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Essentials of Pulmonology

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CHAPTER 11

MAINTENANCE OF ADEQUATE GAS exchange and delivery is a fundamental goal of anesthesia. Although the lungs play an important role in acid-base balance, temperature regulation, metabolism, and endocrine signaling, the preservation of oxygen and carbon dioxide (CO_2) equilibrium is the principal pulmonary function of immediate concern to the anesthesiologist. Respiratory problems are common in children and are frequently encountered by anesthesiologists during perioperative consultations, intraoperatively, or in intensive care units. Problems range from mild acute respiratory tract infections to chronic lung disease with end-stage respiratory failure. In this chapter we discuss the basics of respiratory physiology, assessment of pulmonary function, and practical anesthetic management of specific pulmonary problems. Airway and thoracic aspects pertinent to ventilation are discussed in Chapters 12 and 13, whereas pulmonary issues specific to neonates, intensive care, or other disease states are addressed in the relevant chapters.

Respiratory Physiology

The morphologic development of the lung begins several weeks into the embryonic period and continues into the first decade and beyond 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. The respiratory system is an outgrowth of the ventral wall of the foregut. During the embryonic period of development of the first few postconceptual weeks, lung buds form as a projection of the endodermal tissue. During the pseudoglandular period, extending to the 17th week of life, 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. Proliferation of capillary networks surrounding these air spaces become sufficient for pulmonary gas exchange by 26 to 28 weeks, when extrauterine survival of premature neonates becomes possible. Formation of alveoli occurs by lengthening of the saccules and thinning of the saccular walls and has begun by the 36th postconceptual week in most human fetuses (Fig. 11-1). The vast majority of alveolar formation occurs after birth, however, typically continuing to as late as 8 to 10 years postnatally. The neonatal lung at birth commonly has 10 to 20 million terminal air sacs (many of which are saccules rather than alveoli), which is one tenth of the number in the mature adult lung. Growth of the lungs after birth is primarily due to an increase in the number of respiratory bronchioles and alveoli and not due to an increase in the size of the alveoli.

Respiratory rhythmogenesis, as seen by rhythmic thoracic movement, begins well before birth and may be necessary for normal anatomic and physiologic lung development. At birth, interruption of umbilical blood flow initiates 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 P_{O_2}, P_{CO_2}, and pH cause an acute decrease in pulmonary vascular resistance and a consequent increase in pulmonary blood flow. Increased left atrial and decreased right atrial pressure reverse the pressure gradient across the foramen ovale, causing functional closure of this left-to-right one-way flap valve. Expansion of the lungs combined with increased pulmonary blood flow initiates the abrupt transition to

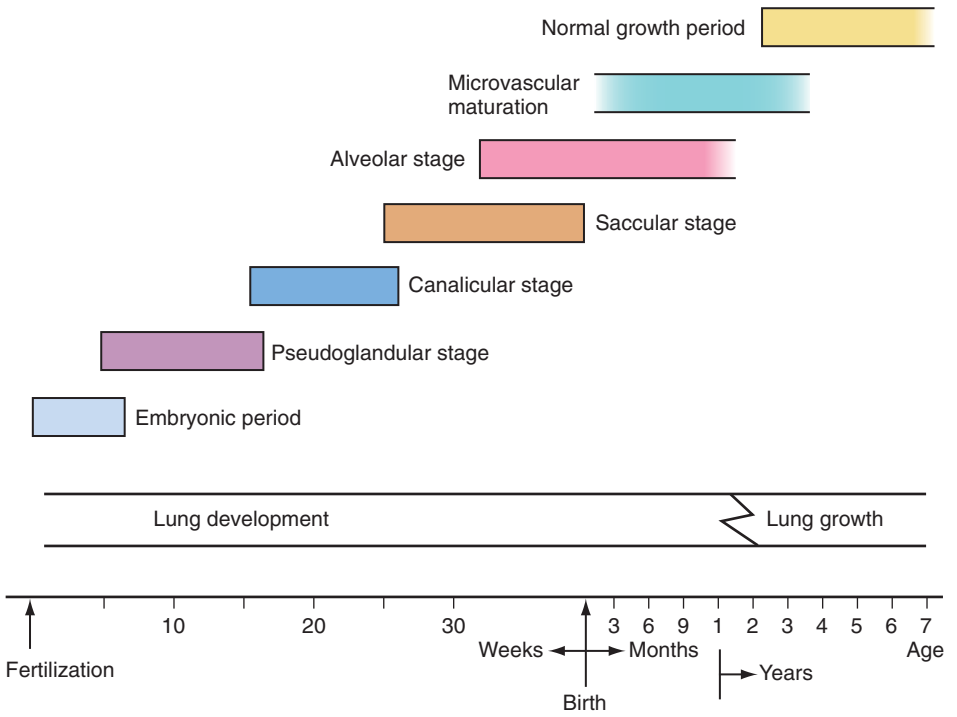


Figure 11-1. Timetable for lung development. (Reproduced and modified with permission from Guttentag S, Ballard PL: Lung development: embryology, growth, maturation, and developmental biology. In Tausch HW, Ballard RA, Gleason CA [eds]: Avery's Diseases of the Newborn, 8th ed. Philadelphia, WB Saunders, 2004, p 602.)

extrauterine gas exchange. Continuous increased arterial oxygen levels following birth, in comparison with intrauterine levels, augment and maintain ventilatory rhythm.

Breathing is controlled by a complex interaction of input from sensors, integration by a central control system, and subsequent output to effector muscles.[2] Afferent signaling is provided by peripheral arterial chemoreceptors, central brainstem chemoreceptors, upper 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 in humans. The carotid bodies sense both Pao_2 and hydrogen ion concentration. The central chemoreceptors are responsive to $Paco_2$ and hydrogen ion concentration and 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, or 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. The rapidly adapting receptors lie between the airway epithelial cells and are triggered by noxious stimuli such as smoke, dust, and histamine. Parenchymal receptors, or 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 proprioreceptors. Mechanoreceptors in the muscle spindle endings and tendons of respiratory muscles sense changes in length, tension, and movement.

Central control of respiration is maintained by the brainstem (involuntary) and cortical (voluntary) centers. Although the precise mechanism of the neural ventilatory rhythmogenesis is unknown, the pre-Bötzinger complex and retrotrapezoid nucleus/parafacial respiratory group, neural circuits in the ventrolateral medulla, are thought to be the respiratory rhythm generators.[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 respiratory nuclei and neural complexes in the pons and medulla, which 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 cyclical contraction of the pharyngeal dilator muscles. The diaphragm produces the majority of tidal volume during quiet inspiration, with the intercostal, abdominal, and accessory muscles (sternocleidomastoid and neck muscles) providing additional negative pressure. The elastic recoil of the lungs and thorax produces expiration, with inspiration 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.

Preoperative Assessment

The preoperative assessment of the respiratory system in a child is based on history, physical examination, and evaluation of vital signs. 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 ventilation is a complex process involving many systems beyond the lung, preoperative pulmonary appraisal must include airway, musculoskeletal, and neurologic assessment that might impact gas exchange under anesthesia or in the postoperative period. The potential impact of esophageal reflux, cardiac, hepatic, renal, or hematologic disease on gas exchange and pulmonary function should also be considered. The child's reaction to the presence and approach of medical staff may determine the order and even the position of the history and examination.

The history should establish the current respiratory status, the presence of chronic and present status of pulmonary disease. Because children may be unwilling or unable to give a reliable history, parents or caregivers are often the sole or an important supplemental source of information. Respiratory issues especially pertinent to the pediatric population include upper respiratory tract infections (URIs), reactive airway disease/asthma, ventilatory problems relating to prematurity, and congenital diseases. Viral URIs are common in children, and the time, frequency, and severity of infection should be established. Reactive airway disease is also widespread in the pediatric population, and the precipitants, frequency, severity, and relieving factors should be determined. Chronic pulmonary diseases often have a variable clinical course, and a history of acute exacerbations of chronic problems should be elicited. The conceptual age at birth, the current postconceptual age, neonatal respiratory difficulties, and prolonged intubation in the neonatal period are particularly important to ascertain in the younger child because subglottic stenosis and/or tracheomalacia are common sequelae. Whereas congenital lesions may manifest at birth, symptoms of airway obstruction may only become evident later in life.

