	
Pregnancy-related liver diseases	Preexisting liver diseases	Liver diseases coincident with pregnancy
Intrahepatic cholestasis of pregnancy (ICP)	Hepatitis B and C	Biliary disease
Preeclampsia and eclampsia	Autoimmune liver disease	Budd–Chiari syndrome
Hemolysis, elevated liver enzymes, low platelet (HELLP) syndrome	Wilson's disease	Drug-induced hepatotoxicity
Acute fatty liver of pregnancy (AFLP)	Cirrhosis and portal hypertension	Viral hepatitis A and E
Hyperemesis gravidarum		

- Additional tests—peripheral smear, serum lactate dehydrogenase levels, reticulocyte count, and Coombs' test—to exclude thrombotic thrombocytopenic purpura (TTP).
- Ultrasonography is considered safe and is the preferred abdominal imaging modality during pregnancy.
- MRI with contrast is preferable to CT scanning during pregnancy to avoid ionizing radiation.
- Transthoracic echocardiography.

Step 5: Differential Diagnosis

The various conditions that can cause acute hepatic failure can be divided into those related to pregnancy and those unrelated to pregnancy (Tables 18.3 and 18.4).

Table 18.4 Comparison of severe preeclampsia–eclampsia, intrahepatic cholestasis of pregnancy, HELLP syndrome, and AFLP

	Severe preeclampsia–eclampsia	Intrahepatic cholestasis of pregnancy	HELLP syndrome	AFLP
Trimester	Second to third	Second to third	Third	Third
Incidence (%)	1–5	0.1	0.2–0.6	0.005–0.01
Family history	Occasionally	Often	No	Occasionally
Presence of preeclampsia	Yes	No	Yes	50%
Typical clinical features	Hypertension, edema, proteinuria, neurological deficits (headaches, seizures, coma)	Pruritus, mild jaundice, elevated bile acids	Hemolysis thrombocytopenia (<50,000 often)	Liver failure with coagulopathy, encephalopathy, hypoglycemia, disseminated intravascular coagulation
Aminotransferases	None/mild	Mild to 10- to 20-fold elevation	Mild to 10- to 20-fold elevation	300–500 typical but variable
Bilirubin	Normal—<5 mg/dL	<5 mg/dL	<5 mg/dL unless massive necrosis	Often <5 mg/dL, higher if severe
Hepatic imaging	Normal—hepatic infarcts	Normal	Hepatic infarcts hematomas, rupture	Fatty infiltration
Histology (usually not performed)	Periportal hemorrhage, necrosis, fibrin deposits	Normal–mild cholestasis, no necrosis	Patchy/extensive necrosis and hemorrhage	Microvesicular fat in zone 3 long-chain 3-hydroxyacyl-CoA dehydrogenase defect—yes fatty acid oxidation defect—rare
Recurrence in subsequent pregnancies	20% risk	60–70%	4–19%	

- Use of gestational age of the pregnancy is the best guide to the differential diagnosis of liver disease in the pregnant woman
- Hyperemesis gravidarum should be considered in the differential diagnosis of abnormal liver tests in the first trimester
- Cholestasis of pregnancy should be considered in the differential diagnosis of abnormal liver tests presenting initially in the second trimester. Early delivery should be considered to prevent prematurity and stillbirth
- HELLP (hemolysis, elevated liver tests, low platelets) syndrome and acute fatty liver of pregnancy should be considered in the second half of pregnancy
- Patients with acute fatty liver of pregnancy have true hepatic dysfunction, and may, or may not, have signs of pre-eclampsia and HELLP syndrome
- Consider viral or drug-induced hepatitis, gallstone disease, or malignancy in the differential diagnosis of abnormal liver tests in any of the trimesters of pregnancy
- Chronic hepatitis B or C poses a risk of transmission to the offspring

Step 6: Management

1. *AFLP*

   Prompt delivery is essential; expectant management is not appropriate
   - Caeserian if required, consider coagulopathy and DIC for anesthesia and surgical risk.
   - Manage complications:
     - Renal failure, hypoglycemia, encephalopathy.
     - Acute pulmonary edema or acute respiratory distress syndrome
     - Coagulopathy/disseminated intravascular coagulation
   - Rarely, liver transplantation is indicated for liver rupture with necrosis, fulminant liver failure, hepatic encephalopathy, or worsening coagulopathy.
2. *Hyperemesis gravidarum*
   - Treatment is supportive and need hospitalization with intravenous rehydration and antiemetics.
   - Vitamin supplementation, including thiamine, is mandatory to prevent Wernicke's encephalopathy.
   - There is no role of steroids.
   - Relapse and recurrence in subsequent pregnancies is common.
3. *Intrahepatic cholestasis of pregnancy*
   - Treatment of choice is ursodeoxycholic acid (10–15 mg/kg/day), which helps to relieve pruritis and improve hepatitis.
   - Owing to increased risk of fetal complications, early delivery at 37 weeks is recommended or if clinical condition is deteriorating despite treatment.

- Mechanism of action is unknown.
- Other drugs are cholestyramine, dexamethasone, and vitamin K supplementation.

4. *Management of severe preeclampsia–eclampsia and HELLP syndrome*
5. *Preeclampsia with hepatic involvement is severe preeclampsia an*d should be managed appropriately. After 36 weeks, women with severe preeclampsia should be delivered promptly to limit maternal and fetal complications.

   The HELLP syndrome is a medical emergency and should be managed by prompt delivery, especially after 34 weeks gestation. Target platelet count 40,000–50,000/cu.mm before delivery.
   - Anticipation and management of hepatic rupture requires surgical referral and tertiary care hospital care with liver transplant team expertise.
6. *Viral hepatitis*

   All pregnant women presenting with acute hepatitis should be tested for common etiologies of acute liver injury including viral hepatitis HAV, HBV, HCV, HEV, and HSV.
   - Treatment is mainly supportive and similar to nonpregnant patients.
   - Course is not altered by delivery.
   - Herpes simplex hepatitis can be effectively treated with acyclovir if the diagnosis is recognized promptly.

Suggested Reading

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Acute Respiratory Failure During Pregnancy

19

Rajesh Chawla, Prashant Nasa, and Aakanksha Chawla Jain

A 25-year-old female at 36 weeks of pregnancy was admitted to hospital with complaints of breathlessness, right sided chest pain, and swelling of the left leg for 3–4 days. Her BMI was 40 kg/m^2. She was tachypneic, chest was clear, and SpO_2 on room air was 90%.

Acute respiratory failure during pregnancy can occur due to many disorders. It can result in significant maternal and fetal morbidity and mortality.

Step 1: Initiate Assessment and Resuscitation

Airway

- Airway evaluation and management remains the first priority in the initial resuscitation as in nonpregnant patients.
- Definitive airway (tracheal intubation) is needed in persistent hypoxemia, airway obstruction, impaired laryngeal reflexes, or in altered consciousness.
- Difficult airway equipment for airway management must be thoroughly checked before proceeding to intubation, and an alternative plan for definitive airway including surgical access should be identified.
- Intubation should be performed by a senior intensivist/anesthesiologist especially in later part of pregnancy due to upper airway edema and narrow airway caliber.

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Breathing

- Supplemental oxygen may be required in some patients depending on their oxygen saturation.
- High Flow nasal Oxygenation or Noninvasive ventilation (NIV) can be tried only in the controlled ICU setting. Signs of failure of NIV and requirement of intubation should also be identified sooner than later. This includes increased work of breathing, mental status deterioration, hemodynamic instability, and inability to protect the airway or manage secretions.
- Always target SpO_2 of more than 95%. For adequate fetal oxygenation, a maternal arterial oxygen tension (PaO_2) of more than 70 mmHg is required, which corresponds to an oxyhemoglobin saturation of 95%.

Circulation

- Two large-bore intravenous cannulae (14G or 16G) should be placed to administer fluids.
- Administrate fluid judiciously to optimize preload and at the same time to avoid overload.
- Maintain high cardiac output.
- Nursing in the left lateral (30° wedge to the right hip) position is needed to prevent supine hypotension syndrome.

Step 2: Take History and Physical Examination

- Take detailed history of pregnancy, antenatal evaluation and immunization, respiratory disease (e.g., asthma and tuberculosis), and family history of active respiratory infections.
- Detailed history of respiratory symptoms such as dyspnea, cough, expectoration, and chest pain should be evaluated.
- The physical examination includes assessment of the severity of respiratory failure by general assessment, respiratory rate, use of accessory respiratory muscles, and signs of impending respiratory arrest (e.g., fatigue, drowsy, silent chest, and bradycardia).
- Assessment of the fetus is also important. Fetal heart sounds and its variability—to ascertain the fetal well-being—should be assessed along with the maternal assessment.

Step 3: Understand Physiological Changes in Pregnancy

- Pregnancy causes various mechanical, immunological, biochemical, and hemodynamic changes on the cardiorespiratory system (Table 19.1).

Table 19.1 Effects of pregnancy on pulmonary physiology

	Anatomical changes	Physiological alterations
Airway	Edema, mucosal friability, rhinitis	Increased respiratory drive
		Hyperventilation
Thorax including lung parenchyma	Widened diameters, widened subcostal angle, elevated diaphragm	Reduced functional residual capacity
		Increased tidal volume
		Preserved vital capacity
		Respiratory alkalosis
		Normal oxygenation
Abdomen	Enlarged uterus	Reduced chest wall compliance
Cardiovascular system	Increased left ventricular (LV) mass	Increased cardiac output
	Increased blood volume	
Arterial blood gas		7.40–7.45 pH
		28–32 mmHg $PaCO_2$
		106–110 mmHg PaO_2

- Normal $PaCO_2$ on ABG should be interpreted as a sign of impending respiratory failure as there is a mild respiratory alkalosis in pregnancy (see Table 19.1).
- Inability to maintain a PaO_2 of more than 70 mmHg, or a SaO_2 of more than 95%, with conservative therapy should also be interpreted as a sign of respiratory compromise.

Step 4: Send Investigations

- Complete hemogram.
- Liver function tests.
- Renal function tests and serum electrolytes.
- Arterial blood gas.
- Coagulation profile (prothrombin time [PT], activated partial thromboplastin time [aPTT], and fibrinogen international normalized ratio).
- When appropriate send sputum examination/tracheal secretions—Gram stain and aerobic culture sensitivity, Throat swab for viral panel including H1N1
- Paired percutaneous blood cultures.
- Additional tests if indicated—D-dimer does not help in pregnancy.
- Chest X-ray only if absolutely necessary.
- Multidetector computed tomographic (MDCT) pulmonary angiography if clinical situation demands.
- Ultrasonography is used to assess the status of the fetus, to evaluate growth, and in suspected case to evaluate deep venous thrombosis.
- Transthoracic echocardiography

Step 5: Make a Diagnosis of Respiratory Failure in Pregnancy

The various causes of acute respiratory failure are summarized in Table 19.2.

1. *ARDS*
   - The criteria for diagnosis of ARDS are similar to nonpregnant women (see Chap. 6, Vol. 1).
   - The pregnant state is associated with higher risk of ARDS from both pregnancy associated and other conditions. The proposed mechanisms of ARDS in pregnancy are increased circulating blood volume, capillary hyperpermeability, hypoalbuminemia and may be upregulation of acute inflammatory response.
2. *Asthma in pregnancy*
   - Rule of thirds—one-third of patients with asthma in pregnancy improve, and one-third shows no change. One-third worsens and can present in acute severe asthma.
   - The risk of severe asthma exacerbation tends to revert by 3 months' postpartum similar to non-pregnant. The risk of asthma exacerbation is generally same during successive pregnancies.
   - This explains the unpredictable effect of pregnancy on asthma.
3. *Pulmonary embolism in pregnancy*
   - Pregnancy itself is a hypercoagulable state and an independent risk factor for pulmonary embolism (PE).
   - Clinical prediction models that are used to predict pretest probability of PE have not been validated in pregnant patients.
   - D-dimers should not be used in pregnant as false positive rates are high.
   - The initial diagnostic test for venous thrombosis in pregnancy should be duplex ultrasonography if suspicion of DVT or PE is present.

Table 19.2 Differential diagnosis of acute respiratory failure during pregnancy

Conditions unique to pregnancy	Conditions can be affected by pregnancy	Conditions unaffected by pregnancy
Peripartum cardiomyopathy	Acute pulmonary edema	ARDS—direct/pulmonary
		Bacterial pneumonia
Amniotic fluid embolism	Aspiration of gastric contents	Fat embolism
Tocolytic therapy-induced acute pulmonary edema	Asthma	Inhalational injury
Severe preeclampsia	Venous thromboembolism	Indirect
Chorioamnionitis, endometritis	Bacterial and viral pneumonia	Sepsis, trauma, burns
Ovarian hyperstimulation syndrome (OHSS)	Malaria, fungal infections	Acute pancreatitis, transfusion-related acute lung injury (TRALI)

- Radiographic imaging remains the primary testing modality for diagnosing PE, and it should not be delayed because of concerns about radiation exposure.
- The diagnosis of pulmonary embolism in pregnant women can utilize ventilation-perfusion (V/Q) scanning or CT pulmonary angiography.

  The exposure of radiation to the fetus is same for V/Q scan or CT pulmonary angiography. However risk of radiation to pregnant women breasts is higher with CT angiography. So V/Qscan is preferred in patient with normal X-ray. The ventilation portion of the study can be avoided if perfusion is normal. An algorithm for diagnosis of pulmonary embolism is mentioned in Fig. 19.1
- Compression ultrasonography and transesophageal echocardiography (TEE) can be used for provisional diagnosis in case of unstable patient with suspected PE.

4. *Ovarian hyperstimulation syndrome (OHSS)*
   - Gestation of 3–8 weeks.

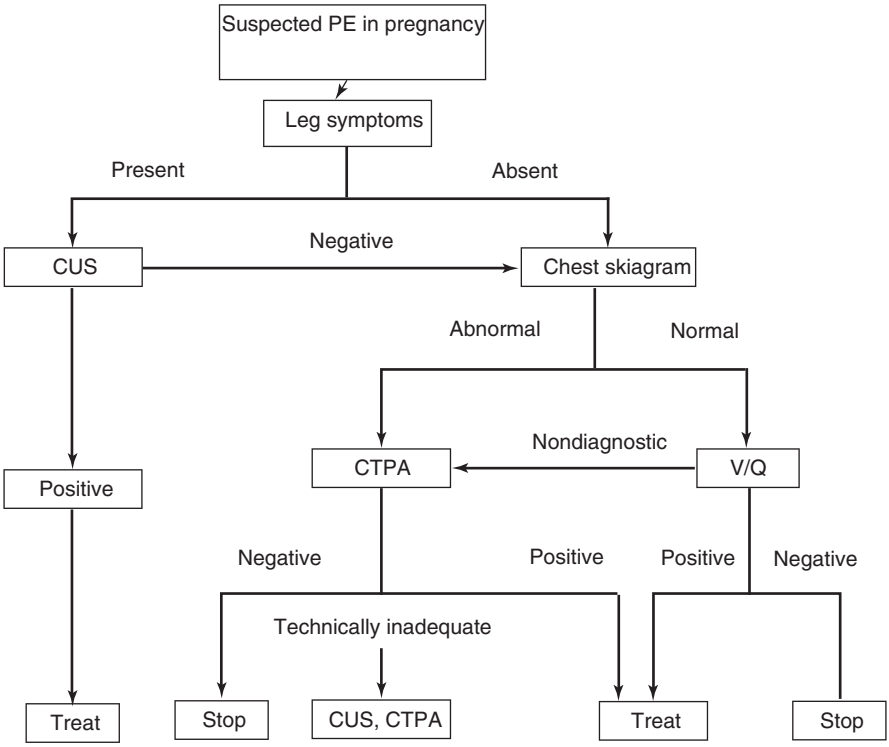

Fig. 19.1 Algorithm for the diagnosis of pulmonary embolism in pregnancy. *PE* pulmonary embolism, *CUS* compression ultrasound, *CXR* chest radiography, *CTPA* computed-tomographic pulmonary angiography, *V/Q* ventilation-perfusion

Table 19.3 Criteria that define the severe and life-threatening stages of OHSS

Severe OHSS	Life-threatening OHSS
Variably enlarged ovary	Variably enlarged ovary
Massive ascites with or without hydrothorax	Tense ascites with or without hydrothorax
Hematocrit >45%	Hematocrit >55%
WBC count >15,000	WBC count >25,000
Oliguria	Oliguria
Creatinine level 1.0–1.5 mg/dL	Creatinine level ≥1.6 mg/dL
Creatinine clearance ≥50 mL/min	Creatinine clearance <50 mL/min
Liver dysfunction	Renal failure
Anasarca	Thromboembolic phenomena
	ARDS

- Increased vascular permeability—fluid shift from the intravascular to extravascular space—causing pleural or pericardial effusions, ascites, electrolyte imbalances, dyspnea, oliguria, severely enlarged polycystic ovaries, hemoconcentration, and hypercoagulability, electrolyte imbalance are the common presentations.
- The common criteria for severe and life-threatening OHSS are described in Table 19.3.

5. *Peripartum cardiomyopathy (PPCM)*

   The cause of the disease remains unknown.
   - The associated conditions include hypertension, preeclampsia, multiparity, multiple gestations, and older maternal age.
   - Signs and symptoms are paroxysmal nocturnal dyspnea, chest pain, nocturnal cough, new regurgitant murmurs, pulmonary crackles, increased jugular venous pressure, and hepatomegaly.
   - Identify other cardiac and noncardiac disorders such as coronary, rheumatic, or valvular heart disease; arrhythmias; and family history of cardiomyopathy or sudden death and other risk factors of cardiac diseases such as hypertension (chronic, gestational, preeclampsia), diabetes, dyslipidemia, thyroid disease, anemia, prior chemotherapy or mediastinal radiation, sleep disorders, current or past alcohol or drug abuse, and collagen vascular disease.
   - The diagnosis of PPCM is a diagnosis of exclusion and should be made when other possible causes of acute/subacute heart failure have been ruled out (Table 19.4).

6. *Tocolytic induced pulmonary edema*

   Terbutaline (beta 2 agonist) use to inhibit preterm labour may induce pulmonary edema. This is more commonly seen in pregnancy with multiple gestations. It is also seen sometimes with magnesium sulphate infusion.

   Exclude other causes of cardiogenic or non cardiogenic causes of pulmonary edema.

   Give supplemental oxygen, fluid restriction and diuresis.

   Most cases resolve within 24 h.

Table 19.4 Clinical criteria for the diagnosis of PPCM

Development of cardiac failure in the last month of pregnancy or within 5 months postpartum
Absence of another identifiable cause for the cardiac failure
Absence of recognizable heart disease before the last month of pregnancy
LV systolic dysfunction shown by echocardiographic data such as depressed shortening fraction (e.g., ejection fraction less than 45%, M-mode fractional shortening less than 30%, or both, and an LV end diastolic dimension of more than 2.7 cm/m^2)

Step 6: Treat the Specific Cause

The general management of respiratory failure in pregnancy is similar to the management in nonpregnant women, although one should be careful about normal physiologic alterations that occur in the parturient state and effect of ventilator strategies.

1. *Management of ARDS and mechanical ventilation in pregnant patients*
   - Lung-protective strategy to avoid volutrauma, biotrauma, atelectrauma, leading to less ventilator-induced lung injury has been found to reduce mortality and improve outcome in patients with ARDS.

     Lung-protective strategy causes hypoventilation, which is tolerated to maintain (permissive hypercapnia) the pH between 7.25 and 7.35. This strategy has not been assessed in pregnancy. If necessary, in case of severe ARDS, mild hypercapnia with $PaCO_2$ should be maintained less than 60 mmHg.
   - Permissive hypercapnia can cause fetal acidosis, an increase in intracranial pressure, and a right shift in the hemoglobin dissociation curve and in first 72 h may lead to retinopathy of prematurity, so lung-protective ventilatory strategy in pregnant patients should be used with close monitoring of the fetal status with the biophysical profile.
   - Oxygen levels should be closely monitored in pregnancy and kept higher than in nonpregnant women (preferably $SpO_2 \geq 95\%$) and pO_2 above 70 mmHg.
   - Chest wall compliance is reduced by the enlarging uterus, and the usual pressure limits (e.g. plateau pressure of 35 cmH_2O) may not be appropriate. This may lead to increase need of higher airway pressures (without increased trans-pulmonary pressure) for appropriate tidal volumes in pregnant women especially in last trimester.
   - Hyperventilation and alkalosis should be avoided to prevent uterine vasoconstriction.
2. *Management of asthma in pregnancy*
   - Management of asthma in pregnancy is similar to nonpregnant women.
   - Beta-agonists bronchodilators with or without ipratropium are given with spacer and metered dose inhaler or in nebulisations.
   - IV corticosteroids are the mainstay of the treatment in severe asthma exacerbation like in a normal adult.
3. *PE during pregnancy*

- Acute treatment of PE can be done with low-molecular-weight heparin (LMWH) or unfractionated heparin (UFH) and should be started without delay whenever PE is suspected or confirmed.

  LMWH is first-line therapy for the treatment of acute PE in the general population and in pregnancy and is associated with fewer adverse effects than unfractionated heparin.
- Thrombolysis can have obstetric and neonatal complications such as pregnancy loss, abruption, and preterm labor. However complications have been found no more than non-pregnant. Therefore, the use of thrombolytics in pregnancy should be reserved for women with PE who are hemodynamically unstable or with refractory hypoxemia.
- The anticoagulation is continued for 6 weeks in postpartum or total duration of minimum 3 months whichever is later.
- Warfarin is usually avoided in pregnancy for this indication as it crosses the placenta and associated with fetal nasal, ophthalmologic, or central nervous system abnormalities.

  Heparins are thus the mainstay treatment during the entire period of pregnancy. Start oral anticoagulants only after delivery.

4. *OHSS*
   - Syndrome is self-limiting, and resolution parallels the decline in serum HCG levels: 7 days in nonpregnant patients and 10–20 days in pregnant patients.
   - Monitor frequently for deterioration with physical examinations, daily weights, and periodic laboratory measurements of complete blood counts, electrolytes, and analysis of renal and hepatic function.
   - Severe disease—placement of two large-bore peripheral intravenous catheters or a central venous catheter (preferred) for fluid management may be required.
   - Use the Foley's catheter for close monitoring of the urine output.
   - Normal saline with or without glucose is the crystalloid of choice, and potassium-containing fluids should be avoided because patients with OHSS could develop hyperkalemia.
   - In more severe cases with significant hypovolemia, hemoconcentration (hematocrit >45%), hypoalbuminemia (serum albumin level <3.0 g/dL), or severe ascites, albumin can be given as a plasma expander along with diuretics (furosemide) once hematocrit is 36–38%.
   - If respiratory symptoms worsen, thoracentesis/paracentesis should be performed.
   - If ARDS develops and mechanical ventilation is required, lung-protective strategies must be used.
5. *PPCM*
   - Diuretic agents, including loop diuretics, and nitrates are initial agents for symptom relief, in most patients because they cause symptomatic relief of pulmonary and peripheral edema.
   - Angiotensin-converting enzyme inhibitor or angiotensin receptor blockers are contraindicated before delivery and can be used only in post-partum female.

Table 19.5 Treatment of PPCM

Nonpharmacological measures	Drugs for routine use	In selected patients	Therapies avoided
Hypertension control (salt restriction)	Diuretics	Aldosterone antagonists	Angiotensin-converting enzyme inhibitors
Fluid restriction	β-Blockers	Inotropes	Angiotensin receptor blockers
	Digoxin	Anticoagulation	Many antiarrhythmic drugs
	Vasodilators	Implantable defibrillators	Nonsteroidal antiinflammatory drugs
		Biventricular pacing	Nondihydropyridine calcium channel blockers
		Cardiac transplantation	

- Hydralazine and nitrates are the vasodilators of choice for pregnant women.
- β-Blockers (sustained-release metoprolol succinate, carvedilol, and bisoprolol) have been shown to reduce mortality with current or prior heart failure and reduced ejection fraction and therefore constitute the first-line therapy for all stable patients unless contraindicated (Table 19.5).
- Digoxin if required is safe in pregnancy with same level of monitoring as in nonpregnant.
- Anticoagulation to prevent systemic thromboembolism is recommended in all females till resolution of cardiomyopathy or 3 months postpartum whichever is earlier.

Suggested Reading

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Severe Preeclampsia

20

Rajesh Chawla, Prashant Nasa, Renu Chawla, and Bharat G. Jagiasi

A 23-year-old female at 30 weeks of pregnancy was admitted to the hospital with an episode of seizure, epigastric pain, and decreased urine output. She had pedal edema, and her blood pressure (BP) on admission was 190/110 mmHg. Her urine output was 300 mL in the past 24 h. Urine examination showed protein 4+ and hemoglobin 8 g%. Liver function test showed elevated aspartate aminotransferase and alanine aminotransferase.

Hypertensive disorders (preeclampsia, chronic hypertension, preeclampsia superimposed on chronic hypertension and gestational hypertension) complicate 5–10% of all pregnancies. Preeclampsia either alone or superimposed on chronic hypertension may be associated with adverse outcomes.

Pre-eclampsia is new onset hypertension systolic blood pressure >140 mmHg or diastolic blood pressure more than 90 mmHg on at least two occasions at least 4 h apart presenting after 20 weeks with significant proteinuria.

These findings are usually seen after 34 weeks gestation and progress until delivery but some may develop it earlier, intrapartum and even postpartum.

Delivery of placenta usually results in resolution of maternal organ dysfunction and results in normotension.

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R. Chawla, S. Todi (eds.), *ICU Protocols*, https://doi.org/10.1007/978-981-15-0902-5_20

Step 1: Initial Assessment and Resuscitation

- Always anticipate difficult airway in pregnant patients (Table 20.1).
- Endotracheal intubation should be performed by a senior intensivist/anesthesiologist.
- Difficult airway equipment for airway management must be thoroughly checked before proceeding to intubation, and alternative plan for definitive airway including surgical access should already be identified.
- Supplemental oxygen may be required in some patients depending on their oxygen saturation.
- Target SpO_2 more than 95% with oxygen or ventilation.

Circulation

- Two large-bore intravenous cannulae (14G or 16G) should be placed to administer fluids.
- The Foley catheter should be placed to monitor urine output.
- Judicious fluid administration is needed to optimize preload and at the same time to avoid overload.
- Nurse in the left lateral position (30° wedge to the right hip) to prevent supine hypotension syndrome.

Disability (Neurological)

- Magnesium sulfate is a drug of choice for control of seizures.
- 4–6 g is diluted in 100 mL of IV fluid bolus over 5 min.

Step 2: Taking History and Physical Examination

- Detailed history should be taken about previous pregnancy, antenatal evaluation, immunization, hypertension, pregestational diabetes, and PIH (pregnancy induced hypertension) during the previous pregnancy.

Table 20.1 Risk factors for difficult airway during pregnancy

Progesterone-induced airway edema is further exacerbated in pregnancy-induced hypertension (PIH)
Thick neck, large breasts
Increased risk of hypoxemia—decreased cardiopulmonary reserve and increased metabolic requirements
Increased risk of aspiration of gastric contents

- Complications and outcome of the previous pregnancy and family history of hypertension should be required.
- History includes symptoms displaying end-organ effects to detect presence of severe preeclampsia:
  - Headache
  - Visual disturbances—blurred, scintillating scotomas
  - Altered mental status
  - Blindness
  - Dyspnea
  - Edema
  - Epigastric or right upper quadrant abdominal pain
  - Weakness or malaise—may be evidence of hemolytic anemia
- The physical examination includes the evaluation of end-organ dysfunction for diagnosis of severe preeclampsia:
  - Altered mental status
  - Decreased vision or scotomas
  - Papilledema
  - Epigastric or right upper quadrant abdominal tenderness
  - Peripheral edema
  - Seizures
  - Focal neurologic deficit
- PIH (preeclampsia) is defined as presence of hypertension (BP ≥140/90 mmHg) on two occasions, at least 6 h apart in more than 20 weeks' gestation in women with previously normal BP and who have proteinuria (≥0.3 g protein in 24-h urine specimen or urinary protein: creatinine ratio is greater than 30 mg/mmol), with or without pedal edema.
- Severe preeclampsia is defined in Table 20.2.

Table 20.2 Criteria for diagnosing severe preeclampsia

Systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg on at least two occasions at least 4 h apart after 20 weeks of gestation in a previously normotensive patient AND the new onset of one or more of the following
• Proteinuria ≥0.3 g in a 24-h urine specimen or protein/creatinine ratio ≥0.3 (mg/mg) (30 mg/mmol) in a random urine specimen or dipstick ≥2+ if a quantitative measurement is unavailable
• Platelet count <100,000/μL
• Serum creatinine >1.1 mg/dL (97.2 μmol/L) or doubling of the creatinine concentration in the absence of other renal disease
• Liver transaminases at least twice the upper limit of the normal concentrations for the local laboratory
• Pulmonary edema
• Cerebral or visual symptom (e.g., new-onset and persistent headaches not accounted for by alternative diagnoses and not responding to usual doses of analgesics; blurred vision, flashing lights or spark, scotomata)
• If systolic blood pressure is ≥160 mmHg or diastolic blood pressure is ≥110 mmHg, confirmation within minutes is sufficient

Adapted from American College of Obstetricians and Gynecologist (ACOG) Practice Bulletin No. 202: Gestational Hypertension and Preeclampsia. Obstet Gynecol 2019; 133:e1–e25

Criteria for superimposed preeclampsia In a women with chronic/preexisting hypertension are new onset of proteinuria, significant end-organ dysfunction, or both after 20 weeks of gestation.

- Eclampsia is defined as seizures that cannot be attributable to other causes in a woman with preeclampsia.

Step 3: Send Investigations

- Complete blood cell count.
- Liver function tests.
- Renal function tests and serum electrolytes.
- Arterial blood gas and blood glucose.
- Coagulation profile (prothrombin time [PT], activated partial thromboplastin time [aPTT], and fibrinogen, international normalized ratio).
- Lactate dehydrogenase.
- Uric acid.
- Urine routine microscopy, 24-h urine protein, and creatinine, urinary protein: creatinine ratio.
- Additional tests—peripheral smear, serum magnesium levels.
- Ultrasonography is used to assess the status of the fetus as well as to evaluate growth retardation.
- Fetal monitoring
- Transthoracic echocardiography.

Step 4: Make a Differential Diagnosis (Table 20.3)

Principal differentiation includes exacerbation of underlying preexisting renal disease, acute fatty liver of pregnancy, thrombotic microangiopathy (TTP or HUS) and exacerbation of systemic lupus.

Step 5: Admit to the ICU and Monitor Closely

- ICU admission is indicated with:
  - Eclampsia
  - Haemorrhage
  - Hyperkalaemia
  - Severe oliguria
  - Coagulation support
  - Intravenous antihypertensive treatment—initial stabilisation of severe hypertension—evidence of cardiac failure

Table 20.3 Differential diagnosis

Severe preeclampsia (abdominal pain)
Abruptio placentae
Abdominal aneurysm
Acute appendicitis
Blunt abdominal trauma
Cholecystitis and biliary colic
Hypertensive emergencies
Ovarian torsion
Eclampsia (seizure)
Cerebrovascular accidents
Brain tumors
Brain infections—meningitis, encephalitis, abscesses
Thrombotic thrombocytopenic purpura
Metabolic disorders
Hypertensive encephalopathy
Illicit drug use
Postdural puncture syndrome
Epilepsy
Posterior reversible encephalopathy syndrome

  - Abnormal neurology
  - Placental abruption
  - Severe preeclampsia
  - Hemolysis, elevated liver enzymes, and low platelet (HELLP) syndrome
  - Chorioamnionitis
  - Acute pulmonary edema
  - Respiratory failure
  - Acute respiratory distress syndrome
  - Acute renal failure
  - Maternal monitoring is required with severe preeclampsia:
  - Repeated clinical assessment including neurological examination (deep tendon reflexes for magnesium toxicity).
  - ECG monitoring.
- Arterial BP—noninvasive BP can be tried initially but may be incorrect with inadequate cuff size.
- Pulse oximetry.
- Foley catheterization—urine output monitoring.
- Blood gas monitoring.
- CVP monitoring—infusion of vasopressors.
- Additional—intra-abdominal pressure during resuscitation, serum magnesium levels.

Step 6: Management of Severe Preeclampsia

The definitive treatment of preeclampsia is delivery of placenta. Timing of delivery depends on gestational age, severity of preeclampsia, and maternal and fetal condition.

Other important aspect in the management of severe preeclampsia is control of hypertension.

1. *BP control*
   - Arterial pressure greater than 160/110 mmHg in preeclampsia can increase the risk of complication, and it should be controlled.
   - BP control should only be done in the ICU, preferably with arterial line monitoring.
   - BP control should also be done along with fetal monitoring. Avoid sudden fall in BP as it can result in fetal distress.
   - Goal of BP control is 15–25% reduction in the mean arterial pressure, and reduction of pressure to normal levels (<140/90 mmHg) should be avoided as it may compromise placental perfusion.
   - *Drugs*
     – Labetalol (IV 20 mg) can be given initially followed by doubling the dose every 10 min to a cumulative dose of 300 mg. This drug can result in severe bradycardia. A continuous infusion of labetalol at a rate of 0.5–2 mg/min can also be used.
     – Hydralazine (5–10 mg) can be given every 20 min (maximum of 40 mg) until BP is controlled.
     – Nifedipine or nicardipine can be given (sudden precipitous decrease in BP or tachycardia can occur).
     – Intravenous nitroglycerin (10–100 mg/min) or sodium nitroprusside (2–8 mg/min) can be given. Prolonged use of nitroglycerin may lead to methemoglobinemia. Cyanide toxicity in the mother and fetus may occur with sodium nitroprusside, limiting its use to less than 4 h and only as a last resort.
2. *Seizure control*
   - The initial management of eclampsia includes airway, breathing, and circulation.
   - Seizure prophylais is given intrapartum or postpartum with magnesium sulfate in cases of severe preeclampsia
   - The initial bolus of magnesium (4–6 g over 5 min) is followed by an infusion of 1–2 g/h maintained for 24 h.
   - The mechanism of action of magnesium is unknown, but magnesium suppresses excitatory neurotransmitter release by replacing calcium at nerve endings.
   - Monitor toxicity—loss of deep tendon reflexes; loss of patellar reflex occurs when the plasma magnesium level is more than 10 mg%. Look for respiratory muscle weakness.

Table 20.4 Clinical manifestations related to serum concentration of magnesium

Serum magnesium levels (mg/dL)	Effects
5–8	Therapeutic
8–12	Loss of deep tendon reflexes
12–16	Muscular paralysis and respiratory difficulties
>17	Conduction disturbances
>25	Cardiac arrest

- Magnesium has a relatively narrow therapeutic range, and target magnesium serum concentrations are 5–8 mg/dL.
- Infusion dose should be reduced in case of renal dysfunction. Serum magnesium level should be monitored Table 20.4.
- In recurrent seizure, additional 2–4 g of magnesium sulfate can be given over 5 min concurrently with the magnesium sulfate infusion.
- Calcium gluconate 15–30 mL of a 10% solution intravenously over 2–5 min is given to women with cardiac arrest or severe cardiac toxicity related to magnesium toxicity.
- If seizures are not controlled by repeat magnesium bolus, then diazepam or lorazepam can be administered (see Chap. 30, Vol. 1).
- Discontinue magnesium sulfate 24 h after delivery.

3. *Fluid management*
   - Despite the peripheral edema, patients with preeclampsia are volume depleted with high peripheral vascular resistance. Diuretics should be avoided.
   - Aggressive volume resuscitation, on the other hand may lead to pulmonary edema, which is a common cause of maternal morbidity and mortality. Because volume expansion has no demonstrated benefit, patients should be fluid restricted when possible, at least until the period of postpartum diuresis.
   - Central venous or pulmonary artery pressure monitoring or other hemodynamic monitoring modality may be indicated in critical cases.
   - Careful measurement of fluid input and output is advisable, particularly in the immediate postpartum period.
4. *Delivery*
   - As maternal morbidity is very high with severe preeclampsia, prompt delivery is indicated regardless of gestational age.
   - Women with severe preeclampsia who are managed expectantly (nonsevere disease) must be delivered under the following circumstances:
     - Severe hypertension develops refractory to treatment
     - Nonreassuring fetal heart status
     - Uncontrollable BP
     - Oligohydramnios, with amniotic fluid index of less than 5 cm
     - Severe intrauterine growth restriction
     - Oliguria (<500 mL/24 h)
     - Serum creatinine level of at least 1.5 mg/dL

  - Pulmonary edema
  - Shortness of breath or chest pain with pulse oximetry of <94% on room air
  - Headache that is persistent and severe
  - Right upper quadrant tenderness with deteriorating liver function test
  - Development of HELLP syndrome
- Severe hypertension after 34 weeks when their blood pressure has been controlled and a course of corticosteroids has been completed (if appropriate).
- Offer delivery to women with pre-eclampsia before 34 weeks only after discussion with neonatal and anaesthetic teams and a course of corticosteroids has been given
- Preeclampsia is not an indication for caesarian delivery and many patients can have normal vaginal delivery

Step 7: Watch for Complications

- Abruptio placentae
- Disseminated intravascular coagulopathy (DIC)
- Renal insufficiency and acute renal failure
- HELLP syndrome
- Eclampsia
- Cerebral hemorrhage
- Fetal changes—intrauterine growth restriction, abruptio placentae, oligohydramnios
- Intrauterine fetal death

Step 8: Managing Complications

HELLP syndrome

- HELLP syndrome can complicate 4–12% of patients with severe preeclampsia.
- Signs and symptoms are right upper quadrant or epigastric pain, nausea and vomiting, malaise, and nonspecific viral-like symptoms. Physical examination findings include right upper quadrant or epigastrium tenderness and generalized edema.
- Delivery is the definitive treatment for HELLP syndrome.
- Delivery is indicated for women with HELLP syndrome at greater than 34 weeks' gestation. During labor and for 24-h postpartum, patients should receive intravenous magnesium sulfate for seizure prophylaxis.
- If gestation is less than 34 weeks, delivery may be delayed for a steroid course of betamethasone (12 mg intramuscularly, every 24 h) in two doses, with delivery 24 h after the last dose.

- Platelets are generally transfused when the platelet count is less than 20,000/mm^3. For cesarean delivery or with any significant bleeding, platelets should be transfused if the platelet count is less than 50,000/mm^3.

Acute pulmonary edema

- Management is similar as in nonpregnant patients.
- Intravenous furosemide (bolus 20–40 mg over 2 min) is used to promote diuresis. The repeated doses of 40–60 mg are given after 30 min or infusion if there is inadequate diuretic response (maximum dose 120 mg/h).
- Careful fetal monitoring, fluid restriction, and strict fluid balance and positioning (such that the head is elevated) are required.

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Part VI

Perioperative Care

General Issues in Perioperative Care

21

Prakash Shastri and L. N. Yaddanapudi

A 25 year old woman who developed severe post-partum haemorrhage after home delivery of a still-born baby was taken up for emergency hysterectomy under general anaesthesia with rapid sequence intubation using 150 mg thiopentone, rocuronium 50 mg, fentanyl 50 mcg, 7.5 mm tracheal tube, and controlled ventilation with FiO_2 of 1.0 and 0.8 MAC sevoflurane. During the procedure the patient was administered 3 units of whole blood, 1 unit FFP, and 2 L of Ringer's lactate solution. Dopamine infusion was used to maintain the mean blood pressure around 70 mmHg. At the end of the procedure the patient was transferred to the ICU without reversal of neuromuscular blockade.

In the ICU the patient was mechanically ventilated and the dopamine was tapered off. The patient was hypothermic and anuric, with a haemoglobin of 6.5 g/dL, platelet count of 37,000/mm^3, INR of 5.1, urea of 50 mg/dL, creatinine 2.7 mg/dL and raised liver enzymes. ECG showed tall T waves and a blood gas analysis showed serum potassium of 6.1. Corrective measures for hyperkalemia were instituted and the patient was allowed to rewarm. After overnight ventilation and one episode of hemodialysis, the patient was extubated. Hemodialysis continued for another 2 days till the patient's urine output improved.

Intensive care physicians have become an integral part of the perioperative care of high-risk patients, those undergoing complicated surgical procedures, and those who experience perioperative major adverse events. The usual principles of co-ordinated evidence-based resuscitation, monitoring, nursing and medical care are applicable to these patients as well. There are, in addition, a number of special circumstances that operate in these patients. This chapter attempts to summarize these principles and factors.

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Step 1: Assess the Reason for Perioperative Admission to the ICU

– Elective preoperative admission for monitoring and optimization of hemodynamics and respiratory status in high-risk cases.
– Elective postoperative admission for monitoring and organ support for high-risk and major surgeries
– Airway monitoring in major oral, head, and neck surgery
– Flap monitoring in major plastic surgery
– Elective ventilation after prolonged surgery
– Emergent postoperative admission for unexpected intraoperative complications
– Intraoperative severe blood loss
– Hemodynamic instability due to arrhythmia and myocardial ischemia
– Intraoperative cardiac arrest
– Respiratory complications after elective extubation

- Initial resuscitation, monitoring, investigations and continuing care differ in each of these scenarios.
- Attempts have been made to predict the risk of ICU admission after surgery. It has been identified that intraoperative requirement of vasopressors (adrenaline, noradrenaline and vasopressin) at the end of surgery and emergency surgery are good predictors of ICU admission.
- A strong case can be made for upgrading the post-anesthesia care units and staffing them round the clock to reduce the demand for ICU beds for short-term observation/ventilation.

Step 2: Obtain a Structured Handover from the Anesthesia and Surgical Teams. Take Focused History. Perform Physical Examination

- Confirm the patient's identification
- Intraoperative findings and surgical procedure performed
- Duration of surgery
- Anesthesia chart and postoperative notes: pay attention to any airway problems encountered, placement of venous and arterial lines.
- Intraoperative complications, estimated blood loss, and transfusions of blood and blood products, nature and volume of other fluids administered
- Postoperative instructions
- Placement of surgical drains and current drainage
- Urinary catheter and output
- Fluids, antibiotics, analgesia, antiemetic prescription
- Epidural catheters or patient-controlled analgesia (PCA) pumps
- Review of the medical records of the patient for comorbid conditions
- Drug history—aspirin, other antiplatelet agents, oral anticoagulants, and oral hypoglycemic agents.

Step 3: Identify Problems of Immediate Concern

- Hemodynamic instability
  - Intraoperative blood loss, inadequate resuscitation, bridging vasopressor infusions, transport
  - Assess volume status of the patient using clinical signs and noninvasive techniques such as IVC collapsibility on ultrasound examination. Decide whether intravenous fluid is required and administer in a titrated fashion.
  - Titrate any vasopressors.
- Coagulation and dyselectrolytemia
  - Massive blood loss and transfusion, excessive crystalloid administration, especially isotonic saline will lead to dilutional coagulopathy and dyselectrolytemia.
  - Any obvious bleeding should be looked for and treated.
  - Dyselectrolytemia should be corrected.
- Hypothermia
  - Causes: Bleeding, massive fluid and blood transfusion, anesthesia (dry gases, muscle relaxants, medication), surgical causes (evaporative cooling and lavage), transport causes increased oxygen demand which can be detrimental in patients with low cardiorespiratory reserve.
  - Hypothermia may lead to tissue ischemia with delayed wound healing and increased surgical site infection.Other adverse effects include deranged coagulation and immunosuppression.Patients with coronary artery disease and those with vascular anastomoses and skin grafts are particularly vulnerable.
  - Hypothermic patients with core temperature less than 35 °C should be actively rewarmed with forced air rewarming devices, warm intravenous fluids and adequate covering.
- Pain
  - Appropriate and adequate pain relief is an essential component of postoperative care and these patients are no exception. Consultation with the pain management team is helpful.
  - Pain should be assessed formally using a validated instrument such as VAS on a regular basis. Analgesia should be titrated according to the patient's response.
  - The modalities of pain relief usually available are:

    Opioid analgesics such as morphine and fentanyl used as iv aliquots or as infusions or in patient-controlled analgesia (PCA) devices or transdermal patch.

    Intravenous paracetamol

    NSAIDs such as diclofenac (iv/im/rectal). These should be avoided in patients at risk of renal injury, including elderly patients and those who had intraoperative hypotension.

    Intravenous tramadol

    Neuraxial local anesthetic/opioid combinations

    Intra-articluar injection of local anesthetics/opioids

    Peripheral nerve blocks

- Sedation and altered mental states
  - Causative factors include residual effects of anesthetic drugs, hypothermia, hyponatremia and hypercarbia
  - Rule out residual neural blockade using a neuromuscular junction monitor. (Train of Four monitor)
  - Other abnormal behaviour is usually due to effects of medication and rarely due to hypoxia, acidosis or hypotension. Depending on the clinical scenario, you may need to rule out hypoglycaemia.
  - Reassurance and correction of underlying derangement is usually sufficient.
- Nausea and vomiting
  - Post Operative Nausea and Vomiting (PONV) after general anesthesia is very troublesome to the patient.
  - Management strategies include reducing the dose of opioids and alternative analgesics.
  - 4–8 mg ondansetron can be effective. Be aware of the occurrence of side effects such as arrhythmias and intractable headache.

Step 4: Identify and Correct Fluid Imbalance

- Conventional intake-output charts do not reflect fluid balance in critically ill patients or postoperative patients.
- Stress due to surgery and pain cause an increased secretion of ADH and aldosterone resulting in a high incidence of SIADH. Fluid sequestration in the gut wall, interstitial fluid accumulation due to increased capillary leak, all cause fluid disturbances.
- A low urine output may not indicate hypovolemia. Alternative measures of volume status should be used such as using ICU beds with in-built weighing facility, abdominal ultrasound assessment of IVC collapsibility, transthoracic echocardiography to assess filling of the left ventricle, or other dynamic measures of fluid responsiveness.
- Postoperative patients tend to retain free water. Hypotonic fluid administration should be restricted due to the risk of hyponatremia.
- In patients with chronic diuretic use, hypertension, and cardiac dysfunction, cautious use of diuretics could be tried if urine output remains low in spite of normal hemodynamics and no evidence of sepsis.
- Renal Replacement therapy should be instituted as necessary, in consultation with the nephrology team.

Step 5: Identify and Correct Cardiac and Pulmonary Problems

- Pre- and intraoperative management
  - Cardiovascular status should be assessed and optimized preoperatively by careful preoperative cardiovascular and pulmonary risk assessment,

optimizing medications and other measures. These will include cessation of smoking, incentive spirometry, treatment of chest infections and bronchospasm.
  - It is to be kept in mind that these measures are not possible in emergent surgeries.
  - The risk indices for postoperative complications such as that developed by Shoemaker for cardiac and others for pulmonary complications may be followed to identify patients at high risk (Table 21.1).
  - Validated Surgical risk calculators may also be used
  - These patients may be managed using perioperative goal-directed therapy using minimally invasive cardiac output monitoring techniques to improve outcomes.
- Postoperative management
  - High risk patients should be monitored for chest discomfort/pain, ST segment changes, hemodynamic instability and pulmonary oedema. A low threshold for investigations such as 12-lead ECG and cardiospecific enzyme tests is useful.
  - Postoperative respiratory failure is usually due to one or more of the following:
    Atelectasis
    Aspiration
    Pain leading to splinting of the diaphragm and hypoventilation
    Tracheobronchitis and pneumonia
    Noncardiogenic pulmonary edema
  - Measures to avoid pulmonary complications include:
    Early ambulation and assisted coughing
    Continuation of incentive spirometry
    Intermittent positive pressure breathing exercises
    Adequate hydration

Table 21.1 Shoemaker criteria for identifying patients at high risk of cardiac complications

Patient factors
Prior severe cardiac illness, acute myocardial infarction (AMI), stroke, congestive heart failure (CHF)
Age more than 70 years
Severe sepsis with septic shock
Severe nutritional problems
Respiratory distress, chronic obstructive pulmonary disease, requiring mechanical ventilation
Acute hepatic failure and acute renal failure
Severe CNS problem—head injury with coma (Glasgow coma score <8)
Surgical factors
Extensive ablative surgery for cancer, more than 8 h
Severe multiple trauma—three organs or two body cavities
Massive blood loss of more than 8 units
Acute abdominal catastrophe—peritonitis, perforated bowel with gangrene
Aortic aneurysm and end-stage vascular disease

Humidification of inspired air and oxygen, High Flow nasal Cannula
Noninvasive ventilation, especially in patients with COPD and hypercapnia
Measures to reduce risk of aspiration (positioning, minimizing use of NG tube, prokinetics, etc.)
Optimizing analgesia and avoiding excessive sedation
Early identification and treatment of sepsis
Early external stabilization of long bone fractures using a damage-limitation philosophy

Step 6. Other Measures

- Safe intrahospital transportation of patients, with adequate monitoring, structured handover, and documentation checklist.
- Early identification of ongoing haemorrhage by inspecting volume and type of drain, hemodynamic instability, falling haematocrit and correcting volume deficit, hypothermia, acidosis, coagulopathy, and thrombocytopenia.
- Identification of the site of bleeding and preparing the patient for re-exploration if necessary, in consultation with the surgical team.
- Judicious use of blood and blood products. In a hemodynamically stable patient, without active bleeding or active coronary artery disease, keep the haemoglobin level at 7–8 g/dL.
- Early identification of sepsis and judicious use of antibiotics. Institutional protocol should be followed as per established guidelines for perioperative antibiotic prophylaxis.
- Surgical patients are in a hypercoagulable state in the perioperative period. Institutional protocols should be followed for deep vein thrombosis prophylaxis. A combination of pharmacological and mechanical methods (pneumatic compression or graduated compression stockings) are advocated in patients at high risk.
- Early enteral nutrition should be instituted as soon as possible. If early enteral nutrition cannot be initiated, parenteral nutrition should be started especially in patients with established malnutrition. Consideration should be given for immunonutrition in patients with cancer surgery.
- Stress ulcer prophylaxis with H_2 blockers should be instituted in selected case i.e. patient on mechanical ventilation, previous history of g.i. bleed and on anticoagulants/aspirin.
- Thyroid status should be optimized in hypothyroid patients. Supplemental corticosteroid should be given to patients with history of chronic use of systemic steroids.

There are certain risk factors which help to predict postoperative pulmonary complications (Table 21.2).

Table 21.2 Risk factors for postoperative pulmonary complications

Age more than 50 years
Obesity
Smoking
Chronic obstructive pulmonary disease
Location of incision (upper abdominal, thoracic)
FEV_1 less than 1 L
FVC less than 1.5 L
FEV_1/FVC less than 30%
Use of pancuronium
Surgery lasting more than 3 h
Functional dependence
Serum albumin less than 3.5 g/dL

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Website

www.surgicalriskcalculator.com

Specific Issues in Perioperative Care

22

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A 60-year-old male patient with triple-vessel disease with reduced left ventricular function and diabetes mellitus underwent coronary artery bypass graft (CABG) with extracorporeal support. He was transferred to the ICU, and his blood pressure was 90/60 mmHg on epinephrine infusion.

A 50-year-old male patient with road traffic accident had undergone an emergency decompressive craniectomy due to an expanding intracerebral hematoma. He had arrived in the ICU postoperatively on the ventilator and was paralyzed. His blood pressure was 110/70 mmHg without any vasopressor support.

A 50-year-old male patient had undergone an emergent thoracotomy and left upper lobe resection due to massive hemoptysis not getting controlled with conventional measures. He had arrived in the ICU ventilated with a saturation of 90% on FiO_2 of 0.8.

Due to increasing specialization of intensive care, patients with organ-specific surgery (thoracic, cardiac, neurosurgery) are being managed in dedicated ICUs. As these patients have specific perioperative problems, the intensive care physician taking care of these patients should have a working knowledge of their specific perioperative critical issues and should work in close consultation with the surgical and anesthetic team.

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Cardiac Surgery

Traditionally, cardiac surgery has been performed via a median sternotomy incision with the use of a cardiopulmonary bypass (CPB) machine that maintains total body oxygenation and perfusion despite cardioplegia. After CPB is initiated, injection of hyperkalemic cardioplegic solution directly into the coronary circulation produces cardiac standstill. Cardioplegic solution also provides necessary nutrients for myocardial preservation despite the absence of cardiac blood flow. Traditional surgical approaches are associated with varying degrees of hypothermia, coagulopathy, and hemodilution. Usually the patients need varying period of mechanical ventilation postoperatively.

Minimally invasive surgery (MIS) modifies one or more of these techniques to accomplish similar surgical goals through small surgical incisions without CPB (i.e., off-pump), or both. MIS has been shown to reduce blood requirements, length of stay, and resource use.

Step 1: Take Handover Information from Operating Room Staff

- Patient identification details
- Preoperative details
  - Type of coronary artery disease, valve dysfunction, left ventricular function, and pulmonary hypertension
  - Medications used—antiplatelets, diuretics, angiotensin-converting enzyme inhibitors, statins, and calcium channel blockers
  - Comorbidities—diabetes, hypertension, peripheral vascular disease, stroke, renal dysfunction, and thyroid status
  - Preoperative functional capacity
  - Previous medical records
- Operation performed (on- or off-pump, arterial, venous graft) and problems encountered
- Current drug infusions
- Pacemakers and antiarrhythmic drug information
- Estimated blood loss, blood and blood product administered, and urine output
- Intraoperative fluid balance
- Antibiotics administered and timing
- Drains (number, placement)
- Latest arterial blood gas analysis, hematocrit, blood sugar, and electrolytes

Step 2: Checklist on Arrival of the Patient (A to I)

- *Airway*
  - The patient is connected to the ventilator.
  - Note the size of the tube, position of fixation at the angle of mouth, and cuff pressure.

- *Breathing*
  - Look for chest movement. Auscultate and confirm air entry to both the lungs.
  - The usual initial ventilator setting are as follows:
    Breath rate of 12–15/min
    FiO_2 of 0.6–0.8
    Tidal volume of 6–8 mL/kg
    Depending on arterial blood gas (ABG) report, settings are modified subsequently
- *Circulation*
  - Set up the monitor.
  - Check
    ECG for rate, rhythm, and ST segment changes.
    Arterial pressure, oxygen saturation.
    Pulmonary artery pressure/central venous pressure—measure the pulmonary artery wedge pressure (PAWP), cardiac output (CO), and systemic vascular resistance.
    Mixed venous oxygen saturation
    Temperature probe—if temperature is less than 37 °C, warming blanket should be placed.
    Low urine output, acidosis, and peripheral examination are not a good indicator of the low perfusion state in these patients, and direct measurement of cardiac output is preferable in unstable patients.
- *Drugs*
  - Vasoactive drugs—check infusion pumps labeled with proper drug dosing and dilutions, and calculate infusion rate (mcg/kg/min).
- *Electrolytes*
  - Maintain K^+ at 4–4.5 mmol/L.
  - Maintain Mg^+ at 0.8–1.5 mmol/L.
- *Fluids*
  - Intravenous maintenance fluids (crystalloid) are started at the rate of 1–1.5 mL/kg/h.
  - Blood transfusion to keep hematocrit at more than 25–30%.
  - Maintain urine output at 0.5–1.0 mL/kg/h.
- *Glucose control*
  - Maintain serum glucose between 140 mg and 180 mg/dL.
  - Hypoglycemia should be avoided
- *Hemorrhage*
  - Causes of bleeding after cardiac surgery include:
    Inadequate surgical hemostasis
    Inadequate platelet number or function
    Inadequate reversal of heparin
    Dilutional coagulopathy
    Hypothermia
  - Chest tubes are connected to underwater seal. If bleeding is significant, and coagulation profile is normal, the patient needs to go back to the operation theater for re-exploration.

  - In adult patients, bleeding is significant when:
    >400 mL for 1 h
    >300 mL/h for 2 h
    >200 mL/h for 3 consecutive hours
    >100 mL/h for 4 consecutive hours
  - CPB may induce coagulation abnormalities in these patients and this may be the cause of excessive bleeding.
  - Anticoagulation protocols:
    Valve surgery: Anticoagulation is maintained with intravenous heparin. With mechanical valve prosthesis, oral anticoagulants (warfarin) should be started as soon as oral intake is permitted (48–72 h). Initial overlapping therapy of warfarin with heparin is recommended for 48–72 h to prevent warfarin-induced hypercoagulability.
  - Coronary artery bypass graft—aspirin/clopidogrel in low doses is started as soon as oral feeds are started.
  - Reverse heparin effect by protamine if needed.
- *Investigations*
  - Investigations should be done within 30 min of arrival.
    ECG
    ABG
    Hct and electrolytes
    Chest X-rays—look for pneumothorax, hemothorax, position of endotracheal tubes, chest tubes, intravascular catheters, pacing wires, lung infiltrates, and cardiac size.
    Coagulation profile (Prothrombin Time (PT), APTT, ACT)
    Thromboelastogram (if available)

Step 3: Take General Care of the Patients

- Position—head end elevated at 30–45°
- Neurological assessment
  - Awake and obeying commands
  - Able to move all four limbs

Step 4: Look for and Manage Specific Complications

- The most common complications after cardiac surgery are mechanical complications, physiological complications (inadequate preload, excessive afterload and poor ventricular pump function), dysrhytmias and myocardial infarction.
- *Arrhythmias* are common, occurring in 25–60% of patients. Advanced age, prior atrial fibrillation, and combined bypass graft/valve surgery are risk factors. Exclude precipitating causes such as hypoxia, hypercarbia, lack of analgesia, and electrolyte imbalance (hypokalemia and hypomagnesemia) before instituting antiarrhythmics. Treat arrhythmias only if hemodynamically significant.

Arrhythmias with signs of ischemia may signal perioperative infarction, inadequate revascularization, and blocked graft requiring urgent reoperation.

- *Low-output state*: Keep high index of suspicion if unexplained postoperative hypotension,tachycardia or pulmonary edema occurs.Urgent echocardiogram should be performed to exclude pericardial tamponade. Assess left ventricular function and volume status.
  - In cases of pericardial tamponade, the patient should be re-explored with evacuation of hematoma. The chest may have to be reopened in the ICU if tamponade is sudden and severe, leading to hemodynamic collapse.
  - In low-output states, rewarming should be gradual. Decrease metabolic demand by proper analgesia, sedation, and muscle relaxant to decrease shivering. Optimize preload by judicious use of fluid and blood (keep hematocrit 0.25–0.35) under monitoring. Add inotropes and if blood pressure permits decrease afterload by adding vasodilators. Due to ischemia reperfusion injury, a phase of stunned myocardium persists, which usually resolves over a variable period and is helped by inotropic support. This phenomenon should be distinguished from ongoing ischemia where inotropic support is detrimental.
  - An intra-aortic balloon pump is sometimes used to maintain coronary perfusion in low-output states (see Chap. 50).
- *Postoperative hypertension*: It is usually transient but may lead to left ventricular dysfunction, myocardial ischemia, graft and suture line disruption, and increased bleeding. Ensure proper analgesia and sedation. Parenteral vasodilators like nitrates may be used.
- *Atelectasis*: Ensure early mobilization and incentive spirometry.
- *Fluid overload*: Maintain strict input–output chart. Low-dose diuretics may be needed.
- *Myocardial ischemia* or *infarction* may be difficult to diagnose in postoperative settings as ECG, echocardiogram, and cardiac enzyme may not be able to detect early ischemia and may be false positive.
- *Right ventricular dysfunction*: This may occur due to pulmonary hypertension or ischemic reperfusion injury. It presents with low cardiac output syndrome, which may initially be volume responsive. The patient has high right-sided filling pressure disproportionate to left-sided pressure, low cardiac index, and low systemic blood pressure. It is managed by maintaining sinus rhythm, appropriate heart rate (by pacing if necessary), optimizing preload, reducing afterload (with pulmonary vasodilators such as inhaled nitric oxide or epoprostenol infusion), inotropic support, and mechanical assist devices if needed.
- *Significant neurological deficit*: It occurs in 2–3% of patients undergoing coronary artery bypass surgery. This can present as stroke, transient ischemic attack, or global cerebral dysfunction.Early recognition is important.
- *Prevent occurrence of renal failure*: Acute Kidney injury occurs in up to 30% of patients and is associated with increased mortality. Best strategy is to prevent AKI.Optimise renal perfusion (avoid hypotension and hypovolemia), avoid nephrotoxic drugs.
- Pulmonary dysfunction: Pleural effusion, Atelectasis, Pneumonia, Difficulty weaning,diaphragmatic dysfunction and ARDS

Step 5: Take a Fast-Track Approach to Extubation

- The increasing use of off-pump surgery, short anesthesia, and lower doses of sedatives has led to early liberation of patients from ventilators. Many patients can be extubated within 4 h of surgery or even in the operating room.
- The key to a successful fast-track program is proper patient selection, high-level supervision by a disciplined team, and absence of surgical complications.

Thoracic Surgery

Step 1: Take Care of Immediate Postoperative Issues

- Immediate concerns include assessment of oxygenation, volume status, cardiovascular support, provision of ventilatory support if needed to ensure adequate oxygen delivery and status of chest drains that accompany the patient from the operating room.
- Special concerns apply to pain control, which is especially important, as pain will limit respiratory effort and can also precipitate delirium and agitation.

Step 2: Be Cognizant of Potential Problems Following Thoracotomy

- Poor respiratory effort and sputum retention (chest wall trauma and pain)
- Atelectasis, pneumonia, and sepsis
- Alveolar and minor bronchial air leaks
- Localized or generalized pulmonary edema
- Intercostal, pulmonary, or bronchial vessel hemorrhage
- Cardiac arrhythmias, myocardial infarction, and heart failure
- Pulmonary and systemic embolism
- Chest wall hematoma, wound infection, and wound dehiscence

Step 3: Be Cognizant of Potential Problems Following Lung Resection

- Respiratory insufficiency due to extensive lung resection
- Bronchopleural fistula and massive air leak
- Early and late mediastinal shift
- Atrial fibrillation and other supraventricular arrhythmias
- Torsion of lobe or segment
- Cardiac herniation (usually after pneumonectomy with a partial pericardium excision, when the heart herniates through a gap in the pericardium; may be manifested by supraventricular arrhythmias and/or severe hypotension)
- Residual venous or arterial lung infarction

- Blood loss into the pleural space, mediastinum, or bronchus
- Bronchial obstruction from accumulated secretions, blood, and pus
- Empyema following air leaks, insufficient lung volume, or overwhelming sepsis
- Paradoxical chest wall movement following extensive rib resection
- Pulmonary hypertension and acute right-sided heart failure

Step 4: Get a Chest X-ray in the Hypoxic Patient

- In all postoperative thoracic surgery patients who are hypoxic on arrival, after a careful physical examination, urgent chest X-rays should be requested.
- A daily chest radiograph must be performed in unstable patients, to confirm endotracheal, nasogastric, and chest tube placement, as well as to identify any pneumothorax, mediastinal shift, or significant atelectasis.

Step 5: Assess Chest Drain Sites and Amount of Drainage

- Hourly output from chest tubes should be recorded, and the operative team should be notified if drainage is greater than 100 mL/h for more than 4 h, or if greater than 200 mL of drainage is recorded in any 1-h observation period.
- Expected chest tube drainage from major thoracic procedures in the first 24 h is roughly 300–600 mL, tapering to less than 200 mL by the second day.
- Daily chest radiographs are usually obtained while chest tubes are in place.
- Once all air leaks resolve and drainage is minimal (<100 mL/24 h), chest tubes may be removed during the expiratory phase of ventilation or while the patient performs a Valsalva maneuver.
- After pneumonectomy, surgeons usually keep the intercostals drain on the operated side clamped so that the fluid fills the pneumonectomy space and maintains the mediastinum central.
- This drain may be occasionally unclamped for a short period to note whether there is bleeding.
- The drain may need to be unclamped if there is very rapid accumulation of fluid in the pneumonectomy space, manifested by dyspnea, mediastinal shift to the opposite side, high jugular venous pressure (JVP), or central venous pressure. This may be mistaken for congestive cardiac failure.

Step 6: Address Airway Concerns and Plan for Extubation

- Extubation can often be accomplished in the operating room, but continued ventilation may be necessary in the presence of concurrent cardiac illness, inability to protect the airway, malnutrition, or coexisting lung disease.
- Ideally, the patient should be awake and following instructions and have an adequate gag reflex (signifying airway protection) and cough (for secretion clearance).

Step 7: Control Pain

- Adequate pain control is important not only to ensure patient comfort but also to avoid potential cardiac and pulmonary complications. Early pain management is also important in an effort to reduce the chances of developing long-term post-thoracotomy pain.
- Various options exist for pain management. They include systemic analgesics, neuraxial opioids, and local anesthetics via the epidural route, regional anesthesia such as intercostal and paravertebral nerve blocks, and adjuvant therapies such as transcutaneous electrical nerve stimulation (TENS) or applied heat. Exercise caution when using TENS in the patient with the temporary pacemaker in situ as it may interfere with sensing function of the pacemaker.
- The mainstay of postoperative pain control is systemic analgesics in the form of opioids. Agents such as morphine and fentanyl are frequently used, with the intravenous route providing the most predictable responses. Opioid side effects remain the greatest issue, with respiratory depression, nausea, vomiting, and ileus being the most common.
- Nonopiate medications such as paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs) are reasonable adjuncts to the opioids. Because NSAIDs may exacerbate renal dysfunction, it is necessary to exercise caution when using them in the presence of underlying renal insufficiency.
- Neuraxial opioids and local anesthetics via the epidural route provide excellent regional pain control. Epidural catheters are the preferred route, and when local anesthetics, either with or without opioids, are infused in this manner, the incidence of pulmonary complications decreases relative to that with systemic opioids.
- In addition, patients requiring prolonged postoperative mechanical ventilation may benefit from the centrally acting α-adrenergic agonist, dexmedetomidine, as an analgosedative.

Step 8: Optimize Fluid Balance

- Fluid management in the postoperative period requires special attention due to the high risk for pulmonary edema.
- Traditional markers of perfusion help determine if a patient is adequately volume-resuscitated. These include urine output (usually >0.5 mL/kg/h), mental status, blood pressure, heart rate, blood lactate level, capillary refill time, venous oxygen saturation, filling pressures, and cardiac performance.
- Ideally, the clinician should limit crystalloid infusion to 20 mL/kg for the first 24 h.

Step 9: Start Respiratory Therapy

- Thoracic surgical patients often have significant underlying chronic obstructive pulmonary disease, impaired mucociliary clearance, excessive secretions, and/or increased closing volumes, all of which predispose to atelectasis.
- The respiratory therapist plays an important role in providing secretion management and performing chest physiotherapy (percussion and vibration) and incentive spirometry.
- Other modalities supporting recovery include adequate hydration, aerosolized bronchodilators, humidified oxygen, and early identification and treatment of infection of the tracheobronchial tree.
- Chest physiotherapy should begin as soon as the patient has recovered sufficiently from anesthesia to cooperate.

Step 10: Manage Bronchopleural Fistula

- Early postoperative bronchopleural fistula in a pneumonectomy patient is a surgical emergency. The typical presentation is sudden expectoration of copious amounts of pink, frothy sputum, which may be misdiagnosed as pulmonary edema. Further management will likely include bronchoscopy to assess the stump closure and immediate reoperation if a leak is detected.
- A double-lumen tube may need to be introduced to prevent soiling of the opposite lung by contents of the pleural space and to prevent loss of tidal ventilation through the fistula.
- Always insert an intercostal drain on the side of the fistula and keep it draining at all times.

Step 11: Manage Postoperative Hypoxemia

- Postoperative hypoxemia is common and may be due to hypoventilation, atelectasis, aspiration, sepsis, acute respiratory distress syndrome, pneumonia, or pulmonary embolization.
- Noninvasive ventilation may be useful to treat respiratory failure after lung surgery.
- If pulmonary emboli are suspected, manage the patient accordingly (refer to Chap. 5, vol. 1).
- Systemic tumor emboli, though uncommon, may be seen after pulmonary resections for primary bronchogenic carcinomas or metastatic sarcomas.
- Meticulous attention must be given to prevent dehydration, overtransfusion, and infection.

Step 12: Address Special Concerns in Esophageal Surgery

- Patients who undergo esophageal resection for carcinoma tend to be malnourished and have complications, including atelectasis, pneumonia, aspiration, and retained secretions.
- One-third of patients experience respiratory complications. The most dreaded complication of esophageal surgery is leakage from the surgical site. Factors impacting the incidence include high estimated intraoperative blood loss, cervical location of the anastomosis, and the development of postoperative acute respiratory distress syndrome.
- Anastomotic dehiscence or ischemia of the gastric tube should be suspected when the following signs/symptoms appear: hydropneumothorax, bronchospasm, atrial fibrillation, dyspnea, hypotension, raised lactate levels, and tachycardia.
- Mortality associated with anastomotic leaks is historically high, but with improved surgical techniques, the patients now have a more promising outcome.
- Intraoperative nasojejunal tube placement or jejunostomy is vital to maintain enteral nutrition throughout the postoperative period.
- A multimodal approach including epidural analgesia, judicious fluid administration, early mobilization, and enteral nutrition contributes to a good outcome.

Neurosurgery

Step 1: Maintain Airway, Oxygenation, and Ventilation

- Adequate oxygenation is mandatory for proper neuronal functioning. Hypercarbia is detrimental to the brain injury patient as it leads to rise in intracranial pressure (ICP), and therefore proper ventilation should be ensured (see Chap. 31, vol. 1).
- Maintain arterial oxygen saturation of more than 94% and $PaCO_2$ in the normocapnic range. Reserve hyperventilation for management of sudden increases in the ICP.

Step 2: Maintain Adequate Fluid Balance while Preventing Brain Swelling

- Avoid hypotonic fluids (like 5% dextrose) to prevent brain swelling. Note that lactated Ringers' solution is also mildly hypotonic.
- Use isotonic fluid like normal saline to maintain euvolemia.
- Fluid restriction and active diuresis should be avoided as it will lead to reduced circulating blood volume and hypoperfusion of the brain.
- Maintain normal or slightly high serum sodium values (145–150 mEq/L).

Step 3: Maintain Normoglycemia

- Hyperglycemia is associated with worse outcome after brain injury. This is because during low oxygen supply state intracellular sugar is converted into lactate, which causes intracellular acidosis and is detrimental to neuronal cells.
- On the other hand, for normal neuronal function, continuous supply of glucose is mandatory and hypoglycemia is equally detrimental.
- Thus, a fine balance of glucose control between 140 and 180 mg/dL should be maintained, with insulin infusion and ensuring adequate carbohydrate intake.

Step 4: Treat Fever Aggressively

- Fever is detrimental to brain tissues, and on the other hand, mild hypothermia is beneficial.
- Any febrile episode should be actively controlled with antipyretics and external cooling measure.

Step 5: Maintain Blood Pressure in the Normal Range

- Excessive swings of blood pressure should be avoided as autoregulation of cerebral blood flow is disrupted with the injured brain and flow will increase or decrease with changes in blood pressure leading to hyperemia with increased ICP during hypertension or hypoperfusion leading to decreased cerebral blood flow and neuronal injury during hypotension. Mean arterial pressure should be kept in the range of 65–75 mmHg in most patients.

Step 6: Decrease Cerebral Metabolic Demand

- Judicious use of sedatives (e.g., barbiturates and propofol) and analgesics is useful in these cases.

Step 7: Prevent and Treat Convulsions Aggressively
(See Chap. 30, Vol. 1)

- Anticonvulsant prophylactic may be given perioperatively for cortical surgeries.
- All episodes of new onset seizures should be actively managed to prevent secondary brain injury.
- In patients with persistent or fluctuating level of consciousness, nonconvulsive status should be ruled out.

Step 8: Monitor the Patient for Increases in ICP and Neurological Deterioration Frequently

(See Chap. 33, Vol. 1)

- Hourly Glasgow coma score, pupillary size and reaction
- ICP monitoring where appropriate
- Maintain CPP (MAP−ICP > 65 mmHg).
- Measurement and management of raised ICP (refer to Chap. 33, vol. 1)
  - Basics
    Normal ICP is less than 15 mmHg.
    Raised ICP is more than 15–20 mmHg for more than 1–5 min.
    CPP = MAP − ICP.
    Always measure cerebral perfusion pressure (CPP) along with ICP.
    The ICP monitor (intraventricular drain or subarachnoid bolt) is inserted if indicated.
    Transducer (without flush system) has to be kept at midventricular level which is at the level of tragus in supine position.
    Start treatment if ICP is more than 20–25 mmHg for more than 5 min.
  - Management of intraventricular drain (IVD)
    Drain cerebrospinal fluid (CSF) whenever ICP is more than 15–20 mmHg.
    Drain CSF till ICP is 10–15 mmHg.
    Measure daily CSF drain required to maintain ICP.
    Examine CSF every day.
    Take full sterile precautions.
- Lumbar drain
  - If IVD is in situ, do lumbar puncture and compare opening and closing ventricular and lumbar pressures.
  - If there is comparable drop, IVD can be removed, and CSF is drained by Lumbar punctures (LPs).
  - If there is no fall in ventricular pressures, drain CSF from IVD and avoid further LPs.
- Approach to an acute rise of ICP in a previously stable patient
  - Check the transducer level and rezero.
  - Confirm waveform of ICP trace.
  - Position the head, neck, and endotracheal tube tape properly to minimize increase in ICP.
  - Check ventilation, ABG, and X-rays and increase mechanical ventilation to decrease pCO_2 if necessary.
  - Exclude anxiety, pain, or seizures.
  - Drain CSF or give mannitol bolus.
  - Perform a CT scan if appropriate.

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Part VII

General Issues

Initial Assessment and Resuscitation

23

Jeetendra Sharma and Apoorva Tiwari

A 52 year old male patient with past history of chronic active alcoholism and history of endoscopic variceal ligation (EVL) for Grade III Esophageal varices 2 years back was admitted to ICU with complaints of upper gastrointestinal bleeding and altered sensorium. His vitals on arrival were axillary temperature of 37.0 °C, non-invasive BP of 80/51 mmHg, rapid thread pulse with rate of 142/min, respiratory rate of 27/min with SPO_2 of 87% on ambient air with Glasgow Coma Scale (GCS) of 12.

Managing a patients in ICU, arriving in morbid condition is a challenging task, with underlying concept of timely intervention directly proportional to morbidity and mortality, and a prompt and protocolized resuscitation regimen will help in salvaging these patients.

Step 1: Assign Responsibilities

- Quickly make a team and assign job responsibilities to every member clearly and appropriately.
- In the initial phase, the patient should be seen by a senior member of the ICU team for initial resuscitation, investigation, management planning, and family briefing.
- Assign two doctors for initial resuscitation.
- Assign two nurses initially for unstable patients.
- Take early assistance whenever needed from other members of the team.

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Step 2: Start Initial Assessment and Resuscitation

- Initial aim is to determine immediate life-threatening problems. Time is usually short and not enough to be certain about the cause of the problem, and correcting physiological abnormalities should take precedence over arriving at an accurate diagnosis. However, a working diagnosis is essential for deciding treatment options once physiological stability is achieved.
- For the patient in cardiorespiratory arrest, follow ACLS protocol.
- Pertinent History taking, physical examination, sending investigations, and resuscitation need to be carried out simultaneously rather than sequentially as time is limited.
- For hemodynamically unstable patients, resuscitation should be systematic and aimed toward assessment and management of A (airway), B (breathing), and C (circulation and consciousness).
- All three components can be managed simultaneously; sequential approach is not necessary.

Airway (A)

Assess the airway. Need for definitive airway by endotracheal intubation or airway adjunct (oral/nasal airway), supralaryngeal devices, or surgical cricothyrotomy in a patient is mainly based on clinical assessment and should not be delayed.

- Ask for assistance whenever in doubt about a difficult airway.
  - Look, listen, and feel for features of airway obstruction and secure airway and intubate when necessary (for details, see Chap. 1, vol. 1).
  - Snoring—due to obstruction of upper airway by tongue and oropharyngeal soft tissue—insert oro/nasopharyngeal airway.
  - Gurgling—due to obstruction of upper airway by secretions—perform suctioning.
  - Stridor—due to obstruction by foreign body or stenosis of upper airway, usually inspiratory—remove foreign body or intubate.
  - Wheeze—due to spasm in small airways—give bronchodilators.
  - Complete airway obstruction is silent—intubate.

Breathing (B)

- Assess the need for oxygen and ventilation. It can be assessed clinically along with pulse oximetry and arterial blood gas analysis:
  - Look for clinical signs of respiratory distress:
    Breathlessness
    Tachypnea
    Inability to talk

Table 23.1 Clinical features of inadequate oxygenation

• Restlessness • Delirium • Drowsiness • Cool extremities • Cyanosis	• Tachycardia • Arrhythmia • Hypotension • Flapping tremor (asterixis)

Open-mouth breathing
Flaring of alanasi
Use of accessory muscles of respiration
Paradoxical breathing (inward movement of abdomen during inspiration)

– Look for clinical features suggestive of inadequate oxygenation or ventilation (Table 23.1):
Remember that these clinical presentations are a very late feature of respiratory failure and imply impending cardiorespiratory arrest. Patients need to be identified much earlier, and appropriate management should be instituted.
Look for features of tension pneumothorax and evidence of massive pleural effusion or hemothorax and drain immediately.
Any evidence of massive lung collapse with desaturation requires intubation, suctioning, and positive-pressure ventilation.
Some clinical conditions, for example, deep unconsciousness (GCS <8), severe hemodynamic instability, or severe respiratory distress, require immediate endotracheal intubation and mechanical ventilation.
Noninvasive ventilation can be tried in relatively stable patients if they are suffering from a condition where noninvasive ventilation has been shown to be effective.

- Use High Flow oxygen device whenever indicated
- Normal oxygen saturation does not exclude compromised airway and need for intubation and ventilation.

Circulation (C)

- Assess adequacy of circulation. Assessment and management should go side by side.
  – Examine the following:
Peripheral and central pulse for rate, regularity, volume, and symmetry
Skin temperature
Heart rate and rhythm
Blood pressure (supine and sitting for orthostatic hypotension)
Capillary refill
Jugular venous pressure
Urine output

Bedside echocardiography—e-FAST (Extended Focused Assessment with Sonography in Trauma), RUSH (Rapid Ultrasound for Shock and Hypotension) or FATE (Focus Assessed Transthoracic Echocardiography) can be performed
Consider invasive monitoring—Invasive Arterial Pressure, Central Venous Pressure Monitoring
Advanced hemodynamic monitoring including, Cardiac Output (If indicated).
Judiciously use volume, inotropes, and vasopressor support.
Early volume challenge is appropriate in most hypotensive patients.
Identify cardiogenic shock and rapidly triage to appropriate facility.
Look for pericardial tamponade causing hemodynamic instability requiring immediate pericardiocentesis.
Any suspicion of pulmonary embolism should lead to urgent anticoagulation if not contraindicated, and then arrange for appropriate investigation.
Patients presenting with features suggestive of aortic dissection should have urgent control of hypertension and heart rate and should be urgently investigated to confirm diagnosis.
In patients with features of sepsis and septic shock apply sepsis bundle along with prompt broad-spectrum antibiotics administration.

- *Consciousness*—frequent neurological examination needs to be performed in drowsy patients.
  - Lateralizing features like hemiplegia are usually a feature of neurological disease.
  - A depressed conscious level in the absence of a primary neurological cause is indicative of severe systemic disease.
  - Check for hypoglycemia and correct urgently.
  - Control ongoing seizures with appropriate measures.
  - Consider urgent antibiotics for patients with features suggestive of bacterial meningitis (Table 23.2).

