Asthma

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Jeffrey A. Elo and Marissa R. Shams

Introduction

Patients of varying ages with asthma are commonly referred to oral and maxillofacial surgeons (OMSs) for surgical treatment under intravenous sedation/anesthesia. A thorough understanding of the disease process is a prerequisite for the proper management of asthmatic patients. Practitioners may run into trouble if they possess inadequate basic knowledge of the disease process or fail to appreciate the potential for respiratory/airway compromise and bronchospasm in patients with asthma.

Bronchial asthma is a chronic disorder characterized by inflammation and increased responsiveness (hyper-reactivity) of the tracheobronchial tree to diverse stimuli resulting in a varying degree of airway obstruction and constriction. The constriction subsequently causes episodes of wheezing, dyspnea, chest tightness, coughing, and breathlessness. The severity of symptoms can range from mild to life-threatening. The narrowed airways are acutely treated with inhalational bronchodilators and systemic glucocorticoids to resolve inflammation. This often results in improvement within minutes to hours, but occasionally the exacerbation can last for several days.

Asthma is characterized by spasmodic contraction of the smooth muscle of the airways, increased production of an abnormally viscous mucus by bronchial mucous

J. A. Elo (✉)
Division of Oral and Maxillofacial Surgery, College of Dental Medicine, Western University of Health Sciences, Pomona, CA, USA

Department of Oral and Maxillofacial Surgery, Loma Linda University, Loma Linda, CA, USA
e-mail: jelo@westernu.edu

M. R. Shams
Department of Internal Medicine, Division of Pulmonary, Allergy, Critical Care & Sleep Medicine, Emory University School of Medicine, Atlanta, GA, USA
e-mail: Marissa.reiter.shams@emory.edu

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glands and, in severe attacks, by airway obstruction from mucus that has accumulated in the bronchial tree. This results in symptoms of shortness of breath, cough, wheezing, and chest tightness. According to the Centers for Disease Control (CDC), asthma affects approximately 25 million people in the United States, or 7.7% of American adults and 8.4% of American children. Asthma is more common in urban areas and is described as the most common chronic disease of childhood. The World Health Organization (WHO) estimates 235 million people suffer from asthma worldwide. Patients with persistent or uncontrolled asthma are at increased risk of perioperative morbidity and mortality due to the possibility of bronchospasm and hypoxemia. Preoperative identification and optimization of asthmatic patients are critical elements in preventing harm.

Clinical Manifestations

The clinical manifestations of asthma include the classic triad of symptoms: wheezing, cough, and dyspnea. Other signs and symptoms include chest discomfort/tightness and sputum production. The symptoms of asthma are typically chronic with episodic exacerbations. The presence of these symptoms may interfere with school, work, and physical activity due to chronic fatigue, daytime sleepiness, and poor performance. In children, the most common symptom of asthma is a persistent nighttime cough and cough after running, crying, or cold exposure.

Clinically, patients experiencing an acute asthma attack may demonstrate any of the following signs and symptoms:

- Dyspnea
- Tachypnea
- Wheezing
- Hypoxemia
- Tachycardia
- Hypercapnia
- Accessory muscle use with retractions
- Prolonged expiratory phase
- Diaphoresis
- Pulsus paradoxus

Pathophysiology

Asthma is recognized as a heterogeneous disease with several different underlying processes contributing to a patient's symptoms. Identifiable clusters of clinical and pathophysiologic characteristics have allowed asthma to be categorized into the following phenotypes: allergic, non-allergic, eosinophilic, and adult onset. Certain phenotypes may respond better to specific medications or treatment approaches although more research is needed in understanding the utility of asthma phenotypes.