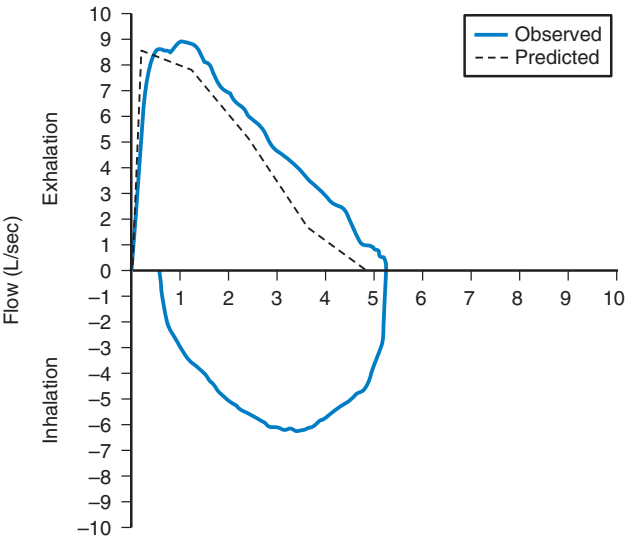
Physical examination begins when you enter the room. Particularly with young children, your best opportunity to observe them before they react to your presence is from across the room, and inspection from a distance can provide useful information. Respiratory rate is a sensitive marker of pulmonary problems, and scrutiny before a young child becomes agitated and hyperventilates is an important means of assessment. Pulse oximetry, the "fifth vital sign," 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, whereas intense cyanosis can also be detected from a distance. Weight may relate to pulmonary function: patients 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. 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 will improve diagnostic yield and patient satisfaction.

Pulmonary Function Tests

Further investigations of pulmonary function include chest radiography, 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 times when 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 will be adequate to establish an appropriate anesthetic plan. Before requesting a new investigation, the clinician should have a clear idea of what question is being asked and how the answer will modify anesthetic management and outcome.

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.[4] Figure 11-2 illustrates a normal pulmonary function test (normal flow-volume loop and spirometry parameters). Pulmonary function studies include dynamic studies, measurement of static lung volumes, and diffusing capacity. The



Spirometry Parameter	Units	Predicted Value	Observed 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 11-2. Normal pulmonary function test (*broken line, predicted curve, solid line, measured curve*). The normal flow-volume curve obtained during forced expiration rapidly ascends to the peak expiratory flow. Shortly after reaching the peak expiratory flow (highest point on curve), the curve descends with decreasing volume following a reproducible shape that is independent of effort. In this normal flow-volume curve, the FEV_1/FVC, FEV_1, and FVC 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.

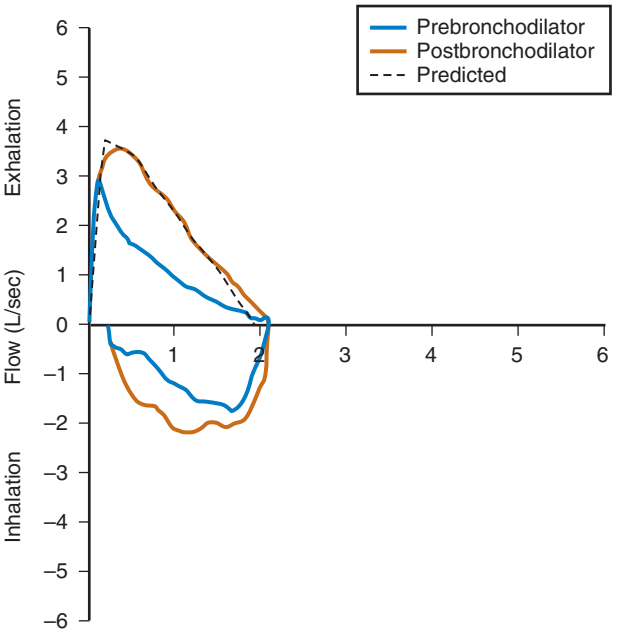
dynamic studies, which are the most commonly used, include spirometry, flow-volume loops, and measurement of peak expiratory flow. A reliable study requires patient effort and cooperation, accurate testing equipment, as well as a skilled and knowledgeable staff. Although the maneuvers needed to obtain measurements appear straightforward, studies are valid only if they reflect maximal effort and are reproducible. Children older than the age of 6 years can often perform adequately, although children as young as age 3 years have been shown to be able to perform spirometry with coaching. There must be three acceptable maneuvers and two studies need to have values for both FVC and FEV_1 that are within 0.15 L of each other before the study can be accepted. Table 11-1 presents common indications for pulmonary function testing in children.

An obstructive process is characterized by decreased velocity of airflow through the airways (Fig. 11-3), whereas a restrictive defect produces decreased lung volumes (Fig. 11-4). Examining the ratio of airflow to lung volume assists in differentiating these components of lung disease. Spirometry measures the volume of air inspired and expired as a function of time and is by far the most frequently performed test of pulmonary function in children. With a forced maneuver, the volume exhaled from full inhalation in the first second is referred to as the forced expiratory volume in the first second (FEV_1). The maneuver is completed when the subject has completed exhaling as fast as possible after a maximal inhalation. This is referred to as the forced vital capacity (FVC). Normally, a child should be able to exhale more than 80% of the total lung volume in the first

Table 11-1. 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 prediction of the prognosis and quantitate 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, 2006, p 168.

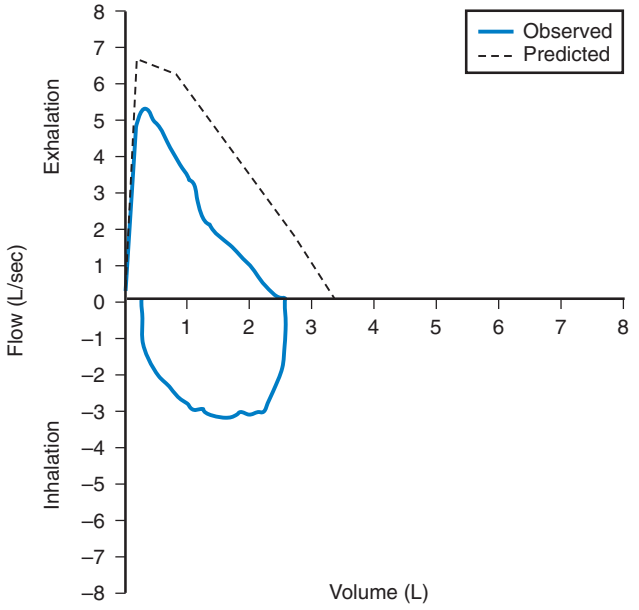


Spirometry Parameter	Units	Predicted Value	Observed Pre	Observed Percent Pred	Observed Post	Observed Percent Pred	Percent Change
FVC	Liter	1.94	2.15	111	2.14	110	0
FEV_1	Liter	1.71	1.30	76	1.82	106	40
FEV_1/FVC	Percent	90	60	67	85	94	42

Figure 11-3. This flow-volume curve demonstrates a reversible obstructive defect. The forced expiratory volume over 1 second (FEV_1) as a percentage of forced vital capacity (FVC), or total volume exhaled, is decreased in patients with airway obstruction. The pre-bronchodilator curve shape (*blue*) is scooped. After administration of a short-acting bronchodilator, the curve shape (*brown*) appears normal and there is an increase in both the 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.

second of exhalation. Children with obstructive lung disease have decreased air flow in relation to lung 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 11-2, see Fig. 11-3). The FEV_1 needs to be interpreted in the context of the FVC. A low FEV_1 itself is not sufficient to make the diagnosis of airflow obstruction. Those with restrictive lung disease have a 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 11-2 and Fig. 11-4).