Table 23.2 Rule out 7H and 5Ts

7H	5T
• Hypovolemia • Hypoxia • Hydrogen ion excess (acidosis) • Hypoglycemia • Hypokalemia • Hyperkalemia • Hypothermia	• Tension pneumothorax • Tamponade—cardiac • Toxins • Thrombosis (pulmonary embolus) • Thrombosis (myocardial infarction)

Reversible causes of unstable patient may lead to cardiac arrest

Step 3: Take Focused History

- Obtain history from relatives and medical and nursing staff in the unstable patient.
- Review patients' clinical chart and perioperative note.
- Presenting problem in chronological order with duration and temporal profile of illness needs to be documented.
- Take history of mechanism of injury in trauma patients.
- Ask for significant comorbidities such as cardiac, pulmonary, renal diseases, previous surgery, or any other significant past medical problem.
- Enquire about previous hospitalization or use of NIV at home.
- Enquire about functional state at home—bedbound, ambulatory with support or independent.
- Enquire regarding exercise tolerance.
- In the elderly, enquire about mental state and cognition.
- Take detailed medication history with doses and duration. Enquire about any recent change of medication, drug allergies, over-the-counter medications, alternative medication, and self-administration of medications.
- Ask for any routine use of sedatives or psychiatric medication.
- Enquire about addictions such as alcohol and tobacco.
- A problem list of active and inactive problems needs to be documented in the clinical notes.
- Ascertain patients' resuscitation status as per family's wish.

Identify next of kin for family briefing

Step 4: Perform Focused Physical Examination

- Check for vital signs.
- Look for warning signs of severe illness (Table 23.3).
- Examine for any life-threatening or limb-threatening abnormalities systematically.

Table 23.3 Warning signs of severe illness

– BP systolic <90 or mean arterial pressure <60 mmHg
– Glasgow coma score <12
– Pulse rate >150 or <50 beats/min
– Respiratory rate >30 or <8/min
– Urine output <0.5 mL/kg/h

Complete blood count, blood sugar, sodium, potassium, urea, creatinine, aspartate transaminase (AST), Alanine Transaminase (ALT), PT, APTT, arterial blood gas, and lactate level in septic patients are important initial investigation

Table 23.4 Examples of investigations requiring urgent corrective action

– Blood sugar <80 mg/dL or >600 mg/dL
– Sodium <110 or >160 mmol/L
– Potassium <2.5 or >6.0 mmol/L
– pH < 7.2
– Bicarbonate <16 mmol/L

- Examine for pallor, cyanosis, jaundice, clubbing, or pedal edema.
- Examine skin for rash, petechiae, urticaria, and eschar.
- Examine other organ systems systematically.
- Examination needs to be repeated frequently for any new features or findings missed previously. In neurological patients, Glasgow coma score needs to be assessed frequently.
- Patients should be fully exposed with proper privacy during initial examination.
- A detailed physical examination should be performed later once the patient stabilizes after initial resuscitation.
- Chest X-rays and a 12-lead ECG should be performed.
- Appropriate microbiology cultures should be sent.
- Further investigations should be based on finding from history and physical examination.
- In unstable patients, investigations should be performed at the bedside as much as possible.
- If transport outside the ICU is needed, the patient should be properly monitored and accompanied by qualified personnel (see Chap. 25, vol. 2).
- Maintain an investigation flow sheet in chronological order.
- Red flag investigations require immediate corrective actions (Table 23.4).

Step 5: Recognize the Patient at Risk

- Take special precautions in the following group of patients:
  - The elderly and immunocompromised may not show features of decompensation such as fever and tachycardia.
  - Polytrauma patients, due to multiple injuries and effect of distracting pain, are difficult to assess.
  - In young adults, decompensation is late due to physiological reserve.

Step 6: Assess Response to Initial Resuscitation

- Assess changes in vital signs with initial resuscitation—pulse rate, rhythm, blood pressure, oxygen saturation, urine output, and mental state.
- Continuous assessment is mandatory, and one needs to be vigilant and present at the bedside.

- Preload assessment and volume responsiveness with bedside 2 D Echo, SVV, PPV, PLR, etc.
- Repeat Arterial Blood Gas at timely interval
- Comprehensive Hemodynamics and Neurological Monitoring

Step 7: Assess Intensity of Support

- Inspired oxygen fraction needed to maintain saturation above 90%
- Intensity of ventilatory support—positive end-expiratory pressure, minute ventilation
- Dose of vasopressor and inotrope needed to maintain mean arterial pressure above 60 mmHg
- Need for volume support to keep adequate urine output
- Need for blood transfusion to keep hemoglobin above 7 g/dL
- Need for sedation in agitated patients
- Need for dialysis support
- Need of temporary intravenous pacemaker
- Refractory cardiogenic shock may require urgent Veno-arterial extracorporeal membrane oxygenation (VA ECMO)
- Refractory severe hypoxia in ARDS may necessitate Veno-venous extracorporeal membrane oxygenation (VV ECMO)

Step 8: Seek Help for Specific Problems That Might Require Expertise (Multispeciality Consultations)

- Cardiologist—complete heart block, acute coronary syndrome, cardiogenic shock, intra-aortic balloon pump insertion, pericardial tamponade, massive pulmonary embolism
- Nephrologist—Need of urgent dialysis
- Neurologist—acute stroke or undiagnosed depressed conscious level
- Neurosurgeon—intracranial hemorrhage, head injury, severe cerebral edema
- Trauma surgeon—polytrauma, abdominal trauma, thoracic trauma, compartment syndrome
- Obstetrician—ruptured ectopic pregnancy, postpartum hemorrhage
- Intervention Radiologist—Control of ongoing hemorrhage by vascular embolization.
- Cardiothoracic Surgeon/ECMO team—ECMO Installation

Step 9: Construct a Working Diagnosis and Plan for Further Management

- Initial resuscitation, assessment, investigation and response are helpful in arriving at a working diagnosis or make ground for differential diagnosis.
- Reassess the patient frequently to modify initial plan if needed.
- Problem oriented goals to be defined and steps to achieve to these goals within stipulated time must be incorporated in plan of management (Table 23.5)

Table 23.5 Examples of plan of management with list of relevant goals[a]

Goals	Plan
Mean arterial pressure >65 mmHg	– Continuous invasive arterial blood pressure monitoring – Appropriate fluid resuscitation – Vasopressor/inotropic support if require
Hb > 7 mg/dL	– Monitoring of Hb level in blood 8 hourly – Packed red cells transfusion if Hb < 7 g/dL
Blood platelets count >10,000 per cu. mm	– Monitor blood platelets count 8 hourly – Watch for bleeding, if occur transfuse one unit of single donor platelets collected by apheresis (SDP) – If platelets count <10,000 cu. mm transfuse one unit of SDP – 4–6 units of Random donor platelets collected from multiple donors (RDP) may be transfused if SDP not immediately available
PaO_2 > 65 mmHg	– Use Oxygen supplement Methods-Prongs/Mask – Consider NIV/Invasive Ventilatory Support/High Flow nasal cannula (HFNC)
Adequate and smooth breathing	– Provide ventilatory support with endotracheal intubation if GCS < 9 – Bronchodilator nebulization if bronchospasm – Breathing exercises – Chest physiotherapy – Non-invasive ventilation where indicated
Conscious and alert	– Close neurological monitoring – Consider CNS imaging – Consider osmotic therapy
Urine output >30 mL/h	– Ensure adequate resuscitation – Consider renal replacement therapy
Sedation score = 0-1	– Adjust infusion rate of sedative according to sedation score – Every day sedation interruption
Intra-abdominal pressure (IAP) < 12 mmHg	– Continuous IAP monitoring – Apply non-surgical measures to reduce IAP – Consider surgical intervention if medical measures fail to reduce IAP

[a]Please note this list is not comprehensive

Step 10: Brief Relatives

- After initial resuscitation, assessment, investigation, and response, the family should be briefed about the likely diagnosis, treatment plan, and approximate prognostication, and duration of stay and consent should be taken for any invasive procedures.

Step 11: Documentation and Consents

- Family briefing should be documented in clinical notes; preferably, counter signed by participant relative(s).

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Website

www.aha.org

Comprehensive ICU Care

24

Tariq Ali, Yatin Mehta, Rajesh Chawla, and Subhash Todi

A 60-year-old male patient with urosepsis and multiple organ failure was admitted to the ICU for 10 days. He was requiring ventilator support, vasopressor, and dialysis support. He was under continuous sedation and not tolerating enteral feeding fully which was being supplemented with partial parenteral nutrition.

ICU management of the multiorgan failure patient is getting increasingly complex due to the availability of the advanced organ support system. A systematic and multidisciplinary approach to multiple critical-care-related issues encountered by these patients should be initiated by the ICU team to minimize chances of hospital-acquired complications or infections and maximize chances of recovery. For an experienced intensivist, the comprehensive ICU care begins before he/she enters the ICU. Having a plan ready for each patient and modulating it with the current condition drives confidence in both the staff and the patient.

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Step 1: Perform a Quick Overview

- Perform a quick overview of ICU occupancy, patient–nurse ratio, and medical staff available for the day. It helps in identifying staffing problems early.
- Check and allocate staff for remote calls (emergency department, wards, high-dependency units [HDUs], cardiac arrest and Rapid Response).
- Planned shifts are best worked up early to accommodate the transfer in timely manner.
- Ensure proper allocation of residents and nurses.

Step 2: Take Proper Handover

- Continuity of patient care in the ICU is dependent on accurate and timely handover. Due to shift work of junior doctors, this may need to be done once or even twice in 24 h and is a common source of medical error.
- Structured method of handover has been shown to critically influence the transfer of clinical information, and this process should be implemented for a smooth and correct transfer of information.
- Only 2.5% patient information is retained in verbal handover, 85.5% is retained when using the verbal along with note-taking method, and 99% is retained when a printed handout with all clinical information of the patient is used.
- Handover should take place in an unhurried manner at a set time and place with minimal interruptions and under senior supervision. Each handover session should last 20–30 min to cover 10–15 patients.
- A structured written format like ISBAR should be maintained for all new patient handover. The essentials of this format are as follows:
  - *I*dentity of the patient—age, gender, and primary consultant.
  - *S*ituation—symptoms/problems, patient stability/the level of concern.
  - *B*ackground—the date of admission, history on presentation, diagnosis, and relevant past medical history.
  - *A*ssessment and action—what has been done so far and assessment of situation.
  - *R*esponse and rationale—response to intervention, what needs to be done, investigation, treatment pending, review by whom and when, further plan, and recommendations.
- For patients known to the ICU team, ISBAR may be shortened to SAR only.

Step 3: Take Relevant History, Perform Clinical Examination, and Review Investigations, Nursing Charts, and Clinical Notes

- After taking proper handover, the patients assigned should be thoroughly reviewed and examined afresh rather than relying on previous information.
- Enquire about any recent events from the duty nurse.

- Observe the patient from the bedside for a minute for any evidence of respiratory distress, restlessness, patient ventilator asynchrony, and paucity of spontaneous movements.
- After taking the bedside nurse's permission, ensuring proper hand hygiene, and maintaining patient privacy, introduce yourself and take patient's consent before examination. Examine from head to toe in a systematic way without causing any discomfort to the patient. Always thank the patient at the end of your examination and ensure proper covering.
- In the head and neck region, examine for pallor, jaundice, pupils, conjunctival hemorrhage, evidence of exposure keratitis, jugular venous pressure, carotid pulse, carotid bruit, thyromegaly, and cervical lymphadenopathy. Avoid manipulating the neck in trauma patients and ensure proper placement of cervical collar if present.
- Examine the conscious level by Glasgow coma scale scoring.
- In intubated patients, note the length of the endotracheal tube at lips and whether properly secured. Check proper placement of heat and moisture exchanger (HME) filters with dates changed and condition of the filter whether clogged with secretions. Check the ventilator circuit for not causing undue traction on the endotracheal tube, water accumulation, and attachment to heated humidifiers. Ensure proper attachment of nebulizer or metered-dose inhaler devices. Check inline suction assembly and endotracheal tube cuff pressure. In tracheotomized patients, check tracheostomy site for erythema, purulence, proper tying of the tracheostomy tube, and functioning of supraglottic suction, if present, and measure cuff pressure. In the uncuffed tube, check patency by blocking the tube and asking the patient to vocalize. Enquire about the frequency of suctioning and the amount and type of respiratory secretions.
- Check placement of orogastric or nasogastric tube position, patency, and attachment to the enteral feeding pump.
- In patients with central venous catheters at jugular or subclavian venous sites, ensure proper dressing and inspect the entry site for erythema and purulence. Palpate over the dressing for tenderness. Ensure stopcocks are properly cleaned and securely attached.
- Examine the chest systematically. Inspect for proper electrocardiograph lead placement, any skin changes, and flail chest in trauma patients. Palpate for any crepitus and percuss for dullness of effusion and hyperresonance of pneumothorax. Auscultate for breath sounds, cardiac sounds, adventitious breath sounds, and cardiac murmurs.
- Examine the abdomen for fullness, tenderness, visceromegaly, ascites, and bowel sounds. Also check the position of the gastrostomy or jejunostomy tube if any.
- Rectal examination in all patients and pelvic examination in women should not be ignored. Enquire about bowel movements, consistency, and color of stool.
- Check penile area for urinary catheter position and proper tying of the urinary bag at the thigh to avoid traction and reverse drainage. Examine the color and quantity of urine in the drainage bag.
- Examine upper extremities for radial and brachial pulse, blood pressure, hand grip, and thrombophlebitis. Check radial artery line if in place for proper

functioning by performing a flush test, date of insertion, and capillary refill for ensuring hand perfusion.

- Examine lower extremities for edema, calf swelling, muscle strength, proper fitting of anti-embolism stockings, or pneumatic compression. Look for any femoral lines and if present whether properly secured and any evidence of groin hematoma.
- Roll the patient on the side with nurse's help and examine the back. Feel the back of scalp and ears for pressure areas, auscultate for basal crepitations, or diminished breath sounds. Look for decubitus ulcers at the sacral area, scrotal swelling, and any perineal soiling or evidence of candidiasis.
- In postoperative and trauma patients, look at the wound or surgical incision site for erythema and purulence, palpate for induration and tenderness, and check proper dressing. Check the drainage bag for proper labeling, amount, and type of drainage.
- Take note of bedside monitor readings of vital signs—cardiac rate and rhythm (print out a rhythm strip), any obvious ST changes, and mean arterial pressure—noninvasive or invasive, and confirm yourself by checking manually if in doubt about correct values. Check pulse oximeter plethysmograph and oxygen saturation, central venous pressure, or pulmonary arterial pressures (after printing out a pressure strip), capnograph, and core temperature readings.
- Check ventilator parameters—mode, FiO_2, positive end-expiratory pressure (PEEP), tidal volume, pressure limit, ventilator rate, inspiratory–expiratory ratio, and inspiratory flow. Monitor minute ventilation, auto-PEEP, pleateu pressure and Driving Pressure. Measure lung compliance and airway resistance.
- Check intravenous infusions, volumetric infusion pumps, and syringe pumps for proper labeling and functioning.
- Check advanced hemodynamic monitoring if present for Cardiac output, Stroke volume, Stroke Volume variation and Pulse Pressure Variation.
- Perform Straight passive leg raising test when indicated
- Check Intrabdominal pressure in catheterised patient when indicated
- Review recent investigations including hematology, biochemistry, microbiology, and imaging studies and compare it with the previous reports to analyze the trend.
- Use Portable Bedside Ultrasound device for central line placement, assessment of volume status and rule out Pneumothorax,,pleural effusion, pulmonary embolism in appropriate situations
- Familiarize with the ICU nursing chart and review it systematically. Examine previous 24-h trend and worst values. Look for records of vital signs, hemodynamic and ventilator parameters, intake and output chart, enteral feed rate and tolerance, hourly urine output, blood or blood product transfusion in previous 24 h, and any untoward transfusion-related reaction.
- Review cumulative fluid balance till date and cumulative calories or protein deficit or excess.

- Review the medication sheet daily for proper drug dosing and stop any unnecessary medication.
- Review clinical notes for any referral input and any new major event described.
- Review patient's code status and therapeutic support level as desired by the patient and family.
- Review the prior status of the patient.

Step 4: Participate in a Multidisciplinary Ward Round

- ICU care is a teamwork, and a typical ICU round in a tertiary care hospital consists of the ICU consultant, resident doctor, senior sister, duty nurse, physiotherapist/respiratory therapist, dietitian, clinical pharmacist, ICU technician, and social worker.
- Rounds in ICUs are different from a general ward round in many aspects. First, substantially more information is exchanged, which is essential. Second, the emphasis is on physiological derangements rather than on specific problems. Third, the discussion is always goal-oriented so that when goals are met the patient may be transferred to a lower level of care.
- In addition to providing educational value, rounds in ICUs serve two purposes: first to communicate the patient's present status to the entire team and second to establish goals and plans for each patient.
- To ensure that each patient undergoes a comprehensive evaluation each day, think and communicate in terms of systems. These typically include neurological (including analgesia and sedative), pulmonary, cardiovascular, renal, fluid, electrolytes, nutrition, gastrointestinal, metabolic, infectious, and hematologic. Rounds will move more smoothly and efficiently if a structured and uniform format of presentation is adopted by all members.
- Each system should be analyzed and presented according to outcome and process variables. For example, in the renal system, urine output, intake/output balance, and electrolyte levels are outcome variables, and supplemental electrolytes administered, volume of intravenous fluid given, and amount of diuretic used are process variables (Table 24.1).
- Case presentation should start with identifying the patient, the day of ICU or hospital admission, reason for admission, principal diagnosis, and any significant event in the previous 24 h. For new patients, significant medical background and presenting complaint should be presented. Vital signs, pertinent physical examination findings, hemodynamic, ventilator parameters, intake and output, invasive procedures performed, major investigations done with results, and treatment initiated should be described. Area of major concern needs to be addressed; treatment goals and the plan for the day should be elaborated. A summary capsule of case should be presented at the end. The case presentation should be precise and should not take more than 5 min.

Table 24.1 Outcome and process variables

System	Outcome variables	Process variables
Neurological	Motor function	Type/route of analgesics
	Pain level	Type/route of sedative, antiseizure medications
	Sedation level	Intracranial pressure monitors
	Glasgow coma score	
	Intracranial pressure	
	Occurrence of seizures	
Pulmonary	Presence of rales or wheezes	Ventilator settings
	Appearance of the chest X-ray	Administration of nebulized bronchodilators
	Oxygen saturation	Administration of supplemental gases such as nitric oxide
	End-tidal CO_2 concentration	Readiness for weaning and extubation daily assessment
	Arterial blood gas data	
	Spontaneous ventilation rate	
	Forced vital capacity	
	Negative inspiratory pressure	
Cardiovascular	Blood pressure	Estimates of and interventions to adjust preload, such as central venous pressure or pulmonary artery occlusion pressure
	Heart rate	Estimates of and interventions to adjust afterload, such as vasodilator therapy
	Abnormal rhythm	Estimates of and interventions to adjust contractility, such as inotropic therapy
	Presence of rales	Estimates of (e.g., drug level) and interventions to adjust antiarrhythmic
	Peripheral pulses and extremity warmth	
	Cardiac output	
	Evidence of ischemia	
Renal/fluid/electrolytes	Weight	Intravenous fluid composition and rate
	Net intake and output balance	Supplemental electrolytes
	Current electrolytes	Sites of unusual loss of volume
	Blood urea nitrogen, creatinine, ABG	Sites of unexpected loss of specific electrolytes
Gastrointestinal/metabolic/nutrition	Bowel sounds, function	Route/rate/composition of nutritional support
	Absorption of enteral feedings	Use of prokinetic or antiemetic agents
	Fraction of caloric goal attained	Prophylaxis against gastrointestinal bleeding
	Nitrogen balance	Insulin requirements
	Hyper- or hypoglycemia	Hormone replacement therapy (e.g., thyroid)

Table 24.1 (continued)

System	Outcome variables	Process variables
Hematologic/ infections disease	New findings on physical examination suggestive of bleeding	Transfusion requirements
	Hematocrit, platelet count, and coagulation parameters	Deep venous thrombosis prophylaxis
	Temperature; findings suggestive of infection on physical examination; gram stain and culture data, including antimicrobial and sensitivity	Procedures to diagnose and/or control infection
	Leukocyte count and differential count	Antimicrobial prescription, including drug levels where appropriate

Adapted from www.sccm.org
Medical students' guide to intensive care medicine

Step 5: Write Proper Clinical Notes

- Appropriate documentation whether on paper or electronic is of paramount importance and should be done in a systematic and unhurried manner. Writing should be legible, and the proper date, time, and signature should be recorded.
- A uniform format should be maintained during daily case record documentation.
- SOAP (subjective, objective, assessment, plan) format may be utilized for case notes in short-stay cases.
- A more elaborate and comprehensive daily checklist should be utilized in complex and long-stay cases on multiple organ support (Table 24.2). This ensures that all aspects of case management have been addressed.
- Every patient should have a master problem list (active and inactive problems), which needs to be updated periodically.
- Documentation of family briefing and end-of-life care decisions should be done meticulously.

Step 6: Perform Procedures under Supervision

- Acquiring technical skills in different procedures is a requisite for any ICU training program.
- Acquire factual knowledge about the common procedures performed in the ICU with indications, contraindications, complications, and steps of procedure (see Sect. XV).
- Familiarize yourself with procedures performed by observing seniors in ICUs.
- Initial procedures should be performed under elective conditions under proper supervision.

Table 24.2 Daily checklist

I Hug Fast	Continuous Quality Improvement (CQI) checklist
I = Infection control	What needs to be done for the patient to be discharged from the ICU?
H = Hand hygiene and head of bed elevation	What is the patient's greatest safety risk? How can we reduce that risk?
U = Ulcer prophylaxis	Pain management/sedation
G = Glycemic control	Cardiac/volume status
F = Feeding	Pulmonary/ventilator (plateau pressure, elevate head of bed 30–45°)
A = Analgesia	Mobilization
S = Sedation	Infectious disease issues, cultures, drug levels
T = Thromboprophylaxis	Gastrointestinal issues, nutrition
	Medication changes (can any be discontinued?)
	Tests/procedures
	Review morning laboratory results and the chest X-ray
	Consultations
	Communication with primary service
	Family communication
	Can catheters tubes be removed?

Adapted from Vincent (2005) and Pronovost et al. (2003)

- Take informed consent in elective procedure, explain procedure to the patient, and always remember "do no harm."
- Procedure performed should be documented, and any complication should be recorded and countersigned by the supervisor. An individual logbook of procedures should be maintained to acquire sufficient experience to have privileges of unsupervised procedures.

Step 7: Follow Infection Control Practices

- Take leadership and exemplary role in maintaining proper infection control practices.
- Maintain and teach hand hygiene procedures to juniors and nonmedical members of the ICU team.
- Practice isolation practices wherever applicable.
- Be vigilant in detecting and reporting nosocomial infection to the infection control nurse.
- Practice antibiotic stewardship.
- Take proper preventive measures during invasive procedures and during maintenance of invasive devices.

Step 8: Counsel Family Members

- Be observant and listen to seniors discussing a patient with family members and clarify any doubts.

- Start participating in group discussion with the family and document discussions in clinical notes.
- Be sensitive about discussion of end-of-life care
- Above all, be compassionate.

Step 9: Be a Productive Member of the ICU Team

- ICU care is a teamwork where each member of the team has a defined responsibility.
- Many of the ICU tasks are interdependent, and therefore effective communication among team members is essential.
- Familiarize yourself with policies and protocols of the ICU, which may vary between ICUs.
- Create a safe work culture, avoid distractions, and keep ICU environment clean, calm, and acceptable to patients and family members.
- Punctuality, following a dress code if present, and proper mannerism reflect a professional approach.
- Attend departmental meeting regularly.
- Take an active role in quality control programs of the ICU.

Step 10: Keep Yourself Updated

- Actively participate in academic and research activities of the ICU.
- Keep a reference ICU handbook with you and refer to it whenever in doubt.
- Keep hospital drug formulary in the ICU and communicate with pharmacists regarding drug dosing.
- Attend simulation workshop for proper training in ICU skills.
- Participate in e-learning programs available on the web.
- Be familiar with ICU syllabus (see Appendix).
- Work towards gaining an accreditation at the end of your training period.

Suggested Reading

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Websites

www.cobatrice.org
www.isccmcourses.org

Quality Control

25

Subhash Todi and Ashit Bhagwati

Case 1: A 70-year-old male patient with dementia and Parkinson's disease was admitted to the ICU with the confusional state. He fell from his bed on the night of admission and suffered scalp injuries. How would you ensure that similar accidents do not happen in the future?

Case 2: A 60-year-old male patient was admitted to hospital with hypertensive intracerebral bleed and required ventilatory support. On the fourth day of admission, he developed features of ventilator-associated pneumonia. What measures should have been in place to avoid this complication?

Case 3: A 30-year-old male patient was admitted to hospital with gastroenteritis and severe hypokalemia. He was inadvertently administered high concentration of potassium in intravenous infusion through the central line and suffered a cardiac arrest. How could you have prevented such errors?

In a landmark publication, *To Err Is Human: Building a Safer Health System*, a decade ago by the Institute of Medicine USA, it was described that human error was one of the common causes of morbidity, mortality, and increased health care cost in hospitalized patients worldwide. Experts estimate that as many as 98,000 people die every year due to medical errors in hospitals. This number is more than the number of deaths due to motor vehicle accidents, breast cancer, and AIDS—three causes that receive far more public attention. This error is even more evident in the critically ill patients in the ICU. Increasing accountability and demand from public and accrediting agencies have led to a movement of quality care in ICUs.

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Step 1: Understand the Concept of Quality and Safety

- Quality and safety are two sides of the same coin. Quality reflects measures that should have been taken but were not taken or errors of omission, and safety reflects actions that were taken inappropriately or errors of commission.
- Case 1 may be taken as quality issue as proper precautions were not taken, which led to compromise in patient safety.
- Case 2 reflects need for preventive protocols for ventilator-associated pneumonia to be in place, another quality control issue.
- Case 3 reflects not only an error of commission, clearly a safety issue, but also lack of protocol for intravenous potassium infusion, a quality issue.

Step 2: Understand Donabedian's Theory on Quality Control

- Three important ingredients are as follows:
  1. Structure (what we have)
  2. Process (what we do)
  3. Outcome (what we get)
- Structural issues consist of organizational elements, personnel, and finance and are predominantly under administrative control.
- Process issues are the care given to the patient by health care providers. Daily checklists of such issues are always helpful.
- Outcome reflects what happens to the patient from morbidity and mortality point of view, given the structure in place and processes being implemented (Tables 25.1).

Step 3: Implement Standardized Data Collecting and Reporting System

- This should be done for all the three elements: structure, process, and outcome.
- It should follow SMART principle (specific, measurable, achievable, reliable, and time bound). A well-trained data collector is the backbone of any quality control program (Fig. 25.1).

Table 25.1 Donabedian's model of quality control

Structure	Process	Outcome
Closed model of ICU care	Compliance with hand hygiene	Crude ICU mortality
Critical care consultant availability	Family conference	Risk-adjusted ICU mortality
24 × 7 intensivist coverage	End-of-life support policies	Standardized mortality ratio = crude mortality/ predicted mortality
Ward design	Compliance with ventilator bundle	Hospital mortality
Nurse–patient ratio	Compliance with central line insertion bundle	ICU length of stay
Doctor–patient ratio	Antibiotic consumption	Hospital length of stay
Policies and protocols	Implementation of catheter-related blood stream infection prevention policies	Family satisfaction
Infectious disease consultant	Implementation of urinary tract infection prevention policies	Cost of care
Infection control nurse		Resource utilization
Multidisciplinary ward round		
Infection control committee		
Daily goal sheet		
Antibiotic form		
Adequate equipment		

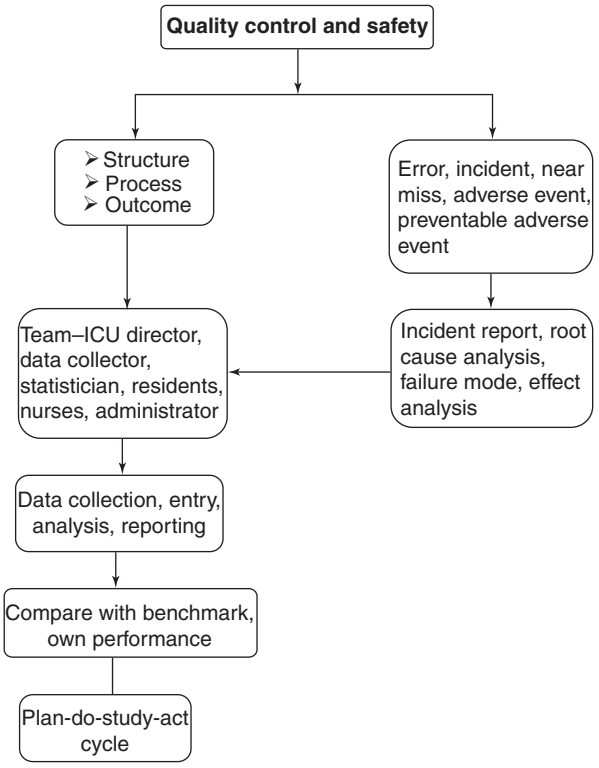

Fig. 25.1 Quality control approach in the ICU

Step 4: Understand Principles of Data Collection

- Any data should have a numerator (affected persons) and a denominator (persons at risk) (Table 25.2).

Step 5: Prioritize

- Identify important elements for which data need to be collected (Table 25.3).

Table 25.2 Formulae for urinary tract infections, central line-associated blood stream infections, and ventilator-associated pneumonia

$\frac{\text{Number of catheter-associated urinary tract infections}}{\text{Number of urinary catheter-days}} \times 1000$
$\frac{\text{Number of central line-associated blood stream infections}}{\text{Number of central line-days}} \times 1000$
$\frac{\text{Number of ventilator-associated pneumonias}}{\text{Number of ventilator-days}} \times 1000$

Table 25.3 Fundamental quality indicators

(a) Early administration of acetylsalicylic acid in acute coronary syndrome
(b) Early reperfusion techniques in ST-elevation myocardial infarction
(c) Semirecumbent position in patients undergoing invasive mechanical ventilation
(d) Prevention of thromboembolism
(e) Surgical intervention in traumatic brain injury with subdural and/or epidural hematoma
(f) Monitorization of intracranial pressure in severe traumatic brain injury with pathologic CT findings
(g) Pneumonia associated to mechanical ventilation
(h) Early management of severe sepsis/septic shock
(i) Early enteral nutrition
(j) Prophylaxis against gastrointestinal hemorrhage in patients undergoing invasive mechanical ventilation
(k) Appropriate sedation
(l) Pain management in unsedated patients
(m) Inappropriate transfusion of packed red blood cells
(n) Organ donors
(o) Compliance with hand-washing protocols
(p) Information of patients' families in the ICU
(q) Withholding and withdrawing life support
(r) Perceived quality survey at discharge from the ICU
(s) Presence of an intensivist in the ICU 24 h/day
(t) Adverse events register

Adapted from Spanish quality control guideline

Step 6: Identify Team Members

- This should be done for data collection, data entry, data analysis, and data reporting.

Step 7: Identify Benchmarks

- This should be done for comparison of data.
- There are national and international benchmarks for various quality control processes and outcomes.
- In the absence of a comparative benchmark, one can follow one's own trend and performance over time.

Step 8: Adopt the Plan-Do-Study-Act Cycle for Quality Control

- After identifying specific elements for data collection, collect, analyze, and compare reliable data with benchmark, take corrective action, and revisit the same process periodically to maintain a standard of care.

Step 9: Understand Terminology for Reporting of Safety Issues

- Patient safety data should be reported in the format including error, incident, near miss, adverse event, and preventable adverse event (Table 25.4).

Table 25.4 Terminology for reporting adverse events

Patient safety	Absence of the potential for, or occurrence of, health care-associated injury to patients
Error	It is defined as mistakes made in the process of care that result in, or have the potential to result in, harm to patients. Mistakes include the failure of a planned action to be completed as intended or the use of a wrong plan to achieve an aim. These can be the result of an action that is taken (error of commission) or an action that is not taken (error of omission)
Incident	Unexpected or unanticipated events or circumstances not consistent with the routine care of a particular patient, which could have, or did lead to, an unintended or unnecessary harm to a person, or a complaint, loss, or damage
Near miss	An occurrence of an error that did not result in harm
Adverse event	An injury resulting from a medical intervention
Preventable adverse event	Harm that could be avoided through reasonable planning or proper execution of an action

Step 10: Implement

- One of the measures for evaluating patient safety such as incident report, root cause analysis, and failure mode effect analysis should be implemented:
  - *Incident report*: It evaluates how a single patient comes to a harm. An incident reporting system should be voluntary, anonymous, and not linked with any form of punitive measures.
  - *Root cause analysis*: This is a more focused enquiry on certain incidents deemed to be important for patient safety. A sentinel event is identified, and important preventive aspects of this event are discussed by the safety team, and safeguards are implemented.
  - *Failure mode and effects analysis*: An error-prone process is identified, and a multidisciplinary team is formed to analyze prospectively the process from multiple perspectives before a sentinel event has occurred.

Step 11: Initiate Safety and Quality Culture

- This has to come from a strong leadership, primarily from the ICU director, backed by a supportive management.
- This has to be backed up by full support and motivation of ICU staff.
- Adequate budget needs to be provided by the administration.
- Computerized physician order entry system and Clinical Decision Support Systems goes a long way in ensuring safety in the ICU by reducing human error.

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Ethical Principles in End-of-Life Care

26

Subhash Todi, Rajesh Chawla, and Raj Kumar Mani

A 70-year-old male patient was admitted with massive intracerebral bleed to the ICU for 6 days. He was on a ventilatory support, with a Glasgow Coma Score of 6. According to the treating physician and neurologist, his survival chances were poor, and even if he survived, he would be fully dependent functionally. His eldest son requested withdrawal of the ventilatory support to provide comfort measures only and transfer out of the ICU.

Recognition of terminal stage of an illness and timely shift of management paradigm to palliative care is essential for appropriate care of those who die in the ICU. This involves weighing of benefit vs. harm and avoiding disproportionate interventions, The focus must shift to eliciting the values and wishes of the patient from a surrogate or a legally appointed healthcare proxy, as most of the time a critically ill patient is unable to decide for himself/herself.

Step 1: Identify Situations When EOL Support Needs to Be Initiated

Identifying these situation needs expertise and experience. The following checklist, though not exhaustive, should help the physician to recognize when to start discussions on EOL issues:

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- Advanced age, coupled with a poor premorbid state due to chronic debilitating diseases, for example, advanced chronic obstructive pulmonary disease requiring home oxygen and/or bi-level pressure support or severe impairment of quality of life, advanced interstitial lung disease on oxygen therapy with failed medical treatment, chronic renal failure requiring long-term dialysis, chronic liver disease, and advanced congestive heart failure.
- Catastrophic illnesses with multiple organ dysfunctions unresponsive to a reasonable period of aggressive treatment.
- Prolonged coma (in the absence of brain death) due to acute nonreversible causes or chronic vegetative state.
- Incurable chronic severe neurological states rendering meaningful life unlikely, for example, progressive dementia or quadriplegia with ventilator dependency.
- Progressive metastatic cancer where treatment has failed or the patient refuses treatment.
- Post-cardiorespiratory arrest, situations with non-restoration of comprehension after a few days.
- Comparable clinical situations coupled with a physician's prediction of low probability of survival.

Step 2: Discuss with Other Team Members Including Nurses Regarding EOL Decision

- Ensure that all members of health care team are on board and agree on initiating this discussion.
- The overall responsibility for the decision rests with the attending physician/intensivist of the patient, who must ensure that all members of the caregiver team including the medical and nursing staff follow the same approach.

Step 3: Identify a Surrogate Decision Maker

Majority of patients in the ICU are not competent to participate in EOL discussion. In these circumstances, the following approaches may be adopted:

- Ascertain whether the patient has executed a valid *Living will or advanced medical directive(AMD)* which is a duly processed legal document, which states patient's explicit wishes while he/she was compos mentis (in full sense). If it exists it should be honored as far as medically feasible. According to the recent Supreme Court judgment Common Cause vs. The Union of India, an AMD) is legally valid. AMD becomes operational only after the patient loses capacity. The treating team must integrate the values and wishes in order to respect the patient's Autonomy.
- *Durable power of attorney*: The patient also has the right to designate a surrogate/Healthcare proxy to take decisions on his/her behalf during the period of incompetency.

- *Surrogate decision maker*: This means spouse, children, parents, siblings, the next of kin who is available, or even a trusted friend. Existing laws for hierarchy of surrogates for EOL decision making, if present, should be applied in these situations.
- If an AMD does not exist proceed to engage with surrogates in counseling sessions to arrive at an end of life decision according to the "shared decision-making" model.

Step 4: Understand Ethical Principles About Withdrawing Life-Support Measures in the ICU

- *Autonomy*
- It is the right of an individual to make a free and informed decision.
  - Competency: The patient should be competent to make decisions and choices. This competency is assessed clinically by the physician and a psychiatrist if necessary.
- *Beneficence*
  - A principle that makes it obligatory on the part of physicians to act in the best interests of patients. In this context, the physician's expanded goals include facilitating (neither hastening nor delaying) the natural dying process, avoiding or reducing the sufferings of the patient and the family, providing emotional support, and protecting the family from undue financial loss.
- *Non-maleficence*
- A principle that directs physicians to first of all not do harm.*Distributive justice*
  - It means that patients in similar circumstances should receive same care.

Step 5: Initiate Discussion on EOL with the Surrogate Decision Maker

- The intensivist in consultation with the primary/admitting physician should initiate this process.
- This should be done in an empathic manner, in an unhurried way, with due time given for discussion. The environment should preferably be a quiet room, ensuring privacy and without any interim disturbance.
- A senior nurse or other members of health care team including family physician may be present during discussion.
- Other senior family members apart from the surrogate can also participate in the process, though total number should be restricted.
- Discussions should be carried out in a language and in terms that the family can understand.
- His/her present understanding of the disease process, expectations, and areas of uncertainties need to be identified. Attentive listening during this process is the key in reaching a consensus.

- The present clinical situation needs to be explained in simple terms avoiding medical jargon.
- The diagnosis, prognosis, and the range of therapeutic interventions available, including their risks, benefits, costs, and consequences, as well as the option of no therapy, should be explained clearly.
- As accurate a prognosis as is possible should be given, clarifying that uncertainty is inherent in the treatment of critical illness.
- Family's wish for a second opinion needs to be clarified and if requested should be complied with.
- The term futile care should be avoided and use of term like "inappropriate care" is advisable
- The possibility of death should be discussed along with the medical and palliative treatment options.
- Any previously stated terminal care wishes or preferences directly or indirectly expressed by the patient should be enquired.
- The discussions should include the relevant economical, ethical, and legal issues.
- The family should be counseled that withdrawal of support does not mean withdrawal of care, and all measures will be taken to ensure that the patient is free of pain and discomfort during EOL care.
- It should be made clear to the family that the decision is not binding and they are at liberty to change their mind if needed later (Fig. 26.1).

Step 6: Hold Multiple Counseling Sessions

- As EOL decisions are very sensitive, these should not be taken in haste. The family should be given adequate time and opportunity to ask questions and to express their views and emotions and to come to term with the situation and make an informed decision.
- There should be multiple counseling sessions of adequate duration.
- Pending consensus decisions or in the event of conflicts between the physician's approach and the patient's/family's wishes, all existing supportive interventions should continue.

Step 7: Reach a Consensus and Discuss Modalities of Palliative Care

- If the family consistently desires that life support should be withdrawn and when the treating physician also considers aggressive treatment non-beneficial, it is ethically justifiable to consider withdrawal of life support within the limits of existing laws of the country.
- The physician should explicitly communicate the available modalities of limiting life-sustaining interventions as follows:

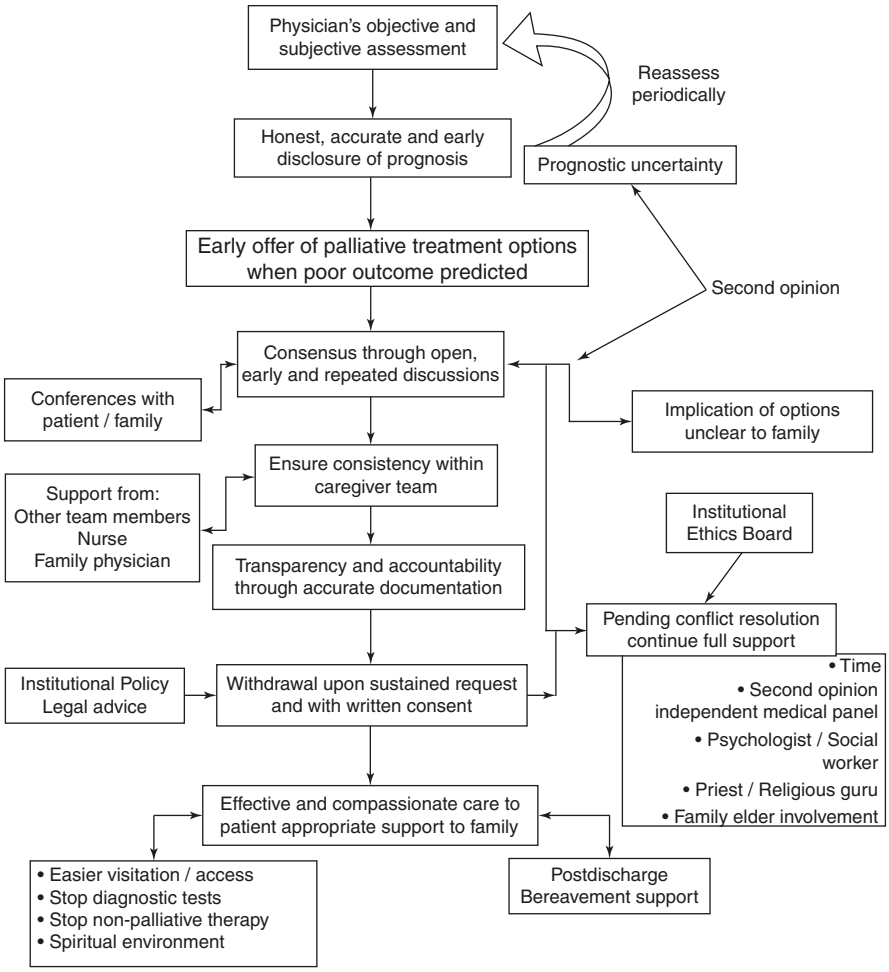

Fig. 26.1 Pathway to end-of-life decision making

- Do not intubate/resuscitate (DNI/DNR)
  - Aggressive ICU management but not including intubation (DNI) or attempts at cardiopulmonary resuscitation (DNR)
- Do not escalate
  - Not to escalate some or all existing life-support modalities (intubation, inotropes, vasopressors, mechanical ventilation, dialysis, antibiotics, intravenous fluids, enteral or parenteral nutrition) in case of clinical deterioration with the understanding that the patient will probably die from the underlying condition.
- *Withdrawal or withholding of life support*
  - All or specific life-support systems such as dialysis or ventilators may be withdrawn.

- Decision not to institute new life-support treatment.
- Ethically, there is no difference between withholding and withdrawing life-support therapy.

Step 8: Document Discussion in Case Notes

- The proceedings of the counseling sessions, the decision-making process, name of health care members and family members present during discussion, and the final decision should be clearly documented in the case records, to ensure transparency and to avoid future misunderstandings.
- Details of the communications between the medical team and the family should be documented accurately and completely.
- The signature of a family representative is not a mandatory requirement but may be kept optional.

Step 9: Institute Palliative Care

- Ensure proper sedation and analgesia (e.g., midazolam/fentanyl), preferably as an infusion. Give proper dose to ensure comfort and analgesia. Avoid excessive doses leading to respiratory depression or hypotension. This is termed as "double effect" in palliative care. Document doses and intention of palliation in the case notes.
- Neuromuscular blockers should be stopped. Ventilators may be disconnected, and the patient may be left on T piece for suctioning or extubated if family desires.
- Family members should be allowed at the bedside and given adequate time to spend with the patient. Monitors may be switched off, and blood draws should be stopped to avoid distraction.
- The patient may be shifted out of the ICU if the family wishes and if permitted even transfer home under supervision within the laws of the country.

Step 10: Resolve Areas of Conflict

When the family may be pursuing unrealistic demands of continuing futile care as deemed by the treating senior physician, or the physician may be seeking to impose his/her wishes on the family in contradictions to their wishes, conflicts may arise. The proposed course of action in these situations may be as follows:

- A second opinion from another physician not hitherto involved in the care of the patient.
- Multiple counseling sessions explicitly informing the family the hopeless prognosis of the patient and the futility of continuing life support.

- If the family is intransigent, then suggest transfer to another treating team willing to continue support.
- With the help of the hospital administration, set up a committee of doctors to counsel the family. The committee may also take the help of a social worker, identified by the family to help resolve barriers to understanding.
- Seek a judicial review.

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ICU Organization and Training

27

Narendra Rungta, Manish Munjal, and Kundan Mittal

A 50-year-old male patient was brought to the emergency department in a shock state. After initial resuscitation, the emergency physician wanted to admit this patient in the intensive care unit (ICU), but there were no beds available. The duty resident in the ICU was unable to shift any patient to make room for the patient in the emergency department.

Organizational issues, anticipating problem areas, and prior planning are of utmost importance for smooth functioning of any intensive care unit (ICU). These organizational aspects may be looked from human resources, infrastructure, and processes of care viewpoint (Table 27.1).

Step 1: Designate the Level of Care That Can Be Provided by the ICU

- ICUs are usually designated by three levels of care provided, with a varying nomenclature for these levels.
- In essence, they are the basic, intermediate, and advanced level of ICU care.
- Minimum requirements for a basic level ICU care:
  - Resuscitation and short-term cardiorespiratory support including mechanical ventilation
  - Noninvasive ventilation

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Table 27.1 Important considerations in organizing an ICU

ICU design
Assessing cost-effectiveness in the ICU
Improving the quality of care in the ICU
Infection control and surveillance in the ICU
Outreach services
Legal issues in critical care
Assessment of severity of illness and likely outcome
Physiotherapy in intensive care
Critical care nursing
Common problems after ICU care
Clinical information system
Clinical trials in critical care
Transportation of the critically ill patients
Telemedicine
Preparedness for catastrophe

  - Facilities for transport to higher centers
  - Basic laboratory, radiology, blood bank outsourcing
  - 24-h coverage by a physician trained in fundamentals of ICU care
  - Adequate support staff
- Minimum requirements for an intermediate level ICU care:
  - All requisites for the basic level ICU.
  - Intermediate or long-term cardiorespiratory support.
  - Expert consultation available on call.
  - The intensivist should be in charge of ICU care.
  - Duty doctors and nurses should have intensive care training.
  - Onsite blood bank facility.
  - Comprehensive ICU care facility.
  - Policies and protocols for the ICU are followed.
- Minimum requirement for an advanced level ICU care:
  - All requisites for an intermediate level ICU
  - Fulltime multidisciplinary critical care team, led by an ICU director
  - A nursing director
  - Subspecialty services such as neurosurgery, cardiothoracic surgery, interventional cardiology, and radiology available round-the-clock
  - Preferably a closed model of ICU care delivery
  - Bedside endoscopy, bronchoscopy, and dialysis facilities
  - Extracorporeal support available
  - A step-down unit
  - Academic program for ICU training

Step 2: Identify the Model of ICU Care Delivery

- Pattern of delivery of care in the ICU varies globally. In essence, it can be described as closed, open, or transitional ICU care.
  - *Closed ICU care*: Patient care is transferred to consultant intensivist, who makes all major decisions including transferring out of patients. Once the patient is transferred out of ICU, the primary physician takes over the care.
  - *Open ICU care*: Patient care remains under the primary physician who may not be an intensivist. Intensivist, if available, consults only on request and can suggest treatment which is not binding.
  - *Semiclosed or transitional ICU care*: This is a hybrid model where the consultant intensivist rounds on every patient as a mandatory consultation. Patient management is a shared decision between the primary physician and the intensivist.
- There is an increasing body of literature that the closed ICU system is a better model of delivery of care in the ICU.

Step 3: Construct a Multidisciplinary Team

- The principal ingredients of a multidisciplinary team in an advanced ICU should consist of the following:
  - Consultant intensivists
    - Conduct daily rounds of all ICU patients preferably twice
    - Available on call or in-house for emergencies
    - Supervise residents in writing clinical notes and during procedures
    - Coordinate admissions and discharges
    - Coordinate with the primary physician
    - Communicate with the patient and the family
    - Coordinate end-of-life decisions (see Chap. 26, vol. 2)
    - Maintain policies and protocols (see Chap. 24, vol. 2)
    - Perform quality control and audit (see Chap. 25, vol. 2)
    - Play an active role in teaching and research
  - Resident doctors
    - One qualified resident doctor for five ICU beds
    - Rotate at 8- or 12-h shift
    - Present cases in rounds, write clinical notes, and perform procedures and proper handover (see Chap. 24, vol. 2)
  - Nurses
    - 1:1 Nursing for patients on the ventilator
    - 1:2 or 1:3 Nursing for less sicker patients

- Health assistants
  Assist nurses in patient care activities such as feeding, giving bath, bed making, etc.
- Respiratory/physiotherapists
  Help in early mobilization
- Nutritionists
  Assess calories and protein goal every day and ensure adequacy of nutrition delivery
  Coordinate with the physician and nurses to ensure early enteral nutrition delivery
- Biomedical technicians
  Maintain, calibrate, and troubleshoot different biomedical devices such as monitors and defibrillators
  Ensure safe transport of these equipments
  Ensure proper disinfection of the equipments
- Clinical pharmacists
  Coordinate with nurses and doctors to identify adverse drug reaction, drug dosing, and drug–drug interaction
  Ensures compliance with the hospital antibiotic policy
- Social workers
  Liaise with family members and coordinate between them and ICU staff
- Secretarial staff
  Keep proper medical records, billing, computer entry of drugs, etc.
  Answer phone calls and check the laboratory and radiology report.
- Cleaning and housekeeping personnel
  Clean the ICU (see Chap. 50, vol. 1)
  Help in transporting the patient and blood samples
  Help with catering services

Step 4: Understand Important Elements of an ICU Design

- Location
  - The ICU should be located ideally near the emergency department and operation theater.
- Number of beds
  - General recommendation for number of ICU beds is usually 10 ICU beds per 100 hospital beds.
  - Bed strength in one ICU should be between 8 and 12.
- Layout
  - The ICU could have separate rooms, two or four bed cubicles, or an open ward with curtains or partition between patients.
  - The isolation room should be present for immunosuppressed patients (positive pressure) or infectious patients (negative pressure).

  - Space per bed has been recommended from 125 to 150 square feet.
  - Each bed should have compressed air, oxygen, vacuum source, and adequate electrical sockets for power source.
  - Beds should have removable headboards and adjustable position ideally motorized.
  - Beds should be equipped with the cardiopulmonary resuscitation (CPR) facility knob.
- Adequate lighting, preferably natural light, and minimum noise level should be maintained.
- Bedside hemodialysis facility should be available in some beds.
- There should be ample storage area and clean and dirty utility rooms.
- Proper hand hygiene, waste disposal, and adequate CSSD facilities should be available.
- Disaster preparedness should be maintained.
- Family counseling room and doctors and nurse resting rooms should be provided.
- Adequate toilet facilities for the patient and staff should be provided.

Step 5: Equip the ICU with the Following Services

- Continuous electrocardiogram monitoring (with high/low alarm) in all beds
- Pulse oximetry monitoring capability in all beds
- Continuous arterial pressure monitoring (noninvasive and invasive)
- Continuous central venous pressure monitoring
- Emergency resuscitative equipment including defibrillators
- Airway maintenance equipment including laryngoscopes and endotracheal tubes
- Difficult airway cart
- Adequate number of ventilators depending on case mix
- Equipment to support hemodynamically unstable patients including infusion pumps, blood warmers, pressure bags, and blood filters
- Hypo-/hyperthermia blankets
- Core temperature monitoring devices
- Temporary pacemakers
- Cardiac output monitoring facility
- Pulmonary artery pressure monitoring
- Glucometer
- Continuous or intermittent hemodialysis
- Peritoneal dialysis
- Capnography
- Fiber-optic bronchoscopy
- Intracranial pressure monitoring
- Continuous EEG monitoring
- Portable X-ray facilities

- Computerized access to laboratories, pharmacy, and imaging
- Immediate access to information—paging numbers, hospital directory, duty roster, online search facility, medical textbooks and journal, and poison center contact number

Step 6: Define ICU Policies and Protocols

- An updated policy and protocol of the ICU should be available to all ICU personnel.
- These policies should be formed with consultation of all stakeholders and approved by the ICU director and hospital management.
- A few examples of such policies are as follows:
  - Interhospital and intrahospital transport
  - End-of-life policies
  - Guidelines for determining brain death
  - Restraint and sedation protocols
  - Organ donation policies
  - Infection control policies
  - Antibiotic policies

Step 7: Make an Organogram

- All ICUs should have a structured organogram depicting various activities carried out by the critical care department, personnel involved, and hierarchal structure.

Step 8: Organize Training Curriculum

- Training ICU residents and fellows should be an integral part of services provided by advanced ICUs.
- Nursing, physiotherapy, and technician training should also proceed in parallel.
- There is a wide variation in credentialing for intensive care training globally with variation in basic specialty requirement, duration of training, etc.
- All residents in training should keep a logbook of procedures performed under supervision and get it signed by the supervisor.
- They should acquire factual knowledge of core critical care syllabus during their training period (see Appendix). These can be obtained through hospital library or over internet.
- Simulation training in ICUs has been found to be the most effective way of training where various ICU scenarios can be simulated and various aspects of critical care training requirements apart from factual knowledge may be evaluated.

- Regular bed side training, online courses, didactic lectures, case discussions, journal club should be conducted for doctors and nurses.
- Regular auditing of ICU performance by data entry personnel should be performed

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Transportation of Critically Ill Patients

28

Sandeep Dewan and Priteema Chanana

A 57-year-old male patient was admitted to the emergency department with complaints of abdominal pain and recurrent vomiting. He was found to be in a state of septic shock. After the initial resuscitation, his abdominal examination was remarkable for abdominal distension with absent bowel sounds. The ultrasonography report of the abdomen was inconclusive, and he was shifted to the radiology department for a contrast-enhanced CT scan of the abdomen. He was still on inotropic and vasopressor support.

The ideal way to consider transport of a critically ill patient is as a "mobile ICU environment." Attention to details during transport ensures patient safety.

Intrahospital Transport

Step 1: Evaluate the Need for Transfer

- The most important initial step is to evaluate the potential benefit which may be derived by shifting the patient against the risks involved.
- The aim or purpose and the justification to transport should be noted in the case record.
- The potential risks can be minimized by careful planning of the procedure and utilization of available equipment and personnel.
- Timing of transport should also be carefully decided, preferably during day time for elective transfers.
- A multidisciplinary team of the physician, nurses, paramedical staff, and transport coordinator is required to plan and coordinate the process.

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- Transport of the patient should not be undertaken in the following circumstances:
  - Inability to provide adequate oxygenation and ventilation during transport or at destination, either by the manual resuscitator bag, portable ventilator, or standard intensive care unit ventilator.
  - Inability to maintain acceptable hemodynamic parameters during transport or at destination.
  - Inability to adequately monitor the patient's cardiopulmonary status during transport.
  - Inability to maintain airway control during transport or at destination.
  - All the necessary members of the transport team are not present.
  - Receiving team is not ready.

Step 2: Pretransport Coordination and Communication

- A physician-to-physician and nurse-to-nurse communication is required to plan the transport.
- The team ensures that the receiving location is ready to receive the patient for immediate procedure and testing.
- Documentation in the medical record should be done, which includes the indication of transport and the clinical status of the patient.

Step 3: Accompanying Personnel

- Minimum of two people, preferably one of them from the treating ICU team, should accompany a critically ill patient.
- It is strongly recommended that a physician with training in airway management and advance cardiac life support accompanies the unstable patient.
- The transport personnel should remain with the patient until return to the ICU.

Step 4: Equipment Requirement

- The equipment to be used during transport should be dedicated and should not be used anywhere else.
  - A blood pressure monitor, a pulse oximeter, invasive and noninvasive ventilators, and defibrillators.
  - Basic resuscitation drugs including epinephrine, nor epinephrine, antiarrhythmic drugs, vasopressin, muscle relaxants, sedatives, narcotics, analgesics, dextrose ampoule, and appropriate IV fluids.
  - Drip medications properly labelled must accompany the patient.
  - All battery-operated equipments must be fully charged and should have adequate battery backup provision.

- In mechanically ventilated patients, endotracheal tube position is noted and secured before and during transport and the adequacy of oxygenation and ventilation is reconfirmed.
- No equipment or drugs should be placed over the patient. Most units will have custom-made shelves, which will fit on the beds or trolleys.
- The monitors and/or ventilators should be properly secured with straps to the bed or shelves so that they do not fall on the patient.

Step 5: Identifying High-Risk Patients

Patients in the following categories are at particularly high risk for deterioration during or after transport:

- The mechanically ventilated patients, particularly those with requirement of high positive end-expiratory pressure and FiO_2 more than 0.5. Extra oxygen reserve for patients with high oxygen requirement should be kept.
- Patients with high therapeutic injury severity score
- Head-injured patients
- Hemodynamically unstable patients requiring continuous infusion of dobutamine, or a continuous infusion of norepinephrine or other potent vasoactive agents
- Specifically trained personnel are required for the transport of neonates, infants, patients requiring extracorporeal life support or an intra-aortic balloon pump and bariatric patient

Step 6: Monitoring During Transport Includes the Followings

- ECG monitoring
- Pulse oximetry
- Periodic measurement of the blood pressure, pulse rate, and respiratory rate
- Selective patients may benefit from capnography, continuous intra-arterial blood pressure monitoring, and intracranial pressure monitoring if required.

Step 7: Care During Transport

- Ideally, the patient should receive the same level of care as in the pretransport area.
- Vital signs should be monitored and recorded at fixed intervals.
- Use of memory-capable monitors should be used. This will allow documentation of data during transport.
- Any adverse events should be noted and immediately acted upon.
- There should be a designated senior physician available for consult in case of an adverse or critical event during transport.

- Ideally, he/she should be available on-site and should be able to arrive at the destination area if required.
- The transport team should be able to communicate with the designated person during transit as well as upon arrival at the destination in case of an emergency.

Interhospital Transport

When a critical care patient requires resources, which are not available in the existing hospital, the patient will be transferred to a facility that has the required resources. Interhospital patient transfer will occur only when the benefits exceed the efforts. If needed, the resuscitation and stabilization of the patient should be carried out before the transport.

Basic requirements are the same for intra- or interhospital transport. Interhospital transport requires more planning, more personnel, vehicle availability, consideration of altitude effects in air transport, weather condition, battery life of equipments, backup equipment, oxygen supply, power supply, contingency plan in case of breakdown, and more documentation for medicolegal purposes.

Step 1: Take Informed Consent

- An informed consent for interhospital transport must be taken from a competent patient, guardian, or legally authorized representative, if the patient is incompetent.
- It includes a discussion of the risks and benefits of transfer.
- It should be documented in the medical records before the transfer is done.
- In case of life-threatening emergencies when an informed consent cannot be taken, the indication of transfer and the reason for not obtaining consent must be documented in the medical record.

Step 2: Communicate and Coordinate Prior to Transport

- The referring physician will contact the receiving physician and will explain the clinical condition to him/her.
- The mode of transportation (ground/air) will be determined by the transferring physician based on the medical condition, the time savings, facilities available, and the medical interventions required.
- The transport service will then be contacted to confirm its availability and coordinate the timing. A copy of the medical record including case summary and all relevant laboratory and radiographic data will accompany the patient.

Step 3: Decide on Accompanying Personnel

- It is recommended that minimum of two people should accompany a critically ill patient.
- The transport team leader should be a treating physician/intensivist/anesthesiologist with additional training in transport medicine.
- It is strongly recommended that a physician with training in airway management and advance cardiac life support accompanies the unstable patient.
- The transport personnel will remain with the patient until reaching the ICU.
- There must be a clear chain of responsibility throughout the transfer. A proper handover from referring physician to transfer physician and then to receiving facility physician is essential.

Step 4: Choose Transport Equipment and Medicines

- When choosing the equipment, the following should be considered: size, weight, battery life, ability to fit to trolley railings, ability to function under condition of vibration, ease of use in poor light, and placement in restricted space.
- Equipments should be adequately restrained and should be easily accessible to the operator.
- Backup equipment may be desirable in some situation.
- The recommended minimum transport equipments and medications are given in Tables 28.1 and 28.2.

The following specialized/controlled medications are added immediately before transport as indicated:

- Narcotic analgesics (e.g., morphine and fentanyl)
- Sedatives/hypnotics (e.g., lorazepam, midazolam, propofol, and ketamine)
- Neuromuscular blocking agents (e.g., succinylcholine, pancuronium, atracurium, and rocuronium)

Additional drugs, should be added depending on specific circumstances (antiarrhythmic or antibiotics that need to be dosed during transport).

Step 5: Monitoring During Transport

This includes followings:

- ECG monitoring
- Pulse oximetry
- Periodic measurement of blood pressure, pulse rate, and respiratory rate
- Selective patients may benefits from capnography, continuous intra-arterial blood pressure monitoring, and intracranial pressure monitoring.

Table 28.1 Recommended minimum transport equipments

Adult/pediatric bags—valve systems and oxygen reservoir
Adult and pediatric masks
Flexible adaptors to connect the bag valve system to the endotracheal/tracheostomy tube
End-tidal carbon dioxide monitors (pediatric and adult)
Infant medium- and high-concentration masks with tubing
Laryngoscope with blades with extra batteries
Endotracheal tubes with stylets
Magill forceps
Nasopharyngeal airways
Oral airways
Scalpel with the blade for cricothyroidotomy kit
Needle cricothyroidotomy kit
Water-soluble lubricant
Nasal cannulae
Oxygen tubings
Adhesive tape
Aerosol medication delivery system
Alcohol swabs
Arm boards
Arterial line tubings
Intraoseous needle
Blood pressure cuffs
Butterfly needles
Communications backups
ECG monitor/defibrillator with electrolyte pads and jelly
Flashlights with extra batteries
Heimlich valve
Infusion pumps
IV fluid administration tubing
Y fluid administration tubing
Extension tubing
Three-way stopcocks
IV catheter (14–24G)
Intravenous solutions (1000 mL, 500 mL of normal saline)
Irrigating syringe (60 mL), catheter tip
Kelley clamp
Hypodermic needles and syringes, assorted sizes
Normal saline for irrigation
Pressure bags for fluid administration
Pulse oximeter with multiple site adhesive or reusable sensors
Soft restraints for upper and lower extremities
Stethoscope
Suction apparatus and catheters
Surgical dressings and tourniquets
Trauma scissors

The followings are considered as needed: Neonatal/pediatric isolette, spinal immobilization device, and transport ventilator

Table 28.2 Recommended minimum transport medication

Adenosine (6 mg/2 mL)
Amiodarone (150 mg/3 mL)
Atropine (0.6 mg/mL)
Calcium chloride (1 g/10 mL)
Dextrose (25%/50%)
Digoxin (0.5 mg/2 mL)
Diltiazem (25 mg/5 mL)
Diphenhydramine (50 mg/1 mL)
Dopamine (200 mg/5 mL)
Epinephrine (1 mg/10 mL)
Furosemide (100 mg/10 mL)
Glucagon (1 mg vial)
Heparin (1000 units)
Isoproterenol (1 mg/5 mL)
Labetalol (40 mg/8 mL)
Lidocaine (100 mg/10 mL)
Mannitol (50 g/50 mL)
Magnesium sulfate (1 g/2 mL)
Metroprolol (5 mg/5 mL)
Naloxone (2 mg/2 mL)
Nitroglycerine injection (50 mg/10 mL)
Nitroglycerine tablets (0.4 mg)
Nitroprusside (50 mg/2 mL)
Normal saline (30 mL) for injection
Nor epinephrine (2 mL)
Phenobarbital (65 mg/mL or 130 mg/mL)
Potassium chloride (20 mEq/10 mL)
Procainamide (1000 mg/10 mL)
Sodium bicarbonate (50 mEq/50 mL)
Sterile water (30 mL) for injection
Terbutaline (1 mg/1 mL)
Verapamil (5 mg/2 mL)

Step 6: Preparing Intravenous Access and Airway Before Transport

- If peripheral venous access is unavailable, central venous access is established. If needed, fluid resuscitation and inotropic support are initiated, with all intravenous fluids and medications maintained in plastic (not glass) containers.
- A patient should not be transported before airway stabilization if it is judged likely that airway intervention will be needed en route (a process made more difficult in a moving vehicle).
- The airway must be evaluated before transport and secured. Finally, the patient's medical record—laboratory and radiological data—is copied for the receiving unit.

- Use appropriate physical restraint.
- Particular attention has to be focused on the personnel, equipment, and monitoring in use to prevent adverse events during transportation of critically ill patients.
- Detailed planning of the process goes a long way in preventing the adverse events related to patient, equipment, and transport personnel.

Step 7: Safety During Transport

- Patients should be secured to the transport trolley by means of appropriate restraint (e.g. 5 point harness/straps).
- Pressure areas (including neurovascular bundles) should be appropriately protected.
- Warming/insulating blankets should be used to keep the patient warm unless otherwise contraindicated.
- Indwelling lines and tubes should be secure and visible/accessible.
- All equipment (including transfer bags) must be securely stowed. Equipment should be either fastened to the transport trolley or securely stored in appropriate lockers in the ambulance. When this is not possible, equipment should be placed on the floor against the bulkhead wall. Under no circumstances should equipment (e.g. syringe pump) be left on top of the patient trolley. This may become a dangerous projectile in the event of a sudden deceleration. Gas cylinders must be held in secure housings.
- Staff should remain seated at all times and wear the seat belts provided. Adequately resuscitated and stabilised patients should not normally require any significant changes to treatment during transport. If, however, despite meticulous preparation, unforeseen clinical emergencies arise and the patient requires intervention, this should not be attempted in a moving ambulance. The vehicle should be stopped appropriately in a safe place before administering treatment.
- High speed journeys should be avoided except where strictly necessary. Blue lights and sirens may be used to aid passage through traffic to deliver a smooth journey.

Step 8: Aeromedical Considerations

- Whether using helicopters or fixed wing aircraft, the transport of patients by air presents medical escorts with many problems unique to this mode of travel.
- Staff involved in aeromedical transport must have both a high level of expertise, specialist knowledge and practical training.
- Issues which may be relevant for those preparing a patient for air transfer.
  - A fall in barometric pressure results in a reduction in alveolar partial pressure of oxygen and may lead to hypoxemia. Increased inspired oxygen concentration is mandatory for all aeromedical transfers.
  - A fall in barometric pressure also leads to an increase in the volume of gas filled cavities within the patient. Endotracheal tube cuff pressure should be

monitored or the cuff filled with saline. Pneumothoraces must be drained. Nasogastric tubes should be inserted and placed on free drainage. Pneumoperitoneum and intracranial air are relative contraindications to air transport. Tissues may also swell, and plaster casts should be "split".
  - Increased altitude is also associated with a fall in temperature and additional measures may be required to keep the patient warm.
  - Noise and vibration may cause nausea, pain and motor dysfunction. Anti-emetic pre-medication should be available for patients and ear protection provided.
- Staff without appropriate training should not undertake aero-medical transfers. Minimum requirements include safety training, evacuation procedures for the aircraft, and basic on board communication skills (particularly for helicopters). More advanced training in aeromedical transfer is however desirable.

Step 9: Documentation and Handover

- Clear records should be maintained of all stages. These should include details of the patient's condition, reason for transfer, names of referring and accepting consultants, clinical status prior to transfer and details of vital signs, clinical events and therapy given before and during and after transport
- On arrival at the receiving hospital, there should be a formal handover between the transport team and the receiving medical and nursing staff who will then assume responsibility for the patients care.
- Handover should include a verbal and written account of the patient's history, vital signs, therapy and significant clinical events during transport. X-rays, scans and other investigation results should be described and handed over to receiving staff.
- Standardised documentation should be developed across networks and should be used for both inter-hospital and intra-hospital transport. This should include a core data set for audit purposes and the transport team should be able to retain a duplicate for such purposes

Suggested Reading

Warren J, Fromm RE Jr, Orr RA, Rotello LC, Horst HM. American College of Critical Care Medicine. Guidelines for the inter and intra hospital transport of critically ill patients. Crit Care Med. 2004;32:256–62. *These guidelines promote measures to ensure safe patient transport during both intra- and interhospital transport and give minimum standard regulations to ensure patient safety during transport by establishing an organized, efficient process supported by appropriate equipment and personnel.*

Waydhas C. Intrahospital transfer of critically ill patients. Crit Care. 1999;3:R86–9. *This review addresses the type and incidence of adverse effects, risk factors and risk assessment, and the available information on efficiency and cost-effectiveness of transferring such patients for diagnostic or therapeutic interventions within hospital.*

Whiteley S, Macartney I, Mark J, Barratt H, Binks R. Intensive care society. Guidelines for the transport of the critically ill adult. 3rd ed. 2011. www.ics.ac.uk. *A comprehensive guidelines for transport of critically ill patients.*

Ultrasound in ICU

29

Swarup Shankar Padhi, Shrikanth Srinivasan, and Deepak Govil

A 50 year old male, known case of COPD presented to the Emergency with complaints of shortness of breath and cold clammy extremities. On examination he was found to be tachypnec, tachycardiac and hypotensive. A decrease in urine output was also noted. How would ultrasound help in evaluation and management of this patient?

Ultrasonography is now considered the stethoscope of the intensivist to diagnose common problems in the intensive care unit. Routinely using the ultrasound in the ICU can rule out various disorders of the lungs, heart, abdomen, vasculature and help in managing fluid balances which is an integral component in the ICU. Repeatability, reproducibility, portability, good quality imaging and lack of hazards from radiation make the ultrasound a handy tool to dynamically evaluate in real time the various pathological conditions.

Step1: Understand Thoracic Ultrasound

Air produces artefacts and taking that as an advantage various abnormalities can be diagnosed with good sensitivity and specificity.

Pleural line

- With the transducer held in a longitudinal orientation to the skin surface and centred over an intercostal space, a horizontally orientated hyperechoic

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R. Chawla, S. Todi (eds.), *ICU Protocols*, https://doi.org/10.1007/978-981-15-0902-5_29

artefactual line approximately 0.5 cm deep to the origin of the rib shadows is seen which represents the interface of the visceral and parietal pleural surfaces and is called the pleural line.

Lung Sliding

- During respiration, the two pleural surfaces slide against each other, and this appears as a shimmering white line artefact which moves in synchrony with the respiratory cycle called lung sliding or pleural sliding and is identified on B-mode.
- On M-mode ultrasound, lung sliding appears as what is known as the seashore sign, which is characterized by a horizontal linear pattern corresponding to the chest wall, the pleural line appearing like bright granularity and a homogeneous granular pattern, an artifact generated by respiratory cycles and air movement below the pleural line (Fig. 29.1).
- Lung sliding is found in normal lungs, and is reduced or absent in various pathologies that affect lung mobility.
- Lung sliding becomes restricted in acute respiratory distress syndrome, chronic adherences, fibrosis, phrenic palsy, high frequency jet ventilation while it is absent in pneumothorax, complete atelectasis, pleural fibrosis and apnoea.

A lines

- The normal lung parenchyma cannot be seen beyond the pleural line, as presence of air prevents penetration of ultrasound wave. When ultrasound beams encounter the air tissue interface there is production of artifacts known as A-lines which are horizontally orientated lines seen deep to the pleural line (Fig. 29.2). They represent reverberation artifacts from ultrasound reflection between the pleural surface and the chest wall.
- A lines with lung sliding is consistent with normal aeration pattern. A lines with no lung sliding could denote a pneumothorax.

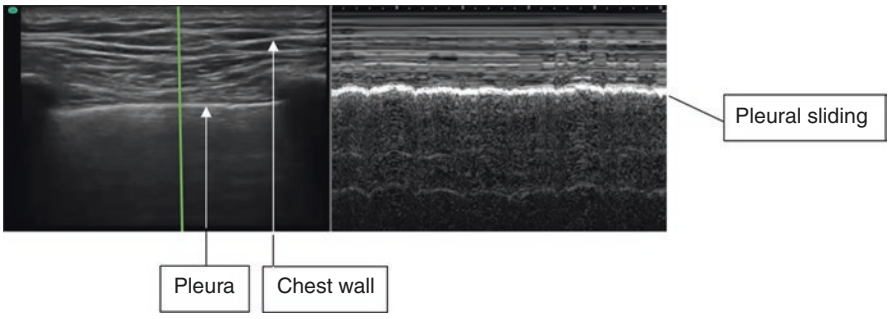

Fig. 29.1 Lung sliding and Seashore sign

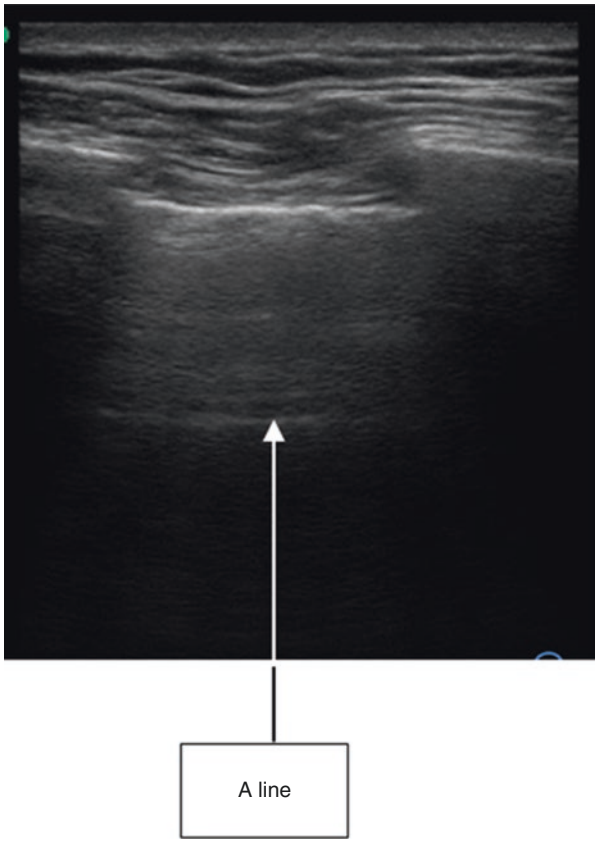

Fig. 29.2 A lines

B-lines

- B lines are artifacts that appear as vertically orientated laser like lines extending from the pleural interface to the bottom of the screen without fading and effacing A lines where the two intersect and they generally move synchronously with lung sliding (Fig. 29.3).
- B-line strongly correlates with interstitial edema and are formed when air and water are simultaneously hit by ultrasound beams (Fig. 29.3).
- Three or more B lines in two adjacent intercostal spaces may be considered as significant finding.
- Diffuse B-lines in lung parenchyma with a distance <3 mm are also called lung rockets corresponds with a ground-glass pattern in chest computed tomography scan.
- Since B lines arise from the pleural line, their presence rules out a pneumothorax in that field.

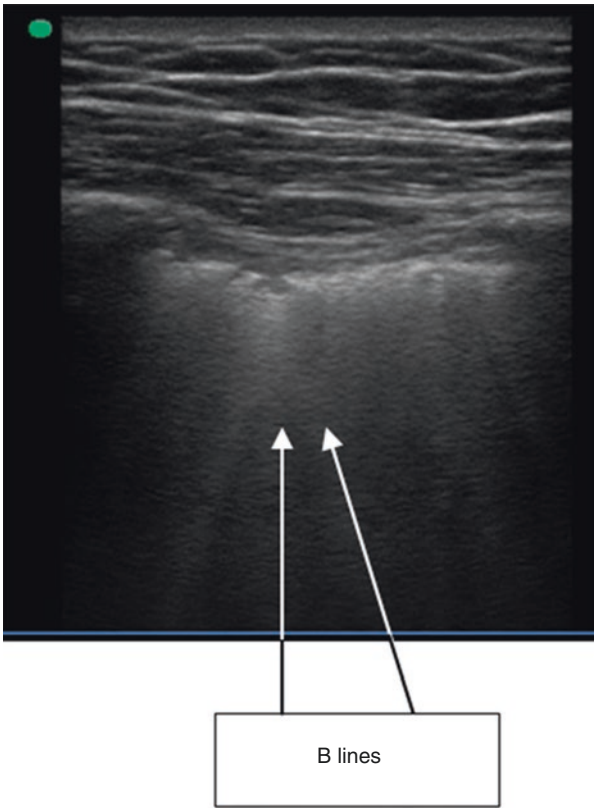

Fig. 29.3 B lines

E lines

- E lines are formed due to subcutaneous emphysema. As the air bubbles infiltrate into the subcutaneous tissues, the tissue air interface moves up from the pleural line to the subcutaneous fat and muscle planes. This leads to formation of vertical artifacts similar to B lines but emerging at different levels from the subcutaneous tissues and muscle planes (Fig. 29.4).

Pleural effusion (Fig. 29.5)

- Using the Curvilinear probe (2–5 MHz), For a proper evaluation of pleural effusion, it is necessary to identify three findings:
  1. Anatomical boundaries chest wall, lung, diaphragm, and adjacent solid organs (liver/ spleen) confirming the intrathoracic location of the collection, especially if a thoracentesis has been planned
  2. Anechoic space—the pleural effusion itself
  3. Dynamic changes: intermittent lung aeration, compressed lung, or both (atelectasis);

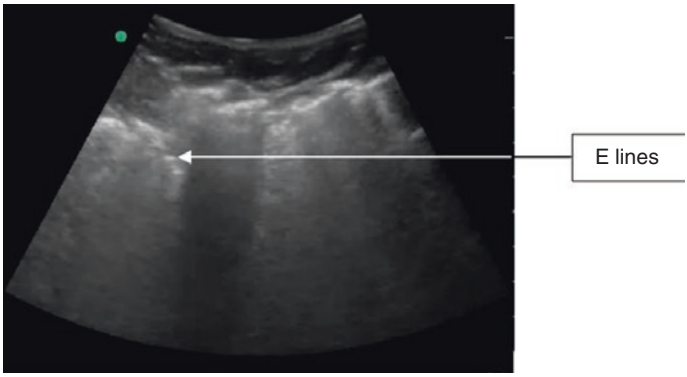

Fig. 29.4 Subcutaneous emphysema

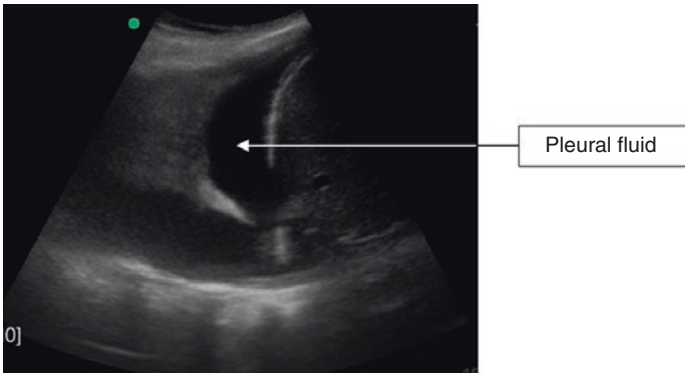

Fig. 29.5 Pleural effusion

- Two signs are associated with pleural effusion:
  1. quad sign: A quadrilateral formed by the chest wall (parietal pleura) above and the pleural line (visceral pleura) below along with the shadow of two adjacent ribs, the intervening space is hypoechoeic which indicates pleural effusion.
  2. sinusoid sign: It's a dynamic sign on M mode wherein the sinusoidal movement of the freely floating lung with each inspiration denotes presence of an effusion.
- A 15-mm distance is considered minimum required for safe diagnostic or therapeutic puncture for pleural effusion.