Exposure to a trigger provokes an innate and adaptive inflammatory response within the respiratory tree triggering recruitment of inflammatory cells, airway hyper-responsiveness, and structural abnormalities that contribute to an acute asthma exacerbation. Inflammatory mediators cause spasmodic contraction of the smooth muscle surrounding the bronchi (bronchospasm), swelling and inflammation of the bronchial tubes, and excessive secretion of mucus into the airways. The inflamed, mucus-clogged airways act as a one-way valve resulting in air that can be inspired but not expired. The obstruction of airflow may resolve spontaneously but often requires acute treatment. Clinically, bronchospasm may present as shortness of breath, wheezing, chest tightness, or coughing.

During normal breathing, inhaled air travels through the two primary bronchi that branch into smaller, narrower bronchioles and finally into the terminal bronchial tubes. During an asthma exacerbation, airway smooth muscle surrounding the bronchioles begins to spasm. This results in constriction of the airways, swelling and inflammation of the inner airway space due to fluid buildup and infiltration by immune cells, and excessive secretion of mucus into the airways. Consequently, air is obstructed from circulating freely in the lungs and cannot be expired. Triggers for an exacerbation of asthma may include the following:

- Respiratory irritants (e.g., cologne, smoke, pollution)
- Allergens (e.g., dust mites, pollen, pet dander, latex)
- Infections (e.g., upper respiratory infections, bronchitis, sinusitis)
- Medications (e.g., aspirin and other nonsteroidal anti-inflammatory drugs [NSAIDs] via prostaglandin and leukotriene release; beta (β)-blockers via antagonism of β2 receptors within the bronchial tree; morphine via histamine release)
- Other (e.g., emotional stress, cold air, secretions, exercise)

Diagnostic Studies

Pulmonary function tests (PFTs) are an adjunct to history and physical examination and provide an overall assessment of the patient's respiratory system. The tests include the following:

- Measurements of airflow (spirometry)
- Lung volumes
- Diffusing capacity for inspired carbon monoxide

The tests are reported as a percentage of predicted normal values based on age, height, and ethnicity (Caucasian, African-American, and Asian). The normal FEV_1/FVC (forced expiratory volume in 1 second/forced vital capacity) ratio is 70–80%. In obstructive pulmonary diseases such as asthma, expiratory resistance increases, which results in an decrease in the FEV_1. The FVC may also decrease, but not to the same degree, resulting in a decreased FEV_1/FVC ratio below 70%. Evidence of

Table 5.1 Classification of asthma severity

Severity	Symptom frequency	Nighttime symptoms	% FEV_1 of predicted	SABA use[a]	Interference with activity	Use of oral steroids in the prior 12 months
Intermittent	≤2/week	≤ 2/month	≥ 80%	≤2 days/week	None	0–1
Mild persistent	>2/week	3–4/month	≥ 80%	>2 days/week	Minor	[a]2 or more
Moderate persistent	Daily	>1/week	60–80%	Daily	Some	[a]2 or more
Severe persistent	Continuously	>7/week	< 60%	≥2/day	Extremely limited	[a]2 or more

Adapted from: Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2020. Available from: www.ginasthma.org
FEV_1 forced expiratory volume in 1 second; *SABA* short-acting β-agonist
[a]Not including prevention of exercise-induced bronchospasm

airway obstruction on spirometry, especially if acutely reversible with a bronchodilator, strongly supports the diagnosis of asthma.

Peak flow meters can also be used to monitor asthma and diagnose asthma exacerbations at home by measuring a decline in peak flow with respect to a previously determined baseline.

The traditional approach to the classification of asthma described asthma as e*xtrinsic* or *intrinsic*. Extrinsic asthma occurs as a result of sensitization to a specific antigen. *Intrinsic* asthma occurs without identifiable antigen or prior sensitization. Current guidelines suggest that asthma is better classified as allergic, non-allergic, eosinophilic, and adult onset. Furthermore, asthma can be classified based on the *severity* and *control* (Table 5.1).

The *severity* and *control* when assessed are based on the worst/most severe marker. For example, if a patient has FEV_1 > 80% (intermittent), nighttime symptoms <2× per month (intermittent), reports minor interference with activity (mild persistent) yet is having daily symptoms (moderate persistent), they would be classified as moderate persistent.

