Oral and Maxillofacial Surgery for the Medically Compromised Patient

A Guide to Management and High-Quality Care

Daniel J. Meara
Rajesh Gutta
Editors

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Foreword

As an educator in Oral and Maxillofacial Surgery for the past 30 years, I have had the opportunity to treat many patients and help train the next generation. The academic environment gives you a unique perspective on so many aspects of our field. The medically compromised population of patients is certainly unique and presents many challenges for the oral and maxillofacial surgeon but also provides so many teachable moments in a residency training program and the community of interest. These opportunities allow the clinicians to broaden their education by thoroughly preparing to manage these patients in an office-based setting.

During residency and in their professional careers, I've gotten to know the authors of this text. It is not surprising and certainly within their character that they have chosen to compose a textbook on this topic. Their qualifications make them distinctively qualified to write this text. Dr. Meara completed a residency in internal medicine before deciding to pursue a career in oral and maxillofacial surgery. Dr. Gutta completed a Master of Science degree while in residency. I had the opportunity to work with them during their residency. Both of them are extremely compassionate and caring individuals. They are well-read and have spent many years preparing and presenting together on this topic at local and national scientific meetings. Together, they bring a unique perspective to the importance of preparedness in managing the medically compromised patient in the office setting.

Through advancements in medicine and pharmacology, patients are living longer with chronic illnesses. Oral and Maxillofacial Surgeons, through their deliberate and dedicated training, are entrusted with the assessment and management of these patients. A critical component in the management of any patient and especially in the medically compromised patient is risk assessment. The focus of this book is the identification and appropriate management of patients who are at high risk during office-based procedures. The authors have assembled a body of knowledge, through review of the literature and their experience in patient care and education, to provide evidence-based guidelines for the management of most common medical condition during office-based surgery. It is designed in such a way to give the reader in-depth knowledge and quick access to common questions in the management of these patients.

Due to the focus of this text, this book will most likely become required reading for all residents during their training. It will also serve as a reference

for many clinicians performing office-based procedures. Due to its subject matter, I know you will find this text as informative as the authors have intended and one that you will keep going back to as you prepare to manage these patients that our profession has been entrusted with.

Birmingham, AL, USA Patrick J. Louis

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Oral and Maxillofacial Surgery is an awesome profession and it is truly an honor to care for patients and educate residents as an academic oral and maxillofacial surgeon. Extreme thanks to my mentors: Drs. Patrick Louis, Peter Waite, Bruce Horswell, and Eddie Granite. Special thanks to my Dad, Dr. John W. Meara, Jr., an OMF surgeon, for being the ultimate role-model, and Dr. BJ Costello for encouraging my pursuit of OMF surgery while I was an internal medicine resident at UPMC. Thanks to my colleague, friend and academic partner, Dr. Raj Gutta, for his teamwork, patience, and enthusiasm. Lastly, thanks to my family, especially my wife Dr. Regina Meara for her sacrifice, support, and encouragement throughout this journey.

—Daniel J. Meara

I am deeply indebted to Drs. Patrick J. Louis and Peter D. Waite for training me as an oral and maxillofacial surgeon and their continued mentorship. Special thanks to the OMS residents, colleagues, and patients for providing the impetus towards this publication. My sincere gratitude to Dr. Dan Meara for all the years of academic partnership. My heartfelt appreciation to Dr. Asvin Vasanthan for his friendship and support.

—Rajesh Gutta

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Introduction

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Daniel J. Meara and Rajesh Gutta

1.1 Patient Safety and Safe Care

The World Health Organization (WHO) defines patient safety as "the absence of preventable harm to a patient during the process of health care and reduction of risk of unnecessary harm associated with health care to an acceptable minimum" [1]. Generally, the complexity of health care systems makes humans more prone towards mistakes which lead to patient harm. According to the Agency for Healthcare Research and Quality (AHRQ), patient safety refers to the freedom from accidental or preventable injuries produced by medical care [2]. The agency further emphasizes that practices or interventions must be implemented to reduce preventable adverse events, and this improves patient safety.

Cardiac complications are the leading cause of death among patients undergoing elective noncardiac surgery [3]. As the baby boomers age, the number of noncardiac surgical procedures is expected to increase. If the patient with complex medical history undergoes general anesthesia or procedural sedation, the anesthesia provider is responsible for preoperative medical assessment and coordinating care to optimize the patient before surgery [4]. For the vast majority of these patients, perioperative risk is attributed to cardiac morbidity and mortality.

In an attempt to provide optimal surgical care, the concept of medical clearance came into existence. It is not uncommon to see the patient's physician stating, "patient is cleared for dental extraction under mild sedation or general anesthesia." What does that mean? Is the risk shared by the physician? Or is the surgeon immune from a complication? There is no universally accepted definition. But the term "medical clearance" is loosely used in clinical practice and has led to a significant use of perioperative testing (Table 1.1). There is a great degree of assumption that a series of laboratory tests prior to any operative procedure would enhance safety for surgical patients and reduce liability for adverse events. In fact, recent studies have indicated adverse outcomes in patients who underwent medical consultation prior to major noncardiac surgeries [5].

1.2 Goal of Medical Clearance

The aim of preoperative medical clearance should be obtained to identify patients with potentially life-threatening cardiac disease that requires preop-

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Table 1.1 Commonly ordered preoperative tests

Renal function tests
Electrolytes
Liver function tests
12-lead EKG
Chest radiography
Urine analysis
Pregnancy tests
Bleeding and coagulation tests
Blood glucose tests
Blood counts
Echocardiography
Cardiac stress testing
Pulmonary function tests
Computed tomography or magnetic resonance imaging
Radionucleotide testing
Coronary angiography

erative assessment and treatment by a cardiologist, to identify the most appropriate testing and avoid unnecessary testing, and to implement medical and interventional cardiovascular treatment strategies as indicated [6]. As an alternative to routine preoperative testing, a wise practitioner would be able to judiciously interview the patient and do a risk assessment based on the patient's functional capacity than mere lab values indicating the presence or absence of a disease state.

According to the American College of Cardiology (ACC) and the American Heart Association (AHA) task force, "the purpose of preoperative evaluation is not to give medical clearance, but rather to; perform an evaluation of the patient's current medical status, make recommendations concerning the evaluation, management, and risk of cardiac problems over the entire perioperative period and to provide a clinical risk profile that the patient, primary physician, anesthesiologist, and surgeon can use in making treatment decisions" [7].

1.3 Preoperative Testing and Its Usefulness

It now has been approximately 25 years since the ACC/AHA first published multispecialty Guidelines on Preoperative Evaluation for Noncardiac Surgery. At the time of publication, the guidelines recommended that testing should be reserved for those patients in whom the results would impact care. Testing a low-risk population not only increases costs unnecessarily but may increase morbidity and causes harm by delaying a noncardiac operation. In fact, 77% of US physicians say the frequency with which doctors order unnecessary medical tests and procedures is a serious problem [8]. The burden to the healthcare system due to such unnecessary testing is approximately $200 billion annually [9]. Other than to discover the previously unknown condition, results of preoperative testing will rarely trigger a change in medical therapies to reduce risk [10, 11]. However, if the risk is deemed less than 1% and even if the patient is shown to be at elevated risk with poor exercise tolerance, it is rare that preoperative tests will change management. In addition, current therapeutic approaches to mitigate the risk of noncardiac surgery are limited. In fact, abnormal lab tests that resulted in a change in management have only ranged from 0.1 to 2.6% of time [12]. Despite evidence demonstrating that routine preoperative testing before elective, low-risk ambulatory surgery is not indicated, more than 60% of all patients underwent at least one laboratory test during their preoperative evaluation [13]. Clinicians should thus use the existing guidelines to identify those patients who require additional testing due to poor or unknown exercise tolerance and thus reduce the probability of a major cardiovascular event. Such a strategy will result in many fewer tests ordered and more cost-effective tests [14].

1.4 Seeking Medical Clearance

Rather than anecdotal evidence, Perioperative management of the patient should be based on the best available scientific evidence, individual patient's risk stratification, and cost-effectiveness. Improvements in preoperative risk assessment,

anesthetic care, surgical technique, and postoperative surveillance have resulted in a significant decrease in postoperative mortality [15].

However, patients with unstable coronary syndromes, decompensated heart failure, major arrhythmias, and severe valvular disease should be evaluated and treated for their conditions before surgery can be considered. Often, it is argued that additional testing is being done to avoid unnecessary medicolegal hassles in the event of an unanticipated complication. In addition, regulations, economic incentives, entrenched practice culture, and medicolegal issues make it difficult to change such habits. However, there is clearly a paradigm shift, and focus should be on appropriate medical interview of the patient and determining their functional status rather than burdening the already strained health care system.

In summation, the questions to be asked for every patient are as follows: (1) Would ordering preoperative tests improve outcomes? (2) Would additional testing improve quality of life or patient satisfaction? (3) Would the testing change patient management or resource utilization? If the answer to the above questions is a no, there is no indication of preoperative testing.

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2 Management of the Cardiac Patient

Rajesh Gutta

Cardiovascular disease represents about 30% of global mortality [1]. A thorough history and physical exam of the cardiac patient should involve appropriate questioning of symptoms and obvious signs of undiagnosed cardiac disease. The physical exam must also include auscultation of the heart for any murmurs, blood pressure in both arms when indicated, and carotid/jugular distention with bruits. In addition, examination of extremities for edema and hepatomegaly would indicate underlying cardiac disease. This chapter will discuss only the most common cardiac issues encountered in daily practice listed under the following subtitles:

1. Hypertension
2. Ischemic heart disease
3. Cardiac arrythmias, pacemakers, and anticoagulation
4. Valvular heart disease
5. Congenital heart disease
6. Anticoagulation
7. Perioperative cardiac risk assessment

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2.1 Hypertension

Hypertension is known to affect over a billion people worldwide with far-reaching consequences of heart disease and stroke in poorly controlled patients [2]. Due to its circadian pattern, blood pressure (BP) can be variable. For morning appointments, the reading can be high and be a normal pattern. It also increases with age and with anxiety. Primary hypertension is defined as a condition without identifiable causative factors. Secondary hypertension, on the other hand, has an identifiable cause. Endocrine and vascular conditions are the predominant causative factors for secondary hypertension. Others include alcoholism and obstructive sleep apnea [3].

Many patients with hypertension remain undiagnosed and poorly controlled in nearly half of them on treatment [4]. Untreated hypertension is one of the most important preventable causes of morbidity and mortality, since it is a major risk factor for stroke, myocardial infarction, heart failure, chronic kidney disease, cognitive decline, and premature death. It is one of the leading causes of death with more than seven million fatalities [5]. According to the Joint National Committee (JNC 8), hypertension is defined as a blood pressure reading >140/90 in otherwise healthy individuals. The committee further defines various stages of hypertension [6] (Table 2.1).

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Table 2.1 Hypertension categories [6]

Definition	Blood pressure measurement
Normal	SBP <120 mmHg and DBP <80 mmHg
Prehypertension	SBP 120–139 mmHg or DBP 80–89 mmHg
Stage I hypertension	SBP 140–159 mmHg or DBP 90–99 mmHg
Stage II hypertension	SBP ≥160 mmHg or DBP ≥100 mmHg
Hypertensive urgency	DBP > 120 mmHg without end-organ damage
Hypertensive emergency	DBP > 120 mmHg with end-organ damage

SBP systolic blood pressure, *DBP* diastolic blood pressure

Proper technique for obtaining accurate blood pressure measurements mandates that a patient be seated quietly for at least 5 min in a chair, feet on the floor and arms supported at heart level. An appropriate-sized cuff, a cuff bladder that encircles at least 80% of the arm, should be used to ensure accuracy, and at least two measurements should be taken during the visit [7]. Oral procedures are inherently associated with elevated levels of anxiety and a potential for increased blood pressure. Such readings should be interpreted with caution since patient's with elevated blood pressure tend to normalize upon administration of anxiolytics [8]. Several antihypertensive medications are available and may have interactions with common drugs used in oral surgical procedures (Table 2.2).

The induction of anesthesia, extubation, surgical pain, hypoxia, hypothermia, and volume overload are the events that could lead to blood pressure elevations and tachycardia [9]. In addition, the use of local anesthesia with epinephrine may potentiate hypertensive state. However, some patients may experience hypotension, cardiac arrythmias, angina pectoris, and myocardial infarction [10]. Injection of local anesthetics with greater concentration of epinephrine can increase blood pressure [11]. However it is open to debate whether such elevations have clinical significance. In addition, maximum dosage of epinephrine for patients with cardiovascular disease has been reported, but these dosage recommendations are based on poorly designed scientific studies and extrapolated data, and the recommendations should be weighed against the likelihood of significant endogenous catecholamine release from inadequate local anesthesia.

Table 2.2 Drug interactions of various antihypertensive agents

Drug group	Drug interactions
Beta-blockers	NSAIDs decrease their effect, decrease the metabolism of amide anesthetics
ACE inhibitors	NSAIDs decrease their effect, risk of angioedema
Diuretics	NSAIDs decrease their effect; erythromycin and fluconazole levels are elevated
Angiotensin II receptor blockers	NSAIDs decrease their effect, may interfere with fluconazole, indomethacin, and cimetidine
Calcium channel blockers	Increased sedation with benzodiazepines, altered drug levels with cimetidine and erythromycin
Alpha blockers	NSAIDs decrease their effect

NSAID nonsteroidal anti-inflammatory drugs, *ACE* angiotensin-converting enzyme

Hypertensive emergencies (i.e., severe elevations in BP [>180/110 mmHg] complicated by evidence of impending or progressive end-organ damage) require immediate BP reduction to prevent or limit end-organ damage. Blood pressure should be reduced by 10–15% (maximum of 20%) in a controlled fashion within the first hour with a continued decrease towards 160/100 mmHg over the next 2–6 h as tolerated by the patient. There was no benefit to deferring long-term treatment of patients with hypertension with diastolic blood pressures between 110 and 130 mmHg and no previous cardiac conditions [12]. Strategies may include having the patient take their usual daily medications, if not already done, as well as anxiety and stress reduction breathing and/or mindfulness exercises. If intravenous (IV) sedation is part of the treatment plan, then often the IV medications will result in blood pressure reduction, but ketamine should be avoided in these cases due to its propensity to increase blood pressure.

2.1.1 Ischemic Heart Disease

Cardiovascular disease remains a major cause of morbidity and mortality, particularly ischemic heart disease (IHD), a common cardiac condition [13]. Angina and myocardial infarction are known diseases as a result of IHD.

2.2 Angina Pectoris

Angina pectoris is classically described as a substernal pressure or squeezing sensation due to increased oxygen demand on the myocardium. The pain can also radiate to the neck and arms and usually is relieved at rest. Sublingual nitroglycerin (NTG) quickly resolves those symptoms, and then it is safe to proceed with the procedure. Coronary atherosclerosis is the common cause for angina. Angina in the dental office is most often a result of anxiety and fear resulting in tachycardia and angina. These patients are usually on nitrates and are prone to the risk of hypotension. If the symptoms persist despite rest and treatment with nitrates, a concern for myocardial infarction should be suspected.

2.3 Myocardial Infarction

Myocardial infarction is a condition due to ischemic death of the myocardium which is often not relieved with nitrates. In addition, patients complain of chest pain, nausea, pallor, and diaphoresis. MI usually results from a ruptured atherosclerotic plaque which then obstructs the coronary vessels leading to obstruction and ischemia. This is a medical emergency, and appropriate emergency activation should commence for timely thrombolysis. Differences between MI and angina are listed in Table 2.3.

Table 2.3 Differences between angina and myocardial infarction

	Myocardial infarction	Angina
Degree of ischemia	Complete	Partial
Myocardial injury	Yes	No
Symptoms relief with NTG	No	Yes
Duration of pain	>30 min	<30 m
EKG changes	ST-elevation, pathological Q-waves	ST-segment alterations

NTG nitroglycerin, *EKG* electrocardiogram

2.4 Perioperative Myocardial Infarction (PMI)

Acute coronary syndrome occurs when an unstable plaque ruptures leading to acute coronary thrombosis, ischemia, and infarction. Physiological and emotional stresses are known to predispose patients to PMI. Tachycardia and hypertension which are common in the perioperative period may lead to rupture of plaques. Anxiety and stress response to surgery leads to a surge in catecholamines that leads to increased ionotropic and chronotropic effects on the heart. This causes coronary oxygen supply-demand imbalance which can also lead to PMI. Perioperative tachycardia is the most common cause of oxygen supply-demand imbalance. Stress-induced coronary vasoconstriction can also impair coronary perfusion leading to PMI. Heart failure is another common condition in patients with coronary artery disease. This condition can be aggravated by ischemia and volume overload, leading to cardiac decompensation and subsequent PMI. Contrary to popular belief, these patients are in fact better served with anxiolytic techniques such as nitrous oxide or sedation protocols safely [14].

During the 1980s, the rule prevailed to wait 6 months after a myocardial infarction before embarking on noncardiac surgery [15]. This recommendation was based on risk of cardiac events for general surgical procedures under general anesthesia [16]. Studies have shown that the cardiac risk after a previous infarction is less related to the age of the infarction than to the functional status of the ventricles [17]. In that context, a small infarction without residual angina in the context of a good functional status allows essential noncardiac surgery as soon as 6 weeks after the ischemic

episode [18]. Current practice guidelines consider the period within 6 weeks of infarction as a time of high risk for a perioperative cardiac event, because it is the mean healing time of the infarct-related lesion [19]. The period from 6 weeks to 3 months is considered as intermediate risk for cardiac complication. In patients with ischemic event-related complications such as arrhythmias, ventricular dysfunction, or continued medical therapy, this risk period is extended beyond 3 months after the ischemic event. In uncomplicated cases, there is no reason for delaying surgery more than 3 months after an ischemic attack.

Heart failure is an outcome of IHD and is associated with significant morbidity and mortality. Signs and symptoms include shortness of breath, rales, extremity edema, elevated jugular pulse, and fatigue. Heart failure is a major independent predictor of adverse perioperative outcome in noncardiac surgery. It carries a greater perioperative risk than ischemic heart disease. In the Framingham study, the overall mortality at 2 years was 25%. The overall prevalence in the general population is 1–2% [20]. This patient population must be expected to be taking multiple, long-term medications, including angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers, b-blockers, aldosterone antagonists, and diuretics, all with associated side effects (mostly electrolyte disturbances, renal insufficiency, and intraoperative therapy-resistant hypotension). The most important consideration when categorizing heart failure is whether left ventricular ejection fraction (LVEF) is preserved or reduced (less than 50%). A reduced LVEF in systolic heart failure is a powerful predictor of mortality. As many as 40–50% of patients with heart failure have diastolic heart failure with preserved left ventricular function [21, 22]. The New York Heart Association classification system is the simplest and most widely used method to gauge symptom severity [23].

2.5 Local Anesthesia in Cardiac Patients

When properly injected, vasopressors in local anesthesia can cause clinically insignificant arrythmias, and several systematic reviews have shown that the use of low concentration vasopressors in local anesthesia is safe for cardiac patients [24]. Despite the lack of absolute scientific evidence, various authors and guidelines recommend limiting the quantity or advise against the use of local anesthetics with vasopressors in these patients. However, there recommendations ignore the fundamental role that vasoconstrictors prolong the effects of local anesthetics. A patient who experiences pain and anxiety due to lack of appropriate local anesthesia can release endogenous catecholamines that could increase up to 10 times the base level and may reach significantly concentrations than the very low concentration of epinephrine used in local anesthesia [25]. The most frequent complications in cardiac patients after local anesthesia with a vasoconstrictor agent were identified on EKG as arrythmias. Most of these arrhythmias were clinically insignificant. The use of ≤4 carpules of lidocaine with epinephrine 1:100000 as a local anesthetic seems to be relatively safe for cardiovascular compromised patients [24].

2.6 Cardiac Arrythmias/ Implantable Electronic Cardiac Devices

Cardiac arrythmias occur when there is an abnormality in impulse generation or conduction or both. Benign arrythmias sometimes occur in patients without cardiac disease and rarely pose a problem. Many episodes are asymptomatic, and extra beats are very common in normal people. However, tachyarrhythmias are often associated with a diminished cardiac output leading to symptoms like angina, dyspnea, palpitations, or syncope. These patients present with implanted electronic cardiac devices to manage arrythmias. Approximately 250,000 implantable cardiovascular electronic devices are placed each year in the United States [26]. Patient with implantable cardiac devices should provide the details of implantation date, device manufacturer, mode of the implant, model number, and serial number. Cardiac arrythmias are most commonly seen in surgical procedures under local anesthesia with or without vasoconstrictors [27]. Patients with

preexisting rhythm disorders or heart failure are more prone to such arrythmias [28]. Insufficient local anesthesia and lighter plane of general anesthesia are the most common intraoperative factors leading to cardiac arrythmias. Effective pain and anxiety control are important in such patients.

2.6.1 Automated Implantable Cardioverter Defibrillators (AICD) and Pacemakers

AICD have been widely used in patients with a higher risk of sudden cardiac death due to ventricular fibrillation and tachyarrhythmias. These devices deliver shock immediately upon sensing such arrythmia providing defibrillation and cardioversion [29]. Symptomatic bradycardia is often managed by a pacemaker. Various types of pacemakers are available and implanted by the individual needs of the patients. Pacemakers have cardiac leads and the pulse generators. The leads may be single or dual lead depending on whether the atria or ventricles are paced. They can also be dual lead where both the chambers are stimulated. In addition, there are also biventricular pacing devices. In patients with implanted cardiac devices, caution should be exercised in the use of anesthetic adjunctive agents such as anticholinergics, beta-blockers, local anesthetics, and vasopressor agents [30]. Malfunction of pacemakers may lead to symptomatic bradycardias or tachycardias, although upper rate-limiting programming is done in recent devices to limit such tachyarrhythmias. Antiarrhythmic drugs may be considered to covert such rhythms [31].

Electromagnetic interference with these cardiac devices is a concern when cautery devices or lasers are used in these patients. The grounding pad of the cautery device should be placed as far away as possible from the pacemaker/ICD. In addition, use of bipolar cautery is recommended over monopolar cautery. To reduce the risk of interference, an external magnet placement may allow for asynchronous cardiac pacing. This depends on the type of pacemaker, and the manufacturing company should be contacted for guidance [32]. However, this approach is seldom employed nowadays.

Review of the EKG or consultation with the cardiology team can determine whether the patient is device dependent; information of the procedure, patient positioning, and anticipated sources of intraoperative electromagnetic interference should be discussed. Specific recommendations from a cardiologist regarding the cardiac device should be carefully documented [33]. Battery function of these devices is another concern. Usually, the lithium-ion batteries in the devices last over 10 years. Patients should be asked about the year of placement and if there has been any replacement of the devices for a changed battery.

2.7 Valvular Heart Disease

According to the American Heart Association, approximately five million people are diagnosed with valvular heart disease in the United States each year. Valvular heart disease is a common condition which can either be stenosis or regurgitation. Most commonly, the aortic and mitral valves are involved resulting in a heart murmur. It is not uncommon to detect murmurs during physical exam which have not been detected in the past. While most murmurs are benign and asymptomatic, a high-grade murmur warrants further evaluation by a cardiologist. Aortic valve stenosis is an independent risk factor for cardiac morbidity and mortality. Prosthetic heart valves require long-term anticoagulation depending whether they are mechanical or biological. The risk of thromboembolism is significantly higher in patients with mechanical prosthesis, particularly the mitral valve due to relatively low flow compared to aortic valve. These patients are anticoagulated, and any interruption of anticoagulation can predispose them to thrombosis. If there is appropriate indication to discontinue anticoagulants prior to extensive maxillofacial surgery, such a decision should be made in consultation with the patient's cardiologist or primary care provider. Valvular heart disease poses a risk for developing bacterial endocarditis and exacerbat-

Table 2.4 Cardiac risk stratification of patient with congenital heart disease [35]

Type of condition	Low risk	Moderate risk	High risk
Conduction defects		Wolff-Parkinson-White syndrome	
		Long QT syndrome	
		Pacemaker dependence	
Structural lesions	Repaired ASD or VSD	Simple unrepaired lesions, such as atrial or ventricular septal defect	Unrepaired complex cardiac lesions
	Mild regurgitation or stenosis of a single valve	Complex cardiac defects with full repair Single ventricle with Glenn or Fontan palliation	Systemic arterial to pulmonary arterial shunts Severe valvular disease
Pulmonary hypertension		New York Heart Association functional class 1 Normal cardiac index	Pulmonary artery pressure equal to or higher than systemic Decreased cardiac index Severe heart failure
Miscellaneous		Heart or lung transplant	Ventricular assist devices William's syndrome Hypertrophic obstructive cardiomyopathy

ing a preexisting congestive heart failure. According to the recent ACC/AHA guidelines, endocarditis prophylaxis before invasive oral procedures is recommended in patients with valvular heart disease [34].

2.7.1 Recommendations for Endocarditis Prophylaxis [34]

1. Prosthetic cardiac valves, including transcatheter-implanted prostheses and homografts
2. Prosthetic material used for cardiac valve repair, such as annuloplasty rings and chords
3. Previous infective endocarditis (IE)
4. Unrepaired cyanotic congenital heart disease or repaired congenital heart disease, with residual shunts or valvular regurgitation at the site of, or adjacent to the site of, a prosthetic patch or prosthetic device
5. Cardiac transplant with valve regurgitation attributed to a structurally abnormal valve

2.8 Congenital Heart Disease

Congenital heart disease represents a common developmental anomaly. Atrial septal defect (ASD), ventricular septal defect (VSD), patent ductus arteriosus (PDA), congenital pulmonary stenosis, and aortic stenosis are some of the common conditions. A majority of these are repaired early in life upon detection, although some may go undiagnosed until later in life and some into adulthood. Saettele et al. developed a risk stratification chart (Table 2.4) of patients with congenital heart disease undergoing major surgery. The risk of conduction defects increases with the use of certain drugs (Table 2.5). However, currently no data exists on outpatient anesthesia for these patients. Until such evidence is available, these patients should undergo preoperative evaluation by their cardiologist, and their recommendations should guide the anesthesia plan. In addition, according to the current AHA guidelines, patients with unrepaired congenital heart diseases require endocarditis prophylaxis.

2.9 Anticoagulation

Various antiplatelet or anticoagulant drugs are available to reduce the risk of thrombus formation (Table 2.6). Cardiac conditions such as IHD, valvular heart disease, and cardiac arrythmias are indications for anticoagulant therapy. Surgical procedures of the oral cavity have an increased risk of bleeding. In the past interruption of anticoagulation therapy was commonly done to reduce the risk of oral bleeding. However, this

Table 2.5 Drugs that affect cardiac repolarization and prolong the QT interval, with documented cases of torsades de pointes

Class of drugs	Drug name
Class Ia antiarrhythmics	Quinidine, disopyramide, procainamide
Class Ic antiarrhythmics	Flecainide
Class III antiarrhythmics	Sotalol, amiodarone
Antipsychotics	Droperidol, haloperidol, phenothiazine, thioridazine, quetiapine, risperidone, zotepine
Serotonin reuptake inhibitors	Fluoxetine, paroxetine, sertraline
Macrolide antibiotics	Erythromycin, azithromycin, clarithromycin
5-HT1 agonists	Zolmitriptan, naratriptan
Antimalarial agents	Halofantrine
Antihistamines	Terfenadine
Prokinetic agents	Cisapride

Table 2.6 Various anticoagulant agents and their mechanism of action

Drug name	Mechanism of action
Aspirin	Inhibition of platelet aggregation
Clopidogrel	Inhibition of platelet aggregation
Coumadin	Inhibits vitamin K-dependent coagulation factors (II, VII, IX, X, protein C, and protein S)
Prasugrel	Inhibition of platelet aggregation
Ticagrelor	Inhibition of platelet aggregation
Apixaban	Selective coagulation factor Xa inhibitor
Dabigatran	Reversible direct thrombin inhibitor
Rivaroxaban	Selective coagulation factor Xa inhibitor
Edoxaban	Selective coagulation factor Xa inhibitor
Betrixaban	Selective coagulation factor Xa inhibitor
Vorapaxar	Inhibition of platelet aggregation
Dipyridamole	Decreases platelet aggregation
Cilostazol	Phosphodiesterase III inhibitor and reduces platelet aggregation

inherently increased the risk of ischemic stroke or myocardial infarction.

Atrial fibrillation is the one of the most common cardiac arrhythmic conditions that may require anticoagulation. Several risk factors were identified in these patients to reduce the risk of thromboembolism (Table 2.7). A score of greater than 2 requires managing these patients with anticoagulant therapy [37]. In addition, those with bioprosthetic valves and valve repair are considered increased risk and should be anticoagulated regardless of score.

The risk of perioperative stent thrombosis in cardiac patients is increased by noncardiac surgical procedure, when surgery is performed early after stent implantation and if dual antiplatelet therapy is discontinued [38]. Dual platelet therapy is known to cause more bleeding than single drug. Despite this, interruption of antiplatelet therapy is not indicated for routine oral surgical procedures [39]. In patients who are anticoagulated with warfarin, oral surgical procedures can be safely performed with therapeutic levels of anticoagulation up to INR 4.0 [40]. However, the type of surgery, including the number of extractions, and the technique, such as staged extractions or quadrant procedures, are critical to perioperative success. A meta-analysis study involving aspirin (ASA) and a control group showed longer bleeding time in the aspirin group. However, this increase is not shown to be statistically significant compared to the control group. Hence disruption of antiplatelets therapy was not indicated [41]. Several studies have overwhelmingly concluded against the interruption of antiplatelet therapies prior to oral and maxillofacial surgery although some authors have recommended the use of local hemostatic agents [42, 43]. Further, evidence suggests an approximately 5% stroke risk with cessation of anticoagulation medications in patients on such medications for atrial fibrillation [44].

In order to obtain local hemostasis, it is advisable to take into account all the hemostatic agents known. The local hemostatic measures include the use of hemostatic gauze with regenerated oxidized cellulose, gelfoam consisting of animal origin gelatin, topical thrombin, fibrin sealants, bone wax, sutures, electrocautery, and the use of tranexamic acid. In addition, recently, the US Food and Drug Administration approved idarucizumab, a monoclonal antibody fragment, for the treatment of patients taking dabigatran when

Table 2.7 Risk factors development of stroke in patient with atrial fibrillation: the CHA2DS2-VASc score [36]

Abbreviation	Risk factors	Points
C	Congestive heart failure/left ventricular dysfunction	1
H	Hypertension	1
A2	Age >75 years	1
D	Diabetes mellitus	1
S2	h/o CVA/TIA/thromboembolism	2
V	Vascular disease (MI, PVD)	1
A	Age 65–74 years	1
Sc	Gender; female	1

reversal of the anticoagulant effects of dabigatran is needed for emergency surgery/urgent procedures or in life-threatening or uncontrolled bleeding.

2.10 Perioperative Cardiac Risk Assessment and Testing

The aims of cardiac risk stratification are to:

1. Identify potentially life-threatening cardiac conditions
2. Consider appropriate preoperative testing in high-risk patients
3. Implement optimal perioperative management strategies to reduce the risk of cardiac morbidity and mortality

The risk of perioperative cardiac complications is the summation of the individual patient's risk and cardiac stress related to the surgical procedure. The first step in cardiac risk stratification is to identify patients at risk for perioperative cardiac events. Historically, several indices have been described towards risk assessment in a surgical patient [45–47]. Recent studies have indicated the Goldman index may actually overestimate risk for today's ambulatory surgical patient [48]. However, these indices are outdated due to significant advances in surgical and medical management of patients with cardiac disease. In addition, these indices were used to assess the cardiac risk in patients undergoing major noncardiac surgeries and do not provide optimal data to assess the risk in outpatient oral and maxillofacial surgery. Major noncardiac surgery patients who undergo general anesthesia may experience the risk of significant hemodynamic changes, renal dysfunction, pulmonary failure, and hypermetabolic states. However, such conditions are extremely rarely encountered in the oral surgical patient. Within the oral and maxillofacial surgical procedures, majority of the procedures are considered low risk for cardiac mortality and morbidity. Perhaps, the head and neck reconstructive procedures are considered as intermediate risk. Although not evaluated, patients with severe obstructive sleep apnea (pulmonary hypertension, uncontrolled HTN, diabetes, and renal failure) undergoing a combination of maxillomandibular advancement and soft tissue airway surgery could be classified as intermediate risk.

The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) risk calculator (https://riskcalculator.facs.org/RiskCalculator/PatientInfo.jsp) is a more comprehensive online tool and procedure specific [49]. Another simple yet valuable risk assessment tool is the myocardial infarction or cardiac arrest (MICA) calculator (https://www.mdcalc.com/gupta-perioperative-risk-myocardial-infarction-cardiac-arrest-mica) [50]. Recent studies have shown the MICA calculator outperformed several indicators. Preoperative functional status is another predictor of perioperative outcome. Studies in the past have shown that low exercise tolerance is associated with poor perioperative outcome [51, 52]. The Duke Activity Status Index (DASI) is based on a questionnaire and grades exercise ability related to physical activity such as:

- Can take care of self, such as eat, dress, or use the toilet (1 MET)
- Can walk up a flight of steps or a hill or walk on level ground at 3–4 mph (4 METs)
- Can do heavy work around the house, such as scrubbing floors or lifting or moving heavy furniture, or climb two flights of stairs (between 4 and 10 METs)
- Can participate in strenuous sports such as swimming, singles tennis, football, basketball, and skiing (>10 METs)

One metabolic equivalent of task (MET) is defined as 3.5 mL of oxygen consumed per kilogram body mass per minute. A cardiac patient with a functional capacity of more than 4 METs is considered low risk. However, the inability to climb a flight of stairs (4 METs) is significant because it is associated with cardiac events during major noncardiac surgery. At this time, it is unknown if this data can be extrapolated to oral surgical procedures considered as low risk. A recent study however concluded that subjectively assessed preoperative functional capacity did not accurately identify patients with poor cardiopulmonary status or predict postoperative morbidity or mortality in major noncardiac surgery [53]. A surgical classification system that identifies risk based on blood loss can be a valuable tool in risk stratification (Table 2.8).

Table 2.8 Surgical classification system [54]

Category 1	Minimal risk to patients independent of anesthesia Minimally invasive procedures with little or no blood loss Operation done in an office setting
Category 2	Minimal to moderately invasive procedures Blood loss <500 mL Mild risk to patients independent of anesthesia
Category 3	Moderately to significantly invasive procedure Blood loss 500–1000 mL Moderate risk to patients independent of anesthesia
Category 4	Highly invasive procedure Blood loss >1500 mL Major risk to patients independent of anesthesia

Despite evidence that routine preoperative testing before elective, low-risk ambulatory surgery is not indicated, studies have shown that more than 60% of all patients underwent at least one laboratory test during their preoperative evaluation [55]. A systematic review of the current literature found that the incidence of abnormal test results that changed perioperative management ranged from less than 0.1% (CBC) to 2.6% (renal function tests) [56]. Inappropriate and unnecessary preoperative testing can lead to significant financial burden on the patient but may also lead to morbidity and mortality as a result of the testing [57]. According to the ACC/AHA perioperative guidelines, if the patient has had a cardiovascular evaluation in the previous 2 years and has not experienced new or worsening symptoms, further testing is usually unnecessary. If there has been no diagnostic workup, or if new or worsening cardiopulmonary symptoms are present, then additional testing may be indicated. Also, asymptomatic, functionally active patients with previous successful coronary revascularization within the last 6 years are in a low-risk category and should not be investigated further for a noncardiac operation [58].

In summary, perioperative cardiac management of the patient should be based on the best available scientific evidence, individual patient's risk stratification, and cost-effectiveness. The focus should be on appropriate medical interview of the patient and determining their functional status, rather than burdening the already strained health care systems with unnecessary testing. Discussion with primary care providers or other consultants should focus less on preoperative "clearance" and more on determining if the patient is optimized. In addition, conditions like stress, anxiety, and fear of oral surgical procedures can cause endogenous release of catecholamines, particularly norepinephrine, which in turn can precipitate autonomic responses leading to conditions like hypertension and arrhythmias. Hence, control of anxiety and pain plays a major role in reducing complications related to cardiovascular disease.

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3 Patients with Respiratory Disease: High Yield Concepts for Optimal Clinical Care

Habib Asmaro and Daniel J. Meara

3.1 Introduction

Obstructive lung disease is a respiratory illness that is characterized by airway obstruction. It includes asthma and chronic obstructive pulmonary disease (COPD). COPD has several subtypes that include emphysema, chronic bronchitis, and chronic obstructive asthma. In this chapter we will review basic definitions, pathophysiology, and anesthetic considerations for the common obstructive lung diseases.

3.2 Asthma

Asthma is one of the most common chronic airway diseases worldwide [1]. It is characterized by chronic inflammation resulting in reversible airflow obstruction with recurrent episodes of wheezing, breathlessness, chest tightness, and cough that are brought on by specified triggers and relieved by broncho-dilating medications. Some of these triggers include exercise, cold air, and exposure to aeroallergens such as dust mites, molds, and pollen.

According to the CDC, the prevalence of asthma in the United States is approximately 7.9% with incidence, and severity of asthma continues to increase [2]. The reasons for continued increase in asthma incidence, despite decrease in number of smokers and secondhand smoke exposure, remain unknown. The leading theory is "hygiene hypothesis" that suggests children's immune system, in developed countries, is understimulated [3]. COPD prevalence was 6.0% (among smokers) and 2.2% (among nonsmokers) and varies considerably by state with highest clusters along the Ohio lower Mississippi Rivers [4]. Costs attributable to having COPD were $32.1 billion and with a projected increase to $49.0 billion by 2020. Respiratory events accounted for 28% of claims due to anesthesia-related brain damage and death [5]. Closed claims data from OMSNIC indicates respiratory distress as the most frequent cause for transfer of an OMFS patient to the emergency department.

The most common technique in detecting airflow obstruction includes peak expiratory flow rate (PEFR) and spirometry measurements [6]. In PEFR, a handheld flow meter is used to measure peak flow. If peak flow is less than 80% of predicted value, then the patient should be further evaluated with spirometry. Pre and post

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bronchodilator spirometry involves measurement of maximal inhalation to total lung capacity followed by maximal exhalation. This provides the forced vital capacity (FVC) which is the total volume of air exhaled, the forced expiratory volume in 1 second (FEV_1), and the ratio of FEV_1/FVC. When the ratio is reduced below 0.7, then airflow obstruction is present. The reversibility of the obstruction is assessed by administration of quick-acting bronchodilator such as albuterol. The characteristic physiologic feature of COPD is partial reversibility, or irreversibility, of the airway obstruction with bronchodilator administration.

The Expert Panel Report 3 of the National Asthma Education and prevention Program characterizes asthma severity as intermittent, persistent mild, persistent moderate, and persistent severe (Table 3.1). There are multiple systems for staging of COPD. There is the GOLD system that combines patient's individual symptoms and exacerbation history and the BODE index which is calculated based on the BMI, FEV_1, dyspnea, and exercise capacity. The COPD Foundation system incorporates spirometry, symptoms, oxygenation, emphysema, presence of bronchitis, and comorbidities placing the patient into 5 spirometric grades (Table 3.2).

As with any patient, the first step in assessing patient with history of obstructive lung disease includes a thorough history and physical. Some of the key information to emphasize during preoperative assessment includes the following:

- Patient's perception of the severity of the asthma
- Frequency of use of short-acting inhaled beta-2 agonist
- Current asthma medication regimen
- Triggering factors
- History and frequency of hospitalizations and emergency department visits pertaining to asthma exacerbations
- History of intubation due to severity of attacks
- Recent use of oral glucocorticoids or antibiotics
- Current smoking status
- Recent hospitalization due to COPD exacerbation
- Baseline functional status and need for supplemental oxygen
- Dyspnea at rest or with minimal exertion
- Recent illness, fevers
- Recent increase in sputum production

It is also important to identify certain risk factors that are associated with relapse of an asthmatic patient. Some of these risks factors include having made 3 or more visits to an emergency department within the past 6 months or difficulty performing work or activities as a result of physical health in the 4 weeks prior. Based on the

Table 3.1 Classification of asthma severity [7]

Component	Intermittent	Persistent mild	Persistent moderate	Persistent severe
Symptoms frequency	≤1–2 days/week	>2 days/week (not daily)	Daily	Throughout the day
Sleep interruption	≤1–2 events/month	3–4 events/month	Multiple weekly (not nightly)	Frequently (7/week)
Short-acting β_2 agonist use frequency	≤2 days/week	>2 days/week (not daily and no more than once on any day)	Daily	Several times/day
Interruption of daily activities of life	None	Minor interferences	Some interferences	Limited activities
Lung function	FEV_1 normal between exacerbation (FEV_1> 80% and FEV_1/FVC normal)	FEV_1> 80% and FEV_1/FVC normal)	60% < FEV_1 < 80% FEV_1/FVC reduced by 5%	FEV_1 < 60% FEV_1/FVC reduced by >5%

information, the level of asthma control can be classified as well-controlled, not well-controlled, or very poorly controlled (Table 3.3). If the asthma is not well-controlled or exhibiting acute symptoms, such as wheezing, then the planned procedure should be delayed, and the patient should be referred to his or her primary care provider for further optimization.