Atelectasis

- The pleural line may move in synchrony with cardiac pulsation in addition to lung sliding that occurs synchronous with the respiratory cycle. This movement, termed lung pulse, is caused by the force of the cardiac pulsation being transmitted to the lung and the visceral pleura. The **lung-pulse** is useful for immediate diagnosis of an atelectasis which is seen as a marked reduction in sliding with pulsation transmitted from the heart.
- Presence of lung pulse also rules out a pneumothorax in that field because it is produced when the two layer of pleura are opposed to each other allowing the transmitted cardiac pulsations to be visualized.
- Absence of dynamic air bronchograms (see below)
- Loss of lung volume and raised hemi diaphragm on the affected side

Consolidation

- Consolidations can either be nontranslobar or translobar.
- **Shred sign** (Fig. 29.6) indicates non translobar consolidations and the border between consolidated and aerated lung is seen as an irregular line known as the fractal line.
- **Tissue-like sign** is used for translobar consolidations which mean it looks like liver.
- The dynamic air bronchogram: seen in the form of air artifacts appearing and disappearing with every inspiration and expiration respectively within a deaerated or tissue like hepatized lung. This denotes the patency of the bronchi and bronchioles while the alveoli are flooded and deaerated. The presence of this sign distinguishes consolidation from atelectasis.

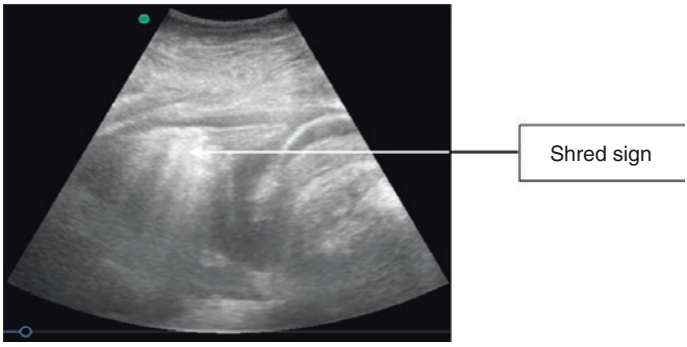

Fig. 29.6 Shred sign

Interstitial syndrome

- B-line is a comet-tail artefact arising from the pleural line, and moves synchronously along with lung-sliding.
- Presence of B lines 7 mm apart suggests interstitial edema
- As the number of B lines increase and become confluent (3 mm) apart, it represents alveolar edema

Pneumothorax (Fig. 29.7)

- Absent lung-sliding that is the visceral pleura doesn't move against the parietal pleura with respiration using real-time ultrasound assessment.
- **Lung point** is pathognomonic which is the junction between the sliding and the non sliding lung. M-mode shows the **stratosphere sign** which are laminar and horizontal artefacts seen below and above the pleural line.

Airway

- Passage of endotracheal tube in the trachea can be visualized real time during intubation by placing the linear probe on the trachea during intubation. Bilateral ventilation is confirmed by visualizing bilateral lung sliding

BLUE-protocol (Fig. 29.8) (Bedside lung ultrasound in emergency) evaluates three standardized points which is formed when two hands are placed on the chest side by side, the upper BLUE-point(middle of the upper hand), lower BLUE-point (middle of the lower palm) and PLAPS-(Postero Lateral Alveolar and/or Pleural Syndrome)point(defined by the inter-section of a horizontal line at the level of the lower BLUE-point; a vertical line at the posterior axillary line) (Tables 29.1 and 29.2).

The profile combining A-profile, free veins, and PLAPS is called A-V-PLAPS-profile.

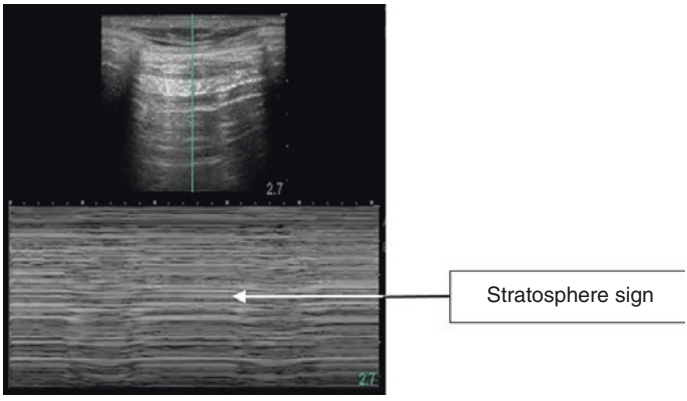

Fig. 29.7 Pneumothorax on M mode: Stratosphere sign

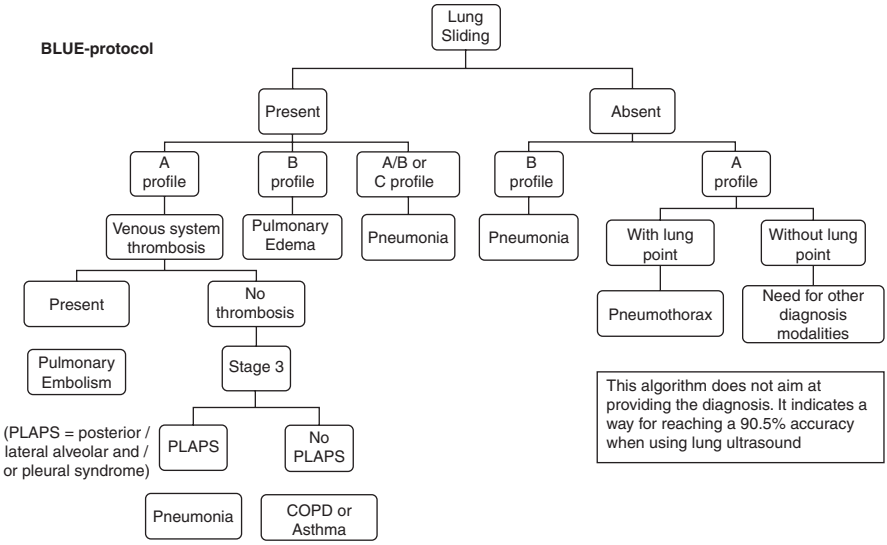

Fig. 29.8 Blue protocol

Table 29.1 Various profiles and their correlation with the pathology

Profile	Definition	Pathological process
A profile	Anterior lung-sliding with A-lines	Normal or if lung sliding absent-pneumothorax If DVT positive—Pulmonary embolism If DVT negative with PLAPS—Pneumonia If DVT and PLAPS negative—Nude profile s/o severe asthma or COPD
B profile	Lung-sliding with lung-rockets	Acute cardiovascular pulmonary edema
B′ profile	B-profile with abolished lung-sliding	Pneumonia
C profile	A thickened, irregular pleural line	Pneumonia
A/B profile	Half A-profile at one lung, a half B-profile at another	Pneumonia
PLAPS-profile	Postero Lateral Alveolar and/or Pleural Syndrome	Pleural effusion, Consolidation, Pneumonia

Table 29.2 Various signs and their correlation

Seashore sign	Normal lung
Quad sign or sinusoidal sign	Pleural effusion
Shred sign or tissue like sign	Consolidation
Lung rockets	Interstitial syndrome
Stratosphere sign	Pneumothorax
Lung point	Pneumothorax

Step 2: Hemodynamic Assessment of Circulatory Failure Using Lung Ultrasound: FALLS-Protocol (Fig. 29.9)

- FALLS-protocol follows Weil and Schubin's classification of shock where it first considers obstructive shock followed by cardiogenic, hypovolemic and then distributive shock

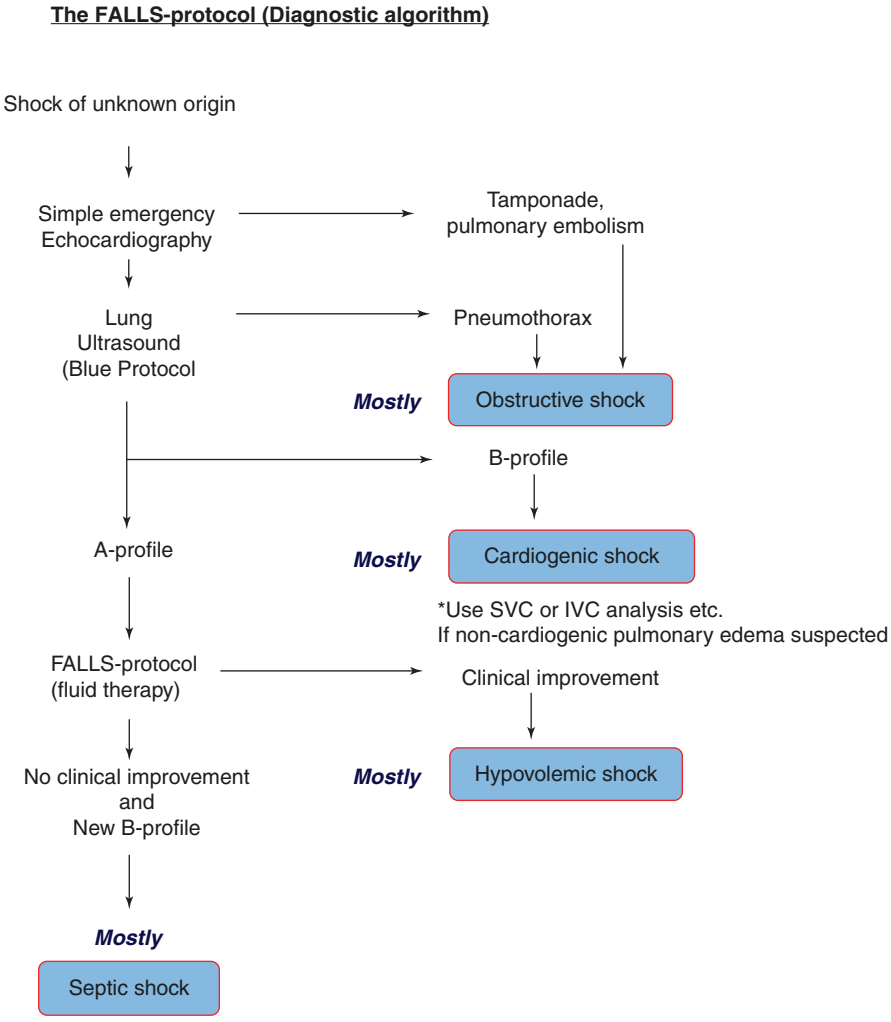

Fig. 29.9 The FALLS-Protocol

Table 29.3 Essential views using ultrasound

Window	Footprint position	Structures assesses
Parasternal long axis (PLAX) view	3rd/4th ICS near the sternum with beam towards the right shoulder	Aortic and mitral valvular abnormalities
Parasternal short axis view	Rotating the transducer to 90 degrees clockwise from the PLAX view and tilting it	EF by eyeballing method mitral valve, papillary muscles and apex
Apical 4 chamber view	At the apex of the heart	4 chambers of the heart along with size and the mitral and tricuspid valves, right ventricular free wall, left lateral wall, interventricular septum
Apical 5 chamber view	Tilting of the transducer from the 4 chamber view	LVOT and the aortic valve
Subcostal view	Below the xiphoid process	4 chambers along with valvular functions. Septal defects, pericardial effusion
Suprasternal view	Suprasternal notch	Aortic flows, arch of aorta with branches, ascending and descending aorta and pulmonary artery

Step 3: Cardiac Ultrasound

Goal directed echocardiography is performed by the intensivist to know hemodynamic instability in a patient and it differs from the detailed examination of the heart as done by the cardiologist (Table 29.3).

To Evaluate Hemodynamic Instability in a Patient

Hypotension in ICU patients can be due to hypovolemia, valvular disorders or ventricular dysfunction or pericardial tamponade. Using point of care Echo, several indices can be used to predict fluid responsiveness like Inferior Vena Cava Imaging and Variation, Ventricular Size, Aortic Flow Variations and Passive Leg Raising Test.

Inferior Vena Cava Size and Variability

- Respiratory variations in IVC size can predict fluid responsiveness, both in mechanically ventilated and in spontaneously breathing patients.
- During spontaneous ventilation, the IVC collapses in inspiration, whereas during mechanical ventilation the IVC dilates during inspiration.
- IVC distensibility index is measured for fluid responsiveness in mechanically ventilated patient and IVC collapsibility index in spontaneously breathing patient.
- A dispensability index of more than 18% in mechanically ventilated and collapsibility of >50% in spontaneous ventilation is indicative of fluid responsiveness. IVC diameter and its respiratory variations is assessed in the subxipoid ECHO view. It can be measured either close to its entrance to the right atrium

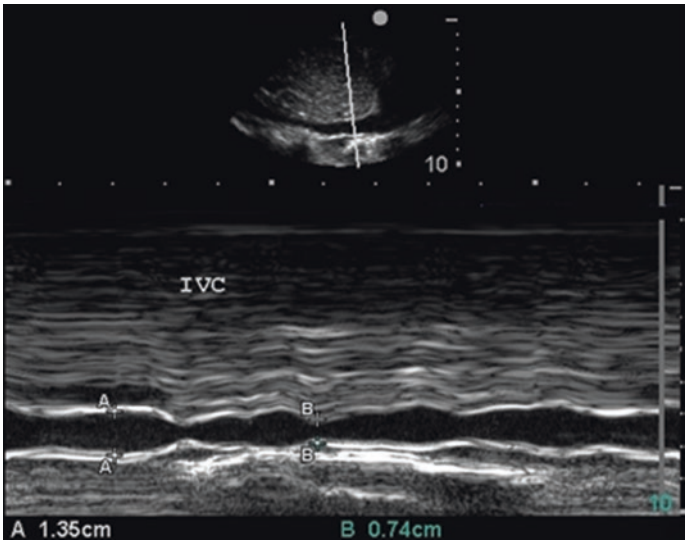

Fig. 29.10 IVC variation with respiration in 2D mode and M mode

(less susceptible to motion artefact but can be influenced by diaphragmatic contraction) or 1–2 cm caudal to the hepatic vein–IVC junction (approximately 3–4 cm from the junction of the IVC and the right atrium) (Fig. 29.10)

- IVC can 'inappropriately' collapse in a fluid resistant patient when the patient is inspiring excessively or the intra-abdominal pressure is abnormally high as in ascites and intra-abdominal hypertension.

Right Ventricular Dysfunction

RV dysfunction accompanies a dilated IVC in almost all cases. Right ventricular dilation can be assessed by ultrasound if its size is similar or larger than Left ventricle. PSAX view will demonstrate flattened interventricular septum or better known as **D-sign** in case of RV overload states.

Left Ventricular Dysfunction

To assess the LV size whether it is dilated or hypertrophied along with the ejection fraction or Regional wall motion abnormalities. Parasternal short axis view in particular is best for detecting RWMA although it is best accomplished by a trained intensivist.

Pericardial Tamponade (Fig. 29.11)

Right atrial collapse during ventricular systole and RV diastolic collapse along with the presence of pericardial fluid in hemodynamically unstable patient indicates cardiac tamponade and this is best visualised either in the apical 4 chamber view or subcostal view.

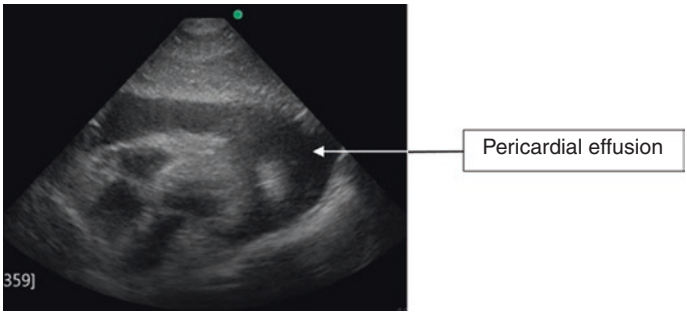

Fig. 29.11 Pericardial tamponade

Step 4: Procedures

- Venous cannulation: IJV or subclavian vein cannulation can be done by out of plane or in plane technique. In plane technique is one where the entire course of the needle penetrating the soft tissue till the vein is seen while cannulation which minimises the risk for arterial puncture and pneumothorax. Out of plane technique is where the needle is directed towards the plane of ultrasound beam and only the tip of the needle is visualized.
- Ultrasound guidance arterial cannulation minimises the number of attempts as well as shortens the procedure time.
- Thoracentesis and abdominocentesis
- Percutaneous tracheostomy to exclude the presence of vascular structures and visualising the course of needle and guidewire insertion.

Step 5: Evaluation of DVT

- Using the three-point compression test that evaluates common femoral vein, Proximal deep femoral vein and popliteal vein can give an idea about the presence of DVT. lack of compressibility of the veins during scanning suggests DVT.

Step 6: FAST Protocol-Focussed Assessment of Sonography in Trauma

- Assesses four areas, the hepatorenal pouch or Morissons pouch, Splenorenal recess, pelvic and pericardial space for any collection of fluid. Assessing the lungs for pneumothorax or hemothorax along with the FAST scan is termed e FAST (Table 29.4).

Table 29.4 FAST protocol

Quadrant	Transducer position	Structures identified
RUQ	• Right subcostal, anterior axillary line • Mid axillary line approx. In seventh ICS	Liver Diaphragm Kidney Hepatorenal recess
LUQ	• Left subcostal, anterior axillary line • Mid-posterior axillary line in seventh ICS	Spleen Kidney Lung Diaphragm Splenorenal recess
Subcostal	• Below the xiphoid process	IVC, pericardial collection
Pelvic	• Above pubis with inferior angulation	Bladder, uterus, prostate, Cul de sac, retrovesical space

Step 7: Ultrasound in Cardiac Arrest

- This is for patients receiving CPR to rule out potential reversible causes of cardiac arrest like pneumothorax, cardiac tamponade, pulmonary embolism along with assessing the contractility of the heart.
- The SESAME-protocol abbreviated from SESAMOOSIC which stands for sequential emergency scanning assessing mechanism or origin of shock of indistinct cause, a fast protocol devoted to cardiac arrest, assesses the lung before the heart.

Step 8: Measuring Optic Nerve Sheath Diameter (ONSD) as a Surrogate for Increased ICP

- **ONSD** is normally less than 5.5–5.7 mm in diameter. Using the linear transducer over the eyelid measure the optic nerve sheath diameter at a distance 3 mm posterior to the globe. It has a good negative predictive value i.e. if less than 5.7 mm then the ICP is unlikely to be more than more than 20 mmHg. Increased ICP could be due to various reasons like traumatic brain injury, intracranial bleeding, hydrocephalus or hypertensive emergency.

Conclusion

US has the potential to become a reference tool for bedside diagnosis, dynamic monitoring and guide therapy in the ICU. It is non-invasive, easily repeatable and provides rapid and accurate evaluation of the patient's physiological state. It minimizes radiation exposure to medical personnel Standardized training and a systematic use should be advocated to fully utilize its potential.

Suggested Reading

Lichtenstein D. Lung ultrasound in the critically ill. Curr Opin Crit Care. 2014;20(3):315–22. *A concise review on the subject*.

Lichtenstein DA. BLUE-protocol and FALLS-protocol: two applications of lung ultrasound in the critically ill. Chest. 2015;147(6):1659–70. *This review article describes two protocols adapted from lung ultrasound: the bedside lung ultrasound in emergency (BLUE)-protocol for the immediate diagnosis of acute respiratory failure and the fluid administration limited by lung sonography (FALLS)-protocol for the management of acute circulatory failure*.

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Zanobetti M, Scorpiniti M. Point-of-care ultrasonography for evaluation of acute dyspnea in the ED. Chest. 2017;151(6):1295–301. *PoCUS represents a feasible and reliable diagnostic approach to the patient with dyspnea, allowing a reduction in time to diagnosis. This protocol could help to stratify patients who should undergo a more detailed evaluation*.

Zieleskiewicz L, Muller L, Lakhal K. Point-of-care ultrasound in intensive care units: assessment of 1073 procedures in a multicentric, prospective, observational study. Intensive Care Med. 2015;41(9):1638–47. *Among 1954 patients hospitalized during the study period, 1073 (55%) POCUS/day were performed in 709 (36%) patients. POCUS served for diagnostic assessment in 932 (87%) cases and procedural guidance in 141 (13%) cases. POCUS utilization for procedural guidance remains insufficient. In contrast, POCUS for diagnostic assessment is of extensive use. Its impact on both diagnosis and treatment of ICU patients seems critical. This study identified factors associated with an improved clinical value of POCUS.*

VV ECMO

30

Deepak Govil and G. Praveen Kumar

32-Year-old female, presented with 3 days history of shortness of breath. On evaluation patient was found to be hypoxic (oxygen saturation of 46%), with severe respiratory distress. Patient was intubated and initiated on lung protective ventilation. X-ray and USG examination revealed bilateral pneumonia. In view of persistent hypoxemia, P/F ratio of 55 mmHg, patient was initiated on prone ventilation. After 6 h of prone ventilation, patient is on 100 FiO_2, respiratory rate of 32/min, tidal volume of 6 mL/kg and Arterial blood gas (ABG) revealed pH 7.19, pCO_2 75 mmHg, pO_2 56 mmHg, SaO_2 78%.

Extra Corporeal Membrane Oxygenation (ECMO) is the only treatment modality currently available that can completely replace the cardiorespiratory function and remains the rescue therapy of choice for refractory hypoxemia in patients with severe acute respiratory distress syndrome (ARDS). The use of ECMO for worsening oxygenation has been on the rise since H1N1 influenza pandemic in 2009. Veno-venous ECMO (VV ECMO) is preferred unless patient is in septic shock or has associated myocardial dysfunction leading to cardiogenic shock. In these circumstances veno-arterial ECMO (VA ECMO) can be considered.

Step 1: Planning for Ecmo

- Initiate discussion with family members of the patient for probable need of ECMO immediately after prone ventilation and ECMO team should be communicated regarding potential ECMO patient
- Percutaneous ECMO cannulation trolley should be checked for the following items:
  - Echo/USG machine
  - Appropriate size drainage and return cannulas (preferably reinforced)

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- J tipped Guide wires (0.035–0.038 in, 150–180 cm long)
- Dilators of various sizes (8F to 26F)
- 11 size surgical blades
- Sterile surgical whole body drapes
- Isotonic crystalloid solution
- Heparin
- Sutures (non-absorbable)
- Large transparent dressings
- 3 way stopcocks
- Pressure monitoring kits

• Continue with lung protective ventilation throughout before initiating ECMO, with target plateau pressure of less than 30 and driving pressure of less than 15.

Step 2: Indication of ECMO

• Patients with severe but potentially reversible acute respiratory or cardiac failure that is unresponsive to conventional mangement are suitable candidates for ECMO.
• Patients who are in a medical centre not equipped with ECMO, transfer to ECMO equipped medical centre should be considered, ideally after the referral retreival team has assessed the patients and if necessary transfer on ECMO.

1. Criteria for initiation of ECMO in ARDS

- After 6 h of prone ventilation and maximum ventilator optimization, if the patient's blood gas reveals following parameters
- P/F < 80 mmHg with $FiO_2 > 0.8$
- pH <7.25 with $pCO_2 > 60$ mmHg

• ECMO can also be initiated after 3 h of prone ventilation if P/F ratio remains less than 50 mmHg with FiO2 > 0.8

2. CO_2 retention on mechanical ventilation despite high Pplat (>30 cmH_2O).
3. Severe air leak syndromes.
4. Need for intubation in a patient on lung transplant list.
5. Immediate cardiac or respiratory collapse (PE, blocked airway, unresponsive to optimal care).
6. Failure to wean from cardiopulmonary bypass after cardiac surgery.
7. As a bridge to cardiac transplant or placement of ventricular assist device.

• **Contraindications for ECMO**
  - No absolute contraindication for respiratory ECMO

Relative contraindications include

- Mechanical ventilation >7 days prior to ECMO
- Contraindication for anticoagulation (high bleeding risks, expanding intracranial haemorrhage)

- Comorbid conditions like terminal malignancy, severe brain injury and patients who are immunosuppressed
- Morbidly obese (BMI >45 kg/m^2) patients have been excluded in certain studies

- **Timing of initiation**
  - VV ECMO should never be initiated as an emergency
  - In patients with severe hemodynamic compromise, VA ECMO or VAV ECMO should be considered instead

Step 3: Selection of Cannula

- Assess the vessels (femoral and jugular) for diameter and flows: size of drainage cannula should not be more than 2/3rd of total diameter of femoral vein
- Measure patient's cardiac output by echocardiography: cannula size should accommodate highest ECMO flows possible (at least 60% of native cardiac output) with least revolutions per minute on the ECMO machine
- Essentially, ECMO cannulas should be short and fat
- In an adult 70 kg person
  - Drainage cannula: 23–29 Fr
  - Reinfusion cannula: 21 Fr
- Multi stage drainage cannula is preferred
- Kink free reinforced cannulas with heparin/bioline coating should be used

Step 4: Percutaneous ECMO Cannulation

- Can be done by critical care physicians, cardiologists, emergency physicians and cardiac surgeons
- Cardiac surgical team should always be available at cannulation site, for rescue surgical cannulation if the percutaneous approach fails
- Configuration of VV ECMO: always Femoro-Jugular or Double lumen cannula unless specifically indicated
- Percutaneous cannulation should always be done under ECHO/USG or fluoroscopy guidance
- Femoro-Jugular VV ECMO
  - Tip of drainage cannula: junction of inferior vena cava and right atrium
  - Distance between drainage and reinfusion cannula: at least 10–15 cm to minimize reperfusion
- Double lumen cannula
  - Tip of cannula: in the inferior vena cava
  - Reinfusion:lumen should face the tricuspid valve

Step 5: Initiation of VV ECMO

ECMO settings

- ECMO flow and inspired oxygen on membrane: titrated to target PaO_2 of at least 60 mmHg
- ECMO flow—increase slowly to avoid hypotension on initiation
- Target ECMO flow—at least 60% of native cardiac output. ECMO flows should be increased till the target oxygenation is achieved.
- Sweep gas flow: at initiation sweep gas flows should be as low as possible. During ECMO initiation, sweep gas flow of 2 L is recommended.
- Sweep gas can be titrated gradually based on pH and pCO_2. Rapid correction of CO_2 should be avoided as it increases the risk of intracranial haemorrhage.

Mechanical ventilation settings

- Ultra-lung protective ventilation
- Respiratory rate: 5–10 breaths/min
- Tidal volume: 1–3 mL/kg
- Plateau pressure: <20 cmH_2O
- PEEP: at least 10 cmH_2O. Ideally, the same peep on mechanical ventilator as before initiation of ECMO should be continued.
- FiO_2: 30–50%

Step 6: Anticoagulation and Blood Product Management on VV ECMO

- Heparin/Bioline coated circuits should be used to minimize the need for anticoagulation
- Anticoagulation should be initiated immediately after insertion of drainage cannula
- Unfractionated heparin infusion is the drug routinely used
- Bivalirudin and Argatroban can be used in patients with heparin induced thrombocytopenia

Anticoagulation monitoring parameters (with heparin anticoagulation)

- ACT (Activated Clotting Time)
- Most commonly used monitoring parameter
- It is a measure of whole blood clotting
- Deranged ACT could be because of various factors other than anticoagulation
- Excessive anticoagulation
- Thrombocytopenia
- Coagulopathy
- Since ACT is deranged in many situations in ECMO patients, it is not an ideal monitoring tool

- aPTT (Activated Partial Thromboplastin Time)
  - Measures both intrinsic and final common pathway of coagulation
  - Deranged aPTT is seen in following factors, other than heparin anticoagulation
    - Lupus anticoagulant
    - Deficiency of coagulation factors
- Anti Xa activity
  - Assay of anti Xa is dependent on heparin anticoagulation and anti-thrombin levels.
  - Not influenced by any other parameter
- Thromboelastography can been used for anticoagulation monitoring
- Anticoagulation targets
  - ACT: 160–180 s
  - aPTT ratio: 1.5–2 times the normal value
  - Anti Xa levels: 0.3–0.7 IU/mL
- VV ECMO at high ECMO flows (>4 L/min) can be maintained with minimal to no anticoagulation, especially in patients with high risk of bleeding
- ECMO flows of 2.5 L/min or less have extremely high risk of thrombosis and thus necessitates higher anticoagulation
- Anti-thrombin III activity should be checked in patients who require high dose of heparin, to achieve a given anticoagulation target.

Blood product management

- The targets for blood component therapy is discussed in Table 30.1.
- If the patient develops massive life threatening coagulopathy, entire ECMO unit should be changed

Table 30.1 Blood component therapy on ECMO

Blood component	Management	
	ELSO (Extra corporeal life support organisation recommendation)	Recent evidence
Platelets	Transfuse if <80,000/mm^3	Platelets as low as 20,000/mm^3 is found to be safe in absence of bleeding. In bleeding patients: Transfuse if <50,000/mm^3
Fresh frozen plasma	Transfuse if INR >2	No new evidence
Fibrinogen	Transfuse Cryo-precipitate to maintain fibrinogen >100 mg/dL In bleeding patients, target >150 mg/dL	If fibrinogen persistently <100 mg/dL, consider changing the ECMO circuit
Red blood cells	Target haematocrit of 30%	No higher targets needed on ECMO. Transfuse when Hb is <7 g%

Step 7: Clinical Care on ECMO

1. **Sedation and ventilation**
   - Continue with deep sedation with or without neuromuscular blockage for initial 24–48 h on ECMO
   - Patient can be initiated on spontaneous respiration at the earliest, with targets of lung protective to ultra-lung protective ventilation
   - Aggressive physiotherapy of chest and limbs to be performed routinely
   - Patient should be mobilized at the earliest possible opportunity and all measures to prevent ventilator associated pneumonia should be carried out
   - Assess every day for the readiness of weaning from ECMO and ventilator
2. **Nutrition**
   - Enteral nutrition should be initiated at the earliest and nutrition care should be the same as any critically ill patient
   - Glycemic control should be achieved with target blood sugars of 140–180 mg/dL
3. **Antibiotics**
   - Routine antibiotics is not necessary for patients on ECMO
   - Appropriate antibiotic cover for the primary illness should be continued according to local protocols
4. **Drug dosing**
   - Significant alteration in drug pharmacokinetics occur in patients on ECMO
   - Most common one include:
     – Increased volume of distribution
     – Absorption of the drug to the ECMO circuit and membrane, leading to enhanced clearance
     – Renal dysfunction and non-pulsatile flow, leading to reduced clearance
   - Appropriate dosing of drugs is of paramount importance and drug monitoring should be used whenever indicated clinically

Step 8: Monitoring and Trouble Shooting on ECMO

1. **Clinical monitoring**
   - Every ECMO patient should be examined from head to toe, drainage cannula to reinfusion cannula at least once during every shift and as and when required
   - Clinically look for the following:
     – Insertion sites of cannula for infection, and bleeding
     – Circuit for signs of thrombosis
     – Colour difference of the blood in the inflow and outflow tubings of the ECMO circuit. If the colour difference is minimal, one should rule out recirculation and also check if the sweep gas is disconnected or turned off.
     – Chattering of the ECMO tubings
     – Membrane: for thrombosis and fibrin deposition
     – Pressure sores
     – Perfusion of limbs: signs of ischemia, discolouration and mobility

2. **Monitoring on ECMO console**
   - Mode on the ECMO machine
   - Power connection on the ECMO console
   - Charge on the battery (battery back-up)
   - ECMO flows
   - RPM (Revolution per minute)
   - Temperature on the heat exchanger
   - Sweep gas flows
   - Inspired oxygenation to the membrane
3. **Blood gas analysis and ventilation**
   - Arterial blood gases: hourly to second hourly till stabilization of blood parameters. Once, the parameters have settled, routine measurement is not needed
   - Ventilatory parameters: tidal volume, plateau pressure, driving pressure and PEEP should be routinely monitored
   - Trans pulmonary pressure guided ventilator management can be considered, if available
   - Central venous oxygen saturation (ScvO2)
     - Certain ECMO machines has in-built monitoring of central venous saturation
     - Routine monitoring of $ScvO_2$ is not required
     - High $ScvO_2$ is a marker of recirculation
4. **Anticoagulation lab**
   - Anticoagulation lab schedule is discussed in Table 30.2.
   - Plasma free haemoglobin (PFH)
     - Should be measured every day on patients with ECMO
     - Higher PFH (>5 g/dL) is an indicator of significant hemolysis and needs immediate steps to identify the cause and initiate corrective measures
     - Cause of high PFH (high hemolysis)
       Hypovolemia
       Position of drainage cannula- too low in the inferior vena cava

Table 30.2 Anticoagulation monitoring

Parameter	Frequency of monitoring
ACT	2nd hourly initially Once stabilized-6th hourly
APTT ratio	6th–12th hourly initially Once stabilized- daily
Anti Xa levels	6th–12th hourly initially Once stabilized-daily
Platelets	12th hourly to once daily
Fibrinogen	Once daily
Plasma free hemoglobin	Once daily
Anti-thrombin III assay	As and when needed
Thromboelsatography	As and when needed
Hemoglobin	Once daily

Small drainage cannula
Thrombosis of the membrane
Repetitive episodes of chattering of the lines

5. **Other laboratory tests**
   - Blood cultures should be sent daily
   - Renal function tests and electrolytes—as and when appropriate
   - Liver function tests—as and when clinically appropriate
   - All other tests as deemed necessary according to the clinical profile of the patient
6. **ECMO circuit pressure monitoring**
   - The interfaces where pressure monitoring should be done on ECMO is explained in Fig. 30.1
     – P1: inflow pressure in to the pump and is always negative
     – P1 should not exceed more than 100 mmHg in negative to avoid extreme turbulence and hemolysis
     – P2: pressure between the pump and membrane oxygenator. It is pressure generated by the non-occlusive pump to propel blood forward
     – P2 is always positive, with normal values ranging from 150 to 280 mmHg depending on ECMO flows
     – P3: pressure post membrane.
     – The difference between P2 and P3 (membrane pressure drop) should always be less than 50 mmHg.
     – Higher pressure drops suggest membrane thrombosis
     – The various reasons for the changes in pressures is discussed in Table 30.3.

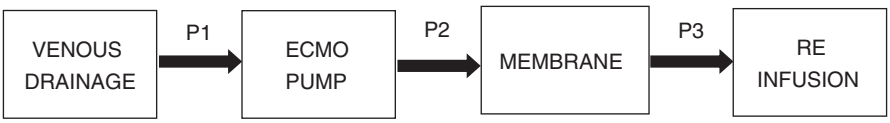

Fig. 30.1 ECMO circuit pressure monitoring

Table 30.3 Circuit pressure monitoring

P1	P2	P3	Cause
↓	↓	↓	Hypovolemia, tension pneumothorax, tamponade, kinking or malposition of drainage cannula
↑/N	↓	↓	Pump failure
↑/N	↑/N	↓	Oxygenator failure (thrombosis)
↑/N	↑	↑	Increased afterload, hypertension, kinking or malposition of infusion cannula

7. **Radiological investigations**
   - Chest X-ray
     - To check for position of ECMO cannulas
     - Radiological improvement in lung parenchyma
     - Position of other tubings like endotracheal tube, central venous lines, naso gastric tubes etc.
     - Identification of pleural effusions, pneumothorax
   - Ultrasonography and Echocardiography
     - Check for lung parenchyma, pneumothorax, pleural and pericardial effusion
     - Position of ECMO cannulas
     - Evidence of venous thrombosis and pseudoaneurysm
     - Cardiac output of the patient
     - Volume status of the patient
     - Examination of valves—especially tricuspid for fungal endocarditis

Step 8: Hypoxemia on VV ECMO

- There is no defined cut off for hypoxemia on ECMO
- Patients with SaO2 of less than 80 despite best ECMO optimization should be considered to be hypoxic
- A fraction of patients would continue to remain hypoxic despite initiation of ECMO and a fraction of them will develop episodes of significant hypoxemia during the treatment period.
- A simplified algorithm (Figs. 30.2 and 30.3) explains the approach to identify the cause of hypoxemia on vv ECMO

Step 9: Weaning from VV ECMO

- Weaning trial can be considered once the support on ECMO is less than 30% of total lung function
- Step wise weaning protocol
  - Increase the ventilator support
  - Tidal volume: 6 mL/kg
  - FiO_2: <60%
  - PEEP: 5–12 cmH_2O
  - Plateau pressure: <30 cmH_2O
  - Reduce the sweep gas flow to zero and cap the oxygenator

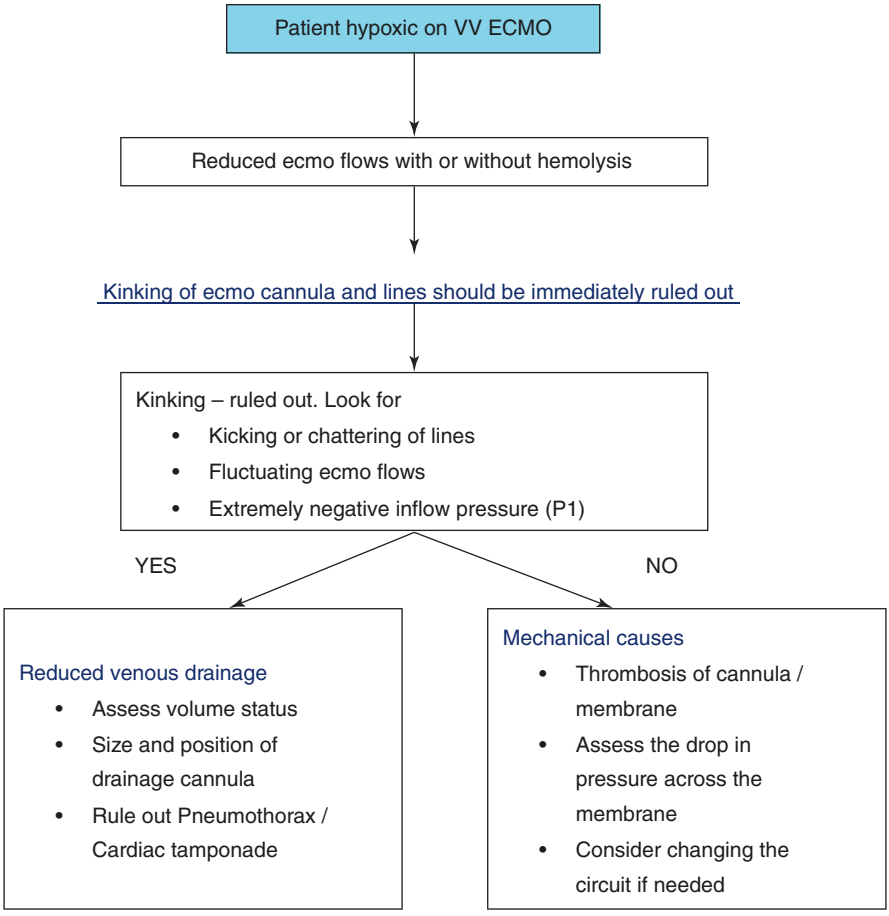

Fig. 30.2 Hypoxic patient with reduced ECMO flows with or without hemolysis

  - Observe the patient for 1–4 h
  - Do not stop anticoagulation or reduce ECMO flows
- Monitor PaO_2, $PaCO_2$, look for evidence of reduced tissue oxygenation like lactates and $ScvO_2$
- $PaO_2 > 60$ mmHg, with acceptable carbon-di-oxide levels and normal tissue oxygenation is an indicator that patient can be weaned off from vv ECMO
- Patient should be stable for minimum of 4 h before considering decannulation

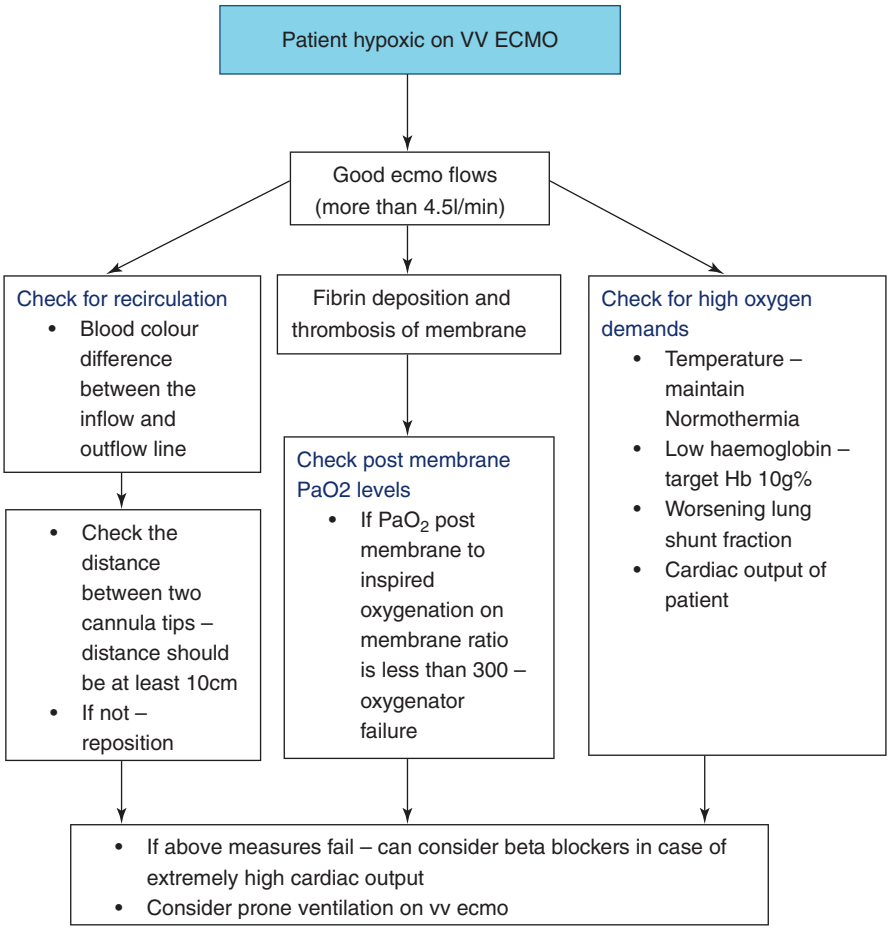

Fig. 30.3 Hypoxemic patient on ECMO with good ECMO flows

Step 10: ECMO Decannulation

- Stop heparin anticoagulation for at least half an hour
- Measure ACT or aPTT before decannulation
- ACT should ideally be less than 150 s
- Percutaneous cannulas can be just pulled out, followed by compression for over 30 min

- Ask the patient to perform a Valsalva maneuver to minimize the risk of air embolism during decannulation
- Observe the patient for at least 6 h before mobilizing the limb and patient

Step 11: Critical Care Post ECMO

- Every aspect of critical care should continue
- Aggressive chest rehabilitation should be pursued
- Daily examination of vessels for evidence of thrombosis and pseudo aneurysm should be done

Suggested Reading

Brogan TV, Lequier L, et al. Extra corporeal life support: the ELSO red book. 5th ed. *This book is official text of extra corporeal life support organization*.

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Peek GJ, et al. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. Lancet. 2009;374:1351–63. *This study concluded that in severe but potentially reversible respiratory failure, whose Murray score exceeds 3.0 or who have a pH of less than 7.20 on optimum conventional management, they should be transfered to a centre with an ECMO-based management to significantly improve survival without severe disability*.

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Scoring Systems

31

Jigeeshu V. Divatia

A 60-year-old male patient with cirrhosis of the liver and portal hypertension was admitted to the hospital with pneumonia. He developed septic shock and became encephalopathic and anuric. The family wanted to know the chances of survival. Can a scoring system be used to predict the chances of survival?

The annual mortality in the ICU patients of hospital A is 5% and of hospital B is 15%. Can it be concluded that the ICU patients of hospital B are poorly managed compared to that of hospital A?

Performance measures of ICU care are usually subjective and difficult to compare. An objective measure of the structure, processes, and outcome by prognosticating in a cohort of ICU patients makes it more meaningful and easier to compare. This also helps in rational allocation of resources. A severity scoring system also helps in controlling risk factors in intervention and control groups in clinical trials.

Step 1: Understand the Type of Scoring Systems Used in ICU Population

- General risk-prognostication scores (severity of illness scores)
  - Acute physiology and chronic health evaluation (APACHE II, III, and IV)
  - Simplified acute physiology score (SAPS II and III)
  - Mortality prediction model (MPM II0 and MPM II24)
- Disease and organ-specific risk-prognostication scores
  - Ranson's score for acute pancreatitis
  - RIFLE and AKIN classification for acute kidney injury
  - Trauma scores

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  - Glasgow coma score
  - KILLIP—heart failure
  - CURB—pneumonia
  - CAM-ICU—delirium
- Organ dysfunction score—sequential organ failure assessment (SOFA)
- Nursing workload measurement—therapeutic intensity scoring systems (TISS)
- Population-specific—pediatrics—APGAR score
- Postoperative—PRISM

Step 2: Understand General ICU Scoring Systems

- All scoring systems are developed from large databases of ICU patients called the derivation cohort
- Statistical modeling is used to determine the variables that are likely to impact survival.
- A summary score is derived from these variables, and the predicted mortality is calculated using predictive equations which is validated in another set of ICU patient called validation cohort
- The performance of the scoring system depends on the size and case mix of patients in the reference database and the methodology used to assign weights to different elements of the scoring system.
- APACHE II and SAPS II scoring systems were derived from datasets of patients in North American and European ICUs in the mid-1980s and early 1990s.
- The APACHE II scoring system assigns points to age, acute physiological observations based on the worst values in the first 24 h after admission for 12 variables, and specified preexisting chronic diseases. It also requires selection of a single diagnostic category for each patient. The predicted mortality is based on the APACHE II score and the diagnostic category (Table 31.1).
- The SAPS scoring system does not require ICU admission diagnosis for calculating the score.
- Both APACHE II and SAPS II did not account for lead-time bias (i.e., the time lag between the onset of critical illness and admission to the ICU).
- APACHE III was developed as a further refinement of APACHE II, but its mortality prediction equations are not in the public domain.
- The APACHE IV system (2006) is based on 110,558 patients in 104 North American intensive care and coronary care units between 2003 and 2004. It uses 129 variables derived from the worst values from the initial 24 h of ICU admission. It has equations to predict both hospital mortality as well as length of ICU stay.
- SAPS III, published in 2005, was based on 16,789 patients aged 16 years or more from more than 300 ICUs in 35 countries across all continents. Three subscores—namely, patient characteristics before admission (5 variables), circumstances of admission (5 variables), and acute physiology (10 variables)—are summed up to produce the SAPS III score. A diagnostic category is essential for estimating mortality.

Table 31.1 The APACHE II scoring system

	High abnormal range					Low abnormal range			
Physical variable	+4	+3	+2	+1	0	+1	+2	+3	+4
Temperature—Rectal (°C)	>40.9	39–40.9		38.5–38.9	36–38.4	34–35.9	32–33.9	30–31.9	<29. 9
Mean arterial pressure (mmHg)	≥160	130–159	110–129		70–109		50–69		≤49
Heart rate (ventricular response)	≥180	140–179	110–139		70–109		55–69	40–54	≤39
Respiratory rate (nonventilated or ventilated)	≥50	35–49		25–34	12–24	10–11	6–9		≤5
Oxygenation: A-aDO$_2$or PaO$_2$(mmHg)									
(a) FiO$_2$ ≥ 0.5 record A-aDO$_2$	≥500	350–499	200–349		<200				PO$_2$
(b) FiO$_2$ < 0.5 record PaO$_2$					PO$_2$ > 70	PO$_2$ 61–70		PO$_2$ 55–60	PO$_2$ <55
Arterial pH	≥7.7	7.6–7.69		7.5–7.59	7.33–7.49		7.25–7.32	7.15–7.24	<7.15
Serum sodium (mMol/L)	≥180	160–179	155–159	150–154	130–149		120–129	111–119	≤110
Serum potassium (mMol/L)	≥7	6–6.9		5.5–5.9	3.5–5.4	3–3.4	2.5–2.9		<2.5
Serum creatinine (mg/100 mL) (double-point score for acute renal failure)	≥3.5	2–3.4	1.5–1.9		0.6–1.4		<0.6		
Hematocrit (%)	≥60		50–59.9	46–49.9	30–45.9		20–29.9		<20
White blood count (total/mm^3) (in 1000 s)	≥40		20–39.9	15–19.9	3–14.9		1–2.9		<1
Glasgow coma score (GCS) score = 15 minus actual GCS									
[A] Total acute physiology score (APS) sum of the 12 individual variable points									
Serum HCO$_3$(venous mMol/L) (not preferred, use if no ABGs)	≥52	41–51.9		32–40.9	22–31.9		16–21.9	15–17.9	≤15
***[B]** Age points*									
Assign points to age as follows:									
Age (years)					Points				
≤44					0				
45–54					2				
55–64					3				
65–74					5				
≥75					6				

(continued)

Table 31.1 (continued)

	High abnormal range					Low abnormal range			
Physical variable	+4	+3	+2	+1	0	+1	+2	+3	+4
[C] Chronic health points									
If the patient has a history of severe organ system insufficiency or is immunocompromised, assign points as follows:									
(a) For nonoperative or emergency postoperative patients, 5 points									
(b) For elective postoperative patients, 2 points									
Definitions									
Organ insufficiency or immunocompromised state must have been evident prior to this hospital admission and conform to the following criteria:									
Liver: Biopsy-proven cirrhosis and documented portal hypertension, episodes of past upper GI bleeding attributed to portal hypertension, or prior episodes of hepatic failure/encephalopathy/coma.									
Cardiovascular: New York heart Association class IV.									
Respiratory: Chronic restrictive, obstructive, or vascular disease resulting in severe exercise restriction (i.e., unable to climb stairs or perform household duties, or documented chronic hypoxia, hypercapnia, secondary polycythemia, severe pulmonary hypertension (>40 mmHg), or respirator dependency).									
Renal: Receiving chronic dialysis.									
Immunocompromised: The patient has received therapy that suppresses resistance to infection (e.g., immunosuppression, chemotherapy, radiation, long-term or recent high-dose steroids), or has a disease that is sufficiently advanced to suppress resistance to infection (e.g., leukemia, lymphoma, and AIDS).									
APACHE II score									
Sum of **[A]** + **[B]** + **[C]**									
AAPS Points_____									
BAge points_____									
CChronic health points_____									
Total APACHE II_____									

- Both APACHE IV and SAPS III account for lead-time bias, but have not been tested and validated as extensively as APACHE II and SAPS II.
- MPM II0, published in 1985, was the first general severity model to assess risk of death based on parameters assessed at ICU admission. Prediction models for assessment at admission and after 24 h (MPM II24) were developed originally. The models consist mainly of dichotomous variables. Data entry is the easiest for all the MPM systems as they use only clinical variables and bedside physiological parameters, and no laboratory data.
- All ICU scoring system predict the likelihood of hospital mortality for patients admitted in ICU
- Some scoring system (e.g. APACHE IV also predicts the ICU length of stay)

Step 3: Understand Organ Failure Scoring System

- The SOFA score is a descriptive score that uses routinely collected data for the calculation of a score of 0–4 for each organ, the higher number meaning more severe failure (Table 31.2).
- Daily scoring enables monitoring of the progress of organ dysfunction or failure.

Table 31.2 The SOFA score

SOFA score					
	0	1	2	3	4
Respiration PaO_2/FiO_2	>400	≤400	≤300	≤200 with respiratory support	≤100 with respiratory support
Coagulation Platelets (10^3/mm^3)	>150	≤150	≤100	≤50	≤20
Liver					
Bilirubin (mg/dL)	1.2	1.2–1.9	2.0–5.9	6.0–11.9	>12.0
(μmol/L)	<20	20–32	33–101	102–204	>204
Cardiovascular					
Hypotension	No hypotension	MAP <70 mmHg	Dopamine ≤5 or dobutamine (any dose)[a]	Dopamine ≥5 or epi 0.1 (or norepi ≤0.1)[a]	Dopamine >15 or epi 0.1 (or norepi ≥0.1)[a]
Central nervous system					
Glasgow coma score	15	13–14	10–12	6–9	<6
Renal					
Creatinine (mg/dL)	<1.2	1.2–1.9	2.0–3.4	3.5–4.9	>5.0
(μmol/L)	<110	110–170	171–299	300–400	>400
Or urine output				Or < 500 mL/day	Or < 200 mL/day

Epi epinephrine, *norepi* norepinephrine
[a]Adrenergic agents administered for at least 1 h (doses given are in μg/kg/min)

- There are no equations to estimate mortality. However, high initial SOFA scores and worsening of SOFA scores over time correlate with increased mortality.
- The logistic organ dysfunction system (LODS) was developed for the evaluation of organ dysfunction on the first day of the ICU.
- It provides probability of hospital mortality, distinguishing it from merely descriptive models such as SOFA.
- The SOFA score has recently been incorporated into the definition of sepsis.
- Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.
- Organ dysfunction can be identified as an acute change in total SOFA score ≥2 points consequent to the infection. The baseline SOFA score can be assumed to be zero in patients not known to have preexisting organ dysfunction.
- A qSOFA (quick SOFA) score consisting of any two of the following parameters altered mentation, systolic blood pressure ≤100 mmHg and respiratory rate ≥22/min is a simple bedside score to identify adult patients with suspected infection who are likely to have poor outcomes

Step 4: Evaluate the Scoring System

- The ability of the model to distinguish between patients who survive and patients who do not survive is termed discrimination. e.g. if a scoring system predicts mortality of 90% the discrimination is perfect if the observed mortality is 90%
- The area under the receiver operating characteristic curve (AUC) is used to give a graphical and numerical estimate of discrimination. If AUC is 0.5, it means the system is only as good as flipping a coin, and if AUC is 1, this indicates excellent discrimination.
- Calibration of a system examines the difference between the observed and expected deaths in patients grouped into different severity of illness. e.g. A scoring system will be highly calibrated if it were accurate at mortalities of 90, 50 and 20%.
- This can be evaluated graphically as well as by goodness-of-fit statistics using the Hosmer-Lemeshow test. If the *p* value is more than 0.05, the model provides a good fit for the data.
- The standardized mortality ratio (SMR = actual mortality/predicted mortality) also takes into account severity of illness and evaluates risk-adjusted ICU performance.

Step 5: Understand Limitations of the Scoring System

- None of the scoring systems are accurate enough to make predictions in individual patients and hence cannot be used to predict outcomes of individual patients.

- Most systems require data to be collected in the first 24 h after ICU admission; hence, the severity score cannot be used to decide whether to admit a patient to the ICU.
- Erroneous conclusions can be drawn if data are not collected correctly according to the original database and definitions of the scoring system.
- The score cannot be applied to patients excluded from the original database (e.g., patients younger than 16 or 18 years and patients with burns).
- Missing data and interobserver variability can affect accuracy.
- APACHE IV poses a heavy burden for manual data entry as it scores 129 variables. This is not a problem in health systems where data is captured directly from the monitors and the electronic health record, but is currently a major limitation in Indian ICUs.
- These scores may not be accurate in geographical regions, and case mix significantly different from that in the original database.
- The performance of a scoring system tends to deteriorate over time, due to changes in practice, therapy and casemix. It often leads to overestimation of mortality
- All the scoring systems can only predict the behavior of a group of patients that matches the patients in the original database population.
- The commonly used APACHE II and SAPS II do not account for lead-time bias, i.e., the effect of treatments offered prior to arrival in the ICU, which includes the time between the onset of critical illness and arrival in the ICU, as well as the location in which the patient was treated prior to transfer to the ICU.
- All the scoring systems need to be updated periodically to reflect contemporary practice and patient demographics to avoid deteriorating performance over time.

Step 6: Understand Utility of Scoring System

- No single scoring system has been proven to be superior to the other, though APACHE systems are reasonably accurate and are widely used.
- Scoring systems can be updated and customised to represent current practice and case-mix in particular countries or regions.
- Scoring systems may be used to evaluate the performance of an ICU using the SMR.
  - The SMR of 1 implies that mortality in the ICU is equal to what is predicted by the system. The SMR of less than 1 indicates that ICU performance is better than predicted, while the SMR of more than 1 implies poor performance.
  - The SMR may be used to compare different ICUs, or the performance of the same ICU over a period. Differences in the SMR may represent differences in case mix, or differences in ICU practices between observed ICUs and the ICUs that contributed patients to the derivation dataset, or differences in quality of care.
  - The trend of SMRs can be used to evaluate ICU performance over time, or to compare ICUs.

- Scoring systems have been used in clinical trials to ensure similarity of study groups in terms of severity of illness at baseline.
- APACHE IV gives predictions for ICU mortality as well as hospital length of stay.
- TISS can be used to quantify and optimize nursing workload, staffing patterns, and costs.
- The daily SOFA score is useful to monitor progress of organ dysfunction. If an ICU treats a large number of patients belonging to a specific group (e.g., trauma, cancer, and coronary), specific scoring systems may be used.

Suggested Reading

Khwannimit B. Serial evaluation of the MODS, SOFA and LOD scores to predict ICU mortality in mixed critically ill patients. J Med Assoc Thai. 2008;91(9):1336–42. *Serial assessment of organ dysfunction during the ICU stay is reliable with ICU mortality. The maximum score is the best discrimination comparable with APACHE II score in predicting ICU mortality*.

Moreno RP, Metnitz PG, Almeida E, et al. SAPS 3 investigators. SAPS 3—from evaluation of the patient to evaluation of the intensive care unit. Part 2: development of a prognostic model for hospital mortality at ICU admission. Intensive Care Med. 2005;31:1345–55. *The SAPS III admission score is able to predict vital status at hospital discharge with use of data recorded at ICU admission. Furthermore, SAPS III conceptually dissociates evaluation of the individual patient from evaluation of the ICU and thus allows them to be assessed at their respective reference levels*.

Vincent JL, Bruzzi de Carvalho F. Severity of illness. Semin Respir Crit Care Med. 2010;31:31–8. *This article reviews the most commonly used severity-of-illness scoring systems and discusses some of their uses and limitations*.

Vincent JL, Moreno R. Clinical review: scoring systems in the critically ill. Crit Care. 2010;14(2):207. *The different types of scores should be seen as complementary, rather than competitive and mutually exclusive. It is possible that their combined use could provide a more accurate indication of disease severity and prognosis. All these scoring systems will need to be updated with time as ICU populations change and new diagnostic, therapeutic, and prognostic techniques become available*.

Zimmerman JE, Kramer AA, McNair DS, et al. Acute physiology and chronic health evaluation (APACHE) IV: hospital mortality assessment for today's critically ill patients. Crit Care Med. 2006;34:1297–310. *APACHE IV predictions of hospital mortality have good discrimination and calibration and are useful for benchmarking performance in US ICUs. The accuracy of predictive models is dynamic and should be periodically retested. When accuracy deteriorates they should be revised and updated*.

Websites

http://www.sfar.org/article/316/scoring-systems-for-icu-and-surgical-patients. For calculation of various scores.

http://www.medcalc.be/manual/roc.php. Understand the ROC curve.

Research Methodology in Critical Care

32

Anirban Hom Choudhuri, Ajeet Bhadoria,
and Surabhi Mishra

Medical research is the only reliable way through which our insight can be focused towards the best practices in medicine. The Health Insurance Portability and Accountability Act define medical research as "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge." Medical research is inevitable for ensuring high quality patient care.

Critical care medicine is a unique discipline which is practiced by physicians from several primary specialties. The execution of good research is vital for intensivists to provide state-of-the art care for patients confronting life threatening illnesses, to improve patient outcomes and better utilisation of ICU resources. Most importantly, good research is inevitable for advancement in the theory and practice of critical care medicine.

A Guide to the "Research Process"

The entire "Research process" can be guided through an eight step model consisting of three phases as outlined in Table 32.1.

Step 1: Formulate the Research Question

The research question is the first and the most important step of medical research. If the research question is good, the research may or may not be good but if the

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Table 32.1 Table showing the phases and steps of Research process

Phase 1 (Decide what to Research)	Phase 2 (Plan a Research)	Phase 3 (Conduct Research)
Step 1: Formulate the research question	Step 2: Conceptualize the study design Step 3: Construct an instrument for data collection Step 4: Select a sample Step 5: Write a research proposal	Step 6: Collection of data Step 7: Process and display of data Step 8: Write a research report

Table 32.2 "FINER" approach for research question

F	Feasible	Access to an adequate number of participants Research team has technical expertise to conduct the study Costs are reasonable and funding is available Can be completed in a reasonable time period
I	Interesting	Results of the study will be of interest to the research community
N	Novel	Provides new findings, extends or refutes previous findings
E	Ethical	Risk to participants is low/acceptable Considered ethical by peers and the IRB
R	Relevant	To improve scientific knowledge, inform clinicians and health policy, and to impact future research

Table 32.3 Format of a research question

P—Population I—Intervention C—Control O—Outcome (T)—Time	e.g. In a comparison of outcome after off pump and on pump CABG, population are the CAD patients Intervention would be surgery (on pump or off pump) Control would be patients on medical treatment (placebo), outcome can be survival or death Time or period of outcome can be chosen accordingly in days, months, years, etc.

research question is poor, the research definitely becomes poor. The most important aspect to be considered while framing a good research question is the "FINER" approach (Table 32.2).

One should be careful in avoiding waste of resources and intellectual energy while framing a research question. This can be done by: (i) doing a pilot or proof of concept study, (ii) consulting a biostatistician beforehand to choose a less costly design and common outcomes and (iii) calculating the feasibility of enrolling the intended number of subjects from the population of interest.

Once framed, the research question should be in the PICO (T) format (Table 32.3).

If the research question has never been studied and is interesting, it is worthwhile pursuing. If the scientific question has been answered before, the question can be modified to get an answer about some other behavior or variable.

Some examples of flawed research question is shown in Table 32.4.

Table 32.4 Example of flawed research questions

Question	Reason of flaw
What is the childhood BSI rate in my ICU?	Too narrow
What are the effects of ICU stay on quality of life in India?	Unfocused and too broad
How much time do pneumonia patients sleep daily?	Too subjective
How many ICUs have an antibiotic protocol for meningitis?	Too simple

Table 32.5 Choice of study design according to the study objective

Study objective	Choice of design
Prevalence	Cross sectional
Incidence	Cohort
Cause (in order of reliability)	Cohort, case control, cross sectional
Prognosis	Cohort
Treatment effect	Controlled trial

Step 2: Conceptualize the Study Design

The next important step is to choose the proper study design. This depends on the research question and the study objective. The table below shows the choice of the design as per the study objective (Table 32.5).

In this connection it is important to recognize the differences in the study designs. There are two broad categories: observational and experimental. In observational, there can be case control, cohort and cross sectional study while in experimental it is usually either randomized or non randomized clinical trial.

Table 32.6 shows some characteristics of the different observational and experimental studies.

While the biggest advantage of the observational studies is the better generalizability due to high external validity, their major drawback is the effect of bias due to low internal validity. This is opposite for the randomized control trials. The Randomized Controlled Trial (RCT) is the gold standard for determining the efficacy and adverse effect of any intervention.

Step 3: Construct an Instrument for Data Collection

The next step is to construct an instrument for data collection which is called Case Record Form (CRF). One can choose either a paper or electronic document to record all the information required in a standard format. Both the study protocol and CRF must be designed in parallel to establish consistency between them.

The components of a standard CRF is shown in Table 32.7.

The table below shows the differences between a poorly designed and well-designed CRF (Table 32.8).

Table 32.6 Different types of observational studies

Study design	Randomized control trial	Cross-sectional	Cohort	Case-control
Study population	Highly selected population, highly controlled environment	Diverse population observed in a range of settings	Diverse population observed in a range of settings	Diverse population observed in a range of settings
Directionality	Exposure is assigned before outcome is ascertained	Exposure and outcome ascertained simultaneously	Exposure is ascertained before outcome is ascertained	Outcome is ascertained before exposure is ascertained
Primary use	Demonstrating efficacy of an intervention	Screening hypotheses, prevalence studies	Assessing association between multiple exposures and outcomes over time	Assessing association between exposures and rare outcomes
Analysis	Straight-forward	Sophisticated, multivariate techniques may be required to account for confounding	Sophisticated, multivariate techniques may be required to account for confounding	Sophisticated, multivariate techniques may be required to account for confounding
Internal validity	High	Low	Low	Low
External validity	Low-moderate	High	High	High

Table 32.7 Components of an ideal CRF

Study title and number
Investigator's name
Study subject/patient ID (number and initials)
Inclusion/exclusion criteria
Demographic data
Detailed description of dosage regimens of investigational drug
Concomitant treatment
Adverse events (side effects and intercurrent diseases)
Conclusion on subject's health
Investigator's signature and date

Step 4: Select a Sample

Sample means a group of people who share a common character or a condition. If we want to conduct a study on patients with sepsis, it will be difficult to include the whole population of sepsis all over the world. Therefore, the practical approach in clinical research is to include a part of this population, called "sample population" which is representative of the "target population", as much as possible with the least possible error and without substitution or incompleteness.

Table 32.8 Poorly designed versus well designed CRF

Poorly designed versus well designed CRF

Poorly designed	Well designed
Date of visit: _____	Date of visit: ☐☐ / ☐☐ / ☐☐☐☐ (DD/MM/YYYY)
Blood pressure: _____/ _____	Blood pressure: ☐☐☐ / ☐☐☐ (mmHg)
Pulse: _____	Pulse: ☐☐☐ (beats/min)
Temperature: _____	Temperature: ☐☐ . ☐ (°C)
Respiration: _____	Respiration: ☐☐ (/min)

The general principles which should be followed while designing CRF are-

a) When capturing dates, include a note of what format the date should be recorded in e.g.

Date of birth: ☐☐ / ☐☐☐ / ☐☐☐☐ DD/MMM/YYYY (e.g. 01/JAN/2013)

b) Coding wherever possible
c) Use subscripts to note the variable codes (e.g. 1. Yes 2. No) and be consistent with coding across all forms e.g.

DEMOGRAPHY	
Date of birth (DD/MM/YYYY)	☐☐☐☐☐☐☐☐
Gender	Male ☐ 1 Female ☐ 2
Height (cm)	☐☐☐.☐
Weight (kg)	☐☐☐.☐☐
Smoker	Yes ☐ 1 No ☐ 2
Family history	Yes 1 No 2

Coding on the case report form module

d) Include units where applicable(e.g. mm Hg, ml/L etc)
e) Collect raw data rather than calculated data e.g. for age collect month and year of birth and visit date rather than age in years
f) Do not collect the same data twice e.g. month/year of birth and age at visit
g) Remember to note whether the person completing the page should "Tick all that apply" or "Select one".
h) Limit the use of free text to as little as possible
i) Data collection should follow the flow of the study and a CRF should only reflect data collected at one time point

The process of selecting a sample population from the target population is called the "sampling method".

Table 32.9 shows the different sampling methods. It is advisable to take help from the Biostatistician or Senior Researcher while selecting the sampling method.

Table 32.9 Sampling methods

Probability sampling	Non probability sampling
Simple random Stratified random Systematic Clustered random	Convenience Judgmental Snow-ball

Table 32.10 Basic components of a Research Protocol

Title of the study
Administrative details
Project summary
Introduction to the research topic, background (literature review)
Preliminary studies
Study objectives and/or questions. Statement of the problem.
Methodology: Study design, study population and methods of recruitment, variables list, sample size, methods of data collection, data collection tools, plan of analysis (analysis of data)
Project management: Work plan (Timeline—proposed schedule)
Strengths and limitations of the study
Issues for ethical review and approvals

Step 5: Write a Research Proposal

It is mandatory for any research project to obtain the approval of IRB/IEC before its commencement. This is achieved upon expression of satisfaction by the IRB/IEC on certain basic points-

(a) The research project is worth undertaking for scientific gains
(b) Investigator(s) have the necessary competence and work experience
(c) No ethical violations and infringements of participants' rights
(d) Requirements and limitations are adequately explained
(e) All these are clearly documented in Research protocol (Table 32.10).

The protocol should be strictly adhered to during the entire period of study. Extra time spent on writing a good protocol will help at a later stage for analysis. If it is poorly prepared and not adhered to, it is unlikely to yield the information that is expected from research.

Step 6: Collection of Data

This is an important step for the reason that wrong means of data collection can give rise to 'GIGO' (Garbage in Garbage out) effect. This can be ensured by: (i) Selecting proper method of Data collection and (ii) establishing the validity and reliability of data collection instrument (Table 32.11).

Table 32.11 Table showing the methods for proper data collection methods and testing the validity of the instrument

Selecting proper method of data collection	Establishing the validity of data collection instrument
Primary sources: Those sources where information is collected directly from respondents for specific purpose for which a study is undertaken. These include interviewing, observation and use of questionnaires. *Secondary sources*: All other sources, where information required is already available, viz. government publications, reports and previous research are called secondary sources	*Quantitative research* External consistency procedures: Test/retest and parallel forms of same test Internal consistency procedures: Split-half technique *Qualitative research* Measured by two indicators: 'Dependability' (paralleling reliability) and 'confirmability' (paralleling objectivity)

Step 7: Process and Display of Data

Since the data collected is a 'raw' data, its processing includes all operations undertaken from when a set of data is collected until it is ready to be analyzed either manually or by a computer.

This involves

(a) Data Processing—starts with data editing (also known as basic 'cleaning'), followed by coding of data, pre-testing it, coding per se and verifying the coded data.

In the frame of analysis the type of analysis to be undertaken (e.g. frequency distribution, cross-tabulation, content analysis) and applied statistical procedures should be specified.

Computers primarily help by saving labor associated with analyzing data manually.

Statistics are desirable though not essential for the study. Their extent of application depends upon the purpose of the study. Statistics primarily helps to generate sense of data, 'read' data, explore and ascertain the magnitude of an existing relationships or interdependence between variables, if any.

(b) Data presentation: In quantitative studies, the text is often combined with other forms of data presentation such as tables, graphs and statistical measures. These make communication better, clearer, more effective and easier to understand.

Tables have the advantage of containing a great deal of information in a small space. It has five parts: title, stub, column headings, body and supplementary notes or footnotes. Depending upon the number of variables about which information in a table is stored, there are three types of table: univariate (frequency), bivariate (cross-tabulation) and polyvariate. For its interpretation, simple arithmetic procedures such as percentages, cumulative frequencies or ratios can be used. Other simple descriptive statistical procedures such as mean, median, or mode, chi-square test, *t*-test and coefficient of correlation can also be used. In certain cases, advanced statistics can also be applied.

Graphs make it easy for readers to absorb information at a glance. While there are many types of graphs, the common ones are histogram, bar diagram, stacked bar chart, 100% bar chart, frequency polygon, stem-and-leaf display, pie chart, line or trend diagram, area chart and scatter gram.

The method of data presentation to be used is entirely based on the discretion of the researcher to suit his/her knowledge and comfort, and which enhances the understanding of research.

Step 8: Write a Research Report

It is a crucial step in the research process. A badly written report can spoil all the hard work that has been put into the research study.

There are certain obligations in terms of accuracy and objectivity. Before beginning to writing the research report, it is necessary to develop a general outline. All sections should be written around main themes of the study.

Abstracts

Length can vary from one paragraph to several, but they follow the IMRAD format and typically spend 25% of their space on Introduction, 25% of their space on Methods, 35% of their space on Results, 15% of their space on conclusion. Abstracts do not discuss the study. They should not be too long.

Introduction

It is not a historical perspective or a review. It should not be vague and general. Don't put discussion material here. Stay sharp and much focused.

Methods

What did we do? It describes the methodology to make reader visualize how it was executed. It is written in past tense with a passive voice with headings and subheadings. It describes statistical tests for comparison of the data captured and the statistical software. Those working in this field would read it with interest, for others it is the least-read section of an IMRAD report.

Results

What are the findings? What did we find? It is like presenting the findings and outcomes of the research. It contains tables and figures. It may contain things like Forest plot, Kaplan Meyer's graph, ROC curves. All tables and figures are labelled and numbered separately. Captions go above tables and beneath figures.

Discussion

What does the study mean? What are the message/ Inference of the study? It may summarize the main findings/significant findings of the study, allowing the readers to skip reading the entire report. It is like the "headlines" in a news bulletin. If interested listen to the full broadcast, it connects these findings to other research. It

discusses the strengths and flaws in the present study. It may include a concluding remark. It often mentions the limitations of the present study and suggests the need for future research. It may state the implications of their findings for future policy or practice.

Conclusion

An example of conclusion of a research report could be as follows: The quality of care provided in ICUs worldwide has improved enormously over the past decade. Nevertheless, many disorders like ARDS (adult respiratory distress syndrome), sepsis and Hospital acquired infections (HAI) remain foci of interest, and are difficult to manage and associated with high mortality rates. Consequently, further research studies on several fields are urgently needed.

Suggested Reading

Murad MH, Montori VM. How to read a systematic review and meta-analysis and apply the results to patient care: users' guides to the medical literature. JAMA. 2014;312(2):171–9. *Clinical decisions should be based on the totality of the best evidence and not the results of individual studies. When clinicians apply the results of a systematic review or meta-analysis to patient care, they should start by evaluating the credibility of the methods of the systematic review, ie, the extent to which these methods have likely protected against misleading results*.

O'Sullivan D, Wilk S. Using PICO to align medical evidence with MDs decision making models. Stud Health Technol Inform. 2013;192:1057. *PICO-(evidence based search strategy focusing on Patient/Population, Intervention, Comparison and Outcome)-based framework for (indexing and retrieving medical evidence*). *Students reported that the PICO-based framework for organizing evidence provided an intuitive way of accessing and evaluating evidence and would be useful for their clinical tasks.*

Speckman RA, Friedly JL. Asking structured, answerable clinical questions using the population, intervention/comparator, outcome (PICO) framework. PM R. 2019;11(5):548–53. *An analysis of PICO format for clinical research*.

Sun X, Ioannidis JP. How to use a subgroup analysis: users' guide to the medical literature. JAMA. 2014;311(4):405–11. *This article provide 5 criteria to use when assessing the validity of subgroup analyses: (1) Can chance explain the apparent subgroup effect; (2) Is the effect consistent across studies; (3) Was the subgroup hypothesis one of a small number of hypotheses developed a priori with direction specified; (4) Is there strong preexisting biological support; and (5) Is the evidence supporting the effect based on within- or between-study comparisons*.

Part VIII

Pediatrics

Mechanical Ventilation

33

Praveen Khilnani and Rajiv Uttam

A 2-year-old girl with fever and cough for the past 4 days was admitted to the hospital with worsening respiratory distress and tachypnea. Her SpO_2 on room air was 83%. She was put on oxygen at 12 L/min. In spite of high flow of oxygen, SpO_2 was still 91–88%. Chest X-ray showed fluffy shadows bilaterally. In view of clinical exhaustion, severe hypoxemia, and evidence of respiratory acidosis on blood gas, she was intubated.

Mechanical ventilation is the process of delivery of tidal volume with a set FiO_2 at a predetermined rate by presetting the peak inspiratory pressure (pressure ventilation) or tidal volume (volume ventilation) on the ventilator, with a purpose to remove CO_2 from lungs and deliver oxygen to the pulmonary capillaries. This is based on gradient of mean airway pressure in the alveoli resulting from delivery of peak inspiratory pressure (PIP) and positive end-expiratory pressure (PEEP) for the entire duration of the respiratory cycle (inspiratory time and expiratory time). Two main issues are important physiologically during mechanical ventilation: Ventilation and Oxygenation. Partial pressure of oxygen in alveolus (PAO_2) is the driving pressure for gas exchange across the alveolar-capillary barrier determining oxygenation. FiO_2 and mean airway pressure will control oxygenation. Ventilation washes out carbon dioxide from alveoli keeping arterial $PaCO_2$ between 35 and 45 mmHg. Minute ventilation = respiratory rate × effective tidal volume. Adequate minute ventilation is essential to keep $PaCO_2$ within normal limits.

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Table 33.1 The eight "P"s of RSI

Time	Action
Zero minus 10 min	Preparation
Zero minus 5 min	Preoxygenation
Zero minus 3 min	Pretreatment
Time zero	Paralysis with induction
Zero plus 20–30 s	Protection and positioning
Zero plus 45 s	Placement
Zero plus 45 s	Proof
Zero plus 1 min	Postintubation management

Step 1: Initial Resuscitation

- Patient is resuscitated and rapid sequence intubation (RSI) is planned within 1 min (Table 33.1 and Fig. 33.1).
- The main purpose of RSI is to avoid positive-pressure ventilation by bag and mask and prevent gastric inflation in patients at risk of aspiration.
- Bag-and-mask ventilation may be necessary in apneic patients or those with ineffective spontaneous breathing.
- In such patients, Sellick's maneuver is performed to prevent air entering into stomach, and gentle AMBU bagging can be done.

Step 2: Initiation and Ventilator Management

Monitor the status of oxygenation and ventilation and titrate ventilator parameters accordingly (Fig. 33.2).

Initial Ventilator Settings: Pressure Limited

- Mode—pressure control.
- FiO_2—start with 1 and wean down to get good SpO_2 (>90%).
- Optimal positive end-expiratory pressure (PEEP)—to achieve adequate alveolar recruitment so that saturations are maintained at minimum FiO_2 (<0.6) and compliance is best with no hemodynamic compromise.
- Respiratory rate—normal for age (adjust if there is air trapping).
- Pressure control above PEEP (peak inspiratory pressure [PIP]-PEEP)—so that tidal volume equal to 6–8 mL/kg is delivered with adequate chest rise.
- Inspiratory time—normal for age, 0.4 s for neonates, 0.5–0.6 s for infants, 0.6–0.8 s for toddlers, and 0.9–1.0 s for older children (adjust in case of air trapping or severe acute respiratory distress syndrome [ARDS]).