The signs and symptoms of *intermittent* as well as *mild*, *moderate*, and *severe persistent* asthma include the following:

Intermittent

- Symptoms are present no more than 2 days per week.
- Nighttime awakenings no more than 2 times per month.
- Short-acting (β_2)-agonist needed less than 2 days per week.
- No limitation of normal activity.
- FEV_1 is normal between exacerbations.
- FEV_1 is greater than 80% of the predicted value.
- FEV_1/FVC ratio is normal.

Mild Persistent

- Symptoms are present more than 2 days per week but not daily.
- Nighttime awakenings 3–4 times per month.
- Short-acting β_2-agonist needed more than 2 days per week but not daily and not more than 1 time on any day.
- Minor limitation of normal activity.
- FEV_1 is greater than 80% of the predicted value.
- FEV_1/FVC ratio is normal.

Moderate Persistent

- Symptoms daily.
- Nighttime awakenings greater than 1 per week but not daily.
- Short-acting β_2-agonist needed daily.
- Some limitation of normal activity.
- FEV_1 is greater than 60% but less than 80% of the predicted value.
- FEV_1/FVC ratio is reduced no more than 5%.

Severe Persistent

- Symptoms are continuous throughout the day.
- Nighttime awakenings – often nightly.
- Short-acting β_2-agonist needed several times daily.
- Extreme limitation of normal activity.
- FEV_1 is less than 60% of the predicted value.
- FEV_1/FVC ratio is reduced more than 5%.

Prevention

When a patient with asthma presents for surgery, determining whether their asthma is well controlled or poorly controlled is an important factor to mitigate the risk of complications. Elective surgery should be postponed until the patient's asthma is well controlled. Taking a good history and performing a focused chest/lung physical examination (auscultation) are requisite in making this determination. Preoperative laboratory studies, chest radiographs, and/or pulmonary function tests have not been shown to correlate with perioperative respiratory adverse events and are rarely recommended.

The Asthma Control Classification provides the opportunity to assess asthma control and hence the significant risk of a perioperative complication in the face of uncontrolled asthma. The following screening tool is ideal to identify poorly controlled asthma:

- In the past 4 weeks, has the patient had:
  - Daytime symptoms more than 2× per week?
  - Any night waking due to asthma?
  - SABA reliever use for symptoms more than 2× per week?
  - Any limitation of activity due to asthma?

- *Well-controlled asthma:* Report "no" to all questions.
- *Partially controlled asthma*: Report "yes" to 1–2 of these questions.
- *Uncontrolled asthma:* Report "yes" to 3–4 of these questions.

Risk factors for the development of perioperative respiratory adverse events in asthmatic patients include the following that are common in an individual with poorly controlled asthma:

- Prior history of sudden severe exacerbations
- Wheezing with exercise
- Wheezing >3 times in the past 12 months
- Nocturnal dry cough
- Recent upper respiratory infection (<2 weeks)
- Hay fever
- Passive/second-hand smoking
- >2 hospitalizations in the past year for asthma-related illness
- >3 emergency room visits for asthma-related illness
- >2 metered-dose inhaler usages of short-acting β_2-agonists in the past month
- Obesity
- Low socioeconomic status
- Illicit drug use
- An $FEV_1 < 1$ L with spirometry

Several important factors should be considered in patients with a history of asthma to help reduce the likelihood of developing an asthmatic attack during an intravenous sedation or general anesthesia. General guidelines include the following:

- Never induce a wheezing patient.
- Defer elective oral and maxillofacial surgical sedation/anesthesia treatment until the patient's asthma is controlled and wheezing is no longer present.
- Recent upper respiratory infection (<2 weeks) and a history of asthma will increase the likelihood of an asthma exacerbation.
- Use a short-acting β_2-agonist inhaler prior to the sedation or general anesthesia.
- Manage possible adrenal suppression if the patient is taking corticosteroids.
- Stress reduction.
- Avoid erythromycin if the patient is using theophylline.
- Avoid histamine-releasing drugs such as morphine.
- Avoid barbiturates due to the increased risk of wheezing.
- Monitor depth of anesthesia as stage 2 is the most excitatory stage where the airway is the most responsive.

