Chapter 8

Anesthesia and Sedation

Jeffrey A. Elo and Ho-Hyun Sun

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/63539

Abstract

Anxiety control and patient comfort are integral components of everyday oral and maxillofacial surgery (OMFS) practice. Moderate sedation, deep sedation (DS), and general anesthesia (GA) have been successfully administered by and in the offices of oral and maxillofacial surgeons (OMSs) and their anesthesia teams for more than 50 years. The goal of moderate sedation, DS, or GA in the OMFS office is to establish an environment in which patients are comfortable and cooperative while allowing the surgeon to safely perform the operation. This requires meticulous care in which the practitioner balances the depth of sedation and level of responsiveness while maintaining a patent airway, proper and adequate ventilation, and optimal cardiovascular hemodynamics. The record of safety among OMSs with this form of outpatient anesthesia is exemplary. The impressive morbidity and mortality statistics support the concept that the OMFS anesthesia team model is a safe, efficient, and cost-effective model for office-based ambulatory surgical-anesthesia care. Safe anesthesia practice depends on various items, including goals of anesthesia, selecting the proper patient, anesthetic technique utilized, drug regimen selection, monitoring, anesthetic team (staff and anesthesia provider) training, and the team's preparedness to handle unanticipated complications and medical/anesthetic emergencies.

Keywords: general anesthesia, pediatric anesthesia, levels of sedation, anesthetic agents, local anesthetics

1. Introduction

Moderate sedation, deep sedation, and general anesthesia have been successfully and safely administered by and in the offices of oral and maxillofacial surgeons (OMSs) and their

anesthesia teams for more than 50 years. [1–5]The goal of moderate sedation, deep sedation (DS), or general anesthesia (GA) in the oral and maxillofacial surgery (OMFS) office is to establish a safe environment in which the patient is comfortable and cooperative while allowing the surgeon to safely perform the indicated operation. This requires meticulous care in which the practitioner balances the patient's depth of sedation andlevel of responsiveness while maintaining a patent airway, proper and adequate ventilation,andoptimalcardiovascular hemodynamics. Several recent nationwide morbidity studies in the United States have demonstrated that these techniques are safe when used by OMSs who have completed an accredited OMFS residency program with formaltraininginanesthesiology. The impressivemorbidityandmortality statistics support the concept that the OMFS anesthesia team model is a safe, efficient, and cost-effective model for office-based ambulatory surgical-anesthesia care.

A preanesthetic patient assessment is a critical component of an OMS' practice. The standardization of the method of evaluating and documenting a patient's medical history and physical examination findings, as well as any pertinent diagnostic tests (laboratory and radiographic), is essential to formulating an accurate diagnosis and developing an effective anesthetic treatment plan. A comprehensive evaluation provides the basis for determining the surgical and anesthetic risk of each patient, and minimizes perioperative morbidity and complications associated with comorbid systemic health conditions. It is important to note that many comorbid medical conditions require consideration by the OMS. However, as each OMS has been trained during his/her surgical residency to complete a thorough pre-operative patient assessment, this chapter is not intended to describe the steps in how to perform an assessment; rather it will attempt to organize its process.

The processes described here establish a foundation for patient assessment and management as described in the American Association of Oral and Maxillofacial Surgeons' (AAOMS) Parameters of Care—2012 (AAOMS ParCare 2012) [9]. Specific diagnostic techniques and physical assessment protocols are purposely not defined, as it is not the authors' intent to dictate the methods for performing a patient assessment. The OMS has the freedom and ability to complete a patient assessment based on his/her training, the clinical circumstances of the patient, and the institutional standards under which the OMS practices.

The OMS is responsible for an initial history and physical examination necessary to determine the risk factors associated with the management of each patient. In some circumstances, the patient's primary care medical doctor may perform the history and physical examination, but it is ultimately the responsibility of the OMS to review such information and to ascertain whether it is complete to his/her level of satisfaction or whether further assessment and/or laboratory studies are indicated based on the specific patient and planned procedure. In cases when another health care provider (such as a primary care physician, cardiologist, or pediatrician) assesses the patient preoperatively, the OMS must ensure that the documented assessment also meets the parameters set forth in the AAOMS ParCare 2012 [9] The OMS is solely responsible for the final risk assessment of the patient and, ultimately, the decision to perform or not perform the surgical procedure. No other provider may assume this responsibility.

http://dx.doi.org/10.5772/63539

1.1. American Society of Anesthesiologists (ASA) Physical Status Patient Classification System

ASA class I	A normal healthy patient
ASA class II	A patient with mild systemic disease
ASA class III	A patient with severe systemic disease
ASA class IV	A patient with severe systemic disease that is a constant threat to life
ASA class V	A moribund patient who is not expected to survive without an operation
ASA class VI	A declared brain-dead patient whose organs are being removed for donor purposes

*Note: If a surgical procedure is performed emergently, an "E" is added to the previously defined ASA classification.

Table 1. American Society of Anesthesiologists Physical Status Patient Classification System

On the basis of a thorough patient assessment, an ASA physical status should be assigned to all surgical patients according to the guidelines set forth by the ASA (**Table 1**).

1.2. Preoperative fasting guidelines

Every healthy patient without a risk of gastroparesis who will undergo a sedation or general anesthetic procedure should maintain a "nothing per mouth" (NPO) status (**Table 2**). The ASA [10] recommends a 2-h fasting period of clear liquids for all patients. The ASA recommends a fasting period for breast milk of 4 h and for infant formula or nonhuman milk of 6 h for neonates and infants. For solid foods in most adult patients, the ASA recommends fasting periods of at least 6 h (light meal such as toast and clear liquid) or 8 h (fatty or fried foods or meat). For infants and children, the fasting period for solids should be at least 6 h.

Ingested material	Minimum fasting period
Clear liquids	2 h
Breast milk	4 h
Infant formula	6 h
Nonhuman milk	6 h
Light meal	6 h
Fatty meal	8 h

Table 2. American Society of Anesthesiologists Fasting Guidelines [10]

The preoperative use of gastric stimulants, gastric acid secretion blockers (histamine H_2 receptor antagonist agents), antacids, antiemetic agents, and/or anticholinergic medications (to decrease the risk of pulmonary aspiration) is not routinely recommended [10] Their use should be based on the individual patient assessment.

1.3. Discharge criteria

All patients who have undergone outpatient surgery using moderate sedation, DS, or GA must meet minimal criteria to permit safe discharge from the OMFS office or outpatient surgical facility. Such criteria may include either the use of an Aldrete Score (**Table 3**), Post-Anesthesia Discharge Scoring System (PADSS or modified PADSS), or another equivalent. The patient must arrive at the office or surgical facility with a responsible adult escort for discharge after surgery and anesthesia.

Criteria	Points
Oxygenation	
SpO_2 > 92% on room air	2
SpO_2 > 90% on oxygen	1
SpO_2 < 90% on oxygen	0
Respiration	
Breathes deeply and coughs freely	2
Dyspneic, shallow, or limited breathing	1
Apnea	0
Circulation	
BP ± 20% of normal	2
BP ± 20–50% of normal	1
BP ± > 50% of normal	0
Consciousness	
Fully awake	2
Arousable on calling	1
Not responsive	0
Activity	
Moves all extremities	2
Moves two extremities	1
No movement	0

A total score of 9 or 10 shows readiness for discharge.

Table 3. Post-anesthetic Aldrete recovery score.

1.4. Special considerations for pediatric patients

When performing physical examinations on pediatric patients, it is critical to remember the differences between children at various ages and adults with regard to anatomy (e.g., airway), vital signs (e.g., heart and respiratory rates), and physiology (greater body surface area or mass

and cardiac output). Cardiac output is more heart rate dependent in the child than in the adult. When assessing the child for anesthesia, the OMS must also pay particular attention to the patient's allergy history for the common childhood precipitants of asthmatic attacks: pollen, other indoor or outdoor airborne irritants, animal hair, physical exercise, and/or anxiety. Upper respiratory tract infections that produce airway irritability are exceedingly common in young children. Specific reactions to suspected drug allergens should be ascertained through allergy testing with, for example, an allergy panel. Noted differences between the pediatric and adult airways include: higher, more anterior position of the glottis opening in the child; relatively larger tongue in the infant; larger and more floppy epiglottis in the child; the subglottic region as the functionally narrowest portion of the pediatric airway versus the vocal cords in the adult; and larger relative size of the occiput in the infant.

1.5. Preoperative cardiac and pulmonary assessment

It comes as no surprise to the seasoned OMS/anesthesia provider that the two most important systems to consider on patient evaluation are the cardiac and pulmonary systems. Perioperative adverse cardiac events may occur in the OMFS patient. High-risk patients can usually be identified during a comprehensive history, review of systems, and physical examination. The history should elicit conditions such as stable (ASA 3) or unstable (ASA 4) angina, recent or past myocardial infarction with or without cardiac stent and appropriate anticoagulation, heart failure—compensated or decompensated, significant arrhythmias, valvular disease, and the presence of a pacemaker or a defibrillator. Patients should be questioned on their smoking status (current or former use, how many cigarettes per day, how many years), management and control of their blood sugars in diabetes mellitus, and renal insufficiency. Functional status should be quantified based on the metabolic equivalent (MET) (**Table 4**), which is used in the American College of Cardiology/American Heart Association Guidelines (ACC/AHA) [11]. For example, a person functioning at 1 MET is limited to simple activities such as eating, dressing, and using the toilet. A person with 4 METs can climb a flight of stairs, walk up a hill, or walk on level ground at 4 mph, and would generally not require an extensive cardiac workup. Physical examination should be used to look for jugular venous distention, arrhythmias, and abnormal heart sounds such as an S_3 gallop or murmur. The information obtained from the history and examination can be used to assess risk and to direct further testing.

