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CHAPTER 4

Respiratory Diseases

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KEY POINTS

- Pulmonary arteriovenous fistulas have congenital and hereditary etiology, and patients are at risk for life-threatening rupture requiring surgery.
- Wegener's granulomatosis can affect any organ system, although renal and pulmonary involvement is most common; men ages 40 to 50 are at increased risk.
- Lymphomatoid granulomatosis affects cardiopulmonary, neurologic, and myeloproliferative systems; may result from opportunistic infection, and frequently progresses to lymphoma; men age 50 to 60 are at increased risk. Spontaneous remission occurs in some cases; mortality is 60% to 90% at 5 years.
- Churg-Strauss syndrome is usually associated with long-standing asthma, with men and women affected equally, and can affect any organ system; major cause of death is cardiac related.
- Primary pulmonary hypertension is a diagnosis of exclusion; women are affected twice as likely as men; right-to-left shunt may occur in 30%, secondary to patent foramen ovale; hypoxia with resultant heart failure is typical cause of death.
- Cystic fibrosis is an autosomal recessive disease, eventually fatal, with increased risk for airway obstruction, fluctuating pulmonary function, and chronic hypoxia; risk for spontaneous pneumothorax is 20%.
- Bronchiolitis obliterans organizing pneumonia is a pulmonary obstructive disease that may be reversible and usually resolves spontaneously.
- Idiopathic pulmonary hemosiderosis is associated with autoimmune disorders; patients have recurrent hemorrhage,

pulmonary fibrosis, restrictive lung disease, and pulmonary hypertension, with some cases of spontaneous remission.
- Chronic eosinophilic pneumonia may be preceded by adult-onset asthma; women are at increased risk; prognosis is good.
- Goodpasture's syndrome is a genetic autoimmune disorder involving the pulmonary and renal systems.
- Pulmonary alveolar proteinosis, a lipoprotein-rich accumulation in alveoli, has three forms: congenital, decreased alveolar macrophage activity, and idiopathic; some cases of spontaneous remission occur.
- Sarcoidosis may affect any organ system; African American, northern European, and females are at greater risk; many patients are asymptomatic.
- Systemic lupus erythematosus may affect any organ system; women of childbearing age are at increased risk.
- Idiopathic pulmonary fibrosis is a rare interstitial lung disease, with smokers at increased risk for pulmonary malignancy; survival is usually 2 to 3 years from diagnosis; no effective treatment exists, with lung transplant the only therapeutic option.
- Acute respiratory distress syndrome (ARDS) is associated with underlying critical illness or injury, developing acutely in 1 to 2 days; mortality is 25% to 35%.
- Pulmonary histiocytosis X is an interstitial lung disease associated with cigarette smoking and an unpredictable course; some spontaneous remission occurs.
- Lymphangioleiomyomatosis involves progressive deterioration of lung function, associated with tuberous sclerosis and exacerbated by pregnancy, with women at increased risk; possible spontaneous pneumothorax and chylothorax; death usually results from respiratory failure.
- Ankylosing spondylitis is a genetic inflammatory process resulting in fusion of axial skeleton and spinal deformities, with men at increased risk; radiologic bamboo spine, sacral to cervical progression, and restrictive lung disease with high reliance on diaphragm; extraskeletal manifestations may occur.
- Kyphosis (exaggerated anterior flexion) and scoliosis (lateral rotational deformity) are spinal/rib cage deformities with idiopathic, congenital, or neuromuscular etiology; corrective surgery done if Cobb thoracic angle >50% lumbar angle >40%.
- Bleomycin is an antineoplastic antibiotic used in combination chemotherapy, with no myelosuppressive effect; toxicity can cause life-threatening pulmonary fibrosis.
- Influenza A is highly infectious, presenting with flulike symptoms and possible progression to ARDS; human-to-human exposure is through droplets or contaminated surfaces, with high risk for infants, children, pregnancy, chronically ill, or renal replacement therapy patients. No prophylactic treatment exists; treat patients with high index of suspicion without definitive testing; rRT-PCR and viral cultures are sensitive for pandemic H1N1 strain.
- Severe acute respiratory syndrome (SARS) is highly infectious, transmitted by coronavirus with human-to-human exposure via droplets or surfaces, and may progress to ARDS.
- Echinococcal disease of lung is from canine tapeworm, transmitted by eggs from feces; rupture of cyst may result in anaphylactic reaction or spread of disease to other organs; children are at increased risk. No transthoracic needle aspiration is done; surgery is only option.