Volume Limited

- Mode—volume control
- Tidal volume—6–8 mL/kg of ideal body weight, look for adequate chest rise
- Inspiratory time—normal for age (adjust in case of air trapping or severe ARDS)

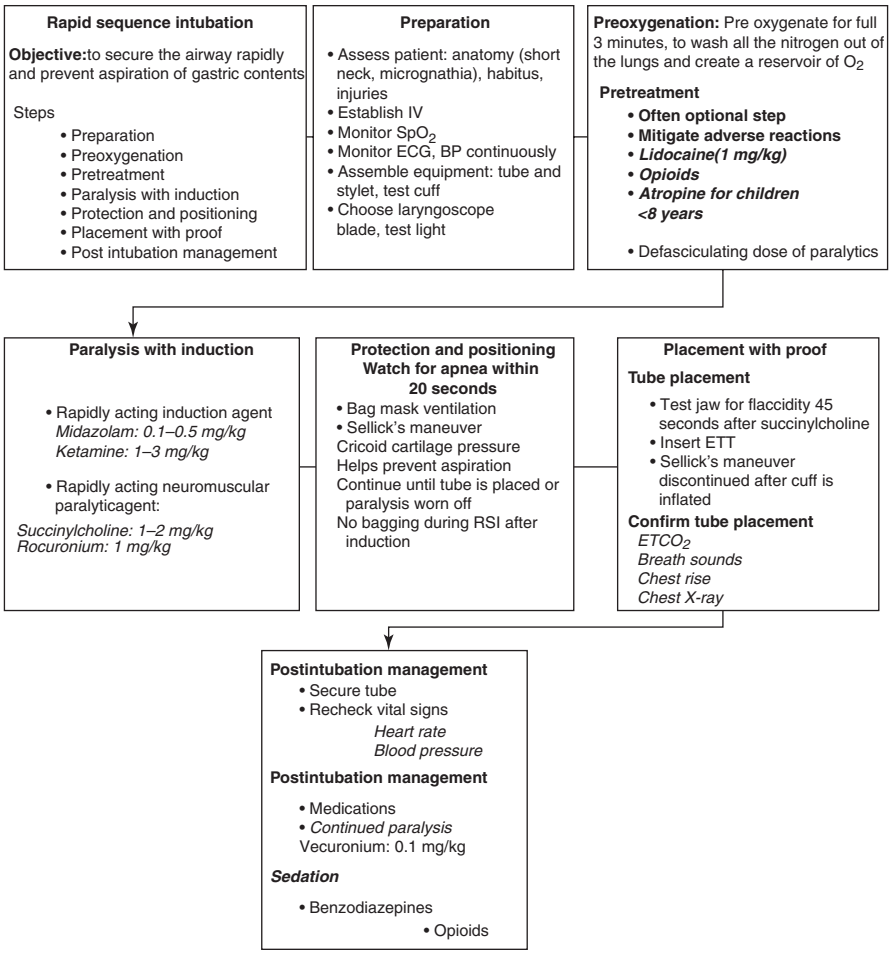

Fig. 33.1 Rapid sequence intubation protocol

- Optimal PEEP—adequate alveolar recruitment so that saturations are maintained at minimum FiO_2 (<0.6) and compliance is best with no hemodynamic compromise
- Respiratory rate—normal for age (adjust if there is air trapping)
- FiO_2—to get good SpO_2 (>90%)

Sedation and Analgesia

- Most patients can be managed with adequate sedation and analgesia without muscle relaxants. Muscle relaxants should never be started without adequate sedation.
- Midazolam and morphine or fentanyl are used for most of the cases. In case of specific scenarios, other agents can be tried.

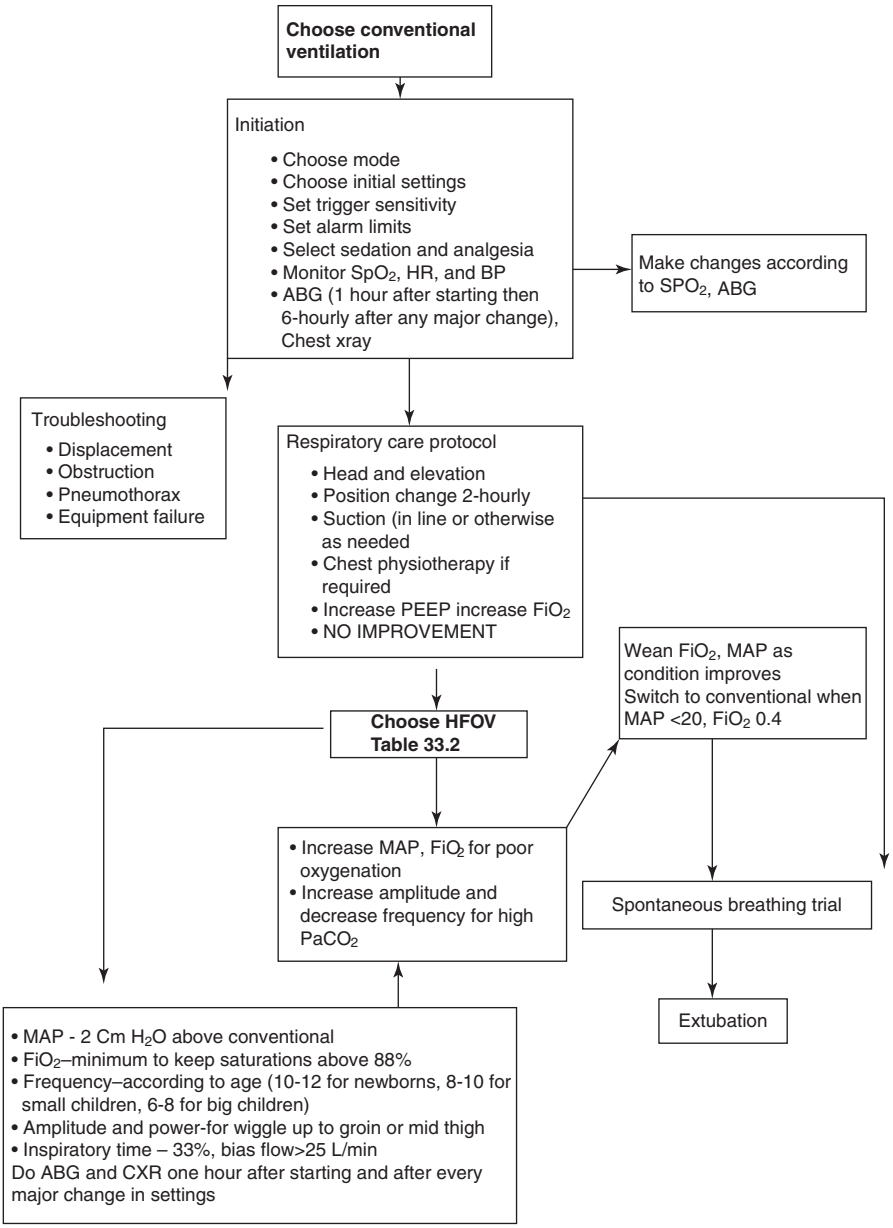

Fig. 33.2 Ventilator management protocol

- Morphine is not preferred in hemodynamic instability and wheezing. Ketamine can be used.
- Midazolam is not preferred in severe hemodynamic instability and liver failure.
- Ketamine is preferred in shock and wheezing. Ketamine is generally not used in raised intracranial pressure.

Step 3: Change Settings According to Arterial Blood Gas

- Poor oxygenation—increase FiO_2, optimize PEEP, increase inspiratory pressure or tidal volume (Vt) if chest rise is not adequate, increase inspiratory time (Ti), and try inverse ratio ventilation if severe ARDS. After PEEP titration Prone positioning may be tried
- High $PaCO_2$—ignore if pH is acceptable (>7.2) unless there is increased intracranial pressure or severe pulmonary hypertension (permissive hypercapnia).
- To decrease $PaCO_2$, increase rate or increase PIP or Vt. In bronchospasm, decrease rate and increase expiratory time to prevent air trapping.
- High PaO_2—decrease FiO_2.
- Low $PaCO_2$—decrease rate and decrease Vt.
- HFOV May be tried after PEEP titration and Prone positioning not working well in patients with refractory hypoxemia

Step 4: Weaning

Ventilatory settings are reduced once the primary pathology or condition that led to ventilation is improving. There are no set protocols for weaning. Different protocols are followed by different institutions. Generally, the following pattern is adopted:

- FiO_2 is weaned first to 0.4, maintaining saturation in acceptable range.
- Mode is changed to Synchronized intermittent mandatory ventilation (SIMV) with pressure support mode or pressure support mode only.
- PEEP is decreased gradually in steps of 2 cmH_2O to 4–5 cmH_2O.
- SIMV rate is decreased to 5–10.
- The patient is reassessed after each change in the settings, and if the oxygen requirement goes up or the patient develops respiratory distress or is hypercarbic on blood gas, weaning process is paused and the support level is increased.

Some patients (especially when the lung is normal or short ventilation for neurological indications) can be directly given a spontaneous breathing trial after stopping sedation and extubated without weaning.

Step 5: Spontaneous Breathing Trial

- Spontaneous breathing trial is done before extubation to assess extubation readiness. It can be done with a T piece after disconnecting ventilator, endotracheal continuous positive airway pressure (CPAP), or minimal pressure support with CPAP.
- Usually the pressure support (PS) level is adjusted to the size of endotracheal tube (ETT) (6 cmH_2O PS for ETT >5 mm, 8 cm for ETT 4–5 mm, and 10 cm for ETT 3–4 mm).

Duration of the trial ranges from 30 min to 2 h. The following are the criteria for terminating a spontaneous breathing trial.

- Inability to maintain gas exchange (needing more than 0.5 FiO_2 for saturations greater than 95%)
- Inability to maintain effective ventilation (measured exhaled tidal volume < 5 mL/kg; $PaCO_2$ > 50 mmHg or increase >10 mmHg above baseline)
- Increased work of breathing (tachypnea or use of accessory muscles or paradoxical breathing pattern)
- Other signs of distress (e.g., diaphoresis, anxiety, rise in heart rate, change in mental status, and hypotension)

If the patient tolerates the spontaneous breathing trial, proceed to extubate.

Step 6: Extubation

The following criteria should be met before extubation:

- Alert or easily arousable
- Presence of airway reflexes, manageable secretions
- Minimal oxygen requirement less than 0.4 and PEEP less than 5 with saturations above 94%
- Good spontaneous tidal volume with minimal pressure support (5–10 above PEEP depending on the tube size) during spontaneous breathing trial
- Nil orally for at least 4 h before extubation
- Hemodynamically stable (dopamine requirement <5 mic/kg/min)
- $PaCO_2$ less than 50 mmHg
- pH 7.3–7.47
- Core temperature below 38.5 °C
- Leak around the endotracheal tube is good but not a prerequisite for extubation
- No major metabolic derangements

Injection dexamethasone (0.2 mg/kg) q6h can be given prior to extubation, the first dose given 12 h before extubation. It can be continued 48 h after extubation. It decreases postextubation stridor.

High-frequency oscillatory ventilation is. not recommended in adults but used in neonates and Pediatric age group if conventional ventilation fails (Table 33.2).

Table 33.2 Indications for high-frequency oscillatory ventilation

Patients requiring mean airway pressure more than 20
Not maintaining saturations with PEEP more than 14, FiO_2 more than 0.6
Oxygenation index more than 16 (oxygenation index = mean airway pressure × FiO_2 × 100/PaO_2)
Consider early use rather than as a rescue therapy once PEEP titration and prone positioning fails

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Acute Severe Asthma

34

Krishan Chugh

A 6-year-old girl developed worsening of her asthma symptoms one early morning. Her mother administered her two puffs of salbutamol with spacer. Not seeing any improvement after 15 min, she gave her two more puffs and moved her to the neighborhood nursing home. At arrival there the pediatrician found her to be dyspnoeic, diaphoretic, and unable to talk in full sentences. Auscultation of the chest revealed B/L ronchi. Her SpO_2 was 90%.

Acute severe asthma is classical example of obstructive airway disease in children. Ventilation perfusion mismatch results in hypoxemia and obstruction being more in expiration causes air trapping and accumulation of CO_2 requiring bronchodilator aerosol therapy, systemically administered anti-inflammatory agents (steroids), and sometimes mechanical ventilation. A protocolized approach to assessment and management is described below.

Step 1: Initial Resuscitation

Assess airway, breathing, and circulation and take resuscitative measures as described in Chap. 23, vol. 2.

Step 2: Assess Severity of the Asthmatic Attack (Table 34.1)

Hypercapnia (hypoventilation) develops more readily in young children than in adults and adolescents

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Table 34.1 Severity of asthma exacerbations

	Mild	Moderate	Severe	Respiratory arrest imminent
Breathing difficulty	On walking	On talking	At rest	
		Infant softer cry	Infant short cry	
		Difficult feeding	Infant stops feeding	
	Can lie down	Prefers sitting	Hunched forward	
Talk in	Sentences	Phrases	Words	
Alertness	May be agitated	Usually agitated	Usually agitated	Drowsy or confused
Respiratory rate	Increased	Increased	Increased	
	Normal rate of breathing in awake children:			
	Age	Normal rate		
	<2 months	<60/min		
	2–12 months	<50/min		
	1–5 years	<40/min		
	6–8 years	<30/min		
Accessory muscles and suprasternal retractions	Usually present	Usually present	Usually present	Paradoxical thoracoabdominal movement
Wheeze	Moderate, often only end expiratory	Loud	Usually loud	Absence of wheeze
Pulse/min	Mild tachycardia	Moderate tachycardia	Severe tachycardia	Bradycardia
	Guide to limits of normal pulse rate in children:			
	Age	Normal rate		
	2–12 months	<160/min		
	1–2 years	<120/min		
	2–8 years	<110/min		
Pulsus paradoxus (can be observed on SpO_2 monitor waveform)	Absent	May be present	Often present	Absence suggests respiratory muscle fatigue
	<10 mmHg	10–20 mmHg	20–40 mmHg	
Peak expiratory flow rate (PEFR)	>80% predicted or personal best	~60–80% predicted or personal best	<60% predicted or personal best or response	
After initial bronchodilator effect lasts	>2 h	>2 h	<2 h	
PaO_2 (on air)	Normal	>60 mmHg	<60 mmHg	Possible cyanosis
and/or $PaCO_2$	<45 mmHg	<45 mmHg	>45 mmHg	Possible respiratory failure
SaO_2% (on air)	>95%	91–95%	<90%	

- The rapid assessment of a child with status asthmaticus should focus on determining the severity of airway obstruction.
- Wheezing, which reflects turbulent airflow in obstructed airways, is usually equally audible on both hemithoraces. Asymmetric wheezing may imply unilateral atelectasis, pneumothorax, or foreign body. Expiratory wheezing alone is found in mild-to-moderate illness, whereas expiratory plus inspiratory wheezing is present in moderate-to-severe status asthmaticus.
- The silent chest is an ominous sign and may indicate either pneumothorax or the complete absence of airflow due to severe airway obstruction and imminent respiratory failure.
- Blood gas analysis may support the clinical judgment of severity; an increasing level of CO_2 is an ominous sign. During a moderate asthma attack, a capillary blood gas analysis may be sufficient; in patients admitted to an intensive care unit, arterial blood gas analyses should be a routine. Sequential measurements are important as respiratory alkalosis with hypocarbia is common during the early phases of an asthma attack, while normalization and a subsequent increase in the $PaCO_2$ may be important indicators of clinical deterioration. Thus, a normal $PaCO_2$ with even borderline low PaO_2 indicates a phase of rising $PaCO_2$, hence, need for more intensive therapy.
- A chest X-ray may be relevant in search for underlying complications such as pneumonia or air leakages.

Step 3: Review Ongoing Treatment

- Take into consideration the treatment that the child may have received in the past few hours. This helps us in deciding where in the treatment algorithm (Fig. 34.1) we should start. For example, in a child who has received several doses of salbutamol in the past 1 h, it may be futile to begin treatment at the top end of the algorithm.

Step 4: Start Treatment (Fig. 34.1)

- Follow the algorithm for treatment.
- Generally children tolerate repeated doses of salbutamol very well and tachycardia as a side effect is less worrisome.

Step 5: Monitor Closely

- At all stages, the child should be constantly monitored and escalation or de-escalation of therapy should be done accordingly. For example, a child who is showing signs of exhaustion may have to be intubated straightaway even if IV β-agonist or aminophylline has not yet been tried.

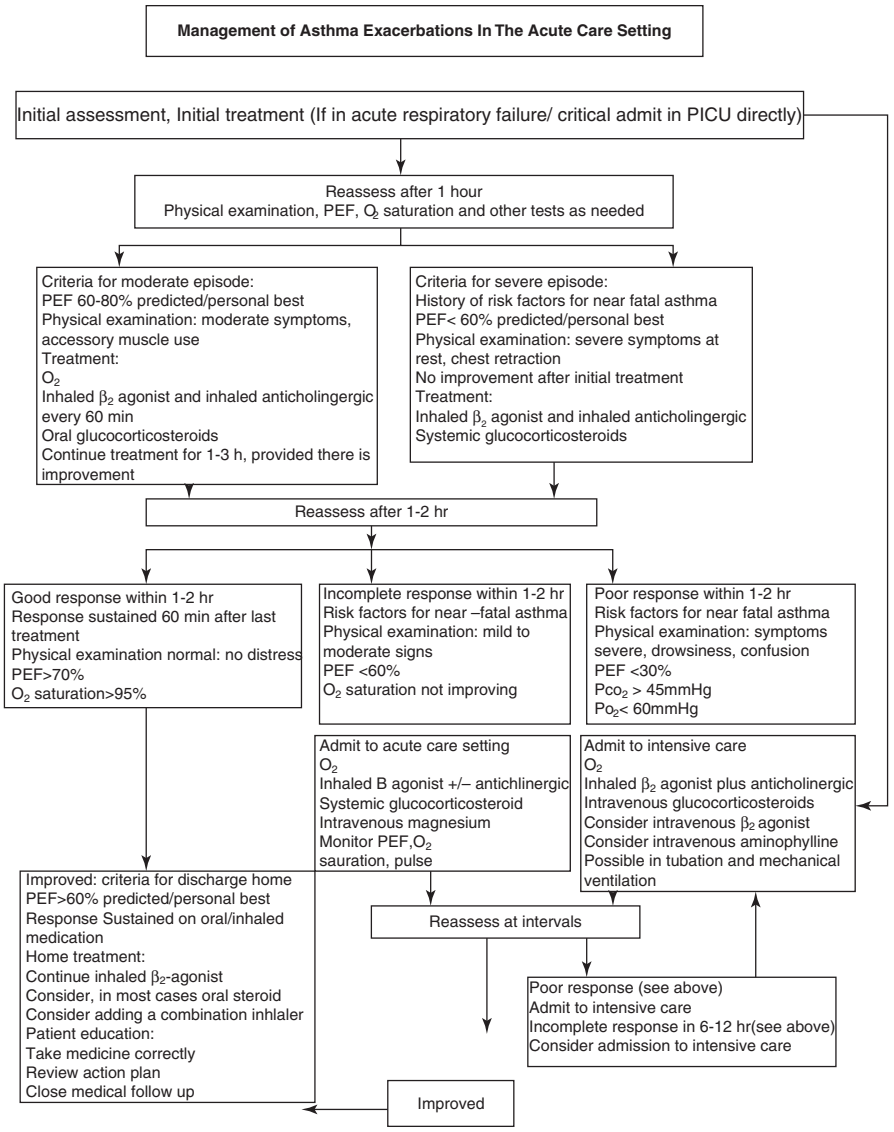

Fig. 34.1 Management of asthma exacerbations in the acute care setting

Step 6: Further Treatment

- Intravenous ketamine can be tried in children who are not improving on intravenous β-agonist, intravenous steroids, and supportive therapy. It is a sedative that has bronchodilator properties. Generally, it is started in the dose of 1 mg/kg/h after a loading dose of 1 mg/kg. The infusion can be increased to 3 mg/kg/h. However, all preparations should have been made for intubation and ventilation before starting IV ketamine.

Step 7: Assess the Need for Intubation and Ventilation

- Generally, decision to intubate and ventilate an asthmatic child is made on clinical grounds.
- Thus, cardiac arrest, respiratory arrest or severe bradypnea, extreme physical exhaustion, and altered sensorium are taken as absolute indications.
- Blood gas analysis and worsening pulsus paradoxus as assessed on the bedside monitors can be additional parameters in making a decision for intubation and ventilation.

Step 8: Initiate Ventilation

- Rapid sequence intubation should be done and avoid overventilation with Ambu bag during preoxygenation.
- Ventilation is started in the controlled mode. Both pressure- and volume-controlled modes (or the combined modes like pressure-regulated volume control) can be used initially. As soon as possible, the child is shifted to assist/synchronized intermittent mandatory ventilation modes. Experience with pressure-support mode in the initial stages of ventilation is very limited in pediatrics.
- Gentle ventilation with a long expiratory time is the recommended strategy.
- Permissive hypoventilation (deliberately tolerating high CO_2) is an accepted strategy to ventilate asthmatic children. Similarly even oxygenation targets are kept in the moderate range.
- Use of graphics in the modern ventilators can facilitate safer ventilation.
- Synchronized abdominal compression has recently been tried as a novel treatment for asthma ventilation in preschool children
- Standard rules of sedation and muscle relaxation are followed with some preferring to use ketamine.
- Noninvasive ventilation for status asthmaticus in children can be tried in fully equipped PICUs where trained and experienced pediatric intensivist is available to monitor the child carefully. In such PICUs a careful trial of High Flow Nasal Cannula (HFNC) can also be given. Temptation to try these much simpler modalities of respiratory support in place of intubation and mechanical ventilation must be avoided in level II PICU as the window of safety is very narrow in such patients and inability to escalate therapy in a timely manner can end in a disaster.

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Status Epilepticus

35

Soonu Udani

A 13-year-old boy with no known seizure disorder was brought to the emergency department with generalized tonic–clonic seizures for the past 30 min. He was unresponsive with a temperature of 99 °F, heart rate 140/min, systolic blood pressure 100 mmHg, respiratory rate 30 breaths/min, and SpO_2 94% on room air. Both pupils were equal and reactive.

Step 1: Identify Status Epilepticus and Resuscitate

- Status epilepticus may be defined as follows:
  - ***A child having a seizure lasting for more than 5 min***
    - A child brought to hospital with a seizure
    - A child having a series of seizures without return to baseline mental status between episodes
- For purposes of quick identification and timely treatment to prevent brain damage, the other definitions used as the working one in practice.
- The initial priority in an ongoing seizure is airway protection. This can be achieved by proper positioning, oral suctioning, and an oral airway device. If necessary, the patient should be intubated.
- Urgent peripheral intravenous access (preferably two) should be established.

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Step 2: Terminate Seizures

- While monitoring heart rate, blood pressure, and respiratory rate, give a benzodiazepine.
- Give lorazepam 0.1 mg/kg, maximum 2 mg, slow IV. The same dose can be given via the intraosseous, per rectal or buccal route.
  Or
- Diazepam or midazolam (MDZ) 0.2 mg/kg can be given, slow IV. The same dose can be given by intraosseous route. Rectal dose is 0.3–0.5 mg/kg.
- Respiratory depression or hypotension can occur, and this needs to be monitored closely.
- Out-of-hospital intranasal or buccal MDZ is an easily available option. The intranasal easy calculation is 1 puff for every 2 kg weight of the current available medication MIDAZIP
- If the seizures do not stop in another 10 min, go to the next step.

Step 3: Treat Resistant Seizure

- Give phenytoin 20 mg/kg IV by slow push over 20 min.
  Or
- Fosphenytoin (20 mg/kg of phenytoin equivalents (PE)) IV by slow push over 5–10 min. This dose can also be given by the intraosseous route.
- If seizures do not stop within 5 min after dose completion, go to next step
- This is also to be used if diazepam is the first benzodiazepine used but not needed if lorazepam is used.
- Phenobarbitone should be given 20 mg/kg IV. It can cause respiratory depression and hypotension, particularly if given with benzodiazepines. If required, secure the airway with endotracheal intubation. This could be the first choice in neonates and infants.
- If seizures continue, then go to step 4—the patient is now in refractory status epilepticus (RSE). One of the discussed drugs could be given depending on the patient's evaluation and availability of resources.
- A general caveat is that it is best to optimize the levels of one drug before adding another, and hence a repeated dose of these may be given.

Step 4: Manage Refractory Status Epilepticus (RSE) 30–45 min Have Passed

- An accelerated protocol can be used here where the step of an additional drug in step 3 is now not advocated as it is deemed a waste of precious time and the drugs in step 4 are given together. i.e. VPA or LEV + MDZ infusion started simultaneously

Step 4.

- IV valproic acid (VPA) 30–35 mg/kg diluted with normal saline is administered over 20 min as profound hypotension can occur.
- Levetiracetam (LEV) at a dose of 30–35 mg/kg loading infusion and then 10 mg/kg 12-hourly can also be tried where intubation and ventilation need to be deferred for transport.

However, by now an hour may have passed and the clock is ticking, so if seizures are not aborted, coma-producing therapies need to be started**.**

Transfer to a center capable of long-term life support is needed as the respiratory depression and hemodynamic instability is unpredictable and varies from patient to patient.

- *Midazolam (MDZ) infusion*
  - A loading dose of 0.2 mg/kg is followed by infusion of 2–6 mcg/kg/min. MDZ 3 mg/kg added to 50 mL normal saline when given 1 mL/kg will deliver 1 mcg/kg/min.
  - Start at low dose and increase by 1–2 mcg/kg/min every 15 min until control is achieved.
  - Maximum rate, 20–22 mcg/kg/min, is recommended or till hemodynamic instability is a problem to manage.
  - Once control is achieved, maintain the same dose for 24 h and then wean by 1 mcg/kg/min every 2–3 h.

If in 24 h the seizures have not stopped, the child is now in super refractory status epilepticus (SRSE) and needs advanced medication as well as advanced neuromonitoring and hemodynamic monitoring and support.

- Propofol: Start with 2–4 mg/kg bolus and then 1–5 mg/kg/h. This is not recommended for children younger than 12 years. Approval for this drug is for usage for 12 h only, so informed consent before usage is advised. (Vigilance for the propofol infusion syndrome is required).
- Thiopentone infusion (cautionary warning for non-intensivists)
  - This general anesthesia drug is reserved for super refractory status epilepticus (SRSE).
  - The patient should be intubated and ventilated prior to starting the infusion, and inotropes should be put on standby.
  - Invasive BP monitoring and real-time EEG monitoring will be needed, at least intermittently if not continuously.
  - A separate IV line is needed. The loading dose is 3–5 mg/kg slowly immediately, followed by an infusion of 1–5 mg/kg/min.

  - Hemodynamic support in terms of extra fluids, vasopressors, and inotropes may be required. Hence, this needs to be done within a fully equipped PICU.
  - Burst suppression with 6–8 bursts/min is the target, and hence it should be done with EEG monitoring.

Step 5: Anesthetic Agents

- Once this stage is reached, the mortality and morbidity of refractory status epilepticus is more than 50%.
- These agents need to be delivered through a proper circuit and monitoring done by an anesthetist who understands the drug.
- Aborting the seizures is usually easy, but maintenance and survival are a universal issue.
- In addition to these drugs, oral drugs like topiramate can be started. Other drugs that have been tried with success are as follows:
  - Give lidocaine 1.5–2 mg/kg IV over 2 min and then give a drip at 3–4 mg/min—same class of drugs as phenytoin and an excellent membrane stabilizer. Neonatal studies have shown this drug to be effective.
  - MDZ infusion as in older children can also be used in neonates because the same principles of quick resolution apply.
  - Pyridoxine (vitamin B6) should be given to all neonates and infants with resistant seizures (B6-responsive seizures). Dose is 100 mg IV.
  - Steroids for autoimmune encephalitis, ketogenic diet as an adjunct need to be considered

Step 6: Tapering of Infusion

- Tapering of any infusion should only be done after complete electrical seizure freedom for at least more than 24 h.
- Very gradual tapering should be done as seizures will return and will often be nonconvulsive and only be detected by EEG monitoring.
- The most toxic drug or last introduced should be removed first.
- Hence, long-term agents should be on board and all levels are well maintained before new drugs are added or tapering is begun
- An algorithm for control of seizure is described in Fig. 35.1

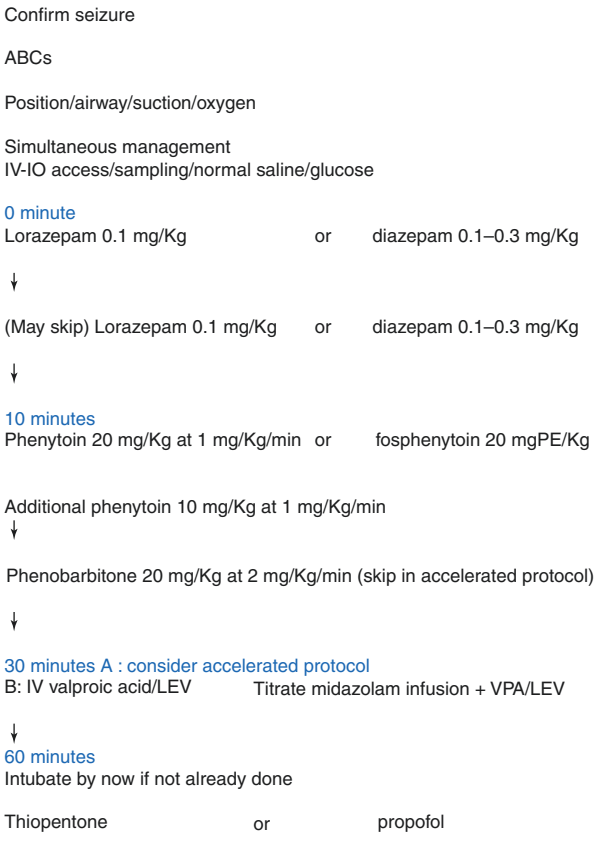

Fig. 35.1 Algorithm for seizure control

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Sepsis and Septic Shock

36

Praveen Khilnani

A 2-year-old boy was brought to the emergency department with lethargy, poor feeding, fever for the past 24 hours, cold extremities, mild respiratory distress for the past 3 h, and no urine output for the past 8 h. He was lethargic but arousable. His rectal temperature was 104 °F, with heart rate 170/min, blood pressure 60 mmHg, respiratory rate 45 breaths/min, and SpO_2 92% at room air. Capillary refill time was 5 s, and extremities were cold with palpable but feeble pulses.

Sepsis is life-threatening organ dysfunction due to a dysregulated host response to infection. Sepsis clinical criteria: organ dysfunction is defined as an increase of 2 points or more in the Sequential Organ Failure Assessment (SOFA) score.Though SOFA score may not be frequently done in pediatrics and hypotension is a late sign of shock, therefore Sepsis 3 definition may miss early septic shock in children. This chapter describes the systematic step-by-step management of sepsis and septic shock in the case described above.

Step 1: Recognition Bundle

- This includes fast recognition and action done almost simultaneously (Table 36.1)
- Shock should be clinically diagnosed before hypotension occurs by clinical signs, which include the following:
  - Hypothermia or hyperthermia
  - Altered mental status
  - Peripheral vasodilation (warm shock) or vasoconstriction with capillary refill more than 2 s (cold shock)
  - Tachycardia
  - Tachypnea out of range for age and level of fever or anxiety

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Table 36.1 Recognition bundle

Zero minutes
Recognize decreased mental status and perfusion
Maintain and establish vascular access—Use intraosseous if IV fails in 90 s
5–15 min: Push 20 mL/kg normal saline/colloid × 3 up to 60 mL/kg
Assess between each push
Correct hypoglycemia and hypocalcemia

Step 2: Resuscitation Bundle

- There should be no time wasted in gaining vascular access. If access is not easily obtained in about 90 s, the interosseous route is a must, as almost everything can go in by that route including inotropes.
- Because mortality goes up with delay in time to inotrope drug use, now it is recommended to use the peripheral line for inotropes—dopamine and dobutamine (not vasopressors)—until central access is attained.
- *Optimizing fluids in the first 15 min or as soon as possible*: Pediatric septic shock is associated with severe intravascular volume depletion, and children frequently respond well to aggressive volume resuscitation.
- The continued emphasis is on the first-hour fluid resuscitation, and appropriate inotrope drug therapy is directed to achieve the following goals:
  - Reducing heart rate to the threshold level for age
  - Getting peripheral pulse to match central pulse volume
  - Improving mentation
  - Improving urine output to at least 1 mL/kg/h
  - Reducing clot retraction time to less than 3 s.
  - This assessment for quick check for overload is done after each bolus of fluid.
    - Rapid expansion of the liver span
    - Rales and increased work of breathing
    - Enlargement of the cardiac silhouette on chest X-ray
    - Drop in SPO_2
  - Establish central venous access.
  - Start Epinephrine via peripheral IV
  - Start dopamine 10 mcg/kg/min if epinephrine not available.
  - Establish arterial access.
  - Continue maintenance fluids 4 mL/kg/h and boluses of 0.9% normal saline/colloid as needed.
  - Thirty to sixty minutes have passed—persistent shock: Cold shock titrate epinephrine.
  - Warm shock titrate Norepinephrine.

Scenarios

1. When pediatric patients are normotensive with a low cardiac output (CO) and high systemic vascular resistance (SVR), initial treatment of fluid-refractory patients consists of the use of an inotropic agent such as dobutamine. Fluid-refractory shock is an important defining step.
2. When pediatric patients are hypotensive with a low CO and high SVR (cold shock), EPI (epinephrine) is started at a dose of 0.1 μg/kg and titrated to effect. When BP improves, an inodilator (dobutamine, milrinone, and nitroglycerine) is added to improve tissue perfusion. This can be done using the same clinical parameters described above or additional laboratory data such as base excess of more than 5 or increasing lactate levels.
3. When pediatric patients are hypotensive with a high CO and low SVR (warm shock), then norepinephrine is the vasopressor of choice. Since the pulse pressure is wide and diastolic pressures are usually low, the need is to increase the mean arterial pressure (MAP). Here, a vasodilator can be added.

There is no magic formula for inotrope or fluid titration. The guidelines are there to give a framework for initiating and adding drugs based on clinical examining and parameter readings of central venous pressure (CVP), BP, etc. Many children by now may be on more than three agents including vasopressors and vasodilators.

Step 3: Give Antibiotics As Soon As Possible Within the First Hour and Control the Source

- An increased mortality rate due to delay in the administration of an appropriate antibiotic has been clearly shown in several pediatric and adult studies. Therefore, every attempt should be made to get appropriate cultures earlier, but this should not hold up the administration of the drug.
- The choice should be on the basis of the site of infection and local patterns. A broad-spectrum antibiotic like a third-generation cephalosporin should be used. De-escalate antibiotics once the culture results are available.
- Along with this, there must be an active search for a source of infection, and immediate action for source control should be taken wherever possible.

Step 4: Mechanical Ventilation and Sedation

- There are many reasons to ventilate patients with septic shock. This step should be considered in any patient who is not rapidly stabilized with fluid resuscitation and peripherally administered inotropes.

Step 5: Give Steroids

- If a child is at risk of absolute adrenal insufficiency (e.g., purpura fulminans, congenital adrenal hyperplasia, prior recent steroid exposure as in asthma, or nephrotic syndrome) and remains in shock despite epinephrine or norepinephrine infusion, fluids and inotropes are optimized for an hour (catecholamine-resistant shock) then hydrocortisone can be administered.
- Hydrocortisone may be administered as an intermittent or continuous infusion at a dosage of 50 mg/m^2/day (2 mg/kg 6-hourly) till hemodynamic stability is achieved.

Step 6: Glucose Control

- Glucose-containing fluids D5 or D10 along with insulin should be used for maintenance, and insulin is titrated to keep blood glucose between 100 and 150 mg/dL. This prevents catabolism as well as the ill effects of hyperglycemia.
- Tight glucose control leads to hypoglycemia and this can be brain damaging, so avoid this and maintain higher glucose value. Hyperglycemia should not be treated by reducing fluid concentrations to glucose-free fluids and removing insulin as there is poor glucose utilization and insulin is needed.

Step 7. Stabilization and Performance Bundles

Stabilization and performance bundles are to be followed as described in recent guidelines. These may be modified and institutionally protocolised.

Summary of guidelines for pediatric Sepsis and septic shock management
Follow Recognition,resuscitation,stabilization and performance bundles

Immediate recognition of shock state from decreased perfusion state and altered mental status.

- Airway, breathing, and circulation approach with high-flow O_2.
- Rapid intraosseous access immediately, if IV is not available.
- Up to 60 mL/kg isotonic nonglucose-containing fluid can be given for 0–15 min.
- Clinical evaluation of improvement of shock by decreasing heart rate, clot retraction time less than 2 s, improved mental status, improved peripheral pulse and central pulse, improved urine output, warmer extremities, and MAP more than 60 mmHg (age-related values).
- Evaluate for fluid overload.
- Rapid decision to start epinephrine (or Dopamine if epinephrine not available) by the peripheral line, not wait for the central line.
- Start appropriate antibiotics as soon as possible in first hour.
- Continue fluid boluses as needed throughout the process—in the first few hours—and continue maintenance fluids.

- Mechanical ventilation with sedation and analgesia.
- If fluid-refractory, dopamine-resistant shock, insert CVP and arterial line.
- Epinephrine for cold shock, norepinephrine for warm shock ± vasodilators.
- Steroids for catecholamine-resistant shock.
- Keep $ScVO_2$ more than 70%, monitor lactate, hemoglobin 10 g/dL and MAP more than 60 mmHg.
- Source control as soon as possible.
- Glucose control with insulin if needed (<150 mg/dL).

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Acute Intracranial Hypertension

37

Sunit Singhi

A 2-year-old unconscious child was brought to the emergency department following fall from the first floor of a building. Initial Glasgow coma score was 6. Both pupils were reactive, blood pressure was 95 mmHg systolic, and heart rate was 120/min. Head CT on admission revealed multiple contusions with cerebral edema. Within 30 min of admission, blood pressure shot up to 130 mmHg, heart rate dropped to 70/min, and the right pupil got dilated.

Acute intracranial hypertension (AIH) is a medical emergency requiring prompt diagnosis and management. Appropriate and timely management strategies result in better patient's outcome in an otherwise severely debilitating or fatal disease process.

Step 1: Initiate Resuscitation

- Airway (A): Secure airway, do rapid sequence intubation, and maintain/induce sedation with midazolam and/or diazepam.
- Breathing (B): Perform hyperventilation using Ambu bag while waiting for intubation, and maintain $PaCO_2$ of 30–35 mmHg.
- Circulation (C): Assess for euvolemia, give normal saline bolus, bring systolic blood pressure between 50th and 90th percentile prior to instituting osmotic therapy.

Step 2: Understand Intracranial Hypertension

A. *Monro–Kellie doctrine*

The pathophysiology and management of AIH is based on the Monro–Kellie doctrine. Intracranial pressure (ICP) is the sum total of pressure exerted by the

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brain tissue (≈80%), blood volume (≈10%), and cerebrospinal fluid (≈10%) in the noncompliant cranial vault.

B. *Normal value*
ICP is not a constant value but is variable with various activities such as coughing, sneezing, and age. Single measurement is not a true representation of ICP; it needs to be measured over the period (24–72 h). Usually normal limits are taken as 5–15 mmHg.

C. *Acute intracranial hypertension*
AIH is a clinical condition defined as the persistent elevation of ICP of more than 20 mmHg for more than 5 min in a patient who is not being stimulated and as a threshold to define intracranial hypertension requiring treatment. Sustained ICP values of more than 40 mmHg indicate severe, life-threatening intracranial hypertension.

- An algorithmic approach to management of ICP (Fig. 37.1) helps put things into perspective so that all aspects of care are attended to.

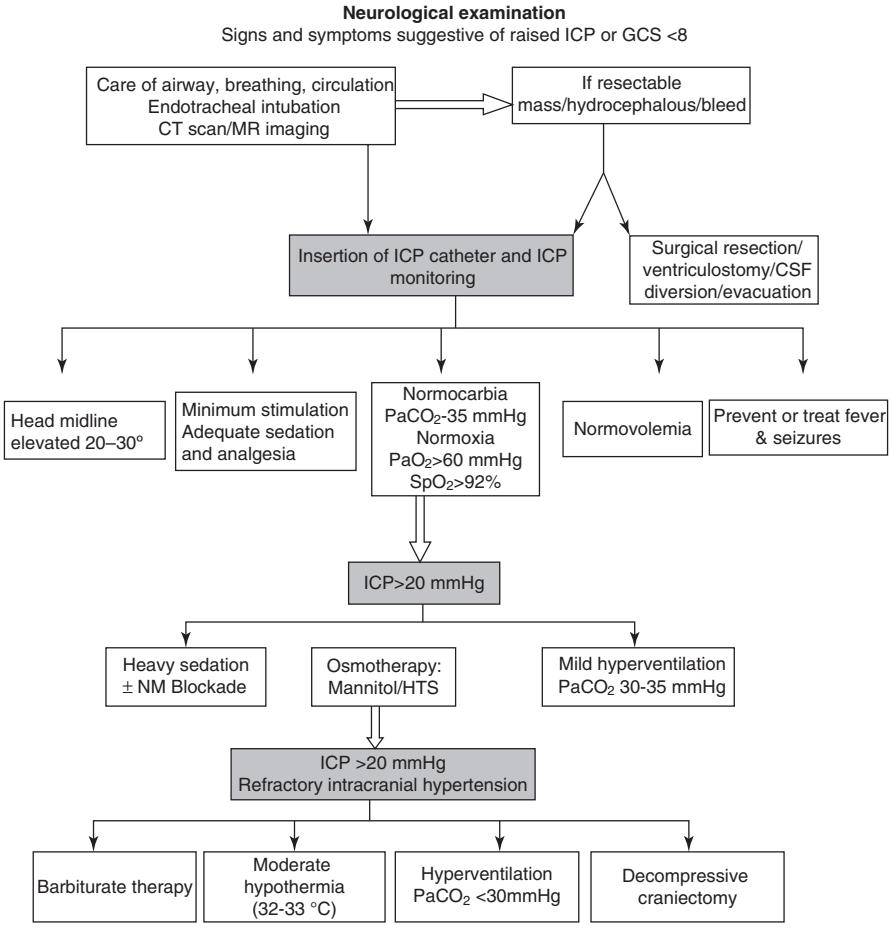

Fig. 37.1 An approach to the management of intracranial hypertension. *ICP* Intracranial pressure, *GCS* Glasgow coma score, *HTS* hypertonic saline

Step 3: Management Goal and General Management

The primary goal is to prevent herniation and maintain cerebral perfusion by elevating the blood pressure to upper limits of normal, prevention of spikes of raised ICP; by reducing the ICP to less than 20; and decreasing cerebral metabolic rate, in that order.

- Head in midline and elevated to 30° (to ensure smooth jugular venous outflow)
- Keep temperature below 38 °C (round-the-clock oral acetaminophen 15 mg/kg 6 hourly if needed).
- Maximize oxygenation and ventilation:maintain Normoxia (PaO_2 80–120 mmHg and SpO_2 > 90%) and normocarbia ($PaCO_2$ 35–40 mmHg).
  Maintain systolic blood pressure and mean arterial pressure (MAP) up to 90th centile to keep cerebral perfusion pressure (CPP) around 55–60 mmHg.

$$\text{CPP} = \text{MAP} - \text{ICP}; \text{MAP} = 1/3\text{rd systolic pressure} + 2/3\text{rd diastolic pressure}$$

- Avoid noxious and painful stimuli that aggravate or precipitate elevated ICP.
- Adequate sedation–analgesia.
- Glucose control—keep blood glucose between 80 and 140 mg/dL.
- Seizure prophylaxis (Phenytoin 20 mg/kg loading, then 5–8 mg/kg/day), for patients at high risk.
- Nutrition—enteral (preferred) to be started within 72 h.

Step 4: Start First-Tier ICP-Specific Treatments

- Ventilate to normocarbia (PCO_2 35 mmHg).
- Sedation and pharmacologic paralysis.
- Hyperventilate to $PaCO_2$ of 30–35 mmHg (moderate and transient only, do not prolong, >6 h, and no prophylactic hyperventilation).
- Increase MAP.
- Mannitol infusion (0.25–1 g/kg IV bolus if ICP >20; serum osmolality not >320 mOsmol/kg).
- Saline infusion (3%) (loading 10 mL/kg; 0.1–1 mL/kg/h infusion; serum osmolality not >360 mOsmol/kg).
- Consider ventriculostomy—drain 3–5 mL cerebrospinal fluid.

Step 5: Consider Second-Tier Therapy if ICP Is Persistently High

- Barbiturates coma (thiopental loading 1–5 mg/kg IV; if complete response [ICP <20 mmHg], return to first-tier agents or repeat bolus doses as necessary; if incomplete response [ICP >20 mmHg but reduction <25%], start IV 1–5 mg/kg/h infusion or until burst suppression EEG pattern at 1–2 bursts/min).

- Moderate hypothermia (32–34 °C with surface or endovascular cooling method for 24–72 h, followed by passive rewarming over 12–24 h.

Step 6: Consider Third-Tier Therapy

- Decompressive craniectomy or temporal lobectomy (if medical AIH management has failed but the patient does not have overt herniation syndrome yet).
- Hyperventilation for acutely symptomatic patients may be lifesaving.
- Two osmotic agents are currently in use: mannitol and hypertonic saline (3%).
- Induced hypothermia is effective in reducing ICP by suppressing all cerebral metabolic activities.

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Multiorgan Failure

38

Anitha Janjanam and Sajith Kesavan

A 1-year-old infant was admitted to pediatric intensive care unit (PICU) with fever, shock, and lethargy. After administering fluid boluses and starting on inotropes, he was intubated and shifted to PICU. Investigations showed leukocytosis and thrombocytopenia with severe metabolic acidosis. Within 6 h of admission, urine output decreased, and he started bleeding from the nasogastric tube. He had persistent tachycardia with cold extremities. Investigations showed persistent metabolic acidosis, elevated liver enzymes, and severe coagulopathy (both prothrombin and partial thromboplastin time were prolonged) with rising serum creatinine.

Multiple organ failure (MOF) defined as dysfunction of more than two organs, is quite frequently seen in the PICU and is associated with high mortality. Mortality increases with increasing number of organs involved. Early identification and appropriate management involving multiorgan support improves outcome in these patients.

Step 1: Initial Resuscitation

- This involves securing airway, fluid resuscitation,Inotropic and vasopressor support, and lung protective mechanical ventilation, sending cultures and antibiotics at earliest and target age appropriate blood pressures and heart rates.

Step 2: Assess Renal Function: Identify AKI

- AKI is characterized by decline in GFR and resultant altered fluid, electrolyte and acid base homeostasis.

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Table 38.1 Modified pediatric RIFLE criteria

	Serum creatinine criteria	Urine output criteria
Risk	eCCL decreased by 25%	Urine output <0.5 mL/kg/h × 8 h
Injury	eCCL decreased by 50%	Urine output <0.5 mL/kg/h × 16 h
Failure	eCCL decreased by 75% or eCCL <35 mL/min/1.73 m^2	Urine output <0.3 mL/kg/h × 24 h or anuria × 12 h
Loss	Persistent failure (>4 weeks)	
End-stage kidney disease	End-stage kidney disease (>3 months)	

- AKI in children is defined and staged commonly by modified pediatric RIFLE criteria with three classes of increasing severity i.e. Risk, Injury, Failure and two outcome classes (Table 38.1).

eCCL—**estimated creatinine clearance (assessment of GFR)**

- eCCL is derived from modified Bedside Schwartz formula–

$$\frac{0.431 \times \text{height in cm}}{\text{Se.creatinine in mg / dL}}$$

- This formula uses 0.431 as the constant (k) for all children below 13 years, irrespective of age and sex.
  - *Previous Schwartz formula overestimates the GFR as the creatinine estimation now is enzymatically determined and not the Jaffe method based on which the old formula was devised.*
- Schwartz formula is not accurate in a sick child with rapidly changing physiological status. Measuring creatinine clearance directly by using the following formula is a better estimate of GFR:

$$\frac{\text{urine creatinine} \times \text{volume of urine in mL / min}}{\text{plasma creatinine}} \times \frac{1.73}{\text{body surface area in m}^2}$$

- Baseline eCCL is taken as normal age specific GFR or the child's previous baseline value.

$$\text{Term infants} - 15 - 40\,\text{mL / min/ 1.73 m}^2$$

- eCCL or urine output or both are considered, classification based on the worst parameter.
- Other criterias include the AKIN (Acute kidney Injury Network) and the more recent KDIGO criteria (Kidney Disease: Improving Global Outcomes), both based on increase in serum creatinine and urine output.
- A combination of elevated urine and serum Biomarkers like NGAL, Cystatin C, Interleukin 18, Kidney Injury Molecule-1, L-FABP, NAG are gaining significance, with high sensitivity for early detection of AKI, evidenced by studies among children post Cardio pulmonary bypass.

Table 38.2 Classification using renal failure indices

	Prerenal	Renal—Tubulo interstitial
Urine sediment	Bland	Broad, brownish granular casts, WBC casts
Urine sodium (mEq/L)	<10	>20
Urine osmolality (mosm/L)	>500	< 350
Fractional excretion of urea	< 35%	>35%
Fractional excretion of Na	<1	>2
Urine specific gravity	>1.020	<1.010

Step 3: Send Investigations

- Urine routine examination
- Renal function test with electrolytes
- Urine sodium
- Urine osmolality
- Urine-specific gravity
- Arterial blood gas analysis
- ECG
- Ultrasound abdomen
- Drug levels—aminoglycosides, paracetamol, vancomycin

Prerenal and Renal AKI

Renal failure can be identified as prerenal or renal based on renal failure indices (Table 38.2).

$$\text{Fractional excretion of Na} = \frac{\text{urine sodium} \times \text{plasma creatinine}}{\text{plasma sodium} \times \text{urine creatinine}} \times 100$$

Step 4: Manage Renal Failure

- Follow oliguria algorithm (Fig. 38.1).

Medical management

- Avoid nephrotoxic drugs.
- Maintain renal perfusion with fluids and inotrope/vasopressors—use fluids judiciously to prevent fluid overload and further ischemic damage to the kidney.
- Adjust drug dosages according to eCCL. Assume GFR to be <10 while on RRT.
- Monitor and manage hyperkalemia medically.
- Severe acidosis can be treated with iv Sodium bicarbonate—watch for fluid overload and hypocalcemia.
- Early nutritional support—high-calorie enteral diet with adequate protein.

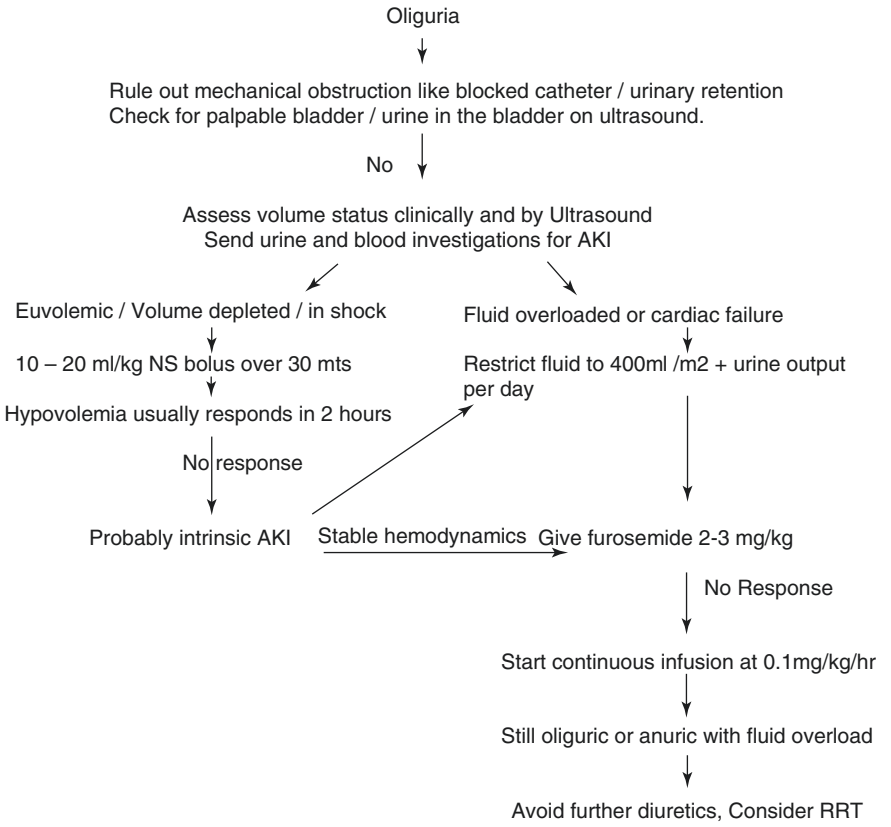

Fig. 38.1 Algorithm for oliguria

Monitor

- Hourly intake output chart, daily weight if possible. Calculate

$$\text{cumulative fluid overload} = \frac{\text{Total fluid input} - \text{Total fluid ouput in litres}}{\text{ICU admission weight in kg}}$$

- Continuous hemodynamic monitoring, sixth hourly electrolytes, once daily RFT.

Step 5: Renal Replacement Therapy

Indications of renal replacement therapy are as follows:

- Oliguria/anuria with fluid overload, refractory to diuretic therapy—Cumulative fluid overload >10%.
- Persistent hyperkalemia refractory to medical treatment

Table 38.3 Types of dialysis

Type	Complexity	Use in hypotension	Dialysis efficiency	Fluid removal	Anticoagulation
Peritoneal dialysis	Low	Yes	Moderate	Moderate	No
Intermittent hemodialysis	Moderate	No	High	Moderate	Yes
CVVH	High	Yes	Moderate	High	Yes
CVVHDF	High	Yes	High	High	Yes

- Severe other dyselectrolytemias
- Severe metabolic acidosis unresponsive to medical management
- Uremic complications like encephalopathy, pericarditis, coagulopathy.

The choice of renal replacement therapy depends on the clinical circumstances, availability of expertise, good vascular access, size of the child and hemodynamic stability.

Types of Dialysis (Table 38.3)
- Peritoneal dialysis
- Intermittent hemodialysis
- Continuous renal replacement therapy (CRRT)—Includes Continuous venovenous hemofiltration (CVVH),Continuous Venovenous Hemodialysis (CVVHD) and Continuous Venovenous hemodiafiltration (CVVHDF).

Peritoneal Dialysis
- Most commonly used mode of RRT in children, best suited for neonates and infants.
- Involves exchange of fluid and solute between peritoneal blood vessels and dialysate filled in the peritoneal cavity.
- Solute clearance occurs by diffusion and solvent drag. Fluid removal is by osmosis.
- Acute PD catheter is placed at the bedside or surgically (Tenckhoff catheter).
- Suitable sizes of catheter include 10, 12, 14F, 45 cm long. Dialysate fluid with varying Dextrose concentrations available (1.5, 2.5, 4.25%).
- Initial prescription—Dialysate volume of 10–20 mL/kg, dwell time of 30–40 min.
- To increase ultrafiltration - Increase dextrose concentration of the dialysate, increase dwell volume up to 30 mL/kg, shorten the dwell time to do more cycles.
- For efficient solute removal—Increase dwell volume and dwell time.
- Avoid instillation of cold dialysate to prevent hypothermia. Hypertonic solutions can cause hyperglycemia.
- Additives for dialysate fluid:
  - Heparin (500 units/L) to prevent catheter blockage.
  - Potassium up to 40 mEq/L in presence of hypokalemia.
  - Bicarbonate in presence of severe acidosis (or use bicarbonate based fluid).

- Suspect catheter kinking, malposition or fibrin plugs in case of failure of inflow or outflow. Mostly a new catheter has to be placed, if simple maneuvers fail.
- Suspect peritonitis in case of cloudy effluent, fever, malfunction. If PD cell count >100 with >50% neutrophils, give intraperitoneal antibiotics.
- Continuous Flow PD—Two catheters in place, one each for in and outflow with the fluid in continuous transit. Achieves higher clearance of solute and fluid.

Vascular access—IHD and CRRT require vascular access, the ideal site being Right Internal Jugular Vein.

Size of dual lumen HD catheter	up to 10 kg	8F
	10–25 kg	10F
	>25 kg	12.5–14F

Intermittent hemodialysis

- Highly efficient for rapid metabolic correction and fluid removal, usually done over 4 h.
- Is best suited for hemodynamically stable children, needing rapid toxin clearance.
- Solute removal is by diffusion, Ultrafiltration by transmembrane pressure gradient.
- Children with multiorgan dysfunction and shock may not tolerate IHD, due to the large extracorporeal blood volume and rapid ultrafiltration, causing hypotension.
- To overcome this, an extension of IHD over longer periods called SLED is being recommended.

SLED: Sustained Low Efficiency Dialysis—Hybrid of IHD and CRRT

- Best cost effective alternative for RRT in critically ill children as it reduces hemodynamic fluctuations of IHD and also obviates the high resource demands of CRRT.
- Uses conventional HD machine and dialyzer at lower UF rates and lesser solute removal, done over 8–10 h daily.
- Priming the circuit with albumin/blood at initiation of dialysis,hiking the dose of vasopressors temporarily,adjusting flow rates will facilitate reasonable RRT in spite of unstable hemodynamics in critically ill children.
- Use of heparin can worsen coagulopathy, regional anticoagulation with citrate containing dialysate is preferred with ionized calcium monitoring.
- Time any PRBC transfusion during dialysis, to remove excess potassium.
- Medications need to be rescheduled as dialysis removes most of them.
- Comparative trials in adults found no difference from CRRT in renal function recovery, fluid removal,mortality or length of ICU stay.

CRRT

- Preferred in hemodynamically unstable critically ill children, in view of the slower flow rates running 24 h, achieving equivalent clearance with less metabolic variation than IHD.
- Enables liberal input /nutrition even in volume overloaded children with accurate Ultrafiltration control, even in the smallest infants.
- Solute clearance is by Convection in CVVH requiring a replacement fluid and by diffusion in CVVHD, needing a dialysate fluid. CVVHDF uses both.
- Ultrafiltration rate should include desired fluid removal, net non CRRT intake and the replacement fluid rate. Typical range is 10–30 mL/kg/h and is adjusted as per the clinical needs, monitoring the weight and cumulative fluid balance.
- Blood flow rate is at least three times the ultrafiltration. A flow of 6–9 mL/kg/min or 8% of circulating blood volume prevents excessive hemoconcentration in the filter.
- Heparin may worsen coagulopathy or cause thrombocytopenia, while Citrate anticoagulation needs close ionized calcium monitoring and infusion.
- Periodic Saline flush (100 mL every 30 min) of the blood filter can safely avoid any anticoagulant (Ultrafiltration rate should include the saline).
- Blood volume in the extracorporeal circuit should be less than 10% of the patient's circulatory volume. Albumin or blood priming of the hemofiltration circuit is necessary in small babies.
- An inline heater in the CRRT machine avoids hypothermia.
  - SCUF—Slow continued ultrafiltration—slower rate of fluid removal only
  - CVVH—Predominantly Volume and additional solute removal
  - CVVHD—Clears mainly small molecules like urea and controlled fluid removal
  - CVVHDF—highly efficient solute and volume removal.

Advances in Pediatric RRT

- **CARPEDIEM—**Cardio-renal pediatric dialysis emergency machine—CRRT machine with low extracorporeal blood volume of <30 mL and accurate ultrafiltration control. Used successfully in <3 kg.
- **NIDUS**—Newcastle Infant dialysis and ultrafiltration system—syringe based system, withdrawing 5–12.5 mL aliquots of blood from a single lumen central vein catheter, passes through dialyzer filter and returns to patient.

Concurrent Management of Hepatic Dysfunction

Step 1: Make a Diagnosis

Consensus statement of the Pediatric Gastroenterology Chapter—Indian Academy of Pediatrics defines pediatric ALF as

- Evidence of liver dysfunction within 8 weeks of onset of symptoms
- Uncorrectable coagulopathy (6–8 h after administration of one dose of parenteral vitamin K) with INR > 1.5 in patients with hepatic encephalopathy or INR > 2 in patients without encephalopathy.
- No evidence of chronic liver disease either at presentation or in the past.

Step 2: Laboratory Evaluation

- Liver function test
  - Bilirubin high in ALF with MODS
  - ALT/AST can be elevated in thousands IU/L (AST is usually more than ALT)
  - Prothrombin time and INR
- Serum electrolytes and renal function tests
- Hourly Blood glucose
- Serum ammonia

Step 3: Treatment

Stop all potentially hepatotoxic drugs and adjust doses accordingly.

Nutrition and metabolic concerns—Early enteral feeding targeting 100–120% calorie and 1–1.5 g/kg/day of protein. Monitor for and treat hypoglycemia, dyselectrolytemia. Avoid hyponatremia and hypokalemia.

Respiratory and Hemodynamic support—Secure Airway for grade 3 and 4 hepatic encephalopathy.

Maintain euvolemia, use normal saline boluses as required. Vasopressors need may go up, use noradrenaline, vasopressin for persistent hypotension. Hydrocortisone may be beneficial.

Infection—Surveillance cultures recommended. Suspect secondary infection in presence of new onset hypotension after a period of stability. Repeat cultures and add antifungal (echinocandin) and vanco/teicoplanin, escalate gram negative cover.

Coagulopathy—Give Vitamin K and Proton pump inhibitor for all patients. Routine FFP not recommended to correct INR.

In case of bleeding or prior to invasive procedures, give FFP, cryo if fibrinogen <100, platelets if <50,000. Recombinant factor VIIa can be tried in patients with refractory bleeding despite FFP, but its expensive.

Hepatic encephalopathy Grade 3 and 4—Watch for cerebral edema clinically and on CT. 3% NaCl infusion to target Sodium at 145–155 can prevent increase in ICP.

For raised ICP:

- Acute management with Mannitol 0.5 g/kg bolus (if renal function normal) and temporary hyperventilation.
- Head in midline and elevated to 30°, adequate sedation and analgesia, Follow normoxia, normothermia, normotension, normoglycemia, normocapnia. ICP monitor may be placed if facilities available, but no consensus exists.

- One trial showed moderate hypothermia as a bridge to liver transplant.
- Treat seizures with phenytoin/benzodiazepine.
- Use Fentanyl or morphine for sedation. Avoid morphine in concomitant renal dysfunction.

Specific therapies

- N Acetyl Cysteine—Can be used in non paracetamol liver failure as well. May not be required in ischemic hepatitis.
- No proven benefit of lactulose, rifaximin, LOLA.

Liver support Devices: MARS, HF VVH—may be used as bridge to liver transplant. No major benefits compared to standard medical therapy.

Liver Transplant

- Refer for liver transplant based on severity and worsening without improvement. Prognostic scores like Kings college criteria, liver injury unit (LIU score) can be used to predict the risk of death or transplant free survival. Persistent INR > is also used as a cut off for liver transplant.
- Liver dysfunction secondary to sepsis recovers with supportive management including correction of shock and treatment with appropriate antibiotics, rarely needing a transplant.

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Part IX

ICU Interventions

Central Line Placement

39

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A 55-year-old diabetic female patient was brought to the emergency department with history of fever with chills and rigors for the past 3 days. She also had altered sensorium for the past few hours. On arrival she was found to have tachycardia and hypotension.

Central line catheterization is a commonly performed procedure in any ICU. Central venous access is a commonly performed procedure with approximately 8% of hospitalized patients requiring central venous access during the course of their hospital stay. It is now recommended to be performed under ultrasound guidance. This is a fairly safe procedure in expert hands.

Step 1: Assess the Need for Central Line Placement

Insert a central line only for patients in whom it is indicated (as mentioned below) after ruling out contraindications (as mentioned in Step 2):

- For appropriate fluid management where peripheral access is difficult to get
  - Severe sepsis and septic shock
  - Low urine output
  - Intraoperative
  - For patients in shock
- Concentrated vasoactive agent administration (e.g. norepinephrine >0.2 mcg/kg/min)

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- Intervention like thrombolysis, venous stenting, cardiac stenting.
- Difficult peripheral vascular access
- Multiple drug administration
- Concentrated electrolytes (e.g., potassium)
- Total parenteral nutrition
- Chemotherapy
- Agents irritating to peripheral veins (e.g. Amiodarone, Phenytoin, mannitol, concentrated potassium)
- Prolonged antibiotic therapy (e.g., endocarditis)
- Temporary hemodialysis
- ECMO
- During cardiopulmonary resuscitation
- Large-bore venous access for rapid administration of fluids
- For hemodynamic monitoring (ScVo2, CVP)
- Temporary transvenous pacing

Step 2: Check for Any Contraindications

There are no absolute contraindications to central line placement. Relative contraindications are as follows:

- Local site infections or burns
- Anatomic abnormalities
- Coagulopathy/Thrombocytopenia: Platelet count/P.Time/INR/APTT: safe levels in which central cannulation can be performed is unclear.
- Thrombocytopenia poses a greater risk than clotting abnormalities.
- No preprocedural correction is needed for Platelet count >20,000, and INR <3.
- Use Ultrasound guidance and experienced operator.

Coagulopathy, corrections needed if platelets <20,000, INR > 3 (ultrasound guidance will help in minimising the risk of bleed and trauma).

Step 3: Choose the Appropriate Site

The central venous cannulation site can be decided on the basis of the patient's requirement and the comorbid conditions:

- Coagulopathy: Prefer—femoral > internal jugular > subclavian
- To decrease risk of infection: Prefer—subclavian > internal jugular > femoral
- Right internal jugular vein cannulation is generally preferred over the left due to the larger diameter of the right-sided vein, its more direct path to the superior vena cava, the lower dome of the right pleura, absence of the thoracic duct, and the relative ease of access for a right-handed operator. Right-sided access is also associated with a lower rate of catheter malposition.

- Right-handed operators often prefer right-sided subclavian access procedures. Right subclavian anatomy carries the theoretical advantage of lower risk of complications due to the lower pleural apex and absence of the thoracic duct. However, right-sided subclavian access is associated with higher rates of catheter malposition and vessel trauma compared with left-sided access. A left-sided access may be preferred when immediate cardiac access is needed (e.g. temporary transvenous pacer placement, pulmonary artery catheter) since the guidewire and catheter are more easily directed into the superior vena cava and right heart.
- Femoral lines are preferred if severe coagulopathy is present, either left or right depending upon the operator.

Step 4: Choose the Appropriate Catheter

- Single-lumen or multilumen catheters*:* The more is the number of lumens, the smaller is their diameter.
  - If rapid fluid infusion is required—as in trauma—single- or double-lumen catheters are preferred.
  - If the number of infusions is substantial, three- or four-lumen catheters are preferred.
  - The infection risk is directly proportional to the number of lumens, so the more the number of lumens, the more is the risk of infection associated with it.
- Antimicrobial-impregnated catheters*:* Can use a chlorhexidine/silver sulfadiazine or minocycline/rifampin-impregnated CVC in patients:
  - When catheter is expected to remain in place for more than 5 days or infection rate is more than 1.6 per 1000 catheter days.
  - If the catheter infection rates are high in the ICU even after successful implementation of a comprehensive strategy to reduce rates of infection
- Tunneled catheters*:* Tunneling is ineffective in decreasing infection rate in short-term CVCs.

Step 5: Know the Relevant Anatomy

- *The subclavian vein:* It crosses under the clavicle just medial to the midclavicular point. It lies underneath the clavicle at the insertion of the lateral head of the sternocleidomastoid on the clavicle. It is separated from the subclavian artery by the anterior scalene muscle, which lies deep to the vein. The vein lies in proximity to the dome of the pleura.
- *The internal jugular vein:* It is located in the neck at the apex of the triangle formed by the two heads of the sternocleidomastoid muscle and the clavicle. At the apex, the carotid artery is medial and posterior to the vein.
- *The femoral vein:* It lies 1–1.5 cm medial to the femoral artery at the inguinal ligament. If the inguinal ligament cannot be identified as in obese patients, then the femoral artery lies approximately at the centre of the pubic tubercle and the anterior superior iliac spine.

Step 6: Take Informed Consent

- Communicate with the patient or their surrogate.
- Explain the detailed procedure, the benefit, the risk and the alternative in the language they understand.
- Reply to all the queries and concerns.
- Document the consent and get it signed.

Have a peripheral venous access before attempting central cannulation except probably during cardiopulmonary resuscitation.

Step 7: Keep All Equipment Ready for Cannulation and Pressure Transducing System

- Turn up the volume on the monitor so that it can be heard.
- ECG, pulse oximetry and BP monitoring instruments.
- Material for sterile preparation—cap, mask, sterile gown, gloves and drapes(full body length).
- 2% chlorhexidine with alcohol.
- Shoulder roll.
- A 25-gauge needle and a syringe with 2% lignocaine.
- Sterile saline flush.
- A sterile cannulation set with CVCs, a guidewire, and a locator needle with the syringe.
- A needle holder with suture material.
- Sterile dressing.
- The pressure transducing system.

Step 8: Set Up the Pressure Transducing System

This consists of a pressure transducing assembly with a flushing system. Details have been discussed in Chap. 40, vol. 2.

Step 9: Central Line Placement

- Wear a cap and a mask.
- Wash hands with alcohol-based hand rub for 3–5 min and minimum three applications.
- Put on a sterile gown and gloves.
- Clean the skin of the patient with 2% chlorhexidine in alcohol preparation.
- Give a frictional scrub in a circular manner to at least 10 cm area from the insertion site.

- Do not shave if hair is present, hair clipping preferred.
- Place large sterile drapes over the insertion site. Do not occlude the air supply or field of vision when draping neck areas of conscious patients.
- 1–2% lidocaine for local infiltration before cannulation.
- Use Seldinger technique for cannulation
  - The desired vessel is punctured with a sharp, hollow needle called a trocar.
  - A round-tipped (J-tipped), long guidewire is then advanced through the lumen of the trocar into the vessel.
  - The trocar is withdrawn, leaving the guidewire in the vessel.
  - The tract is dilated with a dilator introduced in rotating motion.
  - A hollow catheter can now be passed over the guidewire into the vessel.
  - The guidewire is then withdrawn and the catheter remains in situ.
  - Never lose control of the guidewire.
  - Left subclavian vein for cardiac access, PA catheter, Defibrillator.
  - Avoid subclavian vein cannulation for dialysis due to risk of thrombosis.
  - Subclavian vein cannulation (Fig. 39.1)

    Position should be Trendelenburg with the head turned toward the opposite side and a shoulder roll placed along the spine.

    Stand on the side of the patient, where the procedure is planned.

    Ensure maximum sterile barrier precautions.

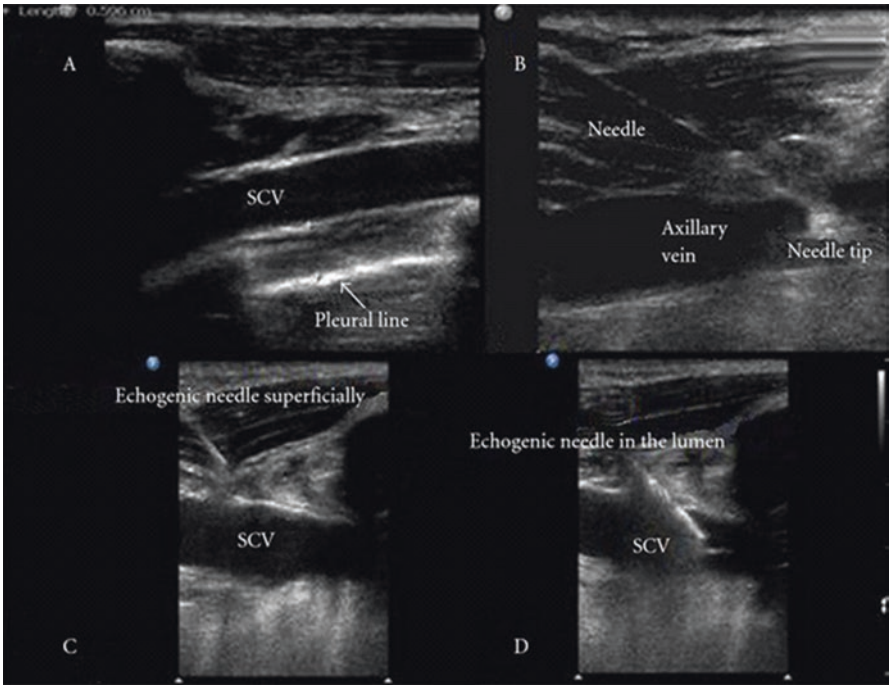

Fig. 39.1 Location of Subclavian vein

Table 39.1 Approaches to subclavian vein cannulation

	Infraclavicular (common)	Supraclavicular
Insertion landmark	2 cm inferior to midportion of the clavicle and walk down the clavicle	Just above the clavicle, lateral to the clavicular head of sternocleidomastoid
Angle with skin	0°	45°
Aim toward	Sternal notch	Contralateral nipple
Depth from skin	Just deep to the clavicle	1–2 cm, just under the clavicle

Locate the landmarks, namely, the clavicle, sternal notch, sternocleidomastoid muscle, and its insertion on the clavicle, lateral end of the clavicle (Table 39.1).
Apply generous local anesthesia.
Insert the needle and syringe (filled with 1–2 mL saline), constantly aspirating for venous blood (Fig. 39.1).
If the rapid flush of blood does not appear during insertion of the needle, gradually withdraw the needle constantly aspirating. Blood may now appear.
If the first attempt is unsuccessful, then withdraw the needle up to the skin and reposition the needle.
Cannulate the vein using Seldinger technique as described above.
Ensure backflow in all ports and flush all the ports.
Ensure local hemostasis.
Fix the catheter appropriately.
Apply sterile dressing.

- *Internal jugular vein* cannulation (Right IJV preferred due to risk of malposition)
  - Position should be Trendelenburg with the head turned toward the opposite side.
  - Stand at the head end of the patient.
  - Feel for the carotid and always keep it under your fingers.
  - Insert the needle at the following landmark and cannulate in a similar manner to subclavian vein (Table 39.2 and Fig. 39.2).
  - It is preferable to first locate the vein with a 25-gauge needle (finder needle) and then puncture with the larger needle.
  - Cannulate using Seldinger technique.
  - Obtain the chest X-ray after cannulation.
- *Femoral vein cannulation* (Fig. 39.3)
  - Position should be supine with the leg slightly abducted and externally rotated.
  - Stand on the side of the patient.
  - Insert the needle 45° angle to the skin at a point 1–1.5 cm medial to the femoral arterial pulsation and about 2–3 cm below the inguinal ligament.

Table 39.2 Approaches to the internal jugular vein (Fig. 39.2)

	Central	Anterior	Posterior
Insertion landmark	Apex of the triangle formed in the neck by the two heads of the sternocleidomastoid muscle and the clavicle[a]	Medial edge of the sternocleidomastoid muscle at level of thyroid cartilage	Lateral edge of sternocleidomastoid muscle, one-third of the way from the clavicle to the mastoid process
Angle with skin	45°	45°	30–45°, dive under the border of the sternocleidomastoid muscle
Aim toward	Ipsilateral nipple	Ipsilateral nipple	Sternal notch
Depth from skin	Within 3 cm	Within 3 cm	Within 5 cm

[a]If the vein is not encountered, then enter the skin slightly more medially and retry (Fig. 39.2)

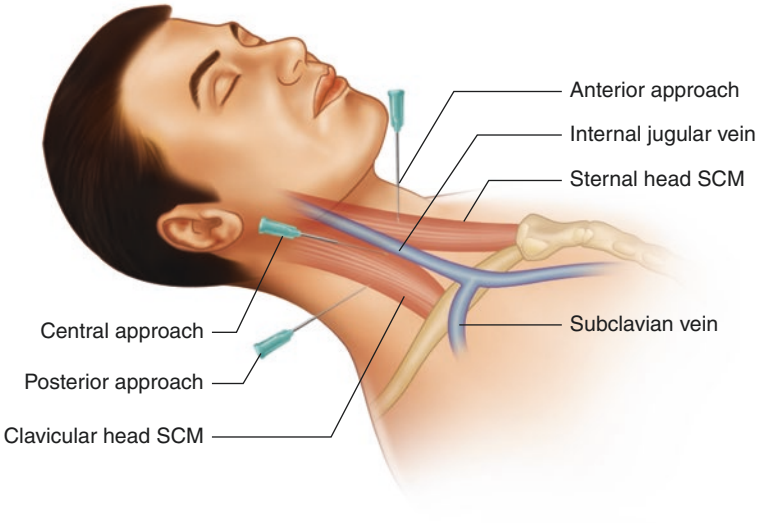

Fig. 39.2 Approaches to the internal jugular vein

  - Direct the needle cephalad.
  - Cannulate using Seldinger technique.
- *Ultrasound use for vascular access*
  - *Advantages*

    Fewer complications
    Fewer attempts for successful cannulation
    Fewer failed procedure
    Shorter time for procedure (can be used in emergency situations)
    Can be used in patient with contraindication to blind technique; patient with coagulopathy

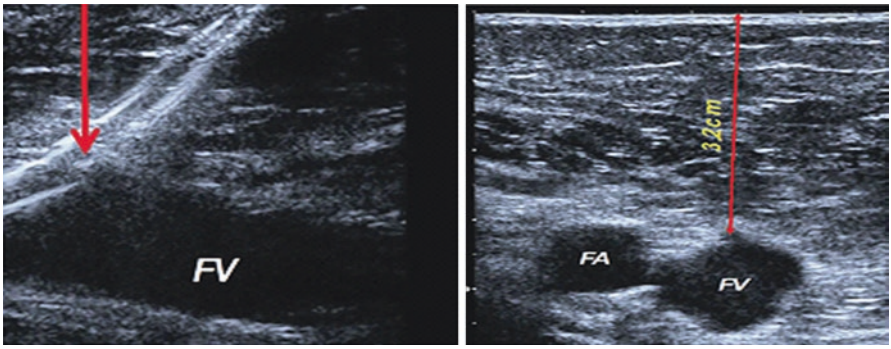

Fig. 39.3 Short and long axis femoral vein

Can be used in "difficult access" category; obesity, short neck, swollen neck, burns/postradiotherapy/postsurgical contracture, etc.
Decrease need of postprocedure radiological confirmation

– *B mode ultrasound*
  B mode ultrasound allows for detailed evaluation of vascular anatomy.
– *Transducer selection*
  For central venous cannulation, high-frequency transducer (5–7 MHz) is ideal. Though in obese patients you may require low-frequency transducer.
– *Technique*
  USG guidance can be:
  • Static guidance: better than landmark approach and inferior to dynamic guidance. USG is used to localize the venipuncture site.
  • Dynamic guidance: here the procedure is performed under real-time guidance, i.e., while doing the puncture, needle is seen puncturing the vessel wall, however more difficult clinically.
– *View*
  Transverse view: here cross section view of vessel is obtained.
  Longitudinal view: here longitudinal view of the vessel is obtained.
– *Method of orientation*
  The transducer has an identification mark on one side which corresponds to mark displayed on one side of image, or alternatively finger can be rubbed on one side of transducer surface to produce an image and confirm orientation.
– *Procedure IJV (Figs. 39.4 and 39.5)*
  Position the patient in supine Trendelenburg position.
  Turn the head to other side.
  Identify the landmark and select the site of puncture.
  Place the USG machine on ipsilateral side.
  Confirm the site puncture with ultrasound.
  Use transverse and longitudinal view to identify the structure around the vein.

