# THE CHEST

# Essentials of Pulmonology 13

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RESPIRATORY PROBLEMS ARE COMMON in children. The anesthesiologist often encounters pulmonary complications ranging from mild acute respiratory tract infections to chronic lung disease with end-stage respiratory failure during perioperative consultations, intraoperatively, or in the intensive care unit. This chapter discusses the basics of respiratory physiology, how to assess pulmonary function, and the practical anesthetic management of specific pulmonary problems. Airway and thoracic aspects pertinent to ventilation are discussed in Chapters 14 and 15; pulmonary issues specific to neonates, intensive care, and various disease states are addressed in the relevant chapters.

## Respiratory Physiology

The morphologic development of the lung begins at several weeks after conception and continues into the first decade of postnatal life.[1] Intrauterine gas exchange occurs via the placenta, but the respiratory system develops in preparation for extrauterine life, when gas exchange transfers abruptly to the lungs at birth.

Development of the lung, which begins as an outgrowth of the foregut ventral wall, can be divided into several stages (Fig. 13.1). During the embryonic period, in the first few weeks after conception, lung buds form as a projection of the endodermal tissue into the mesenchyme. The pseudoglandular period extends to the 17th week of life, during which rapid lung growth is accompanied by formation of the bronchi and branching of the airways down to the terminal bronchioli. Further development of bronchioli and vascularization of the airways occurs during the canalicular stage of the second trimester. The saccular stage begins at approximately 24 weeks, when terminal air sacs begin to form. The capillary networks surrounding these air spaces proliferate, allowing sufficient pulmonary gas exchange for extrauterine survival of the premature neonate by 26 to 28 weeks. Formation of alveoli

occurs by lengthening of the saccules and thinning of the saccular walls and has begun by the 36th week after conception in most human fetuses. The vast majority of alveolar formation occurs after birth, typically continuing until 8 to 10 years postnatally. At birth, the neonatal lung usually contains 10 to 20 million terminal air sacs (many of which are saccules rather than alveoli), one-tenth the number in the mature adult lung. After birth, growth of the lungs occurs primarily as an increase in the number of respiratory bronchioles and alveoli rather than an increase in the size of the alveoli.

The abrupt transition to extrauterine gas exchange at birth involves the rapid expansion of the lungs, increased pulmonary blood flow, and initiation of a regular respiratory rhythm. The development of a respiratory rhythm, detectable initially by intermittent rhythmic fetal thoracic movements, begins well before birth and may be necessary for normal anatomic and physiologic lung development. Interruption of umbilical blood flow at birth initiates continuous rhythmic breathing. Amniotic fluid is expelled from the lungs via the upper airways with the first few breaths, with residual fluid draining through the lymphatic and pulmonary channels in the first days of life. Changes in the partial pressures of oxygen ($PO_2$) and carbon dioxide ($PCO_2$) and in hydrogen ion concentration (pH) cause an acute decrease in pulmonary vascular resistance and a consequent increase in pulmonary blood flow. Increased left atrial and decreased right atrial pressures reverse the pressure gradient across the foramen ovale, causing functional closure of this left-to-right one-way flap valve. Ventilatory rhythm is augmented and maintained in part by the increased arterial oxygen relative to the prior intrauterine levels.

Breathing is controlled by a complex interaction involving input from sensors, integration by a central control system, and output to effector muscles.[2] Afferent signaling is provided by peripheral arterial and central brainstem chemoreceptors, upper
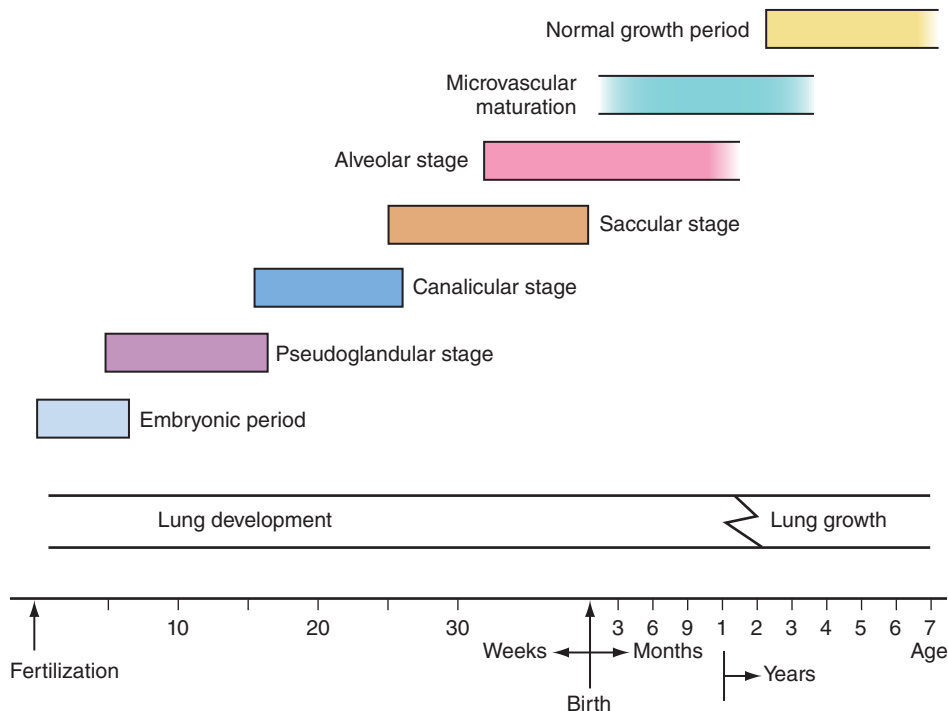
**FIGURE 13.1** Timetable for lung development. (Modified with permission from Guttentag S, Ballard PL. Lung development: embryology, growth, maturation, and developmental biology. In: Tausch HW, Ballard RA, Gleason CA, eds. *Avery's Diseases of the Newborn.* 8th ed. Philadelphia: WB Saunders; 2004:602.)

airway and intrapulmonary receptors, and chest wall and muscle mechanoreceptors.

The peripheral arterial chemoreceptors consist of the carotid and aortic bodies, with the carotid bodies playing the greater role in arterial chemical sensing of both arterial $O_2$ tension ($Pao_2$) and pH. The central chemoreceptors, responsive to arterial $CO_2$ tension ($PaCO_2$) and pH, are thought to be located at or near the ventral surface of the medulla.

The nose, pharynx, and larynx have a wide variety of pressure, chemical, temperature, and flow receptors that can cause apnea, coughing, or changes in ventilatory pattern. Pulmonary receptors lie in the airways and lung parenchyma. The airway receptors are subdivided into the slowly adapting receptors, also called pulmonary stretch receptors, and the rapidly adapting receptors. The stretch receptors, found in the airway smooth muscle, are thought to be involved in the balance of inspiration and expiration. These receptors may be the sensors in the Hering-Breuer reflexes, which prevent overdistention or collapse of the lung. The rapidly adapting receptors lie between the airway epithelial cells and are triggered by noxious stimuli such as smoke, dust, and histamine. Parenchymal receptors, also known as juxtacapillary receptors, are located adjacent to the alveolar blood vessels; they respond to hyperinflation of the lungs, to various chemical stimuli in the pulmonary circulation, and possibly to interstitial congestion. Chest wall receptors include mechanoreceptors and joint proprioceptors. Mechanoreceptors in the muscle spindle endings and tendons of respiratory muscles sense changes in length, tension, and movement.

Central integration of respiration is maintained by the brainstem (involuntary) and by cortical (voluntary) centers. Although the precise mechanism of the neural ventilatory rhythmogenesis is unknown, the pre-Bötzinger complex and the retrotrapezoid nucleus/parafacial respiratory group, neural circuits in the ven-trolateral medulla, are thought to be the respiratory rhythm genera-tors.[3] These neuron groups fire in an oscillating pattern, an inherent rhythm that is moderated by inputs from other respiratory centers. Involuntary integration of sensory input occurs in various respira-tory nuclei and neural complexes in the pons and medulla that modify the baseline pacemaker firing of the respiratory rhythm generators. The cerebral cortex also affects breathing rhythm and influences or overrides involuntary rhythm generation in response to conscious or subconscious activity, such as emotion, arousal, pain, speech, breath-holding, and other activities.[2]

The effectors of ventilation include the neural efferent pathways, the muscles of respiration, the bones and cartilage of the chest wall and airway, and elastic connective tissue. Upper airway patency is maintained by connective tissue and by sustained and cyclic contractions of the pharyngeal dilator muscles. The diaphragm produces the majority of tidal volume during quiet inspiration, with the intercostal, abdominal, and accessory muscles (sterno-cleidomastoid and neck muscles) providing additional negative pressure. The elastic recoil of the lungs and thorax produces expiration. Inspiration is an active and expiration a passive action in normal lungs during quiet breathing. During vigorous breathing or with airway obstruction, both inspiration and expiration become active processes.

Another effect of age is a change in chest wall compliance. In adults the end-expiratory volume is equivalent to the functional residual capacity (FRC). In infants the chest wall is more compliant, so the tendency of the lung to collapse is not adequately counterbal-anced by chest wall rigidity. Infants stop expiration at a lung volume greater than FRC, with the inspiratory muscles braking expiration. When this braking mechanism is impaired, as occurs with general anesthesia, the infant has a tendency to develop atelectasis.

## Preoperative Assessment

The preoperative assessment of the respiratory system in a child is based on the history, physical examination, and evaluation of vital signs. Because ventilation is a complex process involving many systems besides the lung, the pulmonary appraisal must also include an assessment of airway, musculoskeletal, and neurologic pathology that might affect gas exchange under anesthesia or in the postoperative period. The potential impacts of esophageal reflux and cardiac, hepatic, renal, or hematologic disease on gas exchange and pulmonary function should be considered. Further investigations, such as laboratory, radiographic, and pulmonary function studies, may be indicated if there is doubt as to the diagnosis or severity of the pulmonary disease.

Because children may be unwilling or unable to give a reliable history, parents or caregivers are often the sole source or an important supplemental source of information during initial evaluation. Risk factors in the history that are associated with an increased risk of perioperative events include a respiratory tract infection within the preceding 2 weeks, wheezing during exercise, more than three wheezing episodes in the past 12 months, nocturnal dry cough, eczema, and a family history of asthma, rhinitis, eczema, or exposure to tobacco smoke.[1,4] Viral upper respiratory tract infections (URIs) are common in children, and the time, frequency, and severity of infection should be established. If wheezing is present, the precipitating causes, frequency, severity, and relieving factors should be determined. Chronic pulmonary diseases often have a variable clinical course, and the details of acute exacerbations of chronic problems should be elicited.

In younger children the gestational age at birth, the current postmenstrual age, neonatal respiratory difficulties, and prolonged intubation in the neonatal period are particularly important to ascertain. Apneic episodes, subglottic stenosis, and tracheomalacia are possible complications of prematurity and prolonged intubation that may be exacerbated in the perioperative period. Whereas congenital lesions often manifest at birth, symptoms of airway collapse or stenosis may become evident only later in life.

Physical examination begins when you enter the room. Particularly with young children, your best opportunity to observe them before they react to your presence is from across the room, and inspection from a distance can provide useful information. The respiratory rate is a sensitive marker of pulmonary problems, and scrutiny of the rate before a young child becomes agitated and hyperventilates is an important metric. Pulse oximetry is a useful baseline indicator of oxygenation. Nasal flaring, intercostal retractions, and the marked use of accessory respiratory muscles are all signs of respiratory distress. General appearance is also important. Apathy, anxiety, agitation, or persistent adoption of a fixed posture may indicate profound respiratory or airway difficulties, and intense cyanosis can also be detected from a distance. Weight may relate to pulmonary function; children with chronic severe pulmonary disease are often underweight owing to retarded growth or malnourishment, whereas severe obesity can produce airway obstruction and sleep apnea. Inspection of the chest contour may reveal hyperinflation or thoracic wall deformities.

Closer physical examination adds further information. Atopy and eczema may be associated with hyperreactive airways. Auscultation may reveal wheezes, rales, fine or coarse crepitus, transmitted breath sounds from the upper airway, altered breath sounds, or cardiac murmurs. Chest percussion can provide an estimate of the position of the diaphragm and serve as a useful marker of hyperinflation. Patience, a gentle approach, and warm hands improve diagnostic yield and patient satisfaction.

## Pulmonary Function Tests

Further pulmonary investigations include chest imaging, measurement of hematocrit, arterial blood gas analysis, pulmonary function tests, and sleep studies. Special investigations are not routinely indicated preoperatively and should be reserved for cases in which the diagnosis is unclear, the progression or treatment of a disease needs to be established, or the severity of impairment is not evident. In most cases a comprehensive history and careful physical examination are adequate to establish an appropriate anesthetic plan. Before requesting a new investigation, the clinician should have a clear idea of the question the test is expected to answer and how the answer will modify anesthetic management and outcome. Many tests are difficult to perform in children who have short attention spans and who cannot sit still for any length of time. Judgment must be exercised when ordering these tests for young children, and due consideration must be given to the child's age and level of maturity and the influence of the parents.

Pulmonary function tests include dynamic studies, measurement of static lung volumes, and diffusing capacity. Pulmonary function tests enable clinicians to (1) establish mechanical dysfunction in children with respiratory symptoms, (2) quantify the degree of dysfunction, and (3) define the nature of the dysfunction as obstructive, restrictive, or mixed obstructive and restrictive.[5] Table 13.1 presents common indications for pulmonary function testing in children.

The dynamic studies, which are the most commonly used tests, include spirometry, flow–volume loops, and measurement of peak expiratory flow. Spirometry measures the volume of air inspired and expired as a function of time and is by far the most

| TABLE 13.1 | Uses of Pulmonary Function Studies in Children |
|---|---|
| • | To establish pulmonary mechanical abnormality in children with respiratory symptoms |
| • | To quantify the degree of dysfunction |
| • | To define the nature of pulmonary dysfunction (obstructive, restrictive, or mixed obstructive and restrictive) |
| • | To aid in defining the site of airway obstruction as central or peripheral |
| • | To differentiate fixed from variable and intrathoracic from extrathoracic central airway obstruction |
| • | To follow the course of pulmonary disease processes |
| • | To assess the effect of therapeutic interventions and guide changes in therapy |
| • | To detect increased airway reactivity |
| • | To evaluate the risk of diagnostic and therapeutic procedures |
| • | To monitor for pulmonary side effects of chemotherapy or radiation therapy |
| • | To aid in predicting the prognosis and quantitating pulmonary disability |
| • | To investigate the effect of acute and chronic disease processes on lung growth |

Modified with permission from Castile R. Pulmonary function testing in children. In: Chernick V, Boat TF, Wilmott RW, Bush A, eds. *Kendig's Disorders of the Respiratory Tract in Children*. 7th ed. Philadelphia: Elsevier Saunders; 2006:168. Reproduced from National Asthma Education and Prevention Program. Full report of the expert panel: guidelines for the diagnosis and management of asthma (EPR-3). Bethesda, MD: National Heart, Lung, and Blood Institute, National Institutes of Health; 2007.