A thorough knowledge of pulmonary anatomy and physiology is essential to the practicing anesthesiologist, who should be familiar with common clinical conditions such as chronic obstructive lung disease (COPD) and asthma. This chapter presents a comprehensive review of less common pulmonary conditions, organized anatomically (pulmonary vasculature, airways, pulmonary interstitium), and conditions extrinsic to the lungs that affect pulmonary function, such as severe arthritic disorders. Drug-induced lung injury is also discussed, followed by rare infectious pulmonary diseases, including influenza A (H1N1), severe acute respiratory syndrome, and echinococcal disease of the lung.

Many of these conditions are severe, and some are difficult to diagnose. Patients with pulmonary disease may present with varied symptoms, including productive or nonproductive cough, fever, shortness of breath, chest pain, and decreased exercise tolerance. In most circumstances, patients who have these conditions will already be under the care of an internist or pulmonary specialist. The patient evaluation necessary to arrive at an accurate diagnosis often is comprehensive, including detailed history and physical examination; chest radiograph; pulmonary function tests (PFTs), including spirometry, diffusing capacity, and lung volume determination; and perhaps arterial blood gas (ABG) analysis. For some conditions, bronchoscopy and biopsy may be performed, and others require echocardiography or cardiac catheterization for diagnostic certainty. For urgent or emergent surgery, the gravity of the clinical situation often precludes additional diagnostic assessment. For elective surgery, preoperative evaluation should include a review of these diagnostic studies and a determination as to whether the patient's clinical condition has changed substantially. If a diagnosis has already been established, there is no evidence to suggest that additional pulmonary testing will improve pulmonary outcomes after surgery. Spirometry and lung volume determination are the "gold standards" for the presence or absence of pulmonary disease, but are poor predictors of patients who will develop a pulmonary complication after surgery.[1] If a diagnosis has not been established in a patient who has symptoms consistent with one of these respiratory diseases, pulmonary consultation should be obtained preoperatively as the patient's pulmonary disorder may be more urgent than an elective surgical procedure.

Unfortunately, pulmonary complications are common after many surgical procedures, particularly those involving the upper abdomen or thorax, possibly more likely than cardiac

complications.[2–5] Pre-existing lung disease, smoking, congestive heart failure, American Society of Anesthesiologists (ASA) classification, obesity, obstructive sleep apnea, anesthetic time in excess of 180 minutes, and advanced age are also risk factors for pulmonary complications.[4–9] There is no standard definition of exactly what constitutes a pulmonary complication, but the most important complications are those that cause significant morbidity (e.g., postoperative pneumonia) and postoperative respiratory failure. Because all the disorders discussed in this chapter constitute pre-existing lung disease, patients with these disorders who come to the operating room are at increased risk of postoperative pulmonary complications. Effective preoperative and intraoperative treatments are discussed with the individual diseases. In the postoperative period, aggressive treatment with mechanical measures such as incentive spirometry can reduce pulmonary complications.[10,11] Other intraoperative interventions, such as laparoscopic surgery, nasogastric tube decompression, and shorter-acting neuromuscular blockade, may also be beneficial.[12,13]

DISEASES OF THE PULMONARY CIRCULATION

Pulmonary Arteriovenous Fistulas

Pulmonary arteriovenous (AV) fistulas are abnormal communications between the arterial and venous pulmonary circulation that result in shunting of blood from right to left without traversing the pulmonary capillary network. This shunt results in a decreased fraction of the pulmonary circulation participating in gas exchange, mixing of oxygenated and deoxygenated blood, and a consequent reduction in arterial oxygen tension (Pao_2). Many patients with pulmonary AV fistulas are asymptomatic, but some may have associated signs and possible symptoms consistent with chronic hypoxemia (Box 4-1).