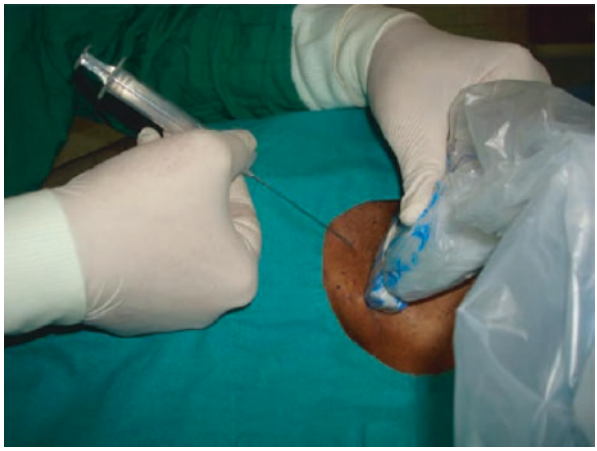

Fig. 39.4 Central line cannulation under USG guidance

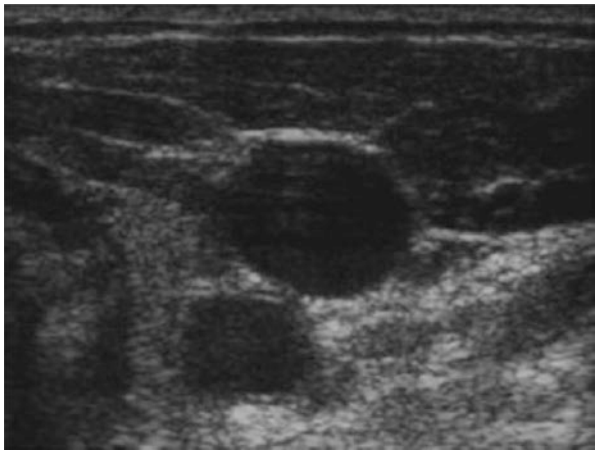

Fig. 39.5 Ultasonographic transverse view of internal jugular vein (*above*) and common carotid artery (*below*)

Can use Doppler to differentiate between vein and artery (depending on the flow velocity).
Identify if there is any thrombus inside the vein
The procedure should be performed under strict aseptic protocol (as described).
Skin is prepared as described.
The assistant holds the transducer and applies ultrasound gel over it.
A sterile sheath (camera cover; used in laparoscopy) is placed on the sterile field.
The operator takes the transducer from the assistant, ensuring that the transducer is covered in the sterile sheath. To maintain sterility, sterile sheath is also stretched over the cord. Then apply band available with the sheath over the transducer to secure the sheath.
Reconfirm the site of puncture. Can apply chlorhexidine over the transducer if image is not clear.

Ensure that the vessel to be punctured is in the center of screen so that the vessel is lying just deep to the center of transducer.
A dummy poke can be done by laying the needle on the skin surface and then pressure is applied near the tip of the needle, and visualize acoustic disturbance in the subcutaneous tissue due to this to ensure that it is positioned directly over the needle.
Perform the skin puncture proximal to transducer, and while puncturing the subcutaneous tissue, ensure that the needle tip is seen advancing. If the tip is not seen, move the probe along the axis of the vein.
Advance the needle further and visualize the needle tip entering the vessel lumen. Aspirate with the syringe to confirm the flash of blood.
Reconfirm the needle position on the ultrasound.
Now keep the probe aside in sterile environment.
Proceed as before with placement of guidewire (Seldinger technique).
Once the line is placed, reconfirm the position of line with the transducer by scanning distally.
Examine with the probe for any pneumothorax.

– *Disadvantages*
  Cost and maintenance of equipment
  Special USG training for operator
  Difficulty to maintain sterility during procedure

Step 10: Check the Post-Central-Line Chest X-ray

The chest X-ray should be done after a subclavian and internal jugular cannulation. The following points should be noted in the X-ray:

- Catheter tip location
  – Catheter tips located within the heart or below the pericardial reflection of the superior vena cava increase the risk of cardiac perforation and fatal cardiac tamponade.
  – Ideally, the catheter tip should lie within the superior vena cava, parallel to the vessel walls, and be positioned below the inferior border of the clavicle and above the level of the third rib, the T4 to T5 interspace or the tracheal carina.
- Pneumothorax
- Pleural fluid/hemothorax
- Connecting with the transducer differentiate venous vs. arterial cannulation.
- Position can be confirmed by Bedside USG,TEE or newer techniques like Endocavitatory electrocardiography.

Step 11: Remove the Line

- As soon as it is not required
- Induration, redness or frank pus discharge from insertion site

- Suspected or confirmed catheter-related infection
- Catheter occlusion/thrombosis
- Vascular erosion caused by the catheter

Step 12: Manage Complications

- *Mechanical complications* (Table 39.3)
  - Never force the guidewire or the catheter; it may cause rupture of the vessel or injury to nearby structures.
  - Do not overdilate—dilating the skin and subcutaneous tissue may be enough.
  - During internal jugular vein and femoral vein puncture, always keep one hand over the artery to prevent arterial puncture.
  - Never lose control of the guidewire, and hold it in one hand.
  - When there is increased risk of bleeding, internal jugular vein route is preferable (with ultrasound guidance).

Table 39.3 Management of mechanical complication

Complication		Management
I. Vascular		
1.	Arterial puncture	Press the artery for at least 15 min or until bleeding stops
2.	Venous bleeding	Compress till bleeding stops
3.	Hematoma	
4.	Hemothorax	Correct coagulopathy, if any; may need drainage if massive
5.	Cardiac tamponade	
	Cardiac perforation	Surgical intervention
6.	Thoracic duct injury, chylothorax	Usually conservative
II. Pneumothorax		Always put an intercostal tube drainage if the patient is on positive-pressure ventilation
		If tension pneumothorax is present, release immediately with the needle thoracocentesis and follow with tube drainage
		Small pneumothorax in the spontaneously breathing patient can be kept under close observation
III. Air embolism		Always position the patient flat if the head is not down while inserting the line
		Never leave the lumen of the catheter uncapped
		If suspected, place the patient the right side up and the head down and aspirate blood mixed with air
IV. Nerve injuries		Conservative management
V. Tracheal/laryngeal injury		May need intubation
VI. Arrhythmia		Pull out the catheter till it is in the superior vena cava
VII. Malposition		May need repositioning

- *Infectious complications*

1. Insertion site infection	Remove the line and treat the infection
2. Catheter related blood stream infection (CRBSI)	
3. Endocarditis	

The following methods are required to prevent infectious complications:

- Use the line only when necessary and remove it as soon as it is not required.
- Use the subclavian vein and avoid femoral or internal jugular vein cannulation.
- Use a CVC with the minimum number of ports or lumens essential.
- Chlorhexidine skin antisepsis—A chlorhexidine solution should be applied by back-and-forth rubbing for at least 30 s. The solution should be allowed to air dry for at least 2 min and should not be wiped or blotted. Chlorhexidine appears preferable to a povidone-iodine solution.
- Use sterile gauze and sterile dressing to cover the catheter site.
- If the patient is diaphoretic or if the site is bleeding or oozing, use a gauze dressing until this is resolved,cap the lumen of port when not required.
- Replace dressings used on short-term CVC sites every 2 days for gauze dressings and every 7 days for transparent dressings.
- Use a chlorhexidine-impregnated sponge dressing if the infection rate is not decreasing despite adherence to basic prevention measures.
- Use a 2% chlorhexidine wash for patients' daily skin cleansing, not the insertion site.
- Evaluate the catheter insertion site daily for signs of infection.
- Use a sutureless securement device.
- Use a chlorhexidine/silver sulfadiazine or minocycline/rifampin-impregnated CVC in patients whose catheter is expected to remain in place for more than 5 days or if the high infection rate is expected.
- Use povidone-iodine antiseptic ointment or bacitracin/polymyxin B ointment at the hemodialysis catheter exit site after catheter insertion and at the end of each dialysis session.
- Do not use guidewire exchanges to replace a catheter suspected of being source of infection.
- Lipid containing Parenteral solution should be infused within 24 h.
- Clean access port with 70% Alcohol,transfuse blood products over not more than 4–5 h.
- Heparin Bonding in catheter used in oncology patients.
- Misinterpretation of data

Suggested Reading

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Ruesch S, Walder B, Tramèr MR. Complications of central venous catheters: internal jugular versus subclavian access—a systematic review. Crit Care Med. 2000;30(2):454–60. *This study shows significantly more arterial punctures with jugular catheters compared with subclavian. There are significantly less malpositions with the jugular access. They further show that the incidence of bloodstream infection is less with subclavian*. Internal jugular vein cannulation using dynamic guidance of ultrasound in the transverse view.

Arterial Catheterization

40

Sheila Nainan Myatra and Mohd Saif Khan

A 65-year-old diabetic male patient was admitted to the ICU with a right lobar pneumonia. He was started on appropriate antibiotic therapy. He was receiving oxygen by a mask at 8 L/min and maintaining an SpO_2 of 94%. His blood pressure was being monitored every 10 min using noninvasive blood pressure measurement. By evening his blood pressure started dropping and reached to 80/50 mmHg at 8 PM, which was not responding to fluid boluses.

Invasive arterial pressure monitoring, using arterial catheterization, is one of the commonly performed bedside procedures in the ICU during shock, when noninvasive blood pressure monitoring becomes unreliable.

Step 1: Assess the Need for Intra-Arterial Pressure Monitoring Indications

- Hemodynamic instability
- Need for frequent blood pressure monitoring during vasopressor therapy
- Need for frequent arterial blood gas analysis
- Assessment of fluid responsiveness using pulse pressure variation or stroke volume variation
- Fine tuning of target blood pressure in management of hypertensive emergencies using vasodilator.

Step 2: Check for Any Contraindications

- Inadequate circulation to the extremity
- Uncontrolled severe coagulopathy

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- Extremities with full-thickness burn or trauma
- Skin infection over the insertion site
- Raynaud's phenomenon
- Multiple punctures or arterial cannulation in the past
- Thromboangiitis obliterans (Buerger's disease)
- Locations near arteriovenous fistulas

Step 3: Choose the Appropriate Site

- The radial artery at the wrist is the most preferred site as the hand has usually good collateral supply, and it is easy to access and maintain.
- Acceptable alternate sites commonly used in adult patients include the femoral, axillary, brachial, and dorsalis pedis arteries.
- All sites are at a risk of ischemic complications due to their small caliber (radial and dorsalis pedis), lack of good collateral supply (brachial and axillary), and presence of atherosclerotic vascular disease (femoral and dorsalis).
- Although infectious complications may be higher with the femoral artery, this may be the only palpable artery amenable to cannulation during severe hypotension. Ultrasound guidance may be useful in locating and cannulating the radial, dorsalis paedis and femoral artery.
- Keeping in mind the above, always choose an artery you are familiar with cannulating.
- When the patient is on high dose vasopressor therapy, the radial arterial site underestimates the intra arterial blood pressure than femoral artrial site, therefore, it is advisable to use femoral arterial site in such scenario to optimally titrate the vasopressors.

Step 4: Check Perfusion of the Extremity

- Peform a **Modified Allen's test:**
  - The patient's hand should be elevated above his or her heart.
  - The patient should clench the fist for 30 s
  - Pressure should be applied to both the radial and the ulnar arteries until distal blood flow is occluded.
  - While maintaining the elevated hand position, the patient should then open the hand. The hand should appear pale and have limited capillary refills.
  - The ulnar arterial pressure should be released (while maintaining enough pressure to occlude the radial artery).
  - The hand should return to normal color within 5–7 s.
  - Delayed return suggests poor collateral circulation
- The test should then be performed on the radial artery circulation in the same manner.

- In the original **Allen's test**, the patient is asked to clench both fists tightly for 1 min, pressure is applied over both radial arteries simultaneously to occlude them. The patient then opens the fingers of both hands, the colour of both are compared. The initial pallor should be replaced quickly by rubor. The test is then repeated by occluding both the ulnar arteries
- There is lack of evidence that these tests can predict hand ischemia after radial artery cannulation. Although the value of these tests has not been established, it may provide some qualitative assessment of collateral circulation.
- In sedated or unconscious patient, to make the interpretation more objective, pulse oximetry, plethysmography, or doppler ultrasound examination may be used along with the **Modified Allen's test**.
- The operator should document the impression of collateral circulation in the procedure note.

Step 5: Keep All Equipment Ready for Arterial Cannulation and Pressure Transduction

- Material for sterile preparation: Chlorhexidine 2% solution, gauze pieces, cap, gown, mask, gloves, sterile drapes
- A wrist board or roller pad under the wrist, 25-gauge needles, and syringes with 1% lidocaine
- An arterial catheters (3 types commonly available)
  - Catheter with needle (cannula over needle)
  - Catheter with needle and a guidewire separately (cannula over guidewire)
  - Catheter with needle and guidewire together (Integral guidewire technique)

  Cannulae for arterial placement should be without an injection port and preferably have an eye to take a stitch
- A needle holder with suture material
- Sterile dressing (preferably transparent)
- An arterial connector
- A pressure transducing system

Step 6: Set Up the Pressure Transducing System

This consists of a pressure transducing assembly with a flushing system. The accuracy of the intra-arterial blood pressure measurement will depend on the proper setup and function of the pressure transducing system.

- *The pressure transducing assembly* consists of a coupling system, pressure transducer, amplifier, signal conditioner, analog to digital converter, and microprocessor that converts the signal received from the artery into a waveform on the a bedside monitor.

- *The flushing system* is set up using a 500-mL normal saline bottle encased in a bag pressurized to 300 mmHg. At this pressure, the catheter will be flushed with 3 mL saline per hour and help keep the catheter patent. Using the flushing device helps flush the assembly as required. Before connecting flush the pressure transducing system with saline, using the flushing device remove all air bubbles, and keep it ready to connect to the arterial catheter. Heparinized saline is no longer routinely used in view of concerns about heparin-induced thrombocytopenia. In addition, continuous heparin flush solution has been shown to affect coagulation studies if the sample is drawn via the arterial line.

Step 7: Positioning and Preparation Prior to Radial Artery Cannulation

- Inform the patient about the procedure (if conscious) and take the informed consent.
- Position the wrist in dorsiflexion. This brings the radial artery in closer approximation to the skin and can be instrumental in success of the procedure.
- This position can be maintained using a roll of gauze below the wrist or with a specially designed arm board and securing the arm with tape.
- Don a mask, cap, sterile gown, and gloves.
- The field can be sterilely prepared and draped using towels. In all invasive procedures, meticulous care should be taken to minimize the risk of infection.
- A small wheal of 1% lidocaine should be raised in the conscious patient to decrease the pain during cannulation and taking stitch.

Step 8: Radial Arterial Cannulation

Blind approach: The radial artery is palpated between the distal radius and the flexor carpi ulnaris tendon. The arterial catheter with needle is inserted at a 30- to 45-degree angle toward the artery.

Over-the-Needle Technique

Once there is blood return, the needle is advanced slightly further to ensure the catheter has entered the vessel. The needle angle is then lowered to 10–15°, and the catheter is guided over the needle and advanced into the vessel.

Over-the-Wire (Seldinger) Technique

- When blood return is noted, the catheter is advanced further, and the needle is then removed. The guidewire is then kept ready, and the catheter is withdrawn till there is pulsatile blood flow. The guidewire is inserted into the vessel, the catheter is advanced over it, and then the guidewire is removed.

- A commonly used variant of this technique is to initially insert only the introducer needle without catheter and then advance guidewire through the needle when in position and finally thread arterial catheter over the guidewire.

Integral Guidewire Technique (Over the Needle and Wire Technique)

- This is a special cannula-needle-guidewire assembly in which, when blood back flow is observed in long hub, the guidewire is advanced freely and then catheter is advanced over the guidewire and needle (Fig. 40.1)
- This is a quick and easy technique, associated with as much blood loss as may occur with the other two techniques.

Real time ultrasonography guided arterial line cannulation

- This can be performed in centres where an ultrasonography (USG) machine and the expertise in USG guided arterial line insertion is available. Success rate of radial arterial cannulation has been shown to be higher with the use of USG guided cannulation. This technique is especially suitable for critically ill patients with feeble pulse (hypotensive), obese, and edematous cannulation site.

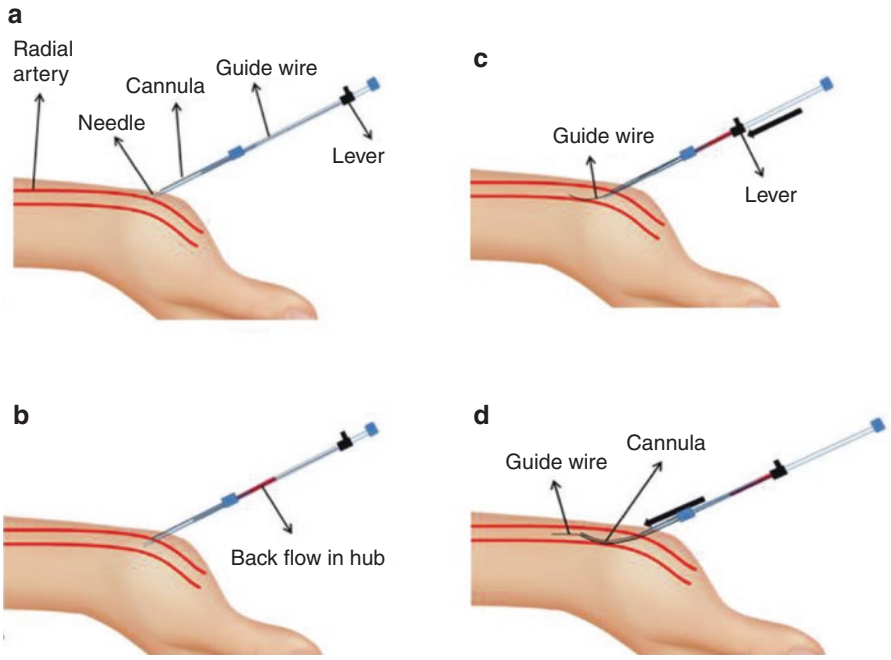

Fig. 40.1 Integral guidewire tehcnique. (**a**) Needle is advanced at 45° to the skin, (**b**) radial artery puncture will be indicated by backflow in the tubing connected, (**c**) advance the lever to push guidewire freely into the aretrial lumen, (**d**) cannula is advanced over the guidewire and needle and then the guidewire is removed

- A sterile probe cover or a sterile glove may be used to cover the ultrasound probe, as a barrier to prevent cross contamination. Full aseptic precuations are taken during cannulation.
- Two approaches are commonly used to visualize the artery and its catheterization---
  - *In-plane approach*
    In this approach, the rafial artery is scanned in-plane (the long axis of probe is kept in line with long axis of artery so that it scans longitudinal section of artery). The advantage of this approach is real time visualization of tip of needle entering inside the lumen. However, it requires good expertize to hold and stabilize the probe during the procedure. (Fig. 40.2)
  - *Out-of-plane approach*
    This technique is easier to learn and quick. In this method the long axis of probe is perpendicular to long axis of artery in such a way that a transverse section of artery is visualized on the screen. The disadvantage is the loss of real time enrty if one is not careful about moving the probe in the direction of needle entry and may result in through and through puncture of arterial wall and posterior wall hemorrhage. The "target sign" is the end point in this technique, when one can see bright spot (needle tip image) inside the lumen of artery.
- The success of either approach is heralded by free and pulsatile back flow of blood in the needle hub.

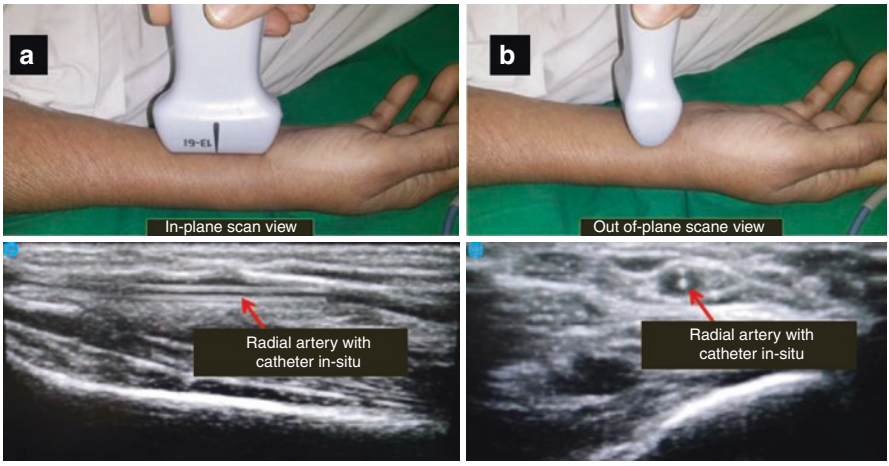

Fig. 40.2 Ultrasound views of radial aretry. a. In-plane scan view of radial artery is obtained when the long axis of probe is parallel to the long axis of the artery b. Out of plane scan view of radial artery is obtained when the long axis of the probe is kept perpendicular to the long axis of artery

Anticipated Difficulties During Cannulation

- In the over-the-needle technique, sometimes there is a blood return, but the artery cannot be cannulated. This may be because the needle has entered into the vessel lumen, but the catheter is still outside it. This can be overcome by advancing the needle further and then guiding the catheter over it. In other technique, advance the needle by 1–2 mm and remove the needle and look for pulsatile blood flow, then pass a guidewire into the vessel over which the catheter can be advanced easily.
- Sometimes the catheter may not easily pass through the skin. To overcome this, make a small nick on the skin with a needle or a blade at the insertion site.
- After multiple attempts at cannulation, the artery may go into spasm. Sometimes, there may be hematoma formation. It is advisable to change the site for arterial line placement at this point. One can use USG at this time to improve success at cannulation without complication.

After cannulation, pressure is given on the artery proximal to the catheter tip to reduce bleeding while the pressure transuding assembly is connected.

Step 9: Check Perfusion and Secure the Catheter

- Immediately after cannulation, check perfusion of the extremity. This should also be checked periodically when the arterial catheter is in place.

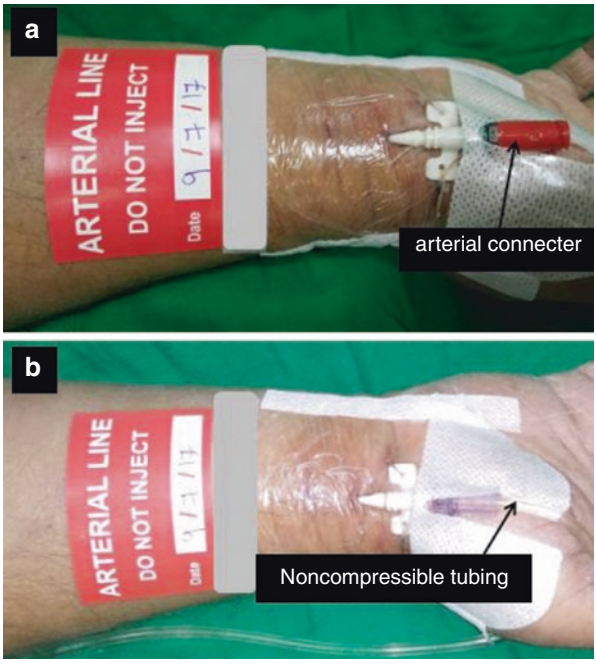

Fig. 40.3 Arterial catheter secured with a sterile transparent dressing and connected to (**a**) an arterial connector (when not transduced) and (**b**) a pressure transducing tubing (when transduced)

- Great care should be taken to make sure the catheter stays in place. Although there are various ways of fixing the catheter with adhesive tape, the best method of securing it is to suture it in place. A moderate-diameter, nonabsorbable suture material can be used.
- Place a sterile transparent dressing over the catheter, to secure it further and allow inspection of the catheter insertion site. Label and date the arterial line. (Fig. 40.3)
- The arterial line should be connected to a pressure transducing assembly or to an arterial connector when the arterial line is not transduced. This will prevent the line from getting blocked. (Fig. 40.3)

Step 10: Zero and Level the Transducer (Static Calibration)

- To obtain accurate pressure measurements, the air-fluid interface must be aligned with the chamber or vessel being measured.
- The reference point is usually at the level of the heart. Use the phlebostatic axis (junction of the fourth intercostal space and midpoint between the anterior and posterior chest walls—Fig. 40.4).
- A spirit level should be used to level this point with the stopcock of the pressure transducing system, which is used for zeroing.
- The transducer is opened to air and the recorded pressure (atmospheric pressure) is used by convention as 0 mmHg reference value.

Step 11: Check If the System Is Optimally Damped (Dynamic Calibration)

- Damping indicates the tendency of an oscillating system to return to its resting state. Anything that takes energy out of the system results in a progressive diminution of amplitude of oscillations.

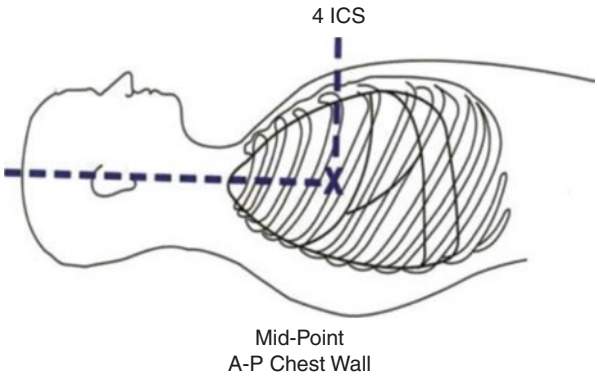

Fig. 40.4 Phlebostatic axis

- *Underdamped waveforms* (will be narrow and peaked tracing and will record higher systolic and lower diastolic pressure) are seen when long tubing is used or with increased vascular resistance.
- *Overdamped waveforms* (will record lower systolic and higher diastolic pressure) are commonly seen when there are air bubbles or blood clots, overly compliant tubing, catheter kinks, stopcocks, no fluid in the flush bag, or low flush bag pressure.
- In both above mentioned, the mean arterial pressure (MAP) will not change. Hence, always rely on the MAP, especially when you are not sure whether the system is optimally damped.
- Damping can be checked by doing a "square wave test" (Fig. 40.5). Activate the flush device, quickly release it, and observe the waveform on the monitor. The waveform will sharply rise and "square off" at the top when the flush is activated and then the tracing returns to the baseline after it is released (Fig. 40.5). Check the number of oscillations:

1. Optimally damped—one or two oscillations before return to tracing
2. Underdamped—more than two oscillations before return to tracing
3. Overdamped—less than one oscillation before return to tracing

Repeat the square wave test every 8–12 h, whenever the waveform looks over- or underdamped, when the accuracy of the measurement is doubtful, especially when you are implementing some interventions based on intra-arterial pressure values.

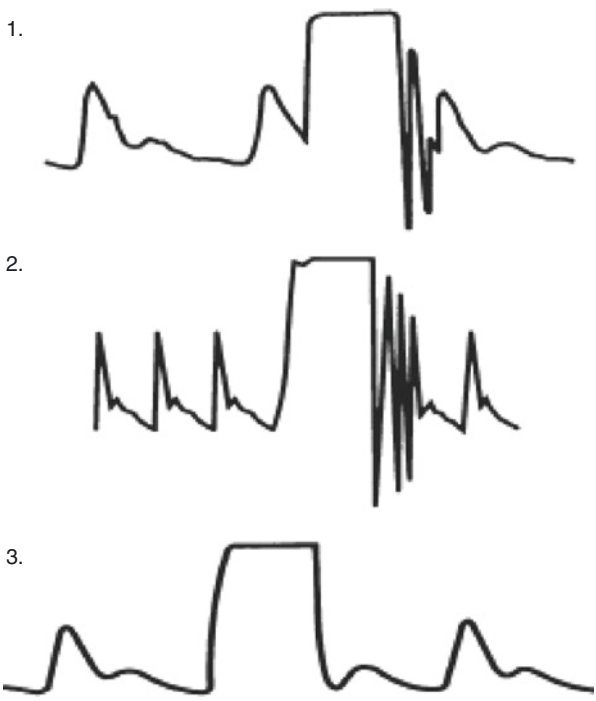

Fig. 40.5 Square wave test

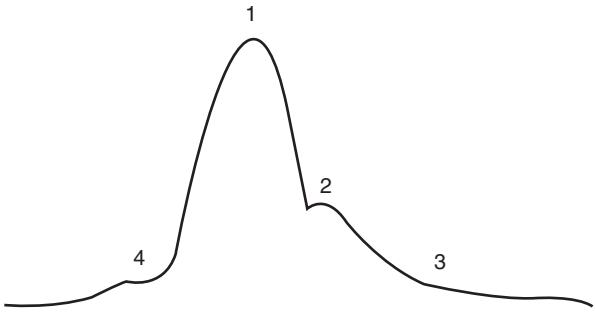

Fig. 40.6 Components of the arterial waveform (*1*—peak systolic pressure, *2*—dicrotic notch, *3*—diastolic pressure, and *4*—anacrotic notch)

Step 12: Check the Arterial Waveform and MAP (Fig. 40.6)

- Arterial pressure waveforms differ from site to site. As the arterial pressure is recorded more distally, the trace gets progressively more peaked and the dicrotic notch migrates away from the peak as a result of reflected waves in the branching vessels and the decreased arterial compliance of the distributing arteries. The MAP however does not vary widely as one measures more distally.
- An under- or overdamped tracing can either under- or overestimate the systolic and diastolic pressures. However, the MAP always remains the same.
- Considering the above, always rely on the MAP, rather than the systolic or diastolic pressure recorded during intra-arterial blood pressure monitoring and titrating therapy.

Step 13: Make Other Interpretations from the Arterial Waveform

Besides more accurate and real-time recording of arterial pressure, a lot of hemodynamic interpretations can be made from the arterial waveform:

- Large variations in pulse pressure (swing in the waveform during mechanical ventilation) can be seen in fluid responsive patients and is used to calculate the pulse pressure variation (PPV) using the arterial waveform analysis. PPV is a dynamic variable to assess fluid responsiveness
- Steep slope of upstroke means good contractility and vice versa.
- Area under the curve represents the stroke volume.
- Position of the dicrotic notch—low (low systemic vascular resistance) and high (high afterload).
- Slope of the decent—steep (low systemic vascular resistance).

Step 14: Optimize the Natural Frequency of the System to Improve Accuracy

- Use a wide-bore, high-pressure tubing no longer than 122 cm (48 in.).
- Avoid tubing extensions and stopcocks.
- All connections should be tight.
- Eliminate air bubbles.
- Ensure that the flush bag external pressure is 300 mmHg.
- Keep cannulated extremity in neutral or slightly extended position.

Step 15: Ensure Proper Maintenance of the Arterial Catheter

- Ensure that the catheter is labeled and has an insertion date at all times.
- Maintain the pressure in saline bag at 300 mmHg, low pressure reduces the saline flush rate and leads to blockage of catheter with a blood clot and overdamped arterial waveform.
- Check perfusion of the extremity at regular intervals.
- Check the insertion site daily through the transparent dressing for signs of inflammation and infection.
- Change the arterial line dressing only if it is not well coated, very dirty, or there is a collection under it.
- Whenever the arterial catheter is not being transduced, block it using an arterial connector (not a venous connectors /stopcock). These colour coded (red) connectors provide high resistance to the blood flow into the catheter, unlike the venous connectors and prevent them from getting blocked. They have a diaphragm through which blood can be collected without removing the connector.
- Special attention should be given while mobilizing and nursing the patient or when a patient is restless, during which the arterial catheter may get accidentally dislodged. An arterial wrist support may be used to prevent such a catastrophe.

Step 16: Watch for Complications

- *Vascular complications* of clinical significance are rare but can be devastating. Attention to the adequacy of distal perfusion is of great importance.
- Absent pulse, dampened waveform, blanched or mottled skin, delayed capillary refill, and painful and cold hands or fingers with motor weakness are presentations of hand ischemia.
- *Infections complications:* Arterial catheters can be responsible for both local and catheter-related bloodstream infections, though the incidence is low. The arterial catheter should be given the same degree of importance as the central venous

catheter as a potential source of sepsis. Remove the catheter if it is suspected to be the cause of infection.
- Bleeding, hematoma.
- Nerve damage.
- Pseudoaneurysm.

Step 17: Treat Ischemic Complications if they Occur

- Black/blue discoularation of fingers—remove the cannula.
- Treatment should be individualized to the patient and expert opinion should be taken early.
- Monitor patient's vital parameters
- If the patient is on vasopressors, taper the dose if possible.
- If the patient's condition is medically stable, consider the following:
  - Arterial duplex sonography
  - Angiography
- Patients with symptomatic vasospasm and thrombosis may be treated with topical or intraartrial vasodilator (nitroglycerin, papaverin, and lidocaine) and anticoagulation therapy. It is advisable to involve a vascular surgeon and interventional radiologist in such cases for expert management.
- If gangrene sets in, it is imperative to involve a vascular and reconstructive surgeons early in the course for operative interventions (thormbectomy and vein grafting for the defect in the involved arterial segment / amputation).

Step 18: Remove the Arterial Catheter at the Earliest

There is no fixed number of days after which the arterial catheter should be removed. Catheter colonization increases with dwell time. Hence, assess the need for the arterial catheter daily and remove it as soon as it is no longer required or earlier if there are any complications.

Suggested Reading

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Chaparro Mendoza K. Radial artery catheterism for invasive monitoring: Preventing complications, a challenge in anesthesia. Rev Colomb Anestesiol. 2012;40(4):262–5. Permanent ischemic hand injuries have been reported to occur in 0.09% of cases. A current theory is that an embolic phenomenon that compromises colateral circulation or the digital arteries could be the cause of distal ischemia and residual injuries in surgical interventions. In case this complication

appeared, the catheter should be removed and patients with symptomatic vasospasm and thrombosis should be treated with vasodilation and anticoagulation therapy.

Del Cotillo M, Grane N, Llavore M, Quintana S. Heparinized solution vs. saline solution in the maintenance of arterial catheters: a double blind randomized clinical trial. Intensive Care Med. 2008;34:339–43. *The use of heparinized solution for arterial catheter maintenance does not seem to be justified as it did not increase the duration of the catheters, nor did it improve their functionality significantly. On the other hand, heparin Na altered aPTT significantly*.

Gu WJ, Wu XD, Wang F, Ma ZL, Gu XP. Ultrasound guidance facilitates radial artery catheterization: a meta-analysis with trial sequential analysis of randomized controlled trials. CHEST J. 2016;149(1):166–79. *The use of dynamic 2-D ultrasound guidance for radial artery catheterization decreases first-attempt failure, mean attempts to success, mean time to success, and the occurrence of hematoma complications. Dynamic 2-D ultrasound guidance is recommended as an adjunct to aid radial arterial catheterization*.

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Morelli A, De Backer D. The ten principles behind arterial pressure. Intensive Care Med. 2018;44:911–4. A recently published update in ICM, about arterial pressure monitoring. The assessment of the arterial pressure values must be interpreted in light of its relationship to cardiac output.

Wallach SG. Cannulation injury of the radial artery: diagnosis and treatment. Algorithm. Am J Crit Care. 2004;13(4):315–9. *Cannulation of the radial artery can result in complications ranging from arterial thrombosis, arterial aneurysm, compartment syndrome, infection, nerve injury, and skin necrosis to possible thumb or even hand necrosis if not recognized and treated early*.

Pulmonary Artery Catheterization

41

Rajesh Chawla, Rahul Joshi, and Aakanksha Chawla Jain

A 65-year-old male patient, a known case of chronic obstructive pulmonary disease with cor pulmonale, hypertension, and coronary artery disease with chronic congestive heart failure, was admitted to the ICU with right lower lobe pneumonia. He was in respiratory failure and in shock. On the second day, he developed renal failure and azotemia. A pulmonary arterial catheter (PAC) was inserted.

The pulmonary artery catheterization (PAC) provides direct pressure measurements from the right atrium, right ventricle, pulmonary artery, and pulmonary artery occlusion pressure. It is also a mean of measuring cardiac output and mixed venous oxygen saturation. Routine use of this should be avoided, but it has still a role in expert hands in cardiac surgery, difficult to treat heart failure, right heart failure, congenital heart disease, and complex fluid management situations.

Despite all the advantages of PA catheter, a number of clinical studies have been published in past 20 years that have shown either no benefit or an increased risk of morbidity or mortality associated with its use.

Step 1: Assess the Need for PAC—Indications

- PAC is used in situations where right-sided pressures (i.e., central venous pressure [CVP]) may not reflect the changes in pressures in the left side of the heart. Right-sided filling pressures are disproportionately elevated compared to the left-sided filling pressures.

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R. Chawla, S. Todi (eds.), *ICU Protocols*, https://doi.org/10.1007/978-981-15-0902-5_41

- PAC should be used in centers with nursing expertise in the management of catheters and sufficient physician experience in the interpretation of data in the following conditions:
  - Management of complicated myocardial infarction
  - For management of heart failure
    Patients with refractory shock not responding to noninvasive management
    Patients with significant azotemia on diuretic therapy and are clinically volume overloaded
    As part of workup or bridge to cardiac transplant or the left ventricular assist device
  - Complex fluid management (shock, burns, acute renal failure, major surgery) in patients with poor left or right ventricular function
  - Cardiac surgery patients on cardiopulmonary bypass or patients with complex cardiac lesions
  - High-risk obstetric cases such as severe preeclampsia and abruptio placentae
  - Surgical procedures such as liver transplant and aortic cross clamping

Step 2: Check for the Contraindications

Relative contraindications are as follows:

- Complete left bundle branch block may convert to complete heart block.
- Wolff–Parkinson–White syndrome and Ebstein's malformation because of possible tachyarrhythmias. A catheter with pacing capability is preferred in these situations.
- Coagulopathy.
- Severe pulmonary hypertension.
- It should not be used in centers that do not have experience and expertise in its use.

Step 3: Know the PAC

- Circumference should be 7–9 Fr, most commonly used external diameter is 5 or 7 French (Fr) (1 Fr = 0.0335 mm)
- Length is 110 cm, marked at 10 cm intervals.
- The distal port (yellow colored) at the catheter tip is used for monitoring of pulmonary artery pressure.
- The second port (blue colored) is 30 cm proximal from the tip and is used for monitoring of CVP and injecting fluid bolus for computing cardiac output with bolus technique.
- The third lumen (red colored) leads to a balloon near the tip, with a locking port.

- The fourth lumen houses wires for a temperature thermistor, the end of which lies just proximal to the balloon. This attaches to the interface cable from the cardiac output monitor.
- The continuous cardiac output PAC has a copper thermal filament embedded in the catheter at 30 cm. Once inserted and connected to the monitor, this filament heats up every few seconds, warms blood around it, and thermistor in the pulmonary artery detects the change in temperature and calculates cardiac output.
- A variety of catheter constructions are available, each designed for particular clinical application.
- Double lumen catheter – balloon inflation through one lumen and distal opening for intravascular pressure measurement and blood sampling.
- Triple lumen catheter- proximal port terminating 30 cm from tip of catheter, allowing simultaneous measurement of right atrial and PA or occlusion pressures.
- Qudrapple lumen catheter (most commonly used in ICU) which has a lumen containing electrical leads for thermistor positioned at catheter surface 4 cm proximal to its tip.
- Five lumen catheter also available (fifth opening 40 cm from tip of catheter, additional access for fluid and medication infusion)
- Several special purpose PA catheter designs are available. Pacing PA catheter incorporates two groups of electrodes on the catheter surface, enabling intracardiac electrocardiographic (ECG) recording or temporary cardiac pacing.
- A five lumen catheter allows passage of a specially designed 2.4 Fr bipolar pacing electrode (probe) through additional lumen (located 19 cm from catheter tip) and allows emergency temporary intracardiac pacing without the need for a separate central venous puncture. The pacing probe is Teflon coated to allow easy introduction through the pacemaker port lumen; the intracavitary part of the probe is heparin impregnated to reduce risk of thrombus formation.
- Continuous mixed venous oxygen saturation measurement is clinically available with the help of fiberoptic five lumen PA catheter.
- Doppler technology for continuous CO monitoring has also been described.

The PAC set also contains the following:

- Large-bore introducer sheath with a one-way valve at its outer end and a side arm extension for intravenous access. (The PAC is introduced through the one-way valve. Some sets may not contain this sheath, but is also available separately.)
- Stiff dilator
- Plastic sheath to cover the catheter
- A 1.5-mL syringe for balloon inflation
- Guidewire
- Puncture needles and syringes
- Three ways and connectors
- A disposable knife

Step 4: Obtain Informed Consent

This has been explained in detail in Chap. 39, Vol. 2.

Step 5: Select the Appropriate PAC for Insertion

- Select the PAC which is appropriate for that patient.
- Catheters are available, which can perform the following additional functions:
  - An extra venous infusion port.
  - Pacing capability.
  - Continuous mixed venous oximetry: Special fiber-optic PACs can be used to monitor mixed venous oxygen saturation (SvO_2) continuously, initially developed as a surrogate for continuous cardiac output.
  - An ejection fraction catheter has a faster thermistor response time so that it can calculate RV ejection fraction in addition to the cardiac output.
  - Continuous cardiac output.

Step 6: Prerequisites

- Establish monitoring of ECG, noninvasive blood pressure, and pulse oximetry.
- Keep ready all emergency medication and transcutaneous pacing equipment.
- Provide sedation in a conscious patient.
- Supply oxygen through the nasal cannula.
- Secure a peripheral venous access.
- Assemble the pressure transducer and flush it.
- An assistant is needed who can prepare the set and closely monitor the patient.
- The patient should be in supine position with the head slightly down and turned toward the opposite side.
- Make use of maximum sterile barrier precautions, described Chap. 39, Vol. 2.

Step 7: Choose the Site of Insertion

- Generally the right internal jugular vein or left subclavian is selected.
- Alternatively any other site used for central venous cannulation can be selected keeping in mind the distance from the puncture site to the right atrium.
- An extra distance of 5–10 cm from the left internal jugular, 15 cm from the femoral veins, and 30–35 cm from the antecubital veins is required. But accurate placement rates are lower from these sites.

Step 8: Prepare the Cannulation Set

With maximum sterile precautions do the following:

- Pass the catheter through the sterile sheet.
- Flush the catheter with heparinized saline.
- Inflate the balloon with 1.5 mL air and check for its shape and any leakage.
- Zero and level the transducer and connect to the saline-filled catheter.
- Place the tip of the catheter at the heart level; pressure on the monitor should read zero.
- Next, raise the catheter tip to 30 cm height; the monitor should show a pressure of 22 mmHg (equivalent to 30 cm H_2O).

Step 9: Insertion of PAC through Internal Jugular Vein

- Use maximum sterile barrier precautions.
- Apply generous local anesthesia.
- Locate the internal jugular vein.
- Puncture the vein with the puncture needle preferably under ultrasound guidance.
- Pass the guidewire through the needle and remove the needle.
- Dilate the skin and subcutaneous tissue with the dilator. This is generally done with the dilator loaded inside the introducer sheath. A small incision is often needed.
- Pass the large-bore sheath using Seldinger technique.
- Confirm placement by aspirating blood, flush it, and secure it with stitches.
- Introduce the prepared catheter through the introducer up to a distance of 20 cm with the balloon deflated. Note the waveform on the monitor—CVP tracing should be seen.
- Rotate the catheter so that curvature is at 11 o'clock position from patient's head end.
- Inflate the balloon gently with 1.5 cc of air and lock it. During pulmonary artery occlusion pressure (PAOP) measurement if the balloon is left inflated, you may cause a pulmonary infarct.
- Advance slowly and keep looking at the monitor for RV waveform with systolic peaks of 25–35 mmHg. Note that the diastolic pressure is close to zero. This is reached at around 30–35 cm length.
- If the RV or PA is difficult to enter:
  - Have the patient take deep breath.
  - Raise the head end of the bed or tilt the table to left or right.
  - Flush the PA port with 1–2 mL cold sterile saline so that the catheter becomes stiff.
- Keep inserting further; PA is reached at 40–45 cm. At PA, there is an increase in the diastolic pressure (Fig. 41.1).

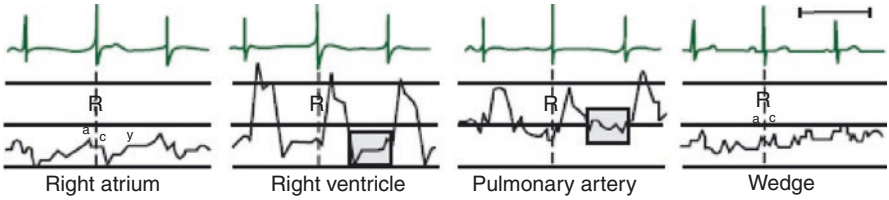

Fig. 41.1 Pressure tracings recorded from the right atrium, right ventricle, pulmonary catheter, and on pulmonary artery occlusion

- Now advance another 5–10 cm or so very gradually keeping an eye on the monitor to look for wedging. When it is wedged, the waveform becomes similar to that of CVP tracing at a pressure near to the PA diastolic pressure. This is the pulmonary artery occlusion pressure PAOP, and it is always lower than the pulmonary artery diastolic pressure (Fig. 41.1).
- Do not advance any further; deflate the balloon.
- Now inflate the balloon with 0.5 cc increments and look for wedging. If it wedges before 1.5 cc, pull the catheter back 3–4 cm. Do not pull with the inflated balloon.
- Fix the catheter at that length. Note the length of the catheter that led to a good PAOP tracing in the case chart.
- Never keep the PAC wedged continuously; deflate the balloon after taking the readings.
- Measured and derived hemodynamic indices values are mentioned in Tables 41.2 and 41.3.
- Special considerations- non flow directed catheters can be put in special disease states (RA or RV dilatation, severe PAH, low CO syndrome) with the help of guidewire although high chances of cardiac perforation (must be done under fluoroscopic guidance with experience personnel)
- Utility of ultrasonography for pulmonary artery catheter insertion- is safe, effective, and fast method of insertion that has advantage over fluoroscopic guidance. Realtime imaging and done at bedside and does not require patient transport and complex equipments.

Step 10: Manage Complications

- Minor complications are seen in up to 50% of patients, but major complications are seen in only 0.1–0.5% of patients.

Besides all the complications of insertion and maintenance of central venous lines, there are a few unique complications of the use of the PAC (Table 41.1).

Table 41.1 Complications of the PAC

Complication	Description	Treatment
I. Catheterization		
(a) Arrhythmias, ventricular fibrillation	Self-limited arrhythmias extremely common during passage	3.1% of patients require treatment, mostly withdrawal of catheter or guidewire
(b) Right bundle branch block, complete heart block	Transient during passage in 5%	May need transcutaneous or transvenous pacing
	Permanent in 0.9%	
	Should rule out ischemia	
II. Catheter resistance		
(a) Mechanical, catheter knots	Suspect if the catheter is blocked or difficulty in withdrawing	Radiological maneuver
	Confirm on a chest X-ray	Surgery
(b) Thromboembolism	Clots seen within hours	The heparin-coated catheter reduces risk
	Thromboembolism rare	
(c) pulmonary infarction	Opacity on a chest X-ray	Removal of the catheter
(d) Infection, endocarditis	Significant risk after 72 h especially in septic patients	Should be removed as soon as feasible
(e) Endocardial damage, cardiac valve injury	53% in autopsy series, but clinically significant regurgitation does not occur	Removal of the catheter
(f) Pulmonary artery rupture	0.02–0.2% of patients	One-lung ventilation to isolate normal lung
	Mortality is 50%	Positive end-expiratory pressure to the affected lung
	Cause:	Reverse anticoagulation
	Excessive insertion depth	May try to reinflate to cause tamponade
	Persistent wedging	May need surgical intervention
	Frequent manipulations	
	Inflation with liquid	
	Presents as hemoptysis and desaturation	
(g) Pulmonary artery pseudoaneurysm	Sequelae of PA rupture	Surgery may be needed
	May cause secondary hemorrhage	
III. Misinterpretation of data		May be widespread
		Use requires expertise and experience
IV. Misuse of equipment		

Step 11: Interpretation of Data Obtained (Tables 41.2–41.4)

Measuring Cardiac Output

- Enter the catheter constant into the monitor; this is generally written on the pack of the set or the insert.
- 10 mL of cold or room temperature saline is smoothly injected from the proximal (blue) port in the right atrium. In small children or patients with volume overload, smaller volumes (2 and 5 mL) may be used.
- A cable from the cardiac output monitor is dipped into the same bottle saline from which the injectant volume was aspirated.
- The temperature of the blood mixed and cooled with the cold saline is measured at the end of the catheter by a thermistor.
- This produces a thermodilution curve, from which the cardiac output is calculated by the monitor. Usually three measurements are made.
- These measurements may have a variability of up to 10%.
- There are various factors that influence the accuracy that include intracardiac shunts, tricuspid regurgitation, pulmonary valve regurgitation, respiratory cycle influences, and rapid injection of saline.

Continuous Thermodilution Cardiac Output

- Near-continuous cardiac output can be measured by a specially designed pulmonary artery catheter.

Table 41.2 Normal cardiovascular pressures

	Pressure	
	Average (mmHg)	Range (mmHg)
Right ventricle		
Peak systolic	25	15–30
End-diastolic	6	0–6
Pulmonary artery		
Peak systolic	25	15–30
End-diastolic	9	4–12
Mean	15	9–19
Pulmonary artery wedge		
Mean	9	4–12
Left ventricle		
Peak systolic	130	90–140
End-diastolic	7	4–12
Central aorta		
Peak systolic	130	90–140
End-diastolic	70	60–90
Mean	90	70–105

Table 41.3 Derived hemodynamic indices

Parameter	Physiologic significance	Formula	Normal value
Systemic vascular resistance	Reflects impedance of the systemic vasculature	80 × (MAP − CVP)/CO	1100–1500 dyne s/cm^5
Pulmonary vascular resistance	Reflects impedance of pulmonary circuit	80 × (PAM − PCWP)/CO	120–250 dynes/s/cm
Cardiac index	Allows for meaningful comparison between patients	CO/BSA	2.5–4.2 L/min/m^2
Stroke volume index	Reflects fluid status and ventricular performance	CI/HR × 1000	40–60 mL/beat/m^2
Left ventricular stroke work index	Estimates work of the left ventricle, reflects contractile state	(MAP − PCWP) × SVI × 0.0136	45–60 g/m^2
Right ventricular stroke work index	Estimates work done by the right ventricle and RV performance	(PAM − CVP) × SVI × 0.0136	5–10 g/m^2

CI cardiac index, *CO* cardiac output, *CVP* central venous pressure, *HR* heart rate, *MAP* mean arterial pressure, *PAM* pulmonary artery mean pressure, *PCWP* pulmonary capillary wedge pressure, *SVI* stroke volume index

Table 41.4 Oxygen transport parameters

Parameter	Symbol	Formula	Normal value
Mixed venous oxygen saturation	SvO_2		70–75%
Oxygen delivery	DO_2	1.34 × Hb × SaO_2 × CO	520–570 mL/min/m^2
Oxygen uptake	VO_2	1.34 × Hb × (SaO_2 − SvO_2) × CO	110–160 mL/min/m^2
Oxygen–extraction ratio	O_2ER	VO_2/DO_2	20–30%

- The RV portion of the catheter has a thermal filament that releases a small amount of heat in a pulsatile manner.
- This temperature variation is measured at the tip of the catheter. It has a measurement delay of 5–15 min, but the measurement is quite reliable.
- Acute changes in cardiac output are detected more slowly, but it has the advantage of ease of operation, minimal handling, and reduced risk of fluid overload.

Pulmonary Capillary Wedge Pressure

- Imagine that the vessel in which the pulmonary artery catheter lies is like a tube connected to the left atrium.

- When there is no flow of blood through the tube, the pressure at the tip of the tube will be the same as the pressure at the left atrium. So, we stop the blood flow by inflating the balloon and measure the pressure at the tip of the pulmonary artery catheter and call it the pulmonary capillary wedge pressure (PCWP), but technically the correct term is pulmonary artery occlusion pressure (PAOP) as PCWP is actually lower than PAOP.
- Pulmonary artery diastolic pressure can be used as an alternative to PCWP to measure left ventricular filling pressure, which we assume predicts left ventricular volume.
- Mean PAOP correlates well with left ventricular end-diastolic pressure (LVEDP) provided the patient has a normal mitral valve and normal left ventricular function. In myocardial infarction, conditions with decreased left ventricular compliance (ischemia and left ventricular hypertrophy) and conditions with markedly increased left ventricular filling pressure (e.g. Dilated cardiomyopathy), the contribution of atrial contraction to left ventricular filling is increased. Thus, the LVEDP may be significantly higher than the mean left atrial pressure or PAOP.

Checklist to Follow Before PCWP Can Reliably Reflect the LV Filling Pressure (Table 41.5)

- The tip of the PAC should be in west zone 3 in the lung. The airway pressure fluctuations are minimum in this zone. On the chest X-ray, the tip of the PAC should be below the level of the left atrium within 2 cm of cardiac silhouette.
- Correct pulmonary artery and wedge pressure waveforms: Pulmonary artery pressure upstroke slightly precedes the radial artery pressure upstroke.
- Rule out abnormal waveforms: There should be no air, clots, or motion-related artifacts (distinguished from normal by their shape and timing). If the balloon is overinflated and occludes the lumen orifice or forces the catheter tip against the vessel wall—or if there is distal catheter migration—overwedging may result. Overwedged pressure is devoid of pulsatility and is higher than expected.
- Measure the pressures only at end expiration. This is because end-expiratory pressure is closest to the atmospheric pressure. This is done by freezing the waveform on the monitor and observing the movement of the trace up or down along with the phases of respiration or on a paper printout.

Table 41.5 Check list for verifying position of pulmonary artery catheter

	Zone 3	Zone Zone 1 or 2
PAOP contour	Atrial waveform seen (A + V waves)	Unnaturally smooth
PAD versus PAOP	PAD > PAOP	PAD < PAOP
Respiratory variation of PAOP	<1/2 P_{ALV}	≥▲P_{ALV}
• Catheter-tip location	• LA level or below	• Above LA level

PAD pulmonary artery diastolic pressure

- Wedge pressure will underestimate the left ventricular end-diastolic pressure if the patient has diastolic dysfunction, aortic regurgitation, pulmonary regurgitation, right bundle branch block, or postpneumonectomy.
- Wedge pressure will overestimate the left ventricular end-diastolic pressure if the patient has pulmonary arterial hypertension, pulmonary veno-occlusive disease, tachycardia, mitral stenosis, or mitral regurgitation.
- Always remember that wedge pressure is a reflection of LV end-diastolic pressure, whereas it is the end-diastolic volume that determines preload. The two measurements may not correlate in up to 58% of measurements.

Suggested Reading

American Society of Anesthesiologists Task Force on Pulmonary Artery Catheterization. Practice guidelines for pulmonary artery catheterization: an updated report by the American Society of Anesthesiologists Task Force on Pulmonary Artery Catheterization. Anesthesiology. 2003;99:988–1014. *A detailed review of the various aspects of the use of the pulmonary artery catheter along with recommendations and practice guidelines on its management and use*

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Connors AF Jr, Speroff T, Dawson NV, et al. The effectiveness of right heart catheterization in the initial care of critically ill patients. SUPPORT Investigators. JAMA. 1996;276(11):889–97. *PAC use was associated with increased mortality and increased utilization of resources. Subgroup analysis did not reveal any patient group or site for which the PAC was associated with improved outcomes. This study started the outcome controversies on PAC use*

Friese RS, Shafi S, Gentilello LM. Pulmonary artery catheter use is associated with reduced mortality in severely injured patients: a National Trauma Data Bank analysis of 53,312 patients. Crit Care Med. 2006;34:1597–601. *Patients aged 61–90 years, with arrival base deficit worse than −11 and injury severity score of 25–75, were found to have a decrease in the risk of death with PAC use*

Swan HJC, Ganz W, Forrester JS, Marcus H, Diamond G, Chonette D. Catheterization of the heart in man with use of a flow-directed balloon-tipped catheter. N Engl J Med. 1970;283:447–51. *The landmark article that completely changed the way people monitored patients in the ICUs. Since its introduction the catheter has hardly undergone change in size or structure. It was at one time the most widely used equipment in the ICU*

Defibrillation and Cardioversion

42

Rajesh Chawla, Roseleen Kaur Bali, and Pradeep Jain

A 70-year-old diabetic, hypertensive, and coronary artery disease male patient was admitted to the hospital with acute myocardial infarction. His pulse was 120/min, and blood pressure was 100/60 mmHg. He was on dopamine and dobutamine infusion. He was being prepared for primary angioplasty. While being shifted to the catheterization laboratory, he collapsed. The cardiac monitor showed ventricular fibrillation (VF).

Electrical shock therapies are capable of terminating arrhythmias due to reentry. Reentry is the predominant mechanism of majorities of arrhythmias in ICUs.

Cardioversion is the delivery of energy that is synchronized to the QRS complex, while defibrillation is the nonsynchronized delivery of a shock randomly during the cardiac cycle.

This terminates arrhythmias by delivering a synchronized shock that depolarizes the tissue involved in a reentry circuit. All excitable tissue of the circuit are depolorized and make the tissue refractory. The circuit is not able to propagate or sustain reentry. So, cardioversion terminates those arrhythmias resulting from a single reentry circuit, such as atrial flutter, atrioventricular nodal reentrant tachycardia, atrioventricular reentrant tachycardia, or monomorphic ventricular tachycardia.

Step 1: Be Familiar with the Device

- *Types of Defibrillators*

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- Manual external defibrillators
  These defibrillators have electrocardiogram (ECG) readers, which the health care provider uses to diagnose a cardiac rhythm. The health care provider will then decide what charge (in joules) to use, based on proven guidelines (ACLS) and experience, and will deliver the shock through paddles or pads on the patient's chest.
  As they require detailed medical knowledge, these units are generally only found in hospitals and on some ambulances.

- Automated external defibrillators (AEDs)
  AEDs are sophisticated, reliable computerized devices, that use voice and visual prompt to guide lay users and health care providers to safely defibrillate the appropriate rhythm.
  They are not designed to deliver synchronized shock (i.e., cardioversion of ventricular tachycardia (VT) with pulse). They will rather recommend a nonsynchronized shock for both monomorphic and polymorphic VTs if the rate and morphology exceed the preset value.
  The AEDs take time (~10–20 s) to diagnose the rhythm. On the other hand, a professional can diagnose and treat the condition far more quickly with a manual unit. This valuable time gap between analysis and application of shock, where the chest compression has to be withheld, is unavoidable for the AEDs.
  These time intervals for analysis, which require stopping of chest compressions, have been shown in a number of studies to have a significant negative effect on shock success. This effect led to the change in the AHA defibrillation guideline (calling for 2 min of cardiopulmonary resuscitation (CPR) after each shock without analyzing the cardiac rhythm), and some recommend that AEDs should not be used when manual defibrillators and trained operators are available.
  There are two types of AEDs: fully automated and semiautomated. Most AEDs are semiautomated. A semiautomated AED automatically diagnoses heart rhythms and determines if a shock is necessary. If a shock is advised, the user must then push a button to administer the shock.
  A fully automated AED automatically diagnoses the heart rhythm and advises the user to stand back while the shock is automatically given. Also, some types of AEDs come with advanced features, such as a manual override or an ECG display.

- Implantable cardioverter defibrillators *(ICD)*
  ICDs analyze the rhythm based on an internal program and shocks appropriately.

- *Types of Shocks*
  - Monophasic
    A monophasic shock delivers current in one polarity.

Biphasic shocks

A biphasic shock delivers current that reverses course during the pulse.

Defibrillation with biphasic waveform improves short-term outcome of terminating VF.

It is safe and has equivalent or higher efficacy in terminating VF than the monophasic.

Recommendation is 120–200 J according to manufacturer's recommendation. If not known, then defibrillate at the maximum dose.

- *The Modes (Defibrillation and Cardioversion)*
  - *Defibrillation*

    Defibrillation is a method of introduction of unsynchronized electrical shock that stuns the heart briefly and terminates all electrical activities including VF and rapid VT, and if the heart is still viable then its pacemakers will eventually resume its normal rhythm, which ultimately results in a perfusing rhythm. It is not synchronized with the R wave in ECG.
  - *Cardioversion*

    Here, the shock delivery is synchronized with QRS complexes. It prevents shock delivery during the relative refractory portion of the cardiac cycle (i.e., ventricular vulnerable period, between 60 and 80 ms before and 20–30 ms after peak of the T wave) when shock could produce VF.
- *Electrodes*
  - *Types*

    Handheld paddles (pediatric and adult)

    Self-adhesive pads (pediatric and adult)
  - *Size*

    8–12 cm for the adult and child (≥8 years)

Step 2: Assess the Need for Cardioversion and Defibrillation—Indications and Contraindications (Tables 42.1–42.3)

Caution: Patients with digitalis toxicity, electrolyte imbalance (more prone to ventricular fibrillation (VF) and ventricular tachycardia (VT) after shock), chronic atrial fibrillation (AF), and atrial flutter (AFL) of more than 48 h who are not adequately anticoagulated.

Table 42.1 Indication of cardioversion and defibrillation

Type	Indications
Immediate	Hemodynamic instability due to tachyarrhythmia of shockable variety
	Congestive heart failure and angina due to shockable tachyarrhythmia
Elective	Hemodynamically stable
	No significant symptoms

Table 42.2 Tachyarrhythmias responsive to electrical therapy

Responsive to cardioversion		Responsive to defibrillation
Supraventricular	Ventricular	Pulseless VT
		VF
		Unstable polymorphic VT with or without pulse
Atrial fibrillation	Monomorphic VT with pulse	
Atrial flutter		
Sinoatrial nodal reentrant tachycardia		
Atrioventricular nodal reentrant tachycardia		
Atrioventricular reciprocating tachycardia		

Table 42.3 Tachyarrhythmias unresponsive to electrical therapy

Unresponsive to cardioversion/defibrillation	
Supraventricular	Ventricular
Sinus tachycardia	Idiopathic monomorphic VT
Focal atrial tachycardia	
Junctional tachycardia	Accelerated idioventricular rhythm

Step 3.1: Method for Cardioversion

- Patient preparation for elective cardioversion
  - It should be done in hospital areas equipped with cardiac monitoring, airway management, and cardiopulmonary resuscitation.
  - Ensure nil by mouth (NBM) status.
  - Patient counseling is required in detail about the procedure.
  - Obtain valid informed consent from the patient or legal surrogate.
  - Confirm adequacy of anticoagulation in chronic AF.
  - Consider starting antiarrhythmics 24–48 h preprocedure.
  - Pre- and postprocedure ECG.
- Preprocedural sedation protocol
  - If the patient requires oxygen or is currently receiving oxygen, oxygen tubings should be kept away from chest
  - Continuous monitoring—ECG, SPO_2, and noninvasive blood pressure (NIBP).
  - Give sedation and analgesia.

    Agents—propofol, midazolam, and etomidate

    Propofol is the best option for its early awakening time and better safety profile. Short-acting agents are preferred.

    Opioid analgesics, such as fentanyl, are used for analgesia.

  - Conscious sedation
    Goal—maintain consciousness but in a somnolent state. It can be done by a trained physician without anesthesiologist's supervision. Midazolam is the preferred agent here.
- Turn the defibrillator on (monophasic or biphasic shock)
  It simultaneously switches the monitor on.
- Suggested electrode position
  - Anterolateral (most common): An anterior paddle is placed in right infraclavicular area, and the lateral paddle is placed lateral to the left breast in longitudinal alignment.
  - Anteroposterior: The anterior paddle is same as before, and the posterior paddle is on the left side of the spine at the level of lower end of the scapula.
    Other two positions include anterior-left infrascapular and anterior-right infrascapular. Anteroposterior placement is found to be more successful in cardioversion of AF with monophasic shock.
    Apply jelly (water-based conducting jelly). Place the negative electrode closer to the heart with both the electrodes adequately separated.
    The conducting jelly should be restricted to the pad area and should not be spread all over the chest.
- Synchronization (for synchronized cardioversion)
  - The device should be in the synchronized mode as most AEDs have a default unsynchronized mode.
  - For each subsequent defibrillation, one needs to reset to synchronized mode. Confirm synchronization by looking at markers on the R wave. It may be necessary to adjust the gain of the monitor to remark the R wave correctly.
- Announce "charging-stand clear"
- Charge
  Press the charge button (present on the paddle as well as on the monitor) to select the level of charge (Table 42.4). Hear the audible sound/alarm when charging is completed.

Table 42.4 Specific energy levels

Rhythm	Mode	Monophasic (initial and consecutive shocks)	Biphasic shock
VF, pulseless VT	Defibrillation	360	120–200
Stable, monomorphic VT with pulse	Cardioversion	100, 200, 300, 360	70, 120, 150, and 170[a]
AF	Cardioversion	100–200, 300, 360	100–120
Atrial flutter, Supravetricular tachycardia (SVT)	Cardioversion	50, 100, 200, 300, 360 (MDS)	70, 120, 150, and 170[a]

[a]The biphasic waveform using the lower energy level is acceptable if documented to be clinically equivalent or superior to reports of monophasic shock success. Initial biphasic dose of 100–200 J with escalation depending on the need is recommended (evidence extrapolated from cardioversion of atrial fibrillation). For specific recommendation consultation from the device, manufacturer is advised

- Clearing
  Say "I am going to shock on three; one, I am clear; two, you are clear; three, everybody is clear." Check and look around after each step and confirm safety.
- Shock
  Check to see the synchronized mode prior to giving a synchronized shock.

Step 3.2: Method for Defibrillation

- Analyze the rhythm
- A bedside cardiac monitor or ECG display of the defibrillator is needed, if already attached.
- Sedation protocol
- As most often patients with pulseless VT and VF present in an emergent condition with unstable hemodynamics and impending cardiac arrest, sedation in such cases is not required.
- Turn the defibrillator on
- In most defibrillators, the default mode is the asynchronized mode.
- Same as step D for cardioversion
- No need for synchronization
- Same as cardioversion up to step H
- Shock (asynchronized)
- Post-shock
- Resume CPR for five cycles, check rhythm, and proceed according to ACLS guidelines.

Step 4: Manage Complications (Table 42.5)

Step 5: Special Circumstances

- *Anticoagulation for reverting atrial fibrillation and flutter*
  - Anticoagulation is indicated in atrial fibrillation and flutter lasting more than 48–72 h.
  - Recommendation is 3–4 weeks of anticoagulation prior to attempt cardioversion. It should be continued for at least 4 weeks post-cardioversion.
  - This approach has an inherent risk of increased bleeding. So, in patients at the higher risk of bleeding, transesophageal echocardiography can be performed to exclude intracardiac thrombus and proceed with cardioversion without adequate prior anticoagulation. In any case, at least 4 weeks of anticoagulation is mandatory in post-cardioversion period.

Table 42.5 Complications and their prevention/treatment

Complications	Prevention/treatment
Thermal burns	The lowest accepted energy level
	Biphasic shock requires less energy
Thromboembolism	More common with AF (incidence in 1–7% patients who are not receiving anticoagulation)
	Ensure adequate anticoagulation
	Exclude left atrial clots with transesophageal echocardiography
Arrhythmia	For expected sinus bradycardia and sinus arrest, prophylactic placement of the pacemaker (transvenous/transcutaneous) in patients with AF with slow ventricular rate
	VT and VF—In patients with digitalis toxicity or hypokalemia, better to avoid cardioversion; if necessary to perform, then be prepared for a more refractory ventricular arrhythmia
Myocardial damage	Clinically insignificant but recommended to give two shocks at least 1 min apart
Loss of airway	Mostly sedation related
	Complications such as aspiration can be reduced by ensuring nil by mouth (in elective cases), supervised cardioversion preferable
Pulmonary edema	Supportive measures and gradual improvement expected
Fire hazard	Reported when shock is given in an oxygen-rich environment
	Avoid direct blowing of oxygen across the chest in the oxygen-rich environment

- *External defibrillation with the ICD/pacemaker in situ*
  - If the ICD is currently delivering shock (as evidenced by external muscle contraction similar to external defibrillation), allow 30–60 s for the ICD to complete the treatment cycle.
  - Place the pads at least 8 cm away from the ICD/pacemaker, but placing the paddle should not be delayed in defibrillation.
  - It is not desirable to place the pads or paddles directly over the device.
- *Pregnancy*
  Cardioversion and defibrillation have been performed in all trimesters of pregnancy. It has been found to have no obvious adverse fetal effects or premature labor. Fetal heart rhythm monitoring is recommended.
- *Pediatric age group*
  - The lowest energy dose for effective defibrillation is not known. The lower and upper limits to safe defibrillation are not known for infants and children.
  - Biphasic shocks appear to be at least as effective as monophasic shocks and are less harmful than monophasic shocks.
  - It is recommended to use an initial dose of 2–4 J/kg, and for refractory VF, increase the dose to 4 J/kg. Subsequent energy levels should be at least 4 J/kg, and higher energy levels may be considered, but not to exceed 10 J/kg or the adult maximum dose.

  - For infants (<1 year of age), a manual defibrillator is preferred. If a manual defibrillator is not available, an AED with pediatric attenuation is desirable. If neither is available, an AED without a dose attenuator may be used.
- *Drowning*
  - Removal of the patient from water and thorough wiping of the chest and the patient is prerequisite before attempting electrical therapy.

Step 6: Remember Factors Affecting Defibrillation and Shock

Equiment Related

Electrode position: Anterolateral electrode position is suggested for persons with an underlying cardiac implantable electronic device (CIED) such as a permanent pacemaker or an implantable cardioverter-defibrillator, it is recommended placing the external electrode pads in the anteroposterior position to avoid any contact with the skin overlying the cardiac implantable electronic device.

Pad size: A larger pad or paddle surface is associated with a decrease in resistance and increase in current and may cause less myocardial necrosis.

Use optimal electrode size (approximately 12.8 cm), above which there is decline in current density.

Hand-held versus patch: Hand-held paddle electrodes are more effective than self-adhesive patch electrodes, specially for cardioversion of persistent atrial fibrillation. No data is available for other arrhythmia needing cardioversion.

Monophasic versus biphasic waveforms: Biphasic waveforms defibrillate more effectively and at lower energies than monophasic waveforms.

Patient Related

1. *Transthoracic impedance*: It depends on the following factors:
   Energy level
   Electrode-to-skin interface
   Interelectrode distance
   Electrode pressure (with hand-held electrodes)
   Phase of ventilation
   Myocardial tissue and blood conductive properties
2. *Types of Arrhythmia*: The type of arrhythmia and the patient's clinical condition are important determinants of defibrillation success
3. Duration of arrhythmia
4. Patients with an underlying cardiac implantable electronic device

Suggested Reading

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Temporary Pacemaker Insertion

43

Rajesh Chawla, Vipul Roy, and Ashutosh Tiwari

A 70-year-old male patient—a case of coronary artery disease on regular treatment—was admitted to the hospital with chief complaints of syncope and giddiness. His heart rate was 38/min and blood pressure was 90/60 mmHg. ECG showed complete heart block. Insertion of temporary pacemaker was planned.

Pacemakers provide electrical stimuli which cause cardiac contraction when the intrinsic myocardial electrical activity is slow or absent. Temporary pacemakers use an external pulse generator with leads placed either transcutaneously or transvenously. During emergency resuscitation, transcutaneous leads are the easiest and most convenient method of choice. Transcutaneous pacing requires mild sedation. For transvenous pacing, a semirigid catheter is placed through central access. ECG monitoring is used for tracking catheter positioning.

Step 1: Assess the Need for the Temporary Pacemaker (Tables 43.1 and 43.2)

Contraindications

For patients especially with life-threatening hemodynamic instability and symptomatic bradyarrhythmias or other indications for temporary cardiac pacing, there are no absolute contraindications.

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Table 43.1 Indications of temporary pacing in the absence of acute myocardial infarction (Electrolyte disturbance/Drug Toxicity/ Myocarditis)

• Symptomatic bradycardia refractory to medical treatment
• Sinus node dysfunction
• Second- or third-degree atrioventricular (AV) block
• Third-degree AV block with wide QRS escape or ventricular rate < 40 bpm
• Prophylactic

Table 43.2 Indications of temporary pacing in acute myocardial infarction

Class I
• Asystole
• Symptomatic bradycardia (includes sinus bradycardia with hypotension and type I second-degree AV block with hypotension not responsive to atropine)
• Bilateral bundle-branch block [BBB; alternating BBB or right BBB (RBBB) with alternating left anterior fascicular block (LAFB)/left posterior fascicular block (LPFB)] (any age)
• New bundle-branch block with Mobitz II second-degree AV block
• RBBB plus fascicular block with Mobitz II second-degree AV block
Class IIa
• Narrow QRS plus Mobitz II second-degree AV block
• Old or new fascicular block with Mobitz II second-degree AV block and anterior myocardial infarction
• Old bundle-branch block and Mobitz II second-degree AV block
• New bundle-branch block plus first-degree AV block
• New bundle-branch block plus Mobitz I second-degree AV block
• RBBB plus LAFB or LPFB (new or indeterminate) with first-degree AV block
• RBBB plus LAFB or LPFB (new or indeterminate) with Mobitz I second-degree AV block

Temporary transvenous cardiac pacing should be avoided or used with caution in the following settings:

- Intermittent, mild or rare symptoms in whom the bradycardia is well tolerated.
  - Symptomatic complete heart block with an adequate and "stable" escape rhythm
  - Symptomatic sinus node dysfunction with only rare pauses
- Patients with a prosthetic tricuspid valve, as the temporary cardiac pacemaker lead could damage the valve or become trapped in the prosthesis.
- Patient with an MI who has received a thrombolytic agent and is being aggressively treated with anticoagulation or antiplatelet agents.

Step 2: Be Familiar with the Device (Table 43.3)

Temporary cardiac pacing techniques — Temporary cardiac pacing can be performed in a variety of ways:

Table 43.3 Temporary pacemaker method and device details

Device	Parts	Current	Benefits	Drawback	Uses
Transcutaneous external pacemakers	• External patch electrodes	Higher current (up to 200 mA) and longer pulse duration (20–40 ms)	• Less time-consuming	Require sedation	• Cardiac arrest
	• Pulse generator (usually a defibrillator)		• Risks of central venous access avoided	Pacing limited to ventricle and minimal capacity for atrial pacing	• Symptomatic bradyarrhythmia
					• Overdrive pacing
					• Prophylactically for arrhythmia in myocardial infarction
					• Unavailability or contraindication to transvenous pacing (prehospital setting during thrombolytic therapy for acute myocardial infarction)
Transvenous pacing	• Transvenous pacing catheters (4–7 F)	Threshold for vent.	Different modes (ventricular, atrial, sequential)	Inherent risk with central venous line	Indications as per Table 43.1
	• Pulse generator	Pacing (<1 mA), atrial pacing (<2 mA)			
		Output three to four times of threshold			

Transcutaneous needle temporary pacemaker should not be used in current technology as it has serious complications

- Internally using transvenous endocardial leads
- Externally via transthoracic patches
- Internally using atrial or ventricular epicardial leads placed at the time of surgery
- Internally via an esophageal electrode, which is primarily used for atrial pacing and recording

Step 3: Transvenous Pacemaker—Procedure

- *Obtain a central venous access*
  - The preferred route: Internal jugular (most common and most preferred), subclavian, and femoral veins, preferably right-sided veins, should be used when possible. Local anesthesia is always indicated.
  - Access blind or ultrasound-guided intracardiac placement of the pacing wire.
- Intracardiac placement of the pacing wire
  - This should only be inserted by experienced practitioners.
  - Preparation:
    A defibrillator and other resuscitation equipments should be immediately accessible.
    Strict aseptic technique.
    ECG monitoring.
  - Cannulate the suitable vein (internal jugular, subclavian, or femoral veins preferably on the right side) using Seldinger's technique of guidewire and dilators to place a sheath of the correct size.
  - Bend the tip of the electrode to give a 20–30° curve for the correct positioning in the heart.
  - Advance the electrode under ultrasound or fluoroscopic guidance until it lies vertically in the right atrium with its tip pointing toward the free wall on the right side.
  - Rotate the wire between the index finger and the thumb so that it points toward the patient's left side; advance the wire steadily through the tricuspid valve and along the floor of the right ventricle to the apex.
  - If blind technique is used, the V1 lead is connected to the distal port (cathode). Endocardial contact is indicated by prominent ST-segment elevation. Placement is facilitated by balloon inflation and floatation in the superior vena cava. Position is confirmed by successful capturing. The anteroposterior X-ray after placement is always indicated.
  - If AV sequential pacing is desired, the atrial J-shaped pacing catheter should be advanced into the right atrium and rotated anteromedially to achieve a stable position in the right atrial appendage; positioning the atrial catheter usually requires fluoroscopy.
- *Setting the Pacemaker*
  - Keep the pacemaker box in off position and attach the leads to the ventricular output position.

- Turn the pacemaker into asynchronous mode and set the ventricular rate 10–20 beats/min higher than the patient's intrinsic rate.
- Set the threshold current for ventricular pacing at 5.0 mA and switch the pacemaker on. See for ventricular pacing as evidenced by a wide QRS complex, with ST-segment depression and T-wave inversion, following each pacemaker depolarization (spike). (Right ventricular apex pacing presents as a pattern of left bundle-branch block on the surface ECG.)
- Output current is slowly reduced and the threshold current (the lowest current at which consistent ventricular capture occurs) is determined. Recommended pacing threshold of less than 0.5–1.0 mA should be achieved.
- If the threshold is high, then consider relative endocardial refractoriness due to fibrosis (rare) or a malposition of the electrode (more common). In any case, the tip of the pacing electrode should be repositioned in the region of the ventricular apex until satisfactory ventricular capture at a current of less than 1.0 mA is consistently maintained.

  The ventricular output is set to exceed the threshold current at least threefold. The pacemaker is now in VOO mode.

  After insertion of the lead and before stitching the lead, withdraw the sheath as it reduces infection rate.

Step 4: Know the Modes (Table 43.4)

Step 5: Know the Complication and Management

Complications

- *Complications as with any route*—pericardial friction rub, arrhythmia, right ventricular perforation, cardiac tamponade, infection, arterial injury, diaphragmatic stimulation, phlebitis, and pneumothorax
- *Complications of internal jugular venous and subclavian access*—pneumothorax, carotid arterial injury, venous thrombosis, and pulmonary embolism.
- *Complication of antecubital venous access*—dislodgement of the pacing electrode from a stable ventricular or atrial position (movement of the arm) and infection (more with this approach than others)
- *Complication of femoral access*—deep venous thrombosis and infection

Management

- Optimum knowledge about the anatomy and the procedure
- Ability to evaluate the correct placement and the desired rhythm
- Strict intra- and postprocedural asepsis.

Table 43.4 Modes

Modes	Paced (A, atrium; V, ventricle; D, dual)	Sensed (A, atrium; V, ventricle; D, dual)	Response (I, inhibit; T, trigger)	Programmability (R, programmable; O, nonprogrammable; M, multiprogrammable)	Multisite pacing (A, multisite pacing; O, nonmultisite pacing)
VVI	Ventricle	Ventricle	A sensed event in the ventricle inhibits the pacemaker from pacing or producing any output	None	None
AAI	Atrium	Atrium	The sensing of an event (e.g., sensing atrial activity within 1 s) inhibits the pacemaker from pacing	None	None
DDD	Both	Both	Response can be both triggering and inhibitory	None	None

Set the mode according to the need and device

Step 6: Troubleshooting

- *Satisfactory pacing not achieved*: Withdraw the wire into the right atrium and repeat the attempt to cross the tricuspid valve.
- *Difficulty in positioning the wire at the apex of the right ventricle*: Pass the tip of the wire into the right ventricular outflow tract and withdraw gently while rotating between the index finger and the thumb. When the tip is at a downward angle, advance toward the apex.
- *No spikes seen and no output*: Suspect failure of the battery or generator or a loose connection.
- *Spikes seen but no capture*:
- Suspect a loose connection but may be due to exit block causing a high threshold. Check the position of the pacing wire and consider repositioning.

Step 7: How to Monitor

Assess rhythm for appropriate pacemaker function:

- *Capture*: Is there a QRS complex for every ventricular pacing?
- *Rate*: Is the rate at or above the pacemaker rate if in the demand mode?
- *Sensing*: Does the sensitivity light indicate that every QRS complex is sensed?

Step 8: Postprocedural Investigations and Precautions

- A chest X-ray is needed to confirm a satisfactory position of the wire and to exclude a pneumothorax.
- Ensure the pacing wire is secured.
- Check and document all connections, battery, and control settings every 4 h and document.
- Sterile precaution is required as in handling a central line.
- Keep the pulse generator dry and the controls protected from mishandling.
- Protect the patient from electromicroshock and electromagnetic interference by covering the exposed wires and the pulse generator, wearing gloves when handling exposed wires; avoid any patient contact with electrical apparatus.