MET	Functional levels of exercise
1	Eating, working at a computer, dressing
2	Walking down stairs or in your house, cooking
3	Walking 1–2 blocks
4	Raking leaves, gardening
5	Climbing 1 flight of stairs, dancing, bicycling
6	Playing golf, carrying clubs
7	Playing singles tennis

MET	Functional levels of exercise
8	Rapidly climbing stairs, jogging slowly
9	Jumping rope slowly, moderate cycling
10	Swimming quickly, running or jogging briskly
11	Skiing cross-country, playing full-court basketball
12	Running rapidly for moderate to long distances

MET, metabolic equivalent of the task. 1 MET is defined as the amount of oxygen consumed while sitting at rest and is equal to 3.5 mL O_2 per kilogram of body weight × min. The MET concept represents a simple, practical, and easily understood procedure for expressing the energy cost of physical activities as a multiple of the resting metabolic rate. The energy cost of an activity can be determined by dividing the relative oxygen cost of the activity (mL O_2/kg/min) by 3.5 [12].

Table 4. Estimated energy requirements for various activities (METs)

Indices for assessment of cardiac morbidity and mortality in noncardiac surgery have been established. The Revised Cardiac Risk Index (RCRI) is one such important assessment tool (**Table 5**). If it is determined that the patient is at significant risk for a postoperative cardiac event, further workup should be conducted and the condition should be optimized prior to the surgical procedure, if possible. Consultation with the patient's cardiologist should be sought when coronary or valvular disease is suspected or if assistance is needed with management of pacemakers or defibrillators.

Risk factors	
Ischemic heart disease	
Congestive heart failure	
Cerebrovascular disease	
Diabetes mellitus requiring preoperative insulin	
Serum creatinine > 2.0 mg/dL	
High-risk surgery (intraperitoneal, intrathoracic, or suprainguinal vascular)	
RCRI classification	**Event rate (%)**
Low risk (0 factors)	0.5
Low risk (1 factor)	1.3
Intermediate risk (2 factors)	3.6
High risk (3 or more factors)	9.1

Table 5. Revised Cardiac Risk Index (RCRI) [13].

1.6. Twelve-lead electrocardiogram (ECG)

A preoperative ECG is indicated within 30 days prior to the surgical procedure in patients with known coronary disease, peripheral vascular disease, or cerebrovascular disease. It may be

reasonable to obtain an ECG in patients with a single clinical risk factor (e.g., diabetes mellitus, renal insufficiency, or congestive heart failure) who are to have an intermediate risk operation (more than "minor" oral surgical procedures). There is no evidence to support the routine use of ECG in patients without risk factors.

1.7. Noninvasive testing of left ventricular function

Evaluation of left ventricular function by radionuclide angiography or echocardiography is reasonable in patients with dyspnea of unknown origin or worsening dyspnea in the setting of known congestive heart failure (decompensated). The routine evaluation of left ventricular function is not otherwise indicated.

1.8. Noninvasive stress testing

Noninvasive stress testing involves radionuclide or echocardiographic imaging combined with pharmacologic stress to evaluate for ischemia and arrhythmias in patients who are unable to exercise. Patients with one or two clinical risk factors and poor functional capacity (<4 METs) should be considered for noninvasive stress testing. Routine noninvasive stress testing is not indicated in patients without clinical risk factors. Patients with active cardiac conditions should usually be evaluated by other methods.

1.9. Pulmonary and airway assessment

Patient-related risk factors for perioperative pulmonary complications include chronic obstructive pulmonary disease (COPD), pneumonia, sleep apnea, dyspnea, advanced age, obesity, and smoking [14, 15]. The most important part of a pulmonary risk assessment is a thorough history and physical examination. Specifically, the patient should be asked about shortness of breath, dyspnea on exertion, productive coughs, and symptoms of sleep apnea. A smoking history should also be obtained. Smoking cessation may reduce postoperative pulmonary complications. Patients experience increased mucociliary response and airway hypersensitivity shortly upon termination of smoking which will increase the risk of pulmonary complications. Ideally, patients should stop smoking for at least 8 weeks prior to the surgical procedure in order to reduce pulmonary morbidity.

Sleep apnea is a common and underdiagnosed problem [16]. Risk factors include obesity, male gender, a short/stout neck, macroglossia, and enlarged tonsils (**Table 6**). Symptoms and signs related to apnea are snoring, nighttime choking, or gasping, observed cessation of breathing by a partner, morning headaches, and daytime somnolence. Premedication with clonidine [17] given the night before and 2 h prior to surgery has been shown to reduce the need for operative anesthesia and to improve perioperative hemodynamics, anesthetic recovery, and pain control.

The Mallampati classification is a scoring system that relates the amount of mouth opening to the size of the tongue, and provides an estimate of space available for oral intubation by direct laryngoscopy. According to the Mallampati scale (**Figure 1**), class one is present when the soft palate, uvula, and pillars are visible, class two when the soft palate and base of the uvula are

visible, class three when only the soft palate is visible, and class four when only the hard palate is visible.

Degree of tonsils blockage	Ratio of the tonsil in the oropharynx
Degree 0	Tonsils in the fossa
Degree 1	Tonsil occupies < 25% of the oropharynx
Degree 2	Tonsil occupies 25–50% of the oropharynx
Degree 3	Tonsil occupies 50–75% of the oropharynx
Degree 4	Tonsil occupies > 75% of the oropharynx

Table 6. Brodsky tonsil classification system

Figure 1. Mallampati classification.

1.10. Renal/endocrine systems assessment

Renal failure has been associated with increased risks of surgical infection and issues with wound healing [18]. It can also lead to disturbances in electrolytes and fluid balance, which may exacerbate the physiologic changes occurring during the perioperative period. In the patient with known or suspected renal failure, it may be prudent to evaluate the serum concentrations of the patient's potassium, magnesium, calcium, and phosphate. Blood urea nitrogen and creatinine assays should be obtained. Patients with newly diagnosed renal failure should be evaluated by a nephrologist prior to general anesthesia and surgery. Dialysis may be indicated if the uremia is found to be significant [19].

1.11. Diabetes and hyperglycemia

The prevalence of diabetes in the United States has been increasing and is currently estimated to be about 10%. Many more individuals likely remain undiagnosed. Hyperglycemia has been associated with immune dysfunction, elevation of inflammatory markers, vascular endothe-

lium dysfunction, and thrombosis. Clinically, hyperglycemia can lead to increased surgical site infection and postoperative mortality [20–23].

At-risk patients should be assessed for hyperglycemia prior to surgery. Known diabetics should have their hemoglobin A1c levels evaluated along with a fasting serum glucose test. Optimization of blood glucose control prior to surgical intervention should be undertaken, if possible. For nondiabetic patients at risk of hyperglycemia (e.g., the obese and the elderly), consideration should be given to measuring the preoperative and intraoperative fasting glucose level. If these levels are found to be elevated, measures to tightly control serum glucose (e.g., insulin infusion) should be initiated [21, 22, 24].

1.12. Summary of preoperative assessment

Risk evaluation should be done for every OMFS patient. A diligent evaluation using the presented guidelines will allow optimization of care throughout the perioperative period. The ultimate goal of achieving improved outcomes should encourage the consistent assessment of all potential risk factors for each patient.

2. Sedation

2.1. Levels of sedation

The American Dental Association (ADA) has incorporated the American Society of Anesthesiology (ASA) definitions for use in its own published guidelines. The categorization as detailed by both the ASA and ADA focuses on the concept that the spectrum of sedation and anesthesia is a continuum extending from mild sedation (anxiolysis) to moderate sedation and analgesia ("conscious sedation") to deep sedation and analgesia to general anesthesia. The ASA and ADA differentiate these levels based on four parameters, which measure responsiveness, airway integrity, spontaneous ventilation, and cardiovascular hemodynamics (**Table 7**).

Minimal sedation (anxiolysis) is a drug-induced state during which patients respond normally to verbal commands. Although cognitive function and physical coordination may be impaired, airway reflexes, ventilatory, and cardiovascular functions are unaffected.

Moderate sedation/analgesia ("conscious sedation") is a drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation. No interventions are required to maintain a patent airway, and spontaneous ventilation is adequate. Cardiovascular function is usually maintained.

Deep sedation/analgesia is a drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully following repeated or painful stimulation. The ability to independently maintain ventilatory function may be impaired. Patients may require assistance in maintaining a patent airway, and spontaneous ventilation may be inadequate. Cardiovascular function is usually maintained.

General anesthesia is a drug-induced loss of consciousness during which patients are not arousable, even by painful stimulation. The ability to independently maintain ventilatory function is often impaired. Patients often require assistance in maintaining a patent airway, and positive pressure ventilation may be required because of depressed spontaneous ventilation or drug-induced depression of neuromuscular function. Cardiovascular function may be impaired.

Characteristic	Minimal sedation	Moderate sedation and analgesia	Deep sedation and analgesia	General anesthesia
Responsiveness	Normal response to verbal stimulation	Purposeful response to verbal or tactile stimulation	Purposeful response after repeated or painful stimulation	Unarousable even with painful stimulus
Airway	Unaffected	No intervention required	Intervention may be required	Intervention often required
Spontaneous ventilation	Unaffected	Adequate	May be inadequate	Frequently inadequate
Cardiovascular function	Unaffected	Usually maintained	Usually maintained	May be impaired

Reproduced with permission of *Anesthesiology* from the American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-anesthesiologists

[†]Reflex withdrawal from a painful stimulus is not considered a purposeful response

Table 7. Continuum of depth of sedation: definition of general anesthesia and levels of sedation and analgesia

In most situations, the primary goal of outpatient sedation in the OMFS office is to achieve comfort and cooperation which is accomplished by a drug-induced alteration in consciousness. Responsiveness can be used as the primary parameter to assess the state of consciousness, which defines the desired anesthetic level. The terms mild, moderate, deep, and general descriptively imply both the desired response and depth of sedation. Given sufficient anesthetic medications, a patient will proceed from a state of relaxation with a normal response to verbal stimulation to a state in which they are unarousable.