Known causes of pulmonary AV fistula formation include congenital malformations (Box 4-2). Patients with hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu syndrome), an autosomal dominant syndrome most often seen in middle-aged women but sometimes diagnosed in early childhood, are more likely to have multiple fistulas and more severe symptoms.[14]

BOX 4-1 ■ PULMONARY ARTERIOVENOUS FISTULA: SIGNS AND SYMPTOMS

Shortness of breath
Dyspnea with exertion
Bloody sputum
Cyanosis
Clubbing
Chest pain
Palpitations
Bruit
Low arterial oxygen saturation
Polycythemia
Anemia
Abnormal vasculature or nodules on chest radiograph

BOX 4-2 ■ PULMONARY ARTERIOVENOUS FISTULAS: ETIOLOGY

Congenital
Hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu syndrome)
Chest trauma
Cavopulmonary shunting*
Hepatic cirrhosis
Pulmonary hypertension

**First stage of a Fontan repair for single ventricle physiology, generally performed at 4 to 6 months of age. A cavopulmonary shunt is constructed and directs superior vena caval blood flow to the confluent pulmonary arteries.*

Patients with pulmonary AV fistula are at risk for rupture, resulting in potentially life-threatening hemothorax and hemoptysis. Thrombus formation within the fistula may also occur, with potential embolization of clot to the brain, resulting in stroke or seizures. Embolization of other organ systems is also possible. If the thrombus becomes infected, septic emboli and potential abscess formation may result.

Surgical intervention in the management of pulmonary AV fistulas becomes necessary when the patient develops more pronounced cardiac symptoms, significant respiratory symptoms, room-air desaturation, or complications such as emboli with central nervous system (CNS) manifestations. Surgical preoperative evaluation requires chest computed tomographic angiography (CTA) or pulmonary arteriography to localize the lesion. Pulmonary lobectomy, segmentectomy, or wedge resection using thoracotomy or video-assisted thoracoscopic surgery (VATS) are the most common procedures. Embolization procedures are becoming the preferred treatment for the majority of patients because embolization is less invasive, is easily repeated, and may be an adjuvant to decrease bleeding and other complications during definitive surgical resection.[15,16]

Anesthetic evaluation focuses on the degree of shunt and hypoxemia, using ABG analysis. Review of the pulmonary angiogram will reveal the size of the lesion and whether multiple fistulas are present. A significant fistula in the nonoperative lung may compromise arterial oxygenation if one-lung ventilation is required for surgical exposure. Efforts to minimize flow through a pulmonary AV fistula involve avoiding both increased pulmonary vascular resistance (PVR) and elevated levels of positive end-expiratory pressure (PEEP), both of which will increase flow through the low-resistance fistula.

Intraoperative management frequently requires one-lung ventilation to optimize surgical exposure. A double-lumen endotracheal tube (ETT) provides the added benefit of isolating the nonoperative lung and airways from any bleeding,

which may occur during a potentially bloody resection. The risk of significant bleeding is decreased if the lesion has been embolized before resection. Large-bore intravenous (IV) access is recommended in the event significant hemorrhage occurs. An arterial catheter is also indicated to monitor oxygenation and guide resuscitative efforts. As mentioned, an important anesthetic goal is to minimize flow through the pulmonary AV fistula. AV fistulas do not have capillary beds and have lower resistance to blood flow than normal pulmonary vasculature. It is important to avoid a general increase in PVR because this will increase flow through the AV fistula. Similarly, minimizing the use of PEEP will minimize increases in PVR and help minimize blood flow through the fistula. Because of the risk of paradoxical emboli passing through the fistula, extra caution must be taken to avoid injection of any air or particulate material into the venous system, because such debris may bypass the pulmonary capillary bed and gain access to systemic arteries, where end-organ embolization can occur (Box 4-3).

Preoperative evaluation should include assessment of neurologic function to rule out prior embolic stroke. Postoperative evaluation should include a neurologic check as well, to look for perioperative CNS embolization.

BOX 4-3 ■ ANESTHESIA CONCERNS FOR PATIENTS WITH PULMONARY DISEASE

Pulmonary Arteriovenous Fistula
Assess for degree of shunt and hypoxemia.
Avoid increases in pulmonary vascular resistance.
Avoid elevated positive end-expiratory pressures.
Extra care is needed to prevent unintentional intravenous air injection or any condition that would result in a venous air embolism.

Wegener's Granulomatosis
Assess for specific organ system involvement (renal and pulmonary insufficiency).
Avoid nasal manipulation (nasal intubation).
Assess for risk of difficult airway (subglottic/tracheal stenosis).

Lymphomatoid Granulomatosis
Assess extent of organ system involvement (obstructive or restrictive lung disease, cardiomyopathy, neuropathy, myelosuppression).
Possible adrenal suppression from long-term steroid treatment.