Most children with respiratory problems have an obstructive pattern, whereas 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, or vocal cord dysfunction. Although the diseases arise from specific isolated genetic disorders, children with cystic fibrosis and sickle cell disease can have very variable pulmonary pathologic processes, with both obstructive and restrictive components of lung disease. Bronchopulmonary dysplasia may also have both obstructive and restrictive pathology. 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 processes such as large bullae or congenital cysts. Alveolar filling defects, such as lobar pneumonia, also reduce lung volume and can be considered as restrictive processes.



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 11-4. Flow-volume curve demonstrating a restrictive defect (*predicted, broken line; measured, solid blue line*). The flow-volume curves in patients with restrictive defects appear to be near normal in configuration but smaller in all dimensions. The FEV_1/FVC ratio is normal, but both the FEV_1 and FVC are reduced. The curve shape appears normal. This child has interstitial lung disease. Pred, predicted.

Table 11-2. Characteristics of Obstructive and Restrictive Patterns of Lung Disease

	Disease Category	
Measurement	*Obstructive*	*Restrictive*
FVC	Normal/decreased	Decreased
FEV_1	Decreased	Decreased
FEV_1/FVC	Decreased	Normal

FEV_1, forced expiratory volume over 1 second; FVC, forced vital capacity.

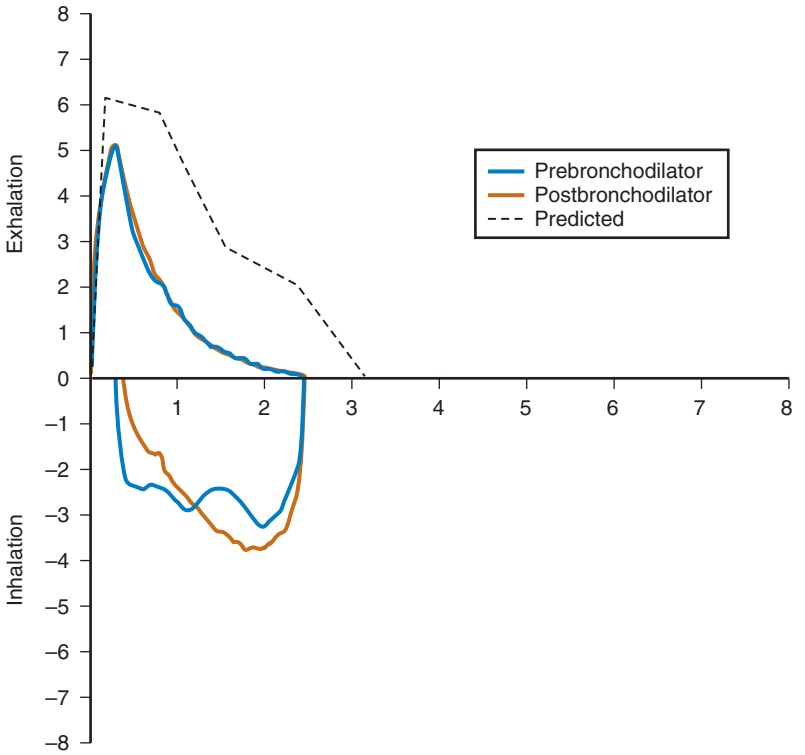
Additional uses of pulmonary function tests are as aids to differentiate fixed from variable obstruction and to locate the obstruction as above or below the thoracic inlet (Figs. 11-5 to 11-7 [see website for Fig. 11-7B]). This information can be gleaned from distinctive changes in the configuration of flow-volume loops, a graphic representation of inspiratory and expiratory flow volumes plotted against time. The flow-volume loop in Figure 11-2 is normal. A fixed central airway obstruction, such as a tumor or stenosis, may obstruct both inspiration and expiration, flattening the flow-volume curve both on inspiration and expiration. The child with tracheal stenosis, for example, has flattening of both inhalation and exhalation curves (see Fig. 11-6). A variable obstruction will tend to affect one part of the ventilatory cycle. When inhaling, 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 intrathoracic lesions will have a more pronounced effect on exhalation. This produces characteristic flow-volume patterns.

Spirometry cannot, however, provide data about absolute lung volumes, because it measures the amount of air entering or leaving the lung rather than the amount of air in the lung. Thus, information about functional residual capacity (FRC) and lung volumes calculated from FRC, such as total lung capacity and residual volume, must be computed via different means. These include gas dilution and body plethysmography. Gas dilution is based 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.

In addition to diagnostic uses, spirometry is used to assess the indication for, and efficacy of, treatment. For example, the obstruction in those 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 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 indication of asthma control. A low FEV_1 or an acute decrease from baseline may reflect a child whose asthma is not under good control and therefore who potentially is at greater risk for a perioperative exacerbation (see Fig. 11-3).

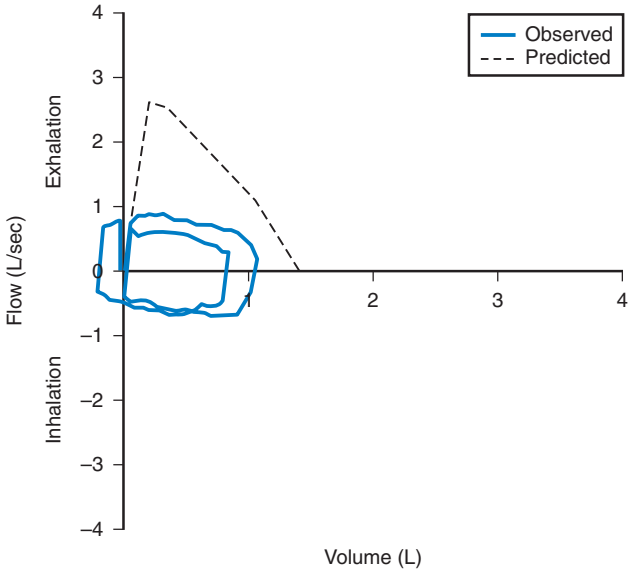
Perioperative Etiology and Epidemiology

Respiratory problems account for the majority of perioperative morbidity in children.[5,6] The triggers of these problems include



Spirometry Parameter	Units	Predicted Value	Observed Pre	Observed Percent Pred	Observed 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 11-5. Pulmonary function test demonstrating a nonreversible obstructive defect. The FEV_1/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 Figure 11-3. This child has cystic fibrosis with a nonreversible obstructive defect. Post, postbronchodilator; Pre, prebronchodilator; Pred, predicted.



Spirometry Parameter	Units	Predicted Value	Observed 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

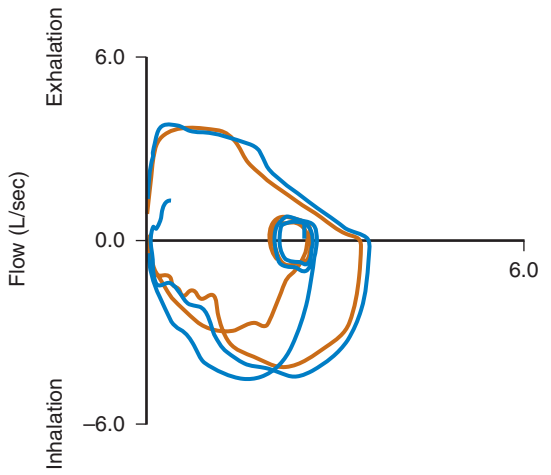
Figure 11-6. Pulmonary function test showing an extrathoracic airway obstruction; both the inspiratory and expiratory limbs of the flow-volume curve are flattened. This child has subglottic stenosis that developed at the site of her tracheotomy 2 years after the tracheostomy had been removed. Pred, predicted.

airway manipulation, the alteration of airway reflexes by anesthetic drugs, the surgical insult, and the depression of breathing by anesthetic and analgesic medications. Adverse events comprise laryngospasm, airway obstruction, bronchospasm, hemoglobin oxygen desaturation, prolonged coughing, atelectasis, pneumonia, and respiratory failure.[7,8] The incidence of respiratory problems in one study of 755 children was 21% intraoperatively and 13% in the postanesthetic care unit.[7] Various disease states can further affect the frequency of respiratory complications in pediatric anesthesia.