Most anesthetic agents cause airway musculature relaxation and depress the hypoxic and hypercapnic respiratory drive, which have the potential to impair airway integrity and patency as well as spontaneous ventilation. As the level of sedation becomes deeper, both airway patency and spontaneous ventilation may and will ultimately require intervention and assistance.

Sedation is a continuous spectrum, and there is always a danger for the patient's airway to become compromised, which can go unnoticed in the absence of diligent monitoring. In addition, patient responsiveness and depth of anesthesia fluctuate depending on the level of stimulation. When the patient is more responsive, there may be a temptation to administer additional sedative medication. However, sustained procedural stimulation is rare and if

http://dx.doi.org/10.5772/63539

additional anesthetic medication is administered to diminish patient responsiveness, respiratory depression may result upon cessation of the procedural stimulation. This presents one of the limitations with the lighter levels of sedation as patient comfort and cooperation may be unachievable without infringing on the potential of adverse events.

It is important for the OMS to be cognizant that levels of sedation are independent of the route of administration or the selection of anesthetic agent. The OMS must also be cognizant that there is a wide variability in patient response to the various anesthetic medications, which could produce a more profoundly sedated patient than desired or anticipated.

2.2. Monitoring in OMFS sedation

The OMS/anesthesia provider is responsible for continuously monitoring the sedated patient. This consists of direct observation as well as utilization and interpretation of cardiovascular and respiratory monitors. Adverse respiratory events have been the primary etiology resulting in adverse outcomes. Standard of care in OMFS offices dictates that the following monitors be applied: pulse oximeter, noninvasive blood pressure monitoring, electrocardiography, capnography, and pretracheal stethoscope auscultation.

Pulse oximetry has been the standard of care for monitoring oxygen saturation for almost three decades. Pulse oximetry measures the amount of oxygen carried by hemoglobin molecules in arterial blood (oxygen saturation), which is displayed as a percentage. Arterial oxygen content is inferred (but not directly measured) from the percent hemoglobin saturation on the oxygen-hemoglobin dissociation curve.

Partial or complete airway obstruction and ventilatory depression from anesthetic medication, if not remediated, will result in an eventual decrease in arterial oxygen content which can be detected by pulse oximetry. However, it is important to realize that there will be at least a 20–30-s delay in the detection of these events as pulse oximetry measures hemoglobin saturation at the fingertip where blood may take up to 20–30 s to travel from the core circulation. Administration of supplemental oxygen will further postpone the onset of desaturation with airway obstruction or ventilatory compromise. For these reasons, pulse oximetry is not an efficient ventilatory monitor.

Ventilation is the movement of gas in and out of the lungs. Ventilatory monitoring for deep sedation and general anesthesia can be best accomplished with both capnography and a pretracheal stethoscope. Capnography typically utilizes infrared gas analysis technology to assess the concentration of carbon dioxide in inspired and expired air. The capnographic unit provides both an absolute end-tidal carbon dioxide ($ETCO_2$) value as well as a graphic demonstration of the patient's ventilation pattern (**Table 8**). In an open system (e.g., nonintubated patient), the exhaled air may be diluted with ambient air, minimizing the benefit of capnography; however, the graphic display can provide visual cues for the respiratory rate as well as an impairment of gas exchange (e.g., obstruction, bronchospasm). In addition, changes in ventilation, such as a change in the graphic display suggestive of airway obstruction, are detected and displayed immediately. The practitioner must be cognizant that capnography can fail in an open system as there is no direct sealed conduit between alveoli and the monitor.

The combination of both capnography and pretracheal auscultation improves the accuracy of ventilatory monitoring, as $ETCO_2$ sampled from the nose in a mouth breather can be inaccurate, and pretracheal auscultation during slow ventilation in an open airway can be silent or difficult to hear.

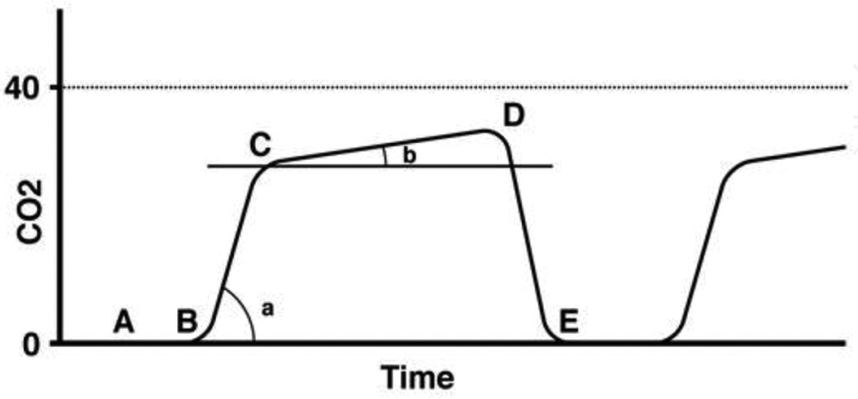

Table 8. End tidal CO_2 monitor graphical recording

3. Anesthetic agents

3.1. Clinical summary

An administered drug's activity is determined by its ability to cross the blood-brain barrier (degree of lipid solubility) to reach and bind respective central nervous system (CNS) receptors [the "vessel rich" group receives 75% of cardiac output (CO)] in sufficient concentration to exert its intended actions such as analgesia, sedation, hypnosis, and/or amnesia. A drug's side effects are usually due to its action at locations other than its targeted receptors. A drug's action is also dependent on the dose given, the rate of administration, and receptor number and

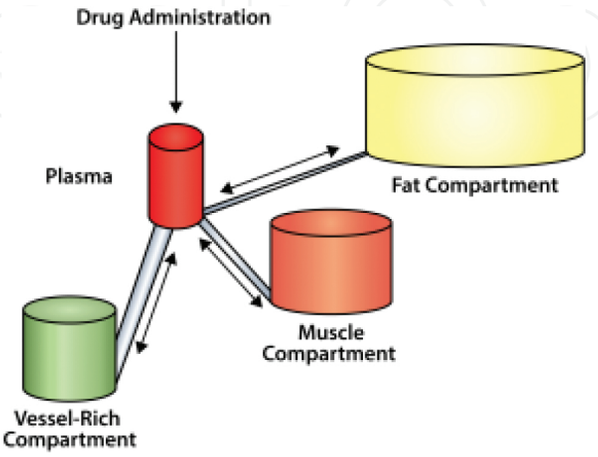

Figure 2. Drug distribution to various body compartments.

http://dx.doi.org/10.5772/63539

sensitivity, with a wide range of variability among patients. The actions of most short-acting drugs are terminated by redistribution ($T_{1/2}\alpha$) to other compartments (**Figure 2**). Longer-acting drugs are terminated by metabolism ($T_{1/2}\beta$) in the liver into smaller, water soluble moieties which can then be filtered and excreted by the kidney (or in sweat, mucus from the lungs, and gastrointestinal excretions to a small extent). Drugs may also "hide" in muscular (20% of CO), adipose (5% of CO) tissues or remain bound to plasma proteins (**Figure 3**), in which cases the intended receptors are not activated and clinical effects are absent (**Figure 4**). "Hidden drugs" can subsequently redistribute from "hidden reservoirs" prior to metabolism, causing a return or additive clinical effect also known as hangover. Hypoproteinemia (e.g., cachexia, anorexia, liver disease) will similarly enhance drug availability and action.

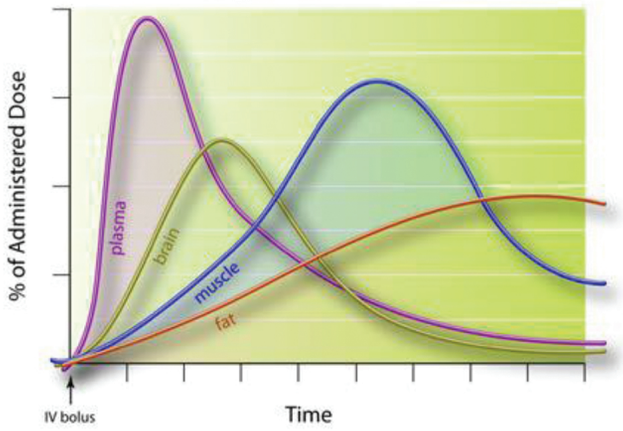

Figure 3. Drug distribution to various compartments over time.

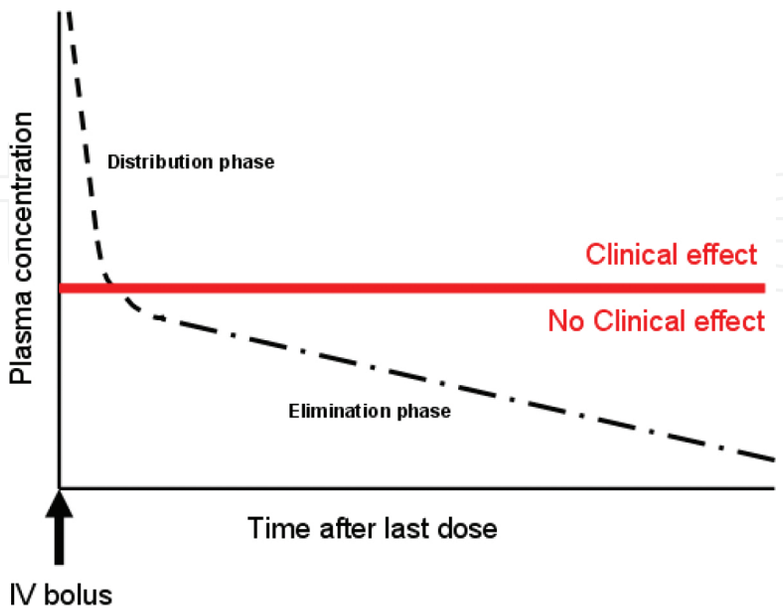

Figure 4. Plasma drug concentration versus time after an intravenous (IV) dose.