The risk of perioperative pulmonary complications is low for a well-controlled asthmatic patient that is not steroid-dependent. Preoperative pulmonary function testing is recommended for patients with moderate to severe asthma. Pulmonary function tests with normal finding should not substitute clinical judgment, as pulmonary function may change. Patient may present with normal PFTs on that particular day which may not reflect the same pulmonary status on the day of the plan procedure. Preoperative laboratory blood testing should be obtained for asthmatic patients on high-dose beta-2 androgenic agonists (4mg QID) as it can result in hypokalemia, hyperglycemia, and hypomagnesemia. Chest x-rays are not routinely indicated for asthmatic patients; however it is recommended for patients reporting dyspnea, cough, and fever or noted to have wheezing or crackles on chest auscultation.

Table 3.2 Assessment of COPD severity [8]

Spirometry grades (SG)	Component
SG0	Normal spirometry; does not rule out emphysema, chronic bronchitis, asthma, or risk of exacerbation or developing COPD
SG1 (Mild)	Post bronchodilator FEV_1/FVC ratio <0.7; $FEV_1 \geq 60\%$ predicted
SG2 (Moderate)	Post bronchodilator FEV_1/FVC ratio <0.7; $30\% \leq FEV_1 < 60\%$ predicted
SG3 (Severe)	Post bronchodilator FEV_1/FVC ratio <0.7; $FEV_1 < 30\%$ predicted
SGU (Undefined)	FEV_1/FVC ratio ≥0.7; $FEV_1 < 80\%$ predicted. Consistent with restriction, muscle weakness, and other pathologies

3.3 COPD

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) defines COPD as "common, preventable, and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases. The chronic airflow limitation that characterizes COPD is caused by a mixture of small airways disease (e.g., obstructive bronchiolitis) and parenchymal destruction (emphysema), the relative contributions of which vary from person to person. Chronic inflammation causes structural changes, small airways narrowing, and destruction of lung parenchyma. A loss of small airways may contribute to airflow limitation and mucociliary dysfunction, a characteristic feature of the disease" [9]. Patients with COPD demonstrate three common symptoms that included dyspnea, chronic cough, and sputum production.

In patients with COPD, preoperative management is no different than asthmatic patient. In regard to maintenance medications, patient should be instructed to continue their usual regiment up to, and including, the day of surgery. This includes inhaled beta-agonists (albuterol, formoterol, salmeterol), glucocorticoids (fluticasone and triamcinolone), anticholinergic (ipratropium, tiotropium) medications, as well as leukotriene inhibitors (montelukast). The excep-

Table 3.3 Assessing asthma control [7]

Component	Well-controlled	Not well-controlled	Very poorly controlled
Symptom frequency	≤2 days/week	>2 days/week (not daily)	Throughout the day
Sleep interruption	≤1–2 events/month	1–3 events/week	≥4 events /week
Short-acting β_2 agonist use frequency	≤2 days/week	>2 days/week	Several times per day
Lung function	FEV_1> 80% of predicted/ personal best	FEV_1 60–80% of predicted/ personal best	$FEV_1 < 60\%$ of predicted/ personal best

tion is theophylline. As a competitive nonselective phosphodiesterase inhibitor, theophylline has a very narrow therapeutic window. Toxic levels could accumulate as its metabolism is affected by many common perioperative medications. This could result in serious arrhythmias and neurotoxicity. It is recommended to hold the medication the evening before surgery.

3.4 Tobacco

Despite awareness of the dangers of tobacco uses, recent studies suggest that almost 20% of the US population still smokes tobacco. Active cigarette smokers are at an increased risk for postoperative pulmonary complications. Thus, it is important to provide smoke cessation counseling during the preoperative evaluation. It is recommended that the patient refrain from smoking 8 weeks prior to surgery. The reason is because of the increased airway secretions after smoke cessation that could result in airway irritation. Airway irritation could be minimized with an oral pack and frequent suctioning of oral secretions with open airway sedation. Furthermore, supraglottic airway (i.e., LMA) can be considered over ET given the increased airway irritation associated with ET intubation.

It should be noted, however, that patients that have quit smoking less than 8 weeks are at increased risk of postoperative complications. One systematic review demonstrated there was no difference in postoperative pulmonary complications between active smokers and recent cessation (less than 8 weeks) [10]. With the lack of evidence of harm with short duration of smoke cessation, it is recommended that all patients anticipating elective procedures to quit smoking as soon as permitted, with 8 weeks of cessation as optimal time.

3.5 Vaping

Vaping, albeit a new phenomenon, is associated with a multistate outbreak of lung injury. Termed EVALI (e-cigarette, or vaping, product use-associated lung injury) is considered a diagnosis of exclusion. The pathophysiology remains unclear, but vitamin E acetate seems to be implicated by lung fluid samples (CDC 2020). Also, THC-containing products play a role in this lung injury, and nicotine-containing products have not been excluded yet. There are no specific tests or markers for its diagnosis. Patients exhibit nonspecific respiratory and gastrointestinal symptoms. Symptoms include cough, chest pain, shortness of breath, abdominal pain, nausea, vomiting, and diarrhea. Fevers, chills, and weight loss were noted in 85% of patients with EVALI. Most exhibit respiratory symptoms first, but GI symptoms can precede respiratory ones. Patients may also have unremarkable auscultation findings despite severe lung injury [11]. Providers should review social history and ask about the use, type of vaping products, and review of system to screen for early symptoms of EVALI. Patients presenting with concerning symptoms should be directed to follow up with their health care provider.

3.6 Respiratory Infections

Acute viral upper respiratory infections (URI) are the most common illness in the general population and are typically caused by rhinovirus and are mostly benign and self-limited [12]. Patients present with a variety of symptoms such as sneezing, nasal congestion and discharge, dry cough, low-grade fever, sore throat, malaise, sinusitis, and/or bronchitis. Upper respiratory infections cause an increased upper airway and bronchial hyperreactivity due to increased vagal tone and decreased function of inhibitory M2 muscarinic receptors on the parasympathetic nerve endings. As a result, the bronchoconstriction reflex and airway hyperresponsiveness are potentiated and predispose to coughing, stridor, development of laryngospasm, and bronchospasms. The airway hyperactivity may last for 2–6 weeks after an URI.

The risk of pulmonary complications in the setting of a viral upper respiratory tract infection is poorly studied. Most of literature pertaining to

the subject is focused on pediatric population. A 1996 retrospective study demonstrated no increase in the incidence of intraoperative bronchospasms in patients with well-controlled asthma setting of a recent URI. For well-controlled asthmatic patients presenting with acute upper respiratory tract infection, it is recommended to postpone elective surgical procedures until 2 weeks for urgent cases and 8 weeks for elective nonurgent, after the symptoms subside. In patients with a history of COPD, it is recommended to postpone elective surgery and setting of COPD exacerbation or in setting of URI. The duration of postponement should be based on individual basis due to variability in time from exacerbation to return to baseline functional status, especially for patients with medical comorbidities. Patient presenting with dyspnea, cough, productive sputum production, and associated fevers should be referred for further medical management, especially if there is suspicion of influenza or coronavirus infection.

3.7 Premedication

Premedication for patients with reactive airway disease is recommended to reduce the risk of pulmonary complications. This includes administering of short-acting beta-2 agonists such as multidose albuterol inhaler, 2–4 puffs, or nebulized 2.5 mg of albuterol 20–30 min prior to planned procedure. For patients that can tolerate resultant tachycardia (~36 beats per min increase) [13], administering anticholinergic agents such as 0.2 mg of glycopyrrolate or 0.4 mg of atropine helps to dry out secretions as well as decrease airway vagal responsiveness.

3.8 Intraoperative Management

Intraoperative anesthetic regimen should be tailored to each individual patient. Propofol is an excellent induction anesthetic for the hemodynamically stable asthmatic patient and is known to attenuate bronchospastic response to airway irritation. However, there have been documented cases of bronchospasms occurring with propofol administration. This is possibly being due to an allergic reaction to sodium metabisulfite used as a preservative in some of the preparations. The authors recommend using propofol with alcohol or calcium edetate as a preservative instead. Ketamine is another agent that could be considered as a part of the anesthetic regiment. Ketamine is known to have sympathomimetic bronchodilatory properties. However ketamine is also known to increase airway secretions, and an anticholinergic agent is recommended when needed.

Opiates are often included as a part of anesthetic regiment, as it supplements anesthetic requirements as well as suppresses airway reflexes such as coughing. Most opiates release some amount of histamines that hypothetically could cause bronchospasms. Synthetic opiates such as fentanyl, remifentanil, sufentanil, and hydromorphone release minute amount of histamines and have been safely used an asthmatic patients during induction, maintenance, as well as in recovery. In contrast, morphine and meperidine are associated with significant histamine release. For example, a randomized study, in 1982, looked at the plasma histamine level in patients receiving morphine compared to those receiving fentanyl. Patients in the morphine group had an average of 750% peek increase in plasma histamine with resultant decrease in medial articular pressure and systemic vascular resistance, whereas the fentanyl group had no change in their plasma histamine and no decrease in arterial or pressure or systemic vascular resistance [14].

In patients with COPD, it is recommended to avoid deep sedation due to susceptibility to hypoventilation resulting in CO_2 retention which causes hypoxic pulmonary vasoconstriction leading to worsening ventilation/perfusion mismatch. Supplemental oxygen should be given to maintain oxygen saturation as close as possible to preoperative baseline. Further administration of oxygen to improve saturation will not improve tissue oxygenation but rather increase the risk of CO_2 retention due to blunting of the hypoxemic respiratory drive noted in COPD patients given the difference in physiologic response to hyper-

carbia seen in COP compared to non-COPD patients.

Beta-blockers are routinely used for management of hypertension and tachycardia during anesthesia. However, in patients with reactive airway disease, beta-blockers increased airway reactivity, bronchial obstruction, and attenuation of the inhaled or oral beta-receptor agonists. Even topical nonselective beta-blockers for glaucoma treatment have been associated with asthma exacerbations. A 2014 systematic review and meta-analysis demonstrated that both beta-1 selective and nonselective beta-blockers reduced FEV_1 and bronchodilator response to inhaled beta-2 agonists with greater attenuation in the latter group [15]. If required, the lowest possible dose of beta-1 selective agents, such as esmolol and metoprolol, can be administered. This is because at higher dosages the selectivity of these agents diminishes.

3.9 Conclusion

Respiratory disease is a risk factor for perioperative complications. Thus, preoperative optimization of a patient's pulmonary status and proper anesthetic treatment planning is essential to the safe provision of surgical care.

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Liver Diseases

4

Shachika Khanna

Oral and maxillofacial surgeons and dentists are often consulted by medical colleagues to evaluate patients with liver disease who complain of pain associated with failing dentition. Some of these patients may present with end-stage liver disease, and poor dentition could put these patients at risk for an acute odontogenic infection. The patient's physician may provide you with a MELD score, Child-Pugh score, and liver enzymes. What do these numbers mean? Why are they important? What else must you know prior planning your surgery? What measures can you take as an oral and maxillofacial surgeon on the multidisciplinary team to achieve the most optimal result for your patient?

4.1 Assessment of Liver Function

For the oral and maxillofacial surgeon, history taking is a very important part of identifying liver disease or risk factors for liver disease in an otherwise healthy-appearing patient. It is important to understand that the term "liver function tests" (Table 4.1) does not measure a recognized function of the liver. Instead, they assess liver injury.

It is important to obtain patient history sensitively to warrant patient safety and the need for referring the patient for further investigation [2]. Details about alcohol consumption including amount, frequency, strength of alcoholic beverage, and abstinence must be addressed. It is also important to review the patient's daily medication list including herbal medications or excessive Tylenol consumption that can result in drug-induced hepatitis; family history of Wilson's disease or hemochromatosis is equally important [2, 3].

An accurate measure of the synthetic functioning of the liver can be derived from tests such a serum albumin, serum bilirubin, and prothrombin time which is standardized to the international normalized ratio (INR) [4]. However, these numbers are usually maintained until late in the disease process resulting in significant decline of liver function.

Albumin is the most important plasma protein produced by the liver in terms of absolute quantity. Given its longer half-life of 22 days, a patient with an acute liver condition such as hepatitis may not appreciate a drop in serum albumin levels which would be expected in a patient with decompensated liver cirrhosis [4].

Serum enzyme tests include aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and gamma-glutamyl transpeptidase (GGT). An increase in ALT is more specific for liver damage compared

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Table 4.1 Liver function tests ([1] modified)

Parameter	Origin	Associated disease
Aspartate aminotransferase (AST)	Liver, skeletal muscle, cardiac muscle, red blood cells, brain, pancreas, lungs	Hepatocellular injury of any cause, myopathies, myocardial infarct, hemolysis, tumors of the liver
Alanine aminotransferase (ALT)	Liver, kidneys, skeletal muscle	Hepatocellular injury of any cause, tumors of the liver, myopathies
Alkaline phosphatase	Liver, bone, placenta, kidneys, intestines	Cholestatic liver disease; inflammation; sarcoidosis; pregnancy; lymphoma; bone, kidney, and intestinal diseases
γ-Glutamyl transferase	Biliary epithelial cells, kidneys, pancreas, prostate	Liver duct injury, biliary or pancreatic disease, myocardial infarct, renal diseases, chronic lung disease, diabetes
Conjugated bilirubin	Hemolysis, insufficient excretion from the liver	Severe liver injury from any cause, Rotor syndrome, Dubin-Johnson syndrome
Unconjugated bilirubin	Hemolysis	Hemolysis, Gilbert syndrome, Crigler-Najjar syndrome
Albumin	Produced in hepatocytes	Low in nephrotic syndrome, malnutrition, protein-losing enteropathy
Prothrombin time	Clotting factors produced in hepatocytes	Prolonged in liver disease, vitamin K deficiency, fat malabsorption, pancreatic insufficiency

to AST due to its comparatively higher concentration in the liver compared to other sites such as the heart, kidney, and skeletal muscles. Elevation of serum aminotransferases is noted in all forms of liver injury, and an elevation of liver enzymes up to 300 U/L is usually nondiagnostic [3]. Notable increases in aminotransferase levels (>1000 U/L) include viral hepatitis A or E, ischemic or autoimmune hepatitis, drug-induced liver injury, and acute obstruction of the biliary tract [3]. Normal values of liver enzymes are listed as follows: alkaline phosphatase is 35–130 iu/L, aspartate aminotransferase is 5–40 iu/L, alanine aminotransferase is 5–35 iu/L, gamma-glutamyl transpeptidase is 10–48 iu/L, albumin is 35–50 g/L, prothrombin time is 12–16 s, and total bilirubin is 5–17 μmol/L. [4] Bilirubin is predominantly unconjugated and insoluble in water and hence undetectable in urine. Hyperbilirubinemia is noted in cholestatic and hepatocellular liver disease [4].

4.2 Acute Liver Failure

By definition, acute liver failure is defined as liver dysfunction, coagulopathy, encephalopathy, and jaundice all ensuing within 26 weeks (6 months) of onset of symptoms in patients with no preexisting liver diseases. The acuity of liver failure is based on the time interval from jaundice to encephalopathy and can range from 7 days to 12 weeks. The most common causes include viral hepatitis and drug-induced hepatitis. The highest chance of survival arises from identification and treatment of the underlying etiology. While viral hepatitis accounts for the most frequent cause of liver failure in developing countries, drug-induced acute liver failure from acetaminophen and paracetamol accounts for the highest number of cases in the USA and United Kingdom (45–60%) [2, 3]. The presence of acute-onset encephalopathy and coagulopathy may preclude any oral surgical treatment. Drug-induced liver injury and acute liver failure can also result from antibiotics such as amoxicillin-clavulanic acid, isoniazid, nitrofurantoin, aminoglycosides, and fluoroquinolones in the Western countries. In addition, herbal medications can also result in liver injury in Asian countries in addition to antibiotics and antituberculosis drugs.

4.3 Liver Cirrhosis

Liver cirrhosis is a diffuse process that results in alteration of the normal liver architecture where the regenerating hepatocytes are surrounded by

Table 4.2 Child-Pugh scoring for severity of liver disease [5]

	Points[a]		
Clinical and lab criteria	1	2	3
Encephalopathy	None	Mild	Severe
Ascites	None	Mild	Severe
Bilirubin (mg/dL)	<2	2–3	>3
Albumin (g/dL)	>3.5	2.8–3.5	<2.8
International normalized ration	<1.7	1.7–2.3	>2.3

Class A = 5–6 points (mild liver disease)
Class B = 7–9 points (moderate liver disease)
Class C = 10–15 (end-stage liver disease)
[a]Child-Pugh score is obtained by adding the points for each parameter

fibrous bands [2, 4]. The causes of cirrhosis include alcoholic cirrhosis, nonalcoholic steatohepatitis (NASH), and viral hepatitis-induced cirrhosis from hepatitis B and C. Cryptogenic cirrhosis is a diagnosis of exclusion where no additional causes of cirrhosis can be determined. The gold standard for the diagnosis of cirrhosis is a liver biopsy although imaging can be helpful as well [4]. The severity and the progression of liver disease can be assessed by the Child-Pugh score/class (Table 4.2). In this classification, points are scored for increasing abnormality. The more severe the disease, the higher the score. The score is determined by presence of jaundice, ascites, encephalopathy, serum albumin concentration, and nutrition (or prothrombin time which can be used instead of nutrition. The 1-year survival rate ranges from 84% in patients with child grade A disease and subsequently drops to 42% in patients with a grade C disease [2]. The Model for End-stage Liver Disease (MELD) score is used to accurately determine the priority for liver transplantation in recipients with cirrhotic livers. Serum creatinine, prothrombin time (INR), and serum bilirubin are used to calculate the MELD score [6]. The predictability of the score is considered high, and it is believed to have successfully lowered the mortality rate amongst the patients waiting to receive a liver transplant, nationally. Clinically cirrhosis can be described as compensated or decompensated. Decompensated cirrhosis will include other clinical signs such as jaundice, ascites, hepatic encephalopathy, and/or bleeding varices with ascites often being the first sign [2, 4]. Patients with compensated cirrhosis will have none of the above [4]. Once cirrhosis has set it, it is not reversible, but measures can be taken to prevent worsening of the condition. Abstinence from alcohol, maintenance of a regular diet and ideal weight, attempts to prevent hemorrhage from varices, and prompt diagnosis of hepatocellular carcinoma and encephalopathy would be the goals to prevent progression of cirrhosis. If the cause of cirrhosis can be identified, then diagnosis and treatment of the specific trigger is key. Antiviral treatment for hepatitis B and C, steroids and immunosuppressive medications for autoimmune hepatitis, strict alcohol abstinence in alcoholic cirrhosis, and weight loss in NASH cirrhosis are recommended to halt further progression of disease [4].

Cirrhotic patients are at a high risk of adverse outcomes including mortality from surgical procedures. Low serum albumin levels, prolonged PT, and presence of an infection are associated with a worse outcome during surgery [4].

4.4 Hepatic Encephalopathy

Hepatic encephalopathy is the term that is used to describe the complex neuropsychiatric changes during liver disease caused by lack of functioning hepatocytes. It is the hallmark of active liver failure and has an unfavorable impact on the patient's quality of life and survival. It includes a myriad of mental and motor disorders that range from subtle changes in a patient's personality to profound changes in cognition and consciousness resulting in coma.

4.5 Portal Hypertension

The superior mesenteric vein and the splenic vein together form the portal vein. The normal pressure in the portal vein is 7 mmHg [2]. An increase in the pressure of the portal vein is referred to as portal hypertension [2]. The pathognomonic feature of portal hypertension is splenomegaly. Absence of an enlarged spleen clinically, on exam or imaging, makes the diagnosis of portal hypertension questionable [4]. Portal hypertension results in the formation of varices and contributes towards the development of ascites [2]. Cirrhosis is the most common cause of portal hypertension, and hematemesis is the most common presentation [4]. Melena may also be seen from bleeding varices [2, 4]. The patient is at an increased risk from bleeding from the varices when the pressure in the portal vein rises above 12 mmHg [2]. Bleeding varices will result in anemia and worsen recovery of the hepatocytes [4]. The treatment of bleeding varices can be complex. Transfusion of blood products and subsequently platelets and FFP must be undertaken (due to dilution of the transfused blood). A transjugular intrahepatic portosystemic shunt (TIPS) is a side-to-side portal systemic shunt that has significant value in lowering portal pressures and in control of hemorrhage from portal hypertension with a success rate of over 90% [4].

4.6 Ascites

Ascites is defined as the presence of free fluid in the peritoneum. The most common cause of ascites is cirrhosis. It can also be seen in conditions unrelated to the liver such as peritoneal malignancies, infections, and cardiac failure [4]. In cirrhotic patients, the onset of ascites signifies the transition to a decompensated states, and in almost half the patients (48%), it is the first incident that marks their evolution to decompensated cirrhosis [2, 4]. Splanchnic and peripheral vasodilation that occur as a sequela of portal hypertension causes ascites [4]. Ascites is usually responsive to diuretics with a natural progression to a point where the ascites eventually become resistant to diuretic therapy, subsequently resulting in hyponatremia and hepatorenal syndrome. While ascites itself is not life-threatening, it does result in a loss of quality of life and could result in spontaneous bacterial peritonitis, which could be fatal. Diuretics are considered the first-line therapy in ascites. Patients who are refractory to diuretic therapy should undergo repeated paracenteses. Fluid restriction must be considered in hyponatremia. Additionally, prophylactic antibiotic therapy should be considered in high-risk patients [4]. These may be immunocompromised patients or patients with additional comorbidities, and the risk may be best determined via detailed review of the patient's medical history. When deemed appropriate, the recommended antibiotic prophylaxis in the patient at risk for SBP is 2 g of amoxicillin and 500 mg of metronidazole 1 h prior to the procedure per the protocol of Firriolo [6].

4.7 Hepatorenal Syndrome

Hepatorenal syndrome (HRS) is characterized by the presence of renal failure in patients with advanced liver disease and with otherwise no known renal pathology [2, 4]. The kidneys are histologically and structurally normal. HRS represents a functional abnormality in the kidneys that is a result of an extreme vascular compromise associated with the severe liver disease [4]. Once the liver is transplanted, the kidney function has been known to return to normal. The diagnosis is based on an elevated serum creatinine >1.5 mg/day in the absence of additional causes of renal failure that shows no improvement following plasma volume expansion and diuretic withdrawal. Prevention of HRS and prophylactic use of diuretics with early correction of electrolyte abnormalities is vital. Care must be taken to avoid nephrotoxic medications and to lower the risk of HRS.

4.8 Viral Hepatitis

Viral hepatitis can be acute or chronic (Table 4.3) [4]. This disease entity can range from a mildly symptomatic, self-limiting infection to chronic hepatitis and liver failure or liver cirrhosis [2]. Hepatitis A virus (HAV) is the most common cause of acute viral hepatitis across the world. It is an infectious, acute self-limiting disease transmitted via the fecal-oral route [2]. Hepatitis E virus (HEV) is also transmitted via the fecal-oral route and is an acute self-limiting disease. However, the immunity to HEV is not lifelong as in the case of HAV [2].

Enteric RNA viruses resulting in hepatitis A and E do not cause chronic hepatitis [4, 7]. Chronic viral hepatitis lasts longer than 6 months and is characterized by hepatocellular necrosis and inflammation which might be accompanied by fibrosis. Causes include hepatitis B, hepatitis B-dependent hepatitis D, and hepatitis C (1). Hepatitis B virus (HBV) is a DNA virus [2]. Chronic hepatitis B is characterized by continued serum presence of hepatitis B surface antigen (HBsAg) and hepatitis B virus envelope protein. The patients with the disease can be broadly divided into those in whom the viral load is high (hepatitis B virus DNA levels exceed 10 [8]–10 [9] IU/mL) and those with a low (undetectable) viral load who have clinically mild chronic hepatitis B with low infectivity and are essential inactive carriers. The spread of hepatitis B occurs in the same fashion as that of other blood-borne diseases such as via sexual activity, contaminated needles from drug use, and occupation exposure to blood and/or contaminated instruments [2, 4]. HBsAg is detectable in patients 2–10 weeks after exposure to the hepatitis B virus. In acute cases, this antigen is undetectable after 4–6 months. The presence of the HBsAg for longer than 6 months is indicative of chronic hepatitis B infection. The symptoms also vary vastly in both situations. In the latter category, symptoms are usually absent with an occasional patient that may complain of chronic fatigue or fullness in upper right quadrant. Patients with a high viral load may present with jaundice and decompensated cirrhosis with ascites, edema, bruising, portal hypertension, hepatic encephalopathy, and cutaneous manifestations such as vasculitis [3].

The goal of treatment in patients with chronic hepatitis B is to prevent delayed complications of liver disease such as cirrhosis, liver failure, and hepatic cellular carcinoma which would increase survival rates in patients with the disease. Amongst the seven drugs approved for treatment of chronic hepatitis B, five are known nucleoside analogs which impede the replication of hepatitis B virus and are known to be more potent than interferon-alpha. The hepatitis B patient in the oral surgery office may present with a medication list which could include one or more of the following—entecavir, tenofovir, lamivudine, telbivudine, and adefovir. While treatment is available, there may be several missed opportunities due to financial and cultural barriers. Hepatitis D virus (HDV), also referred to as the delta virus, requires the HBsAg for survival and is only seen in persons with HBV infection. Hepatitis C virus is the most common cause for liver transplantation worldwide. It is a blood-borne infection and is transmitted most commonly via infected needles. A major risk factor is a history of blood transfusion prior to the screening for HCV infections. There is no vaccine to prevent HCV infection, and the focus is currently on identification and treatment of individuals who are infected to curb the further spread of the disease. However, since around 2013, curative medications including Sofosbuvir (Sovaldi) and Ledipasvir-Sofosbuvir (Harvoni) have revolutionized treatment, long-term outcomes, and disease transmission.

4.9 Jaundice

The final product of heme catabolism is bilirubin, and up to 85% of bilirubin is derived from hemoglobin. Bilirubin is water insoluble and is transported in blood bound to albumin. This is referred to as unconjugated bilirubin. When bilirubin is attached to two glucoronate groups in the liver, it is referred to as conjugated bilirubin. This is eventually converted into stercobilin and is responsible for giving feces its natural color. Yellow discoloration of the sclera, mucous mem-

Table 4.3 Viral hepatitis

	Hepatitis A	Hepatitis B	Hepatitis C	Hepatitis D	Hepatitis E	Hepatitis G
Type of virus	RNA Picornaviridae	DNA Hepandaviridae	RNA Flaviviridae	RNA Deltaviridae	RNA Caliciviridae	RNA Flaviviridae
Transmission	Fecal-oral	Parenteral	Parenteral	Parenteral	Fecal-oral	Parenteral
Symptoms	Fever, malaise, headache, jaundice	Severe liver damage (chronic disease)	Severe liver damage (more chronic disease)	Severe liver damage (high mortality)	High risk in pregnant women (high mortality)	Chronic liver disease
Incubation period	2–7 weeks	1–6 months	2–26 weeks	2–12 weeks	6–8 weeks	2–3 weeks
Carrier state	No	Yes	Yes	Yes	No	No
Passive immunity	Hyperimmune globulin	Hyperimmune globulin	None	Hyperimmune globulin	None	None
Active immunity	Hepatitis A vaccine	Hepatitis B vaccine	None	Hepatitis B vaccine	None	None

branes, and skin due to the presence of excessive circulating bilirubin is referred to as jaundice. The level of circulating bilirubin when higher than 30 μmol/L is referred to as hyperbilirubinemia and for jaundice to be visibly detected is higher than 50 μmol/L. [2] Icterus is the term used to describe yellowing of the sclera which is the pathognomonic feature of jaundice. Jaundice is classified in to prehepatic, hepatic, and cholestatic.

Prehepatic jaundice arises due to an excessive amount of bilirubin prior to its entry into the liver as seen in increased hemolysis during sickle cell disease or thalassemia major. Hepatic jaundice results from an abnormality in the liver itself resulting in reduction of the liver's capacity of excreting the conjugated bilirubin. As a result, there is an excess of circulating conjugated bilirubin, and it is also excreted in the urine. Cholestatic jaundice is the result of failure of bilirubin from reaching the duodenum due to an obstruction of bile flow at any level such as gallstones or a space-occupying neoplasm. The presence of bile in the urine accounts for its dark appearance, and absence of bile in the intestine causes fat malabsorption resulting in steatorrhea. This can also result in the deficiency of fat-soluble vitamins A, D, E, and K which require bile salts for their absorption. Typical symptoms accompanying or preceding jaundice associated with viral hepatitis include nausea, anorexia, and an aversion to smoking (in smokers). Clinical history and timing regarding onset of jaundice is important in diagnosing the underlying cause as are lab tests. Coagulopathy may result due to malabsorption of fat-soluble vitamin K.

4.10 Hematologic Consequences in Liver Disease

The liver is responsible for the production of both procoagulant and anticoagulant factors. The clotting factors—II, labile factor V, VII, IX, X, contact factors XI and XII, fibrin-stabilizing factor XIII, and fibrinogen—are synthesized by the liver. Additionally, anticoagulant factors including anti-thrombin III and proteins C and S are also produced by the liver and subsequently lowered in liver disease as well [3, 10].

From a surgical perspective, the effect of liver disease on the hematological status of the patient must be studied thoroughly. The prothrombin time is the time required for plasma to clot after exposure to tissue factor and phospholipid [4]. The abnormality in PT or INR in liver disease is not always the best indicator of the risk of bleeding. Spontaneous bleeding from mucosal surfaces, frequent bruising, and prolonged bleeding after minimal trauma such as shaving or from a venipuncture are valuable techniques in assessing bleeding in a patient with liver disease. There is a high likelihood of anemia in patient with decompensated liver disease. This often results from gastrointestinal bleeding secondary to esophageal varices or bleeding ulcers from gastritis, epistaxis, and oral bleeding such as gingival bleeding.

The risk of hemorrhage is more accurately measured by the qualitative and quantitative platelet defects. The decrease in platelets arises from splenic sequestration due to hypersplenism. Thrombocytopenia secondary to increased splenic sequestration often results in a platelet count of 60–90 × 10^3/mm^3. This has minimal effect on any necessary surgical intervention. However, a platelet count lower than 50,000/mm^3 may need to be supplemented depending on the extent of surgical intervention. The qualitative effect on platelets arises from a combination of factors including decreased plasma thrombopoietin which is mainly produced by the liver and reduced availability of arachidonic acid in a chronic liver patient.

Management of the decompensated liver patient to undergo necessary oral surgical procedures such as drainage of an acute oral abscess or extraction of non-restorable infected teeth is usually done after thorough evaluation of the trends of the various lab results and in conjunction with the hepatology team. In most instances, the oral and maxillofacial surgeon should be aware that restoration of existing coagulopathies in chronic liver disease patients to normal is not the goal of treatment.

To optimize a patient for surgery, fresh frozen plasma is ideal for restoring clotting factors. Intravenous vitamin K may also be administered in a usual dose of 10 mg vitamin K for 3 days to correct the elevated PT. Even in cases of direct hepatocellular disease, there is a definite improvement in the PT albeit by a few seconds with intravenous vitamin K administration. Transfusion of platelets was considered appropriate if the number was below 50,000/mm^3 [4]. However, several institutions feel comfortable transfusing platelets at a count of 40,000/mm^3 to rationalize the need of a blood transfusion and due to more recent data available [11].

4.11 Management of Patients with Chronic Liver Disease Undergoing Oral Surgical Procedures

The number of patients requiring a liver transplant has increased significantly over the past 15 years. Subsequently, the number of patients requiring extractions and other oral surgical procedures has increased as well [11]. An oral and maxillofacial surgical evaluation forms the basis of prevention of any potential oral foci of infection both in the pre- and post-transplant immunocompromised patient. The oral and maxillofacial surgeon should have a thorough understanding of the patient's lab values as mentioned earlier including the PT, PTT, INR, and platelet count [8, 10]. Further, the surgeon should also be well aware that the final results of the aforementioned studies may not correlate with the clinical scenario in the cirrhotic patient. Chronic anemia from bleeding varices, reduced production of clotting factors by the liver, malnutrition resulting in decreased absorption of vitamin K, thrombocytopenia from splenomegaly, and a host of additional factors all contribute to the altered hemostasis [11]. The oral and maxillofacial surgeon has several local hemostatic measures at his/her disposal. Absorbable hemostatic agents such as gelatin sponge, oxidized regenerated cellulose, microfibrillar collagen, collagen plugs, and topical thrombin are some of the options available. Tranexamic acid or aminocaproic acid rinses are employed to aid in hemostasis as well [9, 11]. Additionally, primary closure of the surgical site, application of cautery and/or bone wax, and local infiltration of vasoconstrictors may be used. The oral and maxillofacial surgeon should place equal importance on the timing of the platelet transfusion as well. Consideration should be given to early sequestration or destruction of platelets soon after they are administered in the patient with chronic liver disease. Hence administration of platelets in the immediate preoperative period or intraoperatively will be most effective at providing the largest volume of circulating platelets that will be available for hemostasis. Advances in medical management have proven that DDAVP has the potential to be a safe and effective alternative to platelet transfusions in cirrhotic patients with underlying coagulopathy in achieving adequate hemostasis [10]. Importantly, quadrant oral surgery should be considered to limit blood loss, and two forms of quadrant surgery exist: the first option is to perform surgery in each quadrant of the mouth and then perform hemostatic techniques and suturing before moving to the next quadrant, as this limits the slow bloody ooze that can result in very underestimated and significant blood loss, when an entire arch or mouth of procedures are completed before wound hemostasis and closure. The second option is to perform only one quadrant of surgery at each visit to limit the surgical insult and wound size. Lastly, procedures that include more than a quadrant of oral surgery likely require observation for an extended period of time, including overnight in a hospital setting, to allow for frequent postoperative checks. Failure to properly consider postoperative monitoring can potentially result in significant adverse events.

The oral and maxillofacial surgeon must realize that it is safe to administer up to 2000 mg of acetaminophen in the chronic liver patient [6]. Also these patients may be prescribed statins in spite of their cirrhosis diagnosis. The medications that are recommended to be avoided in patients with decompensated cirrhosis include

aspirin, NSAIDs, and antibiotics such as aminoglycosides. Additionally, while insulin is considered acceptable for use in diabetic patients with decompensated cirrhosis, oral hypoglycemic agents are only preferred in cases of compensated cirrhosis.

A multi-disciplinary team approach is advocated and encouraged to best serve the chronic liver patient requiring oral surgical intervention.

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5 Oral and Maxillofacial Surgical Management for the Renal Compromised Patient

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5.1 Introduction

Kidney disease is an increasing health problem worldwide and is associated with a number of clinical challenges. In this chapter, we review the most recent strategies and guidelines for the perioperative surgical management of patients with kidney disease. The kidneys serve several important functions including the regulation of fluid volume, the filtration of waste products and toxins, the synthesis and release of hormones, and the metabolism of drugs. Some of the complications of kidney disfunction include anemia, abnormal bleeding, bone disease, cardiac disease, electrolyte and fluid imbalance, and drug intolerance, all which can cause life-threatening complications in a surgical setting. Due to the effects the kidneys have on multiple organ systems, understanding the surgical risks and proper management of a renally compromised patient is crucial for oral and maxillofacial procedures.

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5.2 Definition

Kidney disease can be caused by acute or chronic pathologic conditions. Acute kidney injury (AKI) is often encountered in the setting of toxin ingestion or overdose, urinary tract obstruction, trauma, bacterial infection, and dehydration. If recognized, this typically presents within an onset of hours or days and requires immediate medical intervention. A straightforward and widely accepted method has been established to quantify the severity and outcome of patients presenting with AKI, known as the RIFLE classification (Table 5.1). This is based on serum creatinine (SCr) and urinary output (UO) determinants and considers three severity classes of AKI (risk, injury, and failure), according to the variations in SCr and/or UO, and two outcome classes (loss of kidney function and end-stage kidney disease). The patient should be classified using the criteria (SCr and/or UO) which leads to the worst classification (maximum RIFLE), for instance, if a patient was in the risk class according to the UO but in the injury class according to SCr variation, then the worst criteria (SCr) should be used for classifying the severity of AKI in this patient [1]. The RIFLE classification has been widely accepted in determining the incidence of AKI and its stepwise prognostic accuracy of mortality.

Chronic kidney disease (CKD) manifests as a long-term, progressive decline in kidney function

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Table 5.1 Risk, injury, failure, loss of kidney function, and end-stage kidney disease (RIFLE) classification

RIFLE class	Glomerular filtration rate	Glomerular filtration rate (GFR)	Urine output (UO)
Risk	1.5X increase in serum creatinine	GFR reduction >25%	<0.5 mL/kg/h × 6 h
Injury	2X increase in serum creatinine	GFR reduction >50%	<0.5 mL/kg/h × 12 h
Failure	3X increase in serum creatinine; OR if baseline SCr ≥353.6 μmol/L (≥4 mg/dL) ↑ SCr >44.2 μmol/L (>0.5 mg/dL)	GFR reduction >75%	<0.3 mL/kg/h × 24 h or anuria × 12 h
Loss of kidney function	Complete loss of kidney function >1 month		
End-stage kidney disease	Complete loss of kidney function >3 months		
	SCr, serum creatinine		

Adapted from José António Lopes, Sofia Jorge, The RIFLE and AKIN classifications for acute kidney injury: a critical and comprehensive review, Clinical Kidney Journal, 2013;6(1):8–14. https://doi.org/10.1093/ckj/sfs160

and is often caused by hypertension and diabetes. Patients with CKD often remain asymptomatic for years and are more likely to present for surgical care in an outpatient setting than those with acute disease. The following chapter will address the proper assessment and current knowledge on the surgical management for the chronically renally compromised patient.

Chronic kidney disease is defined as abnormalities of kidney structure or function, present for 3 months or longer, with implications for health. Patients with CKD can be classified for risk assessment depending on their level of kidney function (glomerular filtration rate or GFR) and albuminuria. The presence of severe albuminuria is an indicator that increases the likelihood of further progression of CKD to kidney failure or end-stage renal disease (ESRD) (see Table 5.2). The definition of CKD includes all individuals with indicators of kidney damage (i.e., albuminuria, hematuria, electrolyte abnormalities due to tubular disorders, renal histological abnormalities, structural abnormalities detected by imaging, or a history of a kidney transplantation) or those with a GFR of less than 60 mL/min/1.73 m^2 on at least two occasions 90 days apart [2].

The National Kidney Foundation developed a five-staged classification system based on GFR and albumin: creatine ratios (see Table 5.3). Stage 1 is characterized by a normal or mildly elevated GFR with some evidence of kidney damage as mentioned above. Stage 2 is identified by a slight decrease in GFR. Even in this stage, the patient often remains asymptomatic despite a 10–40% loss of kidney function. Stage 3 is characterized by a moderately decreased GFR (30–59 mL/min) and a loss of 50% or more of renal function. Stage 4 is evidenced by a significant decline in GFR (15–29 mL/min), and stage 5 is identified by a GFR of less than 15 mL/min. At this stage the patient is in end-stage kidney failure with less than 15% of kidney function remaining, ultimately requiring renal transplant or chronic dialysis.

As a patient progresses through the stages of CKD, the loss of nephron function prevents the removal of nitrogenous compounds and other toxins from the blood. The kidneys lose their ability to perform endocrine and excretory function, thus causing a downward spiral of events and ultimately leading to the clinical syndrome of *uremia*.