Suggested Reading

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Percutaneous Tracheostomy

44

Rajesh Chawla, Sudha Kansal, and Munish Chauhan

A 50-year-old male patient, a known case of chronic obstructive pulmonary disease with ischemic cardiomyopathy and renal failure, was admitted to hospital with acute breathlessness. He was drowsy and unable to maintain oxygenation on noninvasive ventilation. He was put on invasive ventilation and he got better. Spontaneous breathing trial was tried a number of times, but he could not be weaned off the ventilator for 10 days. Percutaneous tracheostomy (PCT) was planned.

PCT is a bedside procedure performed usually in an ICU setting. This uses Seldinger technique and is associated with lesser postoperative complications.

Step 1: Assess the Need for Tracheostomy and Advantage of PCT

A. *Indications*

- Securing the airway
  - Temporary—to aid weaning after long-term mechanical ventilation
  - Permanent—airway protection in neurological patients
- Tracheal toileting and airway protection
  - In the patient with excess or thick secretions who is not able to expectorate

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  - Generalized weakness—neuromuscular disease or central cause
  - Altered mentation—unable to maintain airways
- Relief of nonemergent upper airway obstruction
  - Once initial airway stabilization has been done via translaryngeal intubation/emergency cricothyroidotomy

B. *Advantages of PCT over surgical tracheostomy*
- Blunt dilatation causes less tissue trauma and devitalization than sharp dissection.
- It may lead to lower rates of hemorrhage, stomatitis, and cosmetic deformity.
- The tracheostomy tube is fitted tightly against the stoma.
- Interval between decision and actual procedure is shorter.
- It can be done at the bedside in the ICU, avoiding a potentially hazardous transfer of critically ill patients to the operating room.
- Savings in cost of operating room personnel and equipment can be achieved.

Step 2: Select Patient for PCT

- The patient should be hemodynamically stable as much as possible.
- FiO_2 should be below 0.6
- Positive end-expiratory pressure should be less than 10 cm H_2O.
- History of uncomplicated translaryngeal intubation is obtained.
- Cricoid cartilage is palpable at least 3 cm above the sternal angle during appropriate neck extension.

Step 3: Check for the Contraindications

There are no absolute contraindications. Suggested contraindications are not supported by adequate data but are decided on merit depending on the operator experience and protocols of the center involved (Table 44.1).

Table 44.1 Contraindications to PCT

Inability to identify anatomical landmarks	Surgical skin site infection
Previous major neck surgery completely obscuring the anatomy	Midline neck mass
Emergency airway control	High positive end-expiratory pressure (>10–20 cm H_2O)
Repeat tracheostomy	Severe coagulopathy
Age less than 15 years	Tracheomalacia
Cervical fixation/injury/fracture	Obese/thick neck

Step 4: Decide Timing

- The decision about tracheostomy requires anticipation of the duration of expected mechanical ventilation and the expected benefits and risks of the procedure.
- Time of PCT could be 7–14 days of intubation.
- It can be performed earlier (<7 days) for anticipated prolonged ventilation.

Step 5: Obtain Informed Consent

- Discuss the prognosis of the patient and the need for the procedure.
- Explain the advantages and disadvantages of the procedure and the available options in detail. Communicate with the patients or their surrogates.
- Explain the detailed procedure, the benefits, the risks, and the alternatives in the language they understand.
- Document the consent and get it signed.
- In case of emergency, when the patient is unconscious and the surrogates are not available, document the situation clearly and perform the procedure.

Step 6: Form Your Team

- The operating physician.
- One physician, managing the upper airway and bronchoscope, manipulates the ET tube to allow PCT.
- The paramedical staff/technician who assists with the bronchoscope and handling of the endotracheal tube.
- Another paramedical staff monitoring the vitals and administering medication.

Step 7: Prepare for the Procedure

- A PCT set as per the type decided by the physician
- A bronchoscope and its attachments
- Continuous monitoring of ECG, blood pressure, and oximetry
- Functioning intravenous access
- A sterile setup with enough sterile linen and instruments
- A crash cart with a laryngoscope and endotracheal tubes and emergency drugs
- Suction equipment
- Medications
- 1% Xylocaine with epinephrine
- Sedating and paralyzing agents

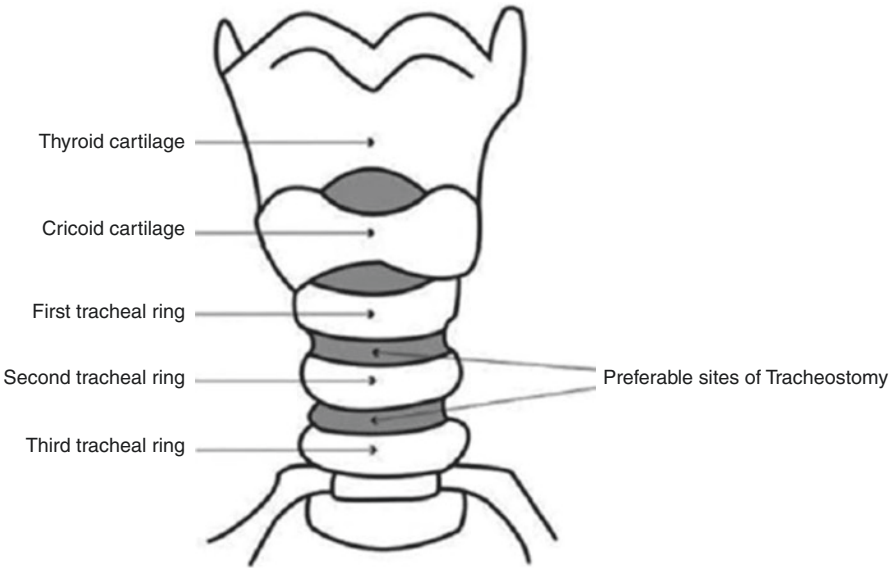


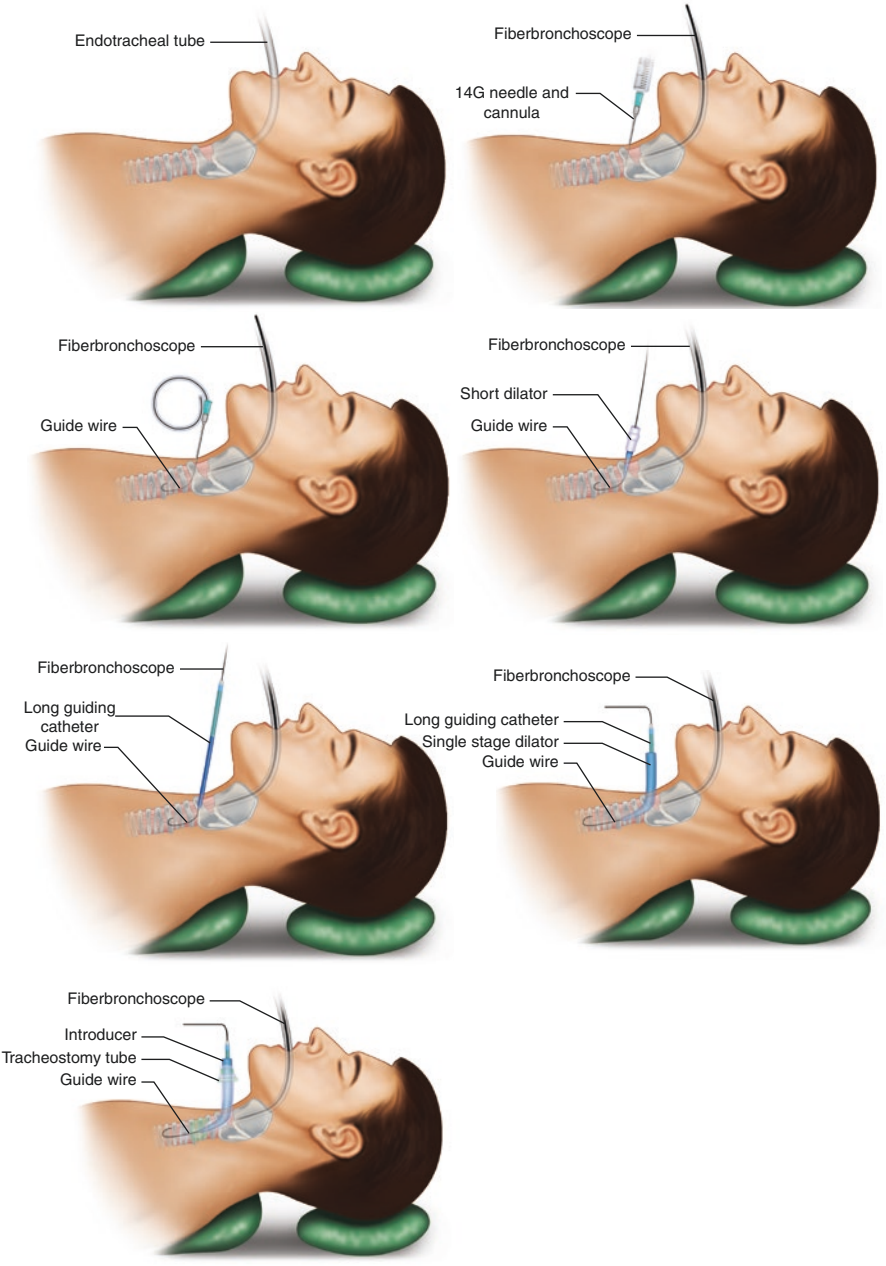
Fig. 44.1 Tracheal anatomy

Step 8: Identify Anatomy (Fig. 44.1)

- Tracheostomy is carried out at least one to two rings beyond the cricoid.
- The tracheostomy tube is entered between the second and third cartilage rings or between the third and fourth cartilage rings.
- In a too high tracheostomy (close to cricoid), there is a risk of a subglottic stenosis.
- In a too low tracheotomy, there is a risk of bleeding from the brachiocephalic trunk.

Step 9: Perform Percutaneous Tracheostomy

- *Ciaglia method (Blue Rhino PCT kit—Cook Critical Care Inc., Bloomington, IN)* (Figs. 44.2–44.8)
  1. Continuously monitor vital signs, pulse oximetry, and complete ventilatory parameters.
  2. Ventilate with 100% oxygen during the procedure.
  3. Counsel and comfort the patient if he/she is conscious.
  4. Sedate and paralyze the patient before positioning.
  5. Extend the neck to open the tracheal interspaces, carefully supporting the vertex using a sand bag beneath the shoulders and the head ring.
  6. Prepare the surgical field with alcohol-containing solution and drape it.



Figs. 44.2–44.8 Ciaglia method

7. Verify the anatomy and identify the neck structures and landmarks. A pre-procedure ultrasound may be done if anatomy is not clear (e.g., morbid obesity).
8. The local anesthetic with epinephrine is infiltrated into the surgical site.
9. Check all parts of the tracheostomy set. Check the tracheostomy balloon by inflating and collapsing it.
10. Make a transverse skin incision approximately 2 cm over the first and second tracheal interspace, approximately two fingers' breadth above the sternal notch.
11. Dissect the wound bluntly with a hemostat through the subcutaneous fascia.
12. Withdraw the endotracheal tube into a position above the first tracheal interspace under bronchoscopic guidance.
13. Insert a 14-gauge cannula over the needle through the skin incision between either the first and second or the second and third tracheal rings under bronchoscopic guidance, aspirating for air (Fig. 44.3).
14. Withdraw the needle leaving the cannula in place.
15. Advance a J-tipped guidewire through the cannula toward the carina and withdraw the cannula (Fig. 44.4).
16. Dilate the opening using a small dilator (Fig. 44.5).
17. Insert a stiffer guide cannula over the guidewire after withdrawing the cannula (Fig. 44.6).
18. Use a single, sharply tapered dilator with a hydrophilic coating and dipped in water-based jelly, for complete dilatation in one step (Fig. 44.7).
19. Withdraw the dilator leaving the guidewire and the stiff white guide cannula assembly in place.
20. Once the tracheostoma has been dilated to the appropriate size, a tracheostomy tube is introduced into the trachea over the same guidewire using introducer dilators as an obturator (Fig. 44.8).
21. The guidewire assembly is removed leaving the tracheostomy tube in place.
22. Position is confirmed by bronchoscopic visualization.
23. The tube is sutured to the skin and also fixed with the provided tie around the neck.

- **Griggs guidewire dilating forceps**
  - Steps 1–15 as above.
  - The cannula is removed leaving the guidewire in place.
  - The Griggs guidewire dilating forceps are threaded over the guidewire into the soft tissue.
  - Open the forceps "dilating" the soft tissue and advance the forceps into the trachea.
  - The trachea is dilated to an aperture sufficient enough to accommodate the tracheotomy tube.
  - An obturator is used to insert the tube over the guidewire.
  - The rest of the steps of fixation of the tube are same as above (Fig. 44.3).

- **PercuTwist technique.** (It contains a J-tipped guidewire, a scalpel, a large-bore introducer needle, the hydrophilically coated PercuTwist dilator, a specially designed 9.0-mm internal diameter PercuTwist tracheotomy cannula, and an insertion dilator.)
  - Steps 1–15 as above.
  - The PercuTwist single dilator is moistened to activate the hydrophilic coating.
  - Advance it over the guidewire into the soft tissue using a clockwise rotation.
  - Further rotation of the device engages the anterior tracheal wall and enlarges the aperture.
  - Once dilated adequately, the device is removed and replaced with the 9.0-mm tracheotomy tube fitted with the insertion dilator.

Ultrasound Guidance in Percutaneous Tracheostomy Instead of Bronchoscope

- Bedside ultrasonography is increasingly being used in ICU settings for various procedures and monitoring purposes. The aim is to decrease the risk profile of procedures and increase the success rate.
- In Percutaneous Tracheostomy, it is becoming increasingly beneficial in a select few scenarios like
  - Morbid obesity
  - Anatomical deformity: Acquired or genetic.
  - Thyromegaly
  - Overlying Vascular structure
- Landmark identification can be difficult in such cases increasing risk of trauma, malposition or failure of procedure.

Technique:

- Steps 1–6 as above
- Step 7: Use a 2D ultrasound using a linear array probe (probe should be covered with sterile camera cover)
  - Sagittal view: Note the position and anatomical relation of all landmarks like the thyroid and cricoid cartilage, the tracheal rings, the thyroid gland and the carotid and jugular vessels.
  - Transverse view: Any aberrant vessels/structure encroaching the proposed surgical area should be noted. Can use colour Doppler also. If needed, Tracheostomy tube size can be decided
- Step 8–12 as above
- Step 13: Insert a 14-gauge cannula over the needle through the skin incision under real time imaging in the sagittal plane to guide the level of insertion in the midline. Then turn the probe by ninety degrees for a transverse view to guide the needle tip (represented by an acoustic shadow) towards the midline. You might need to direct the probe bit caudally to keep track of the needle tip

- The sagittal view can be difficult to attain in some cases like short necked patients. In them, we can use the transverse view for puncture
- Rest of the steps as detailed above for different types of tracheostomy

Step 10: Postoperative Care of the Tracheostomy Tube

- Wound and dressing care
  - Daily examination of the stoma is needed to identify infections or excoriations of the skin.
  - Keep the wound clean and free of blood and secretions, especially in the immediate posttracheostomy period.
  - Dressing changes should be performed at least twice a day and when the dressings are soiled.
  - When changing dressings and tapes, special care is needed to avoid accidental dislodgement of the tracheostomy tube.
  - The inner cannula if used is changed daily or more frequently if necessary.
- Humidification
  - Humidification of inspired gases prevents obstruction of the tube by inspissated secretions and maintains mucociliary clearance and cough reflex.
  - Heat and moisture exchangers are preferred over heated humidifiers.
- Suctioning
  - Airways should be cleared of excess secretions to decrease the risk of lung infection and airway plugging.
  - Suctioning is frequently required in patients with poor or ineffective cough.
  - Suctioning should remove the maximal amount of secretions and cause the least amount of airway trauma. Thus, practice slow suctioning.
    1. Routine suctioning, however, is not recommended.
    2. Upper airway suctioning should also be done periodically to remove oral secretions and to minimize stasis of pooled secretions above the tracheotomy cuff with subsequent potential aspiration into the lower airways.
- Change tracheostomy tube
  - In case of a functional problem with the tube, such as an air leak.
  - If the lumen is narrowed due to the buildup of dried secretions.
  - Switching to a new type of the tube.
  - May downsize the tube prior to decannulation.
  - Do not change the outer cannula, unless the cuff is damaged, in the initial 5–7 days as the tract is not stable.
- Tube cuff pressure
  - Tracheotomy tube cuffs require monitoring to maintain pressures in a range of 20–25 mmHg.
  - Cuff pressures should be monitored with calibrated devices.
  - Record at least once every nursing shift and after manipulation of the tracheotomy tubes.

  - Maintain the tube in a central position, avoiding angling and contact between tracheal mucosa and the tube to avoid damage by the distal end.
  - Avoid traction as well as unnecessary movement of the tube.
- Nutrition
  - Feeding may become complicated because of tube interference with normal swallowing and airway control.
  - It decreases laryngeal elevation during swallowing and an inflated cuff may compress the esophagus. So it may deflate a little.
  - Keep the head end elevated to 45° during periods of tube feeding.
  - Before attempting oral feedings, several objective criteria must be met.

    The patient must be consistently alert and able to follow complex commands.

    Adequate cough and swallowing reflexes.

    Adequate oral motor strength.

    A significant respiratory reserve.

    Assess swallowing function.

    Oral feeding is done under supervision of a caregiver and carefully assessed for aspiration or regurgitation.

Step 11: Manage Complications

- Early complications (until 7 days)
  1. Tube displacement
     - Management—endotracheal intubation to establish airway. Replace the tracheostomy tube under less urgent conditions, always under fiber-optic guidance as there is a danger of entering a false tract. If it fails, intubate orally.
     - Prevention— proper placement of the stoma, avoid excessive neck hyperextension and/or tracheal traction, apply sufficiently tight tracheostomy tube retention tapes, and suture tracheostomy tube flange to the skin.
     - Displacements after 7 days are managed by simply replacing the tube as the tract is well formed.
  2. Tube obstruction
     - By mucus, blood clots, displacement into surrounding soft tissues, or abutment of the tube's open tip against the tracheal wall.
     - Reposition or suction thoroughly; deflate cuff as a temporizing measure.
     - If it fails, replace the tube immediately or intubate orally.
  3. Pneumothorax/pneumomediastinum
     - Pleura can be damaged during tracheostomy.
     - The incidence of pneumothorax after tracheostomy ranges from 0% to 5%.
     - Many surgeons routinely obtain a postoperative chest radiograph, though optional.
     - Immediate tube thoracostomy.

4. Subcutaneous emphysema
   - Positive-pressure ventilation or coughing against a tightly sutured or packed wound causes this.
   - It can be prevented by not suturing the wound around the tube.
   - It resolves spontaneously within a few days.
   - A chest radiograph should be done to rule out a pneumothorax.
5. Hemorrhage
   - Usually, minor postoperative venous ooze is the most common complication.
   - Elevate the head of the bed, pack the wound, and/or use homeostatic materials.
   - Major bleeding can occur in up to 5% of tracheotomies.
   - Hemorrhage from the isthmus of the thyroid gland
   - Injury to the transverse jugular vein
   - May require an exploration
6. Stomal infections
   - Good stoma care
   - Early use of antibiotics but do not use prophylactic antibiotics
7. Others
   - Arrhythmia
   - Hypotension
   - Hypoxia/hypercapnia
   - Loss of airway control
   - Bacteremia
   - Esophageal injury
   - Cardiorespiratory arrest
   - Tracheolaryngeal injury

- Late complications (>7 days)
  1. Tracheoinnominate artery fistula (<0.7% cases)
     - Occurs due to erosion through the trachea into the artery due to excessive cuff pressure or by angulation of the tube tip against the anterior trachea
     - Risk increased by the following:
       – Low placement of tracheotomy
       – High-pressure cuffs
       – Excessive head or tracheostomy tube movement
       – Malnourishment
     - Management
       – Evaluate even minor bleeds
       – Hyperinflation of the cuff; lower neck incision with blind digital compression on the artery may be attempted in a resuscitative effort
       – Operative intervention
  2. Dysphagia and aspiration
     - Due to causes discussed under “nutrition”
  3. Tracheal stenosis

- Approximately 1–2% cases
- Caused by
  - Ischemia
  - Devascularization
  - Chemical erosion
  - Infection
- Due to high-pressure cuffs
- Forced angulation of a stiff tube
- Hyperinflation of the cuff which results in tracheal damage
- Site of stenosis may occur at the:
  - Stoma
  - Cuff
  - Tip of the tracheotomy tube

4. Tracheoesophageal fistula
   - Less than 1% of patients
   - Mostly iatrogenic during procedure
   - Erosion by the tracheotomy cuff
   - Tube angulation with pressure against the posterior tracheal wall
   - More common with a nasogastric tube in place as well
   - Suspect if:
     - Cuff leaks
     - Abdominal distention
     - Recurrent aspiration pneumonia
     - Reflux of gastric fluids through the tracheostomy site
   - Diagnosed by endoscopy or contrast studies
   - Requires surgery or esophageal and tracheal stent
5. Granuloma formation
   - A foreign body reaction to the tracheotomy tube or part.
   - Treated with the YAG laser.
   - Granulomas at the lower end of the tracheotomy tube require bronchoscopic removal providing temporary relief.
6. Persistent tracheocutaneous stoma
   - Can occur when tube has been left in position for a prolonged period.
   - Surgical closure is required.
7. Tracheomalacia
   - Weakening of the tracheal wall
     - Ischemic injury to the trachea
     - Followed by chondritis
     - Then destruction and necrosis of the tracheal cartilage
   - Collapse of the affected portion of the trachea with expiration
     - Airflow limitation
     - Air trapping
     - Retention of airway secretions
   - Cause of weaning failure from mechanical ventilation.

- A short-term therapeutic approach to tracheomalacia is to place a longer tracheostomy tube to bypass the area of malacia.
- Long-term treatment options include stenting, tracheal resection, or tracheoplasty.

Step 12: Decannulation

1. Criteria
   - Stable arterial blood gases
   - Absence of distress
   - Hemodynamic stability
   - Absence of fever or active infection
   - $PaCO_2 < 60$ mmHg
   - Absence of delirium or psychiatric disorder
   - Normal endoscopic examination or revealing stenotic lesion occupying less than 30% of the airway
   - Adequate swallowing
   - Able to expectorate
2. Procedure
   - The deflated-cuff tracheotomy occlusion procedure
     – Occlude the opening of the tube with the cuff deflated by a gloved finger observing the patient for objective signs of respiratory distress.
     – In case of problems, promptly return the patient to breathing through the tracheotomy tube and perform a fiberendoscopic examination to check for upper airway obstruction.
     – If no distress is noticed, the tube can be removed, and the opening is covered with sterile dressings. The wound spontaneously heals in 10 days in most cases.
   - Use tracheotomy button or speech valve in patients with prolonged tracheostomy.

Suggested Reading

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Post-Tracheostomy Care in ICU Patients

45

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A 50 year male with motor neurone disease who has a cuffed tracheostomy for 2 months and is on home ventilation was admitted with respiratory distress. On admission he has laboured breathing, low oxygen saturation and had diminished air entry in right lung. It was difficult to negotiate suction catheter. An emergent change of tracheostomy tube was done with relief of dyspnea.

Caring for Tracheostomy patient in ICU is a challenging task. Tracheostomy is lifesaving in patients of upper airway obstruction, helps in weaning in difficult to wean patients, facilitate secretion removal & early mobilization. Tracheostomy reduces dead space, facilitates vocalisation and improves pharyngeal muscle strength. All these benefits can only be ensured if tracheal tube is patent, properly placed in midline, and is free of complications. If appropriate care is not taken tracheostomy tube itself can be fatal. Patency of tracheostomy tube is ascertained by non-traumatic suction protocol and also as and when required. Midline placement of the tube should be ensured by appropriate suturing or perfectly fitting tie also known as tracheostomy collar. Ventilator circuit weight and patient movement can contribute to tube dislodgement, displacement, life threatening bleeding and in long term trachea-esophageal fistula. Excessive cuff pressure or unmonitored cuff pressure for longer duration can cause tracheal stenosis or tracheomalacia. The very purpose of having a well-placed multidisciplinary tracheostomy team is to provide optimum, complication-free care to get maximum benefit and avoid further harm.

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Step 1. Initiate Tracheostomy Care Immediately after Insertion (Flow Chart 1)

- Tracheostomy tube insertion can be done either by Percutaneous method or Surgical tracheostomy procedure.
- Confirm tube placement by auscultation and monitoring SpO_2, $EtCO_2$, peak pressures and hemodynamics.
- Confirm position of the tube by chest x ray where the distal end of the tracheostomy tube should be 4–6 cm above the carina. USG of airway is more sensitive and specific point of care test for confirming the position of tracheostomy tube in situ.
- Secure the tube properly, tube tie or collar should not be very tight or very loose (movement limited to 1 finger width).

Step 2. Evaluate for Bleeding

Bleeding can be primary as in immediate post op period or can be a secondary bleeding in intermediate period.

- Bleeding can be at the stoma site or in the trachea. Small amount of bleeding is expected and is often self-limiting. However, continuous or profuse bleeding requires surgical re-exploration and vessel ligation. Besides that, anterior tracheal injury, posterior tracheal perforation and injury to paratracheal structures can lead to bleeding.

Step 3. Evaluate for Aspiration

- Tracheostomy cuff should be kept inflated for effective ventilation and further prevention of aspiration.
- Cuff pressure should be frequently monitored and maintained between 20 and 25 cm of water. Higher cuff pressure can cause long term complications such as tracheomalacia, tracheoinnominate artery fistula, tracheal ulcerations, fibrosis, stenosis, and tracheoesophageal fistula whereas lower cuff pressure can lead to leakage of secretions around cuff and subsequent ventilator associated pneumonia (VAP).
- Persistent cuff leak should be promptly recognized and treated. It can be because of malfunctioning of pilot balloon and or trachea must have lost its rigidity owing to tracheomalacia. Tracheomalacia is diagnosed with the help of CT scan of airway and bronchoscopy. However if tracheomalacia is diagnosed, patient may need long flang tracheostomy tube to bypass the damage part and avoid further damage and tracheal collapse.

Step 4. Evaluate for Displacement and Decannulation

- Accidental displacement and decannulation can occur any time and can be life threatening.
- The term dislodgement means when the tube is partially displaced and the tip lies within a false passage anterior to the trachea.
- The term decannulation means when the tube is completely withdrawn from the stoma.
- Replacement tracheostomy tube set should be always kept bedside.
- This complication is commonly observed when, the tie is loose, edema around neck, excessive coughing, agitation, undersedation, morbid obesity, short tracheostomy tube, technical difficulties while placing the tube, and traction caused by the weight of the ventilator circuit.
- Replacement of tube is easier if the stoma is matured. With an immature stoma (less than 1 week old), tissue plans are likely to collapse which makes replacement of tube difficult. Attempt to blindly insert and ventilate may cause formation of false passage leading to subcutaneous emphysema and pneumothorax.
- In case of complete decannulation, immediate intervention is to maintain oxygenation by bag and mask and if required orotracheal intubation if replacement of tube is difficult.
- Replacement of the tube should be with an obturator in place which facilitates tube placement by acting like a stylet.

Step 5. Evaluate for Tube Blockage (Fig. 45.1)

- Suspect tube block if the patient is in stridor, desaturating, using accessory muscles of respiration and manual resuscitator bag has offered some resistance.
- In a patient on ventilator one can find serial drop in tidal volume or increase in peak pressure to diagnose tube blockage.
- Immediate suctioning will help to remove mucus and clear the partial block. It can be done either by close suction or open suction method and should be either at a defined frequency or on request.
- All aseptic precautions and strict hand hygiene protocols should be practiced at all times.
- However, repeated suctioning or even manual ventilation fails to clear the block then immediate replacement of the tube should be done.
- In case of difficult replacement secure the airway and if required revision of tracheostomy site is warranted.

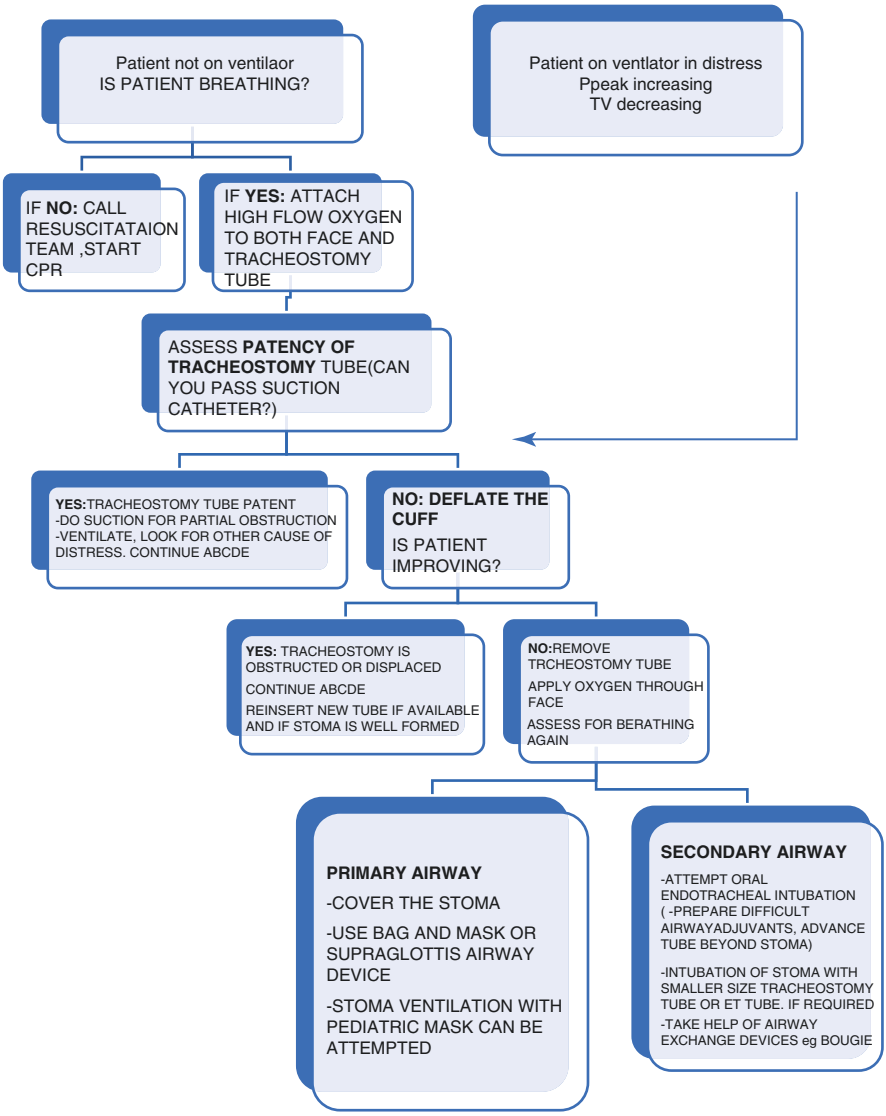

Fig. 45.1 Patient in respiratory distress on tracheostomy

Important Steps of Suctioning

Suctioning can be done by one or two persons.

Step a: Each bedside should be equipped with a functional suctioning system, appropriate size suction catheters, an oxygen source, manual resuscitation bag, and a complete tracheostomy kit.

Step b: Before suctioning, administer 100% oxygen. Choose appropriate size suction catheter and apply correct suction pressure of up to10.6–20 Kpa (80–150 mmHG). Ensure it is not greater than 20 kpa.

Step c: With non- touch technique suction catheter tip should be introduced at premeasured depth. The tip of the suction catheter remains within the tracheostomy tube and not beyond that while suctioning.

Step d: Apply suction only while withdrawing the suction catheter by occluding the suction tubing with a gloved thumb to minimize tracheal injury.

Step e: Ensure suctioning timing should not be more than 10 s and maximum 3 passes of suction catheter at each time.

Step f: The instillation of normal saline, to facilitate sputum clearance, is not a recommended practice, and it may actually be harmful.

Step g: Suctioning should be discontinued if patient desaturates or arrhythmias occur.

Step 6. Take Care of Tracheostomy in the Intermediate Period

- During this period patient should be monitored for stoma infection, tube block, skin breakdown and secondary bleeding.
- Identify stoma infection by features of peristomal bleeding, signs of inflammation, infection, maceration, granuloma formation.
- Stoma should be cleaned with cotton-tipped swabs soaked in normal saline at least once a day.
- Dressings should be done with sterile gauze which should be placed below flanges. Gauze should not be cut as edges will fray and are potential sources of infection. Avoid using loose fibers around stoma as they can cause irritation.
- Ensure stoma & surrounding skin is thoroughly dried after cleaning. Secretions collected above the cuff may ooze out of the stoma site and cause wetness leading to skin maceration, excoriation and infection at the stoma opening as well as at the tracheal opening.
- It is not recommended to use any cream or ointment or powder at stoma site.
- Consider subglottic suctioning as it can reduce incidence of late onset VAP.

Step 7. Ensure Humidification

- In patients with tracheostomy, the natural functions of warming, filtering, and humidifying the airway are also lost which makes secretions thick and prone to cause tube block. This in turn increases risk of infection, impaired secretion removal and micro atelectasis. Thus, humidification is very important aspect of tracheostomy care.
- Humidification techniques such as an active humidifier (presence of an external sources of heat and water), or a passive humidifier (utilization of patient's own temperature and hydration to achieve humidification in successive breaths) can

be used. However, active humidifiers are associated with more condensation and respiratory secretions.

- Passive humidifier, heat moister exchanger (HME) filter also known as artificial noses. It contains a condenser element, which retains moisture from every exhaled breath and returns it back to the next inspired breath and is more physiological. However, shortcomings like impaction of secretions or blood within the device may increase airway resistance and work of breathing. These limitations should be taken in to consideration while using HME filters.

Step 8. Identify and Avoid Skin Breakdown

- Stoma skin should be daily inspected and skin breakdown can be prevented with appropriate dressings.
- Sometimes suture precludes proper skin care till stoma gets matured. Dressing with a gauze is sufficient if secretions are minimum to moderate however if secretions are copious then it is preferable to use polyurethane foam or hydrocolloid dressings.
- Foam dressing acts as an absorptive, moisture retentive, and insulating, keeping the area dry while allowing oxygen to reach the area. If there is evidence of stoma infections then dressings with ionic silver or nylon impregnated silver dressings can be used.
- Ensure tube is in neutral position without any traction on the tube particularly due to oxygen delivery device which aggravates skin break down, tube dislodgement, and inadvertent decannulation.

Step 9. Identify Secondary Bleeding from the Stoma

Frequent deep suctioning may lead to blood tinged secretions. One has to be careful as under suctioning can cause accumulation of secretions, mucus plug formation and tube blockage.

- Tracheoinnominate fistula, is rare but the deadly complication where the innominate artery is eroded through trachea due to pressure necrosis from the tracheostomy tube cuff. It is associated with massive hemorrhage and patient is exsanguinated within minutes. It occurs mostly in 3–4 weeks after the procedure.
- Management includes maintaining oxygenation, cuff over inflation to cause tamponade effect. Definitive options like surgical repair or endovascular embolization can be considered.

Step 10. Consider Weaning and Decannulation of Tracheostomy. (Fig. 45.2)

Prior to decannulation following should be ensured:

- Underlying pathology is resolved
- Underlying airway is patent
- Respiratory support is no longer required

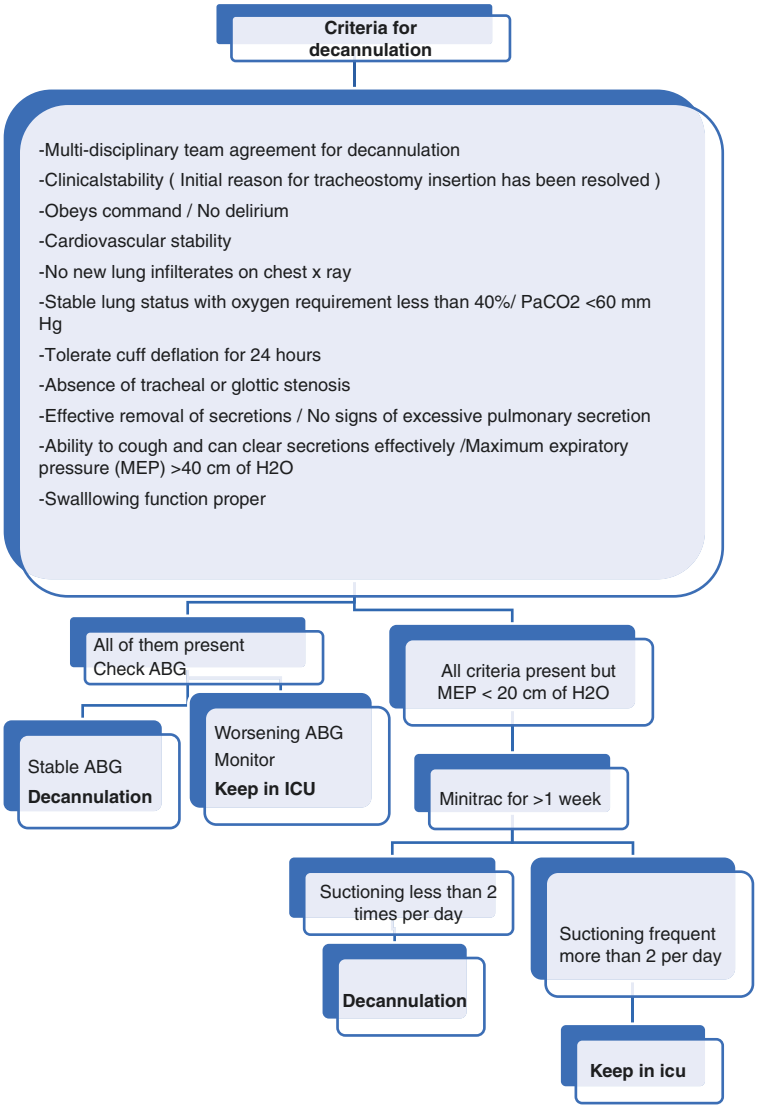

Fig. 45.2 Criteria for decannulation

Table 45.1 Probable complications following weaning

Problem	Cause	Solution
Respiratory distress	Poor airflow past tracheostomy either due to too large size tube, tracheal stenosis, oedema, granulation tissue causing airway obstruction Patient underlying condition not improved	Consider for change to smaller size +/− fenestrated tube Refer to ENT for upper airway evaluation If required fiberoptic bronchoscope evaluation
Excessive coughing	Secretion Anxiety Aspiration	Effective suctioning Reassure and explain procedure to patient Take help of therapist to improve deglutination

- Patient has an effective cough
- Patient is able to swallow secretions
- Patient is sufficiently alert and stress free
- Patient is cardiovascular stable

Techniques of weaning and troubleshooting:

- Cuff deflation- In absence of aspiration continue for 24 h
- Gloved finger occlusion- Observe for stridor
- Connect one way speaking valve
- Decannulation cap
- Look for complications (Table 45.1)
- While usually uncomplicated, decannulation should be undertaken by experienced staff with equipment for immediate recannulation nearby.
- Emergency intubation equipment and a trained airway expert should be immediately available if required.
- Nasogastric feeding should be stopped four hours prior to decannulation and the gastric contents aspirated.
- Following decannulation, the stoma site should be dressed and allowed to heal by itself. The patient should be observed for 24 h prior to discharge to a ward.

Long Term Care of Patient with Tracheostomy

Step 1: Select Proper Tracheostomy Tube

- Polyvinyl chloride (PVC), silicone, steel and silver tracheostomy tubes can be used.
- Single cannula tube is a low pressure design, available which, provides leak protection, aspiration prevention and allows positive pressure ventilation.

- Silicone tubes are reusable, cost effective, withstand repeated sanitization and are, tissue friendly (Fig. 45.3)
- Dual cannula tube are safer for long term care in view of easy inner cannula removal for cleaning and in event of tube obstruction. They help in weaning as inner tube may increase work of breathing (Fig. 45.4)
- Fenestrated tubes are also available (Fig. 45.5) with single and double cannula which facilitates speech and reduce work of breathing in weaning. Not suited for positive pressure ventilation and with unhealthy tracheostomy wounds in view of risk of surgical emphysema.
- Uncuffed tubes are used for patients who can protect their own airways, have an adequate cough reflex and most importantly can manage their own secretions. They remove the risk of tracheal damage caused by inflation of the cuff, may aid swallowing and communication
- Adjustable flange and long length tubes for particularly large neck patients due to obesity, goitre or patients with tracheomalacia

Step 2. Stoma Care and Tube Change

- Inner cannula is regularly inspected at least twice daily to prevent narrowing or blockage but this may be required more or less frequently depending upon the quantity and tenacity of the patients secretions.

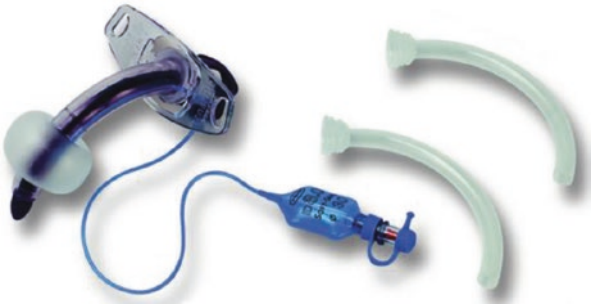

Fig. 45.3 Bivona silicone tubes

Fig. 45.4 Portex blue line ultra-tube

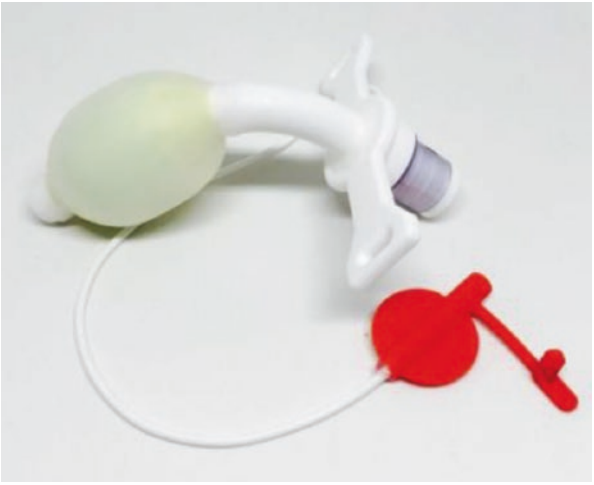

Fig. 45.5 Portex fenestrated tubes red inner cannula with fenestration white simple

- Decontamination from respiratory tract infection by cleansing the inner cannula with mild detergent is as effective as cleansing using an alcoholic chlorhexidine solution in reducing colony counts as per studies.
- Oral care with 2% chlorhexidine mouth wash and daily inspection of oral cavity is mandatory. Stoma should be cleaned with saline and in case of infection with antibacterial solution after sending culture specimen.
- Small granulation tissue can be removed with silver nitrate and large may require surgical excision. Patient and relative should be trained for stoma care and dressings.

Step 3. Provide Long Term Proper Humidification

- In addition to adequate hydration and humidified gas supplies patient may need HME device as in acute care setting. Environmental temperature and humidity also, is an important concern in chronic care. Tracheal filter is a good option for passive humidification. Tracheostomy Mask can used for oxygenation, active humidification and nebulization. (Fig. 45.6)

Step 4: Perform Safe Suctioning

- Suctioning into the tracheostomy tube should not be done as a routine procedure. The patient must be assessed for signs of sputum in the airways. Where the patient can cough secretions independently into the top of the tracheostomy tube these secretions can be can be removed with a clean yankauer suction or tissue paper.

Step 5: Facilitate Speech and Communication

- The purpose of communication for critically ill patients is to help them maintain their identity as well as psychological, structural, personal and social integrity.

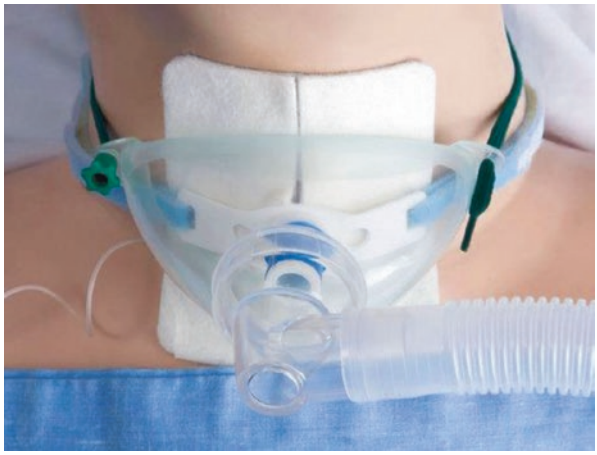

Fig. 45.6 Tracheostomy mask

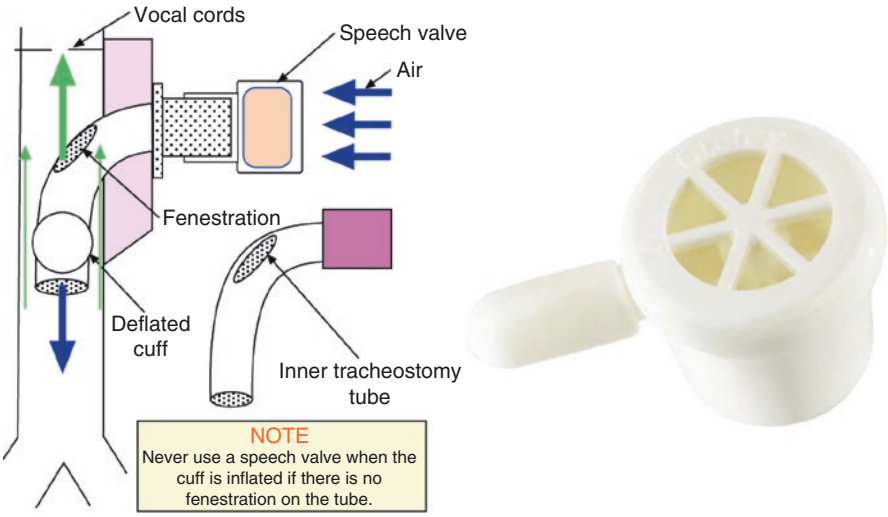

Fig. 45.7 Fenestrated tube and speaking valve

- Non-verbal communication methods to be considered
  - Lip reading
  - Facial expression, coded eye blinking and hand gestures
  - Alphabet Board, Picture Board and Phrase Books
  - Electronic Larynx and Electronic Communication Aids
- Verbal communication- requires special designed double lumen fenestrated tracheostomy tube and speaking valve (Fig. 45.7)

Steps for Speaking with TT Tube

- Explain the procedure
- Do adequate suctioning
- Cuff deflation
- Fenestrated tracheostomy tubes or Double lumen tracheostomy tube
- One way speaking valve if patient is comfortable

Make a Multidisciplinary Team for Tracheostomy Care

- Tracheostomy care is a multidisciplinary approach involving trained personnel like an intensivist, a surgeon, respiratory therapist, speech language pathologist and clinical nurse specialist to minimize tracheostomy related complications and better long-term care.
- Multidisciplinary team assesses patient's ability to tolerate a speaking valve and other augmentative communication strategies. Intensive care unit should have their own tracheostomy care protocol which is subdivided into immediate, intermediate and long-term care.

Check List for Tracheostomy Care in ICU and Afterwards

1. Always keep Tracheostomy replacement kit on bedside of the patient.
2. Always keep ready an intubation set in case of tube blockage.
3. Patency of tube should be checked in each duty shift.
4. Strict non traumatic aseptic suction as and when required.
5. Tube position should be always central.
6. Avoid tube moment and traction due to ventilator circuit.
7. If tube is sutured, always keep a surgical blade on bed side.
8. Never send the patient with sutured tracheostomy tube out of ICU.
9. Cuff pressure should be checked in every shift, and maintain between 20 and 25 cmH_2O
10. Change tube only if it is blocked (partial or complete) not routinely.
11. Daily care should involve stoma care/dressing, watch on bleeding, infection, dryness or granulation tissue formation.
12. Protocol to decannulate should be based on, as and when patient gets better, is able to swallow, cough and there is (10–15%) air leak around deflated cuff.
13. Always be suspicious for tracheal stenosis and tracheomalacia in patient where tracheostomy has been in situ for more than 3 weeks, is difficult to decannulate.

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Thoracentesis

46

Aakanksha Chawla Jain and Rajesh Chawla

A 65-year-old diabetic male patient was admitted to the hospital with severe community-acquired pneumonia and respiratory failure. He was started on antibiotics and other supportive medication. On the second day of admission, his breathlessness increased and he became hypoxic despite oxygen therapy. His chest X-ray showed blunting of the right costophrenic angle. USG chest showed presence of 400 mL of pleural fluid on the right side.

Thoracentesis is the aspiration of fluid or air from pleural space. Thoracentesis is a percutaneous procedure where pleural fluid is removed either through a needle (typically for small volumes e.g., <30 mL), or a small bore catheter. This can be done with or without ultrasound guidance; however, ultrasound guidance is preferred in critically ill patient.

Bedside ultrasonography can be used before the procedure to determine the presence and size of pleural effusion, to assess for loculations, and to guide needle placement.

A, very small free-flowing pleural effusions, with less than 1 cm distance from the pleural fluid line to the chest wall on a decubitus chest radiograph have been considered too small to justify thoracentesis because of the low diagnostic yield and high risk of pneumothorax.

With ultrasound-guided thoracentesis, the "safe window" for thoracentesis has been considered as a point where maximum pleural fluid depth is >1 cm adjacent to the parietal pleura.

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R. Chawla, S. Todi (eds.), *ICU Protocols*, https://doi.org/10.1007/978-981-15-0902-5_46

Step 1: Assess the Need of Thoracentesis

Diagnostic

- Any undiagnosed pleural effusion of any amount

Therapeutic

- Massive pleural effusion and the patient in respiratory distress
- Suspected hemothorax
- Suspected parapneumonic infection and empyema
- Small unresolved pneumothorax

Step 2: Rule out Contraindications

- No absolute contraindications
- Relative contraindications include the following:
  - Uncorrected bleeding diathesis
  - Chest wall cellulitis at the site of puncture
  - Lack of expertise

Step 3: Arrange all Equipments

- A thoracentesis device (This typically consists of an 8 F catheter over an 18-gauge, 7.5-in. (19-cm) needle with a three-way stopcock and, ideally, a self-sealing valve.)
- A self-assembled device, if the thoracentesis device is unavailable (It includes using an 18-gauge needle or 12- to 14-gauge intravenous cannula connected to a 50-mL syringe through stopcock.)
- Injection needles—18, 20, 22, and 25 gauge
- Syringes—5, 10, and 50 mL
- A tubing set
- Antiseptic (preferably, 2% chlorhexidine solution)
- Lidocaine 1% or 2% solution
- The specimen cap for the 60-mL syringe
- Heparin 1000 IU
- Specimen collecting vials or vacutainers
- A drainage bag or vacuum bottle
- Drape (24 in. × 30 in.)
- Sterile towels
- Adhesive dressing (7.6 cm × 2.5 cm)
- Gauze pads (4 in. × 4 in.)

Step 4: Place the Patient in Proper Position

- Ensure proper written consent of the patient or surrogate.
- Collect equipment, and preprocedure diagnostic laboratory studies, as necessary.
- Alert and cooperative patients are most comfortable in a seated position leaning slightly forward, resting their head on their arms on a pillow, which is placed on an adjustable bedside table.
- This position facilitates access to 6th–9th rib space in the posterior axillary line, which is the most dependent part of the thorax.
- Unstable patients and those who are unable to sit up may be in the supine position for the procedure with slight head elevation.
- The patient is moved to the extreme side of the bed, the ipsilateral hand is placed behind the head, and a towel roll is placed under the contralateral shoulder to facilitate dependent drainage.

Step 5: Procedure

1. *Needle thoracentesis*
   - This procedure is preferably done for diagnostic pleural aspiration.
   - Position the patient appropriately as already discussed.
   - After positioning the patient and prior to preparing, ideally perform ultrasonography to confirm the pleural effusion, assess its size, look for loculations, and determine the optimal puncture site.
   - Determine the optimal puncture site by searching for the largest pocket of fluid superficial to the lung.
   - If ultrasonography machine is not available, then identify the correct site of aspiration as a site of maximum dullness on percussion of the chest.
   - Ideally, the site is between the seventh and ninth rib spaces in the middle and posterior axillary line.
   - Use standard aseptic technique for the remaining steps of the procedure.
   - Clean a wide area with an antiseptic bacteriostatic solution such as chlorhexidine.
   - Place a sterile drape over the puncture site and use sterile towels on the bed to establish a large sterile field within which to work.
   - Lidocaine 2% solution should be used for local anesthesia. The skin, subcutaneous tissue, rib periosteum, intercostal muscle, and parietal pleura should all be well infiltrated with local anesthetics.
   - The needle is inserted to the periosteum of the lower rib and is moved up and over the lower rib with frequent injection of small amounts (0.1–0.2 mL) of lidocaine.

- Once this needle is superior to the rib, it is slowly advanced toward the pleural space with aspiration, followed by the injection of 0.1–0.2 mL of lidocaine every 1–2 mm.
- As soon as pleural fluid is aspirated through this needle into the syringe containing lidocaine, the needle should be withdrawn from the pleural space and reattached to a 50- to 60-mL syringe through a stopcock.
- The same needle or large needle (20 gauge) is reintroduced along the same tract slowly with constant aspiration until pleural fluid is obtained.
- Aspiration is then continued until the syringe is filled with pleural fluid.
- Avoid draining more than a liter in one sitting.
- Stop aspirating if the patient coughs and gets dyspneic.
- The needle is then withdrawn, and the procedure is stopped.
- Carefully remove the needle and dress the wound.
- Label the pleural fluid and send it for diagnostic analysis.
- If the effusion is small and contains a large amount of blood, place it in an anticoagulant (heparin) so that it does not clot.
- Reposition the patient appropriately based on his or her comfort and respiratory status.
- Write a procedure note and comment specifically on the descriptive characteristics of the pleural fluid.

2. *Thoracentesis with intravenous cannula*
   - Follow the similar procedure as pleural aspiration with the needle up to anesthetizing the desired intercostal space.
   - Then, arrange a 12G intravenous cannula with a needle and a three-way stopcock and 50-mL syringe.
   - While aspirating, introduce this cannula with the same track up to the pleural space till pleural fluid fills in the syringe.
   - Remove the inner needle from the outer cannula and reattach the three-way stopcock and syringe.
   - Then using the manual syringe pump method or vacuum bottle, aspirate the desired amount of fluid. Follow the rest of steps as described above.
3. *Thoracentesis with commercial kits*
   - Follow the similar procedure as pleural aspiration with the needle up to anesthetizing the desired intercostal space.
   - Initially nick the skin with a No. 11 scalpel blade to reduce skin drag.
   - While aspirating, advance the device over the superior aspect of the lower rib until pleural fluid is obtained.
   - When a free flow of fluid is encountered, the catheter is advanced approximately 1 cm and the needle is withdrawn completely.
   - There is a self-sealing valve so that air does not leak into the pleural space when the needle is withdrawn; however, the needle cannot be reinserted through the catheter.
   - Using either a syringe pump method or a vacuum bottle, drain the pleural effusion until the desired volume has been removed for symptomatic relief or diagnostic analysis.

Step 6: Manage Complications

Major complications

- Pneumothorax (3–11%)
- Tension pneumothorax
- Hemothorax (0.8%)
- Laceration of the artery, liver, or spleen (0.8%)
- Diaphragmatic injury
- Empyema
- Hypotension
- Reexpansion pulmonary edema

Minor complications

- Pain (22%)
- Dry tap (13%)
- Cough (11%)
- Subcutaneous hematoma (2%)
- Subcutaneous seroma (0.8%)
- Vasovagal syncope
- Tumor seeding

Step 7: Send Pleural Fluid for the Laboratory Tests

Routine investigations

- Biochemical analysis—pH level (in heparinised syringe), glucose levels, protein levels, albumin, lactic acid dehydrogenase levels, and adenosine deaminase
- Microbiology examination—Gram stain, fungal stain and culture, AFB stain and culture, and aerobic culture
- Total cell count and differential cell count
- Cytology

Special investigation

- Creatinine levels and pH for urinothorax
- Amylase levels—if there is a pretest suspicion of acute pancreatitis, chronic pancreatic disease, or esophageal rupture
- Triglyceride levels for chylothorax
- Rheumatoid factor for rheumatic lung disease
- Pro-BNP levels for congestive heart failure
- Hematocrit levels for hemothorax

Reasons for Dry Tap

Skin indentation artifact

- Skin movement artifact
- Poor angle replication
- Patient movement
- Needle blockage
- Visceral pleural impingement
- Unexpandable lung
- Inappropriately short needle.

Suggested Reading

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Chest Tube Placement

47

Rajesh Chawla, Ashish Jain, and Roseleen Kaur Bali

A 60-year-old male patient—a known case of chronic obstructive pulmonary disease—was admitted to the hospital with sudden onset of breathlessness. On examination he was found to be tachypneic and had cyanosis. His chest skiagram showed pneumothorax on the right side.

A chest tube placement (tube thoracostomy) is a method to insert a flexible, hollow tube into pleural space to extract air, fluid blood, or pus. It helps in maintaining negative intrapleural pressure and expansion of the lung.

Step 1: Assess the Need of Chest Tube Insertion

- Pneumothorax in any mechanically ventilated patient
- Pneumothorax after initial relief with needle aspiration
- Bilateral pneumothoraces
- Persistent or recurrent pneumothorax after simple aspiration
- Large secondary spontaneous pneumothorax
- Malignant pleural effusion
- Empyema and complicated parapneumonic pleural effusion
- Traumatic hemopneumothorax
- Chylothorax
- Postoperative—for example, thoracotomy, esophagectomy, and cardiac surgery

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Step 2: Rule out Contraindications

There is no absolute contraindication in emergency situation:

- Bleeding diathesis (prothrombin time or partial thromboplastin time more than two times normal, platelets <50,000/ml) should be corrected in nonemergency settings.
- Inability to aspirate pleural fluid or air to confirm correct pleural space before chest drain insertion.
- Caution is required when there is a history of thoracic surgery or pleurodesis on the side of proposed chest tube insertion.
- The lung densely adherent to the chest wall throughout the hemithorax is an absolute contraindication to chest drain insertion.

Step 3: Pre-Drainage Risk Assessments

- Risk of hemorrhage, any coagulopathy, or platelet defect should be corrected prior to chest drain insertion in nonemergency situations.
- Routine measurement of the platelet count and prothrombin time is only recommended in patients with known risk factors.
- A careful radiological differentiation between pneumothorax and bullous disease, collapse and a pleural effusion, is required.
- The drainage of a postpneumonectomy space should only be carried out by or after consultation with a cardiothoracic surgeon.
- For patients with penetrating thoracic trauma, recommendation is to administer prophylactic antibiotics prior to chest tube placement. Patients with penetrating trauma have significantly decreased rates of empyema and pneumonia when given antibiotics prior to chest tube placement, as compared with placebo.

Step 4: Preparation

- Sterile gloves and gown
- Skin antiseptic solution, for example, Betadine or chlorhexidine in alcohol
- Sterile drapes, eye protection, mask, and caps
- Gauze swabs
- Intravenous catheters, tubing
- Supplemental oxygen
- Monitors (cardiac, pulse oximeter)
- A selection of syringes and needles (16–25 gauge)
- Local anesthetic, for example, lignocaine (lidocaine) 1% or 2%
- Scalpel and #10 or #15 blade
- Suture (e.g., “1–0” silk)
- Instrument for blunt dissection (e.g., curved clamp)

- Forceps and the needle holder
- The guidewire with dilators (for intercostal drainage catheter placement)
- Chest tube (No 24–40 French)
- Connecting tubing
- Closed drainage system (including sterile water if underwater seal being used)
- Dressing and adhesive
- Antiseptic ointment
- Resuscitation cart
- Drugs—benzodiazepine, anticholinergics

Step 5: Consent and Premedication

- Written and informed consent should be taken before doing the procedures.
- Intravenous analgesics or mild sedation (benzodiazepine or narcotic) and anticholinergics should be administered.

Step 6: Patient Position

- The preferred position for drain insertion is the patient lying on the bed with the head up, slightly rotated, with the arm on the side of the procedure behind his/her head to expose the axillary area.
- Procedure can also be done while the patient is sitting upright leaning over an adjacent table with a pillow or in the lateral decubitus position.
- For most adults, place the patient in the supine position with the ipsilateral arm abducted and the elbow flexed to position the hand comfortably over the patient's head.
- In the absence of trauma necessitating spine immobilization, the head of the bed can be slightly raised for comfort.

Step 7: Site Selection

- Careful identification of the correct patient, correct side, and correct site should be checked immediately before the procedure. Confirm the indication of chest tube insertion by reviewing the clinical signs and the chest radiograph.
- Ultrasonography can be used as adjunctive guides to the site of tube placement. Ultrasound can localize a fluid collection and image the lung to help prevent lung laceration during tube placement.
- For pleural fluid drainage, the proposed site of chest tube insertion can be confirmed by first performing a thoracentesis using ultrasound guidance. If air or fluid is not obtained during diagnostic thoracentesis, the insertion site is reassessed by reviewing the available chest radiographs or computed tomography.

Occasionally, fluid may not be able to be aspirated with a small needle because of high viscosity of the pleural fluid

- A chest radiograph must be available at the time of drain insertion except in the case of tension pneumothorax.
- The chest tube should be inserted in the fourth to sixth intercostal space in the midaxillary line in the safe triangle.
- The safe triangle is bordered by the anterior border of the latissimus dorsi, the lateral border of the pectoralis major muscle, a line superior to the horizontal level of the nipple, and an apex below the axilla.
- This position minimizes risk to underlying structures such as the internal mammary artery and avoids damage to muscle and breast tissue resulting in unsightly scarring.
- A more posterior position may be chosen if suggested by the presence of a loculated effusion or air. While this is safe, it is not the preferred site as it is more uncomfortable for the patient to lie down after insertion and there is a risk of the drain kinking.
- For apical pneumothoraces, the second intercostal space in the midclavicular line is sometimes selected but is not recommended routinely as it may be uncomfortable for the patient and may leave an unsightly scar. This site can be chosen for needle thoracostomy in tension pneumothorax.
- In hemodynamically unstable patients in whom there is a high suspicion for tension pneumothorax, needle thoracostomy should be performed as a life-saving (albeit temporizing) measure by reducing the intrapleural pressure and restoring venous return to the heart. Following needle decompression of the chest, a thoracostomy tube using a standard technique should be placed as soon as possible because needle thoracostomy may not completely relieve the tension pneumothorax and technical issues may lead to recurrent tension pneumothorax.

Step 8: Select the Drain Size

Drain size depends on the underlying pathology:

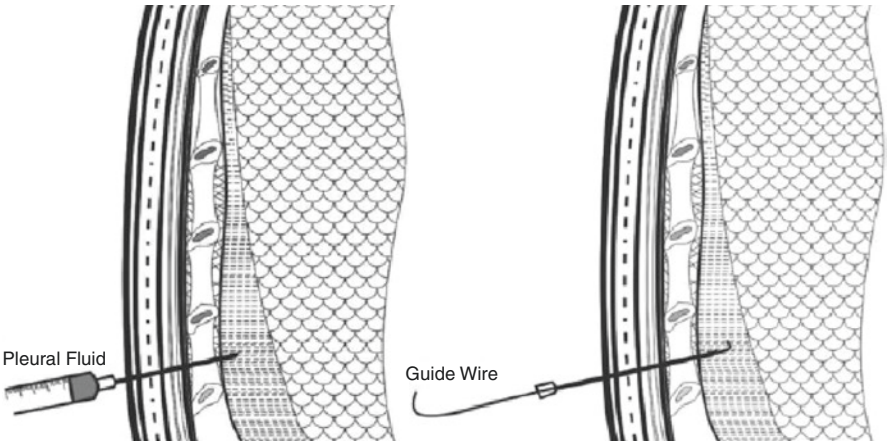
- Small-bore drains are recommended as they are more comfortable than large-bore tubes, but there is no evidence that either is therapeutically superior. These are put in patients with pneumothorax or pleural effusion.
- Large-bore drains are recommended for drainage of acute hemothorax and empyema.

Step 9: Procedure

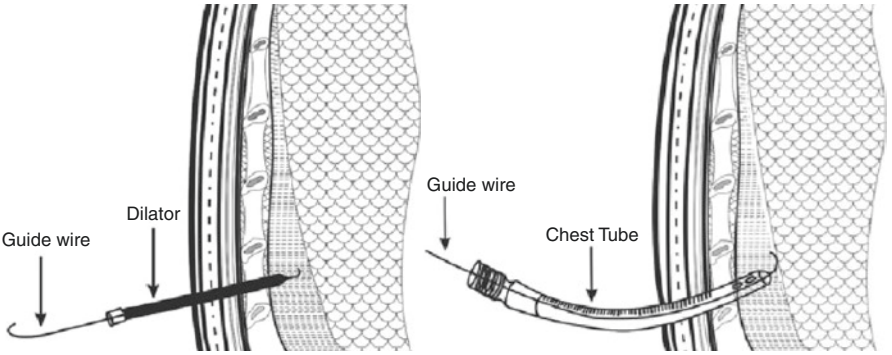
Four methods are described:

1. Guidewire tube thoracostomy
2. Trocar tube thoracostomy

3. Operative tube thoracostomy
4. Single-port thoracoscopy
   A. *Guidewire tube thoracostomy* (Figs. 47.1–47.4)
      - Explain procedure to the patient.
      - Take written consent.
      - Give proper position to the patient.
      - Wear the cap and mask, perform hand hygiene, and wear personal protective equipment (PPE) with sterile gloves.
      - Provide supplemental oxygen, secure intravenous access, and attach all monitors.
      - Ensure adequate lighting.
      - Arrange all equipments on a sterile workplace.
        – Clean the skin of the patient with 2% chlorhexidine in alcohol preparation.



Figs. 47.1 and 47.2 Guidewire tube thoracostomy



Figs. 47.3 and 47.4 Guidewire tube thoracostomy

  - Give a frictional scrub in a circular manner to at least 10-cm area from the insertion site.
  - The field can be draped using towels. In all invasive procedures, meticulous care should be taken to minimize the risk of infection.
  - After locating intercostal space, infiltrate local anesthesia into the skin raising the cutaneous wheel at incision site and subcutaneous tissue.
- Anesthetize rib and pleural space in selected intercostal space.
- Insert the introducer needle just superior to the appropriate rib. Stop just at the point where air or fluid is aspirated (Fig. 47.1).
- Remove the syringe keeping the needle in situ, covering the needle opening with fingers to prevent entry of air.
- Introduce the guidewire through the needle into pleural space and then remove the needle from pleural space while keeping the guidewire in situ (Fig. 47.2).
- Make a small nick at the entry site to allow introduction of dilators and the chest tube.
- Use dilators to dilate the tract over the guidewire (Fig. 47.3).
- Introduce the chest tube over the guidewire into the pleural space. Confirm that all openings are in pleural space. Remove wire.(Fig. 47.4).
- Connect the chest tube to the drainage system.
- Suture the tube in place and dress with gauze and tape.

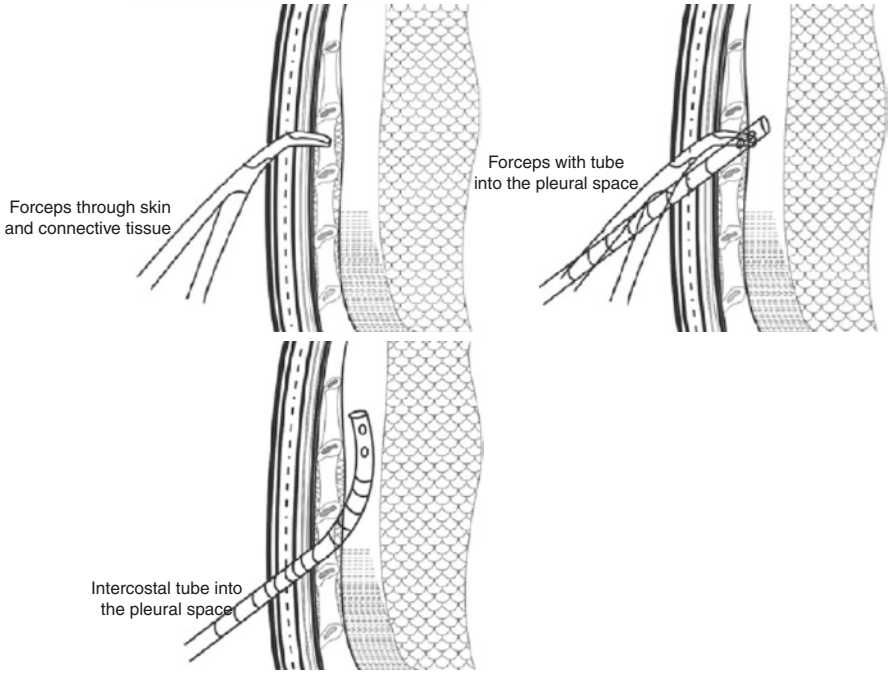
B. *Trocar tube thoracostomy*

- Take written consent.
- Give local anesthesia with 2% Xylocaine.
- This method initially requires a 2–4-cm incision parallel to the superior border of the lower rib through the skin and subcutaneous tissues after local anesthesia.
- This method uses a chest tube with a trocar positioned inside the tube.
- The chest tube with the trocar can then be inserted between the ribs into the pleural cavity, directed toward the opposite shoulder with the flat edge of the stylet tip cephalad to prevent damage to the intercostal vessels.
- Because significant force is often required to insert the trocar, the hand not applying the force should be placed next to the patient's chest wall to control the depth of penetration.
- Once the pleural cavity is entered, the inner trocar is gradually removed from the chest tube. When the proximal end of the trocar clears the chest wall, a clamp is placed between the trocar and the chest wall until the trocar can be completely withdrawn and the tube attached to a water-seal drainage system.
- In critically ill patients, one should avoid the trocar tube thoracostomy.

C. *Operative tube thoracostomy*

- Explain the procedure.
- Position the patient in a semi-recumbent position with the head and shoulder about 30° off the bed.

- The ipsilateral arm is placed above the head for exposure of the axilla and to increase distance between the ribs.
- Follow the first few steps as in the guidewire method.
- After locating intercostal space, infiltrate local anesthesia into the skin raising the cutaneous wheel at incision site and subcutaneous tissue.
- Generously anesthetize parietal pleura and confirm entry into pleural space by aspiration of air or fluid. Then, withdraw syringes and needles.
- Make a skin incision above and parallel to the upper border of the lower rib, one space below the desired site, in intercostals space wide enough to insert a finger.
- The incision should be made down to the fascia overlying the intercostal muscle. This fascia is then incised throughout the length of the incision, with care taken not to cut the muscle.
- Once the fascia has been incised, the muscle fibers are spread with a blunt-tipped hemostat tracking upward until the upper desired intercostal interspace is identified. This will make a tunnel, which helps in keeping the tube in the right place (Fig. 47.5).
- An incision is made in the intercostal fascia just above the superior border of the rib over which the tube will pass.
- Again infiltrate muscle and pleura with the local anesthetic agent.



Figs. 47.5–47.7 Operative tube thoracostomy

- Advance the needle into the pleural space while aspirating fluid or air to confirm the correct location.
- The parietal pleura is then dissected with a blunt-tipped hemostat, ensuring that the tip of hemostat remains on the superior aspect of the lower rib. The hole is then enlarged by means of the operator's index finger.
- At this time, the operator should palpate the adjacent pleural space to detect any adhesions in the pleura.
- Clamp the end of the chest tube with a Kelly clamp and guide into the pleural space with its distal end clamped. Direction is anteroapical for air and inferoposterior for fluid drainage (Figs. 47.6 and 47.7).
- Attach to the external drainage system.
- Suture the tube securely with a purse-string suture to prevent tube displacement.
- Use occlusive gauze to seal the skin around the tube.
- Dress area with a generous amount of gauze and tape.

D. *Single-port thoracoscopy*

- Chest tubes can be inserted through a single-port thoracoscopy. Then under direct visualization, the chest tube is placed into the costodiaphragmatic gutter or in the upper part of thoracic cavity.
- The great advantage is the visualization of the place where the tube will be placed.

Step10: Verification of Chest Tube Placement

- After the chest tube has been inserted and connected to a drainage system, a chest radiograph should be obtained to verify the correctness of its position.
- Ideally, both a posteroanterior view (PA) and a lateral view should be obtained because certain ectopic locations may not be apparent on the PA view alone.
- A CT scan should be obtained when the chest tube does not drain adequately and the chest radiograph is noncontributory.
- With CT, the tube can be visualized over its entire course with accurate location. If there are undrained locules of fluid, additional chest tubes can be inserted.

Drainage System

One-Bottle Collection System

- This system consists of one bottle that serves as both a collection container and a water seal.
- The chest tube is connected to a rigid straw inserted through a stopper into a sterile bottle.

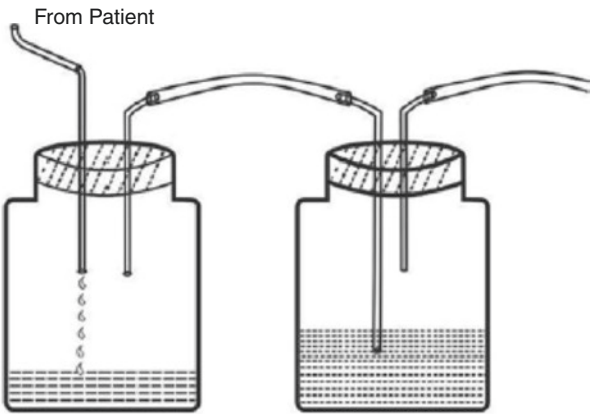


Fig. 47.8 Three-bottle drainage system

- Enough sterile saline solution is instilled into the bottle so that the tip of the rigid straw is approximately 2 cm below the surface of the saline solution.
- The bottle's stopper must have a vent to prevent pressure from building up when air or fluid coming from the pleural space enters the bottle.
- This one-bottle system works well for uncomplicated pneumothorax.
- If substantial amount of fluid is draining from the patient's pleural space, the level of fluid will rise in the one-bottle system, and therefore, the pressure will have to be higher and higher in the rigid straw to allow additional air or fluid to exit from the pleural space. So, in such a case, two-bottle collection system is advised.

Two-Bottle Collection System (Fig. 47.8)

- This system is preferred to the one-bottle collection system when substantial amounts of liquid are draining from the pleural space.
- With this system, the bottle adjacent to the patient acts as a collection bottle for the drainage, and the second bottle provides the water seal and the air vent.
- The degree of water seal does not increase as the drainage accumulates. The water-seal bottle functions identically in both the one- and two-bottle systems.

Suction and Three-Bottle Collection Systems (Fig. 47.9)

- Controlled amounts of suction (usually 15–20 cm H2O) can be readily applied to the system if a third bottle, the suction-control bottle, is added to the system.
- The amount of negative pressure in the system is equal to the depth to which the rigid straw in the suction-control bottle is submerged below the surface of water.
- It is desirable to apply negative pressure to the pleural space to facilitate reexpansion of the underlying lung or to expedite the removal of air or fluid from the pleural space.

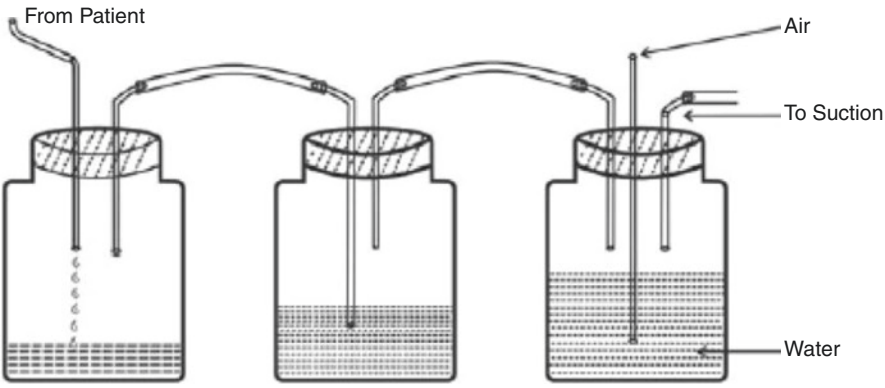


Fig. 47.9 Three-bottle drainage system

Step 11: Care of the Chest Tube

Always see the following things:

- Is there bubbling through the water-seal bottle or the water-seal chamber on the disposable unit?
- Is the tube functioning? Always check for air column movement.
- What is the amount and type of drainage from the tube?

Step 12: Guidelines for Removal

- Fully expanded lung
- Resolution of air leak for 24 h
- For pleural effusion, drainage less or up to 50 ml/day for 3 consecutive days
- Clamp tube and repeat chest Xray in 6 h for recurrence of Pneumothrax

Step 13: How to Remove

- The chest tube should be removed either while the patient performs Valsalva maneuver or during expiration with a brisk firm movement while an assistant ties the previously placed closure suture.
- Obtain an early chest radiograph.

Step 14: Complications

- Local site bleeding
- Hematoma

- Hemothorax from intercostals vessel injury
- The tube misplaced
- The nonfunctional tube
- Laceration of the lung, liver, and heart
- Intra-abdominal placement
- Pneumothorax
- Infection-site cellulitis, track infection, empyema
- Reexpansion pulmonary oedema
- Subcutaneous emphysema
- Clamping a chest tube with presence of air leak may result in tension pneumothorax
- Persistent leak at the site of infection and around the tube

Step 15: Troubleshooting Thoracostomy Tubes

- Many times a closed-suction system becomes disconnected, the tube should be cleaned with an antiseptic (e.g., alcohol, povidone iodine) and the tubing reconnected.
- If a new closed-suction apparatus is immediately available, than the new one should be connected and the old one discarded.
- If patient has an air leak, the chest tube should never be clamped, because doing so can lead to tension pneumothorax.
- Instillation of fibrinolytic agents aids in maintaining flow or restoring flow in obstructed catheters.
- If the chest tube is no longer draining and there is a suspicion that it is full of clot or debris, the tube can be stripped or cleared of obstruction by other maneuvers. These manipulations should only be done by an experienced clinician, typically the physician who places and manages the tube.
- Care should be taken to avoid dislodging the tube during these attempts.
- A tube that has become partially dislodged and exposed to the external environment should not be reinserted.
- When you want to strip the tube, hold the chest tube near its insertion site with the one hand, compress the tube between the first and second fingers of the second hand, and gently pull toward the drainage system.
- If stripping the tube does not clear the tube and reestablish respiratory variation in the drainage system, then following maneuvers should be tried:
  - Twisting the tube 360 degrees,
  - Pulling the tube out 1–2 cm,
  - Passing a sterile endotracheal tube suction catheter,
  - Injecting a small volume of sterile saline with a few drops of povidone-iodine
  - Attempting to clear with a Fogarty balloon catheter.
- If all these fail to resolve the problem and the patient still has indications for thoracostomy, then a new tube should be placed.
- The nonfunctioning tube should be removed only after the correct placement of the new tube is confirmed and it is functioning properly.