4. Review of anesthetic medications

This section focuses on describing many of the characteristics and properties of some of the most commonly used in-OMFS-office sedatives. The list of medications described here is not intended to be exclusive. The authors realize that with variations in OMFS training programs, variations in preferred drug regimens exist.

4.1. Benzodiazepines

Mechanism of action: bind to and enhance $GABA_A$ receptors to the actions of GABA ("GABAergic"), increase chloride conductance, and hyperpolarize neurons, thereby interrupting nerve transmissions. Benzodiazepines can be described as agonists of inhibitory GABA receptors.

Intended effects include sedation, anxiolysis, anterograde amnesia, muscle relaxation, and anticonvulsant activity. Benzodiazepines exert minimal cardiovascular effects and respiratory depression (decreased tidal volume and increased respiratory rate). They suppress psychotomimetic ketamine effects.

Adverse side effects include minimal cardiovascular or respiratory changes when used alone in therapeutic dose; however, benzodiazepines are synergistic with other agents. A paradoxical excitement (disinhibition) reaction is possible in patients at age extremes and in anxious teenage patients.

Benzodiazepines are metabolized via the liver and are excreted renally.

Midazolam: Water soluble until aromatic ring closes at pH > 4 (after injection), which enhances lipid solubility. Can be given by mouth (PO), intravenously (IV), or intramuscularly (IM). Midazolam has minimally active metabolites. Adult sedation/anxiolysis: 5 mg or 0.07 mg/kg IM; or 1 mg IV slowly q2–3 min up to 5 mg. Pediatric premedication dose ~0.25–1.0 mg/kg up to 20 mg maximum PO, or 0.1–0.15 mg/kg IM. Midazolam has an IV onset time of 1.5–5 min, peak effects at 4–8 min, and duration of 15–20 min.

Diazepam: Diazepam is a lipid soluble agent that requires propylene glycol to dissolve in water, which in turn creates a risk for thrombophlebitis. It features erratic IM absorption but can be given PO, IV, or IM. Physiologically, diazepam is metabolized to oxydiazepam, which is an active metabolite and contributes to a longer duration of action and hangover compared to midazolam. Diazepam has an IV onset time of 1.5–5 min, peak effects at 3–5 min, and duration of 15–60 min.

4.2. Flumazenil

Flumazenil is an inhibitory agonist of the GABA-benzodiazepine receptor complex (specifically) with no intrinsic activity. It will occupy a "free" receptor but will not displace other agonists and is therefore not very effective for quick reversal after an overdose. It is characterized by its high affinity, short duration, and possible contraindication in patients with seizure disorders as it may trigger seizures in patients who rely on benzodiazepines for seizure

control. Other side effects may include agitation, arrhythmias, and dizziness, pain on injection, nausea/vomiting (N/V), sweating, headaches, and blurred vision. The dose for benzodiazepine sedation reversal is 0.2 mg IV over 15 s, then 0.2 mg q1 min as needed up to 1 mg total dose. The dose for benzodiazepine overdose reversal is 0.2 mg IV over 30 s, then 0.3–0.5 mg q30 s as needed up to 3 mg total dose.

4.3. Opioids

Mechanism of action: opioid medications bind to multiple opioid receptors, most notably at the central nervous system (brain and spinal cord) mu receptors.

Intended effects of opioids include analgesia, attenuation of the neuroendocrine stress response, blunted laryngeal reflex, sedation, euphoria, and mental clouding. Opioids also provide cardiovascular stability.

Adverse side effects include vagal nerve mediated bradycardia, decreased sympathetic tone (decrease in systemic vascular resistance leading to hypotension), pupillary constriction, respiratory depression (blunted response to hypercarbia), N/V, muscular rigidity with rapid or high dosing (which initiates at the small muscles of the larynx then progresses to the chest wall and skeletal muscles), pruritus, histamine release (seen with morphine and meperidine).

The majority of opioids are metabolized via the liver, though remifentanil is metabolized in the plasma.

4.4. Opioid receptors include the following: mu, delta, kappa, sigma

Mu (μ) receptors are located primarily in the brainstem and medial thalamus. Binding to these lead to supraspinal analgesia, respiratory depression, euphoria, sedation, decreased gastrointestinal motility, and physical dependence.

Delta (δ) receptors are localized largely in the basal ganglia and the neocortical regions of the brain, though their effects are not well studied. It is believed they may be responsible for psychomimetic and dysphoric effects.

Kappa (k) receptors are located in the limbic and other diencephalic areas, the brain stem, and the spinal cord. They primarily induce spinal analgesia, sedation, dyspnea, dependence, dysphoria, and respiratory depression.

Sigma (Σ) receptors have been described as being responsible for dysphoria and hypertonia.

Fentanyl is a commonly used in-office synthetic opioid medication (phenylpiperidine class) that is 100 times more potent than morphine (phenanthrene class). It acts at a variety of receptors within the central nervous system (mu, kappa, delta, and sigma). It produces venodilation, a decrease in heart rate via vagal response, and respiratory depression (dose dependent). It affects respiratory rate more than tidal volume, decreases stress response to surgery, and is metabolized by the liver to be excreted in the urine and bile. Potential side effects include: cough-suppression, constipation, urinary retention, biliary tract spasm, and muscle rigidity. It has an IV onset time of 5+ min, peak effects at 6 min, and duration of approximately 1 h.

Remifentanil is an atypical phenylpiperidine opioid that is metabolized by plasma esterases. It must be delivered as an IV bolus or via continuous infusion. Apnea and hypotension are more common with remifentanil than with other opioids. It has a very rapid onset (due to a small volume of distribution that is 1/10 that of fentanyl) and offset (esterase metabolism) and has a clearance that is more than 2.5 times as rapid as the other opioids'. It has an IV onset time of 1 min, offset time of 5+ min, peak effects at <1 min, and duration of 3–5 min regardless of the duration of infusion, age, or renal and hepatic status. It is supplied as a powder that must be reconstituted.

Meperidine is a pure synthetic opioid that has an active metabolite, normeperidine, which has half the potency but possesses proconvulsant potential. Meperidine has a slight anticholinergic effect, releases histamine, slightly elevates heart rate, and can be effective for controlling postoperative/post-anesthetic shivering, xerostomia, and mydriasis. It is contraindicated for us with monoamine oxidase inhibitors (MAOIs) as both drugs will increase serotonin and can trigger serotonin syndrome (too much serotonin), which consists of cognitive (confusion, agitation, and lethargy), autonomic (hyperadrenergic state), and somatic (myoclonic, twitching, and tremor) symptoms. It has an IV onset time of 5 min and duration of 2–3 h.

4.5. Opioid antagonist

Naloxone is a competitive antagonist of all opioid receptors—it can displace an agonist if the affinity and/or concentration of this antagonist are greater than the affinity and/or concentration of the agonist. The resultant effect is the reversal of the analgesic and ventilatory depressant effects of the opioid. There is a concern about a possible premature termination of the antagonistic effects. If naloxone is used to rescue overdose-induced ventilatory insufficiency, the practitioner must monitor the patient for an additional 1–2 h to ensure against re-sedation. Possible side effects can include flash pulmonary edema (usually in patients with cardiovascular diseases), dysphoria and withdrawal symptoms (in patients who are dependent on opioids for chronic pain relief and where rapid reversal will trigger intense pain), and sympathetic hypertension with possible pulmonary consequences. The usual dosing for adult post-op reversal is 0.1–0.2 mg q2–3 min as needed. Its duration is 30–45 min.

4.6. NMDA receptor antagonist

Ketamine is a phencyclidine derivative. Its pharmacodynamics involves analgesia, anesthesia, and sympathomimetic effects that are mediated by different receptor sites. Non-competitive NMDA (N-methyl-D-aspartate) receptor antagonism is associated with the analgesic effects, opiate receptors may contribute to analgesia and dysphoric reactions, and sympathomimetic properties may result from enhanced central and peripheral monoaminergic transmission. Ketamine blocks dopamine reuptake and therefore elevates synaptic dopamine levels [25]. Inhibition of central and peripheral cholinergic transmission could contribute to induction of the anesthetic state and hallucinations [26]. Ketamine is structurally similar to PCP (phencyclidine), but 10–50 times less potent in blocking NMDA effects. The exact mechanism of action is unclear. Ketamine produces dissociative anesthesia between the thalamocortical and limbic systems; that is, patients do not perceive painful, visual, or auditory stimuli and appear to be

in a cataleptic state. Ketamine is also a direct myocardial depressant. Central sympathomimetics cause a non-dose dependent increase in the heart rate, cardiac output, and blood pressure. It relaxes bronchial smooth muscles but has a minimal effect on the respiratory drive. Ketamine's expected effects are excellent analgesia [27], strong anterograde amnesia, preserved laryngeal reflexes, suppression of convulsive neuronal activities, increased intraocular and intracranial pressures, and increased salivation and lacrimation. Its adverse effects include possible emergence delirium (especially seen with large doses in elderly and pediatric patients, females, and those with underlying personality disorders [28]), dose-related increases in muscle tone, random non-triggered movements, nausea, and vomiting. For common in-office OMFS sedation use, usual dosage (the "low dose IV regimen") is 0.1–0.5 mg/kg which is most often combined with additional benzodiazepines, an opioid, and propofol. Dosages of 1–2 mg/kg IV over 1–2 min or 4 mg/kg IM induce 10–20 min of a dissociative state. Its onset time is very rapid (<1 min), and its duration is 10–15 min. Ketamine is metabolized in the liver and is renally excreted.

4.7. Imidazole derivatives

Etomidate is a GABA agonist that is used for rapid induction of dose-dependent sedation/anesthesia when hypotension cannot be tolerated and cardiovascular stability must be maintained after bolus induction. It has a wide therapeutic index and is the induction agent of choice in patients with severe cardiovascular disease. Induction IV dose is 0.3 mg/kg with maintenance dosing of 5–20 μg/kg/min. It is metabolized by the liver and in plasma and is renally excreted. Possible adrenocortical suppression can be observed, especially when combined with benzodiazepines and opioids. Other potential side effects and precautions include injection pain and phlebitis, hiccups, myoclonic activity on induction, nausea, and vomiting.