5.3 Epidemiology and Etiology

Over 37 million Americans have CKD today. However, most of them are unaware and undiagnosed due to the lack of symptoms in the early stages. The overall prevalence of CKD (stages 1–5) in the United States adult general population

Table 5.2 Classification of renal failure based on GFR and ACR class rubric

CLASSIFICATION OF RENAL FAILURE BASED ON GFR AND ACR CLASS RUBRIC

GFR(Glomerular Filtration Rate- ACR(Albumin to Creatinine Ratio) categories and adverse outcomes

Category	GFR ml/min/1.73 m2 Range	
G1	≥90	Normal or high
G2	60-89	Mildly decreased*
G3a	45-59	Mildly to moderately decreased
G3b	30-44	Moderately to severely decreased
G4	15-29	Severely decreased
G5	<15	Kidney failure

ALBUMINURIA CATEGORIES IN CKD	ACR(MG/G) - compared to young adult
ALBUMINURIA	
ACR SEVERITY A1-2-3	A1 <30mg/g (Normal to mild) A2 30-300mg/g (Moderate) A3>300mg / g (Severe) (ACR>2220mg/g-nephrotic syndrome)

RISK ASSESSMENT WITH GFR & ACR — ACR CATEGORIES

GFR	**A1**	**A2**	**A3**
G1	...	+	++
G2	**...**	**+**	**++**
G3a	+	++	+++
G3b	++	+++	+++
G4	**+++**	**+++**	**+++**
G5	+++	+++	+++

CKD CAUSED BY SYSTEMIC, AUTOIMMUNE KIDNEY DISEASES HAVE TO BE EVALUATED FOR CAUSE IDENTIFICATION

Table information adapted from https://renal.org/information-resources/the-uk-eckd-guide/ckd-stages/

Table 5.3 Staging of chronic kidney disease

As per the National Kidney Foundation, patients presenting with chronic kidney disease are staged based on the estimated GFR (creatinine clearance) as calculated by the Modification of Diet in Renal Disease formula
• Stage 1—Normal GFR (90 mL/min or greater)
• Stage 2—Mildly reduced GFR (60 mL/min to 90 mL/min)
• Stage 3—Moderately reduced GFR (30 mL/min to 59 mL/min)
• Stage 4—Severely reduced GFR (15 mL/min to 29 mL/min)
• Stage 5—ESRD (GFR < 15 mL/min or patient is on dialysis)

is approximately 14.8%, with CKD stage 3 (6.4%) being the most prevalent [2]. Overall, CKD prevalence has remained relatively stable during the last two decades. The majority of patients with ESRD is Caucasian (59.8%), and the remainder is African American (33.2%), Asian (3.6%), or Native American (1.6%). The incidence of ESRD among black individuals, however, is 3.7 times higher than it is among the white population. Similarly, the incidence among Native Americans is 1.8 times greater than it is among whites. Men are 1.2 times more likely than women to develop ESRD, though women are 1.7 times more likely to delay initiation of dialysis [3, 4].

CKD can result from primary renal disorders, for example, IgA nephropathy, focal segmental glomerulosclerosis, membranoproliferative glomerulonephritis, and polycystic kidney disease to common systemic disorders that can lead to renal damage. The four most common causes of ESRD are diabetes mellitus (44%), hypertension (28%), chronic glomerulonephritis (16%), and polycystic kidney disease (4.5%) [5]. Additional causes listed in order of decreasing incidence include neoplasm, obstructive nephropathies, and acquired immunodeficiency syndrome (AIDS) nephropathy [5].

5.4 Pathophysiology

The kidneys filter about 180 L/day through the function of approximately two million nephrons. Progressive damage to the functioning nephrons is the underlying pathological process in renal failure [5]. When the function of the nephrons deteriorates, dysfunction can occur in acid-base homeostasis, electrolyte regulation, fluid balance, hormone production and secretion, and waste elimination. Collectively these abnormalities result in metabolic disturbances and ultimately lead to conditions such as anemia, hypothyroidism, hypertension, metabolic acidemia, and hyperkalemia. It is important to note that chronic kidney disease results in the irreversible loss of nephrons. As a result, few nephrons bear the functional burden of maintaining homeostasis, leading to an increase in glomerular filtration pressure and hyperfiltration. This compensatory hyperfiltration predisposes the kidneys to fibrosis and scarring known as ***glomerular sclerosis***. As a result, the rate of nephron destruction and loss increases, thus speeding the progression to **uremia**, the complex syndrome that occurs due to renal failure. The pathogenesis of uremia derives in part from a combination of the toxic effects of retained products normally excreted by the kidneys (i.e., nitrogen-containing products of protein metabolism), normal products such as hormones now present in increased amounts, and the loss of normal products of the kidney such as erythropoietin [6].

The kidneys have a significant functional reserve—up to 50% of nephrons can be damaged without any acute signs or symptoms of impairment. When the GFR is further reduced, leaving only about 20% of initial renal capacity, elevated blood levels of waste products normally excreted by the kidneys are sequestered, and *azotemia* is observed. Nevertheless, patients may be largely asymptomatic because a new steady state is achieved in which the blood levels of these products are not high enough to cause symptomatic toxicity. However, even at this apparently stable level of renal function, hyperfiltration-accelerated evolution to end-stage chronic kidney disease is in progress. In addition, because patients with this level of GFR have little functional reserve, they can acutely become uremic with the acute stress of surgery, infection, obstruction, dehydration, or the use of nephrotoxic drugs.

5.5 Complications and Clinical Manifestations

5.5.1 Sodium Balance and Volume Status

Patients with CKD typically have some degree of fluid retention, reflecting the loss of proper salt and water excretion by the kidneys. A moderate degree of sodium and water retention may occur without clinical signs of extracellular fluid excess. However, continuous consumption of sodium-containing foods leads to further fluid retention and contributes to heart failure, hypertension, pitting edema, and overall weight gain. Renally compromised patients tend to have a greater sensitivity to sudden extrarenal sodium and water losses due to the impaired conservations mechanisms. Providers must be cautious for excess vomiting, diarrhea, increased sweating, or dehydration—all which can occur in a surgical setting. This extracellular depletion can ensue rapidly, leading to tachycardia, hypotension, nausea, vascular collapse, and AKI.

5.5.2 Potassium Balance

Hyperkalemia is a potentially life-threatening complication of CKD, especially in the later stages (e.g., GFR <15 mL/min). Early in CKD, as the GFR falls, aldosterone-mediated K^+ transport in the distal tubule increases in a compensatory fashion to maintain normal potassium levels [7]. However, treatment with K^+-sparing diuretics, ACE inhibitors, or β-blockers—drugs that may impair aldosterone-mediated K^+ transport—can precipitate dangerous hyperkalemia in a patient with CKD [8]. Patients with CKD are also at greater risk of hyperkalemia in the event of increased loads of K^+ commonly seen in a surgical setting. This includes endogenous sources

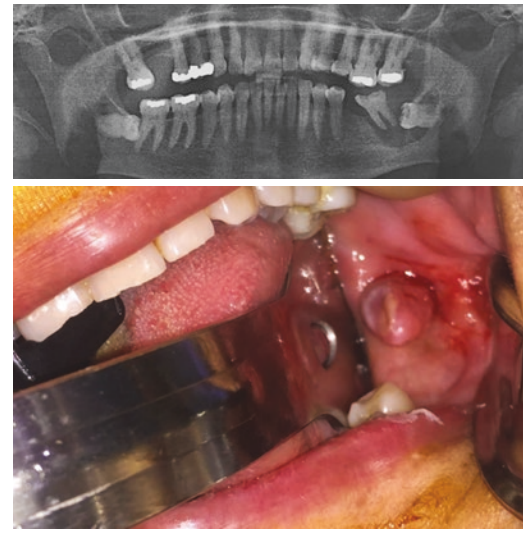
such as hemolysis, infection, and trauma or exogenous sources such as blood transfusions and potassium-containing medications.

5.5.3 Acid-Base Balance

The diminished capacity of the renal tubular cells to regulate acid-base homeostasis results in metabolic acidosis. As kidney failure progresses, there is decreased secretion of hydrogen ions and impaired excretion of ammonium, thus leading to the buildup of phosphate and lactic acid. If not regulated with daily bicarbonate supplementation, the resulting anion gap metabolic acidosis eventually leads to hyperventilation, lethargy, anorexia, muscle weakness, and congestive heart failure. ESRD patients are highly susceptible to metabolic acidosis in the event of ketoacidosis, lactic acidosis, toxic ingestion, or bicarbonate loss such as acute diarrhea. As kidney failure progresses, there is decreased secretion of hydrogen ions, impaired excretion of ammonium, and eventually a toxic buildup of phosphate and additional lactic acid. The resulting anion gap metabolic acidosis eventually leads to hyperventilation, lethargy, anorexia, muscle weakness, and congestive heart failure [5].

5.5.4 Vitamin and Bone Abnormalities

Several disorders of phosphate, calcium, and bone metabolism are observed in CKD. Key factors in the pathogenesis of these disorders include a diminished absorption of calcium from the gut, an overproduction of parathyroid hormone, disordered vitamin D metabolism, and a retention of phosphorus [9]. All these factors contribute to enhanced bone resorption. Hyperphosphatemia contributes to the development of hypocalcemia and thus serves as an additional trigger for secondary hyperparathyroidism, elevating blood PTH levels. The elevated blood PTH further depletes bone calcium and contributes to *osteomalacia* of CKD. These patients can present with



Figs. 5.1 and 5.2 Panogramic radiograph of a lytic left mandibular angle region and clinical picture of the same left posterior buccal area demonstrating a 56 year old female with elevated PTH in secondary parathyroidism, due to renal compromise and a differential of pathology report can be of central giant cell granuloma or "Browns Tumor"

lytic bone lesions and giant cell granulomas known as a brown tumor (see Figs. 5.1 and 5.2).

5.5.5 Cardiovascular and Pulmonary Abnormalities

Heart failure and pulmonary edema can develop in the context of volume and salt overload (see Table 5.4). Hypertension is a common finding in CKD and is often due to fluid and sodium imbalance. However, overproduction of renin due to decreased renal perfusion in the failing kidneys is also one of the main causes for uninhibited feedback resulting in severe hypertension. An increased incidence of cardiovascular disease is observed in patients with CKD and remains the leading cause of mortality in this population [10]. Cardiovascular risk factors in CKD patients include hypertension, hyperlipidemia, glucose intolerance, increased cardiac output, and valvular calcification. As a result, an increased incidence of myocardial infarction, stroke, and peripheral vascular disease is observed in CKD [10].

Table 5.4 Signs and symptoms based on various stages of chronic kidney disease

Symptoms	Signs	Pathophysiology
Fatigue, malaise, confusion, coma, chest pain, shortness of breath	Anemia, pallor, low hematocrit, cardiorespiratory disease, and crackles with pitting edema, mental clouding, headache	Anemia is due to reduced erythropoiesis. Kidneys are the source of erythropoietin (EPO). Individuals with renal failure may need supplementation with EPO Increased fluid retention due to low GFR and albuminuria causes **pulmonary edema** with the ventilation-perfusion mismatch Cerebral encephalopathy and uremic pericarditis can lead to confusion, weakness, and chest pain
Bodyweight changes	Weight loss Weight gain	The kidney regulates hydrogen ion secretion. Metabolic acidosis can cause protein-energy malnutrition(PEM), leading to weight loss Sodium and fluid retention causes hydrostatic pressure changes leading to pitting edema. Low albumin can further reduce oncotic pressure, leading to significant extravascular fluid retention-independent areas like the extremities and abdomen
Bleeding and bruising	Skin bruising and increased duration of bleeding Gastrointestinal bleeding	Platelet dysfunction is secondary to nitrogen and uremia
Electrolyte and metabolite imbalance		
Sodium, potassium, hydrogen, calcium, phosphate, and nitrogen are the most critical	Critical potassium imbalance induced cardiac arrhythmias **Renal osteodystrophy** Calcium and phosphate excretion Secondary and tertiary hyperparathyroidism Metabolic acidosis (H+)	**Hyperkalemia**—Failure of renal potassium excretion can lead to life-threatening arrhythmias Failure of phosphate excretion due to renal failure causes hyperphosphatemia **Hyperphosphatemia** inhibits adequate calcitriol causing low vitamin D3. Advanced CKD and failure causes lack of 1-alpha-hydroxylase leading to reduced conversion of calcifediol (25-hydroxyvitamin D)
Hyperparathyroidism		
Hyperparathyroidism—secondary and tertiary	Osteopenia, osteoporosis, pathological fractures including vertebral compression fractures; ectopic calcifications	The kidney produces 1-alpha- hydroxylase leading to reduced conversion of calcifediol (25-hydroxyvitamin D) to calcitriol. Calcitriol (1,25-dihydroxy vitamin D) increases the uptake of calcium by the intestine Low calcium causes parathyroid gland compensatory hyperplasia with parathormone (PTH), leading to pathological fractures due to bone turnover Long-term parathyroid hyperplasia leads to tertiary hyperparathyroidism

Table adapted from McMasters Pathophysiology Review http://www.pathophys.org/ckd/

5.5.6 Hematologic Abnormalities

Patients with CKD have marked abnormalities in red blood cell count, white blood cell function, and clotting parameters. The normochromic and normocytic anemia is due primarily to the decreased production of erythropoietin, resulting in decreased erythropoiesis. Symptoms of anemia are typically associated with a GFR of less than 50 mL/min (stage 3) or when serum creatinine is greater than 2 mg/mL. Additional causes of anemia include the bone marrow suppressive

effects of uremic toxins, bone marrow fibrosis leading to increased serum PTH, and dialysis-associated hemolysis and blood loss [11].

Patients with CKD display abnormal hemostasis manifested as increased bruising, decreased clotting, and an increased incidence of spontaneous GI and cerebrovascular hemorrhage. Laboratory abnormalities include prolonged bleeding time, decreased platelet factor III, abnormal platelet aggregation and adhesiveness, and impaired prothrombin consumption.

5.5.7 Immunologic Suppression

Uremia is associated with an increased susceptibility to infections, likely due to leukocyte suppression by uremic toxins. This further leads to impaired chemotaxis and overall immunological response. Acidosis, hyperglycemia, malnutrition, and hyperosmolality are also believed to contribute to immunosuppression in CKD [12]. The invasiveness of dialysis and the use of immunosuppressive drugs in renal transplant patients further contribute to an increased incidence of infections.

5.5.8 Neuromuscular Abnormalities

Neurologic symptoms and signs of uremia range from insomnia, impaired mental concentration, memory loss, errors in judgment, and neuromuscular irritability manifested as muscle cramps, fasciculations, asterixis, myoclonus, stupor, seizures, and even coma in severe cases of end-stage uremia.

5.6 Surgical Management and Considerations

5.6.1 Identification and Risk Assessment

The National Kidney Foundation's guidelines suggest screening for CKD in all patients that present with high-risk comorbidities such as hypertension, diabetes, obesity, peripheral edema, smoking history, or a family history of kidney disease. Medical referrals should be made for proper workup and diagnosis, especially if the patient requires a surgical procedure. This simple step in coordinating care not only allows the patient to recognize their disease and receive treatment but also prevents the complications that can arise from surgery with an undiagnosed kidney disorder.

Nephroprotection is imperative for the handling of patients with CKD in the perioperative setting to prevent complications and to avoid the progression of CKD. This requires the identification of CKD patients through risk assessment and preoperative laboratory studies. Evaluation includes measurement of blood pressure; urinalysis for screening of proteinuria, hematuria, and casts; as well as serum analysis for the measurement of GFR, blood urea nitrogen (BUN), creatinine clearance, and electrolytes (see Table 5.5). Once a general assessment and the level of kidney function has been identified, the surgeon can develop a treatment plan accordingly or defer surgery until renal health has been optimized.

Table 5.5 Typical preoperative diagnostic testing in patients with CKD

Hemostasis and anemia	Complete blood count, bleeding time, prothrombin time, partial thromboplastin time, international normalization ratio
Electrolytes and chemistries	Basic metabolic panel: sodium, potassium, chloride, blood urea nitrogen, creatinine, calcium, bicarbonate levels
Volume status	Physical exam, chest x-ray, sodium levels

5.6.2 Antibiotics

Generally, patients in stages 1–3 of kidney failure do not require prophylactic antibiotics. Many physicians recommend that patients with CKD stages 4–5 receive prophylactic antibiotics for surgical procedures. For patients requiring surgery that have recently undergone synthetic vascular grafts for dialysis access, antibiotic

prophylaxis using standard AHA guidelines for endocarditis prevention is recommended for the first several months [13]. The purpose of this is to avoid bacterial seeding of the grafts before epithelialization occurs. Patients who have undergone kidney transplantation may require special surgical prophylaxis and precautions due to long-term immunosuppressant therapy. This includes the need for corticosteroids or antibiotic prophylaxis.

5.6.3 Bleeding

Uremia can cause platelet dysfunction, which can result in increased perioperative bleeding.

Bleeding time is the most sensitive indicator of the extent of platelet dysfunction, although test results are subject to some operator variation [14]. While bleeding times of greater than 10–15 min have been associated with a high risk of hemorrhage, the exact correlation of elevated bleeding times and surgical risk has not been clearly established [15]. Standard options for correcting an elevated bleeding time include desmopressin, conjugated estrogens, cryoprecipitate, and platelet transfusion (Table 5.6) [16–21]. Blood transfusions should try and be avoided if possible, due to immunologic sensitization, which would complicate any need for kidney transplantation in the future.

Antiplatelet agents, including aspirin and dipyridamole, should not be given within 72 h before surgery in patients with end-stage renal disease or uremic chronic kidney disease. In addition, some agents that have only minor platelet effects in patients without uremia can have exaggerated effects in patients with ESRD and may theoretically increase the risk of intraoperative bleeding. These drugs include diphenhydramine, NSAIDs, chlordiazepoxide, and cimetidine. Careful consideration must be taken into account involving treatment of dialysis-dependent patients. A small amount of heparin is used during hemodialysis, with a residual anticoagulant effect lasting as long as 2.5–3 h. Therefore, it is prudent to wait at least 12 h after the last hemodialysis with heparin before any invasive surgical procedure is performed [21]. Lastly, as with any surgical procedure, local hemostatic measures such as topical thrombin, absorbable gelatin, microfibrillar sponge, and epinephrine should be readily available.

Table 5.6 Options for correcting elevated bleeding times in patients with renal failure

Intensive dialysis
Desmopressin (DDAVP), 0.3 mcg per kg IV 1 h before surgery [16]
Cryoprecipitate, 10 units over 30 min IV; effects should be apparent in 1 h [17]
Conjugated estrogens, 0.6 mg per kg per day IV or orally for 5 days; some effect should be apparent in 6 h, but peak effect occurs in 5–7 days [18–20]
Transfusion of packed red blood cells to raise the hematocrit to at least 30 percent, which increases platelet interaction with vessel walls [21]

5.6.4 Blood Pressure

Particular attention should be given to the maintenance of hemodynamic stability, including an adequate blood pressure and preservation of intravascular volume. Preoperative and intraoperative hypertension is very common in patients with chronic kidney disease. Contributing factors include anxiety, a catecholamine response related to the stress of surgery, and baseline hypertension caused by kidney failure. In general, patients who have kidney disease and hypertension should continue antihypertensive drug therapy throughout the surgical period. For more extensive procedures requiring extended surgical time, discontinuation of diuretics should be considered. Unless diuretics are being used for volume management (e.g., congestive heart failure or nephrotic syndrome), they should be discontinued 2–3 days before surgery. Discontinuation of diuretics until after surgery will help avoid possible volume depletion and intraoperative hypotension, which may worsen renal function in the acute setting. Hypoglycemia may also cause hypertension as a result of catecholamine release for mobilization of glycogen stores. This most commonly occurs in patients with diabetes mellitus who are given NPO orders for a prolonged

period before surgery. Inadvertent hypoglycemia can be avoided with perioperative glucose monitoring and the continuous administration of a low-dose dextrose infusion.

Careful cardiac perioperative considerations should be used for patient undergoing dialysis. For example, an extremity with an AV shunt should not be used for obtaining blood pressure measurements, drawing blood, or administering IV fluids and medications. An inflated blood pressure cuff can potentially collapse or damage the shunt, and IV access can potentiate the development of a thrombus or infection of grafts. In general, use of the AV shunt should be left to the discretion of the patient's nephrologist.

5.6.5 Soft Tissue and Bone Considerations

Surgical treatment of a renally compromised patient can present many challenges in soft and hard tissue management. Prior to extraction of teeth, placement of endosseous implants, exogenous bone grafting, or soft tissue augmentation, the following aspects should be carefully considered: Studies have shown that patients on dialysis have poorer periodontal conditions than healthy patients. CKD patients have a higher plaque index and higher dental calculus formation than controls [22]. In addition, many hemodialysis patients present with xerostomia. Dry mouth is caused by many factors such as reduced salivary flow, minor salivary gland parenchymal fibrosis and atrophy, fluid intake restriction (to maintain a correct fluid volume balance), old age, mouth breathing, and the use of xerostomia-causing drugs [23]. Histological evidence shows that 84% of CKD patients have bone disorders [24]. Bone metabolism is regulated by several factors including parathormone (PTH), fibroblast growth factor 23 (FGF23), and dihydroxycholecalciferol ($1,25(OH)_2D$). Complications from CKD, including hyperphosphatemia, hypocalcemia, hyperparathyroidism, and vitamin D deficiency, may interrupt the balance of these factors, impacting bone structural integrity and resulting in CKD-mineral and bone disorder [25]. All of the compromises above have been shown to effect the success and predictably of oral and maxillofacial surgical outcomes in CKD patients.

5.6.6 Drug Considerations

Inappropriate dosing in patients with CKD can cause toxicity or ineffective drug therapy. Chronic kidney disease can affect glomerular blood flow and filtration, tubular secretion, reabsorption, and renal bioactivation and metabolism. Drug absorption, bioavailability, protein binding, distribution volume, and metabolism also can be altered in these patients. Surgeons should pay careful attention when considering drug therapies with active or toxic metabolites that can accumulate and contribute to exaggerated pharmacologic effects or adverse drug reactions in patients with CKD. Dosages of drugs cleared renally should be adjusted according to creatinine clearance or GFR and should be calculated accordingly (see Table 5.7).

5.6.6.1 Antimicrobials

Many antimicrobial agents are eliminated renally and require dosing adjustments in patients with CKD; however, most of the commonly used agents used in an oral and maxillofacial surgical setting do not require adjustments. Excessive serum levels of injectable penicillin G in patients with kidney disease have been associated with neuromuscular toxicity, myoclonus, seizures, or coma [26]. Failure to adjust the dosing of Imipenem/cilastatin in patients with CKD can cause severe seizures [27]. Meropenum has been shown to have a better tolerance for patients with advanced disease [28]. Tetracyclines, with the exception of doxycycline, worsen renal impairment by inhibiting protein synthesis and have been associated with worsening kidney injury in a surgical setting [29]. Nitrofurantoin has a toxic metabolite that can accumulate in patients with chronic kidney disease, causing peripheral neuritis [30]. Aminoglycosides should be avoided in patients with chronic kidney disease when possible. If used, initial doses should be based on an accurate GFR estimate. Renal function and drug

Table 5.7 Medication dosing requirements in patients with chronic kidney disease

Dosage adjustment (% of usual dosage) based on GFR (mL/min/1.73 m²)				
Drug	**Usual dosage**	**>50**	**10–50**	**<10**
Ace inhibitors				
Captopril	25 mg q8h	100%	50–75%	25–50%
Enalapril	5–10 mg q12h	100%	75%	50%
Lisinopril	5–10 mg q12h	100%	50–75%	25–50%
Analgesics				
Acetaminophen	325–650 q4h	100%	q6h	q8h
Aspirin	650 mg q6h	100%	50%	Avoid
Codeine	30–60 mg q4–6h	100%	75%	Avoid
Fentanyl	(per indication)	100%	75%	50%
Hydromorphone	2–4 mg q4–6h	50–100%	50%	25%
Hydrocodone	2.5–10 mg q4–6h	100%	75–100% q8h	50% q8h
Ibuprofen	400–800 mg q8h	100%	Avoid	Avoid
Ketorolac	30–60 mg q6h	50%	Avoid	Avoid
Ketamine	(per indication)	100%	100%	100%
Meperidine	50 mg q4h	100%	75%	Avoid
Morphine	(per indication)	100%	50–75%	Avoid
Oxycodone	2.5–10 mg q4–6h	100%	75–100% q8h	50% q8h
Tramadol	50–100 mg q6h	100%	50% q6–12h	Avoid
Beta-blockers				
Acebutolol	400–600 mg daily	100%	50%	30–50%
Atenolol	5–100 mg daily	100%	50%	25%
Atenolol	40–80 mg daily	100%	50%	25%
Diuretics				
Amiloride	5 mg daily	100%	50%	Avoid
Bumetanide	No adjustment	–	–	–
Furosemide	No adjustment	–	–	–
Metolazone	No adjustment	–	–	–
Spironolactone	50–100 mg daily	q6–12h	q12–24 h	Avoid
Thiazides	25–50 mg daily	100%	100%	Avoid
Torsemide	No adjustment	–	–	–
Antifungals				
Fluconazole	200–400 mg q24h	100%	50%	50%
Ketoconazole	No adjustment	–	–	–
Miconazole	No adjustment	–	–	–
Antivirals				
Acyclovir	200–800 mg q4–12h	100%	100%	200 mg q12h
Valacyclovir	500–1000 mg q8–12h	100%	100%	500 mg q24h
Dosage adjustment (% of usual dosage) based on GFR (mL/min/1.73 m²)				
Drug	**Usual dosage**	**>50**	**10–50**	**<10**
Carbapenems				
Ertapenem	1 g q24h	100%	100%	50%
Imipenem	0.25–1 g q12h	100%	50%	25%
Meropenem	1–2 g q8h	100%	50% q12h	50% q24h
Cephalosporins				
Cefaclor	250–500 mg q8h	100%	50–100%	50%
Cefadroxil	0.5–1 g q12h	100%	q12–24 h	q36h
Cefazolin	0.25–2 g q6h	q8h	q12h	50 q24–48 h
Cefepime	0.25–2 g q8–12h	100%	50–100% q24h	25–50% q24

Table 5.7 (continued)

Cefixime	200 mg q24h	100%	75%	50%
Cefotaxime	1–2 g q6–12h	q6h	q6–12h	q24h or 50%
Cefoxitin	1–2 g q6–8h	q6–8h	q8–12h	q24–48 h
Ceftriaxone	No adjustment	–	–	–
Cephalexin	250–500 mg q6–8h	q8h	q8–12h	q12–24 h
Macrolides				
Azithromycin	No adjustment	–	–	–
Clarithromycin	250–500 mg q12h	100%	50–100%	50%
Erythromycin	No adjustment	–	–	–
Penicillins				
Amoxicillin	250–500 mg q8h	100%	q8–12h	q24h
Ampicillin	0.25–2 g q6h	100%	q6–12h	q12–24 h
Ampicillin/sulbactam 1–2 g q6h	100%	q12h	q24h	
Dicloxacillin	No adjustment	–	–	–
Nafcillin	No adjustment	–	–	–
Penicillin G	0.5–four million U q4–6h	100%	75%	20–50%
Penicillin VK	No adjustment	–	–	–
Piperacillin	3–4 g q6h	q6h	q6–12h	q12h
Piperacillin/tazobactam	3.37–4.5 g q6–8h	100%	2.25 g q6–8h	2.25 g q8h
Quinolones				
Ciprofloxacin	500–750 mg q12h	100%	50–75%	50%
Levofloxacin	250–750 mg q24h	100%	q24–48 h	250–500 mg q48h
Moxifloxacin	No adjustment	–	–	–
Sulfas				
Sulfamethoxazole	1 g q8–12h	q12h	q18h	q24h
Trimethoprim	100 mg q12h	100%	q12–18 h	q24h
Tetracyclines				
Doxycycline	No adjustment	–	–	–
Tetracycline	250–500 mg q6–12h	q8–12h	q12–24 h	q24h
Dosage adjustment (% of usual dosage) based on GFR (mL/min/1.73 m^2)				
Drug	**Usual dosage**	**>50**	**10–50**	**<10**
Other antimicrobials				
Chloramphenicol	No adjustment	–	–	–
Clindamycin	No adjustment	–	–	–
Linezolid	No adjustment	–	–	–
Nitrofuratoin	500–1000 mg q6h	100%	Avoid	Avoid
Other common agents				
Esomeprazole	No adjustment	–	–	–
Famotidine	20–40 mg nightly	50%	25%	10%
Gabapentin	300–900 mg TID	600 mg q12h	600 q24h	300q24h
Lansoprazole	No adjustment	–	–	–
Metoclopramide	10–15 mg TID	100%	75%	50%
Omeprazole	No adjustment	–	–	–
Ranitidine	150–300 mg nightly	75%	50%	25%

Munar MY, Singh H. Drug dosing adjustments in patients with chronic kidney disease. Am Fam Physician. 2007;75(10):1487–96

Gelot S, Nakhla E. Opioid Dosing in Renal and Hepatic Impairment. US Pharm. 2014;39(8):34–38

concentrations should be monitored and dosages adjusted accordingly.

5.6.6.2 Analgesics

Patients with ESRD are more likely to experience adverse effects from opioid use. Metabolites of meperidine, morphine, tramadol, and codeine can accumulate in patients with chronic kidney disease, causing central nervous system and respiratory adverse effects [31]. In general these agents are not recommended or used on a case-by-case-basis with caution in patients with stage 4 or 5 disease. A 50–75% dose reduction for morphine and codeine is recommended in patients with a creatinine clearance less than 50 mL/min. Extended-release tramadol should also be avoided in patients with chronic kidney disease. The dosing interval of tramadol (regular release) may need to be increased to every 12 h in patients with a creatinine clearance less than 30 mL/min [32]. Acetaminophen can generally be used safely in patients with renal impairment.

5.6.6.3 NSAIDS

Adverse renal effects of NSAIDs can be detrimental in renally compromised patients. The risk of acute renal failure is three times higher in NSAID users than in non-NSAID users [33]. Other adverse effects of NSAIDs include decreased potassium excretion leading to hyperkalemia and decreased sodium excretion which can exacerbate peripheral edema and hypertension. NSAIDs can blunt antihypertensive treatment, especially if beta-blockers, ACE inhibitors, or ARBs are used [34]. Although selective cyclooxygenase-2 (COX-2) inhibitors may cause slightly fewer adverse gastrointestinal effects, adverse renal effects are similar to traditional NSAIDs [34].

Short-term use of NSAIDs is generally safe in patients who are well hydrated with good renal function and who do not have heart failure, diabetes, or hypertension. Long-term use and high daily dosages of COX-2 inhibitors and other NSAIDs should be avoided if possible. Patients at high risk of NSAID-induced kidney disease should receive serum creatinine measurements every 2–4 weeks for several weeks after initiation of therapy because renal insufficiency may occur early in the course of therapy [35].

5.6.6.4 Anesthetic Agents

The direct effects of anesthetics on renal function are minor compared with the medications described above. Local anesthetics including lidocaine, articaine, mepivacaine, and prilocaine are generally safe to use within standard dosing guidelines. However, metabolic acidosis in patients with CKD or ESRD may decrease the effectiveness of some local anesthetics.[36] Inhalational anesthetics such as halothane, isoflurane, sevoflurane, and desflurane all cause a decrease in renal vascular resistance. Of special concern, the metabolite of sevoflurane (compound A), has shown to cause acute kidney injury in laboratory animals. This can be avoided by assuring a continuous fresh gas flow rate to prevent its accumulation in the anesthesia breathing circuit. No clinical study has detected kidney injury in humans as a consequence of sevoflurane anesthesia; however a fresh gas flow of at least 2 L/min with sevoflurane is recommended to minimize the risk of this theoretical problem [36]. Intravenous opioids and propofol exhibit minor, if any, effects on the kidney when used alone. Ketamine minimally affects kidney function and may serve a role to preserve kidney function during hemorrhagic hypovolemia. Regardless of the anesthesia used, proper consultation and medical clearance should be ensured prior to surgery.

5.6.6.5 Other Medications

Treatment planning and diagnosis in oral and maxillofacial pathology and trauma often requires the use of imaging with radiocontrast agents. Unfortunately, radiocontrast dye can adversely affect kidney function, especially in the setting of preexisting renal dysfunction. Radiocontrast agents are probably the most common cause of AKI in the acute care setting. In addition to intravenous hydration, pretreatment with *N*-acetylcysteine (600 mg orally every 12 h in four doses beginning prior to contrast administration) has been shown to decrease the risk of radiocontrast agent-induced AKI in patients with

preexisting renal dysfunction [37]. Even though there in no standardization or long-term outcome reviews of this protocols, each institution implements a protocol with prehydration and contrast dose optimization being the key.

5.6.7 Considerations of Patients with Kidney Transplantation

The medical advancements of renal transplantation in the twentieth century have dramatically improved the quality of life of thousands of patients who suffered from chronic end-stage kidney disease. As the life expectancy and total population of renal transplant patients increase, the need of such patients who will seek long-term oral and surgical rehabilitation is becoming more common. Using the guidelines previously discussed, an oral and maxillofacial surgeon plays an important role in the preparation of renal transplantation and also in the continuation of long-term oral rehabilitation. The following considerations will be discussed to aid in the prevention of complications in treatment of these high-risk patients.

Prior to transplantation, the patient's oral health must be optimized and free from any source of possible infection.

In preparation to receive the transplant, the patient is given chronic immunosuppressive medications in an effort to prevent posttransplantation organ rejection. The basis of most immunosuppressive regimens is prednisolone, which is a corticosteroid. Prednisolone suppresses the immune system, but it is usually insufficient by itself to prevent the rejection of the kidney transplant. For this reason, prednisolone is commonly administered in with other nonsteroid immunosuppressive medicines. The most common pharmaceutical regimen currently is a combination of tacrolimus, mycophenolate, and prednisolone. Other regimens include cyclosporine, sirolimus, or azathioprine [38]. While this helps reduce odds of rejection, the ability of the body to cope with systemic infections is also reduced. For this reason, teeth with poor prognosis, which could become sources of bacteremia if left in place, are extracted [39]. Considering the patient's state of immunosuppression in combination with chronic corticosteroid use, antibiotic prophylaxis in addition to a stress dose of steroids should be considered prior to having any invasive oral surgical procedure. Throughout the international bibliography, there are no clear guidelines as to if and when prophylactic antibiotic therapy should be given to transplant patients who are about to undergo oral surgery procedures, in order to prevent transient bacteremia. Through a research questionnaire that was given to a large number of physicians who work in transplant centers in the United States, most physicians stated that they recommend the use of prophylactic antibiotic therapy to all the patients that have been subjected to transplantation prior to any invasive oral procedure. The majority of these physicians adhere to the AHA's standard regimen to prevent endocarditis as a suggested prophylactic therapy [40].

A large number of transplant patients also suffer from hypertension, diabetes, or cardiovascular diseases, so it is essential for them to receive anticoagulant/antiplatelet treatment. If the transplant patient is administered coumarin anticoagulants, a recent INR should be required before surgery. If the INR is above 2.5, there should be a consultation with the nephrologist for dosing adjustments. In the case that the patient receives antiplatelet treatment with aspirin or clopidogrel, minor surgical procedures can typically be done without medication adjustments [41]. For moderate to major surgical procedures, the patient's physician may recommend stopping all antiplatelet medication. If this is suggested, they should be held 5–7 days before and after the scheduled surgery, always in consultation with the treating doctor who administers the medication [41, 42].

The first 6 months following transplantation is a very critical period that requires careful consideration before any surgical procedure should take place. During this period of time, transplant patients receive the highest dosage of immunosuppressive medicines because they are at a higher risk of rejecting the transplant, in addition to developing serious complications. For this reason, only emergency procedures should be con-

sidered and only after the treating nephrologist has been informed [43].

Six months to 1 year following transplantation, it is generally considered safe to perform most oral surgical procedures. This includes all minor surgical procedures, extractions, bone grafting, and even implant placement. A recent study reviewing bone grafting and implant placement in posttransplant patients receiving chronic immunosuppressant medications showed no difference in implant stability and bone loss in comparison to healthy people [44]. The study also demonstrated that corticosteroid therapy had no influence on the effect of dental implant treatment, either at the bone level or soft tissues. Cyclosporin, however, tends to commonly cause diffuse gingival enlargement; therefore implant placement and bone grafting would be delayed unless this medication was discontinued. In general, patients with organ transplants can safely and effectively undergo dental implant treatment. The condition is to adhere to appropriate procedures, and postoperative checkups, and the considerations listed in this chapter.

An additional consideration of transplant/immunosuppressed patients is strict surveillance for oral lesions and malignancies. Many complications and malignancies that are connected with immunosuppressive pharmaceutical therapy are manifested in the mouth. Infections such as candidiasis and secondary recurrent oral herpes tend to appear more often [45]. Malignancies can occur decades earlier in immunosuppressed patients than in the rest of the general population. After kidney transplantation, transplant recipients have been shown to have high susceptibility to developing epithelial dysplasia and squamous cell carcinoma of the lip, as well as viruses that are related to tumors, such as Kaposi's sarcoma and non-Hodgkin lymphoma [46].

In summary, identification and risk stratification is crucial for the perioperative management of patients with kidney disease. To improve clinical outcomes, nonemergent procedures should be postponed, renal function optimized, nephrotoxic drugs avoided, and further kidney injury must be avoided.

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The Immunocompromised Patient

6

Cory M. Resnick

6.1 Introduction

The availability and predictability of organ transplantation, biologic medications for rheumatoid diseases, and other treatments affecting the immune response have burgeoned in recent decades. For example, over 28,000 solid organ transplant operations were performed annually from 2009 to 2013 in the United States [1], and the average life expectancy of transplant recipients now exceeds 10 years [2]. As such, the need to provide outpatient surgical treatment to immunocompromised patients has increased.

Patients may be immunocompromised from a disease, such as human immunodeficiency virus (HIV) or cancer, or from medications, such as immunosuppressive therapy after organ transplantation or for management of autoimmune disease. Moreover, immunomodulation occurs in every patient, including those with normally functioning immune systems, around the time of an insult or operation [3].

Immunodeficiencies are broadly categorized as congenital or acquired. Congenital (primary) immunodeficiencies are typically identified in children and include disorders that impair one or more components of the natural immune response. These include defects of the phagocytic cell (e.g., hyperimmunoglobulinemia and glucose-6-phosphate dehydrogenase deficiency), complement protein abnormalities (e.g., C1 esterase inhibitor deficiency), T-lymphocyte abnormalities (e.g., 22q11.2 deletion syndrome), T-cell and B-cell combined immunodeficiencies (e.g., severe combined immunodeficiency), and antibody defects (e.g., X-linked agammaglobulinemia) [4]. Acquired (secondary) immunodeficiencies occur due to impaired function of one or more organ systems. Examples include diabetes mellitus (endocrine), hepatic insufficiency (gastrointestinal system), HIV, cytomegalovirus, Epstein-Barr virus (infectious), alcoholism and malnutrition (nutritional), nephrotic system and renal insufficiency (renal), rheumatoid arthritis and systemic lupus erythematosus (rheumatologic), and iatrogenic causes (e.g., medication treatment) [3].

The following patient populations may require special consideration for outpatient surgical treatment.

6.2 Rheumatologic Disease

More than 40 million Americans suffer from rheumatologic diseases, and over eight million of them are considered disabled [5]. Over 100 rheumatologic diseases that affect bones, joints, and

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muscles have been identified. Rheumatoid arthritis (RA) is the most common of these in adults, and juvenile idiopathic arthritis (JIA) is the most common chronic rheumatologic disease of children. Systemic lupus erythematous, scleroderma, Sjögren syndrome, gout, ankylosing spondylitis, lyme disease, and giant cell arteritis are other common rheumatologic diagnoses.

RA is an autoimmune disease of unknown etiology. It can affect any joint, but most typically involves the hands, feet, and knees. RA occurs more commonly in females than males and is typically diagnosed between the ages of 35 and 50 years. The disease leads to microvascular endothelial cell activation and injury, primarily affecting the synovial joint lining. This causes slowly progressive joint destruction, pain, and immobility. JIA, which is a distinct entity different from RA, is an autoimmune arthritis that occurs in children under age 16 years and has similar destructive impact. The temporomandibular joints are frequently involved in both RA and JIA [6].

Patients with rheumatologic diseases may be managed with antirheumatic medications. Medication therapy is generally divided in to two types: (1) drugs that decrease joint pain and swelling but have little or no effect on the disease course or joint damage and (2) drugs intended to decrease disease activity and joint damage. The most common class of drugs employed for pain and swelling are nonsteroidal anti-inflammatory drugs (NSAIDs). Corticosteroids are also used when acute control of inflammation is necessary.

Disease-modifying antirheumatic drugs (DMARDs) are a class of medications intended to alter the course of the arthritic disease and decrease joint damage. The most common of these is the antimetabolite methotrexate, which inhibits the enzyme dihydrofolic reductase, thereby blocking the activation of folic acid. Others include hydroxychloroquine, sulfasalazine, leflunomide, and azathioprine. DMARDs are typically initiated early in the arthritis course in order to prevent future joint destruction.

Biologic medications are drugs that target a specific molecular mediator in the inflammatory cascade. Examples include adalimumab (Humira), etanercept (Enbrel), infliximab (Remicade), abatacept (Orencia), anakinra (Kineret), certolizumab (Cimzia), golimumab (Simponi), and rituximab (Rituxan). Biologic medications have been shown to slow the progression of RA even when all other treatments have failed [7].