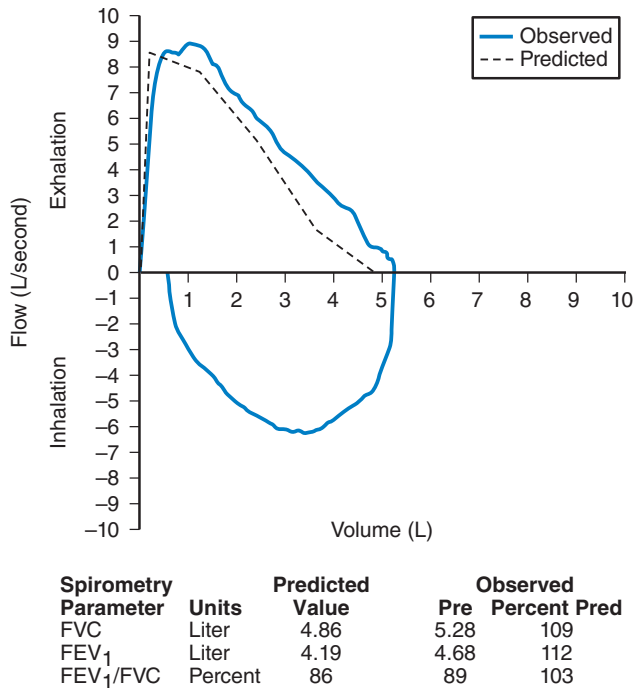| Spirometry Parameter | Units | Predicted Value | Pre | Observed Percent Pred |
|---|---|---|---|---|
| FVC | Liter | 4.86 | 5.28 | 109 |
| FEV$_1$ | Liter | 4.19 | 4.68 | 112 |
| FEV$_1$/FVC | Percent | 86 | 89 | 103 |

FIGURE 13.2 Normal pulmonary function test. The normal flow–volume curve obtained during forced expiration rapidly ascends to the peak expiratory flow (highest point on curve), then descends with decreasing volume, following a reproducible shape that is independent of effort. In this normal flow–volume curve, the forced vital capacity (FVC), forced expiratory volume in 1 second (FEV$_1$), and FEV$_1$/FVC ratio are all within the normal range for this child's age, height, gender, and race. The shapes of both the inspiratory and expiratory limbs are normal as well. *Pre,* prebronchodilator; *Pred,* predicted value.

| TABLE 13.2 | Characteristics of Obstructive and Restrictive Patterns of Lung Disease | |
|---|---|---|
| | **DISEASE CATEGORY** | |
| **Measurement** | **Obstructive** | **Restrictive** |
| FVC | Normal/decreased | Decreased |
| FEV$_1$ | Decreased | Decreased |
| FEV/FVC | Decreased | Normal |

*FEV$_1$,* forced expiratory volume in 1 second; *FVC,* forced vital capacity.

frequently performed test of pulmonary function in children. With a forced exhalation after a maximal inhalation, the total volume exhaled is known as the forced vital capacity (FVC), and the fractional volume exhaled in the first second is known as the forced expiratory volume in 1 second (FEV$_1$). Fig. 13.2 illustrates a normal pulmonary function test (normal flow–volume loop and spirometry parameters).

An obstructive process is characterized by decreased velocity of airflow through the airways (Fig. 13.3), whereas a restrictive defect produces decreased lung volumes (Fig. 13.4). Examination of the ratio of airflow to lung volume assists in differentiating these components of lung disease. Normally, a child should be able to exhale more than 80% of the FVC in the first second. Children with obstructive lung disease have decreased airflow in relation to exhaled volume. If the volume exhaled in the first second divided by the volume of full exhalation (FEV$_1$/FVC) is less than 80%, then airway obstruction is present (Table 13.2; Fig. 13.3).

The FEV$_1$ needs to be interpreted in the context of the FVC. A small FEV$_1$ alone is insufficient evidence on which to make a diagnosis of airflow obstruction. Those with restrictive lung disease have both decreased FEV$_1$ and FVC–decreased flow rate and reduced total exhaled volume. Restrictive lung disease is associated with a loss of lung tissue or a decrease in the lung's ability to expand. A restrictive defect is diagnosed when the FVC is less than 80% of normal with either a normal or an increased FEV$_1$/FVC (see Table 13.2 and Fig. 13.4).

Most children with respiratory problems have an obstructive pattern; isolated restrictive diseases are far less common. Asthma

is the most common obstructive pulmonary disease in children. Rare causes of obstruction include airway lesions, congenital subglottic webs, and vocal cord dysfunction. Restrictive lung disease can arise from limitations to chest wall movement, such as chest wall deformities, scoliosis, or pleural effusions, or from space-occupying intrathoracic pathology such as large bullae or congenital cysts. Alveolar filling defects (e.g., lobar pneumonia) also reduce lung volume and can be considered as restrictive processes. Although the diseases arise from specific isolated genetic disorders, children with cystic fibrosis (CF) and sickle cell disease (SCD) can have highly variable pulmonary pathologic processes with both obstructive and restrictive components of lung disease. Bronchopulmonary dysplasia may also result in both obstructive and restrictive pathology.

Pulmonary function tests can also be used to differentiate fixed from variable airway obstruction and to localize the obstruction as above or below the thoracic inlet (Figs. 13.5 through 13.7, E-Fig. 13.1). This information can be gleaned from distinctive changes in the configuration of the flow–volume loop, a graphic representation of inspiratory and expiratory flow volumes plotted against time. A fixed central airway obstruction, such as a tumor or stenosis, may obstruct both inspiration and expiration, flattening the flow–volume curve on both inspiration and expiration (see Video 14.1). The child with tracheal stenosis, for example, has flattening of both inhalation and exhalation curves (see Fig. 13.6). A variable obstruction tends to affect only one part of the ventilatory cycle. On inhalation, the chest expands and draws the airways open. On exhalation, as the chest collapses, the intrathoracic airways collapse. Variable extrathoracic lesions tend to obstruct on inhalation more than exhalation, whereas variable intrathoracic lesions tend to obstruct more on exhalation. This produces the characteristic flow–volume patterns.

In addition to diagnostic uses, spirometry is used to assess the indication for, and efficacy of, treatment. For example, the obstruction in patients with asthma is usually reversible, either gradually over time without intervention or much more rapidly after treatment with a short-acting bronchodilator. An improvement in FEV$_1$ of 12% and 200 mL in adults or approximately 3 mL/kg is considered a positive response. In addition to confirming the diagnosis of asthma, the degree of airflow obstruction, as indicated by the FEV$_1$, is one measure of asthma control. A low FEV$_1$ or an acute decrease from baseline may indicate a child whose asthma is not under good control and therefore who potentially is at greater risk for a perioperative exacerbation (see Fig. 13.3).

Because it measures the amount of air entering or leaving the lung rather than the amount of air in the lung, spirometry cannot provide data about absolute lung volumes. Information about FRC and lung volumes calculated from FRC, such as total lung capacity and residual volume, must be obtained by different means, such as gas dilution or body plethysmography. Gas dilution is based

**E-FIGURE 13.1** A magnetic resonance angiogram accompanies the flow loop in Fig. 13.7, demonstrating anomalous aortic anatomy compressing the trachea. (Courtesy Brian O'Sullivan, MD.)
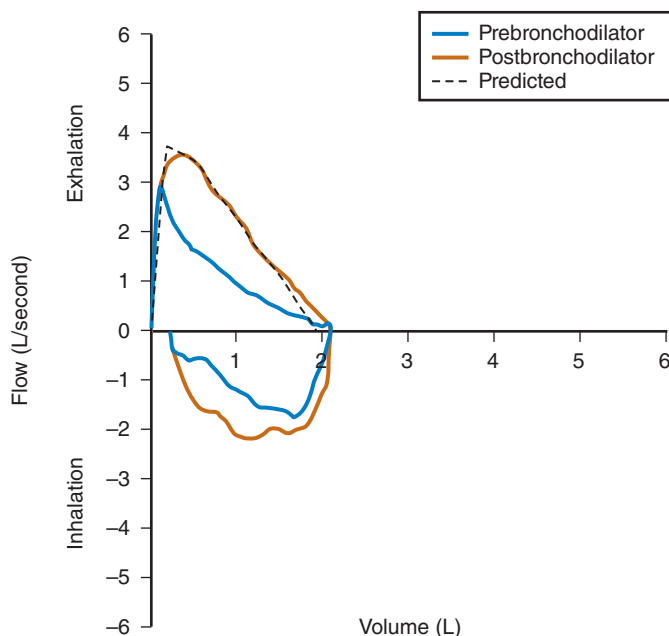
| Spirometry Parameter | Units | Predicted Value | Pre | Observed Percent Pred | Post | Observed Percent Pred | Percent Change |
|---|---|---|---|---|---|---|---|
| FVC | Liter | 1.94 | 2.15 | 111 | 2.14 | 110 | 0 |
| $FEV_1$ | Liter | 1.71 | 1.30 | 76 | 1.82 | 106 | 40 |
| $FEV_1$/FVC | Percent | 90 | 60 | 67 | 85 | 94 | 42 |

**FIGURE 13.3** This flow–volume curve demonstrates a reversible obstructive defect. The forced expiratory volume in 1 second ($FEV_1$) as a percentage of forced vital capacity (FVC), or total volume exhaled, is decreased in patients with airway obstruction. The observed curve shape before bronchodilator use *(blue curve)* is scooped. After administration of a short-acting bronchodilator, the observed curve shape *(brown)* appears normal, and there is an increase in both $FEV_1$/FVC and $FEV_1$. This child has asthma and demonstrates a marked (40%) increase in $FEV_1$ after treatment with a short-acting bronchodilator. Reversible airflow obstruction is one of the hallmarks of asthma. *Post,* postbronchodilator; *Pre,* prebronchodilator; *Pred,* predicted value.

on measuring the dilution of nitrogen or helium in a circuit in closed connection to the lungs, whereas body plethysmography calculates lung gas volumes based on changes in thoracic pressures.

## Perioperative Etiology and Epidemiology

Respiratory problems account for most of the perioperative morbidity in children[6,7] and cause almost one-third of perioperative pediatric cardiac arrests.[8] Adverse events include laryngospasm, airway obstruction, bronchospasm, hemoglobin oxygen desaturation, prolonged coughing, atelectasis, pneumonia, and respiratory failure.[4,9-11] The incidence of perioperative adverse respiratory events in one study of 755 children was 34%,[9] whereas in another observational study of 9297 children it was 15%.[4] The triggers of these problems included airway manipulation, alteration of airway reflexes by anesthetic drugs, surgical insult, and depression of breathing caused by anesthetic and analgesic medications. Various pulmonary diseases common among children can further affect the frequency of perioperative respiratory complications; one retrospective study identified obesity as an additional risk factor.[11]

Studies have consistently reported greater respiratory morbidity among younger compared with older children.[4,6,7,11-14] In particular, neonates are sensitive to respiratory problems for many reasons. Although the FRC approaches adult capacity (in liters per kilogram) within days after birth, a persistently large closing capacity increases

the likelihood of alveolar collapse and intrapulmonary shunt. Residual patency of the ductus arteriosus can also contribute to shunting. The greater metabolic rate of the infant increases oxygen requirements and decreases the time to arterial desaturation after an interruption to ventilation and gas exchange. The work of breathing is also greater in young infants as a result of high-resistance, small-caliber airways, increased chest wall compliance, and reduced lung parenchymal compliance.

### UPPER RESPIRATORY TRACT INFECTION

Upper respiratory tract infections (URIs) are a common problem among young children. Children are typically infected several times a year, possibly even more frequently if they are in day care. Viruses cause the majority of URIs, with rhinoviruses constituting approximately one-third to one-half of etiologic species[15,16]; other common childhood respiratory viruses include adenoviruses and coronaviruses.

Although most URIs are short-lived, self-limited infections and are by definition limited to the upper airway, they may increase airway sensitivity to noxious stimuli or secretions for several weeks after the infection has cleared. The mechanisms probably involve a combination of mucosal invasion, chemical mediators, and altered neurogenic reflexes.[15] URIs may also impair pulmonary function by decreasing FVC, $FEV_1$, peak expiratory flow, and diffusion capacity.[17,18]

Children with a recent or current URI have an increased incidence of perioperative laryngospasm, bronchospasm, arterial hemoglobin desaturation, severe coughing, and breath holding compared with uninfected children (Table 13.3).[4,13,14,19-22] However, most complications can usually be predicted and successfully managed without long-term sequelae by suitably experienced and prepared clinicians.[15,20,22-25] An approach to the child with a URI

is to detect the pathologic process and associated comorbidity, establish the acuteness and severity of the URI, and then decide whether to modify the anesthetic technique or postpone surgery (Table 13.4, Fig. 13.8).

The basis for diagnosing a URI is a careful history and physical examination, with further investigations in limited situations. Because they are usually familiar with their child's state of health, the parents or caregivers can provide helpful insight into the presence and severity of a URI. The child should be evaluated for fever (defined as a temperature >100.4°F [38°C]), change in demeanor or behavior, dyspnea, productive cough, purulent sputum production, nasal congestion, rales, rhonchi, and wheezing. A chest radiograph may be considered if the pulmonary examination is questionable, but because the radiographic changes lag behind clinical symptoms, it is typically of limited value. Although laboratory tests may confirm the diagnosis of a viral or bacterial URI, they are not cost-effective or practical in a busy surgical setting.