4.8. Barbiturates

Barbiturates are both GABAergic and GABAmimetic—they do not require GABA for their intended effects. They are very lipophilic, producing rapid on and offsets but will accumulate in adipose tissue and can lead to a prolonged hangover with high doses.

Intended effects of barbiturates include hypnosis and anticonvulsant properties with no histamine release.

Possible adverse side effects include hyperalgesia in subanesthetic doses (paradoxical excitement), pain on injection (alkaline pH of 11), hypotension (especially with hypovolemia) with compensatory tachycardia, dose-dependent respiratory depression, and excitatory phenomenon such as tremors, twitching, heightened airway reflexes, and laryngospasm.

Methohexital is an ultra-short acting barbiturate that acts by GABA receptor activation and increasing chloride ion channels. It has a rapid onset (1 min) and offset (5–8 min) but does not accumulate in adipose tissue. Expected effects include venodilation, increases in heart rate with stable cardiac output, and central depression of respiratory rate and tidal volume. Methohexital is safe for asthmatics (no histamine release) but does not produce bronchodila-

tion. It is contraindicated in patients with acute intermittent porphyria. Adverse side effects may include nausea/vomiting, laryngospasm, bronchospasm, hiccups, and apnea. It is metabolized by the liver.

4.9. Sedative

Propofol (2, 6 diisopropylphenol) is a short acting ($T_{1/2}\alpha$ 2–8 min, $T_{1/2}\beta$ 4–7 h) hypnotic general anesthetic agent that increases the function of GABA receptors. It is GABAergic and GABA-mimetic and may inhibit the NMDA receptor. It does not provide analgesia or antalgesia but does produce sedation, amnesia, hypnosis, and is a profound antiemetic. There is notable dose-dependent respiratory depression, and it may produce apnea on induction. Propofol also helps relax bronchial smooth muscle and is safe to use with asthmatics (no histamine release). Systolic blood pressure may be reduced 20–40% by blocked sympathetic tone (hypotension without compensatory tachycardia); this effect may be more exaggerated in the medically compromised and elderly patients. Propofol may also reduce the heart rate by 20%. There is a more rapid awakening with propofol and less residual central nervous system side effects with only mild euphoria. There is a low incidence of N/V but patients may experience pain on injection if given in large bolus doses. Propofol is manufactured with no anti-microbial preservatives; therefore, it must be discarded after 6 h once drawn up. As some formulations contain soy or egg products, it may be prudent to use great caution in exposing allergic patients to such solutions. IV sedation infusion dose: 5–50 mcg/kg/min; deep sedation bolus dose: 1 mg/kg IV over 20–30 s, repeat 0.5 mg/kg IV as needed.

4.10. Succinylcholine

Succinylcholine is comprised of two acetylcholine molecules joined together and acts as a depolarizing neuromuscular blocker by binding acetylcholine receptors at the post-synaptic neuromuscular junction end plate. The resultant end plate depolarization initially stimulates muscle contraction; however, because succinylcholine is not degraded by acetylcholinesterase, it remains in the neuromuscular junction to maintain continuous end plate depolarization and subsequent muscle relaxation referred to as a "Phase I Block." Succinylcholine is metabolized by pseudocholinesterase. Its effects may be prolonged in approximately 20% of patients because of atypical or deficient expression of the pseudocholinesterase enzyme. This defect may be diagnosed via the use of the local anesthetic dibucaine, which drastically reduces the action of normal plasma cholinesterase. An atypical patient will not experience the full effects of dibucaine.

Succinylcholine use is a potential etiology behind hyperkalemia and cardiac arrest with expected 0.5–1 mEq/L increases in serum potassium levels following administration. This effect may be exaggerated in patients with neuropathies, denervation injuries, dystrophies, myopathies, strabismus, end-stage renal disease, and burns over a week old as a result of increased acetylcholine receptor expression.

http://dx.doi.org/10.5772/63539

4.11. Volatile anesthetic (VA) agents

With the exception of nitrous oxide (N_2O), inhaled anesthetics do not provide any significant analgesia, though they produce immobility and amnesia. Other than N_2O (which increases skeletal muscle tone), inhaled anesthetics do not affect or, in some cases, decrease skeletal muscle tone. Volatile anesthetic (VA) agents produce immobility via actions on the spinal cord and anesthesia by enhancing inhibitory channels and attenuating excitatory channels. Whether or not this occurs through direct binding or membrane alterations is not known. VAs also depress the cardiovascular system, thereby reducing the mean arterial pressure. Desflurane, isoflurane, and sevoflurane decrease the systemic vascular resistance, which is reflected by a decrease in blood pressure. VAs cause dose-dependent decreases in ventilation. They lead to decreases in tidal volume and compensatory increases in respiratory rate, but a net decrease in min ventilation. A decrease in minute ventilation causes an increase in CO_2.

Ventilation is the most important factor affecting the elimination and dilution of sevoflurane, desflurane, and isoflurane. The time needed for a 50% decrease in sevoflurane, desflurane, or isoflurane is <5 min and essentially independent of case duration. The rate of onset of VAs is indirectly proportional to the blood/gas partition coefficient as a lower coefficient corresponds to rapid equilibration between alveolar gas and capillary blood. The rate is directly proportional to the oil/water partition coefficient as a higher oil/water partition signifies a more rapid uptake through the BBB. All three agents are bronchodilators in general anesthetic doses. However, desflurane and isoflurane are pungent and, upon induction, may precipitate bronchospasm and/or laryngospasm. VAs carry the very serious risk of developing malignant hyperthermia (MH). This risk is decreased with desflurane and sevoflurane (and possibly isoflurane) as compared to halothane, though all potent volatile agents should be avoided in the MH-susceptible patient.

Agent	MAC (potency)	Blood-gas partition coefficient (solubility)
Nitrogen	–	**0.014 (least soluble)**
Desflurane	6.0	0.42
Nitrous oxide	105 (least potent)	0.47
Sevoflurane	2.0	0.65
Isoflurane	1.2	1.4 (most soluble)

MAC: minimum alveolar concentration.

Table 9. Comparison of various common anesthetic agents, potency, and solubility

In general, volatile agents can exist in two phases: gaseous and in solution. The proportion of the agent in its gas phase compared to those dissolved in blood is determined by the blood/gas partition coefficient, which is described using solubility and ambient pressure. If an agent is largely soluble, it resides in solution and exerts no measurable pressure. Pressure—gas tension in an enclosed space—is necessary to drive movement of agents across membranes.

Highly soluble agents are slower in onset and offset, but conversely, they may be held more extensively within the circulating blood. **Table 9** compares various anesthetic gases, their potency, and their solubility.

4.12. MAC

The potency of anesthetic gases are often described using the minimum alveolar concentration (MAC), defined as the concentration of an anesthetic gas administered at 1 atmosphere of ambient pressure required to prevent skeletal muscle movement in response to pain (e.g., surgical skin incision) in 50% of patients. Factors that can increase the MAC include fever, young age, hyperadrenergic states, and chronic alcohol abuse while anemia, old age, hypotension, and other anesthetic agents (such as narcotics, propofol) can lead to its decrease.

4.13. Second gas effect into nitrogen-filled spaces

Nitrogen (N_2) is the least soluble gas and therefore diffuses most rapidly. Nitrous oxide (N_2O) also diffuses rapidly relative to halogenated vapors as the next least soluble gas. When N_2O leaves the alveoli more rapidly than other gases can enter, it creates a gaseous void that shrinks the alveolar volume and increases the concentration (partial pressure) of other gases present, subsequently facilitating their diffusion down the newly amplified concentration gradients. This contributes to the movement of slower moving, more soluble agents, which also creates/enhances a void that theoretically can cause a follow-up "Venturi effect" on other gases. Although N_2 moves more quickly than N_2O because it is less soluble, N_2O is carried in greater concentration in blood; hence, the rate determining step of N_2O moving in more quickly than N_2 moving out is in the blood flow and has little to do with relative solubility differences. N_2O moving in more quickly than N_2 moving out expands compliant nitrogen-filled spaces and pressurizes non-complaint nitrogen-filled spaces.

Nitrous oxide (N_2O) is a GABAergic anesthetic agent that is an NMDA antagonist. It provides analgesia and anxiolysis but can be emetogenic in higher doses. It works in synergy with other volatile anesthetic agents via the second gas effect to lower the MAC. No increased cardiovascular risk has been shown to result from its use; however, increased pressure is noted in non-compliant spaces such as the eyes, middle ears (especially with obstructed Eustachian tubes), and non-draining sinuses. Also noted is increased volume in compliant spaces such as air emboli, pulmonary blebs, bowel distension, and tamponading gas bubbles following retinal surgery. When used in higher elevations/altitudes, the concentration of N_2O must be higher because of less atmospheric pressure needed to drive gas diffusion.

4.14. Anticholinergics

Glycopyrrolate is a quaternary ammonium compound that does not cross the blood-brain barrier (BBB) and causes no sedation. Glycopyrrolate has a delayed onset and possesses more anti-sialagogue effect (its main indication for OMFS in-office use) and less tachycardia than atropine does. Expected effects with glycopyrrolate include tachycardia, bronchodilation, and a reduction in salivary flow. It is metabolized in the liver and renally excreted. Potential side

effects include blurred vision, urinary retention, xerostomia, xerophthalmia, and tachycardia. Dosing for routine use as an anti-sialagogue is 0.1–0.2 mg (0.5–1.0 mL) IV.

Atropine is a tertiary ammonium compound that crosses the BBB. It has a rapid onset but possesses less anti-sialagogue effect and more tachycardia than glycopyrrolate. Expected effects with atropine include tachycardia, bronchodilation, and a smaller reduction in salivary flow. It is metabolized in the liver and renally excreted. Potential side effects include sedation/dysphoria, blurred vision, urinary retention, xerostomia, xerophthalmia, and hyper-vagal responses (tachycardia) with very small doses. Dosing for routine use as an anti-sialagogue is 0.4 mg via IV (1 mL).