Some special considerations are necessary when planning surgical care for patients with rheumatologic diseases:

- Potential for excessive bleeding in light of NSAID treatment. Combination treatment with NSAIDs and corticosteroids can further increase this risk.
- Corticosteroid treatment may be associated with adrenal suppression, and stress dose steroids may be indicated.
- Immunosuppressive drugs can cause bone marrow suppression, resulting in anemia, agranulocytosis, and thrombocytopenia; a current complete blood count should be obtained prior to surgical treatment.
- Many patients with RA will have prosthetic joint replacements. While prophylactic antibiotics are generally not recommended before invasive procedures, a conversation with the orthopedic surgeon regarding specific indications for antibiotic coverage may be prudent.
- Patients taking immunosuppressive drugs, particularly biologic medications, are at increased risk for postoperative surgical site infections. Recommendations for perioperative medication alteration, however, are variable and primarily based on expert opinion rather than scientific evidence. The British Society of Rheumatology recommends holding biologic medications for 2–4 weeks before an operation, and not restarting until here is good wound healing without infection. The French Society for Rheumatology recommends holding biologic medications for 5 half-lives prior to an operation, resulting in a different amount of time for each drug. The American College of Rheumatology recommends holding these medications for 1 week prior and 1 week after an operation [8]. Based on a systematic review of available literature

Table 6.1 Recommendations for holding of biologic medications prior to an operation

Medication	Holding recommendation prior to an operation
TNF-alpha inhibitor	1 dose
Tocilizumab (IL-6 receptor antagonist)	1 dose
Anakinra (IL-1 antagonist)	1 week
Abatacept (CTL4Ig blocker)	1 month
Rituximab (CD20 antibody)	3–6 months

by Polachek, Caspi, and Elkayam in 2012 [8], in combination with the biologic properties of each medication, specific recommendations for holding of medications prior to an operation were developed and are shown in Table 6.1. These authors recommend restarting medications after surgery "in the absence of infection and when wound healing is satisfactory" [8].

6.3 Organ Transplantation

Since the first successful human organ transplant procedure was performed by Joseph E. Murray in 1954, solid organ transplant has saved an improved the lives of countless patients. More than 10,000 renal transplantations, the most common solid organ transplant, are now performed annually in the United States, and more than 75,000 occur each year worldwide [9]. As the 5-year survival rates after renal, heart, and liver transplantation are now above 90% [9], 75% [10] and 70% [11], respectively, clinicians can expect to see increasing numbers of transplant patients seeking outpatient surgical care. Prior transplantation increases the risk for mortality after non-transplant-related surgery [12].

Despite the life-saving effects of organ transplantation, the associated transfer of foreign antigens requires the lifelong use of immunosuppressive medications. Medications that depress the natural immune system non-specifically block T- and B-cell activity and innate immunity effector cells. This significantly increases the patient's risk for infection. Moreover, due to the suppressive effects of these medications, typical signs and symptoms of infection that would be seen in an immunocompetent patient may be subtle or absent [13].

Shortly after transplantation, nosocomial and opportunistic infections, such as methicillin-resistant *Staphylococcus aureus* and aspergillus, are most common. From 1 to 6 months after transplantation, when immunosuppression is most profound, the risk for opportunistic infections such as invasive fungal infections is high, and reactivation of latent infections such as cytomegalovirus is common. After 6 months post-transplant, pathogens are more likely to lead to typical community-acquired infections such as pneumonia and urinary tract infections, though they may have a more profound effect in patients with transplants than they would in otherwise healthy individuals [13].

When planning an outpatient procedure in a patient with prior solid organ transplantation, the surgeon must consider:

- Appropriate timing for the procedure to avoid the highest period shortly after transplantation.
- Potential for infection. While there are no universal guidelines for prophylaxis against infection when performing an operation unrelated to the transplanted organ in patients with a history of a transplant, the increased risk for infection at the surgical site as well as the potential for bacterial seeding of the transplanted organ must be considered. A conversation about antibiotic prophylaxis with the transplant team is critical prior to any elective procedure.
- Potential side effects of the immunosuppressive agents. The major classes of immunosuppressive drugs used in this population include corticosteroids, calcineurin inhibitors, nucleoside inhibitors, and antibodies. Each has specific additional side effects that require consideration. Corticosteroids such as prednisone, for example, have a side effect profile that includes hyperglycemia, hypertension, hyperlipidemia, osteoporosis, and avascular

necrosis. Calcineurin inhibitors such as cyclosporin and tacrolimus can cause renal injury, thereby affecting anesthetic and analgesic medication clearance. Nucleoside inhibitors including azathioprine and mycophenolate mofetil may cause myelosuppression, leukopenia, and anemia. Other common immunosuppressive medications such as mammalian target of rapamycin (mTOR) inhibitors including sirolimus and everolimus are associated with cytopenia and hyperlipidemia.

- The health and function of the transplanted organ and other related systems prior to engaging in elective surgical care. Renal function, for example, will have a significant effect on clearance of anesthetic and analgesic medications. Depending on organ function, medications may require dosing alteration, and/or an inpatient setting may be more appropriate for elective surgery.

6.4 HIV

The retrovirus later named the human immunodeficiency virus (HIV) was first identified in 1983 as the causative agent for the acquired immunodeficiency syndrome (AIDS). Since that time, more than 70 million people have been infected with HIV, and more than 30 million have died from AIDS [13, 14]. Survival and quality of life for patients living with HIV has dramatically increased since the introduction of antiretroviral drugs. As such, many patients with HIV will seek outpatient surgical care [15]. Perioperative considerations include both the effects of the HIV infection itself and of medications used to treat the HIV.

In untreated patients with HIV infection and in those in whom treatment is ineffective, the number of T helper lymphocytes (CD4+ cells) continually declines, thereby impairing the natural immune response to infection. When the CD4+ count drops below 200 cells/μL, the infected patient is considered to have AIDS and is increasingly susceptible to opportunistic infections including pneumocystis pneumonia, toxoplasmosis, histoplasmosis, cytomegalovirus, and others. When CD4+ levels drop below threshold levels, patients may be treated with chemoprophylaxis (i.e., antibiotics, vaccination) to reduce the risk for opportunistic infections.

The 4 most commonly used medication classes in treatment of HIV include (1) nucleoside and nucleotide reverse transcriptase inhibitors (NRTI and NtRTI), (2) non-nucleoside reverse transcriptase inhibitors (NNRTI), (3) protease inhibitors, and (4) fusion inhibitors. These medications are typically provided in combination, utilizing a therapeutic philosophy termed highly active antiretroviral therapy (HAART). Upon introduction of HAART, there is typically an acute increase in CD4+ counts, and, in some patients, this is associated with a clinical deterioration termed immune recovery syndrome [3]. The clinician should be cognizant of this phenomenon and avoid elective surgical treatment around this time.

When considering outpatient surgical management of a patient with HIV, the clinician should:

- Obtain a serum CD4+ count and viral load. In patients with severe immunosuppression, neutropenia (white blood cell count <500/μL) may increase the risk for postoperative infection, and thrombocytopenia can lead to excessive bleeding. Patients that are seropositive for HIV but with CD4+ counts above 350 cells/μL and low or undetectable viral loads, however, can generally be managed without alteration to standard surgical techniques and without additional prophylaxis against postoperative infection.
- Obtain a complete list of antiretroviral medications and understand their potential impact on anesthetic management, wound healing, and infection. There are several dose-related phenomena associated with HAART that may affect outpatient surgical treatment. One is mitochondrial toxicity which can produce lactic acidemia and lipodystrophy, with the latter leading to the potential for airway compromise due to excessive fat deposits in the pharynx [16]. Additionally, HAART may be associated with insulin resistance,

hepatotoxicity, nephrotoxicity, myelosuppression, and/or anemia.
- Consider the potential for medication interactions between anesthetic and prescribed medications and the patient's home regimen.
- Avoid elective procedures shortly after initiation of HAART.
- Use standard precautions for sterility and prevention of needle stick injury for all patients.

6.5 Cancer

Cancer and its treatment may have a profound effect on general health and the response to anesthesia and surgery. When managing a patient with cancer, discussion with the primary care provider and/or oncologist is critical. The surgeon must investigate:

- Current and prior chemotherapeutic agents that the patient has been exposed to. Some agents are associated with known side effects such as pulmonary, cardiac, and/or hepatorenal toxicity.
- The best timing for surgical treatment, for instance, to avoid a leukopenic nadir during chemotherapy treatment.
- Potential need for modification of anesthetic and analgesic medication doses if renal and/or hepatic clearance are impaired.
- The appropriateness of outpatient management must be considered in the context of the patient's general health.

6.6 Congenital (Primary) Immunodeficiencies

Primary immunodeficiencies are a series of disorders affecting components of the immune system and are categorized based on the affected cell line. They are broadly separated into disorders of the innate and adaptive immune systems.

Diseases of the innate immune system are less common than those of the adaptive system. These include phagocytic disorders (e.g., chronic granulomatous disease and leukocyte adhesion deficiency), complement deficiencies, and disorders of cellular signaling. Diseases of the innate immune system are often recognized in childhood due to frequent infections from common pathogens or unusually severe infections.

Disorders of the adaptive immune system affect B cells, T cells, or both. Antibody deficiencies (B-cell disorders) are the most common of the primary immunodeficiencies. These usually become evident around 5–7 months of age when maternal IgG decreases. Affected children tend to have recurrent infections from encapsulated organisms. The most common antibody disorders are *X-linked agammaglobulinemia*, which is the most severe of these diseases and results in a deficiency in all major classes of antibodies; *common variable immunodeficiency*, which often has a later onset (18 months of age or older) and variable presentation with IgG and IgA most commonly deficient; and *IgA deficiency*, which is the most common and also least impactful of the antibody deficiencies.

T-cell disorders increase susceptibility to infections by intracellular pathogens such as cytomegalovirus, *Candida*, and *Pneumocystis jiroveci* [4]. As antibody production is supported by T helper cells, some degree of B-cell dysfunction is common in patients with T-cell disorders. *Severe combined immunodeficiency syndromes* (SCID) is a group of genetic diseases characterized by a complete lack of T-cell function. Some also affect B cells and NK cells. SCID is typically fatal within the first few years of life without bone marrow or stem cell transplantation. *22q11.2 deletion syndrome*, sometimes called DiGeorge syndrome or velocardiofacial syndrome, is a developmental syndrome affecting the third and fourth pharyngeal arches and resulting in characteristic facial and cardiac anomalies. In addition, patients with 22q11.2 deletion syndrome have a variable T-cell deficiency, possibly due to a hypoplastic thymus. This improves spontaneously during growth, typically normalizing by age 2 years. *Wiskott-Aldrich Syndrome* is an X-linked disorder characterized by the triad of eczema, thrombocytopenia, and recurrent infections. T-cell counts are normal at birth but decrease over the first decade of life, and IgM levels are decreased. IVIG therapy is often used to prevent recurrent bacterial infections, but bone

marrow transplantation is the only cure. *Ataxia-telangiectasia* is an autosomal recessive disorder caused by a mutation in the ATM gene, affecting protein stability and DNA repair.

Patients with ataxia-telangiectasia have gross motor dysfunction (ataxia) that presents around the age of 2 years. Later, they have oculocutaneous telangiectasia and a progressive immunodeficiency affecting both T cells and B cells which becomes apparent after the age of 3 years. Recurrent respiratory infections and chronic lung disease are common and can be treated with IVIG. T- and B-cell malignancies are common, and these patients have increased susceptibility to ionizing radiation.

In management of a child or adult with a primary immunodeficiency:

- The nature of the deficiency and susceptibility to infection must be considered.
- Ascetic technique is critical.
- Prophylactic coverage with broad spectrum antibiotics may be indicated.
- Appropriateness for outpatient versus inpatient care must be evaluated.

6.7 Summary

Many patients presenting for outpatient surgical care are immunocompromised, due either to a disease or from medical treatment. Some will appear healthy, and a thorough history will be necessary to uncover the nature of their immunodeficiency. Close collaboration with primary care and specialty physicians to fully understand the state of their immune system and plan for appropriate management is critical.

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7 Metabolic Disorders in the Oral and Maxillofacial Surgical Patient

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7.1 Pituitary Gland Disorders

Many endocrine functions are modulated by the hypothalamic interaction with and regulatory function of anterior pituitary gland function. The hypothalamus produces the releasing hormones thyrotropin-releasing hormone (TRH), corticotropin-releasing hormone (CRH), and gonadotropin-releasing hormone (GnRH). It is also the site of prolactin inhibitory factor production. Secretion of the hypothalamic-releasing hormones stimulates production of trophic hormones by the anterior pituitary gland with feedback from target glands. The hormones produced by the anterior pituitary include thyroid-stimulating hormone (TSH), adrenocorticotrophic hormone (ACTH), growth hormone (GH), luteinizing hormone (LH), follicle-stimulating hormone (FSH), and prolactin. Prolactin release is stimulated postpartum by oxytocin release and infant suckling. The release of hypothalamic prolactin inhibitory factor serves to downregulate the release of prolactin to prevent excesses as well as to curtail breast milk production when nursing has ceased. The posterior pituitary gland has direct neural regulation by the hypothalamus and is the site of production of oxytocin and vasopressin.

7.1.1 Anterior Pituitary Hyperfunction

Disorders of anterior pituitary hyperfunction are often expressed as a result of excessive secretion of the trophic hormones. These disorders of hyperfunction are often the result of adenomas, microadenomas, or hyperplasia. Excessive growth hormone (GH) production often results from acidophil adenoma development with manifestations including gigantism when overproduction of GH occurs in childhood. Acromegaly results from GH overproduction in adulthood with clinical features consisting of coarsening facies, thickened lips, and enlargement of the hands and feet. Impaired glucose tolerance may occur as well as increased risk of developing type 2 diabetes mellitus in those afflicted with acromegaly [1].

Hypercorticism results from overproduction of ACTH due to several potential mechanisms including hypothalamic overproduction of CRH, basophil pituitary adenomas, pituitary microadenomas, or by ectopic ACTH production. In the Cushing disease, ACTH produced in excess by the pituitary leads to excessive production of cortisol by the adrenal cortex. Excessive prolactin production or hyperprolactinemia typically

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results from pituitary adenomas, microadenomas, or hyperplasia. One clinical manifestation that may be seen in affected females is the amenorrhea—galactorrhea syndrome with manifestations including inducible or spontaneous galactorrhea and secondary amenorrhea [1].

7.1.2 Anterior Pituitary Hypofunction

Disorders of pituitary hypofunction are numerous. They may occur as isolated hormonal deficiencies which rarely present. More commonly, global hypofunction may result in producing panhypopituitarism with multiple clinical features. These clinical features are imposed by deficiency of the pituitary hormones resulting in conditions which include hypothyroidism, adrenal insufficiency, hypogonadism, growth failure, or dwarfism. In addition, deficient production of posterior pituitary hormones vasopressin and oxytocin occurs. The causes of panhypopituitarism include the following [1]:

- Tumor compression—primary, metastasis, neighboring tumor
- Iatrogenic: surgical removal; irradiation
- Infarction
- Sarcoidosis
- Empty sella syndrome—etiology unknown

Consultation with specialists in endocrinology is necessary from the onset of this disorder which may result in critical illness in the case of deficiencies in thyroid hormone, ACTH, and vasopressin. Careful replacement therapy is essential throughout life to prevent acute decompensation and to ameliorate lifelong disease manifestations. In patients affected by trauma, severe illness, or in the surgical perioperative phase, stress dosing with corticosteroids should receive high priority.

7.1.3 Posterior Pituitary Disorders

Disorders of the posterior pituitary gland may occur, resulting in derangement in production of oxytocin and vasopressin. Oxytocin is released during active labor resulting in stimulation of uterine contraction and initiation of lactation postpartum. Vasopressin (ADH) plays a major role in regulation of serum osmolarity and blood pressure. Etiologies of ADH deficiency include tumors, irradiation, vascular compromise, trauma, and surgical alteration [1]. Neurogenic or central diabetes insipidus may occur with clinical features of massive polyuria (dilute urine) and serum hyperosmolarity. Critical care management of the underlying cause as well as aggressive targeted fluid and electrolyte management is essential. In addition, administration of vasopressin in the form of DDAVP is critical in the management of these patients to correct hypovolemia and hypernatremia.

Disorders with excessive ADH production may result from brain trauma, stroke, and certain drugs. Pulmonary diseases such as tuberculosis and pneumonia may also result in ADH excess. Malignant diseases may be a source of ectopic ADH production including carcinoma of the pancreas or oat cell carcinoma of the lung [1]. Excessive ADH production results in clinical manifestation of the syndrome of inappropriate antidiuretic hormone (SIADH) with features including oliguria (concentrated urine), hyponatremia, and serum hypoosmolarity. These patients must be managed in the critical care setting with targeted fluid and electrolyte management to treat fluid retention and hyponatremia.

7.2 Adrenal Gland Disorders

Anatomically the adrenal glands are located at the superior pole of the kidneys. Histologically the glands are composed of an outer cortex and an inner medulla. The adrenal cortex is further subdivided into three zones. The outermost zone of the adrenal cortex is the zona glomerulosa. The zona glomerulosa is the primary site of production of the mineralocorticoid aldosterone. Within the intermediate zone, the zona fasciculata, production of the glucocorticoid, cortisol, occurs. The innermost zone is the zona reticularis which is the site of production of the androgens and estrogens.

The adrenal glands are part of the hypothalamic-pituitary-adrenal (HPA) axis which functions in a feedback loop, by which adrenal glandular secretion is normally regulated. Adrenal hypofunction can be of a primary form in which the etiology is dysfunction or destruction of the gland. Secondary forms occur in which HPA dysfunction occurs with diminished ACTH stimulation of the adrenal glands. Secondary adrenal hypofunction may also result from exogenous steroid administration, leading to HPA suppression [1].

7.2.1 Adrenal Insufficiency

Addison's disease is the clinical manifestation of primary adrenal insufficiency which may include:

- Hyperpigmentation of exposed skin, skin creases, and oral mucosa
- Glucocorticoid deficiency—hypoglycemia, anorexia, nausea, weight loss, lethargy, confusion, stress intolerance
- Mineralocorticoid (aldosterone) deficiency—hyponatremia, hyperkalemia, hypovolemia, hypotension, dysrhythmias, stress intolerance

Sources of primary adrenal insufficiency are myriad. This includes autoimmune destruction, infarction, and hemorrhage. Infiltrative processes such as primary tumors, metastatic tumors, or amyloidosis may lead to adrenal insufficiency. Surgical removal also commonly results in adrenal insufficiency. Infectious etiologies of primary adrenal insufficiency include tuberculosis or fungal disease [2].

Perioperative prevention of an acute adrenal crisis is of utmost priority. Physiologic stresses including acute trauma, general anesthesia, major surgery, and critical illness including severe odontogenic infections are common precipitating events. Exogenous steroids are administered for a constellation of diseases and can have lasting negative effects upon the HPA axis. Prevention is predicated upon clinicians having complete familiarity with the patient's medical history, including knowledge of past and present steroid administration. Preventive strategies include dosing regimens that employ alternate day therapy, which generally have less of an effect upon the HPA axis. Steroid-sparing therapies and those which use the lowest doses for the minimum duration also serve to ameliorate impairment of the HPA axis. Recovery of the HPA axis may take at least 1 year after withdrawal of exogenous steroids. Patients at risk should be referred for endocrinology consultation where history and physical and laboratory studies including basal a.m. cortisol levels and ACTH stimulation testing will reveal if the patient is at risk. Low basal cortisol and ACTH stimulated cortisol levels indicate adrenal insufficiency [2]. Those who rule in require lifelong glucocorticoid and mineralocorticoid replacement therapy as well as perioperative stress dose protocols.

Stress dosing may take the following forms:

Mild (fever, minor illness)—40–60 mg hydrocortisone

Moderate (influenza, minor surgery, mild to moderate infection)—100 mg hydrocortisone tapering to maintenance dose

Severe (general anesthesia, trauma, major infection, major surgery)—300 mg/day in 3 divided doses tapering to maintenance dose

Recognition and treatment of an acute adrenal crisis is of utmost importance as this constitutes a critical, life-threatening condition best managed in the critical care setting. The clinical features of acute adrenal crisis [2] are found in Table 7.1.

Critical care management of an acute adrenal crisis includes judicious fluid administration, strict cardiac and hemodynamic monitoring, as well as monitoring of urine output and electrolytes. Administration of the glucocorticoid, cortisol, 100 mg IV over 5–10 min followed by 300 mg over 24 h should take place. In addition the mineralocorticoid fludrocortisone 0.05–0.2 mg is required.

Table 7.1 Clinical features of acute adrenal crisis

• Mental status changes
• Abdominal pain, vomiting
• Electrolyte abnormalities—hyponatremia, hyperkalemia
• Cardiovascular decompensation—hypotension, dysrhythmias

7.2.2 Adrenal Cortical Hyperfunction

The most common manifestation of adrenal gland hyperfunction occurs in the Cushing syndrome. The syndrome may occur in the setting of excessive adrenal gland stimulation by ACTH, HPA axis derangement, or autonomous adrenal cortical hyperfunction.

When a pituitary adenoma is responsible for excessive ACTH secretion and resulting adrenal cortical hyperfunction, the disorder is termed the Cushing disease. Non-pituitary sources of ACTH analogues may also produce the Cushing syndrome. Malignant neoplasms of the lung as well as carcinoid and neoplasms of the thymus gland may be sites of ACTH analogue production [2].The ACTH-independent causes of the Cushing syndrome include adrenal adenomas, adrenal carcinomas, and prolonged exogenous steroid administration [2]. The clinical features of the Cushing syndrome are listed in Table 7.2.

Patients presenting with clinical features consistent with the Cushing syndrome or Cushing disease should have prompt endocrinology evaluation. Diagnosis includes careful medical history, physical examination, and laboratory studies which reveal elevated levels of cortisol and ACTH levels in addition to elevated concentrations of metabolites in urine. The endocrinology workup may also include dexamethasone and cosyntropin (ACTH) suppression tests [2].

Treatment of adrenal cortical hyperfunction may take several forms. Surgical treatments may include adrenalectomy or adrenal adenoma resection for cases of adrenal adenoma. In cases of pituitary adenoma, selective adenoma resection is indicated. In those cases due to ectopic production of ACTH or ACTH analogues, treatment of the tumor source with surgery and medical management is indicated. Medical management with inhibitors of ACTH and/or cortisol secretion may also be indicated in refractory or inoperable cases. Adrenal carcinoma is treated with multiple modalities [2].

Table 7.2 Clinical features of the Cushing syndrome

- Central obesity—"moon facies," "buffalo hump"
- Hypertension
- Abdominal striae, poor wound healing, easy bruising
- Muscle weakness/wasting
- Androgen excess—acne, oligomenorrhea, hirsutism
- Psychologic symptoms
- Edema
- Impaired glucose tolerance
- Growth retardation in children
- Osteoporosis

Management of patients with adrenal cortical hyperfunction presents complex perioperative and postoperative challenges. In cases due to chronic, exogenous steroid administration, perioperative adrenal insufficiency is a major risk, and specialty consultation should be considered in addition to stress dosing prophylaxis. These patients must also have optimization of blood pressure and may also require management of hyperglycemia. Increased fracture risk and the potential for impaired wound healing are additional clinical concerns.

Hyperaldosteronism results in excessive mineralocorticoid secretion. In primary hyperaldosteronism either adrenal adenoma or bilateral adrenal hyperplasia may be the source of excessive aldosterone production. In the primary form, renin activity is suppressed by a feedback mechanism. In secondary hyperaldosteronism, renin oversecretion induces excessive aldosterone secretion [2]. Clinical features of hyperaldosteronism are the result of sodium and water retention leading to elevated intravascular volume and hypertension. Hypokalemia is also seen, and if severe, dysrhythmias, proximal muscle weakness, paresthesias, tetany, and nephropathy may occur. Concomitantly increased renal excretion of hydrogen ions may lead to metabolic alkalosis. Treatment of primary causes of hyperaldosteronism are site specific and include surgical excision where adenomas are involved, or for cases due to hyperplasia, medical treatment with the aldosterone antagonist, spironolactone, is indicated [2].

Congenital adrenal hyperplasia results from relative cortisol deficiency, due to an enzymatic deficiency. This leads reflexively to elevated pituitary ACTH production and overstimulation of

Table 7.3 Clinical features of congenital adrenal hyperplasia

- Androgen excess
  - Females
    - Infants—ambiguous genitalia
    - Prepubertal females—virilization
  - Males
    - Infants—macrogenitosomia
    - Prepubertal males—precocious puberty
- Cortisol deficiency—mild

Table 7.4 Clinical features of pheochromocytoma

- Severe hypertension—paroxysmal in 50% may be induced by exercise, urination, abdominal palpation
- Tachycardia
- Headache, sweating, palpitations, anxiety, tremors, weight loss
- Hyperglycemia, hypermetabolism, postural hypotension in hypertensive patient
- Elevated urinary metabolites, free catecholamines, vanillylmandelic acid, and metanephrine levels

the adrenal cortex. The result is elevated production of sex steroids, primarily androgens, which forms the basis of the clinical manifestations [2] detailed in Table 7.3.

Treatment of congenital adrenal hyperplasia includes replacement therapy via glucocorticoid and mineralocorticoid administration. Administration of anti-androgen agents in pre- and postpubertal females may be necessary. Structural and functional genital reconstructive surgery of affected infants is often required [2]. Due to the cortisol deficiency, perioperative adrenal insufficiency may be a risk, and specialty consultation should be considered in addition to stress dosing prophylaxis regimens.

7.2.3 Adrenal Medullary Hyperfunction

Although it is rarely encountered, pheochromocytoma is the prime manifestation of adrenal medullary hyperfunction (see Table 7.4). The majority of pheochromocytomas are due to a single tumor of adrenal chromaffin cells with excessive production of epinephrine, norepinephrine, and dopamine. These tumors may also occur in extra-adrenal sites at the periphery of major arteries including the abdominal aorta and iliac arteries and are known as paragangliomas. In addition to solitary manifestations, pheochromocytomas may occur as a feature of multiple endocrine neoplasia type II or in association with neurofibromatosis type 1 [2].

Prompt treatment of patients diagnosed with pheochromocytoma is compulsory to prevent the severe, possibly life-threatening sequelae of this condition. Medical management of the physiologic derangements in the critical care setting with alpha-adrenergic blocking agents must be initiated to provide hemodynamic stabilization prior to surgical management. Surgical management includes adrenal exploration and exploration of extra-adrenal sites with surgical excision of tumors. In cases of inoperable tumors, medical management remains the mainstay of treatment and may include measures aimed at reduction of tumor size and function in addition to the adrenergic blocking agents.

Treatment of the primary sources and effects of the pheochromocytoma takes precedence over all oral surgical procedures. Once medical stability and definitive management of the primary source of the adrenal medullary hyperfunction has occurred, specialty evaluation, management, and optimization in the perioperative and postoperative phases is imperative.

7.2.4 Thyroid Disease

7.2.4.1 Hyperthyroidism

There are several disorders associated with hyperthyroidism. The more common ones will be discussed here. Two most common disorders associated with thyroid hyperfunction are those associated with diffuse toxic goiter and those with toxic multinodular goiter. Hyperthyroidism may also be a transient, initial feature of thyroiditis which transitions into hypothyroidism. See Table 7.5 for common clinical features of hyperthyroidism [3].

Grave's disease is the clinical presentation of diffuse toxic goiter, which occurs as a result of

Table 7.5 Common clinical features of hyperthyroidism

- Metabolic—increased metabolic rate, weight loss, heat intolerance
- Cardiovascular—tachycardia, arrhythmias, widened pulse pressure, angina
- Respiratory—tachypnea, increased O_2 consumption
- GI—diarrhea
- Musculoskeletal—weakness
- Neurologic—anxiety, tremulousness
- Skin/hair—warm and moist; thinning of hair

Table 7.6 Clinical features of Grave's disease

- Goiter—diffuse toxic
- Ophthalmopathy—exophthalmos, conjunctivitis, scleritis
- Elevated serum T4, markedly elevated T3, (elevated T3 rU)
- Decreased TSH
- No TSH response to TRH stimulation

production of thyroid-stimulating antibodies which induce excessive production of thyroid hormones T3 and T4 by the thyroid gland. See Table 7.6 for clinical features of Grave's disease.

Treatment of Grave's disease is primarily medical with surgery reserved for cases refractory to medical therapy. Significant, symptomatic glandular enlargement and severe cases of exophthalmos are additional surgical indications. Adrenergic blocking agents are often required to manage hemodynamic manifestations of Grave's disease as well as symptoms resulting from thyroid hyperfunction. Use of the antithyroid medications methimazole and propylthiouracil is often successful in disease modulation. In cases with suboptimal response or with patients intolerant of antithyroid side effects, I-131 radioisotope ablation treatment may be necessary with close monitoring and expectant management of post-ablation hypofunction.

The toxic multinodular goiter often develops in patients with long-standing, nontoxic multinodular goiter and results from prolonged stimulation by TSH leading to autonomous hyperfunction of one or more nodules. Treatment of the patient with toxic multinodular goiter is commonly with antithyroid agents or with I-131 radioisotope ablation for refractory cases [3].

Thyrotoxicosis or thyroid storm represents the acute, severe presentation of hyperthyroidism. This emergent condition has a mortality rate ranging from 50 to 75% if not addressed promptly and effectively [3]. Patients with untreated or undertreated hyperthyroidism are at greatest risk for thyrotoxicosis (see Table 7.7: Clinical features of thyrotoxicosis). In addition it may be precipitated by various causes including trauma, surgery, childbirth, or concurrent serious illness. For treatment principles see Table 7.8.

In patients with thyrotoxicosis, emergent critical care management and stabilization take precedence over all other treatments as these patients may be hemodynamically unstable and may require ventilatory support. Treatment includes specialty consultation, fluid resuscitation, prompt initiation of adrenergic blocking agents and antipyretics, and administration of sodium iodide intravenously. Close monitoring and support of the airway, hemodynamic parameters, ECG, fluid balance, and thyroid function is provided in the ICU.

General treatment principles for the patient with treated hyperthyroidism include obtaining a thorough medical history with close attention to the review of systems and careful physical examination. The clinician must carefully note complaints or clinical findings suggestive of suboptimal management. Prior to performing elective procedures, it is important to confirm that thyroid management has been optimized to minimize risk in the perioperative and postoperative phases. Specialty consultation, thyroid function studies, and ECG should be considered.

Table 7.7 Clinical features of thyrotoxicosis

- Hyperpyrexia
- Tachycardia/arrhythmia
- Cardiovascular collapse
- Declining mental status—agitation → stupor → coma

Table 7.8 Treatment of thyrotoxicosis

- Circulatory support—IV fluids
- Iodide administration—IV sodium iodide 1–2 mg/24 h or oral potassium iodide
- Beta-blockers
- Antipyretics

7.2.4.2 Hypothyroidism

Conditions associated with hypothyroidism may be classified as primary, due to an intraglandular disorder, or secondary due to an alteration in TSH production. The common types of primary hypothyroidism include chronic thyroiditis, iodine deficiency, or iatrogenic cases precipitated by surgical removal or I-131 radioisotope ablation. Forms of thyroiditis include silent or mild presentation, subacute, and chronic thyroiditis. Autoimmune thyroiditis is the chronic form which is often termed Hashimoto's thyroiditis (see Table 7.9: Clinical features of autoimmune thyroiditis) [3]. The most common cause of secondary hypothyroidism is hypopituitarism [3].

Patients with hypothyroidism require lifelong thyroid replacement therapy and titration to a euthyroid state via clinical and laboratory monitoring. Clinical features of hypothyroidism are listed in Table 7.10.

The acute, severe presentation of hypothyroidism is myxedema coma, which when left untreated is associated with a mortality rate of 50–75% [3]. Myxedema coma (Table 7.11) of gradual onset may result from untreated, severe, or undertreated hypothyroidism. Acute onset of this emergent condition may be precipitated by severe infections or by extreme, prolonged exposure to cold temperatures [3].

In patients with myxedema coma, emergent critical care management and stabilization must receive top priority due to potential hemodynamic instability and altered consciousness. These patients may require ventilatory support. Treatment includes specialty consultation; fluid resuscitation; prompt initiation of corticosteroids, especially in the patient with hypopituitarism; and administration of L-thyroxine.

Table 7.9 Clinical features of autoimmune thyroiditis

- Thyroid enlargement—autoimmune damage, lymphocytic infiltration, fibrosis decrease thyroid hormone production
- Pain/tenderness
- May be hyperthyroid or euthyroid initially with progression to chronic hypothyroidism

Table 7.10 Clinical features of hypothyroidism

- Thickened, puffy facial features, non-pitting edema
- Myxedema—deposition of mucopolysaccharide-rich material in tissues
- Weight gain
- Dry skin, coarse hair
- Weakness, lethargy, mood disturbances
- Hoarseness
- Delayed return phase of deep tendon reflexes
- Constipation
- Menstrual irregularities
- Cold intolerance, possible hypothermia
- Hypoventilation, possible pleural effusion
- Bradycardia, decreased C.O., possible pericardial effusion
- Lab findings—decreased T_3, T_4, T_3rU, increased TSH, decreased radioactive iodine uptake

Table 7.11 Clinical features of myxedema coma

- Coma
- Hypotension
- Hypoventilation
- Hypothermia
- Hypoglycemia

Table 7.12 Classification and salient features of hyperparathyroidism

- Primary—autonomous hypersecretion of parathyroid hormone (PTH)
  - Etiology
    - Parathyroid adenoma—single lesion in 80–90%
    - MEN I; MEN II
    - Parathyroid hyperplasia—10–20%
- Secondary—reactive hypersecretion of parathyroid hormone in response to hypocalcemia
  - Etiology
    - Chronic renal disease (renal osteodystrophy)—common
    - Calcium malabsorption (rickets; osteomalacia)—rare
- Tertiary—autonomous oversecretion of parathyroid hormone by parathyroids (hyperplasia) which persists despite normalization of serum [Ca^{2+}] or renal transplantation
  - Etiology
    - End-stage renal disease with secondary hyperparathyroidism

General treatment principles for the patient with treated hypothyroidism include completion of a thorough medical history with detailed review of systems and careful physical examination. Close attention should be given to com-

plaints or clinical findings suggestive of suboptimal management. Prior to performance of elective procedures, it is important to confirm that treatment has been optimized and that the patient has attained a euthyroid state, to minimize risk in the perioperative and postoperative phases. Specialty consultation, thyroid function studies, and ECG should be considered.

7.3 Parathyroid Disease

Clinicians must be familiar with disease states in which hyperparathyroidism (Table 7.12) and hypoparathyroidism exist due to the alteration in calcium and phosphorous metabolism [4]. These conditions have far-reaching effects upon skeletal biology, neurologic function, and cardiac function.

7.3.1 Hyperparathyroidism

The key features of primary hyperparathyroidism [4] (Table 7.13) result from elevated parathyroid hormone (PTH) which leads to hypercalcemia and hypophosphatemia. The elevated PTH levels stimulate increased, active vitamin D production (1,25-dihydroxyvitamin D_3) leading to increased renal tubular calcium reabsorption and decreased renal tubular reabsorption of phosphate and bicarbonate. Gastrointestinal uptake of calcium is also increased. In addition osteoclast activity increases leading to mobilization of calcium from bone [4].

Prompt diagnosis and medical treatment of hypercalcemia is crucial and, due to potential cardiovascular and neurologic impairment, must take place under strictly monitored conditions [4].

- Mild to moderate—serum [Ca^{2+}] 11–13 mg/dL
  - Hydration—increased fluid intake
  - Oral phosphate supplementation
  - Estrogen—postmenopausal females
- Severe—serum [Ca^{2+}]>13 mg/dL
  - IV saline hydration, diuresis
  - Bisphosphonates—bind bone hydroxyapatite
  - Plicamycin—inhibits osteoclastic activity
  - Calcitonin—inhibits osteoclastic activity

Table 7.13 Clinical features of primary hyperparathyroidism

- Skeletal
  - Osteitis fibrosa cystica—focal regions of demineralization
  - Brown tumors—lesions consisting of osteoclasts, osteoblasts, giant cells, fibrous tissue
  - Loss of lamina dura
  - Subperiosteal resorption of distal phalanges, clavicles
- Renal
  - Hypercalciuria—renal calculi
  - Nephrocalcinosis—calcium deposits in parenchyma may lead to renal failure
- Cardiovascular
  - Hypertension
  - Bradycardia
  - EKG changes—shortened QT interval
- Gastrointestinal
  - Increased incidence of peptic ulcer disease and pancreatitis
  - Abdominal pain, anorexia, nausea, vomiting, constipation
- Neurologic/psychiatric
  - Mental status changes—lethargy; drowsiness; stupor; coma
  - Neuromuscular disorders—weakness; fatigue; proximal myopathy; hypotonia
  - Mood disorders—depression

The treatment of primary hyperparathyroidism is often surgical and consists of parathyroid exploration and removal of a single adenoma or subtotal parathyroidectomy for hyperplasia. Expectant management of the resulting hypocalcemia that may occur postoperatively is required.

7.3.2 Hypoparathyroidism

The key features of hypoparathyroidism evolve due to PTH deficiency which leads to hypocalcemia (Table 7.14) and hyperphosphatemia [4]. One of the more common etiologies of hypoparathyroidism is iatrogenic, resulting from surgical removal of all four parathyroid glands in the treat-

Table 7.14 Clinical features of hypocalcemia and hypoparathyroidism

- Neurologic
  - Anxiety
  - Paresthesias—circumoral, fingertips
  - Seizures—tonic-clonic
  - Elevated intracranial pressure, papilledema
  - Muscle fatigue, weakness
  - Chvostek's sign—contraction of muscles of facial expression by tapping over facial nerve course on the face
  - Trousseau's sign—carpal spasm (flexion at MCP joints, extension of IP joints, adduction of thumb/fingers) elicited by inflation of BP cuff to > systolic BP for 3 min
  - Tetany
    Mild—moderate carpopedal spasm, cramping, twitching
    Severe—laryngeal stridor
- Gastrointestinal—intestinal malabsorption
- Cardiovascular—prolonged QT interval; heart block: CHF
- Ectodermal changes—brittle nails, dystrophic skin, enamel defects
- Dystrophic calcifications
  - Basal ganglia – Parkinsonian symptoms
  - Lens – cataracts

ment of parathyroid disease. It may also result from total thyroidectomy without parathyroid preservation. Impairment of PTH secretion may occur in the setting of magnesium deficiency. The DiGeorge syndrome is a congenital cause of hypoparathyroidism due to agenesis of the parathyroid glands and thymus. Hypoparathyroidism is also a feature of an autoimmune disorder termed MEDAC, consisting of multiple endocrine deficiency, autoimmune endocrine destruction, and mucocutaneous candidiasis. In this disorder, the functions of the parathyroid glands and the adrenal glands are destroyed [4].

Timely diagnosis and treatment of hypocalcemia is also crucial given the potentially severe cardiovascular and neurologic impairment that may occur. Careful correction of hypocalcemia must occur under strictly monitored conditions with IV administration of calcium-containing solutions.

Given the multiple systemic manifestations associated with parathyroid disorders, the clinician must perform a thorough history and physical appraisal with close attention to the often subtle findings on the review of systems, maxillofacial, cardiac, neurological, and musculoskeletal, exams. Those with mild to moderate physical complaints and clinical findings consistent with hypercalcemia or hypocalcemia should have non-emergent procedures postponed and referred for evaluation by a specialist in endocrinology. Those with findings consistent with severe hypercalcemia or hypocalcemia should have emergent medical evaluation and treatment.

7.4 Diabetes Mellitus

Diabetes mellitus is a heterogeneous primary carbohydrate metabolic disorder with hyperglycemia as a key feature. The disease involves deficient insulin production that may be absolute or relative. Relative insulin deficiency is often accompanied by insulin resistance. There are several classic signs and symptoms often described leading to the diagnosis. These include polydipsia, polyuria, and polyphagia, in addition to blurred vision and the occurrence of opportunistic infections.