For children with symptoms of an uncomplicated URI who are afebrile with clear secretions and who are otherwise healthy, anesthesia may proceed as planned, because the problems encountered are typically transient and easily managed.[4,15,20,22-25] Elective surgery is usually postponed for children with more severe symptoms that include at least one of the following: *mucopurulent secretions*; *lower respiratory tract signs* (e.g., wheezing) that do not clear with a deep cough; *pyrexia* >100.4°F (38°C); or a *change in sensorium* (e.g., not behaving or playing normally, has not been eating properly).[15,25]

The decision to proceed with surgery becomes much more difficult when the signs of the URI are between the extremes of mild and severe. For these intermediate URIs, other considerations play a greater role in assessing the risk/benefit ratio. These include the presence of comorbidities such as asthma, cardiac disease, or obstructive sleep apnea; a history of prematurity; the frequency of URIs; prior cancellations; the type, complexity, duration, and urgency of the surgery; the age of the child; and the socioeconomic implications for the family. The comfort level and experience of the anesthesiologist may also be an underestimated but important factor in the decision to proceed with or postpone surgery, because less experienced anesthesiologists have a greater incidence of complications.[4] The need to admit a child postoperatively because of anesthetic complications or an exacerbation of the URI may expose other children to a contagious illness.



| Spirometry Parameter | Units | Actual | Predicted | Percent Pred |
|---|---|---|---|---|
| FVC | Liter | 2.59 | 3.34 | 77 |
| $FEV_1$ | Liter | 2.14 | 3.00 | 71 |
| $FEV_1/FVC$ | Percent | 83 | 92 | 90 |

**FIGURE 13.4** Flow–volume curve demonstrating a restrictive defect. The flow–volume curves in children with restrictive defects are near-normal in configuration but smaller in all dimensions. The ratio of forced expiratory volume in 1 second ($FEV_1$) to forced vital capacity (FVC) is normal, but both $FEV_1$ and FVC are reduced. The curve shape appears normal. This child has interstitial lung disease. *Pred*, predicted value.

| TABLE 13.3 | Incidence of Common Upper Respiratory Tract Infection—Associated Perioperative Adverse Events |
|---|---|

| | LARYNGOSPASM (%) | | BRONCHOSPASM (%) | | HEMOGLOBIN DESATURATION (%) | |
|---|---|---|---|---|---|---|
| Study | URI | No URI | URI | No URI | URI | No URI |
| Tait and Knight, 1987[134] | 1.3 | 1.2 | | | | |
| DeSoto et al., 1988[135] | | | | | (<95%) 20.0 | 0[a] |
| Cohen et al., 1990[12] | 2.2 | 1.7 | | | | |
| Levy et al., 1992[136] | | | | | (<93%) 63.6 | 59.0 |
| Rolf and Coté, 1992[22] | 5.9 | 3.3 | 13.3 | 0.6[a] | (<85%) 13.3 | 10.5 |
| Tait et al., 1998[137] | 7.3 | | 12.2 | | (<90%) 17.1 | |
| Tait et al., 2001[20] | 4.2 | 3.9 | 5.7 | 3.3 | (<90%) 15.7 | 7.8[a] |
| von Ungern-Sternberg et al., 2007.[14] | 7.6 | 3.1[a] | | 0.9[a] | 19.3 | 11.4[a] |

[a]$P < 0.05$ versus corresponding URI group.
*URI*, upper respiratory tract infection.
Data in parentheses under hemoglobin desaturation are the limits for desaturation in each study.
Modified from Tait AR. Anesthetic management of the child with an upper respiratory tract infection. *Curr Opin Anaesthesiol.* 2005;18:603–607.
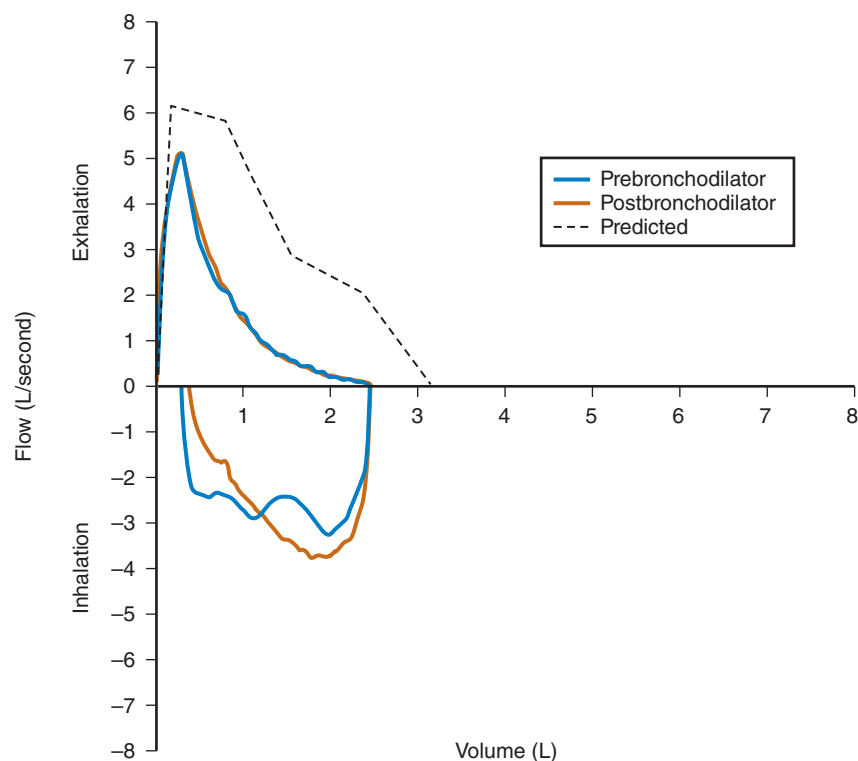
| Spirometry Parameter | Units | Predicted Value | Pre | Observed Percent Pred | Post | Observed Percent Pred | Percent Change |
|---|---|---|---|---|---|---|---|
| FVC | Liter | 3.16 | 2.50 | 79 | 2.45 | 78 | −2 |
| $FEV_1$ | Liter | 2.82 | 1.56 | 55 | 1.56 | 55 | 0 |
| $FEV_1$/FVC | Percent | 91 | 62 | 68 | 64 | 70 | 3 |

**FIGURE 13.5** Pulmonary function test demonstrating a nonreversible obstructive defect. The ratio of forced expiratory volume in 1 second *(FEV₁)* to forced vital capacity *(FVC)* is decreased, as is the $FEV_1$. After administration of a short-acting bronchodilator, there is no significant improvement in the $FEV_1$, in contrast to the pattern in Fig. 13.3. This child has cystic fibrosis with a nonreversible obstructive defect. *Post,* postbronchodilator; *Pre,* prebronchodilator; *Pred,* predicted value.

If the decision is to proceed with general anesthesia, management is directed toward avoiding stimulation of the potentially sensitized airway. Use of an endotracheal tube (ETT) should be avoided, when possible, because it increases the risk of complications, especially in younger children.[4,20] Although managing the airway with a face mask holds the smallest frequency of airway complications,[4] it may be inappropriate for certain cases. The laryngeal mask airway (LMA) is associated with fewer episodes of respiratory events than the ETT, but its use may similarly be contraindicated by the type of surgical procedure and the need to protect the airway from pulmonary aspiration of gastric contents.

Whichever airway technique is chosen, it is essential that the depth of anesthesia be adequate to obtund airway reflexes during placement of an airway device. The optimal depth of anesthesia at which to remove an airway device is less clearly defined. The frequency of emergence complications after awake and deep extubation appears to be similar in children with and without an URI.[4,14,20,26] In contrast the incidence of arterial oxygen desaturation and coughing after removal of the ETT or LMA in awake children was greater.[27,28]

The optimal time when an anesthetic can be given to a child after a URI without increasing the risk of adverse respiratory events remains contentious, but most clinicians wait 2 to 4 weeks after resolution of the URI before proceeding.[4,14,29] This reflects a balance of three critical factors: the time interval to diminish both upper and lower airway hyperreactivity; the perioperative respiratory risk, which includes a recurrence of the URI; and the need to perform the procedure.

The incidence of laryngospasm after maintenance of anesthesia with propofol was significantly less than with sevoflurane in an observation study of more than 9000 children.[4] One might attribute this finding to a differential effect of propofol versus sevoflurane on airway reflexes.[30] The effects of spraying the vocal cords with lidocaine on the incidence of laryngospasm and bronchospasm are unclear.[4] However, after applying topical lidocaine gel lubricant to the LMA in children with URIs, the frequency of adverse airway events was significantly less than without lidocaine lubricant.[31] Prophylactic treatment with glycopyrrolate, ipratropium, or albuterol does not affect the incidence of URI-related adverse events,[32,33] although one observational study reported that prophylactic salbutamol reduced perioperative airway sequelae in children with URIs.[34] Nasal vasoconstrictors (such as phenylephrine or oxymetazoline nose drops) have been recommended for reducing oropharyngeal secretions in children with URIs, but their efficacy remains anecdotal.[25]

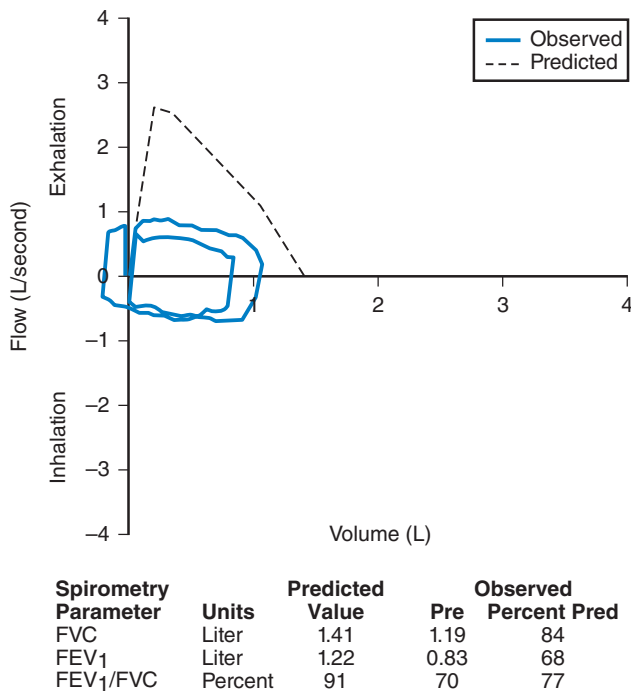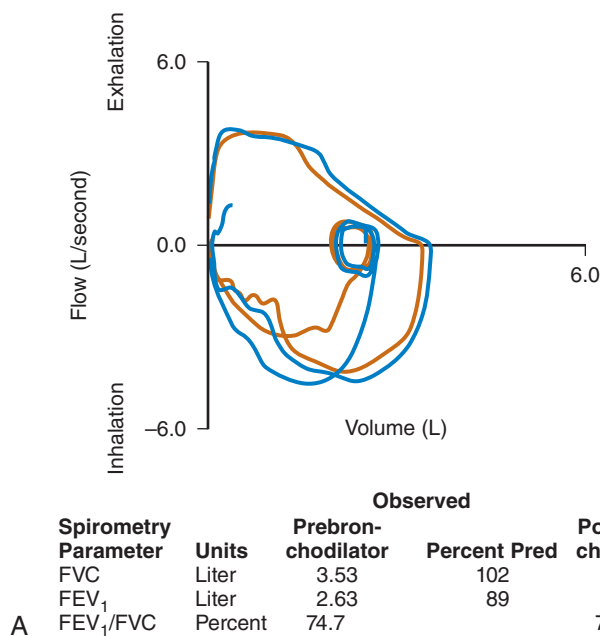| Spirometry Parameter | Units | Predicted Value | Pre | Observed Percent Pred |
|---|---|---|---|---|
| FVC | Liter | 1.41 | 1.19 | 84 |
| FEV$_1$ | Liter | 1.22 | 0.83 | 68 |
| FEV$_1$/FVC | Percent | 91 | 70 | 77 |

FIGURE 13.6 Pulmonary function test showing an extrathoracic airway obstruction; both the inspiratory and expiratory limbs of the flow–volume curve are flattened. This child has subglottic stenosis that developed at the site of her tracheotomy 2 years after the tracheostomy was removed. *FEV$_1$*, forced expiratory volume in 1 second; *FVC*, forced vital capacity; *Pred*, predicted value.

## LOWER AIRWAY DISEASE

Acute lower respiratory tract infections in infants and children may result in rapid deterioration necessitating aggressive intervention, including tracheal intubation and ICU admission. Many children are treated with antibiotics on the presumption that the infection is bacterial. However, many may be affected by viruses. In infants and children up to 18 months of age, respiratory syncytial virus is a very serious and common viral infection that infects the lower respiratory tract.[35] Other viruses that also infect the lower respiratory tract include parainfluenza virus, adenovirus, and human metapneumovirus.[36] Acute inflammation of the small airways may result in bronchiolitis with edema of the small airways leading to desaturation, hypercapnia, and acute respiratory failure. Bronchiolitis management can involve several days of continuous positive airway pressure (CPAP), high-flow nasal prongs, or tracheal intubation until the acute infection has resolved.

Croup or laryngotracheobronchitis, defined as acute inflammation of the airway (below the vocal cords), has been attributed primarily to parainfluenza virus as well as to adenovirus.

Asthma is one of the most common chronic diseases of childhood, affecting an estimated more than 6 million children in the United States.[37,38] A history of wheezing is associated with an increased risk of perioperative bronchospasm.[4] Rare perioperative complications associated with asthma include anaphylaxis, adrenal crisis, and ventilatory barotrauma such as pneumothorax or pneumomediastinum.[39] An anesthetic approach to children with asthma should include a basic understanding of the disease, an assessment of the child's current state of health, modification of anesthetic technique as appropriate, and recognition and treatment of complications if they occur.