4.15. Gastric prokinetics

Metoclopramide is a moderate central dopamine receptor (D_2) antagonist. It increases lower esophageal sphincter tone and upper gastrointestinal forward peristalsis. It is metabolized by the liver and is renally excreted. It must be avoided in patients with Parkinson's disease, and it may cause extrapyramidal reactions. Usual adult dose is 10 mg IV/IM.

4.16. Antiemetics

Patients at increased risk of perioperative/perianesthetic N/V include children, women, the obese, expectant mothers, gastroesophageal reflux disease (GERD) patients, those with a history of motion sickness, gastroparesis, the anxious, and those in acute pain.

Causes of perioperative/perianesthetic N/V include early ambulation, acute pain, unpleasant visual sights, odors, tastes, and physical stimulation of the pharynx. Anesthesia-related causes of N/V include high concentrations of N_2O, opioids, ketamine, gastric insufflation, hypoxia, and hypovolemia. Various surgical stimuli can also account for perioperative N/V. These might include blood in stomach (could be common following oral surgical procedures), throat drape that applies too much pressure on the skin over the larynx, and a Weider tongue retractor placed too deeply or too aggressively.

Treatment of perioperative N/V focuses on the following goals: prevent aspiration, avoid protracted recovery, prevent hypoxia, prevent hypovolemia, achieve meticulous hemostasis, prevent distress to patient, and correction of any possible electrolyte imbalances.

Ondansetron is a serotonin 5-HT3 receptor antagonist used to prevent N/V. It is produced in various forms, both for IV (4 mg) use as well as in oral dissolving tablets (8 mg). It is metabolized in the liver and renally excreted. It has no significant drug interactions and only demonstrates mild side effects such as constipation, dizziness, and headache.

Promethazine is a neuroleptic medication and a first generation histamine H_1 receptor antagonist. It has antiemetic and anticholinergic properties via actions on the Dopamine D_2 receptor. Promethazine can have an additive central nervous system action when combined with antidepressant medications. It is metabolized in the liver and is renally excreted. Possible side effects include excessive sedation, xerostomia, constipation, and rare neuroleptic malignant syndrome. It is recommended to avoid IV push when administering this medication as

extravasation can lead to tissue necrosis. For parenteral use, the IM route in encouraged. Usual dosage is 6.25–25 mg IV, and 12.5–50 mg PO/IM/PR.

Diphenhydramine is a first generation antihistamine and an H_1 receptor antagonist. Antagonism is achieved through inhibiting the effects of histamine more so than its production or release. Diphenhydramine inhibits most smooth muscle vasoconstrictor effects of histamine. This antagonism may also produce anticholinergic effects, antiemetic effects, and significant sedative side effects [29, 30]. Diphenhydramine is metabolized in the liver and renally excreted. Usual adult dosage is 6.25–25 mg IV, and 12.5–50 mg PO/IM/PR.

Dexamethasone is a glucocorticoid and a well-established antiemetic in patients receiving highly emetogenic cancer chemotherapy. Its antiemetic mechanism of action is not well understood. Dexamethasone may antagonize prostaglandin, stimulate the release endorphins that improve mood and a sense of well-being, and stimulate appetite. It is metabolized in the liver and is renally excreted. It may incur interactions with non-steroidal anti-inflammatory medications, and potential side effects include hyperglycemia and euphoria/mania. Usual adult dose is 2–10 mg IM/IV, and 4–10 mg PO.

4.17. Local anesthetics

Local anesthetics (LA) are classified as either esters or amides. Esters include Novocain, procaine, benzocaine, and tetracaine. They are metabolized by plasma pseudocholinesterase. Amides include lidocaine, mepivacaine, and bupivacaine. They are metabolized in the liver by its microsomal enzymes. A commonly used LA, articaine, contains both an amide and an ester link but is classified as an amide.

The mechanism of action of LAs is that once they are injected into tissue, they exist in both ionized and nonionized forms. The nonionized base is able to penetrate many layers of tissue —the lipid nerve sheath and membrane. Re-equilibration between the ionized and nonionized forms occurs once passage is completed. While in the nerve axon, the ionized form is able to block sodium channels, prevent the inflow of sodium, slow the rate of depolarization, and thus preventing an action potential from occurring.

Agent	Lipid solubility	Protein binding	Duration	pKa	Onset time
Mepivacaine	1	75	Medium	7.6	Fast
Lidocaine	4	65	Medium	7.7	Fast
Bupivacaine	28	95	Long	8.1	Moderate

Table 10. Properties of local anesthetics

An ideal LA is one that is very potent, has a quick onset time, and has an appropriate duration of action sufficient to accomplish the procedural goals and then wear off with no permanent adverse effects. Properties often used to compare one LA to another include potency, duration, and onset time (**Table 10**). Potency is determined by lipid solubility. Greater lipid solubility produces a more potent LA (bupivacaine > lidocaine > mepivacaine). Duration is determined

by the protein binding. Greater protein binding creates a longer duration (bupivacaine > mepivacaine > lidocaine). Onset time is determined by pKa. The closer the pKa of a LA is to the pH of tissue (7.4), the more rapid the onset (mepivacaine > lidocaine > bupivacaine). The pKa is the pH at which equal concentrations of ionized and nonionized forms exist.

Anesthetic	pKa	% Conc	Vasoconst	Pulpal (P)/Soft Tissue (ST) duration (min)	Max dose (mg/kg)	Max dose (absolute, mg)
Articaine	7.8	4	Epi 1:100k	P: 60–75 ST: 180–360	7 (adult)	500 (adult)
Bupivacaine	8.1	0.5	Epi 1:200k	P: 90–180 ST: 240–540	1.3 (adult)	90 (adult)
Lidocaine	7.7	2	None	P: 5–10, ST:60–120	4.5 (adult)	300 (adult)
		2	Epi 1:100k	P: 60, ST: 180–300	7.0 (adult)	500 (adult)
Mepivacaine	7.6	2	Levo 1:20k	P: 60, ST: 180–300	6.6	400
		3	None	P: 20–40, ST: 120–180	6.6	400
Prilocaine	7.9	4	None	P: 10–15 (infil), 40–60 (block); ST: 90–120 (infil), 120–240 (block)	6.0	400

Table 11. Comparison of various commonly used local anesthetics

Time	Blood levels of LA	Signs/symptoms
Initial	Minimal to moderate overdose	↑ HR, ↑ BP, ↑ RR Drowsiness, confusion, slurred speech, stuttering, talkative, excited, nystagmus, tinnitus, metallic taste
Progressive	Moderate overdose	Tremors, hallucinations, ↓ BP, ↓ HR, ↓ CO
Late	Moderate to high overdose	Unconsciousness, seizures, ventricular dysrhythmias, respiratory and circulatory arrest

Table 12. Clinical manifestations of local anesthetic toxicity

The most common drugs utilized by OMSs are LAs, so a detailed and intimate knowledge of these agents is essential to ensure a successful practice (**Table 11**). Occasionally, providers do not take into account special patient factors such as age, weight, or medical comorbidities; LA toxicity may result if maximum dosages are exceeded. Clinical manifestations of systemic LA toxicity are varied and may include only the (early) classic sign of circumoral numbness.

However, if left unnoticed, toxicity symptoms may progress and can involve the cardiovascular and central nervous systems (**Table 12**).

Should a toxic reaction or overdose from LA occur, several treatment options exist for the practitioner. One option for treating minimal to moderate LA overdose is to give a reversal agent. OraVerse (phentolamine) is a short-acting alpha blocker. It reverses the vasoconstrictor effect and shortens the LA duration. It is only for use with vasoconstrictor-containing LAs. It is packaged as 1.7 mg in a 1.8 mL cartridge, and the maximum dose is two cartridges. For moderate or high overdose as the symptoms worsen, Intralipid™ 20% IV emulsion can be administered. This drug increases the concentration of serum proteins available for binding the LA. Usual dosing is to administer 1 mL/kg over 1 min and to repeat twice more at 3- to 5-min intervals. Then (or sooner if stability is restored), the practitioner can convert to an infusion at a rate of 0.25 mL/kg/min, continuing until hemodynamic stability is restored. As a last resort, emergency dialysis can be considered.

4.18. Epinephrine

Lidocaine remains the most common local anesthetic medication administered in OMFS and dental offices; therefore, a deeper review of this medication, its properties, and its toxicity is warranted. **Table 13** lists adult dosages for the most common preparations of lidocaine in dental carpules (2% solutions, 1.7 mL total volume/carpule). Most OMSs prefer to use the lidocaine preparation with epinephrine due to its favorable vasoconstrictive properties. A 1:100,000 concentration of epinephrine translates to 0.01 mg/mL or 0.017 mg/carpule. The American Heart Association regards no more than 0.04 mg epinephrine generally as safe for patients with uncontrolled/poorly controlled hypertension or a significant cardiac history. This, however, is based more on anecdotal rather than empiric evidence as injection variables such as the time frame over which the medication is administered or whether the injection was given intravascular become important factors.

Agent	Cartridge size (mg)	Max dose (mg/kg)	Max dose (mg/lb)	Max dose (mg)
2% lidocaine	34	4.5	2	300
2% lidocaine w/1:100k epi	34	7	3.3	500

Maximum dosages are based on an adult weight of 150 lb or 70 kg and taken from the manufacturer (Astra).