Classification of diabetes is divided based upon the pathophysiology and nature of the insulin derangement. Type 1 diabetes mellitus (type 1 DM) is marked by total or near total absence of insulin production due to autoimmune destruction of pancreatic beta cells. Symptoms and signs at onset tend to be significant and often occur prior to age 20. These patients are at extreme risk for the acute complication ketoacidosis, which may be evident at initial disease presentation but more commonly occurs due to severe inflammatory disease, infections, glycemic control aberration, or noncompliance. Type 2 diabetes mellitus (type 2 DM) commonly occurs due to progressive loss of insulin secretion often accompanied by peripheral insulin resistance. Type 2 DM tends to occur beyond the second decade, in those who are overweight, and affected individuals tend to be less prone to ketoacidosis occurrence [5]. A subtype of type 2 DM known as maturity onset diabetes of youth (MODY) may occur earlier in life. A third glucose metabolic disorder, prediabetes, may occur, but the degree of hyperglyce-

mia falls below the range for the diagnosis of diabetes. These individuals are at increased risk for subsequent development of diabetes and cardiovascular disease [6].

Diagnosis of diabetes is made on the basis of the presenting symptoms and signs of hyperglycemia. This may include hyperglycemic crisis. Abnormalities in fasting plasma glucose (FPG) ≥ 126 mg/dL, oral glucose tolerance testing (OGTT) with 75 g anhydrous oral glucose ≥ 200 mg/dL, glycosylated hemoglobin assay (hemoglobin A1C) ≥ 6.5%, and random plasma glucose (RPG) ≥ 200 mg/dL are required to make the diagnosis. Prediabetes is diagnosed when the patient has values including FPG 100–125 mg/dL, OGTT 140–199 mg/dL, and hemoglobin A1C in the range 5.7–6.4% [6]. These patients must have comprehensive medical evaluation as well as risk assessment and frequent monitoring for acute and chronic complications of the disease. Patients and family members must be engaged in self-monitoring and disease management from medication, diet, and lifestyle perspectives. Lifetime glycemic control is imperative and reflective of the delicate balance among overall systemic health, physical activity, diet intake, and pharmacotherapy.

Common therapeutic goals include optimization of glycemic control resulting in hemoglobin AIC of <7%, preprandial plasma glucose 80–130 mg/dL, and maximum postprandial blood glucose of <180 mg/dL, which may vary based upon individual factors [6]. Treatment of type 1 DM requires dedicated glucose self-monitoring and consistent insulin administration which is commonly in the form of multiple daily injections of long-acting, basal insulin with rapid-acting prandial insulin to reduce hypoglycemia risk. Some patients require more intensive therapy in the form of implanted glucose monitors and continuous infusion pump insulin delivery. Additionally, dietary regulation, regular physical activity, and monitoring for hypoglycemia are essential.

Treatment of type 2 DM is through a multifactorial approach with emphasis on lifestyle changes, including regular exercise and behavioral interventions with a goal of attainment and maintenance of >5% weight loss. Weight loss medications may also be utilized to achieve this goal in selected cases.

In addition to management of lifestyle factors, the treatment of type 2 DM places high priority upon glycemic control, as well as the prevention, recognition, and treatment of acute and chronic disease complications. Attention to diet and exercise promotes weight loss as well as amelioration of hyperglycemia through enhanced peripheral sensitivity to insulin, glucose utilization, and regulation of lipid metabolism. When indicated, lipid-lowering agents may be effective in reducing risks of ASCVD, cerebrovascular disease, and peripheral vascular disease. In addition blood pressure management is an essential component of therapy [5, 6].

Pharmacotherapeutic regimens for treatment of type 2 DM include metformin as the initial agent. Insulin may be indicated under the following conditions [6]:

- Ongoing weight loss
- Plasma glucose ≥ 300 mg/dL
- Symptoms of hyperglycemia
- Hemoglobin AIC > 10%

Other agents may be indicated based upon the presence of comorbidities including atherosclerotic coronary vascular disease (ASCVD), heart failure (HF), and chronic kidney disease (CKD) as follows [6]:

Patients with type 2 DM and ASCVD

Sodium-glucose cotransporter 2 (SGLT2) inhibitors or glucagon-like peptide 1 (GLP-1) receptor agonists

Patients with ASCVD with high risk of HF or HF

SGLT2 inhibitors

Patients with type 2 DM and CKD

SGLT2 inhibitor or GLP-1 receptor agonist

The primary effect of the orally administered agent metformin is in the reduction of hepatic glucose production by inhibition of gluconeogenesis. Additionally, enhancement of glucose uptake and utilization occurs via reduction of peripheral insulin resistance and decreasing intestinal glucose uptake. It also exerts desirable

effects on lipid metabolism by lowering lipogenesis and fatty acid production, lowering substrate availability for gluconeogenesis. Metformin is contraindicated in patients at risk for developing lactic acidosis as well as those with renal insufficiency [7]

The major mechanism of action of the orally administered sulfonylureas is through stimulation of insulin secretion by pancreatic beta cells and increased cellular sensitivity to insulin. This includes the long-acting agents, chlorpropamide, glyburide, and tolbutamide, and the short-acting agents, gliclazide, glimepiride, and glipizide. The short-acting sulfonylureas are recommended to reduce the incidence of hypoglycemia. Sulfonylureas may be indicated as adjunctive agents in patients failing to meet treatment goals with metformin alone, when metformin is contraindicated, those with severe hypoglycemia, and in the treatment of MODY [8].

The subcutaneously administered GLP-1 agonists bind to GLP-1 receptors on pancreatic beta cells and stimulate glucose-induced insulin release. Weight loss has also been attributed to the GLP-1 agonists through slowing of gastric emptying, reduction of post meal glucagon release, and reduced food intake. The GLP-1 agonists include the short-acting agents exenatide (twice daily) and lixisenatide (once daily before any meal), and the long-acting agents include liraglutide (once daily) and once weekly administered agents dulaglutide, exenatide, and semaglutide [9].

The SGLT2 inhibitors reduce the reabsorption of glucose in the proximal tubule of the nephron thus enhancing excretion of glucose and functionally achieving osmotic diuresis. These orally administered agents include canagliflozin, dapagliflozin, empagliflozin, and ertugliflozin [10].

The most common acute complications of diabetes mellitus are hypoglycemia, diabetic ketoacidosis (DKA), and non-ketotic hyperosmolar syndrome [5]. It is critical for the surgeon to perform a thorough history and physical assessment and to work in concert with the patient and physician for perioperative glycemic management. Consultation with the endocrinology provider is critical in perioperative management of the type I DM patient or the complex type 2 DM patient.

Surgical patients having ambulatory procedures with local anesthesia alone should have optimized glycemic control and should be instructed to take medications and consume usual meals at the usual times including a breakfast on the procedure day. The postoperative glycemic regimen may require dosage adjustment based upon the potential for impaired oral intake postoperatively with strict home monitoring of plasma glucose.

For those having sedation or general anesthesia, preoperative fasting is required necessitating dosage modifications in the glycemic control regimen. All fasting patients must have appropriate perioperative fluid resuscitation. For type 1 DM patients with implanted monitors/insulin pumps, the device will require program changes which should be made in close consultation with the endocrinologist. It is equally important to manage these patients carefully postoperatively due to the potential for reduced caloric intake. The nature and duration of the impairment must be communicated carefully so that appropriate monitoring and infusion rates may be titrated. For those on multiple daily injections, the basal or long-acting insulin dose should not be altered. The dosages of short-acting insulin must be reduced following frequent measurements of plasma glucose, and a sliding scale may be necessary until the patient's oral intake has normalized. Patients with labile disease may require perioperative hospital admission with plasma glucose monitoring every 2 h and insulin infusion until oral intake is resumed. At discharge strict monitoring and insulin dosage titration must be arranged.

Patients with type 2 DM who require preoperative fasting should hold short-acting oral agents on the morning of the procedure. Those on metformin should place it on hold for 24 h, and patient hydration is essential, as a means to limit the potential for lactic acidosis, especially in patients at risk for renal impairment. Metformin should also be withheld if imaging with iodinated contrast agents is planned [7].

Patients on intermediate-acting and short-acting insulin should take 50% of the morning dosage of the intermediate-acting insulin and place the short-acting agent on hold. The surgeon must obtain a fasting plasma glucose preoperatively and in the immediate postoperative phase. The patient's subsequent insulin doses must then be titrated with caution based upon the anticipated nature and duration of the impaired oral intake. A range of 50–75% of the intermediate-acting insulin dosage may be required until the next day or until oral intake has normalized. A sliding scale regular insulin regimen may be required until the oral intake has returned to baseline. Oral agents should be resumed with careful postoperative inpatient or outpatient glycemic monitoring.

7.4.1 Acute Complications of Diabetes

Hypoglycemia can occur with either type 1 or type 2 DM and commonly results from an imbalance between medication effect and oral intake. In addition, unanticipated increases in physical activity or exercise regimen intensity may precipitate hypoglycemia. Signs and symptoms include anxiety, irritability, tremors, palpitation, tachycardia, and diaphoresis. If profound, hypoglycemia may induce mental status decline including lethargy, stupor, and coma. In very severe states, seizures may occur. Prevention of hypoglycemia includes close attention to medication dosage, diet, and activity and close glycemic monitoring [5].

Prompt recognition and management of hypoglycemia is imperative. For mild to moderate hypoglycemia in patients who have the capacity for oral intake, an oral source of glucose is appropriate. In severe hypoglycemia, an IV is necessary for fluid resuscitation with addition of an ampule of 50 mg of IV dextrose and must be administered through a large bore IV catheter slowly once intravenous position has been verified. Alternatively glucagon may be administered.

Table 7.15 Clinical features of diabetic ketoacidosis

- Hyperglycemia
- Dehydration from osmotic diuresis
- Ketosis
- Metabolic acidosis
- Hyperkalemia
- Altered consciousness
- Respiratory insufficiency

Diabetic ketoacidosis (DKA) results from insulin deficiency with alteration in carbohydrate, protein, and lipid metabolism leading to a catabolic state. In addition metabolic, electrolyte, and acid-base disorders occur [5] (see Table 7.15). This complication occurs with type 1 DM most commonly, but may occur in patients with type 2 DM under rare conditions. Precipitating factors include gradually worsening glycemic control and physiologic stresses including infections, trauma, and ethanol intoxication among others. Patients in DKA often require critical care admission for ventilatory support, fluid resuscitation, hyperglycemia management, and correction of the metabolic and electrolyte disorders.

Critical care management of the DKA patient includes vascular access, frequent plasma glucose readings, arterial blood gas analysis, administration of insulin via infusion, and respiratory support. Fluid repletion and monitoring of urine output are also essential components, in addition to ECG monitoring due to the potential for hyperkalemia-associated dysrhythmia. Bicarbonate administration may be necessary if acidosis persists despite correction of the hyperglycemia, hyperkalemia, and ketosis. Concurrent management of the precipitating cause is imperative.

Non-ketotic hyperosmolar syndrome is a less common diabetic acute complication which is typically associated with type 2 DM. Precipitating factors are similar to those in DKA. The key clinical features of non-ketotic hyperosmolar syndrome [5] are delineated in Table 7.16.

The principles of critical care management of non-ketotic hyperosmolar syndrome are similar to those of DKA management.

Table 7.16 Clinical features of non-ketotic hyperosmolar syndrome

- Hyperglycemia—profound
- Severe dehydration
- Elevated serum osmolarity
- Declining consciousness ranging from lethargy, delirium, to coma
- Possible seizures
- Metabolic acidosis—lactic acid
- Hyperkalemia

Table 7.17 Chronic complications of diabetes mellitus

Microvascular complications
- Retinopathy
- Nephropathy—chronic kidney disease
- Neuropathy
  - Peripheral—sensory and motor
  - Autonomic
    - Postural hypotension
    - Gastroparesis and delayed gastric emptying
    - Urinary retention
- Mononeuropathy—cranial nerve, proximal motor nerve
- Poor wound healing

Macrovascular complications
- Atherosclerotic coronary vascular disease
- Greater MI risk than nondiabetic population
  - May have atypical presentation with anginal equivalents—nausea, acute dyspnea
- Cerebrovascular disease and stroke risk
- Peripheral arterial disease and insufficiency

Immunologic complications
- Impaired neutrophil function
  - Increased susceptibility to bacterial infection to Gram negative and Gram positive
- Impaired lymphocyte function
  - Increased susceptibility to fungal organisms, Candida sp., Aspergillus sp., Mucorales
- Poor wound healing

7.4.2 Chronic Complications of Diabetes Mellitus

Chronic complications of diabetes mellitus are protean and often involve multiple systems [5] (see Table 7.17). Complications tend to present at earlier ages in type 1 diabetics. Diabetes is frequently implicated in chronic kidney disease, atherosclerotic coronary vascular disease, MI, stroke, and peripheral arterial disease [5, 6].

7.4.3 Obstructive Sleep Apnea

Obstructive sleep apnea (OSA) is a disorder in which obstructive apnea, hypopnea, or respiratory effort-related arousals, lead to a multitude of signs and symptoms resulting from sleep disruption. The symptoms include excessive daytime sleepiness, fatigue, and difficulty concentrating which may place the affected individual at risk of injury in the home, workplace, and during operation of a motor vehicle [11]. Multiple signs of disturbed sleep occur often first noticed by family members and/or significant others, foremost among them is snoring as well as sleep disruption or intermittent arousal. In addition restlessness, grunting, and resuscitative snorting are often reported [12]. The overall prevalence of OSA in the United States is rising, with afflicted males typically outnumbering females two to threefold [12]. While primarily a disorder seen in adults as a result of primary upper airway collapse, children may be affected with derangement in ventilatory control as the primary basis [13]. The typical OSA patient suffers reduced or absent airflow with intermittent disturbance of oxygenation and ventilation during obstructive events. See Table 7.18 for Diagnostic Criteria for Obstructive Sleep Apnea. Additionally, anatomical abnormalities of the upper airway, derangements in the arousal threshold, altered upper airway muscle function, and destabilization of respiratory control systems produce the associated disturbances [11, 12]. Risk factors for Obstructive Sleep Apnea are listed in Table 7.19.

Table 7.18 Diagnostic criteria for obstructive sleep apnea [11]

≥5 obstructive events/hour +
- Non-restful sleep, fatigue, or insomnia symptoms
- Awakened by gasping/choking/breath holding
- Observed consistent snoring, pauses, or both
- Hypertension, mood disorder, cognitive dysfunction, CAD, CVA, CHF, atrial fibrillation, or Type 2 DM.

Or

≥15 obstructive events/h regardless of other symptoms or comorbidities

Table 7.19 Risk factors for obstructive sleep apnea [12]

• Obesity – Prevalence increases with increasing BMI, neck circumference, increased waist/hip ratio
– Increased risk for obesity hypoventilation syndrome
• Gender – 2–3× more common in ♂ – Increased frequency in menopausal/postmenopausal ♀
• Age – Prevalence increases from young adulthood to sixth to seventh decades
• Anatomical craniofacial and upper airway abnormalities – Maxillary/mandibular hypoplasia, wide craniofacial base – Tonsillar/adenoid hypertrophy
• Others – Nasal congestion, history of snoring, smoking

Table 7.20 Medical comorbidities of obstructive sleep apnea [12]

• Congestive heart failure
• Chronic kidney disease
• Asthma, COPD, idiopathic pulmonary fibrosis
• Pregnancy
• Strokes, TIAs
• Acromegaly
• Hypothyroidism

Table 7.21 Sequelae of obstructive sleep apnea

• Cardiovascular – moderate, severe, or untreated OSA – Hypertension, pulmonary hypertension – CHF, CAD, dysrhythmias
• Neurologic/psychiatric – Cerebrovascular disease – Cognitive deficits – Fatigue, inattention, poor concentration, diminished alertness – Depression – Disability
• Endocrine – Metabolic syndrome – Independent association with increased glucose, triglycerides, inflammatory mediators, and long-term complications – Type 2 diabetes – Independent association between OSA severity, insulin resistance, and type 2 DM – Patients with severe OSA have 30% higher risk of developing DM vs general population
• GI/hepatic – OSA associated with 2–3× risk for hypoxia-related nonalcoholic fatty liver disease
• Perioperative, anesthesia risks – Obstruction, hypoxia, hypercarbia, respiratory failure – Acute coronary syndromes – ICU transfers
• Mortality – Severe, untreated OSA is associated with 2–3× increased risk of all-cause mortality – For mild untreated OSA there is no difference in mortality risk compared to those without OSA

Prompt diagnosis and effective evidence-based therapy for OSA is crucial, as is the identification and management of the serious comorbidities (Table 7.20) which often occur [12].

OSA is associated with metabolic syndrome, and thus, patients are at significant risk for medical complications as a result of upper airway obstruction [11, 12]. See Table 7.21: Sequelae of obstructive sleep apnea [12].

Sedation with an unprotected airway should be approached with extreme caution or completely avoided given the advanced risk for sedative-induced obstruction, the anatomically difficult airways, and altered respiratory physiology that many of these patients present with. Management of the awake OSA patient with local anesthesia should be approached with the patient in a position of comfort, avoiding the supine or semi-supine positions whenever possible. One helpful survey tool to use when evaluating a patent with suspected OSA is the validated STOP-BANG Survey [14] (Table 7.22). Patients ruling in on the basis of positive responses on the review of systems or on the basis of results of the STOP-BANG survey should have formal sleep testing obtained by a provider with expertise in sleep medicine.

Perioperative management of individuals at risk for OSA or with known OSA should be proactive and include thorough medical history, optimization of all comorbid conditions, and a well-planned difficult airway protocol implemented for intubation. In the postoperative phase, expectant management of airway obstruction should be implemented with airway adjuncts and the use of properly titrated CPAP devices.

Table 7.22 STOP-BANG survey

1.	*S*noring: Do you snore loudly (loud enough to be heard through closed doors)? Yes No
2.	*T*ired: Do you often feel tired, fatigued, or sleepy during daytime? Yes No
3.	*O*bserved: Has anyone observed you stop breathing during your sleep? Yes No
4.	Blood *P*ressure: Do you have or are you being treated for high blood pressure? Yes No
5.	*B*MI: BMI more than 35 kg m^{-2}? Yes No
6.	*A*ge: Age over 50 years old? Yes No
7.	*N*eck circumference: Neck circumference >40 cm? Yes No
8.	*G*ender: Male? Yes No
	High risk = "yes" to ≥3 questions
	Low risk = "yes" to <3

7.5 Summary

Endocrine functions are essential to optimal health, and any dysfunction has significant patient implications. Prior to oral and maxillofacial surgery, any disorders must be understood and addressed, especially when anesthesia is part of the treatment plan. Failure to properly plan can be catastrophic, ranging from wound infections to significant patient morbidity and mortality.

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8 Psychiatric and Behavioral Disorders

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In this chapter, we will discuss the most common mental disorders that patients can present with; however the reader should be aware that there are numerous other mental disorders that exist. Some of these disorders overlap in etiology, presentation, and treatment with others, while others may be rare and can extend a unique challenge in management for the oral and maxillofacial surgeon. Although not all mental disorders can be discussed in this chapter, it is important to be aware of the different categories and disorders that exist. The American Psychiatric Association (APA) has compiled an updated list of these mental disorders in the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) to help aid in diagnosis and treatment of these disorders. Table 8.1 consists of a summarized list of mental health disorders taken from DSM-V.

Table 8.1 Mental disorders

Neurodevelopmental disorders
• Intellectual disabilities
• Communication disorders
• Autism spectrum disorder
• Attention-deficit/hyperactivity disorder
• Specific learning disorder
• Motor disorder (i.e., Tourette's)
• Other neurodevelopmental disorders
Schizophrenia spectrum and other psychotic disorders
• Personality disorder
• Delusional disorder
• Schizophrenia
Bipolar and related disorders
• Bipolar I disorders
• Bipolar II disorder
Depressive disorders
• Disruptive mood dysregulation disorder
• Persistent depressive disorder
• Substance/medication-induced depressive disorder
Anxiety disorders
• Separation anxiety disorder
• Selective mutism
• Specific phobia (i.e., blood-injection-injury, fear of injections and transfusions)
• Social anxiety disorder
• Panic disorder
• Agoraphobia
• Generalized anxiety disorder
Obsessive-compulsive and related disorders
• Obsessive-compulsive disorder
• Body dysmorphic disorder
• Hoarding disorder

(continued)

8.1 Anxiety

Anxiety is characterized by a state of worry and fear in anticipation of a future event. Anxiety is a normal response that a person can have which can be beneficial at times as it keeps a person aware and prepared for possible dangers. When these responses become

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Table 8.1 (continued)

Trauma- and stressor-related disorders
• Post-traumatic stress disorder
• Acute stress disorder
• Adjustment disorders
Dissociative disorders
• Dissociative identity disorder
• Dissociative amnesia
• Depersonalization/derealization disorder
Somatic symptom and related disorders
• Somatic symptom disorder
• Illness anxiety disorder
Feeding and eating disorders
• Bulimia nervosa
• Binge eating disorder
• Anorexia nervosa
Elimination disorders
• Enuresis
• Encopresis
Sleep-wake disorders
• Insomnia disorder
• Narcolepsy
• Breathing-related disorders
• Parasomnias
Sexual dysfunctions
• Erectile disorder
Gender dysmorphia
• Gender dysphoria
Disruptive, impulse control, and conduct disorders
• Oppositional defiant disorder
• Kleptomania
Substance-related and addictive disorders
• Alcohol-use disorder
• Caffeine-related disorders
• Cannabis-related disorders
• Hallucinogen-related disorders
• Inhalation-related disorders
• Opioid-related disorders
• Stimulant-related disorders
• Tobacco-related disorders
Neurocognitive disorders
• Delirium
Personality disorders
• Cluster A personality disorders (paranoid personality disorders, schizoid personality disorders)
• Cluster B personality disorders (antisocial personality disorder, borderline personality disorder)
• Cluster C personality disorder (avoidant personality disorder, dependent personality disorder)

Table 8.1 (continued)

Paraphilic disorders
• Voyeuristic disorder
• Exhibitionist disorder
• Pedophilic disorder
Medication-induced movement disorders and other adverse effects of medication
• Tardive dyskinesia
• Tardive dystonia
• Medication-induced postural tremor

excessive and inappropriate to the situation at hand, or if the person cannot control their response, or their anxiety affects their day-to-day lives, it becomes an anxiety disorder. The two main subsets of anxiety disorders are panic disorder and phobias. Panic disorder is characterized by multiple panic attacks which consist of symptoms such as palpitations, nausea, difficulty breathing, and chest pains. They can occur at any time thus causing those afflicted to seclude themselves to their homes neglecting their normal lives and health. Phobias are another form of anxiety disorder where there is excessive unjustified fear towards an object or situation. Phobias differ from one another by the type of object or situation that triggers the anxious state; an example is claustrophobia which is the fear of confined spaces. Overall, according to the National Institute of Mental Health (NIMH), anxiety disorders are estimated in 19.1% of the US adult population, with a greater prevalence for females (23.4%) than men (14.3%). Common treatments for anxiety disorders include selective serotonin reuptake inhibitors (SSRIs) such as sertraline or beta-blockers such as propranolol. SSRIs are further discussed later in the chapter.

Oral and maxillofacial surgeons commonly treat patients with dental-related anxiety. Dental anxiety refers to the increased fear of dental procedures. Generally, this fear doesn't reach the threshold of the clinical diagnosis of a phobia; however in some patients it does, and when they do it is generally referred to as dentophobia or dental phobia. Since most of the research around dental anxiety and phobia is based on self-reported anxiety and does not contain other factors to diagnose a phobia [1], we will proceed in this chapter by using the term dental anxiety.

Dental anxiety is the irrational fear of a dental-related object or situation which can arise from simply walking into a dental office, encountering the dentist, visualizing a syringe, or simply thinking about going to the dentist. Recent studies have shown that dental anxiety among patients ranges from 10 to 20% [2–4]. The etiology of dental phobia can occur from past traumatic experiences in a dental setting [5] most commonly occurring early during childhood [1]. Other causes of dental anxiety can result from observation of family members either going through a traumatic experience or relaying a traumatic experience with a dentist. There is also some evidence that suggests dental fear has a genetic basis in some patients with a 30% heritability trait [6].

Dental fear is part of a cycle resulting in delayed dental visits which lead to dental problems that lead to symptomatically driven treatment which feeds back into the dental fear [7]. Patients with dental anxiety are less likely to visit the dentist resulting in higher incidences of decayed and missing teeth [7–9]. Due to the fear and anxiety these patients exhibit on clinical presentation, they are most likely to be referred for treatment under sedation secondary to the need for behavioral management. The higher the level of fear of the dentist, the more likely the patient will avoid visiting the dentist [7] and the higher the incidence of missed or canceled dental appointments [10]. These missed appointments can deny other patients from receiving the care they need as well as having a financial impact on a practice where in some specialty practices, an estimated 443 h of lost clinic time per year occurs due to missed appointments [11].

Dental anxiety can range from minimal anxiety such as an elevated heart rate to full-blown anxiety attacks preventing a provider to initiate or complete treatment. Thus, it is important to properly assess a patient to determine if they are suitable candidates for office-based procedures.

The clinical approach to behaviorally manage a dentally anxious patient is to start conservatively and escalate to more complex and medically invasive approaches as necessary. Multiple approaches that are tailored specifically to a unique patient's needs may be necessary.

As previously discussed, dental anxiety patients can be referred to an oral and maxillofacial surgeon's office from a general or specialist's office either due to the need for behavioral management, procedure complexity, or both. These patients may also come to an oral surgeon's office due to word of mouth advertising or through internet advertising and review sites. Regardless of method in which what brought the patient into the office, the initial contact is likely by phone or in-person conversation with front office personnel. Thus, it is important to have a well-trained receptionist who is able to interact with patients in a friendly manner and keep them at ease as they are usually the first impression a patient has of an office. There has been some evidence for the success of using a questionnaire about anxiety in a dental office which helps keep the patient involved and aware that the provider knows of their anxiety [12]. A questionnaire that assess a patient's anxiety levels can be used by the front office receptionist at the time of scheduling the patient's appointment or incorporated in the initial consult visit. For anxious patients, it is recommended to have the first appointment scheduled as a consult, which allows the patient to be comfortable and open about their concerns. Knowing that there will not be any treatment can decrease dental anxiety significantly, allowing the provider to build rapport and a comfortable level with the patient which can help decrease anxiety levels. Good communication skills by way of using layman's terms to explain diagnoses and treatment to the patient is essential in building a strong provider to patient relationship. Avoiding the use of possible triggers such as "needle" and "shot" may also help keep the patient calm. Lastly, acknowledging the patient's anxiety and discussing it with the patient is also important in understanding the basis of the anxiety so that treatment can be modified to help address those fears.

When examining a referred patient with dental anxiety, it is important to be thorough with the examination to confirm the diagnosis sent by the referring provider. Misdiagnosis of a condition, or the site of the condition, can occur by providers examining an anxious patient due to the stress

under which they perform the examination under [13]. Once an understanding of the basis of the patient's fear is known, other approaches can be taken as well. The major cause of dental anxiety is receiving a dental injection [14]. Acknowledging this fear and discussing methods that can be taken to help ease the anxiety and pain that may be associated with a dental injection is necessary. The use of a topical agent prior to anesthetic administration can have positive psychological impacts by reducing dental anxiety [15] although research has shown that it is not effective in reducing pain on injection [16]. Contrary to popular belief, using a smaller gauge needle does not result in less pain [17], and smaller gauge needles should be avoided due to increased risk of fracture [18], specifically in an anxious patient due to the risk of sudden movements that can cause needle fractures [19]. Warming the cartridge of anesthetic helps in bringing the anesthetic temperature closer to normal body temperature and, when done just prior to injection, can also help with decreasing pain on delivery [20–22]. Evidence has also shown that anesthetics are partly painful due to their acidity [23]; thus those anesthetics that are closer to physiologic pH (7.4) such as carbocaine 3% without epinephrine (pH 4.5–6.8) or 4% prilocaine plain (pH 6.0–7.0) compared to 2% lidocaine 1:100K epi which has a pH range of 2.9–4.4 (see Table 8.2) may be ideal to use in an anxious patient. Since carbocaine and prilocaine have short-acting effects, thus it can be used as the initial anesthetic then supplemented with longer-acting anesthetics. In some patients, the thought of getting extra shots however can be traumatic, so an option for those patients rather than the two-step method described above is the use of a buffered anesthetic solution. Sodium bicarbonate can be added to local anesthetics to decrease the acidity and thus decrease the pain of an injection [24]. Other anesthetic delivery options include the use of a computer-controlled anesthetic delivery which has shown to cause less injection pain [25, 26]. Refer to Table 8.3 for a comprehensive list of different methods of decreasing anxiety and pain from a dental injection.

Table 8.2 Anesthetics and their associated pH

Anesthetic	pH
2% Lidocaine 1:100K epi	2.9–4.4
4% Articaine 1:100K epi	3.62
4% Articaine 1:100K epi	3.68
0.5% Bupivacaine 1:200K epi	3.3–5.5
3% Carbocaine plain	4.5–6.8
4% Prilocaine plain	6–7

Table 8.3 A list of methods to decrease dental related anxiety

Areas to improve dental injection-related anxiety	Recommendation	Drawbacks
Topical	Addition of topical anesthetic agent can help decrease anxiety	• May not be effective in reducing pain • Can cause skin irritation, stinging, bad taste
Anesthetic temperature	Increasing the temperature of the anesthetic just prior to delivery helps decrease pain of injection	• Time consuming
Anesthetic pH	Use of a higher pH (closer to physiologic pH) anesthetic, such as prilocaine or carbocaine, decreases pain of injection	• Short acting • Usually requires additional use of longer acting anesthetics
Sodium bicarbonate	Addition can increase pH closer to physiologic pH, less pain on injection	• Time consuming • Costly, especially if commercial brand product is purchased
Delivery method	Slow delivery of anesthetic results in slower tissue expansion and gives time for the anesthetic to work, decreasing the pain of delivery	• Time consuming • Patient's anxiety may worsen due to extended length of injection
Computer-controlled anesthetic delivery	Delivery of anesthetic slowly to decrease pain	• Expensive • Bulky

Pharmacological intervention is another method for the clinical management of dental anxiety patients. Multiple approaches are available pharmacologically either by oral anxiolytics, inhalation sedation, or conscious intravenous (IV) sedation. General anesthesia can usually be avoided in dental anxiety patients as over 90% of patients with dental anxiety had successful completion of their dental work under IV midazolam sedation [27]. Midazolam has been shown to be effective in reducing anxiety for third molar extractions whether used alone or with another sedative drug [28]. A combination of nitrous oxide inhalation sedation and IV midazolam has shown to be more effective than midazolam alone [29]. In addition to better sedation when incorporating nitrous oxide with IV midazolam, nitrous oxide addition has shown to decrease the amount of midazolam required, decrease recovery time, and result in better oxygen saturation levels [30]. The use of nitrous oxide can help reduce the anxiety with obtaining IV access for conscious sedation. Nasal midazolam can also help with reducing anxiety; however due to minimal volumes used and nasal toxicity, supplemental sedation is likely indicated to start a procedure [31]. In patients who need multiple visits for treatment, there is evidence that repetitive anesthesia can help improve patient behavior in subsequent visits [32].

Proper assessment of dental anxiety patients is necessary to determine the method of behavioral management needed. In most patients, office-based procedures can be completed successfully with a mixture of the previously discussed methods. However, in a small portion of patients, general anesthesia in a hospital setting is required due to their behavioral presentation. Whether a patient is treated in the office with conscious sedation or in a hospital setting for general anesthesia should depend on the patient's level of behavioral noncompliance, office staff's comfort in treating the patient, office clinic time consideration required to treat the patient, and the negative effect that the patient's actions may have on other patients present in the office.

8.2 Depression

Depression is a mood disorder that is characterized by prolonged feelings of sadness, irritability, and loss of interest affecting day-to-day activities. According to the NIMH, 17.3 million or 7.1% of the US population of adults over the age of 18 had at least one major depressive episode in 2017, while the prevalence of depression in women is 1.7-fold greater than that in men [33]. Signs of depression include irritability, loss of interest in activities, fatigue, restlessness, and suicidal thoughts among a sequela of symptoms. Depression is usually multifactorial based on genetic makeup, environmental factors, and psychological factors. Individuals who have family members with depression, traumatized individuals, and those with debilitating diseases are susceptible to depression. Treatment of depression can be done with pharmacotherapy of psychotherapy, each of which can be successful on their own; however combination therapy has shown higher rates of success. Medications most commonly used in treating depression include SSRIs, serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and monoamine oxidase inhibitors (MAOIs). Further, recent studies have demonstrated the benefits of ketamine on depression, and thus, patient's undergoing office IV sedation may benefit from ketamine as part of the armamentarium, assuming no contraindications exist.

SSRIs are the drug of choice in the treatment of depression; they are generally associated with a few side effects when dosed correctly. Certain SSRIs such as fluoxetine and sertraline are believed to inhibit cytochrome P450 [34]; thus the use of these medications effects the clearance of medications that undergo hepatic metabolism. Medications such as benzodiazepines, commonly used in sedation, should be carefully used in these patient's due to their dependency on hepatic clearance. However, holding of SSRIs and other antidepression medications should be avoided due to the risks of developing withdrawal symptoms. Discontinuation syndrome occurs when a patient abruptly discontinues their antidepressive

medications which leads to withdrawal symptoms of nausea, difficulty falling asleep, lethargy, headaches, anxiety, depressed moods, abdominal pain, and diarrhea.

On the opposite end of the spectrum, an increase in serotonin can lead to serotonin syndrome which is a group of potentially life-threatening symptoms that can occur when there are increased serotonin levels in the blood. Symptoms include tachycardia, agitation, confusion, nausea, diarrhea, and hyperthermia. Hyperthermia in these patients may lead to renal failure, metabolic acidosis, rhabdomyolysis, seizures, and even death. Increased intake of SSRIs, SNRIs, MAOIs, and TCAs can place a patient at risk of developing serotonin syndrome. In addition to the therapeutics used to treat depressive disorders, many of the medications used in the oral and maxillofacial surgery office with relation to perioperative drug therapies have also been associated with serotonin syndrome. Opioids such as fentanyl and meperidine have been associated with serotonin syndrome and should be avoided or used cautiously in patients being treated for depressive disorders. Tramadol, commonly given postoperatively for pain control, has also been associated with serotonin syndrome. Postoperative administration of an antiemetic such as ondansetron or metoclopramide also increases development of serotonin syndrome [35]. Given these risks, it is important to obtain a proper medical history along with a current medication list and their dosages prior to determining if a patient is an ideal candidate for in office sedation. An updated medication list is essential in determining what medications to avoid and what medications can be used to safely sedate the patient and avoid perioperative complications. An important note with regard to these medications is that as an oral and maxillofacial surgeon you should not solely decide what medications to hold or adjust; thus inter-professional communication and co-management with the primary care physician is important prior to proceeding with treatment in these patients.

Prior to the advent of SSRIs, TCAs were commonly used to treated depression. TCAs (e.g., amitriptyline) like SSRIs inhibit reuptake or serotonin, as well as norepinephrine. However, they also have many side effects, unlike SSRIs, due to their effects on the cholinergic and histaminergic systems that can include dysrhythmias, urinary retention, postural hypotension, and blurred vision. Careful intraoperative anesthetic management is indicated in these patients due to increased norepinephrine availability which can lead to abnormally high responses to the administration of an indirect vasopressor such as ephedrine. In these patients who need intraoperative treatment of low blood pressure readings, the use of a direct acting pressor such as phenylephrine is indicated. These exaggerated responses can also be seen in sympathetic stimulators such as ketamine and epinephrine which should also be avoided in these patients.

Overall, depression is associated with poor oral health [36] and is associated with a higher prevalence of caries and missing teeth [37]. Comorbidity with anxiety is common; thus some patients may exhibit anxiety symptoms. Depending on the patient's presentation in the office, some patients may need specific interventions for behavioral control as previously described for anxious patients, while others may not need significant behavioral management.

8.3 Bipolar Disorder

Bipolar disorder, also known as manic depression, is a chronic illness consisting of unusual changes in mood, irritability, concentration, energy, and a person's ability to function or perform basic day-to-day tasks. Mood swings can consist of a manic phase, which can last weeks or months, in which a person can experience high levels of energy and euphoria. Patients in the manic phase may display hyperactive characteristics such as talking fast, easily irritable, disconnected thoughts, difficulty falling asleep, impulsivity, and abnormal social behaviors. These patients may also experience a depressive phase in which individuals experience sadness, hopelessness, loss of interest, excess sleep, and fatigue, and at times these patients can inflict self-harm on themselves. According to the National Institute of Mental Health (NIMH), approximately 2.8% of adults, or six million

adults, in the United States had bipolar disorder in the last year, with an estimated 4.4% of US adults experiencing bipolar disorder at some time in their lives. According to the NIMH, approximately 83% of individuals with bipolar disorder experience significant impairment, which is the highest percentage among other mood disorders. To understand the qualitative measurement of impairment in bipolar disorder patients, refer to Fig. 8.1 for the Sheehan Disability Scale where a score of seven and above in any category is considered significant impairment [38].

The exact cause of bipolar disorder is not known; however it is thought to occur due to factors relating to the environment, genetics, and altered brain chemistry. Treatment of bipolar disorder can consist of different modalities, most commonly either though medication, psychotherapy, or a combination of both. For the oral and maxillofacial surgeon, understanding the medications used to treated bipolar disorder as well as their adverse effects is important for delivering safe care in the office. Individuals with bipolar disorder are often treated with multiple medications which mainly include mood stabilizers with the addition of antianxiety, antidepressants, and antipsychotic medications. The most common mood stabilizers used in bipolar disorder patients are valproate and lithium. Lithium is used for both acute treatment of mania and chronic treatment to avoid future manic episodes. There is no need to stop lithium treatment when surgery is done under local anesthetic only. For patients undergoing sedation in the office, it is important to understand the effects and interactions it has when used with anesthetic agents. Close attention to the anesthetic requirements in patients on lithium therapy is necessary due to the sensitivity to anesthetics in this population. Lithium prolongs the duration of neuromuscular blockade when using succinylcholine and decreases the amount of anesthetic required to anesthetize a patient due to the blockage of epinephrine, norepinephrine, and dopamine release. Nonsteroidal anti-inflammatory medications can also increase lithium levels in the blood, increasing toxicity risk. ACE inhibitors can reduce excre-

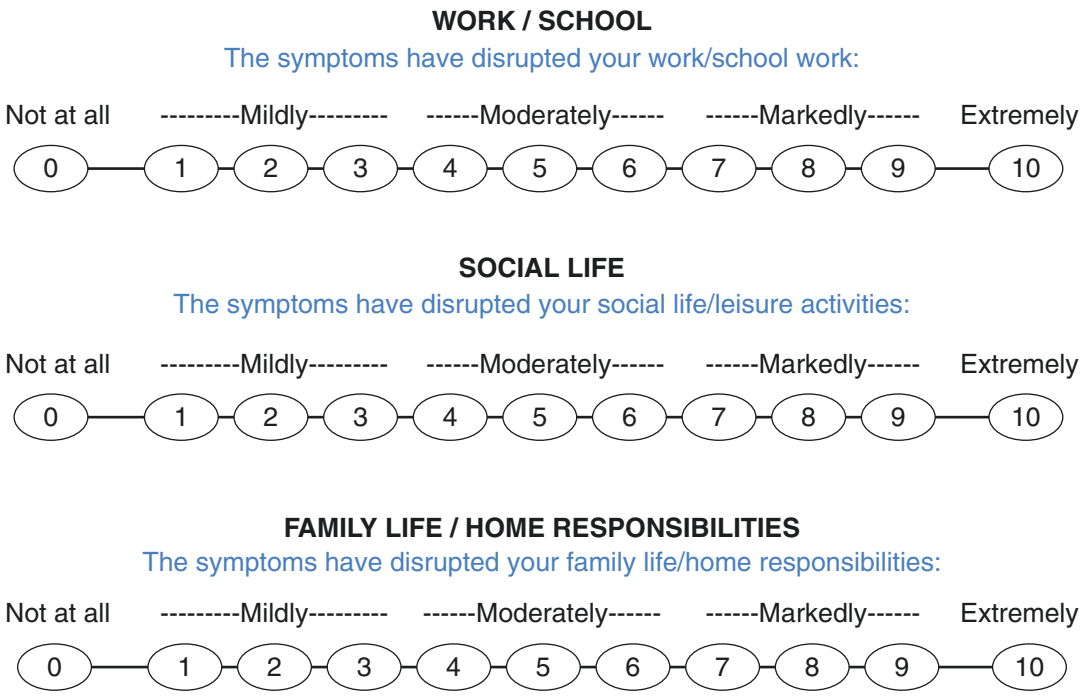

Fig. 8.1 Sheehan Disability Scale

tion of lithium through the kidneys, increasing toxicity risk as well as renal failure especially in individuals with long-term lithium use [39]. Due to lithium's effects on renal excretion and resultant hemodynamic changes, discontinuing lithium preoperatively is recommended approximately 3 days prior to surgery with no concern for withdrawal symptoms [40]. Sodium depletion in individuals on lithium therapy is at risk for lithium toxicity, as lithium transport out of the cell is dependent on the sodium-potassium pump. Preoperative lab work and subsequent perioperative treatment with IV fluids with sodium may be indicated in some of these patients. Postoperatively, lithium should be restarted within 1 week to avoid relapse of a manic episode; however this should be done after the patient's lab work displays hemodynamic stability and normal potassium and sodium ranges.