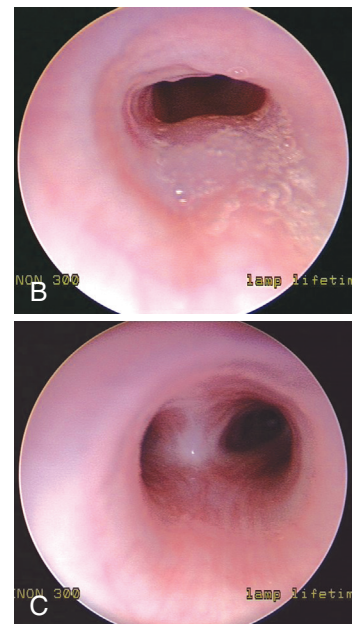| Spirometry Parameter | Units | Observed Prebron-chodilator | Percent Pred | Observed Postbron-chodilator | Percent Pred | Percent Change |
|---|---|---|---|---|---|---|
| FVC | Liter | 3.53 | 102 | 3.63 | 106 | 3 |
| FEV$_1$ | Liter | 2.63 | 89 | 2.65 | 90 | 0 |
| FEV$_1$/FVC | Percent | 74.7 | | 72.8 | | −3 |

FIGURE 13.7 **A,** Pulmonary function test from a child with an intrathoracic airway obstruction (vascular ring). The flow–volume curves suggest a fixed expiratory obstruction. The shape of the inspiratory link is normal; the expiratory flow limb is flattened on both the prebronchodilator *(brown)* and postbronchodilator *(blue)* flow–volume curves. **B,** Slit-like tracheal compression before repair. **C,** Marked improvement in the tracheal lumen after division of the vascular ring. (See E-Fig. 13.1 for a magnetic resonance imaging angiogram of a vascular ring.) *FEV$_1$*, Forced expiratory volume in 1 second; *FVC*, forced vital capacity; *Pred*, predicted value. (Photographs **B** and **C** courtesy Christopher Hartnick, MD.)

| TABLE 13.4 | Risk Factors for Perioperative Adverse Events in Children With Upper Respiratory Tract Infections | | |
|---|---|---|---|
| Study | URI Status | Factors | RR/OR |
| Parnis et al., 2001[19] | URI and no URI | ETT | |
| | | Child has a "cold" | |
| | | Child snores | |
| | | Passive smoker | |
| | | Anesthetic agent | |
| | | Sputum production | |
| | | Anticholinesterase given | |
| | | Nasal congestion | |
| Tait et al., 2001[20] | URI | Copious secretions | 3.9 RR |
| | | ETT in child <5 years | 1.9 |
| | | Prematurity (<37 weeks) | 2.3 |
| | | Nasal congestion | 1.4 |
| | | Passive smoker | 1.6 |
| | | Reactive airway disease | 1.8 |
| | | Surgery of airway | 1.8 |
| Bordet et al., 2002[13] | URI and no URI | Age <8 years | 1.8 OR |
| | | LMA | 2.3 |
| | | Respiratory infections | 3.7 |
| Mamie et al., 2004[9] | No URI | Nonpediatric anesthesiologist | 1.7 OR |
| | | ENT procedure | 1.8 |
| | | ETT without relaxants | 1.2 |
| von Ungern-Sternberg et al., 2010[4] | URI and no URI | Positive respiratory history | 3.05–8.46 RR |
| | | Symptomatic URI | 2.05 |
| | | URI within previous 2 weeks | 2.34 |
| | | Family history of asthma, atopy, or smoking | |
| | | Anesthetic agent | |
| | | Nonpediatric anesthesiologist | |

*ENT,* ear, nose, and throat; *ETT,* endotracheal tube; *LMA,* laryngeal mask airway; *OR,* odds ratio; *RR,* relative risk; *URI,* upper respiratory tract infection.
Modified from Tait AR. Anesthetic management of the child with an upper respiratory tract infection. *Curr Opin Anaesthesiol.* 2005;18:603–607.



FIGURE 13.8 Suggested algorithm for assessment and management of the child with an upper respiratory tract infection (URI). *ETT,* endotracheal tube; *Hx,* history; *LMA,* laryngeal mask airway. (Modified from Tait AR, Malviya S. Anesthesia for the child with an upper respiratory tract infection: still a dilemma? *Anesth Analg.* 2005;100:59–65.)

It is difficult to define asthma with precision because the exact pathophysiology remains unclear. The word *asthma* derives from the Greek *aazein,* which means "to breathe with open mouth or to pant."[40] A working definition of asthma is a common chronic disorder of the airways that is complex and characterized by variable and recurring symptoms, airway obstruction, inflammation, and hyperresponsiveness of the airways.[37]

Clinical expressions of asthma include wheezing, chest tightness or discomfort, persistent dry cough, and dyspnea on exertion. Severe respiratory distress can occur during acute exacerbations and may be characterized by chest wall retraction, use of accessory muscles, prolonged expiration, pneumothorax, and progression

to respiratory failure and death. In some children the development of chronic inflammation may be associated with permanent airway changes, referred to as *airway remodeling,* that are not prevented by or fully responsive to current available treatments. There is a strong association between asthma and atopy, or immunoglobulin E (IgE)-mediated hypersensitivity.[37]

The diagnosis of asthma can be challenging because cough, wheezing, and bronchospasm may arise from many disease processes. Asthma itself is unlikely to be a single disease entity, and the disease process is markedly modified by various genetic and environmental factors.[37,40] Many young children wheeze, and there is no definitive confirmatory blood, histologic, or radiographic

diagnostic test. Given the difficulty with diagnosis, the label "preschool wheezers" may be a more appropriate description for young children with reversible airway obstruction than a diagnosis of "asthma."[40]

The Tucson birth cohort study was the largest longitudinal study in the United States to attempt to differentiate wheezing or asthma phenotypes in children who did not subsequently develop asthma.[41-43] This study examined 826 children at ages 3 years and 6 years from a cohort of 1246 neonates. By the age of 6 years, 48.5% of the children had experienced at least one documented episode of wheezing and were categorized into three groups. "Transient wheezers" were children who wheezed only in response to viral infections, typically during the first 3 years of life. "Non-atopic wheezers" were children who wheezed beyond the first few years of life, often in response to viral infections, but who were less likely to persistently wheeze in later childhood. "Atopy-associated wheezers" were children who had a reversible wheeze together with a tendency toward IgE-mediated hypersensitivity; they had the greatest risk of persistent symptoms into late childhood and adulthood.[41]

The development of asthma is a complex process that probably involves the interaction of two crucial elements: host factors (specifically genetic modifiers of inflammation) and environmental exposures (e.g., viral infections, environmental allergens, pollution) that occur during a crucial time in the development of the immune system.[37] Therefore, the population of young children who wheeze includes a spectrum of disorders rather than one specific pathologic process.

Asthma must be differentiated from other distinct causes that produce similar symptoms (Table 13.5). Tracheomalacia or bronchomalacia may produce wheezing, but this tends to be present from birth (which is unusual for asthma), and the wheezing is commonly of a single pitch heard loudest in the central airways, whereas asthma typically produces polyphonic sounds from the lung periphery. Breathing difficulties owing to chronic aspiration are often related to feeding times. Unremitting wheeze or stridor is often caused by a fixed obstruction or foreign body.

Chronic cough is the most common manifestation of asthma in children. Many children who cough may never be heard to wheeze but still have asthma. A cough with or without wheeze may be caused by a viral infection, whereas a persistent, productive cough may suggest suppurative lung disease such as CF.[39] A positive response of the cough to asthma medications suggests the diagnosis of asthma.

The exact incidence of perioperative complications in the pediatric asthma population is difficult to ascertain because of variations in the definition of asthma, the definition and detection of complications, the presence of coexisting diseases, overlap with adult populations, and changing anesthetic management techniques.

A retrospective review of 706 adult and pediatric patients with a rigorous definition of asthma reported an incidence of documented bronchospasm in the perioperative period of 1.7% and no instances of pneumonia, pneumothorax, or death.[44] Of 211 children younger than 12 years of age, none developed bronchospasm at the time of surgery. A retrospective review of more than 136,000 computer-based anesthesia records found a 0.8% incidence of bronchospasm in patients with asthma.[45] By contrast, older studies from the 1960s reported that 7% to 8% of asthmatic patients wheezed.[46,47] A blinded, prospective study of 59 asthmatic patients detected transient wheezing after tracheal intubation in 25% of cases; however, most events were brief and self-limited.[48] An observational study of 9297 children reported an overall incidence of 2% for bronchospasm; in the subgroup of 2256 children with a history of respiratory problems, the incidence was 6%.[4,39] An editorial review of the subject of asthma and anesthesia concluded that, although the true incidence of major complications is small, severe adverse outcomes do result from bronchospasm, and children with asthma are at heightened risk for severe morbidity.[49]

Both the severity and the control of asthma must be established preoperatively. These two aspects of the current disease state should be clearly differentiated.[50] For example, asthma may be severe yet well controlled, whereas even mild asthma may be poorly controlled. Both situations may present a heightened potential for perioperative complications, because even the child with intermittent but poorly controlled asthma can have a severe exacerbation.

Severity and control of asthma may be assessed by the frequency of symptoms, limitation of effort tolerance, night awakenings, medication use, emergency department attendance, hospitalizations, and need for ventilatory support. An approach to assessment of severity and control in children aged 5 to 11 years is outlined in E-Tables 13.1 through 13.3. A history of a nocturnal dry cough, more than three wheezing episodes in the past 12 months, or a history of past or present eczema is associated with an increased risk of bronchospasm.[4]

Maintenance treatment of asthma is based on a stepwise approach, so that the type of therapy is often an indication of severity. Short-acting inhaled β-agonists are first-line therapy, with inhaled corticosteroids for those patients with persistent symptoms poorly managed by bronchodilators as the preferred second step. Alternative treatments at this step include a leukotriene receptor antagonist, a mast cell stabilizer such as cromolyn sodium or nedocromil, and a methylxanthine bronchodilator such as theophylline. The third step in therapy involves increasing the dose of inhaled corticosteroid or adding an alternative treatment to a smaller dose of corticosteroid; a long-acting β-agonist, a leukotriene receptor antagonist, or theophylline may be considered. Step 4 involves a medium dose of corticosteroid together with a long-acting β-agonist. The final steps of therapy involve a high dose of inhaled corticosteroid or commencing an oral corticosteroid (E-Fig. 13.2). Recently biologics directed at the basic pathophysiology of asthma offer the hope of personalized medicine.[51] Such medicines include

| TABLE 13.5 | Causes of Wheezing in Children |
|---|---|
| **Acute** | |
| Bronchiolitis | Pneumothorax |
| Asthma | Endobronchial intubation |
| Foreign body | Herniated ETT cuff |
| Inhalation injury | Aspiration |
| | Anaphylaxis |
| **Recurrent or Persistent** | |
| Bronchiolitis | Mediastinal mass |
| Asthma | Tracheomalacia/bronchomalacia |
| Foreign body | Vascular ring |
| Bronchopulmonary dysplasia | |
| Cardiac failure | Tracheal web/stenosis |
| Cystic fibrosis | Bronchial stenosis |
| Recurrent aspiration | Roundworm infestation |
| Sickle cell disease | |

*ETT*, endotracheal tube.

| E-TABLE 13.1 | Classification of Asthma Severity in Children 5 to 11 Years of Age Who Are Not Currently Taking Long-Term Control Medication | | | |
|---|---|---|---|---|
| | | | **PERSISTENT ASTHMA** | |
| **Components of Severity[a]** | **Intermittent Asthma** | *Mild* | *Moderate* | *Severe* |
| **Impairment** | | | | |
| Symptoms | ≤2 days/week | >2 days/week but not daily | Daily | Throughout the day |
| Nighttime awakenings | ≤2 times/month | 3–4 times/month | >1 time/week but not nightly | Often 7 times/week |
| Short-acting $\beta_2$-agonist use for symptom control (not prevention of EIB) | ≤2 days/week | >2 days/week but not daily | Daily | Several times per day |
| Interference with normal activity | None | Minor limitation | Some limitation | Extremely limited |
| Lung function | Normal $FEV_1$ between exacerbations | | | |
| | $FEV_1$ ≥80% predicted | $FEV_1/FVC$ >80% | $FEV_1$ = 60%–80% predicted | $FEV_1$ <60% predicted |
| | $FEV_1/FVC$ >85% | $FEV_1$ ≥80% predicted | $FEV_1/FVC$ = 70%–80% | $FEV_1/FVC$ <75% |
| **Risk** | | | | |
| Exacerbations[b] requiring oral systemic corticosteroids | 0–2/year | ≥2 in 1 year | | |
| | Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. | | | |
| | Relative annual risk of exacerbations may be related to $FEV_1$. | | | |

[a]Level of severity is determined by both impairment and risk. Assess impairment domain by patient or caregiver recall of the previous 2 to 4 weeks and results of spirometry. Assign severity to the most severe category in which any feature occurs.
[b]Exacerbation is defined as an acute episode of signs and symptoms requiring oral systemic corticosteroids. More than two exacerbations per year indicates persistent asthma. There are no data indicating correspondence of frequency of exacerbations with severity category within the classification of persistent asthma. In general, more frequent exacerbations and more intense exacerbations (e.g., requiring urgent, unscheduled care hospitalization or admission to an intensive care unit) indicate greater underlying disease severity.
*EIB,* exercise-induced bronchospasm; *FEV₁,* forced expiratory volume in 1 second; *FVC,* forced vital capacity.
Reproduced from National Asthma Education and Prevention Program. Full report of the expert panel: guidelines for the diagnosis and management of asthma (EPR-3). Bethesda, MD: National Heart, Lung, and Blood Institute, National Institutes of Health; 2007.

| E-TABLE 13.2 | Classification of Severity After Asthma Becomes Well Controlled, by Lowest Level of Treatment Required to Maintain Control | | | |
|---|---|---|---|---|
| | **Intermittent Asthma** | **PERSISTENT ASTHMA** | | |
| | | *Mild* | *Moderate* | *Severe* |
| Lowest level of treatment required to maintain control[a] | Step 1 | Step 2 | Step 3 or 4 | Step 5 or 6 |

[a]See E-Fig. 13.2 for treatment steps. Reproduced from National Asthma Education and Prevention Program. Full report of the expert panel: guidelines for the diagnosis and management of asthma (EPR-3). Bethesda, MD: National Heart, Lung, and Blood Institute, National Institutes of Health; 2007.

| E-TABLE 13.3 | Assessment of Asthma Control in Children 5 to 11 Years of Age | | |
|---|---|---|---|
| **Components of Control[a]** | **Well Controlled** | **Not Well Controlled** | **Very Poorly Controlled** |
| **Impairment** | | | |
| Symptoms | ≤2 days/week but not more than once on each day | >2 days/week or multiple times on <2 days/week | Throughout the day |
| Nighttime awakenings | ≤1 time/month | >2 times/month | >2 times/week |
| Interference with normal activity | None | Some limitation | Extremely limited |
| Short-acting β$_2$-agonist use for symptom control (not prevention of EIB) | ≤2 days/week | ≥2 days/week | Several times per day |
| Lung function | | | |
| FEV$_1$ or peak flow | >80% predicted/personal best | 60%–80% predicted/personal best | <60% predicted/personal best |
| FEV$_1$/FVC | >80% predicted | 75%–80% predicted | <75% predicted |
| **Risk** | | | |
| Exacerbations[b] | 0–1/year | 2–3/year | >3/year |
| Reduction in lung growth | Evaluation requires long-term follow-up. | | |
| Treatment-related adverse effects | Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk. | | |

[a]The level of control is based on the most severe impairment or risk category. Assess impairment domain by patient or caregiver recall of previous 2 to 4 weeks and by spirometry or peak flow measures. Symptom assessment for longer periods should reflect a global assessment, such as inquiring whether the patient's asthma is better or worse since the last visit.