Table 13. Adult dosages for lidocaine as commonly used in OMFS practice

Contrary to popular belief, epinephrine will not alter mean arterial pressure as α vasoconstriction is balanced by β dilation. Epinephrine will, however, accelerate heart rate, which will *increase* myocardial oxygen demand secondary to the tachycardia and *decrease* oxygen supply secondary to decreased diastolic fill time and decreased diastolic coronary perfusion time. Since most patients with known coronary artery diseases are stented, the epinephrine-induced tachycardia is only an issue with heart failure and other structural heart diseases. Epinephrine is direct acting and therefore has no interaction with monoamine oxidase inhibitors. It may

http://dx.doi.org/10.5772/63539

increase blood pressure when given to patients taking tricyclic antidepressants, and will increase blood pressure and decrease heart rate when used in patients taking non-selective β blockers.

4.19. Causes and clinical manifestations of local anesthetic (LA) toxicity

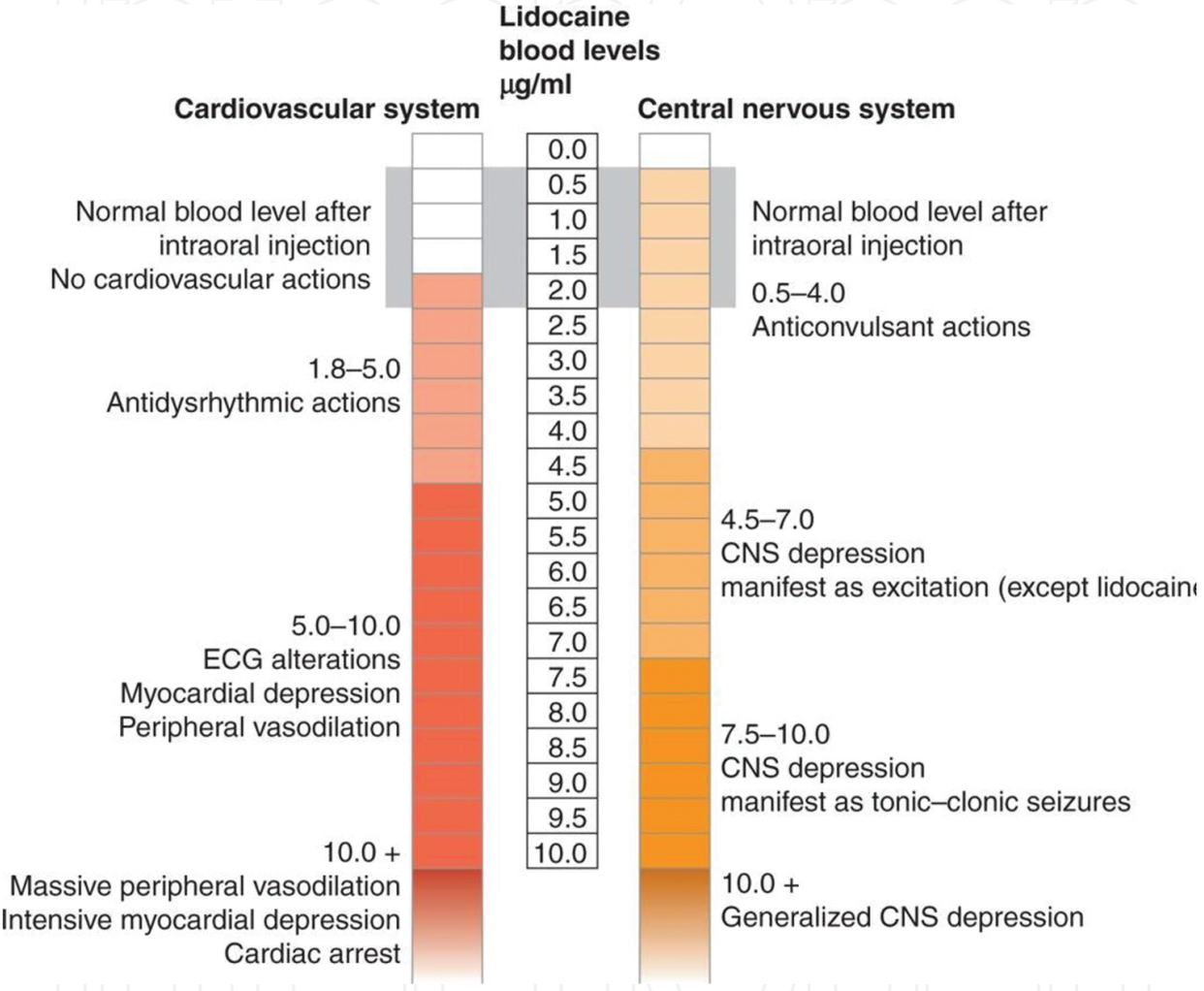

Table 14. Local anesthetic (Lidocaine) blood levels and their actions on cardiovascular and central nervous systems [31].

Elevated plasma levels of the anesthetic could lead to local anesthetic toxicity. This may be caused by an inadvertent intravascular injection or by iatrogenically violating the maximum (mg/kg) dose. Geriatric and pediatric patients are at greatest risks for LA toxicity. Older patients generally metabolize drugs at a slower rate. A geriatric patient who takes multiple medications may experience adverse drug reactions when lidocaine is administered. Cimetidine, a histamine H_2-receptor antagonist, inhibits the hepatic oxidative enzymes (P-450) needed for metabolism, thereby allowing lidocaine to accumulate in the circulating blood. This

adverse reaction is seen only with cimetidine and not with other H_2-receptor antagonists. Propranolol, a beta-adrenergic blocker, can reduce both hepatic blood flow and lidocaine clearance. Toxic reaction could result if high doses of lidocaine are given to patients taking either or both of these medications. A possible additive adverse drug reaction exists with the administration of LAs and opioids in the geriatric and pediatric populations as well. Opioids (fentanyl, meperidine, and morphine) may cause an amide LA additive effect because of their similar chemical structures (both are basic lipophilic amines) and a first-pass pulmonary effect. The lungs may serve as a reservoir for these drugs with a subsequent release back into the system.

4.20. Lidocaine toxicity and cardiovascular effects

Lidocaine has a depressive effect on the myocardium (**Table 14**). Toxic doses of lidocaine cause sinus bradycardia because lidocaine increases the effective refractory period relative to the action potential duration and decreases cardiac automaticity. If a very high dose has been administered, impaired cardiac contractibility, arteriolar dilation, profound hypotension, and circulatory collapse can result [32].

4.21. Lidocaine toxicity and central nervous system (CNS) effects

Lidocaine usually has a sedative effect on the brain (**Table 14**). Initially, lidocaine toxicity depresses brain function in the form of drowsiness and slurred speech. Its effects may progress to unconsciousness and even coma [33].

4.22. Cardiovascular *actions* of lidocaine

Lidocaine is frequently used in the management of various ventricular dysrhythmias, especially ventricular extrasystole (premature ventricular contractions) and ventricular tachycardia. Alterations occur in the myocardium as blood levels of lidocaine increase. In general, the minimal effective blood level of lidocaine for antidysrhythmic activity is 1.8 (μg/mL). In the range from approximately 2–5 (μg/mL), the actions of lidocaine on the myocardium consist only of electrophysiological changes. These include a prolongation or abolition of the slow phase of depolarization during diastole in Purkinje fibers and a shortening of the action potential duration of the effective refractory period. At this therapeutic level, no alterations in myocardial contractility, diastolic volume, intraventricular pressure, or cardiac output are evident. Both the healthy and diseased myocardia tolerate mildly elevated blood levels of lidocaine without deleterious effects. When used to treat dysrhythmias, lidocaine is administered intravenously in a 50–100-mg bolus (1.0–1.5 mg/kg). Overdose is a potential concern, but the generous benefit-to-risk ratio allows for the judicious use of IV lidocaine. Further elevation of the lidocaine blood level (5–10 μg/mL) produces a prolongation of conduction time through various portions of the heart and an increase in the diastolic threshold. This may be noted on the ECG as an increased P-R interval and QRS duration as well as sinus bradycardia. In addition, decreased myocardial contractility, increased diastolic volume, decreased intraventricular pressure, and decreased cardiac output become evident. Peripheral vascular effects observed at this level include vasodilation, which produces a decrease in blood pressure and

occurs as a result of the direct relaxant effect of lidocaine on peripheral vascular smooth muscle. Further increases in blood levels of lidocaine (>10 μg/mL) lead to an accentuation of the electrophysiological and hemodynamic effects such as massive peripheral vasodilation, marked decrease in myocardial contractility, and slowed heart rate, which may ultimately result in cardiac arrest.

4.23. Risk factors for lidocaine toxicity

Older age (>60) and pediatric patients are susceptible to lidocaine overdose and toxicity reactions. Those with decreased body weight, along with patients with medical comorbidities such as congestive heart failure, acute MI, and decreased hepatic function are also at risk. Continued risk includes patients with concomitant use of drugs decreasing P-450 activity (such as cimetidine) that triggers lidocaine accumulation in the blood. Like with other LAs, a possible additive adverse drug reaction exists with administration of lidocaine and opioids in the geriatric and pediatric populations [33].

4.24. Management of mild lidocaine overdose with rapid onset

An overdose in which signs and symptoms develop within 5–10 min following drug administration is considered rapid in onset (**Table 15**). Possible causes include intravascular injection, unusually rapid absorption, or administration of a large total dose. If clinical manifestations do not progress beyond mild central nervous system excitation and consciousness is retained, significant and definitive care is not necessary. The local anesthetic undergoes redistribution and biotransformation, with the blood level falling below the overdose level in a relatively short time.

Method of overdose	Likelihood of occurrence	Onset of signs and symptoms	Intensity of signs and symptoms	Duration	Primary prevention	Drug
Too large of a dose given	Most common	5–30 min	Gradual onset w/ increased intensity; may prove severe	5–30 min	Administer minimal doses	Amides; esters rarely

Table 15. Most common form of local anesthetic overdose

4.25. Toxicity reversal

Increasing evidence suggests that the intravenous (IV) infusion of lipid emulsions can reverse the cardiac and neurologic effects of local-anesthetic toxicity [32]. Although no blinded studies have so far been conducted in humans, studies in animal models and multiple case reports in human patients have shown favorable results. Indeed, case reports support the early use of lipid emulsion at the first sign of arrhythmia, prolonged seizure activity, or rapid progression of toxic manifestations in patients with suspected local anesthetic toxicity. Intralipid™ 20% emulsion IV may be administered at 1 mL/kg over 1 min. This is to be repeated twice more at

3- to 5-min intervals. Then (or sooner if stability is restored), convert to an infusion at a rate of 0.25 mL/kg/min, continuing until hemodynamic stability is restored. This increases the concentration of serum protein available for binding to lidocaine. As a last resort, the practitioner can consider emergency hemodialysis.