8.4 Psychotic Disorders

Individuals with psychotic disorders lose touch with reality and can exhibit long or short durations of symptoms such as hallucinations and delusions. These symptoms are also common in other disorders, thus a full workup is usually done prior to diagnosis. The most common psychotic disorder is schizophrenia, a chronic lifelong disorder where people are unable to interpret reality, hear voices, and have an unusual way of thinking, speaking difficulties, and movement disorders. Schizophrenia is thought to have genetic contribution as well as environmental factors and brain chemistry. Treatment is usually done pharmacologically with antipsychotics.

Whether a patient with schizophrenia is suitable for office-based procedures depends on the extent of the procedure and behavioral presentation of the patient. Medication compliance is important due to behavioral risks postoperatively that may compromise surgical sites. Antipsychotics used in the treatment of schizophrenia include chlorpromazine and haloperidol which can have side effects such as dystonia, tardive dyskinesia, and Parkinson's-like symptoms. Atypical antipsychotics such as clozapine and risperidone do not have the same side effects as typical antipsychotics but may cause other side effects such as weight gain, gynecomastia, and postural hypotension. Patients treated with atypical antipsychotics are susceptible to developing intraoperative hypotension during anesthesia; thus blood pressure monitoring and treatment as necessary is important. It is not recommended to discontinue schizophrenia treatment preoperatively due to withdrawal symptoms which can lead to perioperative psychotic episodes.

8.5 Post-traumatic Stress Disorder

Post-traumatic stress disorder (PTSD) is a condition caused by experiencing or witnessing a physically or psychologically traumatic event. In people who suffer a traumatic event, fear is a normal response yet most people eventually recover. Patients with PTSD however have not recovered from the fear and anxiousness of the trauma-inducing event. Reexperiencing symptoms from the initial traumatic event is common in PTSD patients and one of the criteria for diagnosis. These reexperiencing symptoms can be debilitating, affecting normal day-to-day activities. Other symptoms, which are usually brought on by a trigger, include behavioral changes, mood swings, chills, headaches, and panic attacks. Symptoms of PTSD can last months or years, and some who are afflicted may never recover. The prevalence of PTSD in a person's lifetime is approximately 8.3% [41]. PTSD can occur from traumatic events such as death, violence, and sexual abuse. PTSD is more commonly seen in those who are repeatedly exposed traumatic situations like sexual abuse victims and military personnel. Approximately 30% of Vietnam veterans, 11% of Afghanistan veterans, and 15% of Iraq war veterans suffer from PTSD (Getty Images Iraw War picture) [42–44]. High-risk factors for PTSD include females [45], low education status [46], and family history of mental health disorders [47]. PTSD is diagnosed in patients when they display the following four symptoms for a minimum of 1 month: commonly experience traumatic nightmares and flashbacks also known as reexperiencing symptoms, negative changes in

mood, symptoms of avoidance, and changes in arousal or reactivity [48].

Treatment for PTSD can be done via cognitive behavioral therapies or pharmacological intervention. Behavioral therapy can include desensitization to the traumatic event by excessive exposure to the triggers of their PTSD, helping the patient understand in an objective manner their trauma and how to process it, and eye movement desensitization [49]. Pharmacological treatments include fluoxetine, paroxetine, phenelzine, risperidone, and sertraline; however their efficacy was minimal compared to a placebo [50].

Some dental fears resulting from painful dental treatment may reach levels of a post-traumatic stress disorder diagnosis [5]. PTSD patients have a higher incidence of reported chronic pain in the periodontium [51], poorer oral hygiene, a decrease in dentition, and more temporomandibular disorders than the normal population [52]. When examining a patient with PTSD for nonspecific dental pain with no apparent odontogenic etiology, one should consider tooth clenching as a cause of symptoms [53] as myofascial pain has been seen in 48% of those with PTSD [52].

Oral and maxillofacial surgeons may frequently see patients for surgical interventions to treat obstructive sleep apnea (OSA); some of these patients may suffer from PTSD as evidence points to a high incidence of OSA in PTSD patients [54] as seen in a recent meta-analysis where 76% of veterans with PTSD had OSA [55]. A high incidence of PTSD has also been found in those with maxillofacial trauma [56].

Treatment of PTSD patients in the office may require similar interventions as those with anxiety disorders as anxiety is often a comorbid condition in PTSD; however there are other modalities. Studies in behavioral health have shown positive effects of trauma-informed tailored care. Trauma-informed care (TIC) is a way of tailoring treatment of a patient that takes past traumatic experiences and triggers into account. Evidence has shown the effectivity of TIC in various healthcare fields, which can also be applied in an oral and maxillofacial surgery practice. TIC is a team-based approach which can be applied by all members of an oral surgery staff. The main factors of a trauma-informed approach for treatment is to realize the impact of trauma exposure on a patient and how this exposure can impact the patient, apply that knowledge into practice, and prevent retraumatization of the patient. Examples of TIC in an office, depending on a patient's trigger, can be achieved by decreasing sound levels in a practice when seeing a patient who is triggered by loud noises. This can be achieved by lowering or shutting off the music in an office, closing the door in a procedure room to reduce noise, giving the patient noise cancelling headphones, speaking in softer tones, and other actions of the same nature. Ultimately, TIC is determined by the patient triggers which can be known through observations or questioning, although some patients may not feel comfortable discussing their trauma history as that in itself may be a trigger. The main goal of TIC is to do no harm and avoid retraumatization of the patient.

For those patients with PTSD requiring general anesthesia, there is an increased risk of emergence delirium [57]. Careful care should be taken prior to waking the patient, restraints are an option along with proper awareness among the staff to be prepared. Use of propofol as an induction agent decreases the occurrence of emergence delirium, while using ketamine alone or etomidate can increase the risk of EDL [49].

8.6 Gender Dysphoria

Gender dysphoria is defined as a condition in which a person does not identify with their biological or assigned sex at birth; rather they identify with the opposite sex. Individuals with gender dysphoria usually identify as transgender. Approximately 0.5% of the US population identifies as transgender, roughly 1.5 million people in total. As there has been an increase in tolerance and acceptability of transgender people over the last couple of decades, the frequency in the treatment of transgender individuals will likely increase over time. Having proper understanding of transgender terminology and how to address transgender patients is important for the provider to learn; however that is not the focus of

discussion in this book; rather we will focus on considerations for office-based procedures under sedation in this population.

Transitions from the assigned birth sex to the opposite sex can occur through nonmedical intervention such as change in dress, mannerism, and accessories to a medical transition which can include gender confirming surgery or hormone therapy. For the purpose of this book, we will focus on hormone replacement therapy and its effect on delivering office-based anesthesia care. For those transitioning from being a man to a transgender woman by using hormone replacement therapy, exogenous estrogen is used along with testosterone-blocking therapies to develop female characteristics such as the development of breast tissue and reducing body hair. Oppositely, women transitioning into being transgender men take exogenous estrogen to help build masculine features such as muscle growth and increased body hair volume. Estrogen use increases risk of venous thromboembolism, with a higher incidence in orally administered estrogen [58], and can lead to postoperative vomiting [59]. It is recommended to discontinue estrogen therapy 2–4 weeks prior to surgery due to the clotting risks [60]. However, discontinuation of such therapy can lead to mood changes and depression, and if prolonged it can lead to reversal of physiological and physical feminization characteristics. In female to male transgender therapy with testosterone, there is usually an increase in triglyceride levels; however there is no apparent increased risk in cardiovascular complications with these patients [58].

With regard to pregnancy testing, transgender men may still have fully functioning female reproductive organs, which means that they are capable of becoming pregnant. Thus, it is recommended that questioning of all biologically born females with regard to their pregnancy status be completed, and if indicated pregnancy tests should be done if the patient is unsure of their status. It is important to take into consideration that when a transgender man discontinues their hormone therapy prior to a procedure, their likelihood of becoming pregnant with intercourse increases, and thus they should be made aware. As with most adjustments and changes in medication regimens, consulting and co-management with the patient's primary care physician and specialist(s) is recommended.

8.7 Eating Disorders

Eating disorders are a group of mental health disorders which involve extreme behaviors and thoughts regarding weight and food.

Those who have **anorexia nervosa** view themselves as overweight, even if they are underweight. They go through extreme measures to lose weight by excessive exercising, food restriction, and use of laxatives or vomiting to expel food after they have eaten. Out of all mental health disorders, anorexia nervosa has the highest rate of mortality either by suicide or through complications related to starvation. Starvation in these patients leads to nutritional deficiencies, anemia, brittle nails, lanugo, infertility, lethargy, dehydration, xerostomia, and brain and multi-organ damage. **Bulimia nervosa** is a mental health disorder where individuals affected with the condition go through episodic periods of eating large amounts of food followed by compensatory periods to counteract against their binge eating. Compensatory actions can be by vomiting, taking laxatives, overexercising, and fasting. Individuals with bulimia nervosa can be either normal in weight, underweight, or overweight. Clinical significance of bulimia nervosa is having chronically inflamed oral soft tissue, including the throat, parotid hypertrophy, worn tooth enamel, GERD, dehydration, and electrolyte imbalances. Similar to bulimia nervosa, **binge eating disorder** consists of episodes of excessive eating. However, unlike bulimia nervosa, individuals affected by binge eating disorder do not have compensatory periods to counteract their binge eating. Those affected tend to eat even when they are not hungry, eat their food fast, and have guilt about their eating.

Consults and history and physicals along with blood work may be necessary prior to office-based procedures in eating disorder patients to ensure safe outcomes of anesthesia and postoperative healing. Concerns for anemia and electrolyte imbalances are significant with surgery in this population; thus recent lab work is necessary prior to treatment. Proper counseling may also be indicated as evidence has shown that third molar extractions can cause an increased risk in exacerbation and relapse in eating disorder patients [61]. In individuals with active symptoms from their eating disorder, delay of surgery is recommended when possible [62]. If surgery is indicated, it is not recommended to perform the procedure in an office-based setting of a symptomatic patient with an eating disorder. In those patients, hospital-based surgery is recommended for fluid management along with access to medical specialists and resources [62].

8.8 Summary

Mental health disorders are expanding in number due to our growing understanding of different mental health conditions and their intricacies. Awareness of the most common types of mental health disorders is imperative for the oral and maxillofacial surgeon due to the likelihood of encountering patients that have been referred because of their behavioral condition and complexity of their disorder. Understanding the clinical presentations and etiologies of these major disorders allows proper assessment and determination of the course of care. Decisions are made on whether office-based procedures are suitable or if a patient needs care at a hospital based on these assessments. Those who are candidates for office-based procedures can benefit from tailored care based on their mental health disorder allowing for the surgeon to achieve successful completion of treatment. Table 8.4 summarizes the major mental health disorders discussed in this chapter and their considerations for treatment in the oral and maxillofacial surgery office.

Table 8.4 Summary of mental health disorders and their anesthetic and general considerations for treatment in the oral and maxillofacial surgery office

Condition	Common medications used	Effects of medications	Anesthesia considerations	General considerations
Anxiety	• SSRIs • NRIs • Beta-blockers • Benzodiazepines	• Inhibition of cytochrome P450 enzymes (SSRIs) • Increase of serotonin levels (SSRIs, SNRIs)	• Careful use of medications that are hepatically cleared (i.e., midazolam) • Avoid/cautiously use serotonin-increasing medications (e.g., fentanyl, tramadol)	• Continue anxiety medications in the perioperative period avoiding discontinuation syndrome • Be aware of serotonin syndrome risks and signs
Depression	• SSRIs • SNRIs • TCAs • MAOIs	• Inhibition of cytochrome P450 enzymes (SSRIs) • Increase of serotonin levels (SSRIs, SNRIs, TCAs, and MAOIs) • Increase of norepinephrine levels • SNRIs, TCAs	• Careful use of medications that are hepatically cleared (i.e., midazolam) • Avoid/cautiously use serotonin-increasing medications (e.g., fentanyl, tramadol) • With SNRIs, and TCAs avoid indirect vasopressors; use direct vasopressors instead • Avoid ketamine and other sympathetic stimulators in patients treated w/SNRIs and TCAs	• Continue anxiety medications in the perioperative period avoiding discontinuation syndrome • Be aware of serotonin syndrome risks and signs

(continued)

Table 8.4 (continued)

Condition	Common medications used	Effects of medications	Anesthesia considerations	General considerations
Bipolar disorder	• Mood stabilizers (e.g., lithium, valproate) • Antianxiety medications (see above) • Antidepression medications (see above)	• Lithium prolongs duration of neuromuscular blockage from succinylcholine	• Consider discontinuing lithium 3 days preoperatively • Use perioperative fluids with sodium 2/2 depletion from lithium treatment	• Consult with PCP/Psych provider prior to stopping lithium • Restart lithium within 1 week of surgery to avoid relapse • No need to stop lithium treatment for local anesthetic procedures • Awareness of medications that decrease lithium excretion (i.e., ACEI)
Schizophrenia	• Typical antipsychotics (e.g., chlorpromazine, haloperidol) • Atypical antipsychotics (e.g., clozapine, risperidone)	• Typical antipsychotics: dystonia, tardive dyskinesia, Parkinson's-like symptoms • Atypical antipsychotics: weight gain, postural hypotension, gynecomastia	• Close monitoring and treatment of intraoperative blood pressure—atypical antipsychotics can result in intraoperative hypotension	• Consult with PCP/Psych provider for optimization • Avoid discontinuing antipsychotic medications to avoid withdrawal symptoms and perioperative psychotic episodes
PTSD	• SSRI • Atypical antipsychotics	• SSRI and atypical antipsychotic side effects	• Increased risk of emergence delirium, specifically with ketamine and etomidate when used alone • Propofol induction decreases emergence delirium risk • SSRI and atypical antipsychotic considerations	• Consult with PCP/Psych provider for optimization • Implement trauma informed care (TIC) in all applicable perioperative settings • SSRI and atypical antipsychotic considerations
Gender dysphoria	• Hormone therapy (e.g., estrogen, testosterone)	• Estrogen: development of breast tissue, reduced body hair • Testosterone: muscle growth, increased facial hair	• Pregnancy questioning and testing if indicated on all transgender men due to possibility of functioning female organs	• Increased thromboembolism risk with estrogen therapy • No increased cardiovascular risks with testosterone use
Eating disorders	• N/A	• N/A	• Organ damage: concern for hepatic and kidney clearance of anesthetic meditations • Inflamed oropharynx in bulimia nervosa—possible airway concern • GERD in bulimia nervosa—aspiration risk	• Consult with PCP/Psych provider for optimization • Delay surgery if possible for medical optimization, or consider hospital-based surgery • Electrolyte imbalances can be exacerbated postoperatively

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9 Practice Considerations for Patients with Substance Use Disorder

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9.1 Introduction

Substance abuse is known as a chronic brain disorder which disrupts the normal pathways of rewards, withdrawal, memory, and motivations. The misuse and abuse of substances such as opioids, alcohol, cocaine, and prescription drugs (Table 9.1) have led to a national crisis in the United States and can result in serious medical consequences. Since 2013, the incidence of drug-use-related deaths has surpassed motor vehicle collisions as the number one cause of accidental death in the United States [1]. Despite efforts in education in prevention, the statistical misuse of drugs has escalated, with over 20 million American substance abusers [2]. Over 67,000 Americans died from drug overdoses in 2018, with an upward trend in synthetic narcotics, cocaine, and psychostimulants [3, 4]. The purpose of this chapter is to offer practice considerations for oral and maxillofacial surgeons (OMS) caring for patients with substance use disorder (Fig. 9.1). These considerations include preoperative assessment, perioperative management, and postoperative care of such patients. While the pathophysiology of each substance is beyond the scope of this chapter, clinical assessments, preoperative optimization, and the challenges of treating patients with substance abuse issues will be discussed.

Table 9.1 Commonly abused drugs

Classification	Common drugs
Cannabinoids	Marijuana, hashish
CNS stimulants	Cocaine, amphetamines
CNS depressants	Alcohol, benzodiazepines
Opioids	Heroin, morphine, opium
Hallucinogens	Lysergic acid diethylamide, phencyclidine, mescaline, psilocybin
Volatile Solvents	Varnish, paint thinner, petroleum

9.2 General Considerations

A critical first step in patient management is obtaining a detailed and accurate medical and psychosocial history to formulate a successful plan. Being aware of the drug history of a patient allows safe management, tailored to their needs. Understanding a patient's drug history and predicting their response to office-based anesthetics, for instance, can help determine the most suitable environment for treatment and the optimal anesthetic plan [6]. An overall assessment should be

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	DSM-4 Abuse[a]		DSM-4 Dependence[b]		DSM-5 Substance Use Disorders[c]	
Hazardous use	X	≥1 criterion	–		X	≥2 criteria
Social/interpersonal problems related to use			–		X	
Neglected major roles to use	X		–		X	
Legal problems	X		–		–	
withdrawal[d]	–		X	≥3 criteria	X	
Tolerance	–		X		X	
Used larger amounts/longer	–		X		X	
Repeated attempts to quit/control use	–		X		X	
Much time spent using	–		X		X	
Physical/psychological problems related to use	–		X		X	
Activities given up to use	–		X		X	
Craving	–		–		X	

Fig. 9.1 DSM-4 and DSM-5 criteria for substance use disorders. [a]One or more abuse criteria within a 12-month period and no dependence diagnosis: applicable to all substances except nicotine, for which DSM-4 abuse criteria were not given. [b]Three or more dependence criteria within a 12-month period. [c]Two or more substance use disorder criteria within a 12-month period. [d]Withdrawal not included for cannabis, inhalant, and hallucinogen disorders in DSM-IV. Cannabis withdrawal added in DSM-5 [5]

rendered and may include, but should not be limited to, the patient's general health, current medications, allergies, preexisting conditions, and previous anesthesia history [7]. It is also important to take note of the patterns of use in regard to the substance use, such as known triggers for substance use, duration of use, length of abstinence (if applicable), and most recent use [8].

Implications and considerations of specific substances vary based on their pharmacokinetic and pharmacodynamic effects, but providers should be cognizant of the patient's increased risk of the following [8]:

- Aspiration
- Compromised airway
- Encephalopathy
- Generalized edema
- Hyperalgesia
- Hemodynamic instability
- Hepatomegaly
- Lymphadenopathy
- Subcutaneous abscess
- Venous thrombosis
- Withdrawal tendencies

Medical professionals should remain mindful that not all patients fully declare their entire medical history. Therefore, it is imperative to understand the commonly used recreational drugs, the pathophysiology of their acute and chronic use, and their implication on the planned procedure in order to maintain safe sedation practice while achieving adequate patient response. Of note, procedures performed with local anesthesia only still require a thorough understanding of the patient, to limit untoward outcomes.

9.3 Cannabinoids: Marijuana

9.3.1 Introduction

As more societies move towards decriminalization and legalization of recreational and medicinal use of marijuana, healthcare professionals are likely to find disclosures of such use in patients more commonplace while obtaining a social history. By 2018, more than a third of young adults (ages 18–25) and an estimated 13.3% of adults ages 26 and older reported marijuana use in the past year. Moreover, approximately 4.4 million people aged 12 or older reported a marijuana use disorder in the past year. Marijuana, also referred to as pot, hash, grass, weed, and bud, can be smoked as a cigarette (a joint), using a water

pipe, and using a hollow cigar (a blunt), vaporized, or consumed orally [9]. The primary component of marijuana is tetrahydrocannabinol (THC) which can range between 1 and 65% with hashish oil having the highest amount of THC. Users report a feeling of euphoria and relaxation. When taken in conjunction with alcohol or benzodiazepines, this feeling is accentuated, and when combined with amphetamines or cocaine, a synergistic stimulatory effect can be expected.

9.3.2 Preoperative Assessment

Due to anxiety associated with surgical and dental practices, clinicians are likely to encounter patients who present acutely intoxicated with marijuana during the consultation or surgical appointment. The common presentations are tachycardia, conjunctival injection, and anxiety [10]. The medical questionnaire allows a chance to obtain relevant history regarding use. Obtaining information regarding the amount of daily use, route of administration, and combined use with any other substances will help formulate a safe treatment plan. As a result, the clinician should educate patients on effects of drug use when combined with procedural anesthetics and increased risk of complications.

Marijuana typically tends to accentuate a preexisting emotion. Therefore, if a patient used marijuana to help with preoperative anxiety, the result might be to the contrary, and the practitioner will likely find a highly anxious and somewhat euphoric individual.

9.3.3 Perioperative Management

The ingestion of low to moderate doses of cannabis results in activation of the sympathetic system resulting in tachycardia and increased cardiac output. Acute coronary syndromes are reported in some users with a 25% mortality. High doses result in inhibition of sympathetic activity, presenting as possible hypotension and bradycardia. Cross-tolerance to other drugs such as alcohol, opioids, benzodiazepines, and phenothiazines has been observed. However, during anesthesia, it can create a stacking effect on inhalational agents leading to profound myocardial depression. Further, it also increases the effects of opioids leading to respiratory depression [2]. A study by Flisberg et al. [11] suggested an interaction between cannabis and propofol. Cannabis users needed a significantly higher dose of propofol prior to laryngeal mask insertion, suggesting difficulty in sedation of chronic marijuana users. Anecdotal evidence would suggest that most OMS will concur with their experiences that marijuana users typically will need higher doses of propofol to be sedated comfortably.

Marijuana smoke can cause upper airway irritability, impairment on airway epithelial function, and damage to bronchial tissue. Marijuana also causes increased alveolar permeability and may lead to negative pressure pulmonary edema. Patients are predisposed to bronchospasm, chronic cough, bronchitis, and emphysema [2]. Furthermore, case reports presented patients who suffered from respiratory distress due to isolated uvulitis during general anesthesia. The complication was attributed to heavy marijuana use due to the history of last use within 6–12 h prior to the onset of symptoms [12]. Subsequently, some have recommended for prophylaxis administration of dexamethasone prior to general anesthesia [2].

While life-threatening arrhythmias have not been reported in literature, an increase in supraventricular and ventricular ectopic activity as well as reversible ST segment and T wave abnormalities can be observed [2]. In a patient with a recent history of use, drugs increasing the heart rate such as ketamine, pancuronium, atropine, and epinephrine should be avoided. Patients who consume higher doses of marijuana may have inhibition of sympathetic activity leading to bradycardia and hypotension. Furthermore, adverse autonomic reactions and psychiatric effects may interfere with postoperative recovery. To avoid these effects, anesthesia should be avoided in any patient with cannabis use within the past 72 h [13].

Chronic marijuana smokers are known to present with severe nausea and vomiting which is now characterized as cannabinoid hyperemesis syndrome. These patients have delayed gastric emptying and may present with a prodromal phase of excessive salivation, nausea, and prolonged vomiting.

9.3.3.1 Postoperative Challenges

While postoperative dysphoria, nausea, and vomiting or others have not been identified as a significant complication in marijuana users, those that have habitually used IV drugs such as heroin or synthetic narcotics may have issues with hyperalgesia, and postoperative pain control may be a challenge in these subgroups. Further, marijuana especially as an orally administered form may be considered as adjuvant therapy for postoperative pain control following surgery. More evidence is becoming available to support this in the scientific literature recently.

9.4 Stimulants

9.4.1 Cocaine

9.4.1.1 Introduction

Among polysubstance abuse, addiction to cocaine is one of the most common. Approximately 30% of the drug-related emergency department admissions in the United States are attributed to cocaine. There is no classical socioeconomic, ethnic, or cultural profile when attempting to identify a cocaine user. With five million Americans being regular offenders and 6000 trying the drug for the first time every day, identifying a cocaine abuser is a significant clinical challenge. Concomitant substance abuse of multiple drugs and cocaine is frequently noted, with ethanol being the most commonly observed. During the clinical evaluation, chronic users may present with septal or soft palate perforation. Rarely, cocaine users present with delirium, which is manifested by diaphoresis and agitation and may lead to respiratory or cardiac arrest.

Preoperative Assessment

Given the high probability of complications associated with cocaine abusers, priority should be given to care under local anesthesia. However, should sedation be required, the surgeon should be prepared for management. Increased levels of catecholamines can cause significant cardiovascular effects in a non-dose-dependent manner. Therefore, even small recreational dose amounts can cause myocardial ischemia due to infarction, vasospasm, thrombus, or direct cardiotoxicity. These patients present with a 24-fold risk to develop myocardial infarction (MI). Some studies have reported a 25% of all MIs below the age of 45 years are related to cocaine use. Other cardiac risks include arrhythmias, cardiomegaly, and hypertension. Cocaine users may have hypoxemia and interstitial alveolitis similar to acute respiratory distress syndrome. Patients also may present with bronchospasm, hyperthermia, and agitation. A thorough physical examination at the preoperative stage should detect any cardiovascular abnormalities, which may prompt further investigation of the patient's status. Of note, a 2006 JOMS article by Granite et al. suggests that a patient may undergo necessary surgical and anesthetic care, after an 8-h period of discontinuing of cocaine, if the individual is hemodynamically stable [14].

Perioperative Management

In the setting of general anesthesia, patients may experience severe hypertension due to increased cardiac output, which could furthermore be exacerbated by stimulation during insertion of laryngeal blade at the time of intubation or simply by injections of local anesthetics or the surgery. While it is imperative to treat this hypertension prior to proceeding, that might be challenging. Propranolol is contraindicated in acute intoxication due to potential for unopposed alpha-adrenergic stimulation. Esmolol, labetalol, and hydralazine have been recommended to manage hypertension and tachycardia, commonly seen in this subcategory of patients.

Should general anesthesia be required, it has been postulated that the metabolism of succinylcholine is reduced possibly due to competing

metabolism by plasma cholinesterase. Ketamine should be used with caution due to potentiation of cardiac effects of cocaine by increasing catecholamines. Potent volatile anesthetics may produce cardiac arrhythmias and increase vascular resistance in the intoxicated patient. In addition, administration of succinylcholine may lead to prolonged neuromuscular blockade. Cocaine-related physiological derangements may be mitigated with the use of dexmedetomidine, clonidine, or peripheral alpha-1 antagonists, intravenous hydration, and sedation with benzodiazepines.

In the case that myocardial ischemia is suspected during the procedure, the surgeon should begin initial medical therapy and, once stable, triage the patient for appropriate care. The American Heart Association has revised their guidelines on emergency management of cardiovascular care in cocaine-related myocardial ischemia. The first-line agents should be aspirin, nitroglycerin, and benzodiazepines, and propranolol should be avoided. Due to the high susceptibility of cardiovascular complications, the surgeon should monitor for early signs of arrhythmias, angina, and infarction.

9.4.1.2 Postoperative Challenges

Postoperative monitoring of cocaine patients is imperative to avoid cardiac complications. Intractable postoperative nausea, vomiting, and challenges in postoperative pain control are practical challenges for this group of patients. Counselling about avoidance of cocaine 24–48 h following anesthesia and surgery is prudent.

9.5 Methamphetamines

9.5.1 Introduction

Also known as meth, crystal, and glass, methamphetamine is a synthetic derivative amphetamine, a schedule II drug with high potential for abuse due to its psychostimulant properties [15]. Methamphetamine increases alertness, concentration, and energy and, in high doses, can induce euphoria and enhance self-esteem. Amphetamines are generally used to treat attention-deficit hyperactivity disorder in children and adults, narcolepsy, exogenous obesity, hyperphagia, psychotherapeutic indications such as depression, and Parkinson's disease [15]. The drug is a crystalline powder that can be dissolved in water or alcohol for ingestion via intranasal, inhalational, intravenous, or oral routes. The systemic effects result in activation of the sympathetic system leading to increased release and decreased reuptake of catecholamines. Therefore, increased heart rate and blood pressures can be expected [16].

9.5.2 Preoperative Assessment

Due to high suspicion for intravenous use, and needle sharing, further investigation may be necessary for cardiac, hepatic, hematologic, and immunologic status of patients. Methamphetamines can cause left ventricular hypertrophy and decreased cardiac compliance, presenting as diastolic dysfunction and even heart failure [17]. Therefore, abnormal findings should be addressed with a primary care physician or specialist prior to proceeding with elective surgery.

9.5.3 Perioperative Management

The main challenge of treating patients with a history of methamphetamine use is related to heart rate control and maintenance of blood pressure in light of compromised cardiovascular function. Meth users may present with refractory hypotension leading to hemodynamic instability. Chronic amphetamine exposure and stimulation of the adrenergic and peripheral nerve terminals causes a depletion of catecholamine receptor storage. This depletion, especially norepinephrine, blunts the physiologic and sympathetic response to hypotension. Direct-acting vasopressors like epinephrine or phenylephrine are generally used to treat hypo-

tension. Furthermore, in patients who ingest by smoking the agent, increased risk for intraoperative bronchospasm is similar to that of a heavy tobacco smoker. The management of the airway is further compromised by common presentation of loose and grossly carious dentition and abscesses. Altered drug metabolism and protein binding secondary to hypoalbuminemia and malnutrition can affect the dose of anesthetics administered.

9.5.4 Postoperative Challenges

Postoperative laryngospasms and bronchospasms as well as cardiac complications such us heart failure can occur in these patients. When heavy abuse is suspected, a lower threshold for postoperative admission and in-patient care may be prudent. Postoperative intraoral wound healing is a concern for the obvious reasons as well. These patients often require a high dose of postsurgical prescription pain medications which should be planned pre-operatively with the patient's addiction and pain specialist.

9.6 Depressants

9.6.1 Alcohol

9.6.1.1 Introduction

Preoperative Assessment

Alcohol abuse is generally associated with resistance to the actions of central nervous system depressants. An accurate history of amount and length of consumption is important to determine the need for further workup. If considering performing procedures under general anesthesia, it is necessary to take into consideration hepatic dysfunction, hypoalbuminemia, cardiac failure, and arrhythmias. Chronic alcoholics exhibit myopathy, mostly noted in proximal muscles, and also alcohol-induced cardiomyopathy with reduced ejection fraction presenting similarly to dilated cardiomyopathy. When an alcoholic patient presents with cirrhosis or muscle weakness, an echocardiography is advised before surgery to best evaluate.

Perioperative Management

The effects of alcohol on the gastrointestinal organs are generally related to effects on muscle tone, acid production, and mucosal integrity. Alcoholism may lead to electrolyte abnormalities, hypovolemia, and hypoglycemia. Long-term use can manifest as gastritis, increased gastric volume and acidity, gastric ulcers, gastroesophageal reflux disease, and Mallory-Weiss tears. Alcohol also impairs gastric motility and digestion, housing food in the stomach for prolonged periods. When assigning NPO status, this should be considered. Furthermore, chronic heavy alcohol users are prone to alcoholic liver disease such as hepatitis, fatty liver disease, and cirrhosis. Cirrhotic patients have significant impairment in hemodynamic profile and protein synthesis, such as coagulation factors and albumin. In order to prevent drug toxicity during anesthesia, the standard protocol is modified to half the dose of midazolam increments and double the time between doses [18]. This allows a greater understanding of the effect of each dose, enabling a balance between adequacy of anesthesia and margin of safety. Additional time for recovery should be expected due to impaired metabolism and elimination of sedative.

Alcohol also hinders the natural immune function as well as autonomic functions such as cough and gag reflex. Impairment of these functions can increase risk of aspiration and aspiration pneumonia. Mucociliary function is also blunted which can have a synergistic effect if tobacco is also used.

Postoperative Challenges

Expect a prolonged recovery from anesthesia. Alcoholics with impaired hepatic function may have prolonged postsurgical bleeding issues. Especially following surgery in the mouth and

aerodigestive tract, postoperative malnutrition is not uncommon in these patients. Their already impaired immune system affects normal wound healing deleteriously and predisposes them to infections. Further, the clinician should have a plan regarding the potential for withdrawal, especially if the patient is admitted to the hospital for postsurgical nursing care.

9.6.2 Opioids

9.6.2.1 Introduction

While opioid use can be an effective analgesic therapy when indicated, its euphoric effects are what draws many people to abuse them. Unfortunately, this paves way to rapid tolerance, physical dependence, and a psychological addiction [2]. Opioid overdoses have accounted for more deaths than cocaine and heroin [19]. These patients present with slow and slurred speech, slow gait, constricted pupils, and droopy eyelids. Patient often have reduced appetite and constipation.

According to the National Institute on Drug Abuse, between 21 and 29% of patients that were prescribed opioids for chronic pain misuse them, with 8–12% developing an opioid disorder [20]. With the upward trend of opioid misuse, it is crucial for medical providers to recognize the presenting symptoms, possible drug-to-drug interactions, and overall considerations during and after treatment.

Preoperative Assessment

A history of drug abuse should provoke further medical questions. For example, history of intravenous drug use should prompt an evaluation of cardiovascular, pulmonary, neurologic, and infectious complications such as endocarditis, abscesses, osteomyelitis, hepatitis, and HIV infection. Heroin users present with dry, itching skin and skin infections.

Workup may include toxicology screen, CBC, liver function tests and renal panel. Preoperative consenting may be a challenge especially if the patient tends to be intoxicated at the time of signing it.

Perioperative Management

Anesthetic management of chronic opioid abusers presents with multiple challenges. Vascular access may be challenging. Furthermore, underlying sepsis, coagulopathy, and hemodynamic instability may complicate general anesthesia course. Concomitant malnutrition, liver disease, and altered intravascular fluid volume may require dose adjustment of anesthetic agents [2, 21]. Yet, patients may become hypersensitive to surgical stimuli and require higher doses of anesthetics due to tolerance alone or development of opiate hyperalgesia/hyperesthesia [22]. As each patient will present with unique needs, dosage should be guided by monitoring of vital signs. Also, judicious use of local anesthesia and ketamine may reduce the overall opioid consumption [23].

In patients who may be in the process of detoxification or in recovery, the use of methadone or buprenorphine should be continued. It is recommended that patients continue these agents in the perioperative period. Methadone leads to a decrease in MAC of inhalational general anesthetics. In addition, the risk of torsades de pointes is also reported with methadone. Discontinuation of either agent should be at the discretion of the addiction and pain specialists. Opioid antagonists or agonist-antagonists must be avoided in these patients as it can precipitate acute withdrawal symptoms [2].

9.6.3 Postoperative Management

Inappropriate management of patients on buprenorphine may lead to severe cravings and subsequent relapse. Patients may experience exaggerated postoperative pain secondary to decreased production of endogenous opioids. The subjectivity of pain and conflict between patient's rights and safety pose an ethical dilemma. Coordination with the patient's pain

specialist is of most importance during the preoperative and postoperative phases to establish an appropriate plan. A preoperative pain contract that outlines your responsibility and that of the patient may be beneficial to minimize postoperative negotiations and unnecessary skirmishes regarding prescriptions. Discharge following recovery may be a challenge if the clinician suspects that the escort is also intoxicated.

9.7 Other Drugs

Some patient encounters may also represent drug abuse with MDMA, phencyclidine (PCP), and gamma-hydroxybutyric acid (GHB). Similar to other drug users, these patients also present with psychiatric disturbances, including panic, anxiety, depression, paranoia, muscle tensions, nausea, and blurred vision. Clinical assessment of these patients might reveal hemodynamic instability, tremors, sweating, fainting, chills, and hallucination. Ecstasy users may pose a risk to develop serotonin syndrome and malignant hyperthermia. They consume abnormal quantities of water due to increased antidiuretic hormone production which in turn may lead to hyponatremia and other electrolyte abnormalities. Conduction defects such as long QT interval and torsades de pointes are common. Drug-induced hepatic failure is also common with about 20% of all cases below the age of 20 years.

Patients who abuse GHB may present with tremors, seizures, vomiting, liver failure, and comatose. Fatal respiratory depression is a risk in such patients, and they are prone to life-threatening withdrawals. Physostigmine is reported as a potential agent to reverse toxicity from GHB, although such reports are sparse.

At low to moderate doses, PCP users have increased respiratory rate, pronounced rise in blood pressure and pulse rate, shallow breathing, flushing and profuse sweating, generalized numbness of the extremities, and loss of muscular coordination. In higher doses, drooling, dizziness, loss of balance, seizures, and coma have been reported. Some patients mimic schizophrenia (delusions, hallucinations, paranoia, disordered thinking, a sensation of distance from one's environment, and catatonia), and speech is often sparse and garbled.

Abusers of organic solvents may have arrhythmias, nausea and vomiting, bronchial irritation, pulmonary hypertension, and edema with airway resistance. The risk of methemoglobinemia is also reported in these patients.

9.8 Summary

Oral and Maxillofacial Surgeons, as well as other trained clinicians, are in a unique position to offer anesthesia in the office for surgical management. While questions regarding consumption of alcohol, tobacco, and illicit substances may be overlooked during the preoperative assessment, they certainly bring to light critical information that affects treatment setting and anesthesia. Deeper probing of the social history of our patients have become paramount now than ever. Substance abuse disorder affects patients of all socioeconomic backgrounds, ages, and gender. A thorough understanding of the pathophysiology of the abused substance, probing for underlying medical conditions, and its implication on treatment is of utmost importance. Further workup may be necessary to obtain all relevant information to provide safe treatment and an uneventful postoperative course.

When appropriate postpone elective surgery and consider using a venue other than the office for these patients to mitigate risks. Table 9.2 serves as a summary of physiological implications and considerations during surgical treatment.

Table 9.2 Summary of implications and considerations for the OMS patient with substance abuse disorder. Obtained from an open source article by the American Association of Nurse Anesthetists [8]

Substance	Physiological implications	Considerations
Marijuana	• Airway irritability • Acute airway edema and obstruction • Myocardial depression • Exacerbation of existing tachycardia • Reversible ST segment and T wave abnormalities • Supraventricular or ventricular ectopic activity • Potentiation of non-depolarizing muscle relaxants, norepinephrine • Augmentation of drugs that cause respiratory or cardiac depression • Profound response to inhaled anesthetics • Sensitization of the myocardium due to increased level of epinephrine	• Maintain airway due to potential for airway obstruction • Consider administration of dexamethasone to minimize airway edema • Increased propofol dose may be required for induction and maintenance • Avoid drugs known to affect heart rate (e.g., ketamine, atropine, epinephrine)
Cocaine	• Infection or perforation of nasal septum • Pulmonary edema • Blood vessel constriction • Cardiomegaly, ischemia • Tachycardia, arrhythmia • Thrombocytopenia • Bronchospasm • Hyperthermia • Hypertension • Pneumothorax • Agitation	• Administer medications to control blood pressure • Take precautions with nasogastric and orogastric tubes • If possible, avoid drugs such as ketamine, atropine, halothane, enflurane, and older inhalational agents, which can sensitize myocardium to effects of catecholamines • Cocaine-free interval of at least 1 week prior to elective surgery is recommended • Increased incidence of renal failure may impact anesthetic elimination • Avoid beta-blockers (specifically propranolol) due to possibility of unopposed alpha-receptor activity
Amphetamines	• Hemodynamic instability, refractory hypotension • Decreased catecholamine • Cardiac arrest (during anesthesia) • Poor dentition • Acute intoxication: decreased MAC • Chronic use: increased MAC	• Halothane should be avoided • Take precautions to avoid refractory hypotension – Administer vasopressor (e.g., phenylephrine, epinephrine) in the treatment of hypotension

(continued)

Table 9.2 (continued)

Substance	Physiological implications	Considerations
Alcohol	• Electrolyte abnormalities • Hypoalbuminemia • Hypoglycemia • Hypovolemia due to diuretic effect • Increased gastric acidity and volume • Pulmonary aspiration • Hemodynamic instability • Increased risk of bleeding • Wernicke-Korsakoff syndrome	• Assess need for electrocardiogram, echocardiography, chest x-ray, complete blood count, liver enzyme, liver function, and electrolyte panels • Consider regional analgesia and anesthesia and medications/agents with minimal or non-hepatic metabolism • Administer medications to prevent aspiration • Administer thiamine to prevent Wernicke-Korsakoff syndrome • Appropriately treat symptoms of withdrawal such as agitation and hallucinations on an individual basis • Hemodynamic instability may be exposed by intravenous or inhalational agents in patients with preexisting cardiomyopathy, heart failure, and dehydration
Opioids	• Inadequate analgesia • Respiratory depression • Respiratory depression • Withdrawal • Cross-tolerance • Hypotension • Difficult central and peripheral venous access • Coagulopathy and hemodynamic instability • Liver disease and malnutrition • Reduced intravascular fluid volume	• Difficult central and peripheral venous access • Consider alternative pain management strategies that do not involve the administration of opioids Address opioid overdose • Assess ventilation and provide 100% oxygen • Administer naloxone, as appropriate – Observe patient to ensure they do experience delayed respiratory depression after administration of naloxone • Consider endotracheal intubation and mechanical ventilation if naloxone does not successfully reverse respiratory depression

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10 Oral and Maxillofacial Surgery and Hematologic Diseases

Karen Zemplenyi and Jasjit K. Dillon

10.1 Introduction

Hematologic disorders comprise a wide spectrum of conditions from the inherited to the acquired. The hematological "system" is complex and multiorgan. This family of disorders and diseases can affect cell lineages of the blood, bone marrow, and lymphatic systems. Additionally, disease of non-hematopoietic sites such as the liver, kidneys, and lungs can result in hematological disorder and consequently have impacts on hemostasis and immunocompetency. Patients with hematologic disorders may be prone to bleeding, infection, or complications; all dental practitioners and surgeons should be cognizant of and well-versed in treating. Oral and maxillofacial surgeons must not only be aware of a patient's underlying hematologic condition but should be vigilant for oral manifestations of underlying hematologic disturbance which may otherwise be unknown to the patient. Any decisions of treatment and intervention timing should always be made in concert with a patient's hematologist and/or care team. This chapter will provide an overview of hematological diseases and their management in an outpatient oral maxillofacial surgery setting. Issues with anticoagulation will be covered in more detail in a separate chapter.