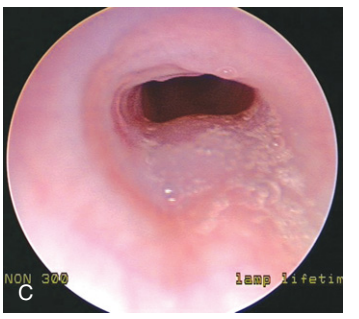
Younger age of the child has consistently been found to be a risk factor for respiratory morbidity.[5,6,9,10] The neonate is particularly sensitive to respiratory problems for multiple reasons. Although the FRC approaches adult levels within days, a persistently large closing capacity increases the likelihood of alveolar collapse and intrapulmonary shunt. Residual patency of the ductus arteriosus can contribute to shunting. The greater metabolic rate increases oxygen requirements and decreases the time to arterial desaturation after an interruption to ventilation and gas exchange. The work of breathing is greater, consequently, because of high-resistance, small-caliber airways, increased chest wall compliance, and reduced lung compliance.

Upper Respiratory Tract Infection

Upper respiratory tract infections are a common problem among young children, typically occurring as often as six to eight times a year, with possibly an even greater incidence among children in day care. Viruses cause the majority of URIs, with rhinoviruses constituting approximately one third to one



Spirometry Parameter	Units	Prebron-chodilator	Observed Percent Pred	Postbron-chodilator	Observed Percent Pred	Percent Change
FVC	Liter	3.53	102	3.63	106	3
FEV_1	Liter	2.63	89	2.65	90	0
A FEV_1/FVC	Percent	74.7		72.8		–3



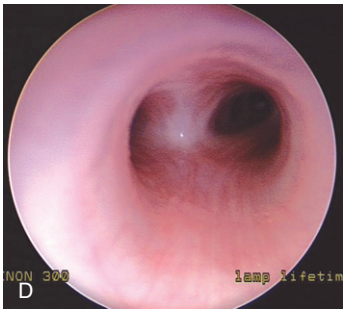


Figure 11-7. A, Pulmonary function test from a child with an intrathoracic airway obstruction (vascular ring). The flow-volume curve shapes suggest a fixed expiratory obstruction. The shape of the inspiratory link is normal; the expiratory flow limb is flattened on both the pre-bronchodilator (*brown*) and post-bronchodilator (*blue*) flow-volume curves. **B,** (see website) A magnetic resonance angiogram accompanies the flow loop. **C,** Slit-like tracheal compression before repair. **D,** Note the marked improvement in the tracheal lumen after division of the vascular ring. (**B** courtesy of Brian O'Sullivan, MD; **C** and **D** courtesy of Christopher Hartnick, MD.) Post, postbronchodilator; Pre, prebron-chodilator; Pred, predicted.

half of etiologic species.[11] Other common causative viruses include adenovirus and coronavirus. Although most URIs are short-lived, self-limiting infections, and by definition limited to the upper airway, they may increase airway sensitivity to noxious stimuli or secretions for several weeks after the infection. The mechanisms probably involve a combination of mucosal invasion, chemical mediators, and altered neurogenic reflexes.[11] URIs may also impair pulmonary function by decreasing FVC, FEV_1, peak expiratory flow, and diffusion capacity.[12,13] These data suggest that children with recent URIs may have an increased incidence of perioperative pulmonary complications and, consequently, may benefit from a postponement of anesthesia.

Despite this suggestive evidence, the practical clinical consequences are less well defined.[14] In 1979, a case series of 11 children noted significant perioperative complications, including atelectasis; all but 1 of the children had a reported respiratory tract infection in the preceding month.[15] Two postoperative deaths in children with URIs have been reported[16,17]: in one case, premature extubation and inadequate monitoring may have been implicated,[18] but, in the other, postmortem examination suggested viral myocarditis.[16] Larger studies, however, failed to detect a high risk of major complications.[19,20] Compared with children without URIs, children with recent URIs desaturate more quickly, but this typically responds rapidly to oxygen administration and alveolar recruitment.[21] Other specific complications include bronchospasm and laryngospasm, breath holding, arterial oxygen desaturations (Spo_2 below 90%), and severe coughing (Table 11-3).[10,19,20,22] Although there appears to

Table 11-3 Incidence of Common Upper Respiratory Tract Infection–Associated Perioperative Adverse Events

	Laryngospasm (%)		Bronchospasm (%)		Spo_2 (%)	
Study	*URI*	*No URI*	*URI*	*No URI*	*URI*	*No URI*
Tait and Knight, 1987[87]	1.3	1.2				
Tait et al., 1998[88]	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*
Cohen and Cameron, 1990[9]	2.2	1.7				
Levy et al., 1992[89]					[<93] 63.6	59.0
DeSoto et al., 1988[90]					[<95] 20.0	0*
Rolf and Coté, 1992[22]	5.9	3.3	13.3	0.6*	[<85] 13.3	10.5

*$P < .05$ versus corresponding URI group.
Reproduced from Tait AR: Anesthetic management of the child with an upper respiratory tract infection. Curr Opin Anaesthesiol 2005; 18:603-607.

be an increased risk of adverse perioperative events, there is little residual morbidity; and most complications can be predicted and successfully managed without long-term sequelae.[11,23]

An approach to the problem of the child with a URI is to detect the pathologic process and associated comorbidity, establish the acuity and severity of the URI, and then decide whether to modify anesthetic technique or postpone surgery (Table 11-4, Fig. 11-8). The presence of a current or recent URI should be established, because this will alert the anesthesiologist to an increased risk of perioperative problems. The basis of diagnosis 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 >38.5°C [101.3°F]), change in demeanor or behavior, dyspnea, productive cough, 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, these 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 generally transient and easily managed.[22] Elective surgery should be postponed for children with more severe symptoms, such as mucopurulent secretions, productive cough, pyrexia greater than 38°C (100.4°F), or pulmonary involvement. There are no definitive data to establish the exact duration of postponement, but 3 to 4 weeks is suggested to be a prudent timeframe, although airway reactivity may last for 6 to 8 weeks.[11] This reflects a balance between the time to diminish airway hyperreactivity and perioperative risk and the incidence of URI recurrence and need to perform the procedure. If bacterial infection is suspected, appropriate antibiotics should be prescribed.

Judgment about the suitability of a child for surgery becomes more difficult when the symptoms of the URI lie somewhere between the extremes of mild and severe. In these instances, other considerations play a greater role in assessment of the risk/benefit ratio. These include the presence of comorbid conditions, such as asthma or cardiac disease, the type and urgency of surgery, the age of the child and history of prematurity, and the frequency of URIs. The comfort level and experience of the anesthesiologist may also be important in the decision to proceed with or postpone surgery. The need for postoperative admission of a child after anesthetic complications or exacerbation of the URI may expose other patients to a contagious illness. Consideration must also be given to the complexity and anticipated duration of the surgery and implantation of foreign bodies such as pins, rods, or other implants (see Chapter 4).

If the decision is to proceed with general anesthesia, management is aimed at minimizing secretions and avoiding stimulation of a potentially sensitized and inflamed airway. Use of an endotracheal tube (ETT) should be avoided, if possible, because it increases the risk of complications, especially in younger children.[20] Although airway management with a face mask is associated with the least incidence of complications, it may be inappropriate for certain cases. Similarly, a laryngeal mask

Table 11-4. Risk Factors for Perioperative Adverse Events in Children with URIs

Study	URI?	Factors	RR/OR
Parnis et al., 2001[19]	URI and non-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
		ETT in child <5 yr	1.9
		Prematurity (<37 wk)	2.3
		Nasal congestion	1.4
		Passive smoker	1.6
		Reactive airway disease	1.8
		Surgery of airway	1.8
Bordet et al., 2002[10]	URI and non-URI	Age <8 yr	1.8
		LMA	2.3
		Respiratory infections	3.7
Mamie et al., 2004[7]	Non-URI	Nonpediatric anesthesiologist	1.7
		ENT procedure	1.8
		ETT without relaxants	1.2