4.26. Stable versus unstable/symptomatic bradycardia

Bradycardia is defined as any rhythm disorder with a HR < 60 beats per minute (bpm). Stable bradycardia can be a normal non-emergent rhythm. For instance, well-trained athletes may have a normal HR < 60 bpm. Symptomatic bradycardia is defined as a rate that is <60 bpm that elicits signs (hypotension, congestive heart failure, myocardial infarction, and hypoxia) and symptoms (chest pain, shortness of breath, decreased level of consciousness). Symptomatic bradycardia will usually manifest with HR < 50 bpm.

4.27. Management of unstable/symptomatic bradycardia with pulse (HR < 50 and inadequate for clinical condition) [34]:

Includes following a treatment protocol resembling this algorithm:

- Establish a secure airway
- Obtain intravenous (IV) access
- Administer oxygen
- Monitor blood pressure and rhythm
- Administer atropine 0.5 mg via IV q3–5 min, maximum 3 mg
- Consider transcutaneous pacing, or
- Consider dopamine 2–10 μg/kg/min, or
- Consider epinephrine 2–10 μg/min, or
- Consider isoproterenol 2–10 μg/min

4.28. Anesthetic preparation

Though significant anesthetic complications in the OMFS office are rare, an American Society of Anesthesiology closed claims analysis reported that up to 80% of anesthetic mishaps were attributable to human error [35] Practitioners and their staff may not be fluent in management of these situations unless they routinely practice emergency scenarios and have made regular preparations for such events. Emergency management preparation must consist of the following components: thinking about the emergency (pathophysiology of the event and decision making), doing (taking responsibility), and interacting (communicating to staff and auxiliary personnel and maintaining leadership). This preparation can be enhanced by staging repeated and simulated rehearsals within the OMFS office.

For most OMSs, anesthetic management is routine, but uncertainties and emergencies are bound to arise. The OMFS office must develop, implement, and practice protocols to optimize

patient care and emergency management that balances practicality with the premises of "do no harm" and "always be prepared."

5. Conclusion

Deep sedation and general anesthesia can be safely administered in the OMFS office. Optimization of patient care requires appropriate patient selection, thorough understanding of medical comorbidities and body systems, selection of appropriate anesthetic agents for the individual being treated, utilization of appropriate anesthetic monitoring, and a well-trained office anesthesia team. Achieving a highly trained team requires emergency management preparation that helps foster decision making in intense circumstances, develops leadership, formulates communication strategies, and perfects task management. Furthermore, the privilege and ability to provide patient care under anesthesia is a continuum that extends beyond this initial training. Safe anesthetic care can be provided, but doing so requires effort that entails constant maintenance of current knowledge, preparation, and teamwork.

Author details

Jeffrey A. Elo[1,2*] and Ho-Hyun Sun[3]

*Address all correspondence to: jelo@westernu.edu

1 Division of Oral and Maxillofacial Surgery, Western University of Health Sciences College of Dental Medicine, Pomona, California, USA

2 Department of Oral and Maxillofacial Surgery, Loma Linda University Medical Center, Loma Linda, California, USA

3 Western University of Health Sciences College of Dental Medicine, Pomona, California, USA

References

[1] D'Eramo EM, Bontempi WJ, Howard JB. Anesthesia morbidity and mortality experience among Massachusetts oral and maxillofacial surgeons. J Oral Maxillofac Surg. 2008;66(12):2421–2433.

[2] D'Eramo EM, Bookless SJ, Howard JB. Adverse events with outpatient anesthesia in Massachusetts. J Oral Maxillofac Surg. 2003;61(7):793–800.

[3] Metzner J, Posner KL, Domino KB. The risk and safety of anesthesia at remote locations: the US closed claims analysis. Cur Opin Anaesthesiol. 2009;22:502–508.

[4] Rodgers SF, Rodgers MS. Safety of intravenous sedation administered by the operating oral surgeon: the second 7 years of office practice. J Oral Maxillofac Surg. 2011;69(10): 2525–2529.

[5] Weaver JM. Comparison of morbidity of outpatient general anesthesia administered by the intravenous or inhalation route. J Oral Maxillofac Surg. 1998;56(9):1038–1039.

[6] Braidy HF, Singh P, Ziccardi VB. Safety of deep sedation in an urban oral and maxillofacial surgery training program. J Oral Maxillofac Surg. 2011;69(8):2112–2119.

[7] Hunter MJ, Molinaro AM. Morbidity and mortality with outpatient anesthesia: the experience of a residency training program. J Oral Maxillofac Surg. 1997;55(7):684–687.

[8] Lytle JJ. Morbidity and mortality with outpatient anesthesia: the experience of a residency training program. J Oral Maxillofac Surg. 1997;55(7):687–688.

[9] http://www.aaoms.org/images/uploads/pdfs/parcare_assessment.pdf.

[10] American Society of Anesthesiologists. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures. Anesthesiology. 2011;114:495.

[11] Fleisher LE, Beckman JA, Brown KA, et al. ACC/AHA 2007 Guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing committee to revise the 2002 guidelines on perioperative cardiovascular evaluation for noncardiac surgery). Circulation. 2007;116:1971–1996.

[12] Jetté M, Sidney K, Blümchen G. Metabolic equivalents (METS) in exercise testing, exercise prescription, and evaluation of functional capacity. Clin Cardiol. 1990;13(8): 555–565.

[13] Lee TH, Marcantonio ER, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. Circulation. 1999;100:1043–1049.

[14] Arozullah AM, Conde MV, Lawrence VA. Preoperative evaluation for postoperative pulmonary complications. Med Clin North Am. 2003;87(1):153–173.

[15] Caplan RA, Posner KL, Ward RJ, Cheney FW. Adverse respiratory events in anesthesia: a closed claims analysis. Anesthesiology. 1990;72:828–833.

[16] Lan CK, Rose MW. Perioperative management of obstructive sleep apnea. Sleep Med Clin. 2006;1(4):541–548.

[17] Pawlik MT, Hansen E, Waldhauser D, et al. Clonidine premedication in patients with sleep apnea syndrome: a randomized, double-blind, placebo-controlled study. Anesth Analg. 2005;101(5):1374–1380.

[18] Cheung AH, Wong LM. Surgical infections in patients with chronic renal failure. Infect Dis Clin North Am. 2001;15(3):775–796.

[19] Hoste EA, De Waele JJ. Physiologic consequences of acute renal failure on the critically ill. Crit Care Clin. 2005;21(2):251–260.

[20] Clement S, Braithwaite SS, Magee MF, et al. Management of diabetes and hyperglycemia in hospitals. Diabetes Care. 2004;27:553–591.

[21] Furnary AP, Zerr KJ, Grunkemeier GL, Starr A. Continuous intravenous insulin infusion reduces the incidence of deep sternal wound infection in diabetic patients after cardiac surgical procedures. Ann Thorac Surg. 1999;67(2):352–360.

[22] Furnary AP, Gao G, Grunkemeier GL, et al. Continuous insulin infusion reduces mortality in patients with diabetes undergoing coronary artery bypass grafting. J Thorac Cardiovasc Surg. 2003;125:1007–1021.

[23] Pomposelli JJ, Baxter JK III, Babineau TJ, et al. Early postoperative glucose control predicts nosocomial infection rates in diabetic patients. J Parenter Enteral Nutr. 1998;22:77–81.

[24] Van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in critically ill patients. N Engl J Med. 2001;345:1359–1367.

[25] Adams VHA. The mechanisms of action of ketamine. Anaesthes Reanim. 1998;23(3): 60–63.

[26] Bowdle TA, Radan AD, Cowley DS, Kharasch ED, Strassman RJ, Roy-Byrne PP. Psychedelic effects of ketamine in healthy volunteers: relationship to steady-state plasma concentrations. Anesthesiology. 1998;88(1):82–88.

[27] Clements JA, Nimo WS, Grant IS. Bioavailability, pharmacokinetics and analgesic activity of ketamine in humans. J Pharm Sci. 1982;71(5):539–542.

[28] Adler CM, Goldberg TE, Malhotra AK, Pickar D, Breier A. Effects of ketamine on thought disorder, working memory, and semantic memory in healthy volunteers. Biol Psychiat. 1998;43(11):811–816.

[29] Gengo F, Gabos C, Miller JK. The pharmacodynamics of diphenhydramine-induced drowsiness and changes in mental performances. Clin Pharmacol Ther. 1989;45:15–21.

[30] Gengo FM, Manning C. A review of the effects of antihistamines on mental processes related to automobile driving. J Allergy Clin Immunol. 1990;86:1034–1039.

[31] Malamed SF. Handbook of local anesthesia, 5 ed., St. Louis, Mosby, 2004.

[32] Neal JM, Mulroy MF, Weinberg GL. American Society of Regional Anesthesia and Pain Medicine checklist for managing local anesthetic systemic toxicity: 2012 version. Reg Anesth Pain Med. 2012;37:16–18.

[33] Bursell B, Ratzan RM, Smally AJ. Lidocaine toxicity misinterpreted as a stroke. West J Emerg Med. 2009;10:292–294.

[34] ACLS 2010 Guidelines, Circ. 2010;122(Suppl 3):S729.

[35] Cooper J, Newbower R, Long C, McPeek B. Preventable anesthesia mishaps: a study of human factors. Qual Saf Health Care. 2002;11(3):277–282.