10.2 Overview

The following chapter is divided into three subsections: malignancies, disorders of platelets/clotting factors, and disorders of red blood cells. These are expansive topics so for practicality only a subset of more common conditions are discussed:

Hematologic malignancies

- Leukemia
- Lymphoma
- Multiple myeloma

Disorders of platelets and clotting factors

- Hemophilia
- von Willebrand disease

Disorders of red blood cells

- Sickle cell disease
- Thalassemia

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10.3 Hematologic Malignancies

Per the National Cancer Institute (NCI), dentists and dental specialists are vital members of an oncologic multidisciplinary team. Given the rapid rate of cell turnover in the oral cavity, the region is highly susceptible to chemotherapies and ionizing radiation. For oncologic patients, it is of upmost importance to evaluate baseline oral health and aim to treat possible complications prior to starting immunocompromising treatment. Caring for patients with hematologic malignancies requires that the provider triage those conditions requiring immediate attention and establish an oral hygiene plan for the patient moving forward. This plan will be made in conjunction with the rest of the oncologic team. On initial exam, one must be vigilant for oral manifestation of systemic diseases and preempt correction of possible sources of oral trauma, i.e., ill-fitting dentures, jagged teeth, and sharp appliances. Prior to maxillofacial surgery, it is important to obtain a complete blood cell count (CBC) looking for isolated abnormalities or pancytopenias in order to assess risk of intervention and in order to plan optimal timing of intervention. In general, oral surgery should be performed at least 10 days prior to start of myelosuppressive therapy. Though there is no strict consensus among organizations or authors, antibiotic prophylaxis is generally recommended in patients with an absolute neutrophil count less than 1000/mm^3, and platelet transfusion should be considered if platelet count is less than 60,000/mm^3 ([1], Table 10.1).

10.3.1 Leukemia

Leukemia is a group of blood cancers broadly categorized as the malignant proliferation of immature blood cells. Leukemia is classified by chronicity (acute vs chronic) and the cell line affected (lymphoid or myeloid). Lymphocytic leukemias refer to abnormalities in cells lines including B lymphocytes, T lymphocytes, and natural killer cells, while myeloid leukemias develop in neutrophils and monocytes. Acute lymphoblastic leukemia is the most common childhood cancer, accounting for ~30% of pediatric cancer cases.

Table 10.1 Recommendations for management guidelines regarding invasive dental procedures (adapted from the NCI)

Medical status	Guideline	Comments
Patients with chronic indwelling venous access lines	AHA prophylactic antibiotic recommendations	Empiric recommendation (no study detailing infectious risk for these lines following dental procedures)
Neutrophils		Order complete blood count with differential
>2000/mm^3	No prophylactic antibiotics	
1000–2000/mm^3	AHA prophylactic antibiotic recommendations	Use clinical judgment to determine aggressiveness of antibiotic regimen
<1000 mm^3	Amikacin 150 mg/m^2 1 h preop Ticarcillin 75 mg/kg IV 30 min preop Repeat both 6 h postop	If organisms are known or suspected, adjust antibiotics appropriately based on sensitivities
Platelets		Order platelet count and coagulation tests
>60,000 mm^3	No additional support needed	
30,000–60,000/mm^3	Optional transfusion for noninvasive treatment, consider transfusion preop and 24 h after surgery for invasive treatment (i.e., dental extractions)	
<30,000/mm^3	Platelets should be transfused 1 h before procedure; obtain immediate postinfusion platelet count; transfuse regularly to maintain counts >30,000–40,000/mm^3 until initial healing	Always consider hemostatic adjuncts such as those in Table 10.2 (i.e., topical thrombin, collagen, aminocaproic acid)

AHA American Heart Association, *IV* intravenous

Systemic signs of leukemia often include pallor, fatigue, easy bruising, fever, petechia, and enlarged lymph nodes. It is not uncommon for a dental professional to diagnose a case of leukemia due to observable signs in the oral cavity: gingival hyperplasia, easy bleeding, and ecchymosis. Diagnosis of leukemias is confirmed with peripheral blood smear and bone marrow aspirate which show blasts and hypercellular marrow, respectively. Patients with leukemia often have white blood cell counts greater than 20,000 per μL. Leukemic infiltration in the bone marrow may lead to reduced number and dysfunction of the main hematologic cell lines making thrombocytopenia, neutropenia, and anemia commonplace laboratory findings.

Treating the different leukemic subtypes usually involves chemotherapy plus or minus radiation and possible bone marrow transplantation [2]. Chromosomal analysis also helps determine leukemia subtypes and may further guide treatments. Dental procedures should ideally be planned prior to treatment start, and emphasis should be placed on oral hygiene and prevention of gingival irritants. As patients undergo treatment, dental and oral maxillofacial providers should also be aware of treatment side effects including xerostomia, bleeding, trismus, osteonecrosis, and oral mucositis, which has been noted in up to 80% of people receiving hematopoietic cell transplantation [3]. Graft-versus-host disease may develop 2–3 weeks after bone marrow transplant and is stimulated by cytotoxic T lymphocytes from the donor. Oral manifestations of this include erythema, xerostomia, gingival erosions and ulcerations. In patients who have undergone allogenic bone marrow transplant, immune system reconstitution can take up to 12 months, leaving the patient at continued risk for opportunistic infection. In general, antibiotic prophylaxis according to the AHA guidelines is recommended prior to invasive dental procedures in the 6 months following chemotherapy [4].

Oral surveillance must continue well after cancer treatment as enamel hypoplasia, arrested tooth development, and subsequent malignancy (mucoepidermoid carcinoma, squamous cell carcinoma) may be sequelae [5]. In addition, dental defects can be associated with relatively low doses of radiation: mature ameloblasts can be damaged by 10 Gy, and tooth development can be halted by doses up to 30 Gy [6]. This is especially true in patients undergoing radiation prior to age 12. Xerostomia from salivary gland dysfunction, often due to radiation to the head and neck, may take 2–3 months to resolve after therapy [7].

10.3.2 Lymphoma

Lymphoma is a broad group of neoplasms disrupting the lymphoreticular system with Hodgkin and non-Hodgkin subtypes. Presenting symptoms often include fevers, night sweats, and weight loss; these are collectively known as "B symptoms." The patient may have painless lymphadenopathy involving the cervical, supraclavicular, and/or axillary nodes. Lab values may show increased erythrocyte sedimentation rate, elevated lactate dehydrogenase, leukocytosis, and anemia. Diagnosis is obtained by lymph node biopsy; Hodgkin lymphoma is characterized by Reed-Sternberg cells on tissue pathology. Intraoral manifestations of Hodgkin lymphoma include ulcerative lesions and swellings to the palate, tonsil, floor of mouth, and mandible [8]. Non-Hodgkin lymphoma is more likely than Hodgkin to present at extra nodal sites. Primary lesions appearing in the oral cavity along Waldeyer's ring comprise 2–3% of cases ([9], Fig. 10.1). Lesions can present with painless swellings and diffuse bony destruction. Lymphomas are often treated with radiotherapy. As with leukemia, the dental provider must plan invasive dental treatment in conjunction with the oncologist. Complete blood count should be obtained prior to treatment given possible pancytopenia. Table 10.2 provides examples of adjunctive hemostatic measure should they be required. Prophylactic antibiotics are required only for absolute neutrophil count <2000.

Table 10.2 Hemostatic measures

Local measures for hemostasis	Derived from	Action
Gelatin sponge	Porcine	Absorbent gelatin promotes fibrin framework and clot. Resorbs in 2 weeks
Oxidize regenerated cellulose	Plant cellulose (polyanhydroglucoronic acid)	Provides meshwork for clot and mechanical pressure Resorbs in 7–14 days *Creates an acidic environment, use caution near nerves
Collagen plugs	Bovine	Causes platelet aggregation Resorbs in 10–14 days
Microfibrillar collagen	Bovine	Promotes platelet adherence and activation of clotting factors
Chitosan-based agents	Chitin	Attracts platelets
Polysaccharide hemospheres	Vegetable starch	Provides scaffold for clot organization
Topical thrombin	Bovine or recombinant human	Reconstituted powder Activates factor IIa (converts fibrinogen to fibrin)
Topical tranexamic acid		Inhibits conversion of plasminogen to plasmin

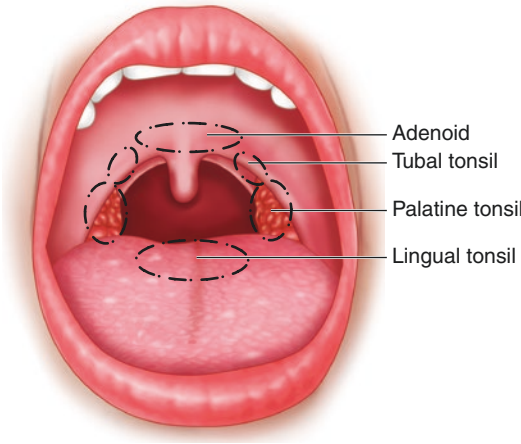

Fig. 10.1 Waldeyer's Ring—lymphoid tissue in the pharynx

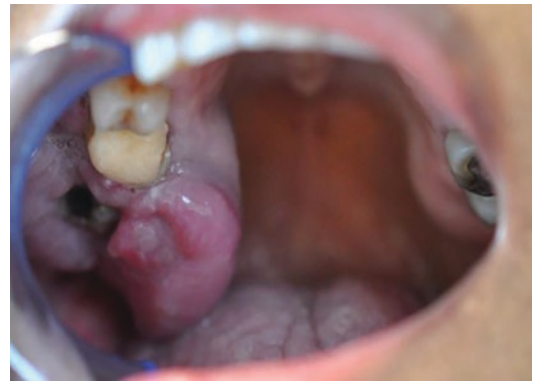

Fig. 10.2 Plasmacytoma

10.3.3 Multiple Myeloma

Multiple myeloma is a cancer of plasma cells making abnormal levels of monoclonal paraproteins. Men are affected twice as often as females with age >45 predominance. Radiographic signs of the disease are characteristic osteolytic punched-out lesions. Bones involved are usually those with high marrow content, e.g., skull, vertebrae, sternum, and hip. Jaws are involved in up to 30% of multiple myeloma cases with jaw pain, swelling, mobile teeth, and easy bleeding as presenting signs and symptoms [10]. The intraoral exam should evaluate for areas of gingival bleeding, ecchymosis, tooth mobility, paresthesia, and swellings—soft tissue and bony. When presenting as a single lesion, it is referred to as a plasmacytoma (Fig. 10.2). It is important to evaluate for evidence of osteolytic lesions and potential for development of osteonecrosis of the jaw (ONJ) as multiple myeloma patients are often treated with bisphosphonates and/or radiation treatment, placing them at increased risk for ONJ. Questions of steroid supplementation may be encountered for patients with multiple myeloma undergoing

invasive dental treatments, as chemotherapy treatment regimens often employ corticosteroids. Adrenal crises secondary to insufficiency are rare in the dental setting; stress dose steroid supplementation before oral surgery is not usually recommended [11]. Patients should, however, continue with their regular daily dose. Stress dosing may be considered in patients who have been treated with a glucocorticoid. Specific details regarding stress dosing can be found in the Endocrine chapter.

10.4 Disorders of Platelets and Clotting Factors

Effective hemostasis requires thrombosis via two interconnected processes: formation of a platelet plug and the coagulation cascade (Fig. 10.3). Platelets are derived from megakaryocytes which differentiate in bone marrow and have a life span of 7–10 days. Thrombocytopenia may result from increased platelet destruction, decreased production, or autoimmune attack. Drugs may also produce thrombocytopenia either directly or by triggering antibody reaction.

Normal platelet levels range between 150,000 and 440,000 with spontaneous bleeding likely with levels <20,000. Henderson et al. [12] have recommended platelet level >50,000 for minor oral surgery and >100,000 for more invasive oral surgery. The platelet count should be evaluated within 24 h of surgery. Prophylactic platelet transfusion can be considered for extensive maxillofacial surgery but must be weighed against transfusion reactions risks (e.g., fever, allergic reactions, viral infections). One unit of platelets can be expected to increase counts by 5000–8000 [12]. Alternatively, desmopressin can be administered in those with acquired or congenital platelet dysfunction (see discussion below regarding desmopressin).

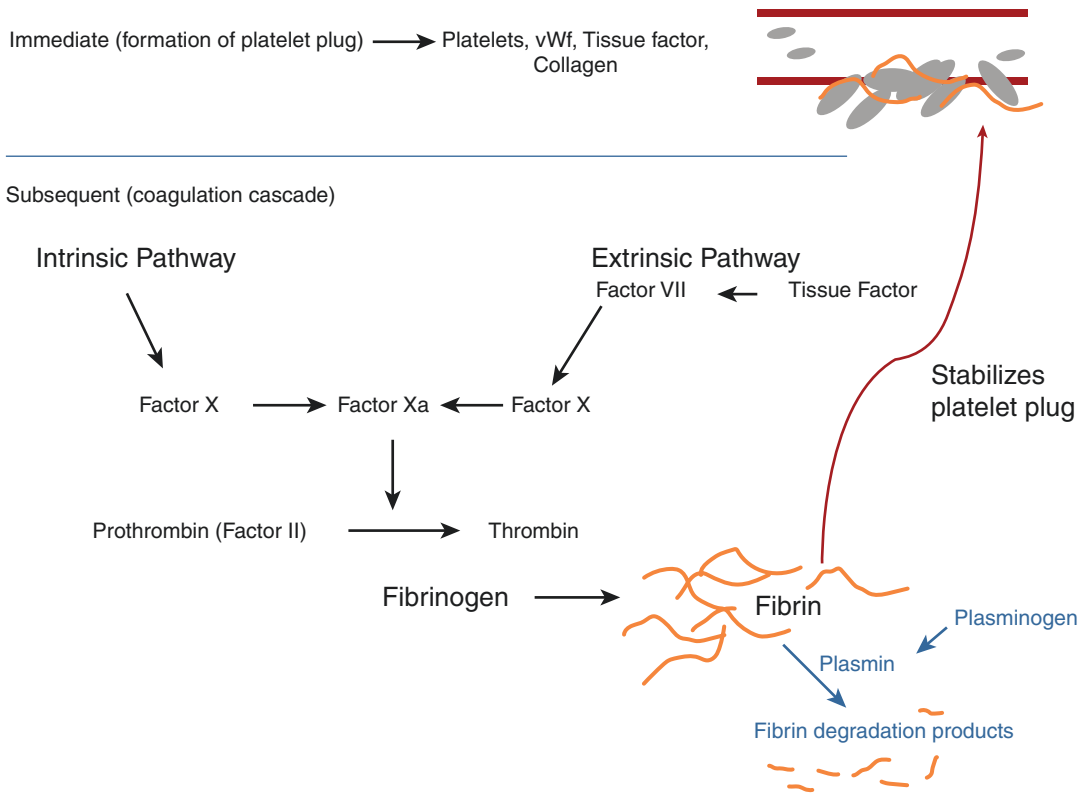

Fig. 10.3 Hemostasis

Other aspects of a patient's medical and social history may also have effects on platelet function. For instance, uremia of chronic kidney disease or those on dialysis often exhibit platelet dysfunction and coagulopathies. Patients with chronic liver disease (i.e., in alcoholism) often have thrombocytopenia and coagulation factor deficiency, increasing bleeding risk.

10.4.1 Hemophilia

Hemophilia is a group of bleeding disorders due to deficiency in coagulation factor VIII (hemophilia A), factor IX (hemophilia B), or factor XI (hemophilia C). Hemophilia C is inherited in an autosomal recessive pattern primarily affecting the Ashkenazi Jewish community and is the rarest of the forms. Hemophilia A is the more common form comprising 80–85% of the total hemophilia population [13]. Hemophilia A and B are inherited via X-linked inheritance, with men most often affected. Hemophilia carriers are generally asymptomatic though factor levels may be below the normal threshold and should be tested prior to any invasive procedures. Expect to have a prolonged activated partial thromboplastin time (aPTT) with low levels of these factors. Common history elicited from those with hemophilia include easy bruising throughout childhood, hemarthrosis, and seemingly spontaneous bleeding into soft tissue and from mucous membranes. Oral hygiene is essential in these patients as they are predisposed to gingival bleeding. Care of a patient with hemophilia starts with treatment planning alongside the patient's hematologist. Preoperative labs should be obtained within a week of planned procedures and should include factor inhibitor screening and inhibitor assay looking for antibodies targeted against specific clotting factors. These antibodies can develop in patients who have required repetitive replacement therapy. Factor levels should be obtained prior to dental extractions with goal levels minimally at 50% of normal ([14], Table 10.3). Factors should be between 75 and 100% of normal levels before maxillofacial surgery and should be repleted 30–60 min prior to surgery [16]. Factor levels should be maintained at these levels for 7 days after surgery to minimize bleeding risk [17]. Treatment with factor-specific concentrates is preferred over cryoprecipitate or fresh frozen plasma (FFP). Cryoprecipitate is preferred over FFP for hemophilia A because it is often difficult to obtain high enough factor VIII with FFP alone, though it is usually sufficient for hemophilia B [18]. Prophylactic antibiotics are not required in the hemophiliac.

Other considerations in caring for the hemophiliac patient include obtaining venous access with small gauge (27 or 30) catheter. In addition, regional anesthetic blocks such as inferior alveolar and lingual blocks should be avoided if possible, opting instead for local infiltration. This is due to propensity for developing hematoma in soft tissue. Minimal recommended clotting factor levels prior to blocks are 20–30% of normal levels [19]. Any extractions or surgical procedures should be carried out with a plan for hemostasis (Table 10.2).

To this end, tranexamic acid (TXA) or aminocaproic acid are useful adjuncts. TXA is an antifibrinolytic acting via competitive inhibition of plasmin (Fig. 10.3). It can be administered

Table 10.3 Severity levels of hemophilia A and general recommendations for dental management (adapted from [15])

Severity	Plasma level of factor VIII (%)	Dental management
Mild	6–50%	Dental treatment can be delivered in the primary care setting. However, shared care with hematologist is recommended
Moderate Severe	2–5% <1%	– Patients at these levels may require preoperative prophylactic factor replacement therapy – Consult with hematologist – Seriously consider treating these patients in a secondary care setting – Preventative dentistry should be emphasized: oral hygiene, pit/fissure sealing, fluoride, etc.

either intravenously (IV), by oral tablet, or by mouthwash. TXA should not be given to patients with factor IX deficiency who are also receiving PCC (prothrombin complex concentrates) as there is an increased risk of thromboembolism [20]. Aminocaproic acid is an antifibrinolytic, similar to tranexamic acid, but has a shorter plasma half-life and is less potent and potentially more toxic [13]. Both TXA and aminocaproic acid can be administered by pouring on gauze or gelatin sponge and using direct pressure on bleeding areas.

Another pharmacologic alternative is desmopressin. This synthetic vasopressin increases levels of factor VIII and vWF by stimulating their release from endothelial cells. It can be the treatment of choice for mild or moderate hemophilia A and may preclude the need for clotting factors. It can be administered IV, subcutaneously, or as a nasal spray. Possible desmopressin side effects to monitor for are tachycardia, hypotension, and headache [16].

10.4.2 von Willebrand Disease

Von Willebrand disease is a bleeding disorder which presents in various subtypes all due to reduced levels of von Willebrand factor (vWF). It can be an inherited or acquired condition and it affects ~1% of the population. vWF's role in the coagulation cascade is as a carrier for factor VIII, increasing its half-life and attaching to collagen, thus supporting clot formation ([15], Fig. 10.3). Laboratory findings with von Willebrand disease include decreased vWF levels, decreased factor VIII, and prolonged aPTT. It is recommended that for planned dental extractions, a level of at least 60% vWF is achieved preoperatively [18]. Desmopressin is the treatment of choice for most forms of mild to moderate vWD as it increases release of vWF and factor VIII from endothelial cells. Desmopressin can be administered within 60 min of surgery. Severe forms of the disorder may require replacement therapy with vWF concentrate. Consultation with the patient's hematologist is required prior to any procedure, and the proper surgical setting must be thoughtfully determined to allow for proper monitoring and treatment, postoperatively.

10.5 Disorders of Red Blood Cells

Anemia is defined as a reduced number of circulating red blood cells (RBCs). This is reflected by low hemoglobin and hematocrit levels—with minimal thresholds defined differently for men and women. Levels vary slightly depending on the institution, but generally anemia is classified as Hb < 13 (Hct < 41) for men and Hb <12 (Hct < 36) for woman. Causes of anemia are numerous but can be broadly organized into three etiologies: decreased RBC production, increased destruction of circulating RBCs, or blood loss. Additional lab values such as mean corpuscular volume (MCV), red cell distribution width (RDW), and mean corpuscular hemoglobin concentration (MCHC) can help distinguish between these causes. Though routine outpatient oral surgery often does not require intervention in patients with anemia, providers should be aware of patients with underlying anemia when invasive procedures are planned and greater blood loss expected. Generally, a minimal hemoglobin of 7 is recommended prior to oral and maxillofacial surgery [21]. The following conditions which may underlie anemia are given special consideration.

10.5.1 Sickle Cell Disease

Sickle cell disease is an autosomal recessive condition which produces red blood cells whose altered shape and function ("sickled") predisposes patients to anemia and occlusive episodes. This is due to a mutated beta hemoglobin chain which results in a deformed hemoglobin, called HbS. The disease and trait are most commonly found in the African, Caribbean, Greek, and Southern Italian populations [18]. Patients with sickle cell disease may suffer from vaso-occlusive complications including bone pain, nephropathy, priapism, acute chest syndrome, and stroke. Pain crisis during these events can be severe, often

accompanied by fever and leukocytosis, and often require hospitalization. For the oral and maxillofacial surgeon specifically, there are intraoral manifestations of sickle disease of which to be aware: aseptic pulp necrosis, pale and/or ulcerative mucosa, and osteomyelitis [22]. Neuropathy due to infarctions of surrounding vascular supply may also be observed in patients with sickle cell. Loss of sensation in the mental nerve distribution has been noted 2.2 times as often in those with sickle cell compared to those without [23].

Treatment in patients with sickle cell disease should be focused around preventing acute sickle crisis. Poorly oxygenated or acidic tissues can trigger "sickling" of hemoglobin S and cause vaso-occlusive crisis. Causes may include infection, altitude, dehydration, or stress generally. For these reasons, patients should be kept warm and hydrated, and oxygen therapy should be administered during and after any procedure. Providers may opt for local anesthetic without vasoconstrictor. Nitrous and anxiolytics should be considered as adjuncts in the outpatient setting.

Patients with sickle cell disease often become functionally asplenic due to repeat splenic infarctions and are consequently left prone to infections—specifically those by encapsulated bacteria: *Streptococcus pneumoniae*, *Haemophilus influenzae*, and meningococcus. Given functional asplenia, it is important for providers to preempt infectious complications prior to oral surgery. In those who are functionally asplenic or who are post splenectomy, antibiotic prophylaxis should be administered within 1 h prior to dental procedures: penicillin, amoxicillin, or clindamycin are acceptable [24].

Prior to treating a patient with sickle cell disease, it is important to ascertain when the last crisis took place, what factors trigger crises for the individual, and if regular blood transfusions have been required. A complete blood count should be obtained within 24 h of surgery. It is recommended to correct any hemoglobin <10 prior to maxillofacial surgeries requiring general anesthesia [22].

10.5.2 Thalassemia

Thalassemias are a group of hemoglobinopathies that result in reduced quality and quantity of hemoglobin. Thalassemias are most prevalent in Italian, Asian, African, Middle Eastern, and Greek ancestry [25]. They are a genetic condition divided into alpha and beta subtypes each resulting in various severities of presenting phenotypes. Presentations can range from mild anemias to dependence on regular blood transfusion or even to death. Patients dependent on transfusions may develop iron overload potentially leading to cardiac dysfunction. They may also suffer from splenomegaly leading eventually to splenectomy and increased susceptibility to infection. In regard to oral maxillofacial surgery, manifestations of thalassemia can be seen secondary to bone marrow proliferation. "Chipmunk face" may develop with frontal bossing, enlarged maxilla, depressed nasal bridge, class II malocclusion, and protrusive maxillary dentition (Fig. 10.4). In addition, marrow proliferation may lead to thinning of the mandibular cortex and propensity towards pathologic fracture [27]. Patients often have pale gingiva secondary to anemia and salivary gland inflammation due to iron deposition. In managing patients with thalassemias, the provider should know baseline hemoglobin and splenectomy status. If post splenectomy, antibiotic prophylaxis is recommended. A complete blood count should be obtained within 24 h of planned procedures with a goal hemoglobin over 7. Any transfusions and preoperative antibiotic administration should be coordinated with the patient's hematologist.

10.6 Summary

Hematologic conditions can come in many varieties and affect multiple cell lineages making preoperative complete blood cell count important. Knowledge of neutrophil and platelet thresholds, requiring prophylaxis and transfusion respectively, is a likewise key point of understanding. Hematologic malignancies may

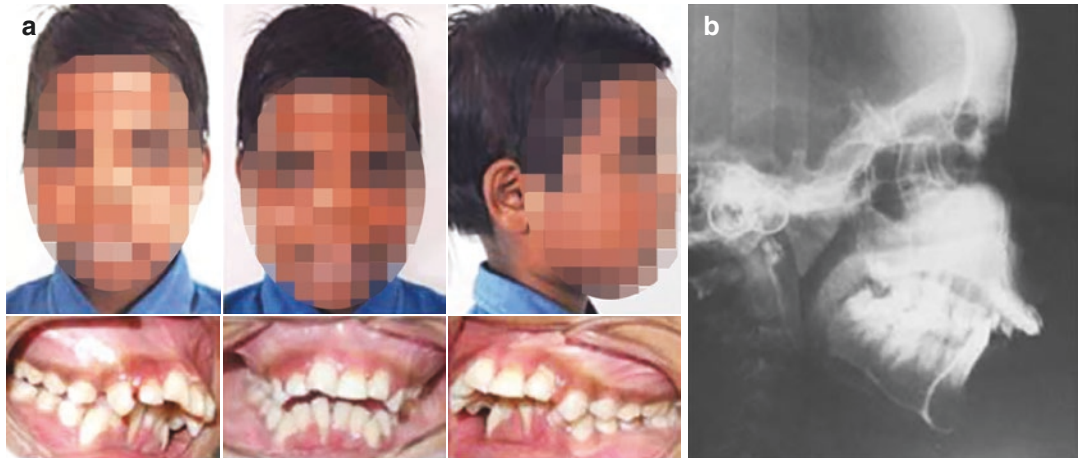

Fig. 10.4 (**a**) 13-year old boy with thalassemia (**b**) lateral cephalometric radiograph of same patient (from [26])

present with oral manifestations as the first signs, requiring vigilance on the part of oral health provider. Finally, care plans for a patient with any hematologic disorder should always be made in conjunction with a hematologist or the oncologic care team.

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11 Preoperative Evaluation of Patients with Neurological Disorders

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Neurological diseases represent a fairly common problem in the general population with a lifetime prevalence of 6% [1]. These conditions can present at any age but are generally more common in older patients, and symptoms tend to worsen over time [2]. As the population ages, these conditions are expected to increase in prevalence necessitating awareness of the disease and proper perioperative management [2, 3]. Additionally, these neurologic impairments are often complicated by additional systemic illnesses, polypharmacy, and the chronicity of the disease itself [4]. A thorough evaluation and assessment of these patients is imperative to prevent adverse perioperative events and decrease susceptibility to intraoperative risks.

Cerebrovascular disease and seizures are the most common neurological conditions that the oral and maxillofacial surgeon will encounter preoperatively. Despite this, familiarity with even uncommon disorders is essential as various neurologic diseases can significantly affect perioperative management, including choice of anesthetic agent, surgical techniques, and postoperative analgesia [2, 5].

In addition to a proper history and physical examination, a thorough neurologic examination should be completed with appropriate documentation of baseline status and any functional or sensory deficits [2]. Particular attention should be paid to cranial nerve examinations and gross motor and sensory functions [5]. In several of the neurologic conditions discussed below, additional cardiac and pulmonary testing is indicated for preoperative evaluation. This is particularly important in diseases such as muscular dystrophy and myasthenia gravis where preoperative cardiac and pulmonary evaluation is imperative [5]. If sedation or general anesthesia is indicated, strict evaluation of perioperative medications is advised as many of these drugs can interfere with the patients prescriptions and neurologic condition [6].

The goal of this chapter is to discuss specific neurological diseases and provide preoperative guidelines for each condition. Patients are generally followed by a neurologist that can provide further insight into the progression of the patient's disease and any recent changes in health status [5]. Consultation with these physicians is highly recommended, especially for elective outpatient procedures which can be delayed until medical optimization is complete.

11.1 Cerebrovascular Disease

Cerebrovascular disease affects a large percent of the patient population and includes a history of stroke and transient ischemic attacks (TIA) [5].

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Stroke is the fifth leading cause of death in the United States and remains a leader in lingering disability and mortality [7]. The majority of strokes (90%) are ischemic and the remaining 10% are hemorrhagic. When evaluating a patient with a history of cerebrovascular disease, it is critical to determine the severity, cause, and recency of the stroke or TIA.

These patients will often have several other risk factors that lead to the initial development of their disease, including hypertension, diabetes mellitus, carotid artery stenosis, cardiac arrhythmias, and hyperlipidemia [5]. In a patient with uncontrolled hypertension, further referral and evaluation by their primary care physician is recommended prior to any elective surgery [8]. If a carotid bruit is heard on physical exam, it is important to discuss visual impairments, numbness, or weakness, which could be suggestive of carotid vascular disease. It is important to remember that a carotid bruit alone does not indicate or correlate with the degree of carotid artery stenosis [8]. If the patient reports symptoms of carotid artery stenosis, then angiography would be indicated for further evaluation and possible endarterectomy prior to elective surgery. Carotid endarterectomy is performed if a patient is symptomatic or if their occlusion is found to be greater than 70%.

The severity of stroke can be elicited through a focused physical exam to evaluate for baseline neurologic deficits. These should also be verified postoperatively to assess for any changes [8]. It is critical to confirm that the patient has not had progressive neurologic changes or worsening of symptoms as these should be evaluated prior to elective surgical intervention. Any recent history of acute loss of visual fields or severe headaches must also be assessed by a primary care physician or neurologist prior to elective surgery [1].

The cause of the stroke should also be known to further stratify the patient's perioperative risk. If the stroke was ischemic or due to atrial fibrillation, the patient will often be on antiplatelet or anticoagulation therapy. Perioperative discontinuation of antithrombotic medications increases the risk of stroke, but this must be weighed with risk of bleeding during surgery [3]. Management of these medications will be discussed in later chapters.

There are no clear guidelines on when an elective surgery can be completed following cerebrovascular accident, but the risk of major adverse cardiac events remains increased for approximately 9 months. Generally, for elective procedures, at least 6 months is recommended following a stroke or TIA to confirm hemodynamic and neurologic stability [1, 3]. Following this time period, it is critical to confirm that there has been medical optimization of the patient's risk factors, including management of diabetes and hypertension. For those undergoing sedation, preoperative evaluation of these patients should also include electrocardiogram, echocardiogram, and possible stress testing to minimize perioperative risk.

11.2 Epilepsy/Seizures

Epilepsy is a disorder that affects approximately 1% of the population and is defined as recurrent paroxysmal seizure activity [9, 10]. When evaluating patients with a history of seizures, a thorough history should be elicited, including type, duration, frequency, inciting events, and current medical management [11]. Seizures can be either partial or generalized. Partial seizures initiate at a localized area of the brain, while generalized seizures involve the entire brain [9]. The risk that a patient will have a seizure perioperatively is directly correlated with the frequency of seizures that he or she has at baseline [12]. Additionally, it is essential to recognize non-epileptic causes of seizures that may have led to previous episodes, including fever, ethanol withdrawal, hypoxia, and hypoglycemia to reduce perioperative recurrences [8].

Aside from a febrile seizure as an infant, patients with a history of seizures should be managed closely by a neurologist with documentation of medications and any recent episodes [8]. Perioperatively it is critical to minimize changes in their current treatment regimen through strict maintenance of antiepileptic drugs (AEDs) and minimization of stress during the procedure. All

antiepileptic medications should be taken on their normal schedule including the morning of surgery and postoperatively [13]. If oral access is unavailable during surgery, then antiseizure medications should be given parentally [2]. Additional seizure precipitating factors should be minimized prior to the procedure including sleep deprivation and alcohol intake.

It is critical to recognize that intraoperative and postoperative medication changes may need to be made due to interactions with AEDs. Common AEDs that the patient may be prescribed include phenytoin, phenobarbital, carbamazepine, ethosuximide, lamotrigine, and valproic acid. Many of these medications can have sedative side effects or inhibit liver enzymes leading to oversedation. Additionally, proconvulsant medications should be limited intraoperatively and postoperatively including ketamine, methohexital, meperidine, and tramadol [9, 14–17] (Table 11.1). However, some controversy exists as to whether the use of ketamine is a relative or absolute contraindication, as the literature is not conclusive of this particular issue.

Perioperatively, the risk of seizures in epileptic patients is estimated at 2–6% [3, 13]. In a patient that had a seizure within the preceding month, this risk is as high as 20% [3]. For this reason, it is critical to be knowledgeable about management if an episode does occur. Most often the seizures that occur perioperatively are due to the underlying condition rather than medications given during the procedure [13].

Finally, and most specific to the oral and maxillofacial surgeon, is a detailed evaluation of treatment options that patients with seizure disorders can receive. Procedures requiring postoperative maxillomandibular fixation are contraindicated, and other alternatives must be evaluated [18].

Table 11.1 Proconvulsant medications

Antibiotics	Isoniazid, metronidazole, penicillins, cephalosporins, imipenem
Antidepressants	TCAs (amitriptyline), SSRIs (sertraline), SNRIs (venlafaxine, duloxetine), bupropion, trazodone
General anesthetics	Enflurane, isoflurane, ketamine, etomidate, methohexital
Immunosuppressants	Cyclosporine, azathioprine
Local anesthetics	Lidocaine, bupivacaine, procaine
Neuroleptics	Clozapine, lithium, haloperidol
Stimulants	Dexamphetamine, methylphenidate
Analgesics	Tramadol, meperidine, fentanyl

11.3 Dementia

Dementia is a slow and progressive decrease in cognitive abilities over time [19]. This can be directly contrasted with delirium which is an acute change in mental status. There are several irreversible causes of dementia including Alzheimer's disease, vascular dementia, frontotemporal dementia, and Lewy body dementia. Alzheimer's is the most common cause of dementia (more than half of all cases) and is characterized by impaired memory, judgment, and emotional liability [9]. Similar to other neurologic impairments, patients with dementia will often be followed closely by a neurologist for progression of disease and pharmacologic intervention (Table 11.2) [20, 21]. A cognitive assessment tool such as the mini-mental status examination can be valuable to provide a baseline status prior to a surgical procedure [1, 21].

Symptoms of Alzheimer's disease and other causes of dementia are highly variable and dependent on the progression of the disease. Patients that have severe cognitive dysfunction must be accompanied by a caregiver to help with a proper

Table 11.2 Common medications prescribed for Alzheimer's treatment

Donepezil, rivastigmine, galantamine	Cholinesterase inhibitors
Memantine	N-methyl-D-aspartate (NMDA) antagonist
Alpha-tocopherol (Vitamin E)	Antioxidant
Selegiline	Monoamine oxidase inhibitor

preoperative assessment, history, and consent [10]. Additionally, in advanced dementia, some patients may require sedation for the procedure due to uncooperativeness. Although delirium is much more common in an inpatient setting, it still must be considered during outpatient surgery, especially if sedation is to be utilized.

Many medications used perioperatively can have a significant association with delirium including opiates, antihistamines, benzodiazepines, high-dose steroids, and anticholinergics [22]. Patients with dementia are much more likely to have postoperative cognitive dysfunction and episodes of delirium [3, 5, 23].

11.4 Movement Disorders

11.4.1 Parkinson's Disease

Parkinson's disease (PD) is an extremely common disorder in the United States and is the second most common neurodegenerative disorder [24, 25]. Both PD and "Parkinson's plus" syndromes appear clinically similar but have different responses to dopaminergic treatment. Similar to many neurologic disorders, PD represents a heterogeneous group of symptoms that include bradykinesia, decreased dexterity, tremor, decreased facial expressions, anosmia, dysphagia, postural instability, dementia, and depression. These patients frequently have motor and postural problems necessitating careful monitoring.

Preoperatively, a detailed history and physical should include medications and progression of the disease. A common rating system for PD is the Unified Parkinson Disease Rating Scale (UPDRS) [6]. This value correlates with the severity of disease and compiles mentation, mood, activities of daily living, and motor difficulties. Due to motor difficulties within the pharynx specifically, patients with PD also often have dysphagia and excessive secretions. This is especially critical to anticipate perioperatively with thorough suctioning of the oropharynx to lower risk of aspiration pneumonia [6, 18]. In addition to dysphagia, patients with Parkinson's will also exhibit sialorrhea secondary to autonomic dysfunction [6]. For this same reason, orthostatic hypotension is extremely common and requires careful postoperative monitoring [26].

All antiparkinsons medications should be continued preoperatively. Most commonly, patients are treated with dopaminergic agents (carbidopa-levodopa), dopamine agonists (pramipexole or ropinirole), MAO-B inhibitors (selegiline and rasagiline), and benztropine [6, 14]. Flares of Parkinson's symptoms often occur with abrupt removal of medications, especially given the short half-life of levodopa [10]. These medications should be continued as close to their regular schedule due to the risk of development of a rare, but potentially fatal, condition called Parkinson-hyperpyrexia syndrome. This syndrome is extremely similar to neuroleptic malignant syndrome and can be triggered by the abrupt cessation of dopaminergic drugs for as short as 6–12 h [3]. If nothing by mouth status is required for surgery, the use of transdermal patches is a viable alternative [12].

Many patients in late state PD may also have deep brain stimulators (DBS) in place which may cause apprehension for preoperative imaging. For those with DBS, ultrasounds, computerized tomography (CT) scans, and plain film radiographs are generally safe modalities for evaluation (Fig. 11.1 [27],). Magnetic resonance imaging (MRI) can be completed in patients with

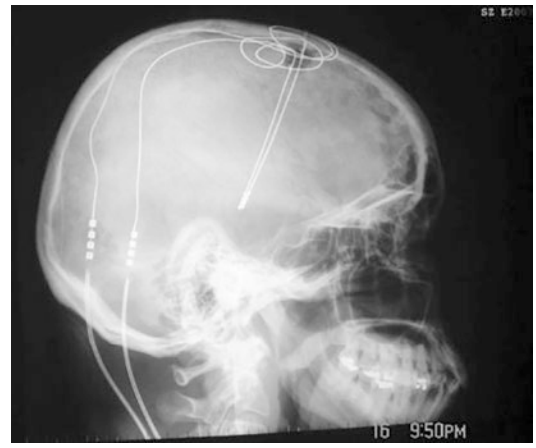

Fig. 11.1 Lateral plain film radiograph exhibiting DBS in place [27]

a DBS in place, but there are specific guidelines and evaluations that must be followed in order to prevent brain injury and edema [12].