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

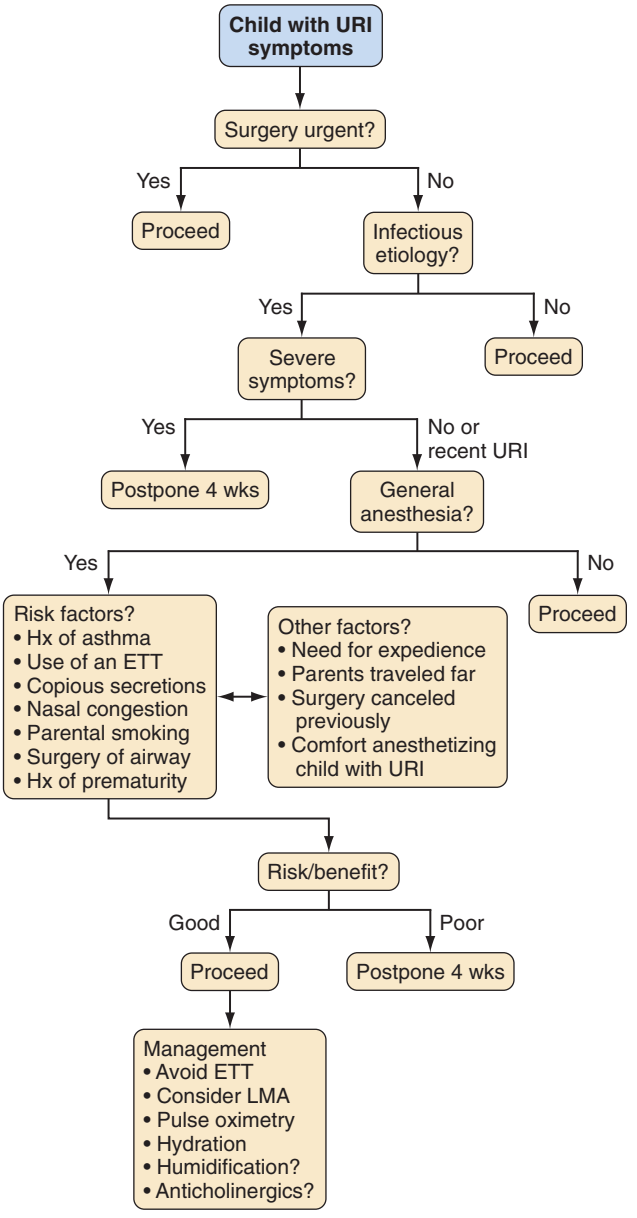


Figure 11-8. Suggested algorithm for the assessment and management of the child with an upper respiratory tract infection. ETT, endotracheal tube; Hx, history; LMA, laryngeal mask airway; URI, upper respiratory tract infection. (Reproduced from Tait AR, Malviya S: Anesthesia for the child with an upper respiratory tract infection: still a dilemma? Anesth Analg 2005; 100:59-65.)

airway (LMA) is associated with fewer episodes of respiratory events than an ETT, but its use may be contraindicated by the type of surgical procedure and the need to protect the airway from pulmonary aspiration of gastric contents. Whatever the choice of airway management, it is essential that the depth of anesthesia is adequate to obtund airway reflexes, particularly during placement of an ETT or an LMA. The data on optimal depth of anesthesia for removal of airway devices are equivocal. Some studies in children with[20] or without[24] URIs found no difference in emergence complications between awake versus deep extubation, whereas others found a greater incidence of arterial oxygen desaturation or coughing on awake removal of ETT or LMA in children with URIs.[25,26]

Because viral infections affect the nature and quantity of secretions, and because copious secretions are identified as risk factors, the airway should be suctioned under deep anesthesia to attempt to decrease the risk of airway irritation or mucus plugging of a bronchus or ETT. For longer cases, adequate intravenous hydration and humidification of inspired gases may minimize inspissation and plugging by secretions. The use of anticholinergics such as glycopyrrolate or atropine may decrease secretions and blunt vagally mediated airway hyperreactivity, but definitive data on efficacy are lacking. Bronchodilators may be of potential benefit, but one study found no effect on URI-related complications.

Lower Airway Disease

Asthma is one of the most common chronic diseases of childhood, affecting an estimated 6.2 million children in the United States.[27] Asthma may be associated with an increased risk of perioperative bronchospasm and, less commonly, anaphylaxis, adrenal crisis, and ventilatory barotrauma, such as pneumothorax or pneumomediastinum. 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, the modification of anesthetic technique as appropriate, and the recognition and treatment of complications if they occur.

Asthma is difficult to define precisely because the exact pathophysiology remains unclear. The word "asthma" derives from the Greek *aazein,* which translates as "to breathe with open mouth or to pant."[28] 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.[27] Clinical expressions of asthma include wheezing, persistent dry cough, chest tightness or discomfort, 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 or fully responsive to current available treatments. There is a strong association between asthma and atopy, or immunoglobin E (IgE)-mediated hypersensitivity.[27] Many aspects of asthma were reviewed in depth by a panel of experts; this review of the world's literature is available elsewhere but serves as the basis for much of our discussion.[27]

The diagnosis of asthma may be challenging because wheezing and bronchospasm may arise from many disease processes. Asthma itself is unlikely to be a single disease entity, with the disease process markedly modified by various genetic and environmental factors.[27,28] Many young children wheeze, and there is no definitive confirmatory blood, histologic, or radiographic diagnostic test. Given the difficulty with diagnosis, the name "preschool wheezers" may be a more appropriate description for young children with reversible airway obstruction than a diagnosis of "asthma."[28] The Tucson birth cohort study is the largest U.S.-based longitudinal study to attempt to differentiate wheezing or asthma phenotypes in children who did not subsequently develop asthma.[29-31] This study examined 826 children at ages 3

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" are children who wheeze only in response to viral infections, typically during the first 3 years of life. "Non-atopic wheezers" are children who wheeze beyond the first few years of life, often in response to viral infections, but who are less likely to persistently wheeze in later childhood. "Atopy-associated wheezers" are children with a reversible wheeze together with a tendency toward IgE-mediated hypersensitivity; they have the greatest risk of persistent symptoms into late childhood and adulthood.[29]

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, and pollution) that occur during a crucial time in the development of the immune system.[27] The population of young children who wheeze, therefore, includes a spectrum of disorders rather than one specific pathologic process.

Asthma must be differentiated from other distinct causes that produce similar symptoms (Table 11-5). Tracheomalacia or bronchomalacia may produce wheezing, but this tends to be present from birth, which is unusual for asthma. The wheezing is commonly of a single pitch and is heard loudest in the central airways, as opposed to asthma, which typically produces polyphonic sounds from the lung periphery. Breathing difficulties due to chronic aspiration are often related to feeding times. Unremitting wheeze or stridor is often due to 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 and still have asthma. A cough with or without wheeze may be due to a viral infection, whereas a persistent productive cough may suggest suppurative lung disease such as cystic fibrosis. The response of the cough to asthma medication suggests the diagnosis of asthma.

The exact incidence of perioperative complications in the pediatric asthma population is difficult to ascertain, owing to 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 found an incidence of documented bronchospasm of 1.7% and no pneumonia, pneumothorax, or death.[32] Of 211 children younger than age 12 years, none developed bronchospasm at the time of surgery. A retrospective review of over 136,000 computer-based anesthetic records found an incidence of 0.8% of bronchospasm in patients with asthma.[33] By contrast, older studies from the 1960s noted incidences of wheezing of 7% to 8% in asthmatic patients.[34,35] A blinded, prospective study of 59 asthmatic patients detected transient wheezing after intubation in 25% of cases; however, most events were brief and self-limited.[36] An editorial review of the subject of asthma and anesthesia concluded that, although the true incidence of major complications is low, severe adverse outcomes do result from bronchospasm and patients with asthma are at heightened risk for severe morbidity.[37]

Table 11-5. Causes of Wheezing in Children

Acute	
Asthma	Pneumothorax
Foreign body	Endobronchial intubation
Bronchiolitis	Herniated ETT cuff
Inhalation injury	
Recurrent or Persistent	
Asthma	Mediastinal mass
Foreign body	Tracheomalacia/bronchomalacia
Bronchiolitis	Vascular ring
Cardiac failure	Tracheal web/stenosis
Cystic fibrosis	Bronchial stenosis
Sickle cell disease	Roundworm infestation
Recurrent aspiration	

Both the severity and the control of asthma must be established preoperatively. The two aspects of the current disease state should be clearly differentiated.[38] For example, severe asthma may be well controlled, whereas mild asthma may be poorly controlled, but both situations may have heightened potential for perioperative complications because even the child with intermittent asthma can have a severe exacerbation. Severity and control may be assessed by the frequency of symptoms, medication use, emergency department attendance, hospitalizations, and need for ventilatory support. Maintenance treatment of asthma is based on a stepwise approach; the type of therapy is, therefore, often an indication of severity. An approach to assessment of severity and control in children aged 5 to 11 years is outlined in Tables 11-6 and 11-7 (see website). Short-acting inhaled β agonists are first-line therapy, with inhaled corticosteroids for those 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 the addition of an alternative treatment to a lower 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 include a high dose of inhaled corticosteroid or commencing an oral corticosteroid (Fig. 11-9, see website).