[b]Exacerbation is defined as an acute episode of signs and symptoms requiring oral systemic corticosteroids.

*EIB,* exercise-induced bronchospasm; *FEV$_1$,* forced expiratory volume in 1 second; *FVC,* forced vital capacity

Reproduced from National Asthma Education and Prevention Program. Full report of the expert panel: guidelines for the diagnosis and management of asthma (EPR-3). Bethesda, MD: National Heart, Lung, and Blood Institute, National Institutes of Health; 2007.
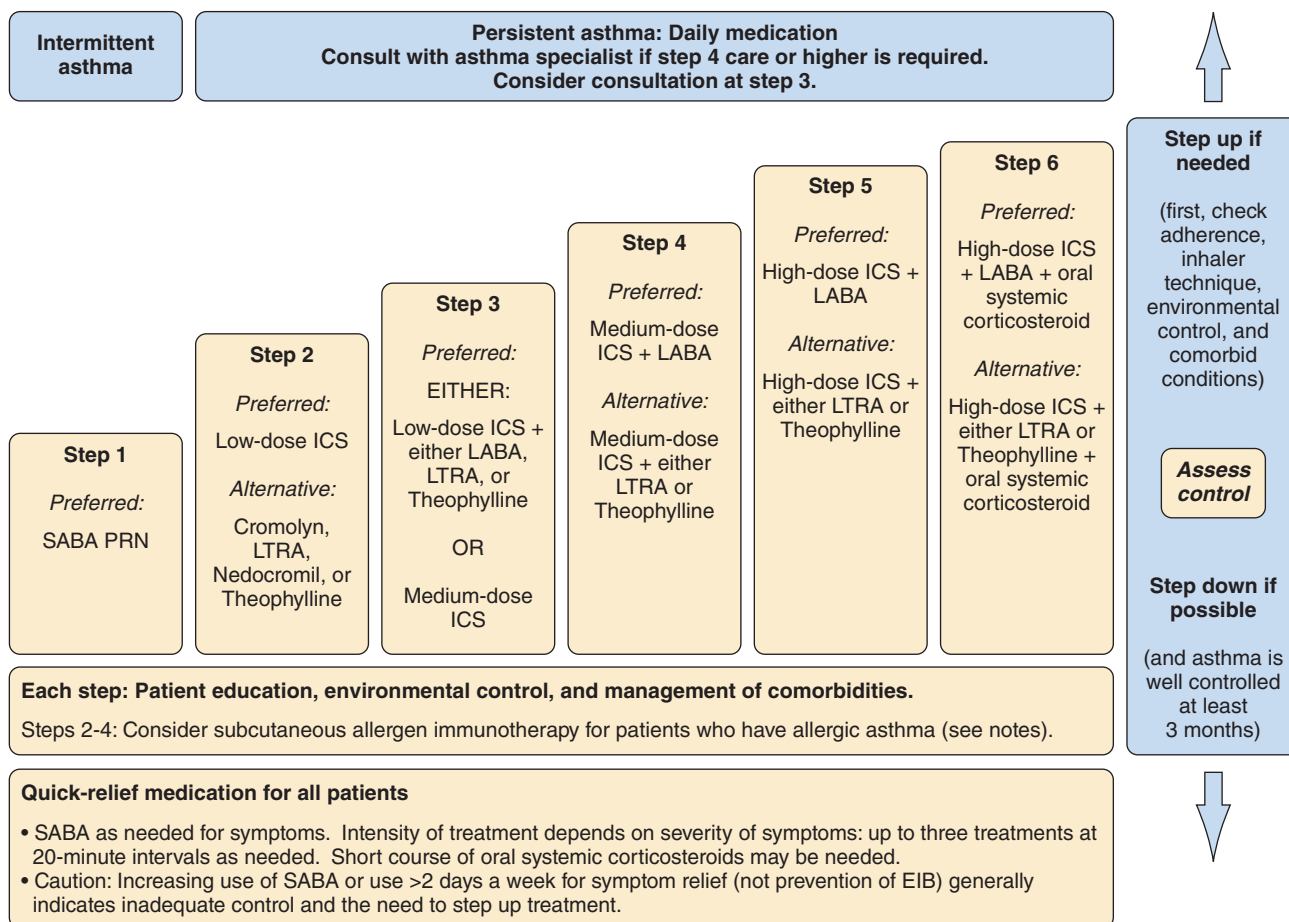
13

| Intermittent asthma | Persistent asthma: Daily medication<br>Consult with asthma specialist if step 4 care or higher is required.<br>Consider consultation at step 3. |
|---|---|

**Step up if needed**

(first, check adherence, inhaler technique, environmental control, and comorbid conditions)

*Assess control*

**Step down if possible**

(and asthma is well controlled at least 3 months)

**Step 6**

*Preferred:*

High-dose ICS + LABA + oral systemic corticosteroid

*Alternative:*

High-dose ICS + either LTRA or Theophylline + oral systemic corticosteroid

**Step 5**

*Preferred:*

High-dose ICS + LABA

*Alternative:*

High-dose ICS + either LTRA or Theophylline

**Step 4**

*Preferred:*

Medium-dose ICS + LABA

*Alternative:*

Medium-dose ICS + either LTRA or Theophylline

**Step 3**

*Preferred:*

EITHER:

Low-dose ICS + either LABA, LTRA, or Theophylline

OR

Medium-dose ICS

**Step 2**

*Preferred:*

Low-dose ICS

*Alternative:*

Cromolyn, LTRA, Nedocromil, or Theophylline

**Step 1**

*Preferred:*

SABA PRN

**Each step: Patient education, environmental control, and management of comorbidities.**

Steps 2-4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma (see notes).

**Quick-relief medication for all patients**

• SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to three treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
• Caution: Increasing use of SABA or use >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.

Key: **Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy.**
*ICS,* Inhaled corticosteroid; *LABA,* inhaled long-acting beta$_2$-agonist; *LTRA,* leukotriene receptor antagonist;
*SABA,* inhaled short-acting beta$_2$-agonist

**Notes:**

• The stepwise approach is meant to assist, not replace, the clinical decision making required to meet individual patient needs.

• If alternative treatment is used and response is inadequate, discontinue it and use the preferred treatment before stepping up.

• Theophylline is a less desirable alternative due to the need to monitor serum concentration levels.

• Step 1 and 2 medications are based on Evidence A. Step 3 ICS + adjunctive therapy and ICS are based on Evidence B for efficacy of each treatment and extrapolation from comparator trials in older children and adults— comparator trials are not available for this age group; steps 4-6 are based on expert opinion and extrapolation from studies in older children and adults.

• Immunotherapy for steps 2-4 is based on Evidence B for house-dust mites, animal danders, and pollens; evidence is weak or lacking for molds and cockroaches. Evidence is strongest for immunotherapy with single allergens. The role of allergy in asthma is greater in children than in adults. Clinicians who administer immunotherapy should be prepared and equipped to identify and treat anaphylaxis that may occur.

**E-FIGURE 13.2** Stepwise approach for managing asthma in children 5 to 11 years of age. (Reproduced from National Asthma Education and Prevention Program. Full report of the expert panel: guidelines for the diagnosis and management of asthma [EPR-3]. Bethesda, MD.: National Heart, Lung, and Blood Institute, National Institutes of Health; 2007.)

omalizumab which is directed against IgE and mepolizumab and reslizumab directed against interleukin 5.

Most children with asthma have disease that is intermittent or persistent but mild and will be treated with inhaled short-acting β-agonists on an as-needed basis, alone or in combination with low-dose inhaled corticosteroids or an adjunctive therapy. Poor control may relate to poor compliance with medication, inadequate inhaler technique, or incorrect diagnosis. Severe asthma is diagnosed when symptom control is poor despite high doses of corticosteroids (see steps 5 or 6 in E-Fig. 13.2). A small group of children have "brittle asthma" that is difficult to control despite optimal therapy and may lead to life-threatening respiratory compromise. A history of severe attacks or admission to intensive care is particularly ominous.

Special investigations are not routinely indicated but may be useful in specific circumstances. A chest radiograph is not usually helpful to assess the severity of asthma but can help diagnose a superimposed infection, pneumothorax, or pneumomediastinum during an acute exacerbation. Pulmonary function tests are important in monitoring long-term responses to therapy but are of little use in the immediate, routine preoperative workup of cases at a stable clinical baseline. Measurements of nitric oxide and various inflammatory markers are primarily of use as research tools at present, but their role in asthma management is evolving.[52]

Although an assessment of disease severity is essential, an important caveat is that many asthma deaths in the community setting occur not in those with severe disease but in those with what was thought to be mild or moderate disease. Asthma is often undertreated,[50] so the sensitivity of medication prescription as a marker of disease activity must be viewed with some caution. Some studies have found a poor correlation between assessment of disease severity and the occurrence of perioperative broncho-spasm. However, disease *activity*, as noted by recent asthma symptoms, use of medications for symptom treatment, and recent therapy in a medical facility for asthma, is significantly associated with perioperative bronchospasm.[44]

Children should continue their regular medications before anesthesia. Midazolam has been reported to be a safe premedication for asthmatics.[53] Corticosteroids may help prevent postintubation bronchospasm in adults,[54] although controlled clinical data to substantiate this practice in children are lacking.[39] Inhaled β-agonists before or shortly after induction of anesthesia attenuate the increases in airway resistance associated with tracheal intubation.[55,56] Ketamine is the traditional choice of intravenous (IV) induction agent in children with severe asthma, although its superiority over other agents has not been substantiated in clinical trials.[57,58] Propofol

is typically preferred over thiopentone because it causes less bronchoconstriction.[48,59] Desflurane is associated with an increased risk of bronchospasm compared with sevoflurane or isoflurane, and because it can increase airway resistance in children, should be avoided in asthmatics.[4]

Tracheal stimulation is a potent stimulus for bronchospasm.[4] In children with a URI, in whom the airways may be acutely hyperactive, the avoidance of tracheal intubation is associated with a reduced incidence of pulmonary complications.[4,19] There are inadequate clinical outcome data on the perioperative manage-ment of asthma to make definitive recommendations about airway management. Nevertheless, avoidance of tracheal and vocal cord stimulation by use of a face mask or an LMA instead of an ETT whenever possible seems a sensible approach. If tracheal intubation is mandatory, a deep plane of anesthesia is preferred to blunt airway hyperreactivity. Similarly, unless contraindicated by other factors, deep extubation is preferred for the same reason. Surgical stimulation is another trigger of bronchospasm, and anesthetic depth and analgesia should be adequate to prevent this response.

Intraoperative bronchospasm is characterized variously by polyphonic expiratory wheeze, prolonged expiration, active expira-tion with increased respiratory effort, increased airway pressures, a slow upslope on the end-tidal $CO_2$ monitor waveform (Fig. 13.9), increased end-tidal $CO_2$, and hypoxemia. Other causes of wheezing must be excluded, such as partial obstruction of the ETT (secretions or herniation of the cuff causing obstruction), main-stem intubation (deep endobronchial intubation), aspiration, pneumothorax, or pulmonary edema. Mechanical obstruction of the circuit or ETT must also be excluded.

First-line treatment for bronchospasm involves removing the triggering stimulus if possible, deepening anesthesia, increasing the fraction of inspired oxygen ($FIO_2$) if appropriate, decreasing the positive end-expiratory pressure (PEEP), and increasing the expiratory time to minimize alveolar air trapping. In severe status asthmaticus, ventilation strategy focuses primarily on achieving adequate oxygenation, rather than attempting to normalize $PaCO_2$ at the potential cost of inducing pulmonary barotrauma. All children who experience anything more than minor bronchospasm should also receive corticosteroids, if they have not already done so.

Inhaled β-agonists can be delivered by nebulizer or by a metered-dose inhaler down the airway device with specially designed adaptors (Fig. 13.10). Alternatively, a 60-mL syringe can be used to deliver doses of the nebulizer into the breathing circuit (E-Fig. 13.3). However, the efficiency of delivery through an inhaler that is actuated at the elbow of the breathing circuit is poor, especially in small-diameter ETTs.[60] To improve the delivery efficiency of
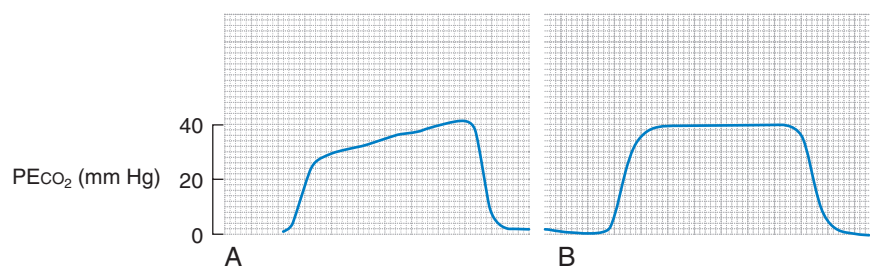
FIGURE 13.9  **A,** Tracing of expired carbon dioxide ($PECO_2$) in a child with acute bronchospasm. Notice the slowly rising $PECO_2$ value. **B,** Tracing from the same patient after administration of inhaled albuterol. Note that the $PECO_2$ waveform now has a flat plateau, indicating relief of the bronchospasm and efficient elimination of $CO_2$ from all areas of the lungs.

13
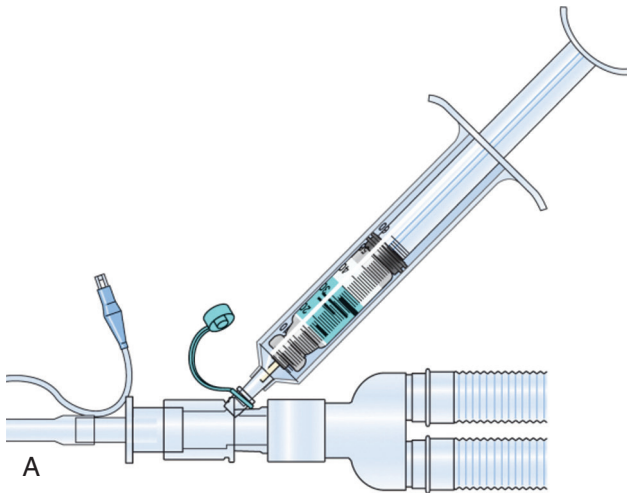


**E-FIGURE 13.3  A** and **B,** A 60-mL syringe may be attached to a port in the circuit to administer aerosolized drugs such as albuterol.