11.4.2 Huntington's

Huntington's disease is a rare inherited movement disorder characterized by progressive motor, neurologic, and cognitive problems. The disease usually presents between 30 and 40 years of age and includes motor symptoms such as choreiform movements of the face, dysarthria, and tongue thrusting [10]. Later stages of the disease are complicated by aspiration pneumonia, cachexia, and cardiac failure. The basal ganglia is most often affected, and early atrophy of these regions predicts advanced motor and cognitive decline [4]. The preoperative evaluation of these patients is heavily dependent on their current functional status especially given the speed of deterioration. Positioning difficulties, uncontrolled movements, and concern for aspiration may necessitate the use of an operating room for the majority of procedures.

11.5 Neuromuscular Disorders

Patients with neuromuscular conditions can experience various complications related directly to surgical interventions and medications used perioperatively. Consultation with the patient's neurologist is often indicated in order to treat the patient at the most medically optimized point in his or her disease [18]. If general anesthesia is indicated in these patients, there are increased risks of life-threatening reactions to neuromuscular blockade and profound responses to volatile anesthetics. Strict consultation with an anesthesiologist is recommended for further preoperative evaluation and stratification of risks [2].

The most common feature that must be evaluated in patients with neuromuscular disorders, especially if they are undergoing sedation, is respiratory weakness. In addition to a formal history and physical, details on dyspnea, fatigue, and orthopnea must be ascertained. Spirometry to document functional vital capacity and an arterial blood gas analysis can be considered to aid in preoperative sedation evaluation. Generally, patients with neuromuscular disorders will also have increased sensitivity to medications that can cause respiratory depression including opiates, benzodiazepines, and barbiturates [3, 12]. Cardiac complications are also of concern in neuromuscular disorders and are discussed in more detail below. Individualized tests for conditions should be considered preoperatively including electrocardiogram and echocardiography [12].

Patients with neuromuscular disorders will often be placed on steroids or immunosuppressant therapy for treatment of their disease. It is important to recognize and discuss possible surgical complications of these medications including poor wound healing and the requirement of a stress dose of steroids prior to the procedure.

11.5.1 Myasthenia Gravis

Myasthenia gravis (MG) is an autoimmune disease that affects the postsynaptic nicotinic acetylcholine receptors [28, 29]. The disease is characterized by fluctuating weakness and fatigue with continued muscle use especially with eye muscles, respiratory muscles, and postural muscles of neck and back [5, 18]. The incidence is highest in African American women followed by Caucasian women. Under 40 years old, women are three times more likely to be affected. Over the age of 50, men are more likely to be diagnosed [4]. Additional autoimmune disorders are also highly correlated with MG including rheumatoid arthritis and systemic lupus erythematosus [4].

Generally, symptoms worsen throughout the first year of the disease but will later plateau by year two. Diplopia, ptosis, dysphagia, dysarthria, and facial weakness are common initial manifestations of the disease. The diagnosis of MG is made by a "tensilon test" (edrophonium) or the "ice pack test" which will notably improve the patient's symptoms following administration.

First-line treatment of patients with mild disease is with acetylcholinesterase inhibitors (pyridostigmine). Preoperative evaluation is critical to determine the severity of disease and current medical therapy. Additionally, a thorough cranial nerve examination should be completed given the common ocular and facial findings of the disease. Only well-controlled patients should be scheduled for elective surgery [18].

If the patient is having worsening symptoms, it is generally recommended to delay elective surgery so that the patient can undergo more aggressive therapy including plasmapheresis, immunotherapy, or thymectomy [4, 5]. Once stabilized, the elective surgery can be completed with clearance from their neurologist.

Preoperative pulmonary function tests for assessment of functional vital capacity are recommended especially if the patient is to undergo sedation [3]. If findings are indicative of significant respiratory weakness, then sedation should be avoided as MG is highly associated with postoperative respiratory insufficiency and prolonged ventilator use [4]. The risk factors that increase this postoperative respiratory insufficiency include duration of disease over 6 years, pyridostigmine requirement of over 750 mg per day, preoperative vital capacity under three liters, and chronic respiratory disease [3, 12].

There are several common medications that worsen MG symptoms including aminoglycosides, fluoroquinolones, macrolides, antiarrhythmics, local anesthetics, and beta-blockers. Medications used perioperatively must be carefully evaluated to prevent exacerbation of the disease (Table 11.3) [30–33]. For local anesthetic use, amides are preferred over esters if a patient is taking pyridostigmine. This is because esters are metabolized by plasma cholinesterase and patients taking acetylcholinesterase inhibitors can have slower breakdown of ester anesthetics increasing risk of toxicity. Additionally, given the poor respiratory reserve in MG patients, opiates should be used cautiously due to potential respiratory suppression [12].

Table 11.3 Medications that can worsen MG symptoms [30–33]

Antibiotics	Macrolides, fluoroquinolones, aminoglycosides, tetracycline, chloroquine
Antidysrhythmic	Beta-blockers, calcium channel blockers, quinidine, lidocaine, procainamide
Antipsychotics	Phenothiazines, atypical antipsychotics
Cardiovascular	Propranolol, quinidine, verapamil, statins
Miscellaneous	Lithium, chlorpromazine, muscle relaxants, levothyroxine, adrenocorticotropic hormone (ACTH), corticosteroids

11.5.2 Muscular Dystrophy

Patients with muscular dystrophy suffer from a genetic defect that leads to the deletion (Duchenne muscular dystrophy) or reduced function (Becker muscular dystrophy) of the structural protein dystrophin [34, 35]. This protein normally supports the sarcolemma in both skeletal muscle and cardiac muscle cells. When absent or reduced, this leads to vulnerable cell walls and tissue necrosis. The onset of Duchenne muscular dystrophy is approximately 3–4 years of age, while the onset of Becker muscular dystrophy is much later with a variable and milder clinical presentation. Patients initially present with lower extremity weakness and muscle degeneration in calf muscles which leads to worsening systemic signs. Significant cardiomyopathy and respiratory dysfunction are commonly seen by 15 years of age in Duchenne muscular dystrophy [4].

Given the pathology of the disease, preoperative evaluation must involve significant cardiac and pulmonary assessment. If deep sedation is to be utilized, preoperative electrocardiogram, echocardiogram, long-term telemetry, and pulmonary function tests are necessary because of the high likelihood of cardiac and pulmonary involvement [13]. Specific guidelines set in place by the American College of Chest Physicians recommend a complete pulmonary evaluation (including spirometry, maximum inspiratory pressure, maximum expiratory pressure, peak cough flow, and oxygen saturation on room air)

for patients with Duchenne muscular dystrophy. A functional vital capacity of under 40% is predictive of postoperative respiratory complications [3].

If acute cardiac or pulmonary symptoms are present, elective surgery should be delayed until the patient is medically optimized [5]. It is important to note that the degree of cardiac dysfunction is not correlated with the degree of skeletal muscle involvement [4]. Additionally, several other cardiac problems are common in muscular dystrophy including mitral regurgitation and mitral valve prolapse. Congestive heart failure is the leading cause of death in these patients.

If general anesthesia is to be considered, succinylcholine is contraindicated in patients with muscular dystrophy as there is a high risk of life-threatening hyperkalemia, rhabdomyolysis, and cardiac arrest. In these cases, a total intravenous anesthesia (TIVA) is recommended in order to avoid use of neuromuscular blockage and inhalational anesthetics.

Due to minimal prospective trials on Becker muscular dystrophy, the disease has the same recommendations for preoperative evaluation as Duchenne muscular dystrophy [36].

11.5.3 Amyotrophic Lateral Sclerosis

Amyotrophic lateral sclerosis (ALS) is an adult-onset neurodegenerative disorder that affects both the upper and lower motor neurons [4, 9]. The disease is rapidly progressive and often presents in the fifth or sixth decade of life with asymmetric weakness, spasticity, and fasciculations. There are no cognitive changes with the disease, and sensory and autonomic functions remain intact. Management of ALS is mainly palliative, and the duration of survival is estimated to be 3–5 years. The etiology of the disease is unknown and 90% of the cases are sporadic [4].

Similar to the above neuromuscular conditions, patients with ALS have increased rates of aspiration and should be closely evaluated if sedation is to be utilized [12]. Progressive respiratory weakness is the leading cause of death, and there are no notable cardiac muscle problems directly attributed to the disease [4, 9]. Patients with late-stage disease will generally have a tracheostomy and be on ventilatory support.

Ideally, outpatient surgery would be completed with the use of local anesthetic alone. Succinylcholine is contraindicated if general anesthesia is to be utilized because of life-threatening complications of hyperkalemia. Additionally, muscle relaxants should generally be avoided in these patients.

11.6 Demyelinating Conditions

11.6.1 Guillain-Barre Syndrome

Guillain-Barre syndrome (GBS) is a disorder that presents with acute onset of ascending motor paralysis and paresthesia [37, 38]. The disease is characterized by an immunologic reaction to the myelin sheath of peripheral nerves often following a gastrointestinal infection or upper respiratory infection—most commonly from *Campylobacter jejuni* (33%) or *Cytomegalovirus* (10%) [4, 9, 39]. GBS frequently presents within 3 days to 6 weeks of initial upper respiratory or gastrointestinal symptoms as a bilateral and symmetric lower limb weakness [4]. Additionally, GBS can present as a complication of human immunodeficiency virus infection or Hodgkin's lymphoma. The treatment of GBS is with plasmapheresis or intravenous immunoglobulin therapy. The most important complication is bulbar involvement that can lead to respiratory muscle paralysis and intubation in approximately 25% of patients [40]. Symptoms of the disease usually peak between 12 h and 28 days of initial diagnosis.

For elective outpatient procedures, GBS should be completely cleared prior to surgery. Most patients do completely recover although sometimes it can take up to a year [4]. If general anesthesia is indicated for treatment, succinylcholine is contraindicated due to risk of cardiac arrest and hyperkalemia. There are no current guidelines on when succinylcholine is safe to use on a patient with GBS, even after complete recovery [4].

11.6.2 Multiple Sclerosis

Multiple sclerosis (MS) is a chronic demyelinating condition that is characterized by central nervous system (CNS) destruction by demyelination and gliosis. The disease can be one of four subtypes: relapsing (80%), primary progressive, secondary progressive, or progressive relapsing [5]. The disease primarily affects women between 20 and 40 years of age, and an increased association exists in Caucasians and higher socioeconomic populations [9]. Patients will have unassociated demyelinating lesions of the brain and spinal cord that intermittently occur leading to both sensory and motor deficits. These demyelinating plaques will be of varying sizes and severity. It is critical to document deficits with a thorough cranial nerve examination prior to surgical intervention as MS can also present with trigeminal neuralgia or hemifacial spasms. Additionally, a thorough eye examination should be performed due to high rates of optic neuritis [4].

Initially, mild neurologic defects present until more permanent chronic problems accumulate [5]. Over time, disease-free remissions are less likely to occur with almost half of patients requiring assistance with walking 15 years after their initial diagnosis. MS can progress to severe disabilities including respiratory dysfunction, spasticity, chronic pain, and loss of bladder function. The goal of treatment is often to delay extensive symptoms of the disease and to treat acute exacerbations.

Preoperatively, it is important to understand that the patient's deficits often worsen with the stress of surgery. In addition to surgical stress, increases in temperature and infection can also precipitate exacerbation of the disease [6]. The patient should be aware that elective surgery can worsen their symptoms.

If a patient is having an acute exacerbation of multiple sclerosis, surgery should be delayed until the symptoms have completely resolved. Symptoms normally develop over the course of a few days and can last several months. Acute attacks are often treated with glucocorticoids to decrease severity. Late-stage disease can also present with various chronic deficits that may increase risks of surgery including cranial nerve deficits and significant respiratory disease.

If general anesthesia is to be utilized, the use of succinylcholine should be avoided if the patient has advanced disease (severe neurologic deficits or atrophy) due to risk of hyperkalemia. The decreased muscle mass in many of these patients can lead to unpredictable nondepolarizing neuromuscular blockade medication levels and should be carefully titrated [10].

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Management Dilemmas

12

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12.1 Treatment Dilemmas

Unique treatment dilemmas often occur in the care of the dental and/or surgical patient. The challenge with these treatment dilemmas is the complexity of management, often the result of:

1. Incomplete understanding of the pathophysiology of a particular disease entity
2. The need to balance between two opposing outcomes, in which one outcome is worsened at the expense of the other
3. Lack of robust scientific evidence to fully guide treatment
4. Lack of standardization and/or care pathways
5. Social determinants of health and patient behaviors
6. Clinical measures resulting in unexpected consequences
7. Controversy or historical dogma around certain treatments

Thus, this chapter provides an update on a variety of conditions and attempt to create clarity, based on current scientific evidence and paradigm shifts in expected standards of care.

12.2 Antiresorptive Drugs and Medication-Related Osteonecrosis of the Jaw (MRONJ)

Antiresorptive drugs have been documented to be effective in the treatment of osteopenia, certain metastatic diseases, osteoporosis, and certain bone conditions [1]. These drugs significantly increase bone marrow density and reduce the risk of fractures and other skeletal-related events [2]. Drugs like bisphosphonates are known to impair bone turnover by suppression of the osteoclastic function. Denosumab, a monoclonal antibody, acts by binding to RANKL thus inhibiting its binding to the RANK receptor which in turn is responsible for maturation of osteoclasts [3]. In general bisphosphonates are recommended for a period of 3–5 years, and denosumab is used for maintenance for 10 years. Other drugs include antiangiogenic agents like bevacizumab, immunomodulators like thalidomide, mTOR inhibitors like sirolimus, etc [4]. These drugs can cause complications such as arthralgias, myalgias, GERD, and osteonecrosis of the jaw. Complications such as hypocalcemia, hypophosphatemia, and fatigue have also been

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reported [5, 6]. However, these risks clearly outweigh the benefits as they can decrease the morbidity and improve quality of life for patients, at risk for vertebral and hip fractures secondary to osteoporosis.

MRONJ has been described as a rare complication with an incidence of 1–18% for the intravenous drugs and 0.001–0.01% for the oral antiresorptive drugs [7]. However certain conditions like multiple myeloma are known to possess the highest risk. In addition, patients who received the intravenous form of these drugs are also known to have a higher risk than the oral forms [8]. Newer evidence however reveals that the condition is also noted in patients who are not exposed to these drugs. Surgical bone procedures are also known to increase the risk of developing MRONJ.

By definition, MRONJ is described as a condition of bone exposure that has not healed in more than 8 weeks within the maxillofacial region in patients with past or current treatment with antiresorptive agents and antiangiogenic agents and who were not previously radiated in the site. The condition has been staged to help develop optimal treatment (Table 12.1).

Table 12.1 Staging of MRONJ and treatment (adapted) [9]

Clinical signs	Treatment
Stage 0—Radiographic alterations, no exposed jawbone, and nonspecific signs/symptoms	Systemic management, including analgesics, and antibiotics
Stage I—Exposed bone or fistulous tract to the underlying skeletal structure without signs/symptoms	Antibacterial oral rinse, close follow-up, patient education
Stage II—Exposed bone or fistulous tract to the underlying skeletal structure with signs/symptoms	Antibiotics, antibacterial oral rinses, analgesics, and localized debridement to relive soft tissue irritation and infection control
Stage III—Exposed bone or fistulous tract to the underlying skeletal structure with signs/symptoms and with involvement of other anatomical structures and/or leading to fractures	Antibiotics, antibacterial oral rinses, analgesics, and surgical debridement/resection for long-term palliative care of infection and pain

12.2.1 Risk Factors

The pathophysiology is not fully understood. Despite many postulated theories, lack of strong scientific evidence has identified several factors may contribute towards the development of MRONJ. Factors like age greater than 65 years, tobacco smoking, local infection, the drug itself (type, form, and duration), immune suppression, females, corticosteroids, and localized trauma were all implicated in the development of MRONJ [10, 11].

12.2.2 Signs and Symptoms

Pain, localized inflammation or swelling, fistula, purulent discharge, exposed bone, loose teeth, halitosis, and neurosensory alterations.

12.2.3 Radiographic Findings

The initial finding of MRONJ on x-rays range from altered trabecular architecture, sclerotic or radiolytic changes of bone, cortical erosion, and bone destruction. Nonhealing or delayed healing of extraction sites should be monitored for disease progression. Often times, the sclerotic and radiolucent changes are subtle and could indicate an early stage of MRONJ in the absence of bone exposure. The osteosclerosis may appear as a diffuse pattern with reactive periosteal bone formation [12].

12.2.4 Risk Reduction in the Development of MRONJ

Several specialty guidelines and task forces have discussed various risk mitigation strategies. While prevention of MRONJ is a subject to debate, various risk reduction measures could help through a team approach involving the patient, oncologist, primary care physician, maxillofacial surgeon, and the dentist. These strategies include a thorough systematic examination (with radiographs) of the oral cavity with emphasis on the health of the alveolar bone and mainte-

nance of good oral hygiene, and completion of invasive procedures should ideally be completed prior to initiation of antiresorptive therapy. If the clinical condition permits, it is advised that the extraction sites heal via complete mucosal coverage prior to initiation of antiresorptive or antiangiogenic agents. Patient education is paramount in identifying the signs of MRONJ and to seek timely diagnosis and intervention. Some have recommended and put forth the concept of drug holiday. However, there is lack of good scientific data to support such effort. In fact, drugs like zoledronic acid has longer half-life which precludes the idea of drug holiday, and till date there is no compelling scientific evidence supporting such theory [13]. Optimistically, it appears that the molecular structure, mechanism of action, and resultant half-life for denosumab result in the meaningful benefit of a drug holiday in terms of limiting MRONJ, compared to bisphosphonates, especially when an invasive procedure is necessary.

If the patient is deemed high risk for the development of MRONJ, the primary dentist should refer the patient to an oral and maxillofacial surgeon for further risk assessment and optimal management. In general, minor noninvasive dental procedures (restorations, root canal treatments, and scaling) can be performed without any risk of developing MRONJ. Focus should be on prevention of advanced oral disease and infection. Dentures should be checked for optimal fit to reduce the risk of soft tissue ulceration and underlying bone exposure. Since localized infection or inflammatory mediators are also implicated in the development of MRONJ, patients with periodontal disease should be treated aggressively, again, to reduce the risk of surgical procedures after the initiation of antiresorptive therapy. Teeth with poor and guarded prognosis should be promptly extracted prior to initiation of treatment.

12.2.5 Treatment of MRONJ

The goal of treatment should be to eliminate any infection via debridement and/or systemic antibiotics therapy. Treatment of the condition varies from nonsurgical management in stage 0 and 1 to aggressive surgical therapy for stages 2 and 3. Nonsurgical treatment includes but not limited to pain oral antibacterial rinses and antibiotics (only in proven cases of infection).

Exposed necrotic bone should be removed completely, and the resultant bone margins should be smoothened to allow for healthy mucosal coverage of the wound. Due to lack of standardized description of surgical technique, a healthy bone margin must be achieved which generally is identified by bleeding points. Excessive bone removal might weaken the underlying basal bone and could result in fracture, which may necessitate preventative application of rigid fixation. Any loose teeth in the area should be removed, and underlying alveolar bone should be debrided to obtain healthy margins.

12.3 Osteoradionecrosis (ORN)

Adjuvant radiation to treat head and neck cancers is a common modality. However, the introduction of 3D radiation therapy and intensity-modulated radiation therapy has decreased the incidence of radiation-induced complications including but not limited to mucositis, trismus, dentition damage, and salivary gland dysfunction.

12.3.1 Definition

Osteoradionecrosis (ORN) is a potentially debilitating chronic complication of the head and neck radiation therapy [14]. The condition is defined as nonhealing necrotic bone in a previously irradiated site that has been present for more than 3 months. There is increasing evidence that necrosis of bone could occur even before any mucosal changes appear.

12.3.2 Pathophysiology

It is postulated that radiation induced fibrosis of the bone due to inadequate osteoblastic activity

and excessive myofibroblasts. The chronic inflammatory phase is followed by fibrosis of the area. Subsequently, there is atrophy of the bone due to loss of bone marrow structure in the region [15]. In general, the mandible is the common site due to limited blood supply compared to the maxilla due to the limitation of collateral blood supply.

12.3.3 Incidence and Risk Factors

Osteoradionecrosis can occur at any point of the disease survivor's life span. ORN has been reported to occur with a relative frequency of 0–22%. However, with current radiation delivery techniques, the reported incidence is between 5 and 7% [16]. Oral cavity tumors are known to have the highest frequency compared to hypopharyngeal tumors. ORN occurs frequently in the mandible than the maxilla [17]. The posterior maxilla and mandible are also more commonly involved.

Radiation dose is a known risk factor in the development of ORN. Patients treated with more than 60 Gy of radiation are more likely to develop ORN. Females are less likely to develop ORN compared to males. Smokers have three times greater risk of developing the condition. In addition, oncological therapy that involves osteotomy of the mandible is another known risk factor in the development of ORN. Adjuvant chemotherapy is also a potential risk factor for the development of ORN due to the excess oxygen free radicals which inhibit DNA repair [18, 19].

12.3.4 Signs and Symptoms

ORN can lead to debilitating pain, dysfunction, and decreased quality of life. It manifests as an area of mucosal ulceration/inflammation with underlying necrotic bone. In addition, patients may present with pain, purulent discharge, halitosis, and even pathologic fracture of the jaws. The condition may be precipitated from local trauma from dental appliances, spontaneous event, and extraction of teeth.

12.3.5 Radiographic Diagnosis

The initial sign of ORN on radiographic images is manifested by altered trabecular pattern. The more common finding is widened periodontal ligament space. In the advanced disease condition, a more radiolucent lesions with mixed radiopaque areas can be seen and sometimes with sequestrum. In severe cases, pathologic fracture of the mandible is also noted with necrotic bone [20].

12.3.6 Staging

Various systems were proposed, but only the clinically relevant and recent staging systems are discussed (Table 12.2) [21, 22].

12.3.7 Risk Reduction

Several factors have been identified to reduce the risk of development of ORN. These include preradiation dental treatment, extraction of nonsalvagable teeth, postradiation extraction of teeth, hyperbaric oxygen therapy (pre- and postextractions), pentoxifylline and tocopherol prophylaxis, and postradiation dental treatment have

Table 12.2 Staging of ORN

	Based on anatomic location of ORN	Based on clinical and radiographic appearance of ORN
Stage I	Confined to the alveolar bone	Minimal soft tissue ulceration and limited exposed cortical bone. Patients are treated with conservative management
Stage II	Extent above the mandibular alveolar canal	Localized involvement of the mandibular cortex and underlying medullary bone
Stage III	Extent below the level of the mandibular alveolar canal with a skin fistula and/or pathologic fracture	Full-thickness involvement of the bone, including the inferior border. Pathological fractures may also be present

been identified. Of note, based on the pathophysiology of ORN, there appears to be an approximately 4-month grace period before the onset of the presumed triad: hypoxia-hypocellularity-hypovascularity. However, to date none have been proven to be effective, and there has been no consensus on the standard of care practice guidelines.

Treatment of carious teeth with restorations, removal of sources contributing to infection, and extraction of teeth with poor or questionable prognosis are considered the mainstays in risk reduction strategies.

HBO therapy has been proposed as a preventative strategy for ORN. However, to date, there has been no scientific data supporting the use of HBO [23]. In fact, one landmark randomized multicenter trial by Annane et al. in 2004 compared the outcomes of HBO vs placebo in the treatment of ORN. The trial was terminated early due to worse outcomes in the HBO arm (19% resolution with HBO versus 32% resolution with placebo) [24]. A recent publication from the Dana-Farber Cancer Institute does not include HBO therapy as a potential treatment strategy. However, they have put forth the below prevention strategy [25].

12.3.8 Patients Who Received Radiation to the Head and Neck Area and Require Dental Extractions

(a) Perform extraction of teeth with minimal trauma to the alveolus and the soft tissue.
(b) Initiation and continuation of topical oral rinses (0.12% chlorhexidine gluconate) and systemic antibiotic therapy as indicated until healing of the extraction sites is noted.

12.3.9 Treatment of ORN

The focus should be on prevention of the condition. However, the treatment of ORN ranges from conservative nonsurgical management to aggressive surgical resection and reconstruction with microvascular tissue transfer.

12.3.10 Patients Who Received Radiation to the Head and Neck Area and Developed ORN

(a) Microbial culture and antibiotic sensitivity in areas of active infection
(b) Conservative therapy—sequestrectomy, topical oral rinses (0.12% chlorhexidine gluconate), and systemic antibiotic therapy as indicated
(c) Novel medication therapy with pentoxifylline, tocopherol, and clodronate. The original trial consisted of patients treated for refractory ORN with 800 mg pentoxifylline, 1000 IU vitamin E, and 1600 mg clodronate 5 days per week alternating with 20 mg prednisone and 1000 mg ciprofloxacin 2 days per week [26].
(d) Surgical Treatment involves debridement of bone and soft tissue; aggressive resection of the involved bone and reconstruction with free or pedicled tissue transfer to manage the defect, soft and hard tissues.

12.4 Antibiotic Prophylaxis

Dentists prescribe more than 10% of all outpatient antibiotics which is a substantial number [27]. In the United States, there is a steady antibiotics prescription pattern among dentists despite a decrease in such prescriptions among other providers [28]. Inappropriate and overuse of antibiotics have led to increasing microbial resistance which in turn leads to increased morbidity and mortality. Studies have shown that bacterial species within the oral cavity can quickly develop genetic expression of antibiotic resistance even if they were used for a shorter period [29, 30]. This section covers antibiotic prophylaxis recommendations based on current scientific evidence for the prevention of bacterial endocarditis and reducing the risk of prosthetic joint infections.

12.4.1 Infective Endocarditis

Infective endocarditis is a rare but one of deadliest infections which occurs in 10/100,000 people [31]. The disease carries significant morbidity including prolonged hospital stay, antibiotic therapy, and the potential need for valvular heart surgery. Infective oral diseases and resulting treatment have long been implicated in the predisposition of infective endocarditis [32]. Hence, the concept of antibiotic prophylaxis prior to invasive oral procedures has been the normal practice across the world. However, there have been significant inconsistencies in administering prophylactic antibiotics [33].

The practice of antibiotic prophylaxis dates back to the early report of bacteremia after a dental procedure in 1923 [34]. This was confirmed in 1935, and the first guidelines for prophylactic antibiotics were developed by the American Heart Association in 1955 [35, 36]. These early guidelines are predominantly consensus based than good scientific evidence. The viridians group of oral streptococci has long been associated in the development of bacterial endocarditis. However due to emerging pattern of antimicrobial resistance patterns, beginning in 2004 various organizations have limited or eliminated the need for antibiotic prophylaxis for the prevention of bacterial endocarditis in all but a small subset of patients [37, 38]. According to the recent ACC/AHA guidelines, endocarditis prophylaxis before invasive oral procedures is recommended in patients with valvular heart disease (Table 12.3).

The current guidelines primarily recommend amoxicillin and clindamycin for prophylaxis. However, recent studies have questioned the effectiveness of such antibiotics, particularly clindamycin, due to developing resistance [40]. In addition, oral hygiene activities are also known to induce bacteremia although less than surgical procedures in the oral cavity. Patients with poor oral hygiene are likely to have much higher rates of bacteremia [41]. Since the latest guidelines have emerged, various studies have shown the decreased trend of infectious endocarditis, while others have observed an increased rate of the disease, although these data do not establish a cause-effect relationship between antibiotic prophylaxis reduction and infectious endocarditis increase [42]. To date there have not been any randomized controlled studies to effectively study the risk of development of infective endocarditis. Majority of the studies have been observational, and the data could not explain the change in disease trends. In addition, the introduction of better diagnostics techniques could perhaps explain the increased detection of infective endocarditis but not necessarily the result of limited antibiotic prophylaxis.

Widespread and indiscriminate use of prophylactic antibiotics still persist within the dental community despite several studies that have questioned the role of dental interventions as a risk factor for infective endocarditis. One study revealed over 80% of patient received antibiotics despite only 20% of them having a cardiac condition at risk of developing infective endocarditis [43].

Table 12.3 Recommendations for endocarditis prophylaxis (adapted) [39]

Prosthetic cardiac valves, including transcatheter-implanted prostheses and homografts
Prosthetic material used for cardiac valve repair, such as annuloplasty rings and chords
Previous infectious endocarditis
Unrepaired cyanotic congenital heart disease or repaired congenital heart disease, with residual shunts or valvular regurgitation at the site of, or adjacent to the site of, a prosthetic patch or prosthetic device
Cardiac transplant with valve regurgitation attributed to a structurally abnormal valve

12.4.1.1 Recommendations

Until further data is available, it is safe to continue with the current antibiotic prophylaxis regimen for patients deemed as high risk towards the development of infectious endocarditis. The protocol is an inexpensive and low-risk approach based on the European Society for Cardiology and the American Heart Association guidelines.

12.4.2 Prosthetic Joint Infections and Antibiotic Prophylaxis

In an attempt to decrease the risk of hematogenous spread of infections to prosthetic joints,

various guidelines have been proposed towards antibiotic prophylaxis. Similar to bacterial endocarditis, oral bacteria have been implicated as a potential source of prosthetic joint infections which have been gradually on the rise. These infections occur in approximately 2% of the patients [44]. In general, *Staphylococcus aureus* is the predominant species implicated in prosthetic joint infections. Oral bacteria have been isolated in less than 10% of the failed joints due to infections [45]. Bacteremia following invasive oral procedures has been described. However, the risk of developing prosthetic joint infections from such bacteremia has not been proven. In addition, the perceived beneficial effect of antibiotic prophylaxis prior to oral procedures on the bacteremia is unclear [46].

The current guidelines recommend the use of antibiotic prophylaxis during the first 2 years of prosthetic joint implantation. However, recent studies have shown the risks of late joint infections are higher, and best available evidence does not support such recommendation [47].

Similarly, the guidelines call for prophylaxis in immunocompromised patients. However, the risk of daily bacteremia from oral hygiene-related activities does not change in these patients, and the evidence does not support the notion of increased risk of joint infection in this patient cohort [48]. In fact, case reports have also indicated the risk of prosthetic joint infection still persists despite prophylaxis in high-risk patients [49]. Similar to the infective endocarditis prophylaxis, the evidence and implementation of these guidelines are based on consensus statements rather than best scientific evidence (Table 12.4) [50].

Table 12.4 Recent international guidelines (modified) [50]

Country/ Region	Recommendations
USA	Antibiotic prophylaxis should be considered in high-risk patients (risk factors not defined clearly) Good oral health maintenance Inconclusive on the routine perioperative use of chlorhexidine oral rinse Inconclusive in oral evaluation before and after prosthetic joint implantation
United Kingdom	Antibiotic prophylaxis should be considered in high-risk patients (risk factors not defined clearly)
Canada	Antibiotic prophylaxis is not indicated
Australia and New Zealand	Antibiotic prophylaxis should be considered in high-risk patients Antibiotic prophylaxis should be considered in specific oral procedures
Europe	Antibiotic prophylaxis should be considered in high-risk patients Antibiotic prophylaxis should be considered in specific oral procedures

12.4.3 Temporomandibular Joint Total Joint Replacement

Interestingly, protocols or evidence-based guidelines for postoperative management of temporomandibular joint total joint replacements are even less robust, but there appears to be less controversy as the dental community has adopted the recommendations found in the 2015 ADA systematic review of antibiotic prophylaxis prior to dental procedures in patients with prosthetic joints. However, some reports suggest few TMJ surgeons do advocate for postoperative antibiotic prophylaxis, even lifetime antibiotic prophylaxis [51].

12.4.3.1 Antibiotic Stewardship

Ultimately, the goal is to assure antibiotic stewardship, by utilizing antimicrobials only when indicated, and to narrow the antibiotic spectrum and duration of treatment as warranted, so as to limit the development of untoward events such as *Clostridium difficile* infection, allergic reactions, and resistance.

12.5 Anticoagulation

Perioperative management of a patient's anticoagulation is critical to a successful surgical outcome. The goal is to find the balance between preventing significant hemorrhage during a pro-

cedure an unnecessary risk of developing a deep vein thrombosis (DVT) or pulmonary embolism (PE). In most all dental procedures and many oral surgical procedures, there is no need to stop or disrupt anticoagulation, as local hemostatic techniques are adequate to create and maintain hemostasis [52]. In contrast, disruption to anticoagulation in a patient with atrial fibrillation can result in an approximately 5% chance of stroke during the period of disruption [53]. As a result, in extraction cases, for instance, the treatment plan may include multiple appointments, for more robust treatment plans, each addressing only one quadrant at a time, in an attempt to limit wounding and the potential for perioperative bleeding when anticoagulation has been uninterrupted. For inpatient cases in which surgery will occur in the operating room, bridging may occur using heparin or lovenox and for expansive treatment can be rendered, and the patient can be monitored, in the hospital, until hemostasis is confirmed, and anticoagulation is normalized.

The aging population has resulted in a significant number of individuals, worldwide, taking some form of "blood thinner." Cardiovascular disease, non-valvular atrial fibrillation, deep vein thrombosis, and valvular heart disease treatments rely on some combination of antiplatelet and/or anticoagulation therapy. Even a short-term interruption of anticoagulants and antiplatelets can be dangerous. The risk of perioperative stent thrombosis in cardiac patients is increased by noncardiac surgical procedure, when surgery is performed early after stent implantation and if dual antiplatelet therapy is discontinued [54]. These patients can suffer a "rebound effect," which increases the danger of a catastrophic event if long-term therapy is interrupted. If interruption is necessary, keep it to the shortest duration possible. A thorough understanding of the disease process, the medication pharmacokinetics, and the surgical procedure allows for an optimal treatment plan in the management of anticoagulation in the perioperative period. Medications of consequence include the following:

The class of anticoagulant drugs

- Vitamin K antagonists (coumadin)
- Low-molecular-weight heparins (lovenox)
- Direct thrombin inhibitors (dabigatran)
- Factor Xa inhibitors (apixaban)

The class of antiplatelet drugs

- Irreversible cyclooxygenase inhibitors (aspirin)
- Adenosine diphosphate (ADP) receptor inhibitors (plavix)
- Protease-activated receptor-1 (PAR-1) antagonists (vorapaxar)
- Thromboxane inhibitors

Discussions with other consultants and the patient's primary care provider are important to in the preoperative setting. For outpatient surgery, the patient can resume normal anticoagulation therapy, if disrupted, almost immediately after surgery. Again, the key with anticoagulation management is balancing the risk of thrombosis against the risk of significant bleeding.

12.6 Obesity

Approximately 13% of the world's population is obese, and about 43% of the United States population is affected by obesity [55]. Body mass index (BMI) is calculated as mass (kg)/height (m^2). BMI of greater than 30 is considered as obese (Table 12.5). Obesity negatively impacts almost every organ system in the body, resulting

Table 12.5 Classification of obesity

BWI (kg/m^2)	Weight category	Obesity class
18.5–24.9	Normal weight	
25–29.9	Overweight	
30–34.9	Obese	Class I
35–39.9	Obese	Class II
40–49.9	Morbidly obese	Class III
50–59.9	Super obese	Class IV
60–69.9	Massively obese	
>70	Mega obese	

in significant multiple medical comorbidities, many of which can negatively impact surgical outcomes. Multiple studies, in various surgical disciplines, have intimated that obesity increases the perioperative risks for operative time, blood loss, surgical site infections, and development of deep vein thrombosis [56]. Further, in the outpatient setting, obesity-associated conditions such as obstructive sleep apnea, acid reflux, metabolic syndrome, depression, hypertension, and chronic pain can complicate the surgical plan, especially if office-based anesthesia is planned [57].

Specifically for the obese patient, perioperative considerations should include the following:

1. Is the patient optimized, despite possibly having multiple medical comorbidities?
2. Is the patient appropriate for office-based surgery?
3. Is anesthesia, sedation or general, necessary to achieve the surgical goals?

If office-based surgery, with anesthesia, is deemed appropriate, based on the questions above, additional considerations are as follows [57–59]:

1. Type of anesthesia, intravenous sedation versus general
2. Patient positioning, reverse Trendelenburg or ramping
3. Airway management, open airway versus supraglottic device versus endotracheal tube
4. NPO status, especially in patients with acid reflux or delayed gastric emptying
5. Difficult airway/emergency equipment available and function verified
6. Medications and dosing
   (a) Use short-acting medications, such as propofol
   (b) Avoid/minimize medications that blunt respiratory drive—consider ketamine in medically appropriate patients
   (c) Optimize local anesthesia and multimodal pain strategies to minimize need for narcotics
   (d) Dosing based on ideal body weight
7. Postoperative recovery location should include direct patient line of sight
8. Postoperative monitoring duration likely needs to be extended, especially in obstructive sleep apnea patients
9. Postoperative pain control should minimize narcotics

The obese surgical patient requires a focused approach to perioperative management to create a treatment plan that results in the safe and effective delivery of care. Weight categories and BMI calculations are useful tools in the management of obese patients, and with obesity levels projected to increase in the years to come, the proceduralist or surgeon must have a detailed plan and approach to this population of patients.

12.7 Postoperative Pain Management

Pain as the fifth vital sign is likely a driver of the opioid crisis within the United States. Nonetheless, pain management is still a critical part of surgical patient management. Thus, in an era of tightened prescription monitoring programs, state prescribing guidelines, and narcotic schedule changes, such as hydrocodone from schedule III to schedule II, pain management requires a multimodal approach. Various non-opioid drugs may be considered for optimal pain control (Table 12.6). Assuming that an individual patient has no contraindication to a medication, such as allergy, adverse reaction, drug interactions, or a medical comorbidity precluding use, nonsteroidal anti-inflammatory medication (NSAIDS) and acetaminophen are the mainstays for opioid-sparing pain control during the acute perioperative period. However, prolonged use of NSAIDS should be avoided due to the FDA warning regarding prolonged use and cardiac disease. Similarly, acetaminophen should not exceed 4000 MG per day and should not be taken in conjunction with alcohol, to avoid liver toxicity.

Regarding opioids and their role in perioperative pain management, it is seemingly clear that historically, there has been an excess of pills pre-

Table 12.6 Non-opioid drugs with analgesic effects

Class of drug	Drug name	Dose	Special considerations
Anticonvulsants	Gabapentin	300–1200 mg tid	Preemptive analgesic caution—drowsiness, fluid retention
	Pregabalin	75–300 mg bid	Start at 75 mg bid
Alpha-2-agonists	Clonidine	0.2 mg bid	Caution—severe hypotension and withdrawal from abrupt stopping
	Dexmedetomidine	0.2–1 mcg/kg/h Start at 0.6 mcg/kg	Caution—bradycardia and hypotension
Nonsteroidal anti-inflammatory drugs (NSAIDs)	Ibuprofen	400–600 mg PO q 4–6 h prn	Caution—GI, renal dysfunction. Gastric ulceration
	Ketorolac	IM or IV 15–30 mg q 4–6 h PO 10 mg q 4–6 h	PO dose—not to exceed 40 mg/day and 5 days
	Diclofenac	18–35 mg PO tid	Not interchangeable with other diclofenac formulations. Reassess dose
	Meloxicam	7.5–15 mg PO qd	All products not bioequivalent
	Nabumetone	1000–2000 mg/day divided qd-bid	Do not exceed 2000 mg/day
	Celecoxib	100–200 mg PO bid	Increases GI ulceration with bisphosphonates
Acetaminophen		325–650 mg PO q 4–6 h IV—1000 mg q 6 h	Do not exceed 4 g/day Potentiates warfarin
NMDA antagonist	Ketamine	IV—0.3–0.5 mg/kg	Euphoric effects and excessive salivation

scribed, as per the third molar study by Resnick et al., compared to the actual patient need [60]. Overprescribing is of particular concern in the opioid naïve patient, as this excess medicating could result in addiction and misuse. In fact, a recent study showed that patients who were prescribed opioids reported higher levels of pain compared to those who were treated with non-opioid drugs [61]. Within the United States, the University of Michigan has created the Michigan Opioid Prescribing Engagement Network (OPEN), and other states, such as Delaware, have followed suit, as a means to study actual opioid needs and create evidence-based guidelines after many different types of surgery, to prevent over-prescribing and addiction (https://michigan-open.org/). Further, a 2017 JAMA article demonstrated no significant difference in pain relief for opioids versus non-opioid analgesics for acute extremity pain in the emergency room [62]. In other cases, preoperative opioid exposure was associated with a higher rate of opioid-related readmissions, compared with naive patients [63]. Hence, it is important to screen patients appropriately for preoperative opioid exposure and create risk mitigation strategies.

Pain management is complex and must be tailored to each individual patient, as patient-specific issues will require a thoughtful approach to perioperative pain control. However, it is clear that most oral surgeries and dental procedures can be managed with non-opioid medications and that when an opioid is necessary, the strength and amount prescribed should be limited, and evidence now exists to guide the clinical team.

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