Churg-Strauss Syndrome
Assess level of organ system involvement (PFTs, chest radiograph, ECG, echocardiogram).
Minimize airway manipulation secondary to airway hyperreactivity.
May need stress-dose perioperative steroids.

Primary Pulmonary Hypertension
Consider increased perioperative morbidity and mortality.
Complete cardiopulmonary workup is needed for all procedures (ECG, echocardiography, chest radiograph, ABGs).
Spinal anesthesia is not recommended.
Maintain cardiac output and systemic vascular resistance.
Minimize increases in pulmonary vascular resistance.
Consider invasive monitoring intraoperatively.
Restrict nitrous oxide or ketamine use.
ABGs, Arterial blood gases; *ECG*, electrocardiogram; *PFTs*, pulmonary function tests.

Wegener's Granulomatosis

Wegener's granulomatosis (WG) is a rare disorder characterized by necrotizing giant cell granulomatosis of the upper respiratory tract and lung, widespread necrotizing vasculitis, and focal glomerulonephritis. WG may also affect the cardiovascular, neurologic, and gastrointestinal systems.[17] Although the etiology of WG is unknown, an autoimmune disorder is suspected. A typical patient is in the fourth or fifth decade, and men are twice as likely to have WG as women. Antineutrophil cytoplasmic autoantibody (ANCA) is a serologic marker that can help confirm the diagnosis.[18] *Staphylococcus aureus* has been implicated as an exacerbating cofactor.[18] Symptoms associated with WG are vague, and diagnosis can be elusive (Box 4-4). Biopsy of a lesion is necessary to make the diagnosis.

If the disease progresses, significant respiratory and renal compromise can occur, as well as hearing and vision loss (Box 4-5). Cardiac involvement is uncommon, although pericarditis, coronary arteritis, valvular involvement, and left ventricular hypertrophy have been reported. Current therapy for WG is often based on disease severity but usually includes cyclophosphamide, corticosteroids, methotrexate, or azathioprine and yields very good results, with long-term remission occurring in the majority of patients. Recent studies have demonstrated possible advantages of antistaphylococcal antibiotics and T-cell inhibitors (leflunomide).[18] Preoperative assessment is directed toward evaluating potential complications of WG, most often renal and pulmonary insufficiency. Blood urea

BOX 4-4 ■ WEGENER'S GRANULOMATOSIS: COMMON SIGNS AND SYMPTOMS

Hematuria
Shortness of breath
Wheezing
Hemoptysis
Bloody sputum
Cough
Chest pain or pleuritis
Sinusitis
Ulcers or lesions around nose
Weight loss
Weakness
Fever
Joint pain

BOX 4-5 ■ WEGENER'S GRANULOMATOSIS: COMPLICATIONS

Chronic renal insufficiency or renal failure
Hearing loss
Subglottic/tracheal stenosis
Pulmonary insufficiency
Functional nasal deformities
Ocular abnormalities
  Vision loss
  Ulcerative keratitis
  Orbital pseudotumor

nitrogen (BUN) and creatinine levels will provide adequate insight into the patient's renal function. A pulmonary flow-volume loop may be indicated if the patient is suspected of having tracheal stenosis and, by providing information about the dynamic changes in tracheal caliber, can supplement static radiographic images. WG may cause either obstructive or restrictive lung disease; the latter can be severe. Spirometry and other PFTs such as formal lung volume measurements can help determine the severity of such disease. Bronchoscopy and neck/chest CT may be necessary to evaluate subglottic stenosis and suggest which EET size can be placed safely.

Several aspects of WG may complicate management of the patient's airway. A significant amount of granulation tissue is likely to be present in and around the nose and nasopharynx. Insertion of a nasotracheal tube or nasal airway may be impossible, or traumatic with hemorrhage, and is best avoided. Additionally, lesions on the epiglottis or oropharynx may inhibit direct laryngoscopy, despite a normal airway examination. Once the vocal cords have been visualized, the ETT may be difficult to place because of subglottic stenosis and may require multiple laryngoscopies. If the patient is receiving corticosteroids at the time of surgery, stress dosing should be considered (see Box 4-3).

In view of these concerns, it is best to proceed with a conservative plan for managing the airway in WG patients, with immediate availability of difficult airway equipment, multiple sizes of ETTs, a videolaryngoscope or fiberoptic bronchoscope, and the means to obtain a surgical airway, as a last resort. If the patient has significant tracheal or bronchial stenosis, care should be taken to prevent air trapping and auto-PEEP by allowing sufficient time for exhalation if the tracheal lesion is below the ETT. (See also Chapter 1.)