- Medications that can reduce the risk of an attack include the following
  - Propofol demonstrates an excellent ability to blunt airway reflex bronchoconstriction but has inferior bronchodilator properties compared to volatile anesthetics.
  - Ketamine is a direct bronchodilator and blunts airway reflex bronchoconstriction, although it may increase secretions which can potentially complicate airway management.
  - Inhalational agents are potent bronchodilators and have been used to treat status asthmaticus.
  - Antihistamine and antiemetic medications.
- Laryngeal mask airways are less likely to precipitate a laryngospasm or bronchospasm than intubation.
- There are no contraindications for the use of nitrous oxide sedation in asthmatic patients, and it may actually be beneficial for managing these patients due to anxiolysis.

Asthmatic patients should continue their usual medication up to and including the day of surgery, with the exception of theophylline, which should be discontinued the evening prior to surgery. Patients with asthma should have their asthma optimized prior to any procedure or sedation/ general anesthesia. Preventive treatment requires a stepwise approach to therapy in which the dose, number of medications, and frequency of administration are increased as necessary. This approach is used to achieve and maintain control. Asthma is a *chronic* inflammatory disorder of the airways with recurrent exacerbations that requires long-term therapy to suppress inflammation. A stepwise approach to the use of medication ensures that patients can be optimized using the most ideal medications (Table 5.2).

Monoclonal Antibody Targets, Route of Administration, and Dosing Frequency

Omalizumab: Anti-IgE, subcutaneous injection every 2–4 weeks
Mepolizumab: Anti-IL-5, subcutaneous injection every 4 weeks
Reslizumab: Anti-IL-5, intravenous infusion every 4 weeks
Benralizumab: IL-5-receptor antagonist, subcutaneous injection every 4 weeks × 3 doses; then every 8 weeks
Dupilumab: Anti-IL-4/13 receptor antagonist, subcutaneous injection every 2 weeks

When performing the initial consultation on a patient with a history of asthma, it is important to ask the following questions:

- Have you been hospitalized or gone to the emergency room in the past 2 years for asthma-related illness?
- Do you use your rescue inhaler daily?
- Do you also use controller medication(s) (ICS, LABA, LTRA, LAMA)?
- What triggers your asthma?
- Has there been any recent modification to your asthma regimen?
- In the past 4 weeks, has the patient had:

Table 5.2 Asthma stepwise therapy

Step 1	Step 2	Step 3	Step 4	Step 5
Rapid-acting β_2-agonists as needed				
Controller options	*Select one*	*Select one*	*Do one or more*	*Add one or many*
	Low-dose ICS	Low-dose ICS + LABA	Medium ICS dose +/− LABA	High-dose ICS + LABA
	LTRA	Medium-/ high-dose ICS	Add LTRA Add LAMA	Add LTRA Add LAMA Monoclonal biologic therapy[a] Add oral steroids (at lowest possible dose)
		Low-dose ICS + LTRA		

Adapted from: Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2020. Available from: www.ginasthma.org

ICS inhaled corticosteroid, *LTRA* leukotriene receptor antagonist, *LABA* long-acting inhaled β_2-agonist, *LAMA* long-acting anti-muscarinic

[a]Biologic medications are injectable or intravenous monoclonal antibodies targeting a specific axis in asthma either IgE, IL-5, IL-5 receptor or IL-4/IL-13 receptor based on asthma phenotype (allergic, eosinophilic). Available agents include omalizumab (Xolair®, Genentech Novartis Pharmaceuticals, NJ, USA), mepolizumab (Nucala®, GlaxoSmithKline, London, UK), reslizumab (Cinqair®, Teva Pharmaceuticals, NJ, USA), benralizumab (Fasenra®, AstraZeneca Pharmaceuticals, Maryland, USA), and dupilumab (Dupixent®, Sanofi-Aventis, Paris, France). Please note that this is a growing field with many new agents due to come to market in coming years

- Daytime symptoms more than 2× per week?
- Any night waking due to asthma?
- SABA reliever use for symptoms more than 2× per week?
- Any limitation of activity due to asthma?