Suggested Reading

Cerfolio RJ, Bass CS, Pask AH, et al. Predictors and treatment of persistent air leaks. Ann Thorac Surg. 2002;73:1727–30. *Steroid use, male gender, a large leak, a leak with a pneumothorax, and having a lobectomy are all risk factors for a persistent leak. Discharge on a Heimlich valve is safe and effective for patients with a persistent leak unless the leak is an expiratory*

Gayer G, Rozenman J, Hoffmann C, et al. CT diagnosis of malpositioned chest tubes. Br J Radiol. 2000;73:786–90. *CT has proved to be extremely accurate in evaluating the position of a chest tube and has often provided additional valuable information with significant therapeutic impact*

Gilbert TB, McGrath BJ, Soberman M. Chest tubes: indications, placement, management and complications. J Intensive Care Med. 1993;8:73–86. *A review article on chest tube management*

Luketich JD, Kiss M, Harshey J. Chest tube insertion: a prospective evaluation of pain management. Clin J Pain. 1998;14:152–4. *In this study, a new protocol, including improved house staff, nursing education, premedication, proper insertion techniques, and more liberal and precise delivery of local anesthetics, allowed the goal of a painless chest tube insertion*

Zgoda MA, Lunn W, Ashiku S, et al. Direct visual guidance for chest tube placement through a single-port thoracoscopy: a novel technique. Chest. 2005;127:1805–7. *A rigid telescope can be safely utilized to accurately place a chest tube after medical thoracoscopy through the same portal used for the pleuroscope*

Pericardiocentesis

48

Rajesh Chawla, Sananta K. Dash, and Vipul Roy

A 60 year old patient post coronary artery bypass grafting returned from theater intubated and ventilated. He had two chest drains (routine post operative) and on arrival to intensive care unit he was on 3 μg/min of noradrenaline infusion. Over next 2 h his drain output has increased from 50 mL/h to 200 mL/h and his noradrenaline requirement has increased upto 20 μg/min to achieve a systolic blood pressure 110 mm Hg. His current blood lactate is 7 mmol/L. This hour there is no drain output, the current BP is 90/78 mm Hg and there is a visible swing in the arterial line trace. His central venous pressure is 22 mm Hg. His blood result showed a drop in Haemoglobin from 9.8 to 6.5 g/dL.

The removal of fluid from the pericardial space is called pericardiocentesis. The abrupt collection of fluid raises intrapericardial pressure, compresses the heart, and decreases cardiac output. This condition is called cardiac tamponade. Echocardiography is recommended to make urgent diagnosis and look for diastolic collapse of the right atrium and ventricle due to cardiac tamponade. Immediate aspiration of fluid is recommended in such a case.

Step 1: Assess the Patient

Assessment of a patient of excessive pericardial fluid is done clinically based on the clinical signs, ECG, and echocardiography (Table 48.1).

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Table 48.1 Differentiating cardiac tamponade and constrictive pericarditis

Clinical signs	Tamponade	Constrictive pericarditis
Pulsus paradoxus	Common	Usually absent
Jugular veins		
Prominent *y* descent	Absent	Usually present
Prominent *x* descent	Present	Usually present
Electrocardiogram		
Low ECG voltage	May be present	May be present
Electrical alternans	May be present	Absent
Echocardiography		
Thickened pericardium	Absent	Present
Pericardial calcification	Absent	Often present
Pericardial effusion	Present	May or may not be present
Right ventricle size	Usually small	Usually normal
Myocardial thickness	Normal	Normal
Right atrial collapse and right ventricular diastolic collapse	Present	Absent
Exaggerated respiratory variation in flow velocity	Present	Present
CT/MRI		
Thickened/calcific pericardium	Absent	Present
Cardiac catheterization		
Equalization of diastolic pressures	Usually present	Usually present

Step 2: Assess the Need of Needle Pericardiocentesis and Contraindications

A. Indications

Emergency

1. Evidence of cardiac tamponade:
   (a) Hypotension (refractory to fluid resuscitation and vasopressors)
   (b) Distended neck veins with cyanosis
   (c) Central venous pressure more than 20 mmHg
   (d) Narrowed pulse pressure
   (e) No other explanation of hypotension (e.g., pneumothorax)
2. Penetrating injury to the chest between the nipples with shock

Elective

Purely diagnostic pericardiocentesis should be limited to selective cases:

1. Cytologic evaluation (discriminate a bacterial, traumatic, neoplastic, or idiopathic cause)
2. Removal of chronic pericardial effusion, which may also produce immediate clinical improvement

3. Placement of a catheter for repeated pericardial drainage and lavage
4. Instillation of antimicrobial agents into the pericardial space
5. Suspicion of purulent pericarditis

B. *Contraindications*
   (i) Septic pleuritis (may introduce infection into pericardial space).
   (ii) External wounds overlying the site of centesis (The approach for the procedure can be from either side of thorax).
   (iii) Thrombocytopenia (<50,000/mm^3), bleeding disorders, and anticoagulant therapy (for elective pericardiocentesis).

Step 3: Know the Options

1. Needle pericardiocentesis: It is decompression of pericardial tamponade by needle aspiration of blood or fluid from the pericardial space.
2. Intrapericardial catheterization: This is a nonsurgical, usually done in a catheterization laboratory under fluoroscopic or echocardiography guidance using dilatational technique.

Step 4: Procedure

- Aggressive resuscitation measures should continue along with preparation for emergency pericardiocentesis.
- Vasopressor and inotropic support should be considered in fluid unresponsive shock.
- The required investigations include complete hemogram, prothrombin time (PT, INR, activated partial thromboplastin time (aPTT), renal functions tests (RFT), and liver functions tests (LFT).
- Blind pericardiocentesis is no longer recommended. Echocardiography-guided procedure is safe and desirable (Table 48.2)

A. *Percutaneous blind technique*
   1. Take written informed consent.
   2. *Patient preparation*: Monitor vital signs and attach cardiac monitor. Keep the head of the bed elevated to approximately 45°. The patient should be placed at a comfortable height for the physician. A central venous catheter is essential for monitoring of right heart pressure and rapid infusion of saline and drugs. Invasive arterial pressure monitoring is indicated. Oxygen supplementation is essential:
      - *Localizing the entry site*: Locate the patient's xiphoid process and the border of the left costal margin using inspection and careful palpation. The needle entry site should be 0.5 cm to the (patient's) left of the xiphoid process and 0.5–1.0 cm inferior to the costal margin.

Table 48.2 Equipment for pericardiocentesis

Equipments for needle pericardiocentesis	Equipments for intrapericardial catheterization
Preparation of the site	*Catheter placement*
Antiseptic	Teflon-coated, flexible J-curved guidewire
Gauze, sterile drapes, and towels	5F or other system
Sterile gloves, masks, gowns, caps	A 35-cm flexible pigtail catheter with multiple fenestrations (end and side holes)
A 5- or 10-mL syringe with a 25-gauge needle	
1% or 2% lidocaine (without epinephrine)	
Emergency drugs	
Procedure	*Drainage system*
No. 11 blade	A three-way stopcock
A 20-mL syringe with 10 mL of 1% lidocaine (without epinephrine)	Sterile tubing
An 18-gauge, 8-cm, thin-walled needle with the blunt tip	A 500-mL sterile-collecting bag (or bottle)
Multiple 20- and 50-mL syringes	Sterile gauze and adhesive bag (or bottle)
Hemostat	Suture material
Electrocardiogram machine	
Three red top tubes	
Two purple top (heparinized) tubes	
Culture bottles	
Postprocedure	
Suture material	
Scissors	
Sterile gauze and bandage	

- *Skin preparation*: Strict asepsis is required with povidone iodine preparation. Local anesthesia is required (lidocaine 2%) prior to the puncture.
- *Puncture*: Puncture at a 45° angle to the skin with the needle toward the inferior tip of the left scapula.
- *Advancement*: Advance the needle posteriorly (while initially pressing the liver hard with the other hand to avoid a tear of the liver) with intermittent aspiration and injection of lidocaine through the path. Pass the tip beyond the posterior border of the bony thorax (usually lies within 2.5 cm of the skin surface). If bone contact occurs, then walk the needle behind the posterior (costal) margin. Reduce the angle of contact to 15° once the tip has passed the posterior margin of the bony thorax, and continue in the same direction.
- Further advancement is done with continuous aspiration. If electrocardiographic guidance is used, the sterile alligator clip is applied to the needle hub. Monitor continuous ECG throughout the procedure. Look for ST-segment elevation or premature ventricular contractions (evidence of epicardial contact) as the needle is advanced.
- *End point*:
  - Advance the needle along this extrapleural path until a definite give-way is felt and fluid is aspirated from the pericardial space (usually

6.0–7.5 cm from the skin). Some patients may experience a vasovagal response at this point and require atropine intravenously to increase their blood pressure and heart rate.
  - If ST-segment elevation or premature ventricular complexes occur (i.e., the needle in contact with pericardium), withdraw the needle toward the skin surface while aspirating, and if unsuccessful, then retry in the same way (caution is not to do any lateral motion as it can damage the epicardial vessels).
  - Collect the samples and send investigations accordingly.
- *Evidence of successful decompression*
- Decreased intrapericardial pressure to levels between −3 and +3 mmHg:
  - Fall in right atrial pressure and separation between the right and left ventricular diastolic pressures
  - Increased cardiac output
  - Increased systemic blood pressure
  - Reduced pulsus paradoxus to physiologic levels (≤10 mmHg)

  Please note that these blind techniques have a high incidence of morbidity and mortality, and they are no longer justified without echocardiography.

B. *Echocardiography-guided intrapericardial catheterization pericardiocentesis* (Fig. 48.1–48.3)
- Take an informed consent.
- The patient is placed in the semi-reclining position, slightly rotated leftward to enhance the fluid collection in the inferoanterior part.
- Define the site of entry and needle trajectory. The site of needle insertion is the place where the pericardial space is closest to the probe and the fluid accumulation is maximum.
- Local site preparation is the same as that for the percutaneous blind technique.

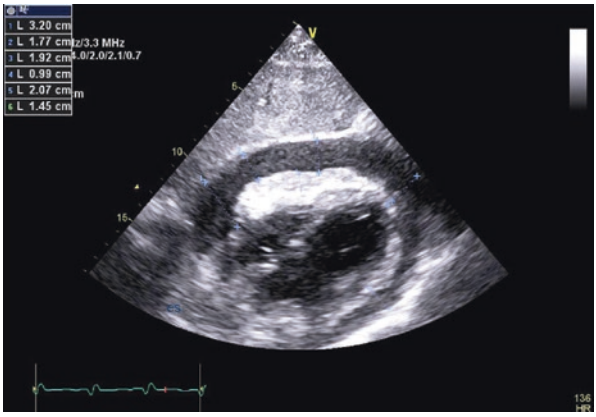

Fig. 48.1 Subcostal view showing measurement of pericardial effusion

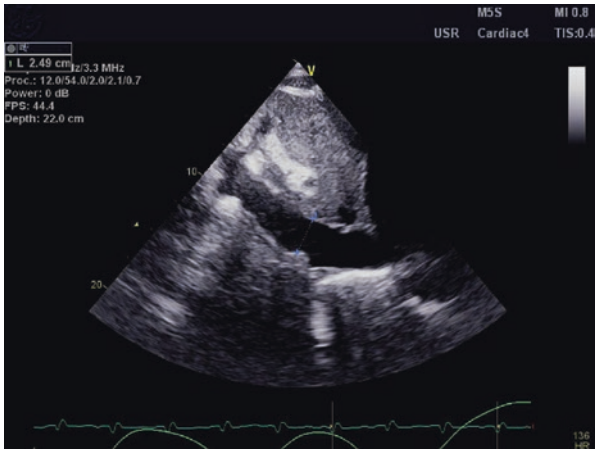

Fig. 48.2 Dilated inferior venacava (IVC)

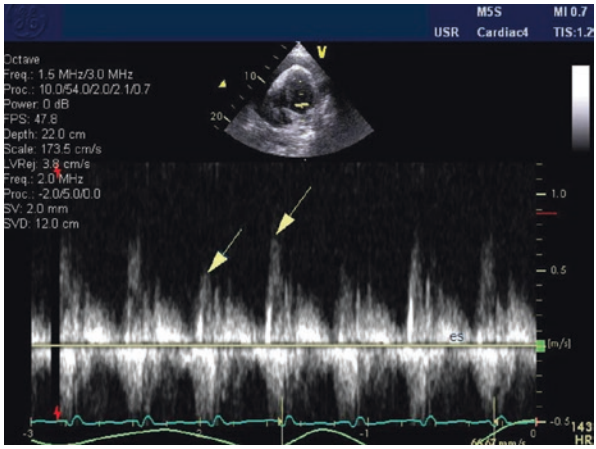

Fig. 48.3 Variation of mitral inflow velocity with respiration (>25%)

- A straight trajectory that avoids puncture of vital organs is chosen. The site should be 3–5 cm from the parasternal border to avoid puncture of the internal mammary artery. The optimal needle trajectory has to be preimagined by the operator.
- A 14–16-gauge Teflon sheath needle attached with a saline-filled syringe is used. On entering the fluid, a further advancement of 2 mm is advised; the sheath is advanced over the needle and the needle is withdrawn. Confirmation of the needle position is done by 5 mL of agitated saline and seen by echocardiography in the pericardial space.
- Seldinger technique is used to place a guidewire through the sheath, and then, sheath is removed. A series of skin dilation is then performed to finally allow an 8 F, 35-cm flexible pigtail catheter to be guided over the guidewire into the pericardial space.

Table 48.3 Echocardiographic findings in Cardiac Tamponade

Views	Findings
Two dimensional (2D) subcostal, parasternal long axis (PLAX), parasternal short axis (SAX)	Pericardial effusion (Fig. 48.1)
2D PLAX (RV collapse), apical 4 chamber (right atrium (RA),right ventricle (RV) collapse)	Systolic collapse of RA & Diastolic collapse of RV
Sub costal	Dilated inferior vena cava (IVC) and loss of respiratory variation(Fig. 48.2)
Apical four chamber	Increased interventricular dependence with respiration
Pulsed wave Doppler (PWD)	>25% of respiratory variation in mitral inflow and tricuspid inflow (Fig. 48.3)

- Maintenance of the system—secure the pigtail with suture and connect it to a reservoir. Flush the drain every 4–6 h with 10–15 mL saline to maintain the patency.
- Other different methods and kits are now available as possible alternate techniques.

C. *In post cardiac surgery patients*

- Cardiac tamponade is a major cause of shock in the post operative period. The subtle signs in the immediate post operative period includes, sudden decrease in an ongoing high drain output, rising Central Venous Pressure (CVP), rising lactate, narrow pulse pressure, deranged LFT and increased vasopressor requirement.
- An immediate bedside echocardiography leads to early diagnosis of this correctable complications. The readiness for opening the chest in ICU and cardiothoracic surgical back-up may be life saving for the patient.
- With the wide spread use and availability of Echocardiography, an ICU practitioner should be aware of "Echcardiographic signs of tamponade" (Table 48.3)
- The resuscitation protocol and CPR for this cohort of patient is different from that the normal Advanced Cardiac Life support (ACLS) protocol. The recommended dose for Adrenaline is 50–100 μg intravenous (as against 1 mg in ACLS protocol). Defibrillation should be done early for a shockable rhythm and three stacked shocks can be given in the situation of recurrent shockable rhythm in spite of defibrillation attempt.

Step 5: Manage Complications (Table 48.4)

Table 48.4 Management of complications

	Complications	Prevention/treatment
Structural damage	Cardiac puncture with hemopericardium	Careful procedure, urgent thoracotomy, and repair
	Coronary artery laceration (hemopericardium or myocardial infarction)	Careful procedure, urgent thoracotomy, and repair
	Fistula formation	Surgical correction
Rhythm disturbance	Arrhythmias, bradycardia, ventricular tachycardia/ventricular fibrillation	Often spontaneously revert, may need cardioversion/defibrillation/ cardiopulmonary resuscitation
	Cardiac arrest (precipitated by pulseless electrical activity, tachyarrhythmia, or bradyarrhythmia)	Cardiopulmonary resuscitation according to ACLS protocol
Dysfunction (cardiopulmonary)	Transient biventricular dysfunction	Often reverts, vasopressors, and inotropes
	Pulmonary edema	Manage according to standard practice
Extracardiac	Hemothorax	Intercostal tube drainage (ICD)
	Pneumothorax	ICD insertion
	Trauma to abdominal organs (liver, gastrointestinal tract)	Careful procedure, better to do under ultrasonographic or fluroscopic guidance
	Infection	Standard therapy

Step 6: Send Investigations of Pericardial Fluid (Table 48.5)

Table 48.5 Investigations of pericardial fluid

Investigations
Hematocrit
White blood cell count with differential count
Glucose, protein, cholesterol, triglyceride
Amylase, lactate dehydrogenase
Gram's stain
Routine aerobic and anaerobic cultures
Smear and culture for acid-fast bacilli
Cytology
Special cultures (viral, parasite, fungal)
Antinuclear antibody
Rheumatoid factor
Total complement, C3

Suggested Reading

Dunning JA, Fabbri AB, Kolh PHC, Levine AD, on behalf of the EACTS Clinical Guidelines Committee, et al. Guideline for resuscitation in cardiac arrest after cardiac surgery. Eur J Cardiothorac Surg. 2009;36:3–28. *This article is the official guidelines of the European Association for Cardio-Thoracic Surgery for the management of cardiac arrest in post cardiac surgery patients. It has an excellent description of logistics, personnel and evidence involved in this scenario*

Fink MP, Abraham E, Vincent JL, Kochanek PM. Pericardiocentesis. In: Textbook of critical care. 5th ed. Philadelphia: Elsevier Saunders; 2005. p. 1833–40. *Gives a comprehensive description of pericardiocentesis*.

Irwin RS, Rippe JM. Irwin and Rippe's intensive care medicine. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2003. p. 80–5. *Detailed procedure and indication with pictorial depiction*

Maggiolini S, Osculati G, Vitale G. Utility and safety of diagnostic pericardiocentesis. Eur Heart J. 2005;26(10):1046–104. *Stresses the view that pericardiocentesis should be performed only on a strong clinical indication, by an experienced operator with the safest technique*

Lumbar Puncture

49

Rajesh Chawla, Charu Gauba, Sudha Kansal, and Ashutosh Tiwari

A 40-year-old male patient was admitted to hospital with altered sensorium, headache, vomiting, high-grade fever and rash. He was drowsy. His pulse was 120/min and blood pressure was 110/80 mmHg. Neck rigidity was positive and CT scan report of the head was normal. A lumbar puncture (LP) was planned.

Lumbar puncture is a commonly performed procedure to obtain cerebrospinal fluid (CSF) for diagnosis of various neurological disorders. The indications for lumbar puncture could be diagnostic or therapeutic and these can be undertaken in urgent or non urgent situations,

Step 1: Assess the Need for Lumbar Puncture

Diagnostic Indications

- Infectious disease
  - Meningitis
    - Tubercular
    - Viral
    - Bacterial
    - Fungal
  - Encephalitis
- Subarachnoid hemorrhage (SAH) with negative CT scan
- Demyelinating/inflammatory diseases
  - Multiple sclerosis/acute disseminated encephalomyelitis

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  - Guillain–Barré syndrome/chronic inflammatory demyelinating polyneuropathy
  - Neurosarcoid
- Neurodiagnostic imaging
  - Myelography
  - Cisternography
- CSF pressure (opening pressure)
  - Normal pressure hydrocephalus (NPH)
  - Idiopathic intracranial hypertension (IIH)
- Oncologic procedures
  - Carcinomatous meningitis
  - Central nervous system lymphoma

Therapeutic indications
  - Neuraxial analgesia and anesthesia
  - Narcotics
  - Local anesthetics
- Ventriculitis and post-instrumentation meningitis
- Antibiotic administration
- Leukemias and lymphomas with cerebrospinal involvement
  - Chemotherapy
  - Methotrexate
- Draining CSF in NPH and IIH

Urgent and Non Urgent Indications

Urgent

Suspected CNS infection (with the exception of brain abscess or a parameningeal process) and Suspected SAH in a patient with a negative CT scan.

Nonurgent

- Idiopathic intracranial hypertension (pseudotumor cerebri)
- Carcinomatous meningitis
- Tuberculous meningitis
- Normal pressure hydrocephalus
- CNS syphilis
- CNS vasculitis

Conditions in Which LP Is Rarely Diagnostic but Still Useful Include

- Multiple sclerosis
- Guillain-Barré syndrome
- Paraneoplastic syndromes

Step 2: Be Familiar with the CSF Analysis

Tests on CSF are determined by:

- Age
- Clinical history
- Differential diagnosis

Basic investigations

- Biochemical
  - Glucose
    Approximately two-third of serum glucose or higher.
    Decreased levels below 40–50% of serum glucose generally imply a bacterial infection.
    Simultaneously random blood sugar must be checked.
  - Protein (<0.5% of plasma)
    CSF total protein: 15–45 mg/100 mL
    Approximately 1000 RBCs = 1 mg% protein (in a bloody tap)
    Increased protein
  - Infective and post-infective state
  - Demyelinating polyneuropathies
- Hematology
  - Cell counts
    Total
    Maximum 5 WBCs/mL; RBCs nil
    In bloody tap, WBC per approximately 700 RBCs can exist
    Differential
- Microbiology
  - Stains: gram/fungal/acid fast/India ink
  - Cultures: aerobic/fungal/tubercular
- Immunology
  - Cryptococcal antigen
  - Bacterial antigens
  - Viral (e.g., herpes simplex PCR)
  - Multiplex PCR
  - Mycobacterial (TB PCR)/ADA
  - Immunoglobulins
  - Oligoclonal band
  - Cysticercus antibody
  - VDRL
- Cytology
  - Malignancies

Step 3: Rule out the Contraindications

- Absolute
  - Infected skin over the needle entry site
  - Risk/signs of cerebral herniation
    - Intracranial lesions especially posterior fossa tumors
    - Intraspinal mass, especially intramedullary
    - Focal neurological signs
    - Brain stem signs
      - Pupillary changes
      - Decerebrate posturing
      - Altered respiration
- Relative
  - Raised intracranial pressure (ICP)
  - Cardiorespiratory compromise: position related
  - Coagulopathy/thrombocytopenia (platelet count < 50,000 or INR > 1.5): risk of spinal hematoma
  - Previous lumbar surgery/congenital defects/degeneration: may require radiology guidance

Step 4: Order CT Head Before Lumbar Puncture

- In all patients to rule out mass effect/frank bleeding, especially if there is:
  - Age > 60 years
  - Immunocompromised patient with known CNS lesions
  - Altered sensorium
  - Focal neurological deficit
  - Seizure within past 1 week
  - Papilledema
  - Suspicion of raised ICP
- CT does not always rule out the risk of herniation completely.
  When the LP is delayed or deferred in the setting of suspected bacterial meningitis, it is important to obtain blood cultures (which reveal the pathogen in more than half of patients) and promptly institute antibiotic therapy. Urgent evaluation and treatment of increased ICP, along with the administration of antibiotics and steroids, should be instituted promptly when this is suspected.

Step 5: Informed Consent

- Discuss the prognosis of the patient and the need for the procedure.
- Explain in detail the advantages and disadvantages of the procedure and the available options.
- Obtain an informed consent.

Step 6: Prepare for the Procedure

- A spinal needle (20G commonly)
- Sterile sheets and instruments
- A manometer
- Antiseptic cleansing agents, Lignocaine 2%
- Numbered collection tubes (at least 4)
- Functioning intravenous access
- Crash cart
- Vital monitoring depending on the patient condition

Step 7: Position the Patient

Explain the procedure to the patient if he/she is conscious.

Lateral recumbent position

- Preferred for an accurate opening pressure.
- Less incidence of post-puncture headache.
- Make the patient acquire a fetal position with the back flexed, to widen the gap between the spinous processes.
- The head flexed, chin close to the chest.
- Hips flexed.
- Knees flexed and as close to the chest as possible.
- Keep the back perpendicular to the bed and close to the edge.

Sitting position

- Lumbar spine should be perpendicular to the bed, leaning forward on a bedside table (Fig. 49.1)
- Preferred for obese/elderly/degenerative spine

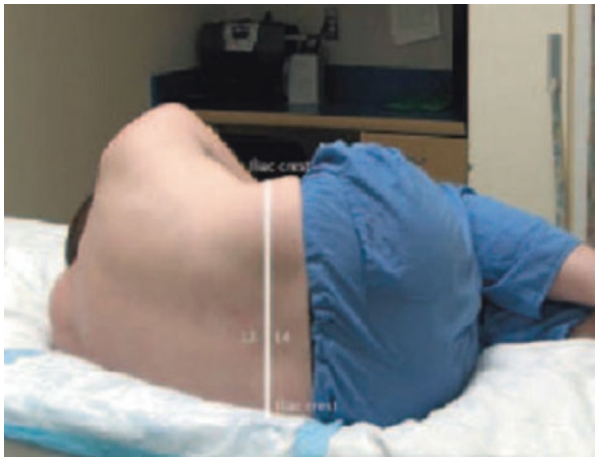

Fig. 49.1 Position for lumber puncture

Step 8: Know Landmarks and Anatomy

Skin-marking pencils should be used to mark before skin preparation:

- Determine the superior point of iliac crests.
- Connect both crests with the imaginary line.
- This line crosses the midline at L4 spine level (spinal cord ends at lower border of L1 in adults).
- Walk the fingers down over the spinous process to palpate L4-L5 and L5-S1 interspaces
- Layers encountered during LP are the following:
  - Skin
  - Superficial fascia
  - Supraspinous ligament
  - Interspinous ligament
  - Ligamentum flavum
  - Epidural space
  - Dura
  - Arachnoid membrane

Step 9: Procedure

- Preparation
  - Wear the cap, masks, and goggles.
  - Scrub appropriately.
  - Wear the sterile gown and gloves.
  - Prepare the skin:
    Use povidone-iodine or chlorhexidine.
    Cover several interspaces.
  - Drape with the sterile fenestrated sheet with the opening over the intended area.
  - Cover the iliac crest with the sheet.
- The procedure
  - Apply local anesthesia (2% lignocaine), use a 25-gauge needle, and infiltrate subcutaneously. Use a 20-gauge needle for deeper tissue and aspirate to see that no blood is aspirated before injecting. Inject while withdrawing the needle. Cover a broad area to allow manipulation.
  - Systemic sedatives and analgesics can be used under close monitoring.
  - Reconfirm the landmarks and interspaces by palpation.
  - Insert the spinal needle with stylet in place at superior aspect of inferior spinous process.
  - Stay in the midline.

- Angle 15–30° cephalad; aim for the umbilicus.
- If the needle is bevel tipped, then keep bevel in sagittal plane. Feel the layers as the needle passes through:
  Popping sensation is felt as the needle passes through the ligamentum flavum.
  Another feeling of giveaway is felt on puncturing the dura.
  Feeling of the layers becomes more consistent with practice.
  Withdraw the stylet to check for flow: if none present, rotate by 90° or advance by 2 mm and recheck.
  If flow is poor, rotate by 90°.
  If bone is encountered, withdraw the needle upto the subcutaneous tissue and redirect the needle superiorly or inferiorly.
- Once the flow is adequate, do the following:
  Measure opening pressure as the height of the fluid via the flexible tube connected to the manometer and needle hub.
  Relax the legs for accurate measurement.
  Measure in recumbent position only (normal pressure 70–180 mm H_2O).
  Collect samples and do not aspirate—it may cause hemorrhage.
  Once minimum amount is collected, replace stylet and withdraw the needle.
  Apply pressure at the puncture site, use tincture benzoin to seal, and apply bandage.
  It was said to keep the patient supine for 1–3 h to reduce severity of post-dural puncture headache, although a meta-analysis of 16 randomized controlled trials of LP performed for anesthesia, myelography, or diagnostic purposes found no evidence in any trial that longer bed rest was superior to immediate patient mobilization or shorter bedrest
  An alternate approach to obtaining cerebrospinal fluid (CSF) with a paramedian needle insertion through the L5-S1 space (Taylor approach) specially in patient with advanced ankylosing spondylosis.

Newer Technique

Fluoroscopic guidance for LP may be required if attempts without imaging are unsuccessful. This is also suggested for patients who are obese or have difficult anatomy because of prior spine surgery or other reasons. Most neuroradiologists perform fluoroscopically guided LPs in the L2-L3 or L3-L4 intervertebral space with the patient in the prone position and rotate the patient to their side for measurement of opening pressure. In addition to improving success rates, fluoroscopic guidance may reduce the incidence of traumatic LP.

Ultrasound guided lumbar puncture can also be performed.

Step 10: Know the Complications and Their Management

- Postdural puncture headache
  - Most common
    - Excessive CSF leak
    - Intracranial hypotension
    - Stretch on pain-sensitive veins
    - Linked to previous history of headaches and psychological factors
  - Risk decreased by
    - Thinner needles
    - Paramedian approach
    - Pencil-point needles (controversial)
    - Bevel parallel to sagittal dural fibers: to split, not cut
    - Replacing the stylet before withdrawing
  - Features
    - Typically occurs within 72 h and lasts 3–5 days
    - Increases on sitting up, better on lying down
    - Usually frontal
  - Treatment
    - Bed rest
    - Hydration
    - Analgesics
    - Methylxanthines—caffeine (most effective), theophylline
    - Epidural blood patch is most effective
    - Epidural injection of saline, dextran, or adrenocorticotropic hormone has been described
- Hemorrhage (uncommon)
  - More risk with bleeding tendency.
  - Spinal SAH: radicular pain, paraparesis, sphincter disturbances.
  - Spinal subdural hematoma (rare): early surgical intervention, else irreversible neurological damage may occur.
- Difficulty in identifying landmarks or subarachnoid space
  - Obesity
  - Ankylosing spondylitis
  - Kyphoscoliosis
  - Lumbar surgery
  - Disk degeneration
  - Calcification of ligaments

Request for an Anesthesiologist or Interventional Radiologist

- Dry tap
  - The misplaced needle tip
  - Dehydration
  - Low CSF volume

- Infection (uncommon)
  - Seeding of skin flora: preventable by aseptic technique
  - More risk with repeated procedures or lumbar drains
- Hemodynamic disturbances
- Cerebral/spinal herniation
  - Raised ICP
  - Cerebrospinal pressure gradient
  - Intramedullary/intracerebral mass lesions
- Hearing loss (rare)
  - Decreased ICP transmitted to cochlear apparatus
  - Reversible
  - Underreported
- Sixth nerve palsy
  - Reversible
  - Traction injury with decreased ICP
- Injury to spinal nerves
  - Usually neuropraxia
  - Local or referred pain
- Subarachnoid epidermal cysts
  - Seeding with skin tissue
  - Avoided by a needle with stylet

Step 11: Managing the Anticoagulated Patient and Timing of LP

Antiplatelets

- NSAIDs: No contraindication
- Ticlopidine: Discontinue 14 days prior
- Clopidogrel: Hold 7 days prior
- GP IIb/IIIa inhibitors: Hold 8–48 h prior

Unfractionated Heparin

- Subcutaneous
  If the total dose is less than 10,000 units/day, twice daily, there is no contraindication.
  If the total dose is more than 10,000 units/day, more than twice daily, safety is not established.
- Intravenous
  One hour prior and 2–4 h after heparin dose.
  No change in next dose timing even if traumatic.

Low-Molecular-Weight Heparin

- Therapeutic dosing
  - 24 h after the last dose
- Single daily dosing
  10–12 h after the last dose.
  Next dose 4 h after the procedure.

Warfarin

- International normalized ratio 1.5 or less

Fondaparinux

Direct Thrombin Inhibitors

- Insufficient evidence should be avoided.
- If still necessary
  - 8–10 h after the last dose
  - 2–4 h after needle placement

Thrombolytics

- Absolute contraindication

For elective procedures in a patient receiving systemic anticoagulation, observational studies and expert opinion have suggested stopping the agents for a specified time period prior to spinal anesthesia or LP

- Unfractionated intravenous heparin drips – 2–4 h.
- Low-molecular-weight heparin – 12–24 h.
- Warfarin – 5–7 days.
- Newer oral anticoagulants (NOACs), apixaban, edoxaban, and Rivaroxaban – 48 h. Dabigatran should be held 48–96 h based on renal function.
- Subcutaneous heparin – <10,000 units/day is not believed to pose a substantial risk for bleeding.

Suggested Reading

Ellenby MS, Tegtmeyer K, Lai S, et al. Lumbar puncture. N Engl J Med. 2006;355:e12. The article presents a simplified and structured review about lumbar puncture in a step-by-step fashion to guide a physician through its practical and diagnostic aspects

Fink MP. Lumbar puncture. In: Textbook of critical care. fifth ed. Philadelphia: Elsevier; 2005. p. 1885. This textbook outlines the preparation and technique adopted for successful and safe execution of lumbar puncture in a crisp and to the point way.

Horlocker TT, Wedel DJ, Rowlingson JC. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy. American Society of Regional Anesthesia and Pain Medicine evidence-based guidelines (third edition). Reg Anesth Pain Med. 2010;35:64–101. The basis of these recommendations is on case reports, clinical series, pharmacology, hematology, and risk factors for surgical bleeding

Irwin RS, Rippe JM. Cerebrospinal fluid aspiration. In: Irwin and Rippe's intensive care medicine. sixth ed. Philadelphia: Lippincott Williams & Wilkins; 2008. p. 151. The text outlines in detail the diagnostic and therapeutic indications of a lumbar puncture along with a review of the techniques involved and the complications one could face during the procedure.

Website

http://emedicine.medscape.com/article/80773-overview#a01

Intra-aortic Balloon Pump

50

Khusrav Bajan

Case

A 60-year-old male patient was admitted to the Emergency room with a history of chest pain for about 3 hours. He was irritable, had cold extremities and was hypotensive with a blood pressure 84/60 mmHg. He has been a Diabetic and a smoker for around 10 years. He persisted to be hypotensive despite being on Adrenaline and Nor-Adrenline. His ECG showed an extensive Anterior wall STEMI. He was taken to the Cardiac Catheterisation laboratory for a Percutaneous Coronary Intervention (PCI) & an Intra-Aortic Balloon Pump (IABP) insertion. After 2 days, the patient's Cardiogenic shock improved & was then discharged on day 7.

The IABP is a mechanical device to support cardiac pump function temporarily by increasing coronary perfusion and decreasing afterload. It augments & counter-pulsates making it useful as a salvage therapy in cardiogenic shock. IABP therapy should therefore be considered for use in patients who have the potential for left ventricular recovery or to support those awaiting cardiac transplantation. The better outcomes of IABP with concomittent PCI/Thrombolysis in earlier studies led to the Class I Recommendations of the use of IABP in Acute Coronary Syndrome with Cardiogenic shock.

Though the IABP Shock II trial, did not show any statistically significant difference in the 30 day mortality in the groups treated with or without IABP in patients with Cariogenic shock, the real life clinical benefits seen on hemodynamics and organ perfusion, has led to the abundant use of the IABP. The IABP as opposed to Left Ventricular Assist Device (LVAD—Impella), is easier to insert and manage.

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R. Chawla, S. Todi (eds.), *ICU Protocols*, https://doi.org/10.1007/978-981-15-0902-5_50

Step 1: Assess the Indications for IABP Insertion

Since the balloon counterpulsation helps to improve myocardial oxygen supply and decrease oxygen demand, the IABP is indicated for conditions with decreased myocardial oxygen supply–demand ratio. The common indication would be a systolic blood pressure <90 mmHg of cardiac origin, not responsive to other interventions.

- Cardiogenic shock
- Acute myocardial infarction with refractory pulmonary edema
- Mechanical complications of myocardial infarction (ventricular septal defect, acute mitral regurgitation)
- Unstable angina refractory to medical treatment
- In conjunction with thrombolysis in myocardial infarction
- Bridge to cardiac transplant
- Bridge to Left ventricular assist devices
- Ventricular arrhythmias secondary to ischemia
- High-risk cardiac surgeries
- Patients undergoing noncardiac surgery with high cardiac risk
- Postoperative low cardiac output syndrome
- Weaning from bypass open heart surgery

Debatable Indication

Prophylactic insertion in High Risk angioplasty.

Step 2: Assess the Contra-Indications for IABP Insertion

- ***Absolute***
  - Irreversible brain damage
  - Chronic end-stage heart disease without the possibility of heart transplant
  - Dissecting aortic aneurysms
- ***Relative***
  - Aortic incompetence
  - Severe peripheral vascular disease where the decision is based on patient risk–benefit ratio
  - Uncontrolled sepsis

Step 3: Apply Principles of IABP (Fig. 50.1)

- The IABP is positioned in the descending thoracic aorta just distal to the left subclavian artery.

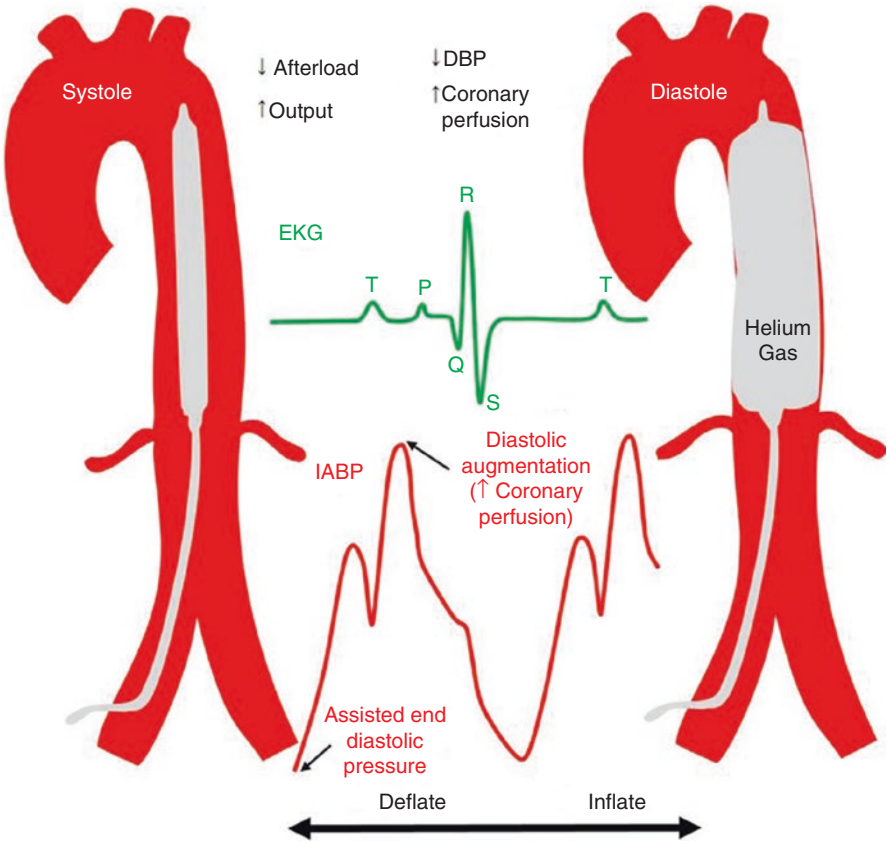

Fig. 50.1 Principles of IABP

- It is connected to an IABP console, which shuttles helium in and out of the balloon, and is timed to inflate and deflate in synchronization with the mechanical cardiac cycle; i.e. the balloon inflates during cardiac diastole and deflates during cardiac systole.
- Inflation at the onset of diastole results in proximal and distal displacement of blood volume in the aorta. This displacement creates elevated pressures by which the coronary artery and systemic perfusion is increased.
- Deflation occurs just prior to the onset of systole. This leads to reduction in the systolic pressure thus decreasing the afterload. Myocardial oxygen demand is decreased as a result of the reduction in systolic pressure and thus improving cardiac output.

  The expected changes in cardiogenic shock after insertion of IABP would be increase in cardiac output, increase in diastolic pressure, decrease in heart rate, decrease in pulmonary wedge pressure and variable effect on systolic pressure.

Step 4: Utilise Techniques of IABP Insertion

- It consists of two principal parts:
  - The first part is a catheter with two lumens, one for flushing and pressure monitoring and another for delivery of helium gas in a closed balloon (20–50 cm^3).
  - The second part is a mobile console for delivering helium, controlling balloon inflation and deflation cycling, and displaying pressure waveform and alarms.
- The balloon is inserted from the femoral artery using a Seldinger technique.
- In rare cases, it may be inserted through the axillary artery in patients with severe peripheral arterial disease with bilateral femoral artery occlusion or graft.

Step 5: Deployment and Positioning the IABP

- The tip of the balloon should lie 2–3 cm below the left subclavian artery so that the entire length of the balloon lies in the descending thoracic aorta.
- The tip of the balloon catheter is radiopaque, and hence, a check X-ray should always be taken after insertion to ensure correct balloon placement.
- The balloon should not be too high, so as to avoid blocking the branches of the arch of aorta, especially the left subclavian artery, and should not be too low, so as to avoid blocking the renal arteries.

Step 6: Set Cycling Time for IABP (Fig. 50.2)

- The mechanical cardiac cycle represented by the arterial pressure waveform is observed to assess appropriate timing.
- Electrocardiographic synchronization may also be done for cycling.
- Inflation of the intra-aortic balloon occurs at the onset of diastole noted by the dicrotic notch on the arterial waveform.
- A sharp deep "V" should be observed when the balloon inflates. As balloon inflates, aortic diastolic pressure is augmented and a second peak is observed. This peak is referred to as diastolic augmentation.
- Diastolic augmentation (30%) is ideally higher than the patient's systolic pressure and is generated by the displacement of blood volume within the aorta.
- Deflation occurs at end-diastole prior to the next systole. The precise timing of deflation is found by observing the arterial pressure tracing. The optimal deflation point is selected to achieve the greatest reduction (20%) in the next unassisted systole.

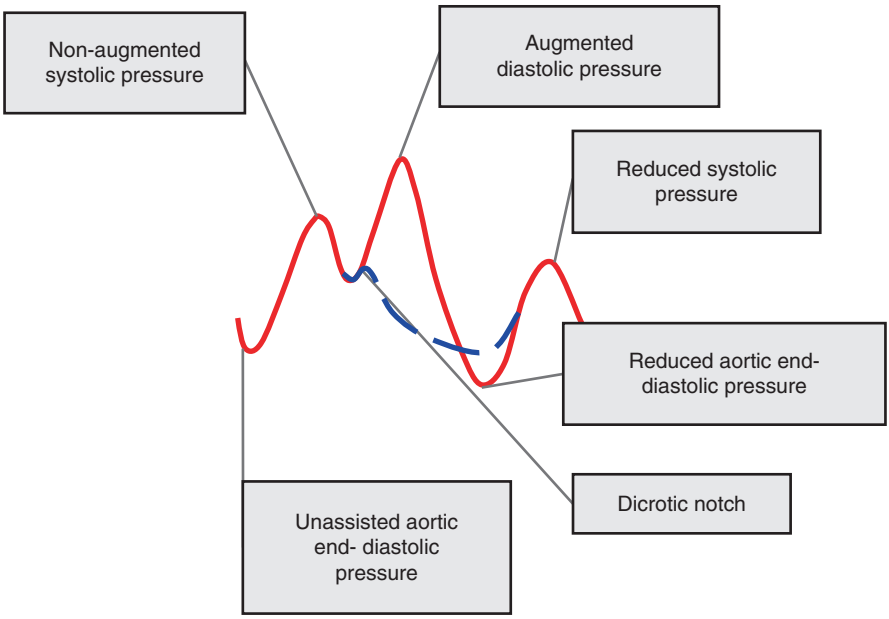

Fig. 50.2 IABP waveform. Suboptimal timing of inflation and deflation of the balloon (Fig. 50.3a–e) will result in haemodynamic instability

- An effective IABP cycling will result in increase of mean arterial pressure, decrease in heart rate, decrease in pulmonary capillary wedge pressure, and increase in cardiac output.

Step 7: Anticipate and Prevent Complications in Relation to IABP

- Trauma to the arterial wall incurred while inserting and advancing the guidewire or balloon (laceration, dissection, subadventitial hematoma) (1–5%)
- Limb ischemia associated with the position of the balloon catheter, which disappears with catheter removal (5–11%)
- Dislodged thrombus created during balloon removal, resulting in distal embolization (peripheral, renal) (1–5%)
- Hematologic (thrombocytopenia, red blood cell hemolysis, hemorrhage) (1–5%)
- Balloon leak/rupture (1–4%)
- Infection (2–4%)
- Cholesterol embolization—presents with fever, thrombocytopenia, livedo reticularis

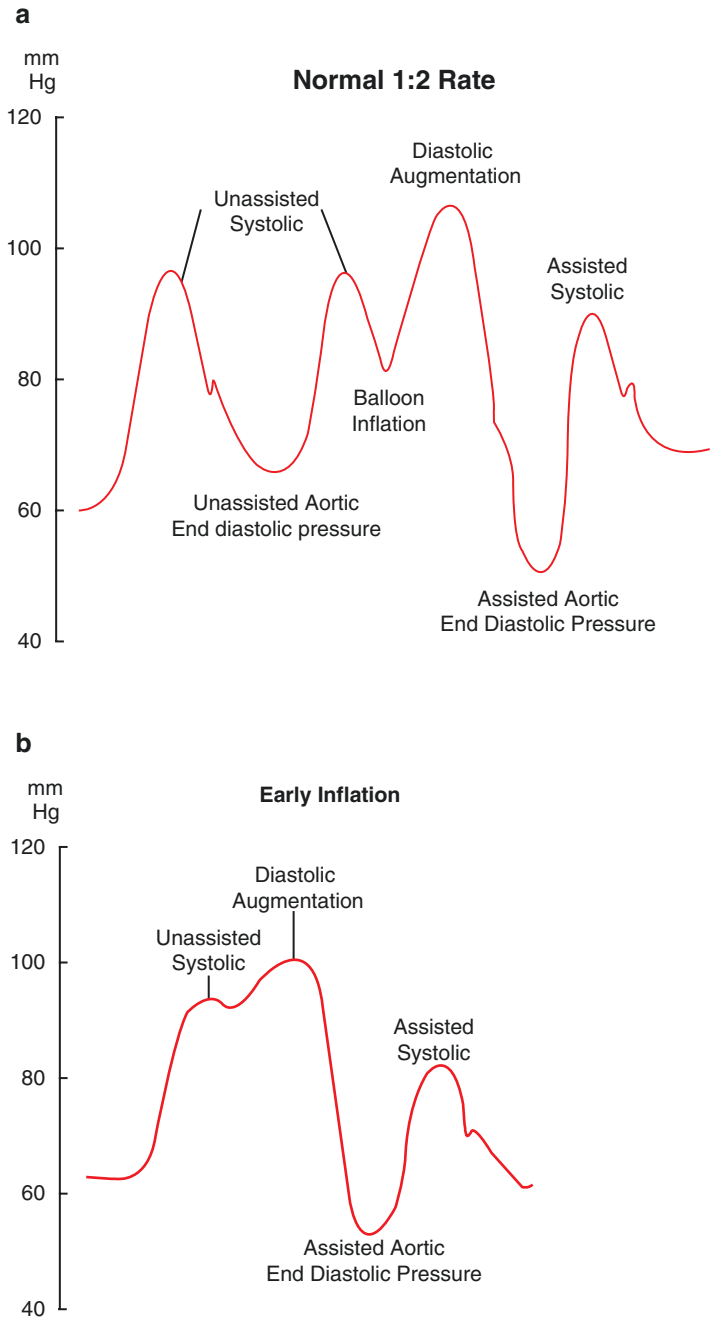

Fig. 50.3 (**a**–**e**) Normal (**a**) Suboptimal timing of inflation and deflation. Early inflation: inflation of the IAB before aortic valve closure (**b**). Late inflation: inflation of the IAB markedly after closure of the aortic valve (**c**). Early deflation: premature deflation of the IAB during the diastolic phase (**d**). Late deflation: deflation of the IAB after the onset of systole (**e**)

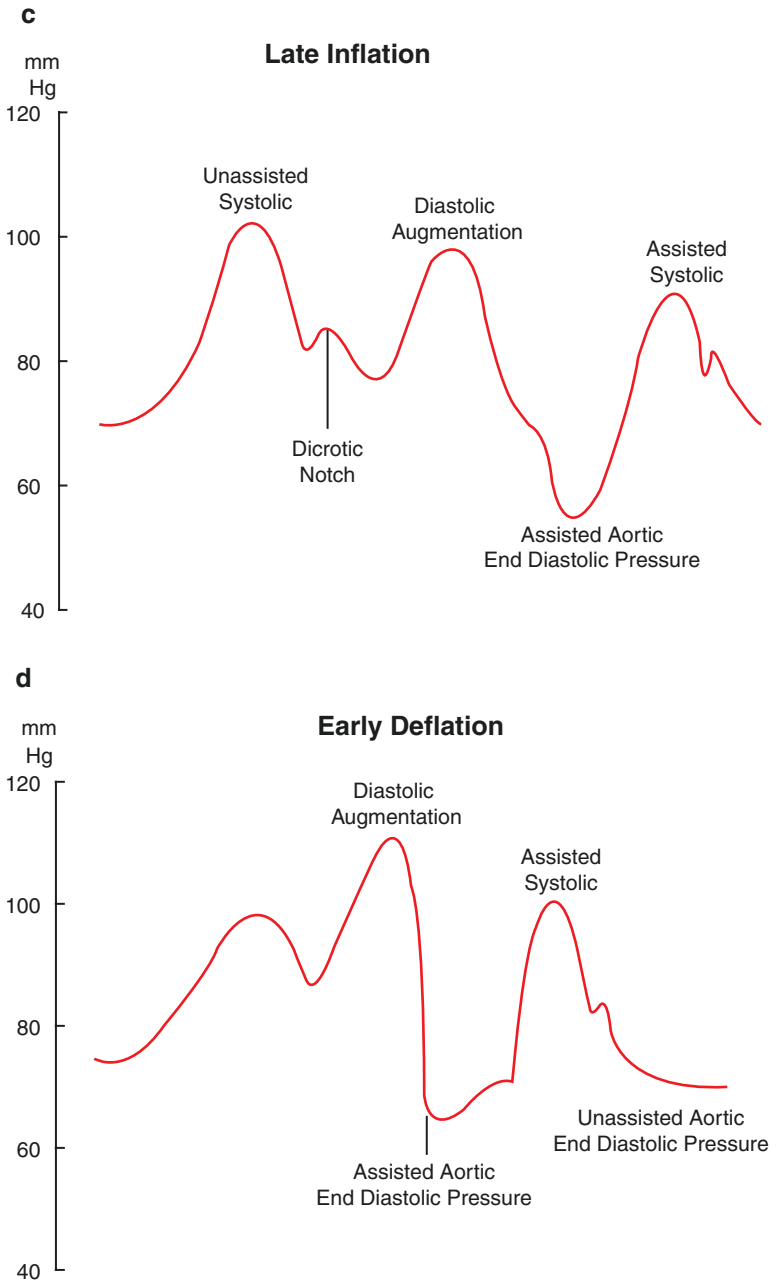

Fig. 50.3 (continued)

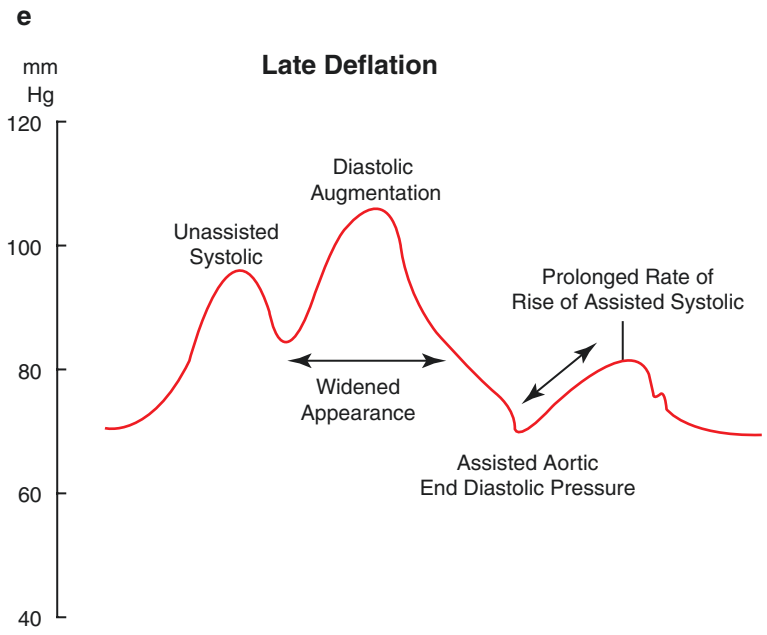

Fig. 50.3 (continued)

Step 8: Identify the Factors Impacting IABP Complications

- ***The following factors increase IABP complications:***
  - Peripheral artery disease
  - Old age
  - Female sex
  - Diabetes mellitus
  - Hypertension
  - Prolonged support
  - Large catheter size (>9.5 Fr)
  - Low cardiac index
  - Low body surface area
- ***The following factors are associated with less IABP complications:***
  - Decrease in balloon size
  - Sheathless technique

Step 9: Monitoring the Patient Whilst on IABP

- Specialized nursing care with 1:1 nursing every shift is needed to take care of patients.
- The chest X-ray to document position of the catheter tip, which should be at the bifurcation of the left and right main bronchi.
- Three times daily documentation of peripheral pulses.
- Daily measurement of hematocrit, platelet count, and creatinine.
- Anticoagulation parameters.

Step 10: Facilitate the Weaning Process off IABP

- The patient can be weaned if the following criteria are satisfied:
  - Urine output is more than 40 mL/h without the use of diuretics
  - Improved mentation
  - Extremities are warm
  - Hemodynamics appear to be getting better and stable on little or no inotropes
  - No evidence of ongoing ischemia

Suggested Reading

Reid MB, Cottrell D. Nursing care of patients receiving: intra-aortic balloon counterpulsation. Crit Care Nurse. 2005;25(5):40–4.

Sjauw KD, Engström AE. A systematic review and meta-analysis of intra-aortic balloon pump therapy in ST-elevation myocardial infarction: should we change the guidelines? Eur Heart J. 2009;30(4):459–68. *All available observational data concerning IABP therapy in the setting of cardiogenic shock are importantly hampered by bias and confounding. There is insufficient evidence endorsing the current guideline recommendation for the use of IABP therapy in the setting of STEMI complicated by cardiogenic shock*

Thiele H, Zeymer U, Neumann F, Ferenc M, Olbrich H, Hausleiter J, Richardt G, Hennersdorf M, Empen K, Fuernau G, Desch S, Eitel I, Hambrecht R, Fuhrmann J, Böhm M, Ebelt H, Schneider S, Schuler G, Werdan K. Intraaortic balloon support for myocardial infarction with cardiogenic shock. N Engl J Med. 2012;367(14):1287–96.

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Appendix A

Table A.1 Drugs and Doses

Drug class/prototypes	Dosing	Common toxicities
ABCD (amphotericin B cholesteryl sulfate complex)	3–4 mg/kg IV q24h	Hypotension, hypokalemia, thrombocytopenia, hypomagnesemia, hepatotoxicity, renal failure allergic reactions
Abacavir	300 mg PO q12h or 600 mg q24h	CNS, Skin Rash
Abciximab	0.25 mg/kg IV bolus, and then 0.125 mcg/kg/min	Hypotension, chest pain, nausea, minor bleeding, back pain
ABLC (amphotericin B lipid complex)	5 mg/kg IV q24h	Hypotension, hypokalemia, thrombocytopenia, hepatotoxicity, renal failure, allergic reactions
Acetaminophen	325–1000 mg PO/IV q4–6h PRN	Rash, anemia, blood dyscrasias, hepatotoxicity
Acetazolamide	250–500 PO/IV mg given q8h	Metabolic acidosis, hypokalemia, hyponatremia, abnormal LFT
Activated charcoal	25–100 g PO	Vomiting, constipation, fecal discoloration (black)

(continued)

R. Chawla, S. Todi (eds.), *ICU Protocols*, https://doi.org/10.1007/978-981-15-0902-5

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Acetylcysteine	Acetaminophen poisoning Oral: 140 mg/kg followed by 17 doses of 70 mg/kg q4h IV: 150 mg/kg over 60 min f/b 300 mg/kg over 21 h Nebulization: 3–5 mL of 20% solution three to four times a day, administer before chest physiotherapy Prevention of radiocontrast-induced renal injury: 600 mg PO q12h for 3 days starting 1 day before procedure, may be given intravenously	Anaphylactoid reaction, angioedema, vasodilatation, hypotension, tachycardia, urticaria, nausea, vomiting, bronchospasm
Acyclovir	10–15 mg/kg/dose q8h IV (HSV encephalitis) 800 mg PO every 4 h (Herpes Zoster) 400 mg bolus	Reversible renal failure Hepatic toxicity Confusional state
Adenosine	6 mg IV, if not effective in 1–2 min, can give 12 mg, may repeat 12 mg	Flushing, light headedness, headache, nervousness/anxiety
Adrenaline (see epinephrine)		
Albumin	0.5–1 g/kg/dose (5% in hypovolemia)	Hypervolemia, anaphylaxis, chills, fever, tachycardia, bronchospasm
Albuterol	5–10 mg nebulized over 30–60 min	Arrhythmias, chest discomfort, palpitation, CNS stimulation, drowsiness, diarrhea, dry mouth, micturition difficulty
Alfentanil	IV bolus 500 mcg every 10 min as necessary IV infusion: 1 mcg/kg/min	Respiratory depression, apnea, bradycardia, delayed gastric emptying, chest wall rigidity
Allopurinol	600–800 mg/day in two to three divided doses	Rash

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Alteplase	15 mg bolus, then 0.75 mg/kg (up to 50 mg) × 30 min, then 0.5 mg/kg (up to 35 mg) × 60 min (maximum 100 mg over 90 min)	Hypotension, bleeding, allergic reactions
	Pulmonary embolism: 100 mg IV over 2 h	
	Stroke: 0.9 mg/kg 10% bolus, rest over 60 min (Max 90 mg)	
Amantadine	100 mg PO q12h	Nausea, vomiting, anorexia, xerostomia
Amikacin	15–20 mg/kg once a day	Ototoxicity, neurotoxicity, nephrotoxicity
Aminophylline	Loading dose; 5 mg/kg IV over 30 min	Tachycardia, arrhythmia, convulsions
	Maintenance: 0.1–0.8 mg/kg/h	
Amiodarone	150–300 mg bolus, then 1 mg/min for 6 h, then 0.5 mg/min for 18 h	Bradycardia, hypotension, AV block, nausea, photosensitivity, hypothyroidism,
	Oral 200 mg 8 hourly, then titrate down to 200 mg q24h	hyperthyroidism, coagulation abnormalities, hepatitis, visual disturbance, pulmonary fibrosis
Amitryptiline	25–75 mg PO q24h	Confusion, dry mouth, retention of urine
Amlodipine	5–10 mg PO q24h	Pedal edema, headache, nausea, vomiting
Amoxicillin/clavulanate	625 mg PO q12h/q8h	Nausea, vomiting, diarrhea, allergic reaction
Amphotericin B deoxycholate Amphotericin B (Liposomal)	0.3–1.5 mg/kg IV q24h (diluted in 5% Dextrose) 3–5 mg/kg /day (diluted in 5% dextrose)	Hypotension, hypokalemia, thrombocytopenia, hepatotoxicity, creatinine increase, allergic reactions Same as Ampho B, Less nephrotoxicity
Ampicillin	250–500 mg IV q4–6h	Fever, allergic reaction, penicillin encephalopathy, diarrhea, pseudomembranous colitis, agranulocytosis, anemia
Ampicillin/sulbactam Andexanet Alpha (Antidote to rivaroxaban and apixaban)	1.5–3 g IVq6h 400–800 mg bolus @30 mg/min 4–8 mg/min iv infusion for up to 120 min	Fever, allergic reaction, penicillin encephalopathy, diarrhea, pseudomembranous colitis, agranulocytosis, anemia
Anidulafungin	200 mg IV bolus, then 100 mg IV q24h	Elevated LFT

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Aqueous penicillin G	2–4 million U IV q4h	Fever, allergic reaction, penicillin encephalopathy, diarrhea
Argatroban	350 mcg/kg bolus, then 25 mcg/kg/min adjust based on aPTT (For PCI) Initial 2 mcg/kg/min, adjust based on aPTT measurements (For prophylaxis in heparin induced thrombocytopenia)	Bleeding, cardiac arrest, dyspnea
Arbekacin (Aminoglycoside)	150–200 mg once a day i.v.	Nephrotoxicity, Ototoxicity
Ascorbic acid	1.5 g over 30 min every 6 h	Oxalate nephropathy
Aspirin	160–325 mg PO q24h	Bleeding, dyspepsia
Atropine	1 mg IV q3–5 min	Dry eyes, dry mouth, urinary retention, tachycardia
Atracurium	0.5 mg/kg IV Bolus then 0.08–0.12 mg/kg bolus every 20–30 min or 5–10 mcg/kg/min infusion	Flushing, allergic reactions, bradycardia, hypotension, bronchospasm, laryngospasm, seizures
Azithromycin	250–500 mg IV/PO q24h	Headache, nausea, vomiting, diarrhea, allergic reactions, fungal infection
Bivalirudin	1 mg/kg IV bolus, then 1.75 mg/kg/h	Hypotension, hemorrhage, pain, headache, nausea, back pain
Bosentan	62.5 mg PO q12h × 1 month, then 125 mg PO q12h, as tolerated	Headache, anemia, transaminase increase, nasopharyngitis, flushing, pruritus
Bromocriptine	2.5–5 mg PO q8h (Max 45 mg for Neuroleptic Malignant syndrome)	Headache, dizziness, nausea, hypotension, nasal congestion
Bumetanide	0.5–2 mg/dose PO q24h	Hyperuricemia, hypochloremia, hypokalemia, azotemia, hyponatremia, hyperglycemia, muscle cramps, creatinine increase
Calcitonin	Initial 4 U/kg IM q12h, up to 8 U/kg IM q6h	Facial flushing, nausea, vomiting
Calcium gluconate/chloride (10 mL of 10%)	1 g IV over 2–5 min	Hypercalcemia, constipation (oral)
Captopril	6.25–50 mg PO q8h	Hypotension, dizziness, abnormal taste, cough, worsening renal function

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Carvedilol	6.25 mg PO q12h, maximum 25 mg PO q12h	Hypotension, dizziness, fatigue, hyperglycemia, weight gain, diarrhea, bradycardia, syncope, deranged LFT, bronchospasm
Caspofungin	70 mg IV bolus, then 50 mg IV q24h	Headache, fever, chills, hypokalemia, flushing, tachycardia, anemia, eosinophilia, neutropenia, nephrotoxicity
Cefazolin	1–2 g IV q8h	Allergic reaction, fever, Stevens–Johnson syndrome, nephrotoxicity, diarrhea, nausea, vomiting
Cefepime	500 mg to 2 g IV q8–12h	Positive Coombs test, fever, headache, rash, pruritus, diarrhea, nausea, vomiting, agranulocytosis
Cefoxitin	1–2 g IV q6–8h	Diarrhea, anaphylaxis, nausea, vomiting, headache, rash, pruritus, diarrhea, agranulocytosis, pseudomembranous colitis
Ceftazidime	500 mg IV to 2 g q8–12h	Diarrhea, hypersensitivity reactions, candidiasis, nephrotoxicity, encephalopathy, headache, fever
Ceftazidime Avibactam	2.5 g every 8 h	Hypersensitivity
Ceftolazone Tazobactam	1.5–3 g every 8 hourly	Hypersensitivity
Ceftriaxone	1–2 g IV q12–24h	headache, rash, pruritus, diarrhea, nausea, vomiting, agranulocytosis
Cefuroxime	0.75–1.5 g IV 6–8 hourly	*C. difficile* diarrhea Hypersensitivity Transient rise in liver function test
Chlordiazepoxide	10–30 mg PO q8h to q6h	Muscle weakness, ataxia, confusion, hypotension
Cyclosporine	IV: 1–5 mg/kg/day Oral: 1.5 times IV dose q12h	Increased urea, creatinine Hypertension Hirsutism, gingival hypertrophy Hyperuricemia, tremor
Cidofovir	5 mg/kg IV weekly plus probenecid 2 g PO 3 h before the infusion and then 1 g at 2 and 8 h after the infusion	Nephrotoxicity, uveitis/iritis, nausea, vomiting

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Ciprofloxacin	500–750 mg PO q12h or 400 mg IV q8–12h	Dizziness, insomnia, restlessness, fever, rash, nausea, vomiting, diarrhea, ALT/AST increase, rhinitis
Clarithromycin	500 mg IV/PO q12h	Headache, nausea, vomiting, diarrhea, abdominal pain, rash
Clindamycin	600–1200 mg IV q8h to q6h, maximum 4.8 g/day PO 150–450 mg/dose every 6–8 h, maximum dose 1.8 g/day	Diarrhea, abdominal pain, hypotension, urticaria, rash, pseudomembranous colitis
Clonidine	0.1–0.3 mg PO q12h/8h	Drowsiness, dizziness, hypotension, bradycardia, dry mouth
Clopidogrel	75 mg PO q24h	Nausea, vomiting, diarrhea, bleeding
Codeine phosphate	30–60 mg PO q4h/q6h	Drowsiness, constipation, respiratory depression
Colistin: Colistimethate Sodium (CMS)	IV: Loading dose 300 mg CBA (Colistin Base activity) (~9 million IU) infused over 0.5–1 h (Body wt/7.5) administer the first maintenance dose 12–24 h later Maintenance dose : 300–360 mg CBA (~9–10.9 million IU), divided into two and infused over 0.5–1 h at 12-h intervals Nebulization: 2–3 million units q8h	Fever, headache, pruritus, rash, GI upset, paresthesia, weakness, apnea, respiratory arrest, renal dysfunction, myopathy
Conivaptan	20 mg IV bolus, then 0.8–1.6 mg/h IV continuous infusion	Diarrhea, hypokalemia
Co-trimoxazole (trimethoprim:sulfamethoxazole 1:5)	PCP pneumonia treatment: 15–20 mg/kg/day of trimethoprim IV for 14 days, followed orally for further 7 days PCP prophylaxis: 80 mg trimethoprim orally daily	Rash, nausea, vomiting, diarrhea, agranulocytosis, thrombocytopenia, hemolysis in G6PD deficiency, rash, allergic myocarditis, peripheral neuritis, aseptic meningitis, hyperkalemia, interstitial nephritis, Steven Johnson
Dalteparin	120 U/kg SC q12h	Bleeding, wound hematoma, pain at injection site, thrombocytopenia, allergic reactions, alopecia

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Dantrolene	1–2.5 mg/kg IV; may repeat q5–10 min to maximum cumulative dose 10 mg/kg	Drowsiness, dizziness, diarrhea, nausea, vomiting
Daptomycin	4–6 mg/kg IV q24h	Anemia, diarrhea, vomiting, peripheral edema, rash, insomnia, UTI, rise in CPK
DDAVP	0.3 mcg/kg slow IV/SC/IM Intranasally: 5–20 mcg daily	Facial flushing
Deferoxamine	1 g IV bolus, then 500 mg IV q4h × 2 doses	Urine discoloration (orange–red)
Dexamethasone	10 mg IV prior to ACTH stimulation test, 4–6 mg IV q6h/q8h	Same as hydrocortisone
Dexmedetomidine	0.2–0.7 mcg/kg/h IV	Hypotension, bradycardia
Dextran (40)	Maximum 20 mL/kg, 20–40 mL/min IV	Allergic reaction, fluid overload, platelet dysfunction
Diazepam	5–10 mg IV over 2 min	Apnea, respiratory depression, drowsiness, hypotension, bradycardia
Diclofenac	75 mg IM 50 mg PO q8h	
Digoxin	Load: 10–15 mcg/kg; give 50% of load in initial dose, then 25% at 6–12 h intervals × 2 *Maintenance*: 0.125–0.5 mg/day (dose should be reduced by 20–25% when changing from oral to IV)	Bradycardia, heart block, arrhythmias, yellow vision, rash, muscle weakness
Diltiazem	0.25 mg/kg bolus (may repeat 0.35 mg/kg bolus after 15 min), then 5–15 mg/h (PO (extended release) 60–120 mg q12h)	Bradycardia, hypotension, constipation (verapamil > diltiazem), headache, flushing, edema
Dobutamine	2.5–20 mcg/kg/min	Tachycardia, hypertension, ventricular ectopics, headache, palpitations
Dopamine	5–20 mcg/kg/min	Ectopic beats, tachycardia, arrhythmia, palpitations, angina, headache, dyspnea
Dopexamine	0.25–6 mcg/kg/min	Tachycardia, hypotension, angina, hypokalemia, hyperglycemia

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Doxycycline	100 mg PO/IV q12h	Intracranial hypertension, pericarditis, angioneurotic edema, skin hyperpigmentation, bone marrow depression, hepatotoxicity
Enalapril	2.5–20 mg PO q12h	Hypotension, dizziness, abnormal taste, cough, worsening renal function
Enoxaparin	1 mg/kg SC q12h	Bleeding, thrombocytopenia
Epinephrine	1 mg IV q3–5 min in cardiac arrest (10 mL of 1 in 10,000 solution) 0.01–0.3 mcg/kg/min IV Infuse via central vein in shock Anaphylaxis: 0.5–1.0 mL of 1 in 1000 solution (50–100 mcg) may be given subcutaneously Bronchospasm: 0.5–1.0 mL of 1:1000 (0.5–1 mg) diluted with normal saline 2.5 mL and nebulized	Tachycardia, hypertension, angina, arrhythmia, sudden death, dry throat, nausea, vomiting, anxiety, headache, dyspnea, urinary retention
Epoprostenol	2–50 ng/kg/min IV 5000–20,000 ng/mL continuous nebulization	Flushing, headache, nausea vomiting, hypotension, chest pain, palpitation, diarrhea, weight loss, weakness, myalgia
Eptifibatide	180 mcg/kg bolus, then 2 mcg/kg/min	Bleeding, hypotension, thrombocytopenia
Ertapenem	1 g IV q24h	Edema, chest pain, tachycardia, headache, fever, rash, diarrhea, nausea, abdominal pain, hepatic enzyme increase
Erythromycin	250–500 mg PO q6h or 0.5–1 g IV q6h	QTc prolongation, torsades de pointes, pruritus, rash, abdominal pain, anorexia, cholestatic jaundice, neuromuscular weakness, hearing loss
Erythropoietin (recombinant human)	50–300 units/kg weekly in 2–3 divided doses subcutaneously	Hypertension, thrombocytosis, flu-like symptoms, hyperkalemia, shunt, thrombosis
Esmolol	500 mcg/kg bolus, then 50–300 mcg/kg/min	Hypotension, diaphoresis, dizziness, nausea, vomiting
Esomeprazole	20–40 mg PO q24h	Headache, dizziness, pruritus, flatulence, diarrhea

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Etomidate	Anaesthesia : 0.2–0.6 mg/kg over 30–60 s	Adrenal suppression
Factor VIIa (recombinant)	Hemorrhagic stroke: (Warfarin related) 10–100 mcg/kg IV: Bleeding episode: 90 mcg/kg every 2 h	Hypertension
Fentanyl	1–2 mcg/kg/dose Infusion: 1–3 mcg/kg/h	Hypotension, bradycardia, CNS depression, confusion, chest wall rigidity, respiratory depression
Flucloxacillin	1–2 g 6 h	Interstitial nephritis Hemolytic anaemia Cholestatic jaundice
Fluconazole	100–800 mg PO/IV q24h	Headache, seizure, rash, angioedema, hypercholesterolemia, hypokalemia, hepatitis, cholestasis
Fondaparinux	2.5 mg SC q24h	Bleeding, fever, nausea, anemia
Flucytosine	25–37.5 mg/kg PO q6h	Nausea, vomiting, diarrhea, rash
Fludrocortisone	50–200 mcg PO q24h	Hypertension, edema, acne, hypokalemic alkalosis, hyperglycemia, peptic ulcer
Flumazenil	0.2–0.5 mg IV q1min, up to 3 mg	Vasodilatation, headache, agitation, dizziness, blurred vision, dyspnea, hyperventilation
Fomepizole	15 mg/kg/IV bolus, then 10 mg/kg IV q12h × 4 doses, then 15 mg/kg IV q12h until ethylene glycol or methanol level <20	Headache, nausea, bradycardia, hypotension, dizziness, metallic taste
Foscarnet	60 mg/kg IV q8h or 90 mg/kg IV q12h	Nephrotoxicity, electrolyte abnormalities (hypocalcemia, hypomagnesemia, hypokalemia, hypophosphatemia), nausea, vomiting, diarrhea, headache
Fosphenytoin 75 mg of fosphenytoin = 50 mg of phenytoin	Loading dose; 15–20 mgPE/kg IV Maintenance; 4–6 mg phenytoin equivalent (PE)/kg/day in two to three divided doses	IV form: hypotension, bradycardia, phlebitis, nystagmus, rash
Furosemide	20–80 mg/day IV/PO in two to three divided doses	Hypotension, blurred vision, cutaneous vasculitis, gout, hyperglycemia, anorexia, allergic interstitial nephritis, fall in GFR, increased blood urea

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Ganciclovir	5 mg/kg IV q12h	Fever, rash, abdominal pain, nausea, vomiting, anemia, leucopenia, thrombocytopenia, confusion, neuropathy, pruritus, paresthesia, retinal detachment
Gemifloxacin	320 mg PO q24h	Headache, dizziness, rash
Gentamicin	3 mg/kg bolus, then 2 mg/kg IV q8h or 5–7 mg/kg extended interval (q24h to q12h or divided dose)	Vertigo, ataxia, gait instability, ototoxicity, nephrotoxicity, edema, pruritus
Glutamine	5 g 6 hourly orally 0.3–0.4 g/kg body weight IV	Increase in AST and ALT
Haloperidol	0.5–5 mg 2–3 times/day/max 30 mg IV/PO 2–10 mg IV bolus, repeat bolus every 15–30 min with sequential doubling of dose	CNS depression, orthostatic hypotension, arrhythmia, alopecia, extrapyramidal symptoms, neuroleptic malignant syndrome, cholestatic jaundice
Heparin	Prophylaxis: 5000 units 8–12 hourly Therapeutic: 60 units/kg bolus f/b 12 units/kg/h infusion maximum 1000 units/h	Bleeding, hyperkalemia, cutaneous necrosis, elevated liver enzymes, peripheral neuropathy
Hydralazine	10–40 mg IV q4–6h or 10–75 mg PO q8h/q6h	Hypotension, tachycardia, flushing, headache
Hydrocortisone	Septic shock: 200–300 mg/day in three to four divided doses or as continuous infusion	Hyperglycemia, mood changes, insomnia, gastrointestinal irritation, increased appetite, GI bleed, hypokalemia, Long-term: osteoporosis, acne, fat redistribution, muscle wasting, cataracts, increased blood pressure, infection
Hypertonic saline (23.4% NaCl)	For mannitol refractory patients: 3–50 mL q3–6h as needed (central line only), 0.686 mL of 23.4% saline is equimolar to 1 g of mannitol	Hypernatremia, hyperchloremia, fluid overload, pulmonary edema
Ibuprofen	200–800 mg PO q3–6h	Edema, dizziness, itching, fluid retention, dyspepsia, tinnitus, hypocalcemia

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Ilioprost	2.5–5 mcg inhaled six to nine times daily	Flushing, hypotension, headache, nausea, trismus, cough, flu-like syndrome, jaw pain, syncope, hemoptysis
Imipenem + cilastatin	500 mg to 1 g IV q6–8h	Tachycardia, seizure, oliguria, nausea, diarrhea
Immune globulin (intravenous)	IV 0.4 g/kg/day for 5 days	Allergic reaction, anaphylaxis, chest tightness, edema, flushing, anxiety, chills, pruritus, bronchitis, abnormal liver function tests
Ipratropium	2–4 puffs (15 mcg/actuation) q12h to q6hNebulised: 500 mcg 3–4 times/day	Bronchitis, upper respiratory tract infection, palpitation, dizziness, rash, nausea
Isavuconazole	IV : initial 200 mg 8 hourly for six doses Maintenance : 200 mg once daily	Peripheral edema
Isoprenaline	Up to 20 mcg/min IV infusion, titrate according to heart rate	Tachycardia, arrhythmia, angina, hypotension
Isosorbide dinitrate	5–40 mg PO q8h	Hypotension, headache, dizziness, flushing
Isosorbide mononitrate (Extended Release)	30–120 mg PO q24h	Hypotension, headache, dizziness, flushing
Itraconazole Kayexalate	200 mg IV/PO q24h Oral: 15 g 1–4 times daily Rectal : 30–50 g every 6 h	Pruritus, nausea, vomiting, chills Ischemic colitis Bezoar
Ketorolac	15–30 mg IV q6h	Headache, abdominal pain, dyspepsia, nausea, edema, drowsiness, diarrhea Tachycardia Hypertension Delirium
Ketamine	20 mg PO f/b 10 mg q6–8h Intubation: 1–2 mg/kg iv over 1–2 min	
Labetalol	100–400 mg PO q8–12h (max 2.4 g/day)	Dizziness, hypotension, bradycardia, nausea, vomiting, transaminase increase, paresthesia, flushing, headache
	20–40 mg IV (maximum 80 mg) as bolus at 10–20 min intervals (Max 300 mg), then 0.5–2 mg/min infusion if needed	
Lactulose	20–30 g (30–45 mL) PO q2h until initial stool, then adjust to maintain two to three soft stools/day	Diarrhea, flatulence, nausea

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Lacosamide	Status epilepticus: 200–600 mg IV daily	CNS
Lansoprazole	30–60 mg PO q12–24h	Headache, abdominal pain, nausea, diarrhea
Lepirudin	0.5 mg/kg IV loading over 5 min as a loading dose (0.2 mg in renal failure) 0.15 mg/kg/h continuous IV infusion adjust based on aPPT measurements	Bleeding
Levalbuterol	Adjust based on aPPT measurements 0.63–0.125 mg q8h 2–4 puff TID (45 mcg/actuation)	Hyperglycemia, hypokalemia, tremors, rhinitis, viral infection, headache, migraine, rash, abdominal cramps
Levetiracetam	500–1000 mg IV/PO q12h	Behavior changes, somnolence, nausea, vomiting, anorexia, weakness, cough, facial edema, bruising
Levofloxacin	500–750 mg IV/PO q24h	Chest, pain, edema, nausea, vomiting, dyspnea, pharyngitis, rash, CNS stimulation, seizure, dizziness, somnolence
Levosimendan	Loading dose (may be omitted) 6–12 mcg/kg given over 10 min 0.1 mcg/kg/min continuous infusion	
Levothyroxine	50–100 mcg IV Q6–8h × 24 h, then 100 mcg IV q24h	Angina, arrhythmia, MI, palpitations, tachycardia, anxiety, headache, hyperactivity, insomnia, alopecia, tremors
Lidocaine	1–1.5 mg/kg IV bolus (may repeat doses 0.5–0.75 mg/kg in 5–10 min up to maximum 3 mg/kg), then 1–4 mg/min	Arrhythmia, bradycardia, heart block, hypotension, edema, flushing, anxiety, hallucinations, seizures
Linezolid	600 mg IV/PO q12h	Headache, diarrhea, insomnia, rash, nausea, constipation, thrombocytopenia, anemia, leucopenia, abnormal liver tests
Liothyronine	200–500 mcg (in myxedema coma)	Tachycardia, arrhythmia
Lisinopril	2.5–40 mg PO q24h	Hypotension, dizziness, abnormal taste, cough, worsening renal function