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 (steps 5 or 6 in Fig. 11-9 [see website]). 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 following long-term response to therapy but are of little use in the immediate routine preoperative workup of cases at a stable clinical baseline. The 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.

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,[38] so the sensitivity of medication prescription as a marker of disease activity must be viewed with some caution. Some studies of asthma have found a poor correlation between assessment of disease sensitivity and the occurrence of perioperative bronchospasm. Disease *activity*, as noted by recent asthma symptoms, use of medications for symptom treatment, and recent therapy in a medical facility for asthma, was significantly associated with perioperative bronchospasm in one study.[32]

Children should continue their regular medications before anesthesia. Midazolam has been reported to be a safe premedication for asthmatics.[39] Corticosteroids may help prevent perioperative bronchospasm, although controlled clinical data to substantiate this practice are lacking.[40] Inhaled β agonists before or shortly after induction of anesthesia attenuate the increases in airway resistance associated with tracheal intubation.[41,42] Ketamine is the traditional choice of intravenous induction agent in patients with severe asthma, although this has not been substantiated in clinical trials.[43,44] Propofol is typically preferred over thiopentone because it causes less bronchoconstriction.[36,45] Both halothane and sevoflurane are used extensively as inhalation induction agents.

Airway manipulation is a potent stimulus for bronchospasm. In children with URIs, when the airways may be acutely hyperactive, the avoidance of intubation is associated with a reduced incidence of pulmonary complications.[19] There are inadequate clinical outcome data on the perioperative management of asthma to make definitive recommendations about airway management. Nevertheless, avoidance of airway stimulation when possible seems a sensible approach. For short cases, a face mask may be adequate; a laryngeal mask airway similarly is less of an irritant than an ETT. If endotracheal intubation is mandatory, a deep plane of anesthesia blunts airway hyperreactivity. Similarly, unless contraindicated by other factors, deep extubation may be preferable 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 expiration with increased respiratory effort, increased airway pressures, a slow upslope on the end-tidal CO_2 monitor, raised end-tidal CO_2, and hypoxemia (see also Fig. 37-9A-B). Other causes of wheezing must be excluded, such as partial ETT obstruction (secretions or herniation of the cuff causing obstruction), mainstem intubation (deep endobronchial intubation), aspiration, pneumothorax, or pulmonary edema. Mechanical obstruction of the circuit or ETT must also be excluded. First-line responses to bronchospasm involve removing the triggering stimulus if possible, deepening anesthesia, increasing F_{IO_2} if appropriate, and increasing expiratory time to minimize alveolar air trapping. In severe status asthmaticus, ventilation strategy should focus primarily on achieving adequate oxygenation, rather than attempting to normalize P_{aCO_2} at the potential cost of inducing pulmonary barotrauma. Inhaled β agonists can be delivered by nebulizer or by a metered-dose inhaler down the airway device with specially designed adaptors (see also Fig. 37-10). Alternatively, a 60-mL syringe can be used to deliver doses of the nebulizer into the breathing circuit (Fig. 11-10). All children who experience anything more than minor bronchospasm should also receive corticosteroids if they have not already done so.

The anesthesiologist may be involved in the management of bronchospasm when consulted to assist a child in the emergency department or on the wards. A drowsy, silent child with a quiet chest on auscultation is in imminent danger of respiratory arrest and requires emergent intubation by an experienced practitioner. Signs and symptoms to assess the severity of an asthma exacerbation are outlined in Table 11-8, and an algorithm for management issued by the American National Heart, Lung and Blood Institute is presented in Figure 11-11 (see website). Oxygen is recommended for most children to maintain the hemoglobin saturation 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 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, intravenous magnesium may decrease the likelihood of intubation, although the evidence is limited. Current recommended drug dosages are listed in Table 11-9 (see website). Methylxanthines such as theophylline are not recommended as treatment for acute exacerbations because they produce no added benefit but expose the child to the complications from toxicity. Antibiotics are not recommended except for comorbid conditions. Aggressive hydration is not recommended for adults or older children, although it may be indicated in younger children who become dehydrated as a result

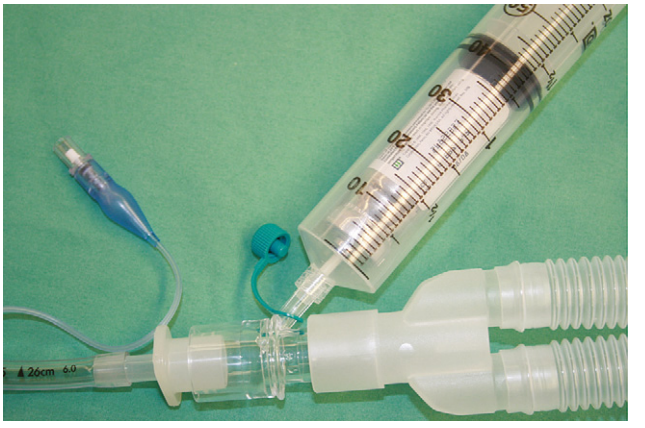


Figure 11-10. A 60-mL syringe may be attached to a port in the circuit to administer aerosolized drugs such as albuterol.

Table 11-8. Formal Evaluation of Asthma Exacerbation Severity

	Mild	Moderate	Severe	Subset: Respiratory Arrest Imminent
Symptoms				
Breathlessness	While walking Can lie down	While at rest (infant—softer, shorter cry, difficulty feeding) Prefers sitting	While at rest (infant—stops feeding) Sits upright	
Talks in	Sentences	Phrases	Words	
Alertness	May be agitated	Usually agitated	Usually agitated	Drowsy or confused
Signs				
Respiratory rate	Increased	Increased	Increased	
Guide to rates of breathing in awake children:				
Age <2 months 2-12 months 1-5 years 6-8 years	*Normal rate* <60/min <50/min <40/min <30/min			
Use of accessory muscles; suprastemal 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	Slightly increased	Increased	Tachycardia	Bradycardia
Guide to normal pulse rates in children:				
Age 2-12 months 1-2 years 2-8 years	*Normal rate* <160/min <120/min <110/min			
Pulsus paradoxus	Absent <10 mm Hg	May be present 10-25 mm Hg	Often present >25 mm Hg (adult) 20-40 mm Hg (child)	Absence suggests respiratory muscle fatigue
Functional Assessment				
PEF Percent predicted or Percent personal best	≥70%	Approx. 40-69% or response lasts <2 hours	<40%	<25% *Note:* PEF testing may not be needed in very severe attacks
PaO_2 (on air) and/or PCO_2	Normal (test not usually necessary)	≥60 mm Hg (test not usually necessary)	<60 mm Hg: possible cyanosis	
	<42 mm Hg (test not usually necessary)	<42 mm Hg (test not usually necessary)	>42 mm Hg: possible respiratory failure (see text)	
SaO_2% (on air) at sea level	>95% (test not usually necessary)	90-95% (test not usually necessary)	<90%	
	Hypercapnia (hypoventilation) develops more readily in young children than in adults and adolescents.			

PEF, peak expiratory flow; SaO_2, oxygen saturation.
Medified 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.

of decreased oral intake and increased respiratory rate. Chest physical therapy and mucolytics are not generally recommended.