Lymphomatoid Granulomatosis

Lymphomatoid granulomatosis (LYG), also known as angiocentric lymphoma, is a rare lymphoproliferative disease that is angiodestructive and frequently progresses to lymphoma. LYG mimics WG clinically and radiographically, although recent advances have identified LYG as a malignant B-cell lymphoma associated with immunosuppression and Epstein-Barr virus (EBV). Diagnosis requires histologic evaluation of a biopsy specimen. LYG was recently categorized as a *lymphoma,* although if diagnosed early (grade I angiocentric immunoproliferative lesions), it is considered benign, although premalignant.[19] Typically, it presents in the fifth or sixth decade of life, affecting men twice as often as women. The etiology of LYG is unknown, although its incidence in populations with immune dysfunction, such as human immunodeficiency virus (HIV) patients and organ transplant recipients, is significantly increased compared with the general population. Speculation that LYG resulted from an opportunistic infection has been confirmed through laboratory investigation.

The disease process primarily involves the lungs, although the skin, kidneys, and CNS can also be affected. Signs and symptoms of LYG include an increased risk of pneumonia (Box 4-6). Unlike WG, glomerulonephritis is not part of this clinical picture. LYG is frequently fatal, with 60% to 90% mortality at 5 years, although a small number of patients may undergo spontaneous recovery and complete remission. The cause of death is usually related to extensive destruction of the lungs and resulting respiratory failure.[20,21]

BOX 4-6 ■ LYMPHOMATOID GRANULOMATOSIS: CLINICAL MANIFESTATIONS

Hemoptysis
Cough
Dyspnea
Chest pain
Pneumothorax
Pleural effusions
Atelectasis
Fever and weight loss
Hepatomegaly
Erythema
Mononeuritis multiplex
Peripheral sensory neuropathy

Corticosteroids and cyclophosphamide are the treatment of choice, resulting in relief of symptoms such as fever, cough, chest pain, weight loss, and sinusitis. If not diagnosed in the premalignant phase, and if the disease has progressed to lymphoma, chemotherapy is necessary. The combination of cyclophosphamide, doxorubicin (hydroxydaunomycin), vincristine (Oncovin), and prednisone (CHOP) is often used. Radiation therapy may be indicated for localized disease. More recently, immunomodulation with interferon alfa-2b and autologous stem cell transplantation have played a role in treatment.[20,21]

In preparation for anesthesia, evaluation of the patient's pulmonary function is the primary concern with LYG. Chest radiography may reveal bilateral nodules, cavitations, pleural effusions, or pneumothorax. In the presence of advanced disease, ABG analysis and spirometry help define the extent of the patient's respiratory compromise and parenchymal destruction. A thorough preoperative neurologic evaluation is advised because of the high incidence of peripheral neuropathy. Toxicities related to any chemotherapeutic agents the patient may have received should also be considered. Toxicity related to the CHOP protocol includes peripheral neuropathy, cardiomyopathy, and myelosuppression.

ANESTHETIC MANAGEMENT

When planning an anesthetic for a patient with LYG, the presence of or potential for peripheral neuropathy may deter the anesthesiologist from using regional techniques, because of concern that subsequent neurologic dysfunction will be attributed to the regional anesthesia. However, the choice of anesthetic must be based on a consideration of risks and benefits, and there is no evidence that regional anesthesia worsens LYG. Respiratory compromise increases the risk of hypoxia under general anesthesia, or if the patient hypoventilates secondary to sedating agents used for premedication or for monitored anesthesia care.

If general anesthesia is chosen, the potential for postoperative intubation and respiratory support should be addressed with the patient. The need for postoperative mechanical ventilation is more likely in patients who have advanced disease with extensive destruction of lung tissue, pleural effusions, or pneumothorax. There is no clear answer to which anesthetic technique is superior, and the approach should be tailored to the individual patient's comorbidities and the surgical procedure. Long-term corticosteroid therapy in this population may result in adrenal suppression, and stress doses of corticosteroids should be considered (see Box 4-3).