Physical examination of a patient with asthma is generally normal if performed when the patient does not have an acute exacerbation. Abnormal findings in the absence of an acute exacerbation may suggest severe disease, suboptimal control, or associated atopic conditions. It remains important to maintain the patient's usual asthma medications immediately prior to the sedation or general anesthesia. Preoperative chest auscultation is important to identify any wheezing or decreased breath sounds that signify an asthma exacerbation. It is also important to obtain the preoperative oxygen saturation.

Preoperative consultation with the patient's physician is important when indicated, as is the delay of surgery in those cases with active disease present as suggested by dyspnea, wheezing, and coughing. Asthmatic patients should bring their rescue and maintenance inhalers with them to their procedural appointment.

Intraoperatively, the anesthetic team should tailor and execute an anesthetic that aims to avoid bronchospasm during sedation and recovery. Narcotics should be used cautiously, as they potentially create respiratory depression-something undesirable in patients with compromising pulmonary disease. Bronchospasm may result from poor control of the airway, irrigating fluid, and blood or saliva present during the procedure. Postoperatively, patients should be monitored closely and then should return to their pre-anesthetic asthma medication regimen as soon as possible.

Recognition

In general, induction of deep sedation/general anesthesia, manipulation of the airway, and emergence from anesthesia represent the most critical times for the development of potential airway complications. Prompt recognition of a patient experiencing a respiratory adverse event is paramount to successful treatment and a good outcome. Bronchospasm should be differentiated from laryngospasm or foreign body aspiration. Bronchospasm is challenging to identify, although a decline or loss of effective respiration can be immediately identified using a precordial stethoscope and capnography. Pulse oximetry will only identify the resultant hypoxemia after several minutes and should not be relied upon as the trigger to intervene. Specific indicators that bronchospasm is present include the following:

- Pre-cordial stethoscope auscultation reveals expiratory wheezing.
- Auscultation of the chest reveals decreased breath sounds and bilateral expiratory wheezing.
- Prolongation of the expiratory phase of ventilation occurs resulting in "shark-finning" on the capnograph and an increase in end-tidal CO_2 (Fig. 5.1).
- Increasing airway pressures during PPV.