FIGURE 13.10 Adaptor that allows administration of albuterol through an endotracheal tube (ETT) and timing of that dose with inspirations to provide maximum delivery; notice that the nebulized albuterol is directed down the ETT *(arrow)*. Use of a long intravenous catheter that extends to the tip of the ETT is an alternative method to further improve drug delivery.

the aerosol in pediatric-size ETTs, the inhaler may be actuated 10 to 20 times at the elbow or once or twice into a narrow-gauge catheter that is passed to the end of the ETT.[60,61]

If IV salbutamol (albuterol) is available, the IV route is preferred over tracheal administration. Onset of bronchodilation in a child with acute symptoms should be rapid with good effect at a plasma salbutamol concentration of 1 μg/L.[62] Salbutamol (10 μg/kg IV) may be repeated, followed by an infusion of 5 to 10 μg/kg per minute for the first hour until there is an improvement in the bronchospasm. Thereafter, salbutamol should be infused at 1 to 2 μg/kg per minute until the bronchospasm resolves. Epinephrine (0.05-0.5 μg/kg per minute) is also an effective bronchodilator.

The anesthesiologist may be involved in the management of status asthmaticus when consulted to assist a child in the emergency department or on the wards. A drowsy, silent child with a quiet chest on auscultation despite therapy is in imminent danger of respiratory arrest and requires emergent tracheal intubation by an experienced practitioner. Signs and symptoms to assess the severity of an asthma exacerbation are outlined in Table 13.6, and an algorithm for management issued by the American National Heart, Lung and Blood Institute is presented in E-Fig. 13.4.

Oxygen is recommended for most children to maintain the oxygen saturation at greater than 90%. Repetitive or continuous administration of short-acting β-agonists is first-line therapy for all children and is the most effective way of reversing airflow obstruction. The addition of ipratropium to a β-agonist may produce additional bronchodilation and may have a modest effect to improve outcome. Systemic corticosteroids should be given to those who do not respond completely and promptly to β-agonists. For severe exacerbations unresponsive to the treatment listed earlier, IV magnesium may decrease the likelihood of intubation, although the evidence is limited. Current recommended drug doses are listed in E-Table 13.4.

There is much debate about the role of methylxanthines such as aminophylline in the management of acute exacerbations of asthma. In some countries, aminophylline is considered a first-line

treatment for asthma, whereas in others it is considered second-line or used less frequently. The difference in practice may be attributed to its equivocal clinical efficacy in the treatment of acute exacerbations of asthma and to complications from toxicity (including vomiting).[63-66]

Antibiotics are not recommended except for comorbid conditions. Aggressive hydration is not recommended in adults or older children, although it may be indicated in younger children who become dehydrated as a result of decreased oral intake and increased respiratory rate. In general, chest physical therapy and mucolytics are also not recommended.

Children with severe atopy-associated asthma are possibly at greater risk for developing anaphylaxis in response to neuromuscular blocking drugs, antibiotics, and latex.[39] Bronchospasm caused by anaphylaxis is differentiated from that due to asthma; it produces additional systemic signs such as angioedema, flushing, urticaria, and cardiovascular collapse.
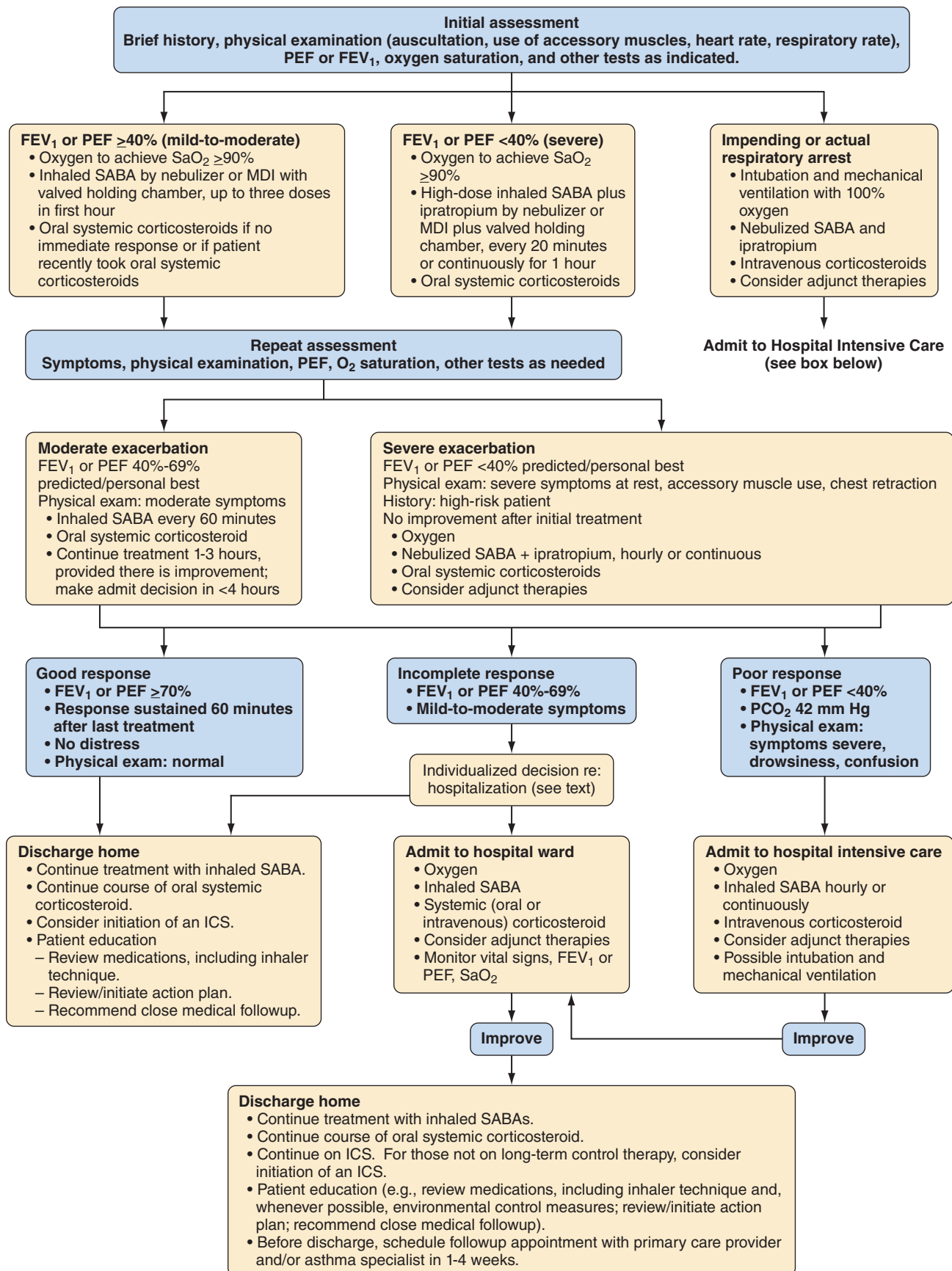
Adrenal crisis during major surgical stress is a potential complication associated with severe asthma caused by iatrogenic suppression of the hypothalamic-pituitary-adrenal axis.[39] Adrenal suppression should be considered in any child who is taking significant doses of corticosteroids for a prolonged period. Short courses of prednisolone used to treat acute flares of asthma may affect function for up to 10 days, but prolonged dysfunction is unlikely. Large doses, prolonged therapy for more than a few weeks, and evening dosing may suppress adrenal function for up to 1 year. Prophylactic corticosteroid administration may be indicated for those receiving prolonged systemic corticosteroids, when their corticosteroid regimen is interrupted by the surgical schedule, or for those who have received high-dose inhaled corticosteroids in the recent past (see Chapter 27).

## CYSTIC FIBROSIS

CF is an autosomal recessive disorder that is caused by one of more than 1500 mutations in the gene coding for the CF transmembrane conductance regulator (located on chromosome 7), a protein that regulates chloride and other ion fluxes at various epithelial surfaces.[67,68] The different gene defects may variously impact the protein's translation, cellular processing, or function as a chloride channel gating. The incidence of CF is approximately 1 of every 2000 births in Caucasians, making it the most common fatal inherited disease in this population.

The disruption of electrolyte transport in the epithelial cells of the sweat ducts, airways, pancreatic ducts, intestine, biliary tree, and vas deferens causes increased sweat chloride concentrations, viscous mucus production, lung disease, intestinal obstruction, pancreatic insufficiency, biliary cirrhosis, and congenital absence of the vas deferens. The clinical outcome is widely variable, even among children with identical mutations at the CF locus. Absence of the gene influences expression of several other gene products, including proteins important to the inflammatory response, ion maturational processing, transport, and cell signaling. These other proteins are potential modifiers of the phenotype and may help explain the substantial differences in clinical severity.

Lung disease is the main cause of morbidity and mortality in CF, and consequently it is the focus of anesthetic concern. The pathophysiology involves mucus plugging, chronic infection, inflammation, and epithelial injury.[69-71] Mucus clearance defends the lung against inhaled bacteria. The mucociliary transport system requires two fully functioning layers to be effective. The base layer of ciliary epithelia bathed in a watery liquid (sol) is overlaid by a more viscous gel (mucus) that is responsible for transporting

**Initial assessment**
**Brief history, physical examination (auscultation, use of accessory muscles, heart rate, respiratory rate), PEF or FEV$_1$, oxygen saturation, and other tests as indicated.**

**FEV$_1$ or PEF ≥40% (mild-to-moderate)**
- Oxygen to achieve SaO$_2$ ≥90%
- Inhaled SABA by nebulizer or MDI with valved holding chamber, up to three doses in first hour
- Oral systemic corticosteroids if no immediate response or if patient recently took oral systemic corticosteroids

**FEV$_1$ or PEF <40% (severe)**
- Oxygen to achieve SaO$_2$ ≥90%
- High-dose inhaled SABA plus ipratropium by nebulizer or MDI plus valved holding chamber, every 20 minutes or continuously for 1 hour
- Oral systemic corticosteroids

**Impending or actual respiratory arrest**
- Intubation and mechanical ventilation with 100% oxygen
- Nebulized SABA and ipratropium
- Intravenous corticosteroids
- Consider adjunct therapies

**Repeat assessment**
**Symptoms, physical examination, PEF, O$_2$ saturation, other tests as needed**

**Admit to Hospital Intensive Care (see box below)**

**Moderate exacerbation**
FEV$_1$ or PEF 40%-69% predicted/personal best
Physical exam: moderate symptoms
- Inhaled SABA every 60 minutes
- Oral systemic corticosteroid
- Continue treatment 1-3 hours, provided there is improvement; make admit decision in <4 hours

**Severe exacerbation**
FEV$_1$ or PEF <40% predicted/personal best
Physical exam: severe symptoms at rest, accessory muscle use, chest retraction
History: high-risk patient
No improvement after initial treatment
- Oxygen
- Nebulized SABA + ipratropium, hourly or continuous
- Oral systemic corticosteroids
- Consider adjunct therapies

**Good response**
- FEV$_1$ or PEF ≥70%
- Response sustained 60 minutes after last treatment
- No distress
- Physical exam: normal

**Incomplete response**
- FEV$_1$ or PEF 40%-69%
- Mild-to-moderate symptoms

Individualized decision re: hospitalization (see text)

**Poor response**
- FEV$_1$ or PEF <40%
- PCO$_2$ 42 mm Hg
- Physical exam: symptoms severe, drowsiness, confusion

**Discharge home**
- Continue treatment with inhaled SABA.
- Continue course of oral systemic corticosteroid.
- Consider initiation of an ICS.
- Patient education
  – Review medications, including inhaler technique.
  – Review/initiate action plan.
  – Recommend close medical followup.

**Admit to hospital ward**
- Oxygen
- Inhaled SABA
- Systemic (oral or intravenous) corticosteroid
- Consider adjunct therapies
- Monitor vital signs, FEV$_1$ or PEF, SaO$_2$

**Admit to hospital intensive care**
- Oxygen
- Inhaled SABA hourly or continuously
- Intravenous corticosteroid
- Consider adjunct therapies
- Possible intubation and mechanical ventilation

**Improve**

**Improve**

**Discharge home**
- Continue treatment with inhaled SABAs.
- Continue course of oral systemic corticosteroid.
- Continue on ICS. For those not on long-term control therapy, consider initiation of an ICS.
- Patient education (e.g., review medications, including inhaler technique and, whenever possible, environmental control measures; review/initiate action plan; recommend close medical followup).
- Before discharge, schedule followup appointment with primary care provider and/or asthma specialist in 1-4 weeks.

**E-FIGURE 13.4** Management of asthma exacerbations in emergency department and hospital-based care. *FEV*$_1$, forced expiratory volume in 1 second; *ICS*, inhaled corticosteroid; *MDI*, metered dose inhaler; *PCO*$_2$, partial pressure carbon dioxide; *PEF*, peak expiratory flow; *SABA*, short-acting β$_2$-agonist; *SaO*$_2$, oxygen saturation. (Reproduced from National Asthma Education and Prevention Program. Full report of the expert panel: guidelines for the diagnosis and management of asthma [EPR-3]. Bethesda, MD: National Heart, Lung, and Blood Institute, National Institutes of Health; 2007.)