Children with severe atopy-associated asthma are possibly at greater risk of developing anaphylaxis in response to neuromuscular blocking drugs, antibiotics, or latex.[40] Bronchospasm due to asthma is differentiated from that due to anaphylaxis by additional systemic signs such as angioedema, flushing, urticaria, and cardiovascular collapse. Adrenal crisis is another potential complication associated with severe asthma, owing to iatrogenic suppression of the hypothalamic-pituitary-adrenal (HPA) axis. This manifests as hypotension, hypoglycemia, or seizures. HPA suppression should be assumed in any child on 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. High doses, prolonged therapy for more than a few weeks, and evening dosing will all cause HPA suppression that may persist for up to a year. Prophylactic corticosteroid cover is indicated for those recently requiring systemic corticosteroids and should be considered for those on high-dose inhaled corticosteroids, when their corticosteroid regimen is interrupted by the surgical schedule (see Chapter 24).

Cystic Fibrosis

Cystic fibrosis (CF) is an autosomal recessive disorder. The incidence of cystic fibrosis is approximately 1 in 2000 white births, making it the most common fatal inherited disease of this population group. In 1989, a mutation that causes CF was localized on the long arm of chromosome 7. The disease syndrome usually arises from one of several mutations in the gene that codes for CF transmembrane conductance regulator, a membrane glycoprotein chlorine channel that contributes to regulation of ion flux at various epithelial surfaces.[46] This disruption of electrolyte transport in epithelial cells in the sweat ducts, airway, pancreatic duct, intestine, biliary tree, and vas deferens can variously cause elevated 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, suggesting that genetic, environmental, and therapeutic factors affect expression. Modifier genes may include genes encoding transforming growth factor and an anti-inflammatory mediator, macrophage inhibitory factor.[47]

Lung disease is the main cause of morbidity and mortality in CF and, consequently, is the focus of anesthetic concern. The pathophysiology involves mucus plugging, chronic infection, inflammation, and epithelial injury.[47] Mucus clearance defends the lung against inhaled bacteria. The mucociliary transport system requires two fully functioning layers to be effective. The base is a layer of ciliary epithelia bathed in a watery liquid (sol), overlaid by more viscous gel (mucus) that is responsible for transporting particles along the tips of the cilia. Normally, mucus is moved at the speed of about 10 mm/min, thus expelling foreign particles and pathogens from the lungs. The efficacy of clearance is dependent on adequate hydration of the mucus.[48] Lack of regulation of sodium absorption and chloride secretion causes decreased liquid on the airway luminal surfaces, slows mucus clearance, and promotes the formation of adherent plugs to the airway.[49] Increased secretions, viscous mucus, and impaired ciliary clearance contribute to airway impaction, providing the nidus for infection. At birth, the lung is normal, or nearly so.[46] However, chronic and recurrent bacterial infections occur early in life, assisted by the pooling of secretions and impaired neutrophil bacterial killing on airway surfaces.[47,50] 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 invades later in life, acquires a mucoid phenotype, and forms a biofilm in the lung, an event 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 death rates from lung disease. Chronic lung damage progresses to bronchiectasis and moderate 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 are commonly obstructive in nature: increased FRC, decreased FEV_1, decreased peak expiratory flow rate, and decreased vital capacity (see Fig. 11-5). Compensatory hyperventilation typically produces a lowered $Paco_2$, 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, consequent on pancreatic insufficiency, failure of enzyme secretion, impaired gastrointestinal motility, abnormal enterohepatic circulation of bile, increased caloric demand due to severe lung disease, and anorexia of chronic disease.[46] 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 age 13 years have insulin-dependent diabetes, and the incidence increases with age. Evidence is accumulating that diabetes contributes to the lung disease and worse outcome.[47] In addition, classic diabetic complications are being reported in CF patients. Hepatic dysfunction results in decreased plasma cholinesterase and clotting factors II, VII, IX, and X, whereas malabsorption of vitamin K may also contribute to coagulation issues.

When CF was first distinguished from celiac disease in 1938, life expectancy was approximately 6 months. Since then, substantial advances in aggressive supportive treatment have improved mean median survival to over 30 years (Fig. 11-12).[46] More than 35% of patients with CF are now older than 18 years of age. The pillars of treatment include nutritional repletion, relief of airway obstruction, and antibiotic therapy for lung infection. Suppression of inflammation has been a more recent focus of therapy. Organ transplantation, in particular, lung transplantation, can also extend life when end-stage organ failure supersedes (see Chapter 29).[46]

The multisystem nature of the disease and changing demographics mean children present for a wide variety of surgical procedures. The most common indications for anesthesia in children are nasal polypectomy and ear/nose/throat surgery, consequent on the frequency of upper airway pathologic processes such as chronic sinusitis and nasal polyps (Table 11-10).[51,52] The investigation or correction of gastrointestinal

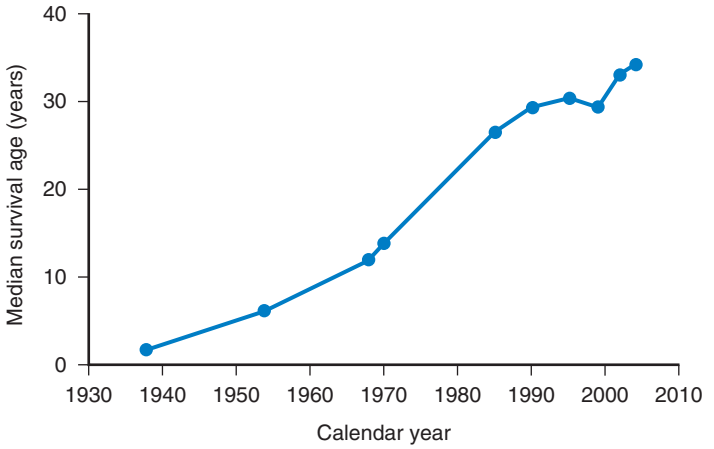


Figure 11-12. Median survival for patients with cystic fibrosis at various times since the first description of the disease. Data before 1970 are gleaned from the then-current literature. Data since 1985 are from the Cystic Fibrosis Foundation Data Registry and represent projections of median survival 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.)

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 due to portal hypertension, insertion of venous access devices, and incidental surgical problems.[52-54] The pediatric anesthesiologist may be involved in the care of adult patients because of the perception that CF remains a "pediatric disease." Surgical procedures 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 an anesthetic. Historically, morbidity and mortality from pulmonary complications were high. A retrospective 18-year review of 133 anesthetics in 93 patients, published in 1964, noted perioperative mortality of 27%, with pulmonary complications occurring in 42% of cases.[55] A retrospective 11-year review of 144 anesthetics, published in 1972, reported a perioperative mortality of 4%.[51] More recent studies record better outcomes. A 1985 study of 126 anesthetics found no mortality and a CF-specific complication rate, predominantly pulmonary, of 9%.[52] A 1984 study of 18 patients for pleural surgery concluded that, although the risks for this procedure were great, the anesthetic hazards of CF could be minimized with careful management.[56] A study of 11 patients undergoing anesthesia for injection of esophageal varices found no serious anesthetic complications but detected significant deterioration in pulmonary function tests shortly after anesthesia[57]; it was unclear if these changes persisted past the immediate postoperative period. A larger study found no difference between pulmonary function tests measured 3 months before and 3 months after surgery.[52] A recent study of 199 anesthetics in 53 patients for ear/nose/throat surgery found a 5% incidence of minor pulmonary problems and no deaths.[58] These limited data suggest that although pulmonary complications are a problem, they can be successfully anticipated and preempted by modern anesthetic management techniques.

Table 11-10. The 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

Reproduced from Della Rocca G: Anaesthesia in patients with cystic fibrosis. Curr Opin Anaesthesiol 2002; 15:95-101.