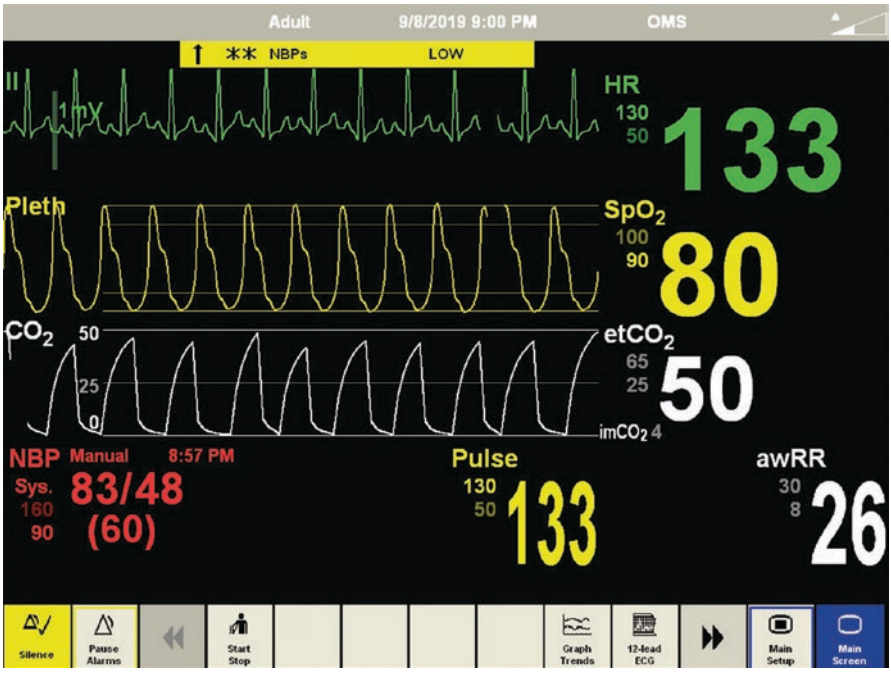

Fig. 5.1 Vital signs monitor demonstrating sinus tachycardia, hypoxemia, hypotension, and "shark-finning" of the capnograph

Management

Place the patient in a somewhat upright sitting position and remove all unnecessary materials from the mouth while employing good suction. Attempts should be made to improve the airway by head tilt, chin lift, jaw thrust, and tongue protraction. Administer 100% oxygen via face mask. Prepare medications for delivery.

Inhaled short-acting β_2-agonist drugs are first-line treatment for intraoperative bronchospasm if the patient is awake or intubated, and the exacerbation relatively mild. Patients who are awake and cooperative may benefit from the use of a metered dose inhaler (MDI) to deliver 6 to 8 puffs of an inhaled β_2-agonist such as albuterol (90 mcg per puff) or levalbuterol (45 mcg per puff). Most office-based deep sedations render the patient unable to cooperate with the use of metered dose inhalers for the delivery of the β_2-agonist. In this situation, consider a nebulized short-acting β_2-agonist (e.g., albuterol 2.5 mg in 2 mL NS) and an anticholinergic (e.g., ipratropium 0.5 mg in 1 mL normal saline) if the exacerbation is mild to moderate and respiration spontaneous. The alternative to a short-acting β_2-agonist is epinephrine. Intramuscular and intravenous modes of administration are considered satisfactory routes to administer epinephrine. Dosing regimens that may be considered include the following:

- *Intramuscular* administration of 0.3 mg (0.3 mL) of 1:1000 epinephrine is generally appropriate for adults (every 5–15 min as needed). (The 1:1000 concentration is available as a 1 mL vial containing 1 mg of epinephrine).
- *Intravenous* administration requires the use of 1:10,000 epinephrine. A slow IV injection of 0.1–0.3 mg epinephrine (1.0–3.0 mL) should be followed with a NS flush or continuous IV fluids. The 1:10,000 concentration is available as a 10 mL injector containing 1 mg of epinephrine. The 1:10,000 concentration can also be reconstituted by drawing up in a 10 mL syringe the 1 mL vial containing 1 mg of epinephrine as well as 9 mL of NS.

Epinephrine is a potent α_1-, β_1-, and β_2-agonist. Therefore, it also has the potential to cause cardiomyopathy, transient left ventricular dysfunction, myocardial ischemia, myocardial infarction, and cardiac arrhythmias. This is more of a concern with overdosing and the intravenous route. The use of epinephrine auto injectors may also be considered in the management of an asthma exacerbation. Most adult and pediatric auto injectors deliver 0.3 mg and 0.15 mg epinephrine, respectively. These devices are for intramuscular injection, but the ability to do so depends on the needle length which, if short, will result in subcutaneous injection and a delayed peak plasma concentration.

Therapy may also include parenteral steroids, such as methylprednisolone (50–250 mg over 4–6 hours). The use of ketamine IV at 1 mg/kg may also be considered as this will result in increased bronchodilation. However, the use of ketamine during an asthma exacerbation in a patient under deep sedation or general anesthesia is not supported by literature. Deepening the anesthesia with propofol

1.0–1.5 mg/kg will also result in bronchodilation, but it will produce a deeper anesthetic that requires proper airway management, likely PPV, or intubation and is not recommended.

Suggested Reading

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