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| E-TABLE 13.4 | Doses of Drugs for Asthma Exacerbations in Emergency Settings or Hospital | | |
|---|---|---|---|
| **Medication** | **Adult Dose** | **Child Dose**[a] | **Comments** |
| **Inhaled Short-Acting β₂-Agonists** *Albuterol/Salbutamol* | | | |
| Nebulizer solution (0.63 mg/3 mL, 1.25 mg/3 mL, 2.5 mg/3 mL, 5.0 mg/mL) | 2.5–5 mg every 20 minutes for 3 doses, then 2.5–10 mg every 1–4 hours as needed, or 10–15 mg/hour continuously | 0.15 mg/kg (minimum dose 2.5 mg) every 20 minutes for 3 doses, then 0.15–0.3 mg/kg up to 10 mg every 1–4 hours as needed, or 0.5 mg/kg per hour by continuous nebulization | Only selective β₂-agonists are recommended. For optimal delivery, dilute aerosols to a minimum of 3 mL at a gas flow of 6–8 L/minute. Use large-volume nebulizers for continuous administration. May mix with ipratropium nebulizer solution. |
| MDI (90 μg/puff) | 4–8 puffs every 20 minutes up to 4 hours, then every 1–4 hours as needed | 4–8 puffs every 20 minutes for 3 doses, then every 1–4 hours inhalation maneuver as needed. Use valved holding chamber. Add mask in children <4 years. | In mild-to-moderate exacerbations, MDI plus valved holding chamber is as effective as nebulized therapy with appropriate administration technique and coaching by trained personnel. |
| *Bitolterol* | | | |
| Nebulizer solution (2 mg/mL) | See albuterol dose. | See albuterol dose; thought to be half as potent per milligram as albuterol | Has not been studied in severe asthma exacerbations. Do not mix with other drugs. |
| MDI (370 μg/puff) | See albuterol MDI dose. | See albuterol MDI dose. | Has not been studied in severe asthma exacerbations. |
| *Levalbuterol (R-albuterol)* | | | |
| Nebulizer solution (0.63 mg/3 mL, 1.25 mg/3 mL) | 1.25–2.5 mg every 20 minutes for 3 doses, then 1.25–5 mg every 1–4 hours as needed | 0.075 mg/kg (minimum dose 1.25 mg) every 20 minutes for 3 doses, then 0.075–0.15 mg/kg up to 5 mg every 1–4 hours as needed | Levalbuterol administered in one-half the dose of albuterol provides comparable efficacy and safety. Has not been evaluated by continuous nebulization. |
| MDI (45 μg/puff) | See albuterol MDI dose. | See albuterol MDI dose. | — |
| *Pirbuterol* | | | |
| MDI (200 μg/puff) | See albuterol MDI dose. | See albuterol MDI dose; thought to be half as potent per milligram as albuterol | Has not been studied in severe asthma exacerbations. |
| **Systemic (Injected) β₂-Agonists** | | | |
| Epinephrine 1:1000 (1 mg/mL) | 0.3–0.5 mg every 20 minutes for 3 doses SC | 0.01 mg/kg up to 0.3–0.5 mg every 20 minutes for 3 doses SC | No proven advantage of systemic therapy over aerosol. |
| Terbutaline (1 mg/mL) | 0.25 mg every 20 minutes for 3 doses SC | 0.01 mg/kg every 20 minutes for 3 doses, then every 2–6 hours as needed SC | No proven advantage of systemic therapy over aerosol. |
| **Anticholinergics** *Ipratropium bromide* | | | |
| Nebulizer solution (0.25 mg/mL) | 0.5 mg every 20 minutes for 3 doses, then as needed | 0.25–5 mg every 20 minutes for 3 doses, then as needed | May mix in same nebulizer with albuterol. Should not be used as first-line therapy; should be added to SABA therapy for severe exacerbations. The addition of ipratropium has not been shown to provide further benefit once the patient is hospitalized. |
| MDI (18 μg/puff) | 8 puffs every 20 minutes as needed up to 3 hours | 4–8 puffs every 20 minutes as needed up to 3 hours | Should use with valved holding chamber and face mask for children <4 years. Studies have examined ipratropium bromide MDI for up to 3 hours. |
| *Ipratropium with albuterol* | | | |
| Nebulizer solution (each 3-mL vial contains 0.5 mg ipratropium bromide and 2.5 mg albuterol) | 3 mL every 20 minutes for 3 doses, then as needed | 1.5 mL every 20 minutes for 3 doses, then as needed | May be used for up to 3 hours in the initial management of severe exacerbations. The addition of ipratropium to albuterol has not been shown to provide further benefit once the patient is hospitalized. |
| MDI (each puff contains 18 μg ipratropium bromide and 90 μg albuterol) | 8 puffs every 20 minutes as needed up to 3 hours | 4–8 puffs every 20 minutes as needed up to 3 hours | Should use with valved holding chamber and face mask for children <4 years. |

| E-TABLE 13.4 | Doses of Drugs for Asthma Exacerbations in Emergency Settings or Hospital—cont'd | | |
|---|---|---|---|
| **Medication** | **Adult Dose** | **Child Dose**[a] | **Comments** |
| **Systemic Corticosteroids** | | | |
| Prednisone | 40–80 mg/day in 1 or 2 divided doses until PEF reaches 70% of predicted or personal best | 1 mg/kg in 2 divided doses (maximum = 60 mg/day) until PEF is 70% of predicted or personal best | For outpatient "burst," use 40–60 mg in single or 2 divided doses for 5–10 days in adults (children: 1–2 mg/kg per day, maximum 60 mg/day, for 3–10 days). |
| Methylprednisolone | As for prednisone. | As for prednisone. | As for prednisone. |
| Prednisolone | As for prednisone. | As for prednisone. | As for prednisone. |

*Notes:*

There is no known advantage for higher doses of corticosteroids in severe asthma exacerbations, nor is there any advantage for intravenous administration over oral therapy, provided gastrointestinal transit time or absorption is not impaired.

The course of systemic corticosteroids for an asthma exacerbation requiring an emergency department visit or hospitalization may last from 3 to 10 days. For corticosteroid courses of less than 1 week, there is no need to taper the dose. For slightly longer courses (e.g., up to 10 days), there probably is no need to taper, especially if patients are concurrently taking inhaled corticosteroids.

Inhaled corticosteroids can be started at any point in the treatment of an asthma exacerbation.

[a]Children <12 years of age.

*ED,* emergency department; *MDI,* metered-dose inhaler; *PEF,* peak expiratory flow; *SABA,* short-acting β-agonists; *SC,* subcutaneous.

Reproduced from National Asthma Education and Prevention Program. Full report of the expert panel: guidelines for the diagnosis and management of asthma (EPR-3). Bethesda, MD: National Heart, Lung, and Blood Institute, National Institutes of Health; 2007.

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| TABLE 13.6 | Formal Evaluation of Asthma Exacerbation Severity | | | |
|---|---|---|---|---|
| | **Mild** | **Moderate** | **Severe** | **Subset: Respiratory Arrest Imminent** |
| **Symptoms** | | | | |
| Breathlessness | While walking<br>Can lie down | While at rest<br>(infant—softer, shorter cry, difficulty feeding)<br>Prefers sitting | While at rest<br>(infant—stops feeding)<br>Sits upright | |
| Talks in | Sentences | Phrases | Words | |
| Alertness | May be agitated | Usually agitated | Usually agitated | Drowsy or confused |
| **Signs** | | | | |
| Respiratory rate[a] | Increased | Increased | Increased | |
| Use of accessory muscles; suprasternal retractions | Usually not | Commonly | Usually | Paradoxical thoracoabdominal movement |
| Wheeze | Moderate, often only end expiratory | Loud; throughout exhalation | Usually loud; throughout inhalation and exhalation | Absence of wheeze |
| Pulse/minute[b] | Slightly increased | Increased | Tachycardia | Bradycardia |
| Pulsus paradoxus | Absent<br><10 mm Hg | May be present<br>10–25 mm Hg | Often present<br>>25 mm Hg (adult)<br>20–40 mm Hg (child) | Absence suggests respiratory muscle fatigue |
| **Functional Assessment[c]** | | | | |
| PEF (% of predicted or of personal best) | ≥70% | Approx. 40%–69% or response lasts <2 hours | <40% | <25% (PEF testing may not be needed in very severe attacks) |
| $Pa_{O_2}$ (while breathing room air) | Normal (test not usually necessary) | ≥60 mm Hg (test not usually necessary) | <60 mm Hg: possible cyanosis | |
| $P_{CO_2}$ | <42 mm Hg (test not usually necessary) | <42 mm Hg (test not usually necessary) | >42 mm Hg: possible respiratory failure (see text) | |
| $Sa_{O_2}$% (while breathing room air) at sea level | >95% (test not usually necessary) | 90%–95% (test not usually necessary) | <90% | |

[a]Guide to rates of breathing in awake children: at age <2 months, normal rate is <60 breaths/minute; at 2–12 months, <50/minute; at 1–5 years, <40/minute; at 6–8 years, <30/minute.
[b]Guide to normal pulse rates in children: at age 2–12 months, normal rate is <160 beats/minute; at 1–2 years, <120/minute; at 2–8 years, <110/minute.
[c]$Pa_{O_2}$ or $P_{CO_2}$ or both may be tested. Hypercapnia (hypoventilation) develops more readily in young children than in adults and adolescents.
$Pa_{O_2}$, arterial oxygen tension; $P_{CO_2}$, partial pressure of carbon dioxide; *PEF*, peak expiratory flow; $Sa_{O_2}$, oxygen saturation.
Modified from National Asthma Education and Prevention Program. Full report of the expert panel: guidelines for the diagnosis and management of asthma (EPR-3). Bethesda, MD: National Heart, Lung, and Blood Institute, National Institutes of Health, 2007.

particles along the tips of the cilia. Normally, mucus is transported at about 10 mm/minute, expelling foreign particles and pathogens from the lungs. The efficacy of clearance depends on adequate hydration of the mucus.[72] Lack of regulation of sodium absorption and chloride secretion decreases liquid on the airway luminal surfaces, slows mucus clearance, and promotes the formation of adherent plugs in the airway.[73] Increased secretions, viscous mucus, and impaired ciliary clearance contribute to airway impaction, providing a nidus for infection.

At birth, the lung structure is almost normal.[67] However, chronic and recurrent bacterial infections occur early in life, assisted by the pooling of secretions and impaired neutrophil bacterial killing on airway surfaces.[69,74] Repeated and persistent infections stimulate a chronic neutrophilic inflammatory response, ultimately destroying the airway walls. Early pathogens include *Staphylococcus aureus* and *Haemophilus influenzae. Pseudomonas aeruginosa* typically invade later in life, acquire a mucoid phenotype, and form a biofilm in the lung, an event that is associated with accelerated decline in pulmonary function. The invasion of the lung by antibiotic-resistant pathogens such as certain strains of *Burkholderia cepacia* is often devastating, markedly increasing the death rate from lung disease.

Various insults such as bacteria, viruses, and airborne irritants can cause acute exacerbations of respiratory symptoms of cough and sputum production. This is often accompanied by systemic manifestations such as weight loss, anorexia, and fatigue. These changes from baseline are termed *pulmonary exacerbations.*[75]

Recurrent exacerbations are associated with progressive airway obstruction, bronchiectasis, emphysema, ventilation/perfusion mismatching, and hypoxemia. Growth of blood vessels with advancing bronchiectasis predisposes to hemoptysis. Bronchial hyperreactivity and increased airway resistance are common, whereas bullae formation can lead to pneumothorax.

Pulmonary function abnormalities typically have an obstructive pattern[76] and include increased FRC, decreased $FEV_1$, decreased peak expiratory flow rate, and decreased vital capacity (see Fig. 13.5). Compensatory hyperventilation typically produces a reduced $PaCO_2$, although hypercapnia may supersede in end-stage pulmonary pathology. End-stage cor pulmonale may lead to cardiomegaly, fluid retention, and hepatomegaly.

Malnutrition is a common problem in CF that follows from pancreatic insufficiency, failure of enzyme secretion, impaired gastrointestinal motility, abnormal enterohepatic circulation of

bile, increased caloric demand owing to severe lung disease, and anorexia of chronic disease.[67] Low weight and body mass index are closely associated with, and can predict, poor lung function.

CF-related diabetes arises from progressive pancreatic disease and scarring that compromises the pancreatic islets. More than 12% of teenagers older than 13 years with CF have insulin-dependent diabetes, and the incidence increases with age. Evidence is accumulating that diabetes contributes to the lung disease and worse outcome.[69-71] In addition, classic diabetic complications occur in older CF patients. Hepatic dysfunction decreases plasma cholinesterase and clotting factors II, VII, IX, and X, whereas malabsorption of vitamin K may also contribute to coagulation issues.[77]

When CF was first distinguished from celiac syndrome in 1938, life expectancy was approximately 6 months. Since then, substantial advances in sustained multidisciplinary supportive care have increased the median survival time to 35 years (E-Fig. 13.5).[67,78] Currently almost half of the CF population are adults.[77]

The pillars of treatment include nutritional repletion, relief of airway obstruction, and antibiotic therapy for lung infection. Organ transplantation, and in particular lung transplantation, has been used in an attempt to improve quality of life and prolong survival, but a clear benefit remains to be demonstrated.[78]

Corrector and potentiator therapies are recently developed treatments that are directed at the molecular defects in the CF transmembrane conductance regulator.[79,80] Correctors are principally targeted at cellular misprocessing, while potentiators aim to correct channel's function. Ivacaftor was the first developed drug in this area, and it is a potentiator that targets a number of mutations in cystic fibrosis transmembrane conductance regulator (CFTR) gene, including the G551D mutation.

The multisystem nature of the disease and changing demographics mean that children present for a wide variety of surgical procedures. The most common indications for anesthesia in children are nasal polypectomy and ear, nose, and throat surgery, as a result of the frequency of upper airway pathologic processes such as chronic sinusitis and nasal polyps (Table 13.7).[81,82] The investigation or correction of gastrointestinal disorders is the next most common procedural category that requires anesthesia in the CF population. Other indications for anesthesia include bronchoscopy and pulmonary lavage, gastrointestinal endoscopy, sclerosing injection of varices resulting from portal hypertension, insertion of venous access devices, and incidental surgical problems.[82-84]

Because of the increasing longevity of this population, the pediatric anesthesiologist may also be involved in the care of adults.[77] Surgical procedures in adults typically include treatment of recurrent pneumothorax, cholecystectomy, and lung or cardiac

transplantation. Consultation may also be requested for obstetric cases as increasing numbers of patients survive to adulthood.