An assessment of the severity, current state and progression of pulmonary disease should guide anesthetic planning. Fitness is a positive predictor of survival,[46] and exercise tolerance is a useful marker of pulmonary function. The quality and quantity of secretions, recent and chronic infections, the use and effectiveness of bronchodilators, and number of hospitalizations are also important points to elucidate on 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.[54] Pulmonary function should be optimized preoperatively, with chest physiotherapy, bronchodilators, and humidified nebulizers to improve clearance of secretions.

Children are often emotionally vulnerable, not simply owing to the usual preoperative anxieties but secondary to 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.[52,58] Prophylactic use of osmotic laxatives may be indicated if opioid-induced ileus is anticipated.[54] Although aspiration has not been reported as a complication in the literature, the incidence of gastroesophageal reflux is high and antacid premedication may be considered.[59]

Inhalation induction may be prolonged due to large FRC, small tidal volumes, and ventilation/perfusion mismatch. Common intraoperative problems include obstruction by inspissated secretions, airway hyperreactivity, and hypoxemia.

Pneumothorax, consequent on high ventilatory pressures and rupture of bullae, is a less common complication. Postoperative tribulations include impaired clearance of secretions, atelectasis, pneumonia, and respiratory failure. Anesthesia should be deep enough to prevent bronchospasm or increased shunting during surgical stimulation or airway suctioning but ideally should not compromise postoperative respiratory function. Regional anesthesia is an ideal option if not contraindicated by coagulopathy or patient refusal. For general anesthesia, short-acting agents are preferred to minimize postoperative respiratory compromise. A cuffed ETT is often required, owing to the great airway pressures needed for adequate ventilation.

Because dehydration of 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 a point just below the carina.[60] This region is known as the isothermic saturation point and ensures that the lower airways are kept moist and warm.[61] 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 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 to a varying extent farther down the airway.[62] This shifts the isothermic saturation point distally, forcing bronchi that normally function in optimal conditions to take part in heat and gas exchange.[61] 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.[63,64] Direct impairment of mucociliary motion by anesthetic medications, as well as blunting of the cough response and ventilatory drive, can contribute further to the problem. Particular attention should, therefore, be directed to hydrating the airway in the perioperative period, to minimize the exacerbation of the primary pathologic pulmonary process of CF. Inhalation of hypertonic saline (7% sodium chloride) accelerates mucus clearance and improves lung function[65-67] and is now part of the routine maintenance management of CF. Nebulized saline treatments should be continued up to the start of anesthesia and recommenced after the procedure is complete. Inhaled gases should be humidified or an artificial "nose" inserted into the circuit to conserve airway moisture and minimize inspissation of secretions. Bronchial washing and suction can be used to clear secretions for more prolonged procedures, under a depth of anesthesia adequate to prevent bronchospasm.

At the conclusion of surgery, complete reversal of neuromuscular blockade should be confirmed. Whenever possible, the child should be extubated and encouraged to breathe spontaneously. A 30- to 40-degree head-up position assists movement of the diaphragm and ventilation. Postoperatively, physiotherapy, airway humidification, close attention to analgesia, and early mobilization should aim to enhance clearance of secretions and minimize atelectasis. The use of regional or local anesthesia, plus non-opioid analgesics, is useful to avoid respiratory depression. Ambulatory surgery is optimal, if feasible, because it minimizes disruption to the patient's schedule and decreases exposure to nosocomial infection.

Sickle Cell Disease

Sickle cell disease (SCD) is an inherited hemoglobinopathy resulting from a point mutation on chromosome 11. 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.[68,69] 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.[70] Perioperative problems and management are covered in more detail in Chapter 9, and this discussion will be limited to a brief review of the pulmonary pathology of SCD.

The 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 38.5° C (101.3° F), tachypnea, wheezing, and cough.[71-73] Precipitants include infection, fat embolism after bone marrow infarction, pulmonary infarction, and surgical procedures.[73-75] Potential risk factors for the development and severity of perioperative ACS include a history of lung disease, recent clustering of acute pulmonary complications, pregnancy, increased age, and the invasiveness of the surgical procedure.[68] However, a study of 60 laparoscopic surgeries noted an association between younger age and ACS, which the authors suggested may be related to reduced temperatures and greater relative blood loss as a proportion of total blood volume in smaller children.[76]

Minor procedures such as inguinal hernia repair or distal extremity surgery have a low risk of pulmonary complications (none to 5%), whereas intra-abdominal or major joint surgery has an ACS rate of 10% to 15%.[75,77,78] Although overall perioperative mortality specifically from SCD appears to be quite small, slightly under 1%,[75] ACS can lead to prolonged postoperative hospitalization, respiratory failure, and death. One study of 604 patients noted that ACS typically developed 3 days postoperatively and persisted for 8 days; 2 patients died in approximately 60 episodes.[74]

SCD also causes chronic lung damage, known as sickle cell lung disease (SCLD).[79] 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.[80] Children appear to have a predominantly obstructive pattern,[81] whereas adults have more restrictive pulmonary findings.[79,82,83] The later stages of lung damage involve decreased vital and total lung capacities, impaired gas diffusion, pulmonary fibrosis, pulmonary artery hypertension, right-sided cardiomyopathy, and progressive hypoxemia.[79,83] 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 heightened risk of sudden death.[82] 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.[79]

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 will serve as a baseline for comparison if post-

operative 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 and right ventricular hypertrophy.[79] Pulmonary function testing can reveal the need for bronchodilators and the presence of obstructive or restrictive lung disease.

The efficacy of preoperative or intraoperative management techniques beyond basic standards of care has not been clearly demonstrated, and well-delivered anesthetic and postoperative care may be the best guarantors of good outcome.[68,69] Because the effect of perioperative red blood cell transfusion versus no transfusion in preventing ACS or other sickle cell complications has not been tested by an adequately controlled study, the efficacy of prophylactic erythrocyte transfusion is controversial. One recent guideline suggests the avoidance of transfusion in low-risk situations, while considering transfusion only for cases assessed as greater risk.[68] If transfusion is undertaken, exchange transfusion aiming to decrease the concentration of hemoglobin S to 30% is no more efficacious than correction of anemia to a hematocrit of 30% in preventing SCD exacerbations but results in more transfusion-related complications.[74] 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.

Sickle cell patients frequently develop postoperative atelectasis. It is unclear if this relates to underlying sickle lung disease, difficulty with analgesia, other causes, or a combination of factors. Pain management can be difficult. Postoperative pain and opioid consumption is often great in SCD patients, and opioid use may lead to respiratory blunting and atelectasis.[84] ACS tends to involve the lower segments of the lung,[73] suggesting an association between atelectasis and ACS. Incentive spirometry can prevent the development of atelectasis and pulmonary infiltrates associated with ACS.[85] 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 continuous positive airway pressure, or intubation and mechanical ventilation are indicated by the degree of dysfunction. Bronchodilators, incentive spirometry, and chest physiotherapy may be useful in preventing progression of the disease. 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. Whereas transfusion has not been clearly shown to improve outcome, both exchange and simple transfusion can improve oxygenation.[73]

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 intelligent 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.

Annotated References

Accurso FJ: Update in cystic fibrosis 2005. Am J Respir Crit Care Med 2006; 173:944-947

A current review of the pathophysiology of cystic fibrosis

Bishop MJ, Cheney FW: Anesthesia for patients with asthma: low risk but not no risk. Anesthesiology 1996; 85:455-456

A thoughtful editorial on the implications, dangers, and practical implications of asthma

Davis PB: Cystic fibrosis since 1938. Am J Respir Crit Care Med 2006; 173:475-482

A succinct discourse on the evolution of management of cystic fibrosis

Doherty GM, Chisakuta A, Crean P, Shields MD: Anesthesia and the child with asthma. Paediatr Anaesth 2005; 15:446-454

A recent review of the perioperative management of asthma

Firth PG, Head CA: Sickle cell disease and anesthesia. Anesthesiology 2004; 101:766-785

A comprehensive review of anesthetic management of sickle cell disease

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

An extensive review of current evidence on the pathophysiology, diagnosis, and management of asthma

Tait AR, Malviya S: Anesthesia for the child with an upper respiratory tract infection: still a dilemma? Anesth Analg 2005; 100:59-65

A broad review of the data on perioperative upper respiratory tract infections and suggested approaches to management

References

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