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Lorazepam	Status epilepticus: 4 mg IV bolus, 0.5–4 mg/h Sedation: 0.02–0.06 mg/kg bolus Infusion: 0.01–0.1 mg/kg/h	Sedation, hypotension, confusion, dermatitis, rash
Magnesium sulphate	4–6 g IV over 15–20 min, then 2 g/h infusion (1 g of Mg So_4 = 98.6 mg of elemental Mg = 8.12 meq of elemental magnesium)	Hypermagnesemia, diarrhea (oral)
Mannitol (10–20%)	1–1.5 g/kg IV bolus, then 0.25–1 g/kg q3–6h as needed	Hypotension, acute renal failure, fluid and electrolyte imbalances
Meropenem	1 g IV q8h	Headache, rash, diarrhea, anemia, phlebitis, agranulocytosis, TEN, glossitis
Meropenem Vaborbactam	4 g 8 hourly	Hypersensitivity
Methimazole	Initial 30–60 mg/day in three divided doses q8h, maintenance 5–30 mg/day PO	Vasculitis, CNS stimulation, alopecia, agranulocytosis
Methylprednisolone	Pulse therapy: 15–30 mg/kg/day for 3 days IV Spinal cord injury: 30 mg/kg over 15 min IV f/b 5.4 mg/kg/h for 23 h (Unlabelled use)	Hypertension, arrhythmia, insomnia, seizure, psychosis, hirsutism, adrenal suppression, diabetes mellitus, hypokalemia, hyperglycemia, peptic ulcer, pancreatitis, osteoporosis, muscle weakness
Metoclopramide	10 mg PO/IV q8h to q6h	Bradycardia, AV block, CHF, drowsiness, dystonic reaction, rash, agranulocytosis, bronchospasm
Metoprolol	IV: 5 mg every 2 min for three doses f/b 50 mg orally q6h for 48 h, then 100 mg q12h	Bradycardia, hypotension, syncopy, Raynaud's disease, dizziness, fatigue, bronchospasm, diarrhea, rash
Metronidazole	500 mg IV/PO q8h	Nausea, vomiting, metallic taste, disulfiram-like reaction
Micafungin	50–150 mg IV q24h	Headache, hypokalemia, hypocalcemia, leucopenia, neutropenia, transaminase increase, rigors
Midazolam	1–5 mg bolus, 1–10 mg/h, 0.2 mg/kg bolus, then 0.75–10 mcg/kg/min	Sedation, hypotension, confusion, dermatitis, rash

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Milrinone	50 mcg/kg/bolus, then 0.25–0.75 mcg/kg/min	Hypotension, arrhythmia
Morphine sulphate	2.5 mg IV q3–4h Infusion: 1–10 mg/h	Constipation, dyspepsia, nausea, drowsiness, dizziness
Moxifloxacin	400 mg IV/PO q24h	
Naloxone	0.4–2 mg IV q2min, up to 10 mg	Narcotic withdrawal
Neomycin	500–2000 mg PO q6–12h	Nausea, vomiting, diarrhea, irritation or soreness of mouth or rectal area
Neostigmine	2.5 mg IV bolus, may be repeated in 3 h	Sweating, salivation, abdominal cramps, diarrhea, bradycardia
Nesiritide	2 mcg/kg bolus, then 0.01–0.03 mcg/kg/min	Hypotension, increased serum creatinine, arrhythmia
Nicardipine	3–15 mg/h IV infusion PO: 20 mg q8h	Hypotension, tachycardia, headache, flushing, peripheral edema
Nifedipine (Immediate release) Extended Release	30 mg once daily PO up to 30 mg q8h 30–120 mg PO q24h	Hypotension, tachycardia, headache, flushing, peripheral edema
Nimodipine	60 mg q6h to q4h orally in subarachnoid hemorrhage 1–2 mg/h in hypertensive emergencies.	Hypotension Elevated liver enzyme
Nitric oxide	5–40 ppm inhalation	Hypotension, flushing, rashes, withdrawal syndrome
Nitroglycerin	10–200 mcg/min IV infusion	Nausea, vomiting, headache, hypotension, tachycardia, thiocyanate and cyanide toxicity
Nitroprusside	Usual, 0.25–3 mcg/kg/min, maximum 10 mcg/kg/min	Nausea, vomiting, hypotension, tachycardia, thiocyanate and cyanide toxicity
Norepinephrine	0.02–3 mcg/kg/min IV infusion	Hyperglycemia, bradycardia, skin necrosis, arrhythmia
Octreotide	25–50 mcg IV bolus, then 25–50 mcg/h infusion 50–100 mcg SC q8h	Diarrhea, flatulence, nausea, abdominal cramps, bradycardia, dysglycemia
Ofloxacin	200–400 mg PO q12h	Chest pain, headache, rash, diarrhea, visual disturbance, pharyngitis
Olanzapine	2.5–5 mg daily	Drowsiness
Omeprazole	20–40 mg PO/IV q12–24h/IV infusion 8 mg/h	Headache, dizziness, rash, vomiting, taste perversion
Ondansetron	8–10 mg PO/q24h/q12h	Headache, malaise, drowsiness, fever, pruritus, diarrhea

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Oseltamivir	Prophylaxis: 75 mg PO q24h Treatment: 75 mg PO q12h	Vomiting, nausea, abdominal pain, allergy, anaphylaxis
Oxacillin	2 g IV q4–5h	Headache, rash, diarrhea, anemia, phlebitis, agranulocytosis, TEN, glossitis
Pamidronate	60–90 mg IV	Renal failure, allergic reaction, hypotension
Pancuronium	50–100 mcg/kg IV bolus f/b 1–2 mcg/kg/min IV infusion	Tachycardia, hypertension
Pantoprazole	20–40 mg PO q12–24h, 80 mg IV bolus, then 8 mg/h × 72 h	Chest pain, headache, rash, diarrhea, visual disturbance, pharyngitis
Paracetamol	IV : 1 g every 4–6 hourly Oral : 0.5–1 g 6 hourly	Hypotension Hepatotoxicity
Pentamidine	Treatment PCP: 4 mg/kg IV q24h for 14–21 days Prophylaxis PCP: 300 mg/dose monthly inhalation	Renal failure, leucopenia, thrombocytopenia, pancreatitis, hypoglycemia
Phenobarbital	20 mg/kg IV bolus	Sedation, nystagmus, ataxia, nausea, vomiting IV form: hypotension, bradycardia, respiratory depression
Phentolamine	2–5 mg IV bolus 0.1–2 mg/min IV infusion	Hypotension, tachycardia, dizziness
Phenylephrine	0.5–10 mcg/kg/min	Arrhythmia, hypertension, chest pain
Phenytoin	20 mg/kg IV bolus, then 5–6 mg/kg/day PO/IV	Concentration-dependent: nystagmus, diplopia, ataxia, sedation, lethargy, mood/behavior changes, coma, seizures
Phosphate salts (over 6 h IV infusion)	0.08–0.16 mmol/kg	Hyperphosphatemia
Piperacillin/tazobactam	3.375–4.5 g IV q6h	Diarrhea, hypertension, insomnia, rash, transaminase increase, moniliasis, fever
Polymyxin B	15,000–25,000 units/kg/day in two divided doses	Neurotoxicity, nephrotoxicity, neuromuscular blockade, respiratory arrest

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Potassium chloride	Daily requirement: 40–80 mEq/day Deficiency correction: 10 mEq/h infusion, maximum 40 mEq/h for first 3–4 h	Rash, hyperkalemia, thrombophlebitis, abdominal pain, constipation (oral)
Potassium iodide	50–100 mg 1–2 drops or 0.05–0.1 mL PO q8–12h	Metallic taste, nausea, stomach upset, diarrhea, salivary gland swelling
Procainamide	15–18 mg/kg bolus, then 1–4 mg/min infusion	Hypotension, rash, diarrhea, nausea, vomiting
Propofol	Bolus: 0.5–3 mg/kg over 3–5 min f/b 5–50 mcg/kg/min infusion	Hypotension, bradycardia, arrhythmia, CNS depression, apnea, hypertriglyceridemia, thrombophlebitis
Propranolol	40 mg PO q12h, maximum 640 mg/day	AV conduction disturbance, cardiogenic shock, Raynaud's syndrome, psychosis, alopecia, anorexia, impotence, agranulocytosis
Propylthiouracil	Initial 300 mg PO in three divided doses q8h, maintenance 50–300 mg/day	Vasculitis, CNS stimulation, alopecia, agranulocytosis
Prostacyclins Epoprostenol	1–20 ng/kg/min	Jaw pain, nausea, headache, flushing, hypotension, infusion-site pain
Protamine	10 mg IV is required to neutralize 1000 units of unfractionated heparin in previous 15 min	Hypersensitivity, hypotension
Pyridostigmine	60–240 mg PO q4h to q6h	Sweating, salivation, abdominal cramps
Quinupristin/dalfopristin	7.5 mg/kg IV q12hr	Hyperbilirubinemia, arthralgia, myalgia
Quetiapine	12.5–200 mg 12 hourly	Dizziness, dry mouth, sedation
Ramipril	1.25–5 mg PO q12h	Hypotension, dizziness, abnormal taste, cough, worsening renal function
Ranitidine	50 mg IV q8h	Hypersensitivity, bradycardia, thrombocytopenia, leucopenia reversible, transient rise in LFT
Rasburicase	0.2 mg/kg IV q24h × 5 days	Nausea, vomiting, fever, headache, rash, diarrhea, constipation
Remifentanil	0.5–1 mcg/kg/min (Induction of anaesthesia)	Hypomagnesemia, bradycardia, hypotension

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Reteplase	10 mg IV, then 10 mg IV 30 min after the first dose	Hypotension, bleeding, allergic reactions
Rifampicin	10 mg/kg/day PO q24h, maximum 600 mg/day	Edema, flushing, ataxia, pemphigoid reaction, adrenal insufficiency, agranulocytosis, hepatitis, myalgias, acute renal failure
Rocuronium	Intubation: 0.6–1.2 mg/kg Maintenance: 0.01–0.012 mg/kg/min infusion	Hypotension/hypertension, arrhythmia, acute quadriparetic myopathy, bronchospasm
Rifaximin	400 mg PO q8h	Headache
Salbutamol	Nebulised : 2.5–5 mg 4–6 hourly	Tachycardia
Sildenafil	20 mg PO q8h (Pulmonary hypertension)	Headache, dyspepsia, flushing, dizziness, diarrhea, anemia, leucopenia, abnormal vision
Sodium bicarbonate (7.5–8.4%)	0.3 × weight (kg) × base deficit (meq/L) = desired increase in sodium bicarbonate 7.5% (8.92 meq/10 mL) 8.4% (10 meq/10 mL)	Metabolic alkalosis, hypernatremia, hypokalemia, fluid overload, tetany
Sodium valproate	10 mg/kg IV bolus, then IV infusion 1–4 mg/kg/h up to 2.5 g/day Oral: 20–30 mg/kg/day in 2–4 divided doses	
Spironolactone	12.5–200 mg PO q24h	Hyperkalemia
Streptokinase	1.5 million units over 2 h IV infusion	Allergic reactions, hypersensitivity reactions, hypotension, bleeding
Sucralfate	1 g suspension 4 hourly	Constipation
Suxamethonium	1.0–1.5 mg/kg IV bolus Rapid sequence intubation	Hyperpyrexia, muscle pain, hyperkalemia
Teicoplanin	400 mg 12 hourly for three doses IV, then 400 mg q24h IV	Raised LFT, hypersensitivity
Tenecteplase	One-time bolus over 5 s: ≤60 kg = 30 mg 61–70 kg = 35 mg 71–80 kg = 40 mg 81–90 kg = 45 mg ≥90 kg = 50 mg	Hypotension, bleeding, allergic reactions

(continued)

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Terlipressin	Hepatorenal syndrome: 0.5–1 mg q6h IV Varices: 2 mg IV bolus, then 1–2 mg q4–6h IV	Hypertension, abdominal cramps
Theophylline	Bolus: 5 mg/kg if no theophylline received in the previous 24 h Maintenance: 0.7 mg/kg/h	Arrhythmia, headache, seizure, nervousness, nausea, diarrhea, tremor, muscle cramp
Thiopental	2.5–4 mg/kg IV bolus for seizure control	Apnea, bronchospasm, hypersensitivity
Thiourea drugs	Initial 300–600 mg q24h PO	Rash, arthralgias, fever, leucopenia, nausea, vomiting
Ticarcillin/clavulanate	3.1 g IV q4–6h	Diarrhea, hypertension, insomnia, rash, transaminase increase, moniliasis, fever
Tigecycline	100 mg bolus, then 50 mg IV q12h	Nausea, hypertension, peripheral edema, phlebitis, fever, headache, insomnia, pruritus, hyperglycemia, hyperproteinemia, hyperkalemia, thrombocytopenia, leukocytosis, hepatic dysfunction, neuromuscular weakness
Tirofiban	0.4 mcg/kg/min × 30 min, then 0.1 mcg/kg/min (In unstable angina)0.4 mcg/kg/min × 3 min, then 0.1 mcg/kg/min (In PCI)	Bleeding, bradycardia, coronary artery dissection, dizziness, vasovagal reaction, thrombocytopenia
Torsemide	10–20 mg IV/PO daily Maximum: 200 mg (PO, IV)	Arrhythmia, chest pain, headache, ototoxicity, dizziness, hyperglycemia, hyperuricemia, hypokalemia
Tranexamic acid	500–1000 mg 8 hourly	Thrombosis
Valproate	1000–2500 mg/day IV/PO q12h to q6h Maintenance Loading (in status epilepticus): 15–45 mg/kg IV at <6 mg/kg/min Infusion (in status epilepticus): 1–4 mg/kg/h	Somnolence, diplopia, nausea, vomiting, diarrhea
Vancomycin	Loading (In severe infection): 25–30 mg/kg f/b 15–20 mg/kg IV q8–12h 125–500 mg PO in C. difficile diarrhea	Bitter taste, nausea, vomiting, chills, fever, eosinophilia, interstitial nephritis, vasculitis, thrombocytopenia, red man syndrome

Table A.1 (continued)

Drug class/prototypes	Dosing	Common toxicities
Vasopressin	40 units IV bolus 0.01–0.04 U/min IV infusion (in refractory septic shock) 0.2–0.4 U/min IV infusion (in variceal hemorrhage)	Arrhythmia, asystole, decreased cardiac output, chest pain, MI, peripheral ischemia, venous thrombosis, urticaria, mesenteric ischemia
Verapamil	5–10 mg iv bolus	Bradycardia
Vecuronium	100 mcg/kg iv	Liver dysfunction
Vitamin K	1–10 mg PO, SQ, or IV q24h	Hemolysis in G6PD deficiency
Voriconazole	i.v. 6 mg/kg for two doses q12h, fist day f/b 4 mg/kg IV q12h Oral maintenance : 200 mg 12 hourly	Photophobia, agranulocytosis, thrombocytopenia, anemia, diarrhea, vomiting, hallucinations, tachycardia, hyper/hypotension, raised liver enzymes, cholestatic jaundice
Warfarin	Initial 1–5 mg PO q24h, adjust based on INR measurements	Bleeding, angina, chest pain, hypotension, alopecia, skin necrosis, agranulocytosis, purple toe syndrome

Table A.2 Dosage modification in renal failure

Medication	Dose for normal renal function	Dose with impaired renal function (GFR mL/min/1.73 m^2)			Supplemental dose in dialysis	
		30–50	10–29	<10	Hemodialysis (HD)	Peritoneal dialysis (PD)
Antimicrobials						
Acyclovir	PO: 80 mg/kg/day, divided q6h IV: 30 mg/kg/day	10 mg/kg, q12h	10 mg/kg, q24h	5 mg/kg, q24h	Yes CVVHD/CVVHDF: 10 mg/kg q12–24h	No
Amikacin	5–7.5 mg/kg/dose, q8–12h or 15–20 mg/kg IV OD	5–7.5 mg/kg, q12–18h	5–7.5 mg/kg, q24h	5–7.5 mg/kg, q48–72h	Yes CVVHD/DF: Loading dose 10 mg/kg f/b maintenance 7.5 mg/kg q24–48h	Yes
Amphotericin B (conventional)	0.5–1.5 mg/kg IV, q24h	No change	No change	No change	No	No
Ampicillin	100–200 mg/kg/day, divided q6h	No change	Usual dose q6–12h	Usual dose q12–24h	Yes CVVHD/DF: Loading Dose 2 g followed by 1–2 g q6–8h	No
Amoxicillin	20–50 mg/kg/day IV/PO, divided q8h	No change	10–20 mg/kg/dose, q12h	10–20 mg/kg/dose, q24h	Yes	No
Azathioprine	1–3 mg/kg, q24h PO	Reduce dose by 25%	Reduce dose by 25%	Reduce dose by 50%	Yes	Yes
Azithromycin	10 mg/kg/day PO/IV	No change	No change	No change	No	No
Caspofungin	70 mg on day 1, then 50 mg IV, q24h	No change	No change	No change	No	No
Co-amoxiclav	IV/PO: 10–20 mg/kg, q8h	No change	Increase interval, q12h	Increase interval, q24h	Yes	No
Cefaclor	20–40 mg/kg/day IV, divided q8–12h	No change	No change	Reduce dose by 50%; divided q12h	Yes	No

Cefepime	50 mg/kg/dose IV, q12h	50 mg/kg/dose, q24h	50 mg/kg/dose, q24h	50 mg/kg/dose, q48h	Yes CVVHD/DF: Loading dose 2 g f/b 2 g q12h	No
Cefixime	8–10 mg/kg/day, divided q12h PO	No change	Reduce daily dose by 25%	Reduce daily dose by 50%	Yes	No
Cefotaxime	100–200 mg/kg/day IV, divided 6–8 h	50 mg/kg/dose q8–12h	50 mg/kg/dose, q12h	50 mg/kg/dose, q24h	Yes CVVHD/DF: 1–2 g q6–8h	No
Ceftazidime	100–150 mg/kg/day IV, divided 8 h	50 mg/kg/dose, q12h	50 mg/kg/dose, q24h	50 mg/kg/dose, q48–72h	Yes CVVHD/DF: loading dose 2 g f/b 2gm q12h	Yes
Ceftazidime Avibactam	2.5 g 8 hourly	1.25 g 8 hourly	0.94 g every 12 h	0.94 every 24 h	Administer post dialysis	
Ceftriaxone	75–100 mg/kg/day IV, divided q12–24 h	No change	No change	No change	No	No
Cefuroxime	PO: 20–30 mg/kg/day, divided q12h IV: 50–100 mg/kg/day, divided q8h	No change	50 mg/kg/dose, q12h	50 mg/kg/dose, q24h	Yes CRRT 1 g q12h	No
Cephalexin	30–50 mg/kg/day PO, divided q6h	5–10 mg/kg/dose, q8h	5–10 mg/kg/dose, q12h	5–10 mg/kg/dose, q24h	Yes	No
Cefoperazone	100 mg/kg/day IV, divided 12 h	No change	No change	No change	Yes	No
Cefoperazone/sulbactam	30–60 mg/kg/day (total), 10–20 mg/kg/day of sulbactam IV	No change	50% dose of sulbactam	25% dose of sulbactam	Yes	No

(continued)

Table A.2 (continued)

Medication	Dose for normal renal function	Dose with impaired renal function (GFR mL/min/1.73 m^2)			Supplemental dose in dialysis	
		30–50	10–29	<10	Hemodialysis (HD)	Peritoneal dialysis (PD)
Ciprofloxacin Colistin	PO: 20 mg/kg/day, divided q12h IV: 10 mg/kg/day, divided q12h 9–10.9 million loading, Maintenance 9 million unit daily divided in two doses 300–360 mg CBA loading 300 mg CBA daily divided in two doses	No change 5.9–6.65 million units/day (195–220 mg CBA/day)	q12–24h 4.85–5.9 million units /days (160–195 mg CBA/day)	q24h 4.4 million/day (145 mg CBA/day)	Yes CVVHD/DF: 200–400 mg q12–24h *intermittent hemodialysis* (IHD): On a nondialysis day,(~3.95 million IU/day). 130 mg CBA/day On a dialysis day, administer a supplemental dose (~1.2 million IU)40 mg CBA – (~1.6 million IU) 50 mg CBA for a 3- or 4-h IHD session, respectively *Sustained low-efficiency dialysis* (SLED) that 10% of the CMS dose be added to the baseline daily dose per 1 h of SLED CRRT, (~13.3 million IU/day) 440 mg CBA/day = (~6.65 million IU every 12 h). 220 mg CBA every 12 h	Yes
Co-trimoxazole	6–10 mg/kg/day (TMP), IV/PO divided q12h	No change	5–10 mg/kg/dose, q12h	Not recommended	Yes	No
Daptomycin	6 mg/kg/dose IV, q24h	No change	4 PO/IV/kg/dose, q24h	4 mg/kg/dose, q48h	No CVVHD: 8 mg/kg q48h	No
Erythromycin	30–50 mg/kg/day IV/PO, q6–8h	No change	No change	50% dose	No	No

Fluconazole	6–12 mg/kg IV/PO, q24h	Reduce dose by 50%	Reduce dose by 50%	Reduce dose by 50%	Yes CVVHD/DF Loading Dose: 400–800 mg f/b 400–800 mg q24h	No
Gentamicin	2–2.5 mg/kg IV, q8h	q12h	q18–24h	q24–48h	Yes CVVHD/DF 1.5–2.5 mg/kg q24–48h (9 redose when concentration <3–5 mg/L)	Yes
Imipenem Cilastatin	60–100 mg/kg/day IV, divided q6h; maximum daily dose 4 g	20 mg/kg, q8h	10 mg/kg, q12h	10 mg/kg, q12h	Yes CRRT: Loading dose 1 g f/b 500 mg q6h	No
Itraconazole	3–10 mg/kg/day PO, q24h	No change	No change	No change	No	No
Linezolid	10 mg/kg/dose PO/IV, q8h	No change	No change	No change	Yes	Yes
Lamivudine	4 mg/kg, q12h PO	4 mg/kg, q24h	2 mg/kg, q24h	1 mg/kg, q24h	Yes	No
Metronidazole	20–25 mg/kg/day IV/PO, divided q8h	No change	No change	Reduce daily dose by 50%	No	No
Meropenem	60–120 mg/kg/day IV, divided q8h	20–40 mg/kg, q12h	10–20 mg/kg, q12h	10–20 mg/kg, q24h	Yes CRRT: Loading dose of 1 g f/b 1 g q8–12h	10–20 mg/kg q24h
Netilmicin	4–7.5 mg/kg IV, divided q8–12h	2 mg/kg, q12h	2 mg/kg, q12h	2 mg/kg, q24–48h	Yes	Yes
Ofloxacin	15 mg/kg/day IV/PO, q12h	7.5 mg/kg/dose, q24h	7.5 mg/kg/dose, q24h	7.5 mg/kg/dose, q48h	Yes	No
Penicillin G	50,000–200,000 U/kg/day IV, divided q4–6h	No change	Reduce daily dose by 25%, divided q8–12h	Reduce daily dose by 50%, divided q12–16h	Yes	No
Piperacillin/tazobactam	150–300 mg/kg/day IV, divided q6–8h	Reduce dose by 30%, q6h	Reduce dose by 30%, q8h	Reduce dose by 30%, q8h	Yes CRRT: 2.25–3.375 g q6h	No

(continued)

Table A.2 (continued)

Medication	Dose for normal renal function	Dose with impaired renal function (GFR mL/min/1.73 m^2)			Supplemental dose in dialysis	
		30–50	10–29	<10	Hemodialysis (HD)	Peritoneal dialysis (PD)
Teicoplanin	10 mg/kg IV, q12h for 3 doses IV, then 10 mg/kg IV, q24h	Normal loading dose, then 1–4 mg/kg, q24h	Normal loading dose, then 1–4 mg/kg, q24h	Normal loading dose, then 1 mg/kg, q24h	No	No
Tobramycin	2.5 mg/kg/dose, q8h	q12h	q24h	q48h	Yes	Yes
Valganciclovir	450 mg/m^2/day or 30 mg/kg/day q24h	50%	25%	25%		Yes
Vancomycin	10–15 mg/kg IV, q6–8h	10 mg/kg, q12h	10 mg/kg, q24h	10 mg/kg, q48–72h	No	No
Voriconazole	6 mg/kg/dose IV/PO, q12h on day 1, then 4 mg/kg, q12h	No change	No change	No change		Yes
Miscellaneous						
Allopurinol	10 mg/kg/dose PO, q24h	Reduce dose by 50%	Reduce dose by 50%	Reduce dose by 75%	Yes	Yes
Amlodipine	0.05–0.15 mg/kg/day PO	No change	No change	No change	No	No
Aspirin	1–5 mg/kg/day PO	No change	No change	Avoid	Yes	Yes
Atenolol	1–3 mg/kg PO, q24h	Normal dose	50% dose, q24h	50% dose, q48h	Yes	No
Cyclosporine	3–6 mg/kg/day	No change	No change	No change	No	No
Digoxin	6–10 µg/kg/day	75% dose	50% dose	25% dose	No	No
Enalapril	0.1–1 mg/kg/day	75% dose	75% dose	50% dose	Yes	No
Enoxaparin	1 mg/kg/day, q12–24h	No change	70% dose	50% dose, q24h	No	No
Furosemide	1–6 mg/kg/day divided PO 6–12 h	No change	No change	No change	No	No

Heparin	50–200 U bolus f/b 20 U/kg/h	No change	No change	50% dose	No	No
Hydrochlorothiazide	2 mg/kg/day, q12h	No change	Avoid	Avoid	Avoid	Avoid
Labetalol	5–20 mg/kg/day, q12h PO	No change	No change	No change	No	No
Metoclopramide	0.2–0.8 mg/kg/day, divided q6–8h	Reduce dose by 25%	Reduce dose by 50%	Reduce dose by 75%	Yes	No
Mycophenolate mofetil	600–1200 mg/m^2/day	No change	No change	No change	No	No
Nitroprusside	0.3–8 μg/kg/min	No change	No change	No change	Yes	Yes
Prazosin	50–500 μg/kg/day	No change	No change	75% dose	No	No
Propanolol	0.5–4 mg/kg/day divided q6–8h	No change	No change	No change	No	No
Ramipril	6 mg/m^2, q24h	No change	50% dose	25% dose	No	NA
Ranitidine	PO: 3–6 mg/kg/day, divided q12h IV: 2–4 mg/kg/day, divided q8h	Reduce dose by 25%	Reduce dose by 25%	Reduce dose by 50%	No	No
Tacrolimus	0.15 mg/kg/day	No change	No change	No change	No	No
Warfarin	0.1–0.3 mg/kg/day	No change	No change	No change	No	No
Antitubercular drugs						
Ethambutol	15–25 mg/kg, q24h	No change	Increase interval, q36h	Increase interval, q48h	Yes	No
Isoniazid	10–15 mg/kg/day, q12–24h	No change	No change	No change	Yes	Yes
Pyrazinamide	30 mg/kg, q24h	No change	50% dose	normal dose after HD, 3 weeks	Yes	Yes
Rifampicin	10–20 mg/kg/day, q12–24h	No change	No change	No change	No	No

(continued)

Table A.2 (continued)

Medication	Dose for normal renal function	Dose with impaired renal function (GFR mL/min/1.73 m^2)			Supplemental dose in dialysis	
		30–50	10–29	<10	Hemodialysis (HD)	Peritoneal dialysis (PD)
Streptomycin	20–40 mg/kg, q12–24h IM	q24–72h	q24–72h	q24–72h	Yes	Yes
Anticonvulsants						
Carbamazepine	10–30 mg/kg/day, divided 8 h	No change	No change	No change	No	No
Clonazepam	0.05–0.5 mg/kg/day	No change	No change	75% dose	No	No
Lamotrigine	2 mg/kg/day in two single doses for 2 weeks, then 5 mg/kg for 2 weeks, then 5–15 mg/kg/day	No change	No change	75% dose	No	No
Levetiracetam	10–60 mg/kg/day, divided 8 h	50% dose	50% dose	50% dose	Yes	Yes
Phenobarbitone	5–8 mg/kg/day	No change	No change	50% dose	Yes	Yes
Phenytoin	5–8 mg/kg/day	No change	No change	No change	No	No
Topiramate	3–9 mg/kg/day, divided 8–12 h	50% dose	50% dose	25% dose	Yes	NA
Valproate sodium	10–60 mg/kg/day	No change	No change	No change	No	No

Appendix B

Common ICU Formulae

A. *Pulmonary equations*

1. *Arterial oxygen tension (PaO_2)*
   On room air = 100 − 1/3 (age)
   On supplemental oxygen = FiO_2 (in decimals) × 500, Room air FiO_2 = 21% (0.21), FiO_2 increases by approximately 4% for each litre increase in Supplemental Oxygen
2. *Alveolar gas equation*

$$PAO_2 = \left(FiO_2 \times \left[Patm - PH_2O\right]\right) - \left(\frac{PaCO_2}{R}\right)$$

$$PAO_2 = 150 - \left(1.25 \times PaCO_2\right)$$

   Normal = 100 mmHg (room air, at sea level)
   where PAO_2 = alveolar partial pressure of oxygen
   FiO_2 = fraction of inspired oxygen (in decimals)
   Patm = barometric pressure (760 mmHg at sea level)
   PH_2O = water vapor pressure (47 mmHg at normal body temperature 37°C)
   $PaCO_2$ = partial pressure of carbon dioxide in the blood
   R = respiratory quotient, assumed to be 0.8
3. *Alveolar–arterial oxygen gradientPAO_2 − PaO_2*
   A-a gradient (on room air) = 2.5 + 0.21 × age in years
   Normal value = 3–15 mmHg
   Varies with FiO_2
   For FiO_2 = 21%; A-a gradient = 5–15 mmHg
   For FiO_2 = 100%; A-a gradient = <150 mmHg
4. *PaO_2/FiO_2 ratio*Normal = 300–500 mmHg
   <300 = acute lung injury (previous definition)
   <200 = ARDS (previous definition)

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Berlin definition:
200–300 (with PEEP/CPAP >5) = Mild ARDS
<200 (with PEEP >5) = Moderate ARDS
<100 (With PEEP >5) = Severe ARDS

5. *Arteriolar–alveolar oxygen ratio* = PaO_2/PAO_2 Normal = 0.77–0.82 (most reliable when FiO_2 <0.5)
6. Oxygenation index =

$$\left[\text{mean airway pressure}\left(\text{cm } H_2O\right)\times\frac{\text{FiO}_{2(\text{fraction of inspired O}_2)}}{\text{PaO}_{22(\text{mm Hg})}}\right]\times 100,$$

$0-25$ = Good outcome

>25–40 = severe hypoxemia

7. *Static lung compliance (Crs stat)*

$$\text{Compliance}_{\text{static}}=\frac{\text{Tidal volume}}{\text{Plateau pressure}-\text{PEEP}\left(\text{positive end}-\text{expiratory pressure}\right)}$$

Normal compliance in an intubated patient = 57–85 mL/cm H_2O

8. *Dynamic lung compliance (Crs dynamic)*

$$\text{Compliance}_{\text{dynamic}}=\frac{\text{Tidal volume}}{\text{Peek pressure}-\text{PEEP}\left(\text{positive end}-\text{expiratory pressure}\right)}$$

Variable depending on peak pressure in an intubated patient
Lung + Thoracic wall compliance = 0.1 L (100 mL)/cm H_2O

9. *Airway resistance*

$$\text{Airway resistance}=\frac{\text{Peak inspiratory pressure-plateau pressure}}{\text{Peak inspiratory flow}}$$

Normal resistance in an intubated patient is 4–6 cm H_2O/L/s

10. ***$PaCO_2$–$PetCO_2$ gradient*** Normal = 4–5 mmHg
11. *Dead space ventilation* $\dfrac{V_D}{V_T}=\dfrac{PaCO_2-PetCO_2}{PaCO_2}$

V_D = Dead Space Ventilation = 1 mL/lb (2.2 kg) of ideal body wt = 150 mL
V_T = Tidal Volume

$$\frac{\text{PetCO}_2=\text{end-tidal CO}_2\text{ measured by capnography}}{\begin{array}{c}\text{Normal } V_D/V_T=0.5\left(50\%\right)\text{ in mechanically ventilated patients}\\ 0.3\left(30\%\right)\text{ in spontaneously breathing patients}\end{array}}$$

12. *Shunt equation (right to left shunt)* $\text{Qs}/\text{Qt}=\dfrac{\left(\text{CcO}_2-\text{CaO}_2\right)}{\left(\text{CcO}_2-\text{CvO}_2\right)}$
Qs/Qt = shunt fraction
CcO_2 is the end-capillary oxygen content (estimated from the PAO_2)
CaO_2 is the arterial oxygen content
CvO_2 is the mixed venous oxygen content

Normal = 5%

Alternate equation (in patients breathing 100% oxygen for 20 min)

$$Qs/Qt = 100 \times (0.0031 \times AaG)/((.0031 \times AaG) + 5)$$

13. *$PaO_2 + PaCO_2 < 150$ mmHg at sea level breathing room air*

B. *Hemodynamic equations*
(see Chap. 18, Vol. 1)

Parameter	Formula	Normal range
Pulse pressure	Systolic − diastolic BP	40 mmHg
Mean arterial pressure (MAP)	1/3 pulse pressure + diastolic BP	65 mmHg
Cardiac output (CO)	SV × HR	4–7 L/min
Cardiac index (CI)	CO/BSA	3.5–4.5 L/min/m^2
Stroke volume (SV)	CO/HR × 1000 End diastolic volume (EDV) (120 mL) – End systolic volume (ESV) (50 mL)	60–80 mL
Stroke volume index (SVI)	CI/HR × 1000, SV/BSA	33–47 mL/m^2/beat
Systemic vascular resistance (SVR)	[(MAP − CVP)/CO] × 80	900–1200 dyn s/cm^5
Systemic vascular resistance index (SVRI)	(MAP – CVP) 80/CI	1970–2390 dyn s/cm^5/m^2
Pulmonary vascular resistance	[(MPAP − PAOP)/CO] × 80	80–120 dyn s/cm^5
Pulmonary vascular resistance index	[(MPAP − PAOP)/CI] × 80	255–285 dyn s/cm^5/m^2
Oxygen delivery (DO_2)	CO (L) × CaO_2 (mL/dL) × 10	700–1400 mL/min
Oxygen delivery index (DO_2I)	CaO_2 × CI × 10	500–600 mL/min/m^2
Oxygen consumption (VO_2)	CO (L) × (CaO_2 − CvO_2) × 10	180–280 mL/min
Oxygen consumption index (VO_2I)	CI × (CaO_2 − CvO_2) × 10	120–160 mL/min/m^2
Oxygen extraction ratio (O_2ER)	VO_2/DO_2 × 100	25%
Oxygen extraction index (O_2EI)	[(SaO_2 − SvO_2)/SaO_2] × 100	20–25%
Arterial oxygen content (CaO_2)	(1.39 × Hb SaO_2) + (0.003 × PaO_2)	17–20 mL/dL
Mixed venous oxygen content (CvO_2)	(1.39 × Hb × SvO_2) + (0.003 × PvO_2)	12–15 mL/dL
A-V oxygen content difference ($C(a\text{-}v)O_2$)	CaO_2 − CvO_2	4–6 mL/dL
Systolic pressure variation (SPV)	[(SPmax − SPmin)/(SPmax + SPmin)/2] × 100	<5 mmHg unlikely to be preload responsive >5 mmHg likely to be preload responsive

(continued)

Parameter	Formula	Normal range
Pulse pressure variation (PPV)	(SVmax − SVmin)/ [(SVmax + SVmin)/2] × 100	<10% unlikely to be preload responsive >13–15% likely to be preload responsive
Stroke volume variation (SVV)	SV × (MAP − PAWP) × 0.0136	<10% unlikely to be preload responsive >13–15% likely to be preload responsive
Left ventricular stroke work (LVSW)	SVI × (MAP − PAWP) × 0.0136	58–104 g m/beat
Left ventricular stroke work index (LVSWI)	SV × (MPAP − RAP) × 0.0136	50–62 g m/m^2/beat
Right ventricular stroke work (RVSW)	SVI × (MPAP − RAP) × 0.0136	8–16 g m/beat
Right ventricular stroke work index (RVSWI)	Diastolic BP − PAWP	5–10 g m/m^2/beat
Coronary artery perfusion pressure (CPP)		60–80 mmHg

CVP central venous pressure, *MPAP* mean pulmonary artery pressure, *HR* heart rate, *BP* blood pressure, *PAOP* pulmonary artery occlusion pressure, SaO_2 arterial oxygen saturation, SvO_2 mixed venous oxygen saturation, PaO_2 arterial oxygen partial pressure, PvO_2, mixed venous oxygen partial pressure

C. *Acid–base equations*

1. *Validity of the data*Henderson's equation

$$\frac{H^+ \times HCO_3}{PaCO_2} = 24$$

H^+ = hydrogen ion
HCO_3 = Bicarbonate
$PaCO_2$ = Partial pressure of carbon dioxide

pH	[H^+] (mmol/L)
7.60	25
7.55	28
7.50	32
7.45	35
7.40	40
7.35	45
7.30	50
7.25	56
7.20	63
7.15	71

Rule of thumb: H^+ = 80 minus the last two digits of pH after decimal (for pH 7.20–7.50)
For example, pH 7.35: H^+ = 80–35 = 45

2. *Respiratory acidosis or respiratory alkalosis*
   - Acute respiratory acidosis or alkalosis: DpH = 0.008 × Delta $PaCO_2$ (from 40)
   - Chronic respiratory acidosis or alkalosis: DpH = 0.003 × Delta $PaCO_2$ (from 40)
   - Acute respiratory acidosis = ↑$PaCO_2$ 10 mmHg = ↑HCO_3 1 mmol/L
   - Chronic respiratory acidosis = ↑$PaCO_2$ 10 mmHg = ↑HCO_3 3 mmol/L
   - Acute respiratory alkalosis = ↓$PaCO_2$ 10 mmHg = ↓HCO_3 2 mmol/L
   - Chronic respiratory alkalosis = ↓$PaCO_2$ 10 mmHg = ↓HCO_3 4 mmol/L
   - Acute respiratory acidosis or alkalosis: SBE (standard base excess) = zero
   - Chronic respiratory acidosis or alkalosis: Change in bicarbonate = 0.4 × SBE
3. *Metabolic acidosis*
   - Predicted $PaCO_2$ = 1. 5 × [HCO_3^- + 8] ± 2
   - Change in bicarbonate = change in standard base excess (SBE)
   - 1 mEq/L fall in HCO_3 = 1.2 mmHg fall in $PaCO_2$
   - Bicarbonate deficit (mEq/L) = [0.5 × body weight (kg) × (24 − [HCO_3−])]
     Rule of thumb : Expected $PaCO_2$ = the last two digits of pH after decimal
4. *Metabolic alkalosis*
   - Predicted $PaCO_2$ = 0.7 × [HCO_3 + 21] ± 2
   - Change in bicarbonate = 0.6 × standard base excess (SBE)
   - 1 mEq/L rise in HCO_3 = 0.7 mmHg rise in $PaCO_2$
   - Bicarbonate excess [0.4 × body weight (kg) × ([HCO_3^-] − 24)]
     Rule of thumb: Expected $PaCO_2$ = the last two digits of pH after decimal
5. *Blood anion gap*
   - Anion gap (AG) = Na^+ − (Cl^- + HCO_3^-)
     - Normal value: 10 ± 4 mmol/L
   - Correction for albumin: For every change (increased or decreased) of 1 g/dL in albumin, a change of 2.5 mmol/L in the anion gap
   - Correction for pH: In acidosis, decrease by 2 mmol/L; in alkalosis, increase by 2 mmol/L
6. *Delta gap/Delta ratio*
   - Delta gap = *delta* AG − *delta* **HCO_3^-**
   - Delta ratio = delta AG/delta HCO_3
   - Where *Delta* AG = patient's AG – 12 mEq/L {normal AG}
   - *Delta* HCO_3^- = 24 mEq/L {normal HCO_3^- } − patient's HCO_3
   - Normal delta gap (in pure anion gap metabolic acidosis) = 0±6
   - Normal delta ratio =1.1
     - High delta gap/delta ratio >1 signifies a concomitant metabolic alkalosis or chronic respiratory acidosis.
     - Low delta gap/delta ratio<1 signifies a concomitant normal anion gap metabolic acidosis or chronic respiratory alkalosis.
7. *Urine anion gap (UAG)*
   - UAG (mmol/L) = urine [(Na + K) − Cl]
     - Normal: usually zero or positive
     - Nonanion gap metabolic acidosis due to gastrointestinal loss: UAG negative
     - Nonanion gap metabolic acidosis due to renal cause (renal tubular acidosis): UAG positive

8. *Stewarts approach*
   - Strong ion difference (SID): $[Na^+] + [K^+] + [Ca^{2+}] + [Mg^{2+}] - [Cl^-] - [\text{lactate}]$
     - Normal value: 40 mEq/L
     - Increase in SID = alkalosis (increase in pH)
     - Decrease in SID = acidosis (decrease in pH)
   - Strong ion gap (SIG): $SID - SID_{eff}$
     - SID_{eff} = effective strong ion difference (depends on pH, albumin, phosphate)
     - $12.2 \times PCO_2/(10 - pH) + [\text{albumin}] \times (0.123 \times pH - 0.631) + [PO^{4-}] \times (0.309 \times pH - 0.469)$
     - Normal SIG = 0
     - Positive SIG = Increase in organic acid

D. *Electrolyte equations*
1. *Hyponatremia*
   - Sodium deficit = (desired $[Na^+]$ − current $[Na^+]$) × 0.6 × body weight in kg
   - Increase in serum sodium = (infusate sodium − serum sodium)/[(0.6 × body weight) + 1]

     Rule of thumb:
     - For hypertonic (3%) saline, infusion rate (mL/h) = weight (kg) × desired rate of correction (mEq/h)
     - e.g. to correct sodium by 0.5 meq/l/h, the desired rate of 3% saline infusion in a 60 kg man would be = 60 × 0.5 = 30 mL/h
     - 0.9% NaCl corrects at 1–2 mmol/L for every 1 L NaCl
   - Calculated urine osmolarity = the last two digits of urine-specific gravity × 30
2. *Hypernatremia*

$$\text{Free water deficit}\left(\text{L}\right) = 0.4 \times \text{body weight} \times \left(\frac{\text{plasma } Na^+}{140} - 1\right)$$

3. *Correction sodium for hyperglycemia*
   - For each 100 mg/dL increase in blood glucose above 200 mg/dL, serum sodium decreases by 2.4 mEq/L.
4. *Serum osmolality*
   - Calculated Sosm = (2 × serum [Na]) + [glucose, in mg/dL]/18 + [blood urea nitrogen, in mg/dL]/2.8
   - Calculated Sosm with standard units (mmol/L) = (2 × serum [Na]) + [glucose] + [urea]
     - Normal value = 270 and 290 mOsm/kg H_2O
   - Osmolar gap = measured osmolality − calculated osmolality
     - Normal value = <10 mOsm/kg H_2O
5. *Corrected calcium*
   - Corrected calcium (mg/dL) = measured total calcium (mg/dL) + [0.8 × (4.0 − albumin)]
   - Corrected calcium (mmol/L) = measured total calcium (mmol/L) + [0.02 × (Normal albumin [40 g/L] – patients albumin)]

E. *Renal equations*
1. *Measured creatinine clearance (CCr) L/day*
   - [24-h urine creatinine (mg/dL) × 24-h urine volume (L/day)]/serum creatinine (mg/dL)
   - CCr mL/min = [(CCr L/day × 1000 mL/L)]/1440 min/day
   - CCr mL/min × 1.73/BSA = CCr mL/min/1.73 sq m
     - Normal values = 95 ± 20 mL/min per 1.73 m^2 in women and 120 ± 25 mL/min per 1.73 m^2 in men
2. *Estimated creatinine clearance (Cockroft–Gault equation)*
   - (140-Age in years × Weight in kg) / Serum creatinine in mg/dL × 72 For female patient multiply with 0.85
3. *Fractional excretion of sodium (FENa+)*

$$\frac{\left[\text{UrineNa}^{+}\right]\times\left[\text{plasma creatinine}\right]}{\left[\text{Urine creatinine}\right]\times\left[\text{plasmaNa}^{+}\right]}$$

   - Normal value = <1
4. *Fractional excretion of urea (FEurea)*

$$\frac{\left[\text{Urineurea}\right]\times\left[\text{plasma creatinine}\right]}{\left[\text{BUN}\right]\times\left[\text{urinecreatinine}\right]}$$

   - <35 in prerenal azotemia, 50–65 in acute tubular necrosis

F. *Nutrition equations*
1. *Ideal or predicted body weight (IBW)*
   - Male IBW (kg) = 50 + (0.91 × (height in cm − 152.4))
   - Male IBW (kg) = 50 kg for 5 ft; add 2.3 kg for every 1 in. above 5 ft
   - Female IBW (kg) = 45.5 + (0.91 × (height in cm − 152.4))
   - Female IBW (kg) = 45.5 kg for 5 ft; add 2.3 kg for every 1 in. above 5 ft
2. *Harris–Benedict equation with Long's modification (calories requirement)*
   - For women, basal metabolic rate (BMR) = 65.5 + (9.6 × weight in kg) + (1.8 × height in cm) − (4.7 × age in years)
   - For men, BMR = 66 + (13.7 × weight in kg) + (5 × height in cm) − (6.8 × age in years)
   - Actual energy needs = BMR × AF × IF (AF, activity factor; IF, injury factor)
   - Activity factor (AF): Confined to bed = 1.2; out of bed = 1.3
   - Injury factor (IF): Minor surgery = 1.2; skeletal trauma = 1.3; major sepsis = 1.6; severe burn = 2.1
   - Normal calories requirement = 25–30 kcal/kg of predicted body weight
3. *Protein requirement*
   - 1 g of nitrogen = 6.25 g of protein
   - Non-protein calories (NPC)–nitrogen ratio = 150:1
   - Nitrogen balance = (protein intake/6.25) − (24-h urinary urea nitrogen + 4)
   - Negative nitrogen balance >5 = severe stress
   - 1 g of nitrogen loss = 30 g lean body mass lost

- 1 g of glucose = 4 kcal
- 1 g of protein = 4 kcal
- 1 g of lipid = 9 kcal
- Protein loss in dialysis = 4–6 g/h in hemodialysis; 40–60 g in peritoneal dialysis

4. *Respiratory quotient (RQ):*
   - Carbon dioxide production (VCO_2)/oxygen consumption (VO_2)
   - Normal value on balanced diet = 0.7–1.0
   - >1: Excess carbohydrate
   - <0.7: Excess fat

G. *Intra-abdominal pressure equation*
- Abdominal perfusion pressure (APP) = mean arterial pressure (MAP) − IAP (intra-abdominal pressure)
- Normal intra-abdominal pressure = 5–7 mmHg
- Filtration gradient (FG) = glomerular filtration pressure (GFP) − proximal tubular pressure (PTP) = MAP − 2 × IAP

H. *Statistical equations*
- Sensitivity: True positives/(true positive [TP] + false negative [FN])
- Specificity: True negative/(true negative [TN] + false positive [FP])
- Positive predictive value: True positive/ (true positive + false positive)
- Negative predictive value: True negative/(true negative + false negative)
- Positive likelihood ratio (LR^+): sensitivity/(1 − specificity)
- Negative likelihood ratio (LR −): (1 − sensitivity)/specificity
- Prevalence (pretest probability): (TP + FN)/(TP + FP + TN + FN)
- Pretest odds: Prevalence/(1 − prevalence)
- Posttest odds: Pretest odds × LR
- Posttest probability: Posttest odds/(posttest odds + 1)
- Event rate (ER): Total events/total subjects (event + nonevent)
- Absolute risk reduction (ARR): Control event rate (CER) − experimental event rate (EER)
- Relative risk reduction (RRR): (CER − EER)/CER
- Relative risk (RR): EER/CER
- Odds ratio: (experimental event [EE]/experimental nonevent [EN])/(control event [CE]/control nonevent [CN])
- Number needed to treat (NNT): 1/ARR
- Number needed to harm (NNH): 1/(CER − EER)
- Rate of Type I error = Number of False positives = Alpha
- Rate of Type II error = Number of False negatives = Beta
- Power of a test = (1-Beta)

I. *Neurology equations*
- CBF = (CAP − JVP) ÷ CVR
  (CBF, cerebral blood flow; CAP, carotid artery pressure; JVP, jugular venous pressure; CVR, cerebrovascular resistance)

- CPP = MAP − ICP
  (CPP, cerebral perfusion pressure; MAP, mean arterial pressure; ICP, intracranial pressure)
  – Keep CPP between 60 and 75 mmHg
- Increased WBC in traumatic tap:
  Rule of thumb: Subtract one WBC for every 500–1500 RBCs (if peripheral WBC is normal)

J. *Hematology equation*

- ANC = WBC × [(segs/100) + (bands/100)]
  (ANC, absolute neutrophil count)

$$\text{Corrected reticulocyte count}\left(\text{CRC}\right) = \frac{\text{reticulocytes}\left(\%\right)}{0.45\,\text{L}/\text{L}} \times \text{Hct}\left(\text{L}/\text{L}\right)$$

- K. Pulmonary Score
- CURB 65: Confusion (1 point), Urea >20 (2 points), Respiratory rate > 30 (1 point), Systolic BP <90 mmHg (1 point), Age >65 years (1 point)
- -1 Low risk of mortality (0–5%), 2 points: Moderate risk of mortality: 9%, 3–5 points: High risk of mortality (15–40%)

Appendix C

Reference ranges for selected clinical laboratory tests

Substance	Fluid[a]	Traditional units	×	k	=	SI units
Acetoacetate	P, S	0.3–3.0 mg/dL		97.95		3–30 μmol/L
Alanine aminotransferase (ALT, SGPT)	S	7–41 U/L		0.016		0.12–0.70 μkat/L
Albumin	S	4.1–5.3 g/dL		10		41–53 g/L
Female albumin	S	4.0–5.0 g/L		10		40–50 g/L
Male albumin	S					
Albumin	CSF	11–48 mg/dL		0.01		0.11–0.48 g/L
Aldolase	S	1.5–8.1 U/L		17.33		26–138 nkat/L
Alkaline phosphate	S	(F) 30–100 U/L		0.016		0.5–1.92 μkat/L
		(M) 45–115 U/L				0.75–1.92 μkat/L
Alpha fetoprotein (adult)	S	0–8.5 ng/mL		1		0–8.5 μg/L
Ammonia, as NH_3	P	19–60 μg/dL		0.587		11–35 μmol/L
Amylase (method dependent)	S	20–96 U/L		0.016		0.34–1.6 μkat/L
Anion gap	S	7–16 mmol/L		1		7–16 mmol/L
Arterial blood gases						
$\left[HCO_3^-\right]$		22–30 mEq/L		1		22–30 mmol/L
PCO_2		32–45 mmHg		0.134		4.3–6.0 kPa
Ph		7.35–7.45		1		7.35–7.45
PO_2		72–104 mmHg		0.134		9.6–13.8 kPa
Aspartate aminotransferase (AST, SGOT)	S	12–38 U/L		0.016		0.20–0.65 μkat/L
B-type natriuretic peptide (BNP)	P	Age and gender specific: <167 pg/mL		1		Age and gender specific: <167 ng/L
Bilirubin	S					
Total (Bilirubin)		0.3–1.3 mg/dL		17.1		5.1–22 μmol/L
Direct (Bilirubin)		0.1–0.4 mg/dL		17.1		1.7–6.8 μmol/L

(continued)

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Substance	Fluid[a]	Traditional units	×	k	=	SI units
Indirect (Bilirubin)		0.2–0.9 mg/dL		17.1		3.4–15.2 µmol/L
β-Hydroxybutyrate	S	<1.0 mg/dL		96.05		<100 µmol/L
Bicarbonate	S	22–26 mEq/L		1		22–26 mmol/L
Blood urea nitrogen (BUN)	P, S	8–18 mg/dL		0.367		3.0–6.5 mmol/L
Calcium-Total	S	8.7–10.2 mg/dL		0.252		2.2–2.6 mmol/L
Calcium Ionized	WB	4.5–5.3 mg/dL		0.25		1.12–1.32 mmol/L
Carboxyhemoglobin (carbon monoxide content)	WB	>20%		0.01		>0.2 proportion of 1
Nonsmokers		0–4%		0.01		0–0.04
Smokers		4–9%		0.01		0.04–0.09
Onset of symptoms		15–20%		0.01		0.15–0.20
Loss of consciousness and death		>50%		0.01		>0.50
Chloride	S	102–109 mEq/L		1		102–109 mmol/L
	CSF	120–130 mEq/L		1		120–130 mmol/L
	U	10–200 mEq/L		1		10–200 mmol/L
Cholinesterase	S	5–12 U/mL		1		5–12 kU/L
Complement						
C3	S	83–177 mg/dL		0.01		0.83–1.77 g/L
C4	S	16–47 mg/dL		0.01		0.16–0.47 g/L
Cortisol Fasting, 8 a.m.–12 noon 12 noon–8 p.m. 8 p.m.–8 a.m.						
	S	5–25 µg/dL 5–15 µg/dL 0–10 µg/dL		27.588 27.588 27.588		138–690 nmol/L 138–414 nmol/L 0–276 nmol/L
Cortisol, free	U	20–70 µg/24 h		2.758		55–193 nmol/24 h
C-reactive protein	S	0.2–3.0 mg/L		1		0.2–3.0 mg/L
Creatine kinase (total) Females Males	S	39–238 U/L 51–294 U/L		0.017 0.017		0.66–4.0 µkat/L 0.87–5.0 µkat/L
Creatine kinase-MB	S					
Mass		0.0–5.5 ng/mL		1		0.0–5.5 g/L
Fraction of total activity (by electrophoresis)		0–4.0%		0.01		0–0.04
Creatinine Female Male	S	0.5–0.9 ng/mL 0.6–1.2 ng/mL		88.4 88.4		44–80 µmol/L 53–106 µmol/L
Creatinine	U	15–25 mg/kg/24 h		0.009		0.13–0.22 mmol/kg/24 h
Cyanide: Nontoxic	WB	<µg/dL		3.8		<19 µmol/L
Cyanide: Lethal		>30 µg/dL				>114 µmol/L
Erythropoietin	S	4–27 U/L		1		4–27 U/L

Substance	Fluid[a]	Traditional units	×	k	=	SI units
Fatty acids, free (nonesterified)	P	<8–25 mg/dL		0.0355		<0.28–0.89 mmol/L
Ferritin Female Male	S	10–150 ng/dL 29–248 ng/mL		1 1		10–150 µg/dL 29–248 µg/L
Fibrinogen	P	150–350 mg/dL		0.01		1.5–3.5 g/L
Fibrin split products	S	<10 µg/mL		1		<10 mg/L
Glucose	P					
Glucose (fasting)	P	70–100 mg/dL		0.06		3.9–6.1 mmol/L
Glucose	CSF	50–80 mg/dL		0.06		2.8–4.4 mmol/L
Impaired glucose tolerance		111–125 mg/dL		0.056		6.2–6.9 mmol/L
Diabetes mellitus		>125 mg/dL		0.056		>7.0 mmol/L
Glucose, 2 h postprandial	P	70–120 mg/dL		0.056		3.9–6.7 mmol/L
Hemoglobin (Hb)	P	0.6–5.0 mg/dL		10		6–50 mg/L
Adult males (Hb)	WB	13.3–16.2 g/dL		10		133–162 g/L
Adult females (Hb)	WB	12–15.8 g/dL		10		120–158 g/dL
Mean corpuscular hemoglobin (MCH)	WB	26–34 pg/cell		1		26–34 pg/cell
Mean corpuscular hemoglobin concentration (MCHC)	WB	33–37 g/dL		10		330–370 g/L
Mean corpuscular volume (MCV)	WB	80–100 μm^3		1		80–100 fL
Hemoglobin A_{1c}	WB	4.0–6.0%		0.01		0.04–0.06 Hb fraction
Homocysteine	P	4.4–10.8 µmol/L		1		4.4–10.8 µmol/L
Iron	S	41–141 µg/dL		0.178		7–25 µmol/L
Iron-binding capacity	S	251–406 µg/dL		0.179		45–73 µmol/L
Lactate	P, arterial	4.5–14.4 mg/dL		0.111		0.5–1.6 mmol/L
	P, venous	4.5–19.8 mg/dL		0.111		0.5–2.2 mmol/L
Lactate: resting	P	<2.0 mEq/L		1		<2 mmol/L
Exercise		<4.0 mEq/L				<4 mmol/L
Lactate dehydrogenase	S	115–221 U/L		0.0171		2.0–3.8 µkat/L
Lipase	S	3–43 U/L		0.166		0.5–0.73 µkat/L
Magnesium	S	1.5–2.3 mg/dL		0.413		0.62–0.95 mmol/L
Methemoglobin	WB	0–1% of total Hb		0.01		0.0–0.01 proportion of total Hb
Microalbumin urine 24-h urine Spot urine	U	0–30 mg/24 h 0–30 µg/mg creatinine		0.001 0.001		0.0–0.03 g/day 0.0–0.03 g/g creatinine
Myoglobin Male Female	S	19–92 µg/L 12–76 µg/L		1 1		19–92 µg/L 12–76 µg/L

(continued)

Substance	Fluid[a]	Traditional units	×	k	=	SI units
Osmolality	P	275–295 mOsm/kg serum water		1		275–295 mOsm/kg serum water
	U	500–800 mOsm/kg water		1		500–800 mOsm/kg water
Phosphatase, alkaline	S	33–96 U/L		0.0169		0.56–1.63 µkat/L
Phosphorus, inorganic	S	2.5–4.3 mg/dL		0.324		0.81–1.4 mmol/L
Potassium	S	3.5–5.0 mEq/L		1		3.5–5.0 mmol/L
Prealbumin	S	17–34 mg/dL		10		170–340 mg/L
Prolactin	S	0–20 ng/mL		1		0–20 g/L
Prostate-specific antigen (PSA) <40 years male >40 years male	S	0.0–2.0 ng/mL 0.0–0.40 ng/mL		1 1		0.0–2.0 µg/L 0.0–0.4 µg/L
PSA, free; in males 45–75 years, with PSA values between 4 and 20 g/mL	S	>25% associated with benign prostatic hyperplasia		0.01		>0.25% associated with benign prostatic hyperplasia
Protein fractions	S					
Albumin		3.5–5.5 g/dL (50–60%)		10		35–55 g/L
Globulin		2.0–3.5 g/dL (40–50%)		10		20–35 g/L
$Alpha_1$		0.2–0.4 g/dL (4.2–7.2%)		10		2–4 g/L
$Alpha_2$		0.5–0.9 g/dL (6.8–12%)		10		5–9 g/L
Beta		0.6–1.1 g/dL (9.3–15%)		10		6–11 g/L
Gamma		0.7–1.7 g/dL (13–23%)		10		7–17 g/L
Total protein	P, S	6.0–8.0 g/dL/L		10		60–80 g/L
	CSF	<40 mg/dL		0.01		<0.40 g/L
	U	<150 mg/24 h		0.01		<1.5 g/24 h
Sodium	S	136–146 mEq/L		1		136–146 mmol/L
Thyroid-stimulating hormone	S	0.34–4.25 µIU/mL		1		0.34–4.25 mIU/L
Thyroxine, free (fT_4)	S	0.8–1.7 ng/dL		12.871		10.3–21.9 pmol/L
Thyroxine, total (T_4)	S	5.4–11.7 µg/dL		12.871		70–151 nmol/L
Triiodothyronine (T_3)	S	75–220 pg/dL		0.015		12–3.4 pmol/L
Troponin I Normal population, 99% tile Cutoff for MI	S	0–0.08 ng/mL >0.4 ng/mL		1 1		0–0.08 µg/L >0.4 µg/L
Troponin T Normal population, 99% tile Cutoff for MI	S	0–0.01 ng/mL 0–0.1 ng/mL		0.1 1		0–0.1 µg/L 0–0.1 µg/L

Substance	Fluid[a]	Traditional units	×	k	=	SI units
Urea nitrogen	S	7–20 mg/dL		0.357		2.5–7.1 mmol/L
Uric acid	S	2.5–5.6 mg/dL		0.06		0.15–0.33 μmol/L
Females		3.1–7.0 mg/dL		0.06		0.18–0.41 μmol/L
Males						
Urobilinogen	U	1–3.5 mg/24 h		1.7		1.7–5.9 μmol/d

Adapted from the New England Journal of Medicine SI Unit Conversion Guide. Waltham, MA: Massachusetts Medical Society, 1992

[a]*P* plasma, *S* serum, *U* urine, *WB* whole blood, *CSF* cerebrospinal fluid, *RBC* red blood cell

Reference ranges for vitamins and trace elements

Substance	Fluid[a]	Traditional units	×	k	=	SI units
Chromium	S	0.14–0.15 ng/mL		17.85		2.5–2.7 nmol/L
Copper	S	70–140 μg/dL		0.16		11–22 μmol/L
Folate	RBC	140–960 ng/mL		2.26		317–2196 nmol/L
Iron	S	(M) 80–180 μg/dL		0.18		(M) 14–32 μmol/L
		(F) 60–160 μg/dL				(F) 11–29 μmol/L
Ferritin	P, S	(M) 20–250 ng/mL		1		(M) 20–250 μg/L
		(F) 10–120 ng/mL				(F) 10–120 μg/L
Manganese	WB	0.4–2.0 μg/dL		0.018		0.7–3.6 μmol/L
Pyridoxine	P	20–90 ng/mL		5.98		120–540 nmol/L
Riboflavin	S	2.6–3.7 μg/dL		26.57		70–100 nmol/L
Selenium	WB	58–234 μg/dL		0.012		0.7–2.5 μmol/L
Thiamine (total)	P	3.4–4.8 μg/dL		0.003		98.6–139 μmol/L
Vitamin A	P, S	10–50 μg/dL		0.349		0.35–1.75 μmol/L
Vitamin B_{12}	S	200–1000 pg/mL		0.737		150–750 pmol/L
Vitamin C	S	0.6–2 mg/dL		56.78		30–100 μmol/L
Vitamin D	S	24–40 ng/mL		2.599		60–105 nmol/L
Vitamin E	P, S	0.78–1.25 mg/dL		23.22		18–29 μmol/L
Zinc	S	70–120 μg/dL		0.153		11.5–18.5 μmol/L

Adapted from the New England Journal of Medicine SI Unit Conversion Guide. Waltham, MA: Massachusetts Medical Society, 1992

[a]*P* plasma, *S* serum, *U* urine, *WB* whole blood, *CSF* cerebrospinal fluid, *RBC* red blood cell

Appendix D: Syllabus for ICU Training

Narendra Rungta and Arvind Kumar Baronia

1. General
   (a) ICU infrastructure: building, equipments and manpower
   (b) Organization of critical care services: models of intensive care and outreach services
   (c) Critical care physiology (system-wise)
   (d) Assessment of critically ill patients
   (e) Monitoring in the ICU
   (f) Principles of critical care pharmacology, Drug interactions and toxicity, Pharmacology of sedatives, hypnotic agents, analgesics and neuromuscular blocking agents
   (g) Pain management
   (h) Scoring system in the ICU
   (i) Enteral and parenteral nutrition
   (j) Care of ICU equipment-electrical safety, calibration, decontamination and maintenance
   (k) Intra and inter-hospital transport of critically ill patients
   (l) Basics of imaging modalities including ultrasound, x-ray, CT, MRI and Angiography in the ICU patients
   (m) Systemic disorders in critical illness
   (n) Obesity-hypoventilation syndrome and obstructive sleep apnea syndrome
2. Fluid and electrolytes
   (a) Fluid requirements in critically ill patients
   (b) Monitoring of fluid therapy and diagnosis of inappropriate fluid therapy i.e. fluid overload and hypovolemia
   (c) Colloid versus crystalloid
   (d) Electrolyte disturbances (calcium, magnesium, potassium, sodium and phosphorus) in ICU
   (e) Hyperosmolar therapies-Hypertonic saline
   (f) Acid-base disorders-Bicarbonate and Anion Gap, Base Deficit, Stewart approach
   (g) Fluid therapy in children

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3. Renal disorders
   (a) Acute kidney injury
   (b) Renal tubular acidosis
   (c) Hepatorenal syndrome
   (d) Peritoneal dialysis, plasmapheresis and apheresis
   (e) Renal replacement therapy
   (f) Drugs in renal failure
4. Nervous system
   (a) Seizure disorders and status epileptics
   (b) Cerebrovascular accident (CVA)
   (c) Acute CNS infections
   (d) Intra-arterial pressure: Physiology, Intracranial hypertension, ICP monitoring
   (e) Coma
   (f) Traumatic brain injury
   (g) Neuromuscular diseases
   (h) Acute Flaccid Paralysis-Guillain-Barré syndrome and other disorders
   (i) Tetanus
   (j) CNS drugs
   (k) Brain death
   (l) EEG in the ICU
5. Cardiovascular system
   (a) Acute coronary syndrome
   (b) Acute heart failure
   (c) ACLS guidelines
   (d) Rhythm disorders
   (e) Basics of echocardiography in the ICU
   (f) Valvular heart diseases
   (g) Cardiomyopathies
   (h) Postoperative cardiac care
   (i) Cardiogenic shock
   (j) Myocarditis
   (k) Hypertensive emergencies
   (l) Cardioversion
   (m) Cardiac drugs
6. Environmental disorders
   (a) Near-drowning
   (b) Thermal injuries
   (c) Biochemical hazards
   (d) Radiation hazards
   (e) Polytrauma
   (f) Disaster management guidelines
   (g) Envenomation
   (h) Acute poisoning

7. Endocrinal disorders
   (a) Thyroid storm and other thyroid disorder in critical care
   (b) Diabetic ketoacidosis (DKA)
   (c) Adrenal insufficiency
   (d) Cerebral salt wasting
   (e) Hyperglycemia and hypoglycemia in the ICU
8. Gastrointestinal disorders
   (a) Upper gastrointestinal bleeding
   (b) Lower gastrointestinal bleeding
   (c) Acute liver failure
   (d) Acute pancreatitis
   (e) Acute abdomen-medical and surgical emergencies
   (f) Stress ulcer prophylaxis
   (g) Postoperative care
   (h) Liver transplant: Basics
9. Respiratory disorders
   (a) Oxygen therapy
   (b) Airway adjuncts
   (c) Basics of mechanical ventilation and applied physiology
   (d) Disease-specific ventilation
   (e) Ventilator-Graphics, monitoring and Troubleshooting
   (f) High-frequency oscillation ventilation
   (g) Acute respiratory distress syndrome
   (h) Pulmonary thromboembolism
   (i) Pneumonias
   (j) Chronic obstructive pulmonary disease
   (k) Noninvasive ventilation
   (l) Chest physiotherapy
   (m) Pulmonary function test (PFT)
   (n) Extracorporeal membrane oxygenation (ECMO) + $ECCO_2$ Elimination: asics
10. Infections
   (a) Hand hygiene
   (b) Asepsis guidelines
   (c) Sepsis syndrome: SIRS, sepsis, severe sepsis, septic shock and multiorgan dysfunction syndrome (MODS)
   (d) Immunocompromised hosts
   (e) HIV and AIDS
   (f) Ventilator-associated pneumonia (VAP)
   (g) New outset fever in the ICU
   (h) Severe Tropical infections: Malaria, Typhoid, Scrub typhus and zoonosis
   (i) Nosocomial infections
   (j) Viral hemorrhagic fevers
   (k) Endocarditis

(l) Opportunistic infections in the ICU
(m) Fungal infections
(n) Infection control measures in the ICU
(o) Antimicrobial therapy
(p) Prevention of Antibiotic Resistance in the ICU
(q) Antibiotic resistance and MDR pathogens

11. Obstetric disorders
    (a) Pregnancy-induced hypertension
    (b) Acute haemorrhage
    (c) Trauma in pregnancy
    (d) HELPP syndrome
    (e) Cardiomyopathy in pregnancy
    (f) Amniotic fluid embolism
12. Procedures
    (a) Endotracheal Intubation
    (b) Percutaneous tracheostomy
    (c) Flexible bronchoscopy
    (d) Intercostal drainage
    (e) Intracranial pressure monitoring
    (f) EEG interpretation
    (g) Peritoneal dialysis
    (h) Continuous renal replacement therapy
    (i) Cardiac pacing
    (j) ECG
    (k) CPR
    (l) Defibrillation
    (m) Pericardiocentesis
    (n) Central venous access
    (o) Echo cardiography(ECHO)
    (p) Emergency ultrasonography
    (q) Emergency radiology
    (r) Percutaneous endoscopic gastrostomy (PEG)
    (s) Intra-abdominal pressure monitoring
13. Hematology
    (a) Blood component therapy
    (b) Thrombocytopenia in the ICU
    (c) Oncology-related life threatening issues in critical care
    (d) Laboratory tests: Interpretation
14. Research
    (a) Basics-statistical definitions
    (b) Sample size calculations, study designs, data collection
    (c) Generation of research ideas and hypotheses
    (d) Interpretation of results
    (e) Understanding evidence-based medicine in critical care

15. Miscellaneous
    (a) Do not attempt resuscitation (DNAR)
    (b) Medical ethics
    (c) Withholding and withdrawing care
    (d) Organ donation
    (e) Legal issues-Laws related to ICU
    (f) Anxiety and stress management in health care providers in ICU
    (g) Communication skills in acute care
    (h) Critical Care nursing-education
    (i) Quality care in the ICU-Bench marking
16. Skills
    (a) Endotracheal intubation
    (b) Difficult airway management
    (c) Flexible bronchoscopy
    (d) Surgical airway
    (e) Percutaneous tracheostomy
    (f) Needle thoracotomy
    (g) Chest tube insertion
    (h) Initiation of ventilation
    (i) Care of equipment
    (j) Central venous access
    (k) Intra-arterial pressure monitoring
    (l) Defibrillation
    (m) Pacing
    (n) Cardiac output measurement
    (o) Gastric tonometry
    (p) Peritoneal dialysis
    (q) Continuous renal replacement therapy
    (r) Intra-abdominal pressure monitoring
    (s) Interpretation of ECG/arterial blood gas/Ventilator waveforms
    (t) Chest physiotherapy
    (u) Lumbar puncture
    (v) Intracranial pressure monitoring
    (w) Intraosseous insertion

Glossary of Statistical Terms

Absolute Risk Reduction (Risk difference) The difference in mortality in treatment and control arm.

Accuracy Number of true positives and true negatives divided by the total number of observations.

Analysis of Variance (ANOVA) Method of comparing means of two or more samples to see whether they come from the same population.

Association Describes relationship between two variables.

Attributable Risk It is calculated by subtracting the incidence of a disease in non-exposed persons from the incidence of disease in exposed persons.

Bayesian Statistics An alternative way of analysing data by combining numerical values for prior belief, existing data and new data.

Bimodal distribution When there are two modes in a set of data.

Binomial distribution If the data can take only one of two values e.g. Male or Female.

Case-control study A case-control study starts with the outcome of interest and works backward to the exposure. For instance, patients with a disease are identified and compared with controls for exposure to a risk factor. In this model relative risk or the incidence of disease cannot be calculated. However, in case-control studies, the odds ratio provides a reasonable estimate of the relative risk.

Categorical Variables Representing different categories of the same feature e.g. different blood group, different eye colours etc. When there is a n inherent order inthe variables like mild, moderate or severe it is called "ordinal" variable.

Chi Square Test Test of association between two categorical variables.

Cohort study A cohort study is a particular form of longitudinal study that samples a cohort (a group of people who share a defining characteristic, typically those who experienced a common event in a selected period, such as birth or graduation), performing a cross-section at intervals through time.

Confidence interval The boundaries of a confidence interval give values within which there is a high probability (95% by convention) that the true population value can be found. The calculation of a confidence interval considers the standard deviation of the data and the number of observations. Thus, a confidence interval narrows as the number of observations increases, or its variance (dispersion) decreases.

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Confounding Effect of a factor that cannot be separated out in an experiment.

Continuous variable A variable which can take any value within a given range.

Correlation When there is a linear relationship between two variables. Measured on a scale of −1 (perfect negative correlation), 0 (no correlation) to +1 (perfect positive correlation).

Correlation Coefficient Measure of strength of the linear relationship between two variables.

Cox proportional hazards analysis Cox proportional hazards analysis is similar to logistic regression because it can account for many variables that are relevant for predicting a dichotomous outcome. However, unlike logistic regression, Cox proportional hazards analysis permits time to be included as a variable, and for patients to be counted only for the period of time in which they were observed.

Cox regression Model A method which explores the effect of different variables on survival.

Descriptive statistics Values which describe the data in a sample.

Discrete variable The data can only be of certain values e.g. number of children in a family.

Fishers Exact Test Test for association between categorical variables.

Histogram A graph of continuous data categorised in a number of classes.

Incidence Number of new events that have occurred in a specific time interval divided by the population at risk at the beginning of the time interval. The result gives the likelihood of developing an event in that time.

Intention to treat The central principle underlying intention-to-treat analysis is that study participants should be analyzed according to the groups in which they were randomized, even if they did not receive or comply with treatment. Such analysis is contrasted to "as treated" (or "per protocol") analysis in which subjects are analyzed according to the actual treatment they received.

Interquartile range The upper and lower values defining the central 50% of observations. The boundaries are equal to the observations representing the 25th and 75th percentiles. The interquartile range is depicted in a box and whiskers plot.

Kaplan-Meier analysis Kaplan-Meier analysis measures the ratio of surviving patients (or those free from an outcome) divided by the total number of patients at risk for the outcome. Every time a patient has an outcome, the ratio is recalculated. Using these calculations, a curve can be generated that graphically depicts the probability of survival as time passes.

Kappa Level of agreement between two categorical measures.

Kruskal Wallis test Non Parametric test which compares two or more independent groups.

Likelihood Ratio Likelihood ratios are an expression of sensitivity and specificity that can be used to estimate the odds that a condition is present or absent.

LoG rank Test A non parametric test used for the comparison of survival estimates.

Logistic regression analysis Models in which the outcome is dichotomous (eg, alive or dead, or a complication occurs or does not occur).

Mann Whitney U test A non parametric test to see whether there is a significant difference between two sets of data that has come from two different set of subject.

Mean Sum of observations divided by the number of observations.

Median Observation in the middle, when all observations are ranked from smallest to largest; when number of observations are even the median is defined as the mean of the middle two data points.

Mode Observation which occurs most frequently.

Multivariate analysis (Regression analysis) Statistical methods that can simultaneously account for multiple variables are known as "multivariate" (or multivariable) analysis. These methods help to "control" (or "adjust") for variables that are extraneous to the main causal question and might confound it.

Negative likelihood ratio It is calculated by dividing 1 minus sensitivity by specificity (1 − sensitivity)/specificity). Positive and negative likelihood ratios of 9 and 0.25, for example, can be interpreted as meaning that a positive result is seen 9 times as frequently while a negative test is seen 0.25 times as frequently in those with a specific condition than those without it.

Negative predictive value It represents the likelihood that a patient who has a negative test is free of disease. The predictive value depend upon the prevalence of a disease within a population.

Nominal Data Data that can be placed in a particular category but have no particular order.

Non Parametric test A test which is not dependent on distribution of data.

Normal distribution Distribution of data that is symmetrical and have a bell shaped curve.

Null hypothesis The null hypothesis is the theory that the exposure or intervention that is being studied is not associated with the outcome of interest. Thus, if a certain level of statistical significance is reached the null hypothesis will be rejected, otherwise the null hypothesis will not be rejected.

Number needed to Harm (NNH) The absolute side effects rate for placebo minus the absolute side effect for treated patients.

Number needed to treat (NNT) NNT is the reciprocal of the absolute risk reduction (the absolute adverse event rate for placebo minus the absolute adverse event rate for treated patients). :1/ARR.

Odds ratio Odds that an individual with a specific condition has been exposed to a risk factor divided by the odds that a individual without that condition (control) has been exposed. The odds ratio is used in case-control studies and is also used in multivariate analyses The relative risk and odds ratio are interpreted relative to the number one.

One tailed Test A test where the null hypothesis can only be rejected in one direction (better or worse).

Ordinal data Data that can allocated to categories in an ordered manner e.g. stages of malignancy.

Parametric test Any test that assumes that the data needs to follow a certain distribution e.g. Normal distribution.

Pearson Correlation coefficient Calculating correlation coefficient if values are sampled from a normal population.

Percentile Percentage of a distribution that is below a specific value. As an example, a child is in 90th percentile for weight if only 10% of children the same age weigh more than she does.

Period prevalence Proportion of individuals with a condition during a specified interval (eg, a year).

Person-years Total number of years that each member of a study population has been under observation or treatment. multiplying the number of years by the number of members of a sample population studied.

Point prevalence Proportion of individuals with a condition at a specified point in time.

Poisson distribution Number of events occurring in a fixed time interval e.g. number of deaths in a year.

Positive likelihood ratio It is calculated by dividing sensitivity by 1 minus specificity (sensitivity/(1 − specificity)).

Positive Predictive Value Likelihood that a patient with a positive test has the disease.

Prevalence Number of individuals with a given disease at a given point in time divided by the population at risk at that point in time. Prevalence has been further defined as being "point" or "period."

P-Value A p-value is a measure of the effect of chance within a study. It is **not** the probability that the result of the study is true or correct. Instead, it is the probability that if the null hypothesis were true, and if the results were not affected by bias or confounding, that we would have seen a result as extreme or more extreme than the one seen in the study.

Randomized controlled trial A randomized controlled trial (RCT) is an experimental design in which patients are assigned to two or more interventions. One group of patients is often assigned to a placebo (placebo control) but a randomized trial can involve two active therapies (active control).

Range Difference between the largest and smallest observation.

Receiver Operating Curve (ROC) curve It plots sensitivity on the Y axis, and 1-specificity (which is the false positive rate) on the X axis.

Regression Finding a relationship between two variables where one is dependent on the other.

Relative risk (or risk ratio) Incidence in exposed individuals divided by the incidence in unexposed individuals. This is used in cohort study.

Sensitivity The number of patients with a positive test who have a disease divided by all patients who have the disease. A test with high sensitivity will not miss many patients who have the disease (ie, few false negative results).

Spearman correlation coefficient An estimate of correlation used for non parametric variables.

Specificity The number of patients who have a negative test and do not have the disease divided by the number of patients who do not have the disease.

Standard Deviation Variability of data around the mean. In "normal" distribution samples (ie, Gaussian), 68 and 95% of values fall within one and two standard deviations of the mean, respectively.

Standard Error of the Mean It describes how much variability can be expected when measuring the mean from several different samples.

tTest (Student tTest) It is a parametric test used to compare means of two groups.

Two Tailed test A test where the null hypothesis can be rejected whether the treatment is better or worse.

Type I Error (also referred to as an "alpha error") It is incorrectly concluding that there is a statistically significant difference in a dataset when it is not present; the probability of making a type I error is called "alpha." A typical value for alpha is 0.05. Thus, a $p < 0.05$ leads to a decision to reject the null hypothesis.

Type II error (also referred to as a "beta error") It is incorrectly concluding that there was no statistically significant difference in a dataset and when actually it is present; the probability of making a type II error is called "beta." This error often reflects insufficient power of the study.

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