Pulmonary disease is the predominant concern when planning anesthesia for these patients. Historically, morbidity and mortality from pulmonary complications were significant–for example, in 1964, a retrospective study reported a perioperative mortality rate of 27%,[85] but by 1972, this incidence had decreased to 4%.[81] More recent studies have confirmed low mortality but an appreciable rate of morbidity after general anesthesia for lung lavage; bronchoscopies; and ear, nose, and throat surgery in children with CF. With a combined cohort of 700 children, the frequency of perioperative complications was between 5% and 13%.[82,86-89] In a study of 18 patients with CF undergoing anesthesia for pleural surgery, the risks for this surgery were considered substantial, although the anesthetic hazards of CF could be minimized with careful management.[90] The effects of anesthesia on pulmonary function in children with CF are unclear. In a small study of children undergoing injection of esophageal varices, pulmonary function test results deteriorated 48 hours after general anesthesia.[91] In contrast, in almost 100 children in two studies, no difference in pulmonary function tests measured before compared with after a variety of surgical procedures was observed.[82,92] Although acute pulmonary morbidity may pose challenges, the effects of the anesthetic management techniques on pulmonary function tests are difficult to predict.

An assessment of the severity, current state, and progression of pulmonary disease should guide anesthetic planning. Fitness is a positive predictor of survival,[67] and exercise tolerance is a useful marker of pulmonary function. The quality and quantity of secretions, recent and chronic infections, use and effectiveness of bronchodilators, and number of hospitalizations are also important points to elucidate in the history. Examination of the cardiopulmonary systems should aim to detect compromise of cardiac, pulmonary, and hepatic function. Special investigations are not routinely indicated but may quantify organ dysfunction in end stages of the disease. Arterial blood gas analysis, chest radiography, pulmonary function tests, electrocardiography, echocardiography, and liver function tests may assist the planning of anesthetic technique in selected children.[84]

Children are often emotionally vulnerable, not simply because of the usual preoperative anxieties but because of the psychological consequences of progression of an ultimately fatal disease. A preoperative visit should aim to allay distress; oral benzodiazepines have been successfully used as anxiolytics.[82,89] Prophylactic use of osmotic laxatives may be indicated if opioid-induced ileus is anticipated.[84]

Because desiccation of mucous secretions is a central pulmonary issue in CF, general anesthesia poses specific problems. During spontaneous ventilation under normal conditions, inspired gases are warmed to body temperature and saturated with water vapor, reaching this state at the isothermic saturation point just distal to the carina.[93,94] This ensures that the lower airways are kept moist and warm. The alveolar environment in optimal circumstances has a saturated water vapor pressure of 47.1 mm Hg and an absolute humidity of 43.4 g/m$^3$ at 98.6°F (37°C).

The inspiration of cold, desiccated anesthetic gases and vapors can impair the warming and humidification of the airways. The use of any airway device (oropharyngeal airway, laryngeal mask, or ETT) bypasses the nasal and oropharyngeal passages and delivers cold, dry gas farther down the airway.[95] This shifts the isothermic saturation point distally, forcing bronchi that normally function in optimal conditions to take part in heat and gas exchange.[94]

| TABLE 13.7 | Most Frequent Indications for Anesthesia in Cystic Fibrosis | |
|---|---|---|
| **Neonates** | **Children/Teenagers** | **Adults** |
| Meconium ileus | Nasal polypectomy | Esophageal varices |
| Meconium peritonitis | Intravenous access | Recurrent pneumothorax |
| Intestinal atresia | Ear/nose/throat surgery | Cholecystectomy |
| | | Lung (liver) transplantation |

Modified from Della Rocca G. Anaesthesia in patients with cystic fibrosis. *Curr Opin Anaesthesiol.* 2002;15:95–101.
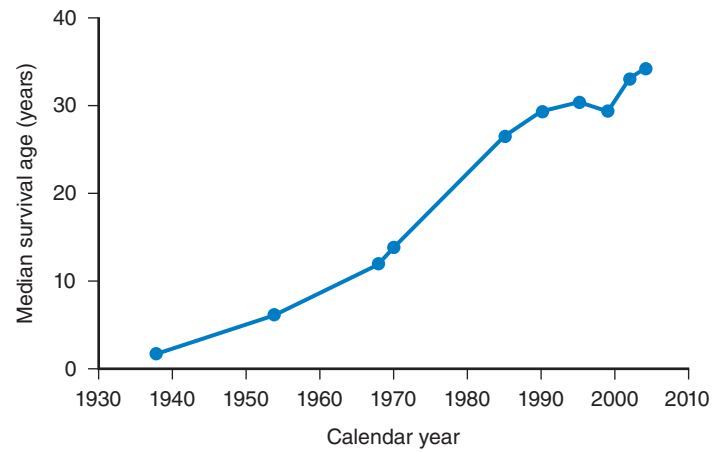
**E-FIGURE 13.5** Median survival age for patients with cystic fibrosis at various times since the first description of the disease. Data before 1970 are gleaned from the then-current literature. Data since 1985 are from the Cystic Fibrosis Foundation Data Registry and represent projections of median survival age for a child born in that year with cystic fibrosis. (Reproduced from Davis PB. Cystic fibrosis since 1938. *Am J Respir Crit Care Med*. 2006;173:475–482.)

These parts of the airway are less adapted to moisture exchange and tend to dehydrate more rapidly, thereby impairing the mucociliary escalator and predisposing to impaction of secretions.[96,97] By directly impairing mucociliary motion as well as blunting the cough response and ventilatory drive, inhalational anesthetics can exacerbate this problem.

It is therefore particularly important to minimize mucus desiccation in the perioperative period. Inhalation of hypertonic saline (7% sodium chloride) accelerates mucus clearance, increases lung function, and improves quality of life[98-100]; this is now typically part of the routine maintenance management of CF. Nebulized saline treatments should continue up to the start of anesthesia and recommence after the procedure. Inhaled gases should be humidified, or an artificial "nose" should be inserted into the circuit to conserve airway moisture and minimize the risk of inspissating secretions. Although removal of pulmonary secretions is considered important in principle, a small prospective trial of intraoperative bronchial wash-out and physical therapy reported an acute increase in airway resistance with no significant long-term benefit in measures of lung function.[101]

At the conclusion of surgery, complete reversal of neuromuscular blockade should be confirmed. Whenever possible, the trachea should be extubated and the child encouraged to breathe spontaneously. A 30- to 40-degree head-up position assists movement of the diaphragm and ventilation. Postoperatively, physiotherapy, airway humidification, carefully titrated analgesics, and early mobilization should enhance clearance of secretions and minimize atelectasis. The use of neuraxial, regional or local anesthesia, as well as nonopioid analgesics, are useful strategies to avoid respiratory depression.[102,103] Ambulatory surgery is optimal, if feasible, because it minimizes disruption to the patient's schedule and decreases exposure to nosocomial infection.

## SICKLE CELL DISEASE

SCD is an inherited hemoglobinopathy that results from a point mutation on chromosome 11 (see also Chapter 10). The mutant gene codes for the production of hemoglobin S, a mutant variant of the normal hemoglobin A. This leads to widespread and progressive vascular damage.[104,105] Clinical features of the disease include acute episodes of pain, acute and chronic pulmonary disease, hemorrhagic and occlusive stroke, renal insufficiency, and splenic infarction, with mean life expectancy shortened to just over 3 decades.[106] Perioperative problems and management are covered in more detail in Chapter 10; the discussion here is limited to a brief review of the pulmonary pathology of SCD.

Acute chest syndrome (ACS) is an acute lung injury caused by SCD. Diagnostic criteria include a new pulmonary infiltrate involving at least one lung segment on the radiograph (excluding atelectasis) combined with one or more symptoms or signs of chest pain, pyrexia greater than 101.3°F (38.5°C), tachypnea, wheezing, or cough.[107-109] Precipitants include infection, fat embolism after bone marrow infarction, pulmonary infarction, and surgical procedures.[109-111] Potential risk factors for the development and severity of perioperative ACS may include a history of lung disease, recent clustering of acute pulmonary complications, pregnancy, increased age, and the invasiveness of the surgical procedure.[104] ACS was associated with younger-age patients, reduced body temperature, and greater blood loss in a study of 60 children with SCD undergoing laparoscopic surgery.[112]

The risk of ACS is small (<5%) after minor surgeries such as inguinal hernia repair and distal extremity surgery, whereas it is severalfold greater (10% to 15%) after intraabdominal and major joint surgery.[111,113,114] Although the overall perioperative mortality from SCD is quite small, <1%,[111,115] ACS can prolong postoperative hospitalization, and cause respiratory failure and death. ACS typically develops about 3 days postoperatively and persists for approximately 8 days, with a 3.3% mortality.[110]

SCD also causes chronic lung damage, known as sickle cell lung disease (SCLD).[116] Because lung function has not yet been assessed longitudinally in a cohort from early childhood to adulthood, the precise pathology of and relationship between the obstructive and restrictive patterns of lung disease is unclear.[117] Children appear to develop a predominantly obstructive pattern,[118] whereas adults develop a more restrictive pulmonary defect.[116,119,120] In the later stages of lung damage, both vital and total lung capacities decrease, gas diffusion is impaired, and pulmonary fibrosis, pulmonary artery hypertension, right-sided cardiomyopathy, and progressive hypoxemia may occur.[116,120] The development of pulmonary artery hypertension, which can precede clinically apparent lung damage, is a particularly ominous sign of disease progression and is associated with a heightened risk of sudden death.[119] Recurrent ACS is an independent risk factor for the development of end-stage SCLD, but subtle evidence of parenchymal and vascular damage commonly precedes clustered episodes of ACS.[116]

Assessment of lung function should include a history of the occurrence, frequency, severity, and known precipitants of ACS and a search for progression of chronic lung damage. A recent chest radiograph can serve as a baseline for comparison if postoperative radiographs are needed and can also delineate lung pathology. Early features of lung damage include decreased distal pulmonary vascularity and diffuse interstitial fibrosis, whereas later stages are characterized by pulmonary fibrosis, pulmonary hypertension, and right ventricular hypertrophy.[116,121] Pulmonary function testing can reveal the need for bronchodilators and the presence of obstructive or restrictive lung disease.

Although the risk of developing ACS in the perioperative period is increased, distinct genotypes, wide variation in disease severity, differing chronic treatment protocols, varied surgical procedures, and logistical complexities have made research into the optimal perioperative management difficult. Well-delivered anesthetic and postoperative care may be the best guarantor of a good outcome.[104,105]

Perioperative management frequently includes red blood cell transfusion in an effort to decrease the risk of perioperative ACS. The Transfusion Alternative Perioperatively in Sickle Cell Disease study prospectively enrolled 67 patients undergoing low- and medium-risk surgery with or without preoperative transfusion.[122] Although limited by early closure of the study, the small sample size, and too few patients enrolled in the low-risk surgery group to allow for subgroup analysis, the prevalence of clinically important events, including ACS, in the nontransfused group exceeded that in the transfused group. The authors concluded that preoperative transfusion may reduce the risk of ACS in patients with a homozygous HbSS genotype.

If preoperative transfusion is performed to attenuate SCD exacerbations, an exchange transfusion aimed at decreasing the concentration of hemoglobin S to 30% is no more effective than simply correcting the anemia to a hematocrit of 30%. However, exchange transfusion is more likely to lead to transfusion-related complications including the development of uncommon antibodies such as Kell and Duffy antibodies.[110] Consequently, if a decision is made to transfuse in the hope of preventing ACS, the target should be a hematocrit of 30% rather than a specific dilution of hemoglobin S.

The risk of ACS after low-risk surgeries or procedures without transfusion appears to be small.[123] A study of patients undergoing magnetic resonance imaging (MRI) with deep sedation reported an incidence of ACS of 1.2% within 1 month of the MRI,[124] whereas nontransfused patients undergoing minor surgery in the Cooperative Study of Sickle Cell Disease had a similar incidence of ACS of 1.4%.[110] A survey of North American pediatric anesthesiologists found that most clinicians do not transfuse children who are at low risk for perioperative complications after minor procedures, whereas a greater number transfuse sicker children undergoing more invasive procedures.[125]

The one group of children with SCD who are at high risk for complications are those who have experienced or are at risk for a stroke. Risk factors for strokes include low hemoglobin, hypertension, and male gender as well as three single-nucleotide polymorphisms.[126,127] Serial transcranial Doppler ultrasound and MRI of the brain have been used to detect pathologic changes in blood flow or subclinical strokes, respectively, and in these children blood transfusion has been effective in reducing subsequent strokes.[128,129] Silent cerebral strokes have been detected in up to 30% of asymptomatic children with SCD.[126] To reduce the risk of stroke, these children have transfusions at regular intervals, based on the results of the serial investigations. However, this approach raises concern about iron overload and other complications associated with repeated blood transfusions. A recent study to limit the number of transfusions in those at risk for a stroke had to be stopped prematurely because two strokes occurred despite serial transcranial Doppler monitoring.[130] Chronic hydroxyurea therapy has also been shown to be effective in reducing the risk of stroke.[131] The perioperative management of children with a history of stroke continues to evolve.

Children with SCD frequently develop postoperative atelectasis. It is unclear whether this relates to an underlying sickle cell lung disease, difficulty with analgesia, other causes, or a combination of factors. Pain management can be difficult in these children. Large doses of opioids can depress ventilation and cause atelectasis.[132] ACS tends to involve the lower segments of the lung,[109] suggesting an association between atelectasis and ACS; incentive spirometry can prevent the development of atelectasis and pulmonary infiltrates.[133] Regional analgesia, supplemental nonopioid analgesics, prophylactic incentive spirometry, early mobilization, and good pulmonary toilet may decrease the incidence of atelectasis and ACS.

Treatment of ACS is focused on supporting gas exchange. Supplemental oxygen, noninvasive ventilatory support such as CPAP, or intubation and mechanical ventilation are indicated by the degree of dysfunction. Bronchodilators, incentive spirometry, and chest physiotherapy may be useful in preventing disease progression. In the presence of a significant ventilation/perfusion mismatch, correction of anemia can improve arterial oxygenation. Erythrocyte transfusion increases oxygen-carrying capacity, decreases fractional peripheral tissue extraction, and increases returning venous oxygen levels. Because the mean arterial oxygen content in the presence of a shunt is significantly affected by the oxygenation of blood returning from nonventilated parts of the lung, increasing venous oxygen levels can improve arterial oxygen content. Although transfusion has not been directly linked to improved outcomes, both exchange and simple transfusions can improve oxygenation.[109]

## Summary

Pulmonary complications are a major cause of perioperative morbidity in the pediatric population. Although preexisting pulmonary pathologic processes in children can present significant challenges to anesthetic delivery, a thorough assessment of the problem combined with meticulous anesthetic management allows most children to undergo surgical interventions without long-term adverse sequelae. Consultation with a pediatric pulmonologist is indicated when appropriate for specific problems as outlined in this chapter; a team approach may markedly improve operative and postoperative outcomes.

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