Churg-Strauss Syndrome

Churg-Strauss syndrome (CSS), also known as *allergic granulomatosis,* is a rare systemic vasculitis that may affect multiple organ systems, particularly the lungs. Diagnosis requires the presence of at least four of six criteria: bronchospasm, eosinophil count greater than 10%, neuropathy (poly or mono), nonfixed pulmonary infiltrates, paranasal sinus abnormalities, and extravascular eosinophils[22] (Box 4-7). Patients frequently present in the fifth or sixth decade and may have a long-standing history of asthma. Both genders are affected equally. Cardiac involvement occurs later in the course and is the major cause of death. CNS manifestations such as cerebral infarcts, subarachnoid hemorrhage, and optic neuritis are common.

Corticosteroids generally result in dramatic improvement or resolution of CSS symptoms. Cytotoxic therapy should be initiated based on the severity of disease. Patients resistant to corticosteroids may respond to interferon-α treatment.[23] Elective surgery should be postponed if management of bronchospasm has not been optimized. Involvement of other organ systems may necessitate neurologic and renal evaluations. Cardiac evaluation may require testing such as echocardiography to assess myocardial function if the patient has congestive heart failure (CHF) or endocarditis.

BOX 4-7 ■ CHURG-STRAUSS SYNDROME: CLINICAL MANIFESTATIONS

Sinusitis
Nasal polyps
Pulmonary infiltrates
Diffuse interstitial lung disease (rare)
Hemoptysis
Pleural effusions
Cutaneous nodules and rashes
Hypertension
Glomerulonephritis
Coronary vasculitis
Endocarditis
Congestive heart failure
Peripheral neuropathy
Mononeuritis multiplex
Cerebral infarct
Subarachnoid hemorrhage
Optic neuritis

Preoperative assessment should include a chest radiograph and PFTs. Chest radiography may reveal multiple small pulmonary nodules or diffuse interstitial disease. Pleural effusions are noted in up to 30% of CSS patients. Spirometry typically demonstrates an obstructive pattern, although restrictive disease may also occur. A decrease in diffusion capacity may be observed from a loss of alveolar capillary surface area. Intraoperative management should include universal asthmatic principles to minimize airway reactivity. If possible, avoidance of airway instrumentation and positive-pressure ventilation (PPV) is desirable. A prolonged expiratory phase may be needed in patients with more advanced obstructive disease if PPV is used, and preoperative spirometry will provide guidance in this area. Nonselective beta-adrenergic blockers should be avoided, if possible, because of the risk of bronchospasm and exacerbation of CHF. If needed for control of ischemic heart disease, selective β_1-adrenergic agents, preferably short acting, should be used. Perioperative corticosteroids should be considered because of the risk of adrenal suppression from long-term corticosteroid therapy (see Box 4-3).

Primary Pulmonary Hypertension

Primary pulmonary hypertension (PPH) is an idiopathic disease and is a diagnosis of exclusion. The prevalence of PPH is thought to be approximately 1:1 million, with women being twice as likely as men to present with the disease. Some cases appear to be genetically linked.[24] Overall, PPH is more severe and aggressive than secondary pulmonary hypertension. Vascular remodeling, an alteration in pulmonary vascular tone, and a loss of cross-sectional pulmonary arterial area are responsible for the increase in PVR seen in this disease. Dyspnea is the most common presenting symptom, and syncope is a particularly poor prognostic sign (Box 4-8). Right-to-left shunting may occur in the 30% of patients with a patent foramen ovale (PFO). Death typically results from hypoxia, a further increase in pulmonary artery pressure (PAP), and eventually right ventricular (RV) failure.[25]

Historically, treatment for PPH relied on oxygen and calcium channel blockers in an effort to decrease PVR (Table 4-1). In addition, warfarin (Coumadin) is used to reduce the risk of thromboembolism resulting from the enhanced platelet activity seen in PPH. Pulmonary embolism or primary pulmonary vascular thrombosis is poorly tolerated in this patient population. Diuretics and digoxin are also employed when RV failure ensues. More recently, prostaglandins (PGI_2, PGE_1; alprostadil)

BOX 4-8 ■ PRIMARY PULMONARY HYPERTENSION: SIGNS/SYMPTOMS

Dyspnea
Fatigue
Syncope or presyncope
Angina
Peripheral edema and other signs of right-sided heart failure
Cyanosis

TABLE 4-1 ■ Current Therapies for Primary Pulmonary Hypertension

Therapy	Advantages	Disadvantages
Nitric oxide (NO)	Pulmonary circulation with selective vasodilation; increased Pao_2	Possible formation of toxic byproducts; prolonged bleeding times; expensive
Prostaglandins (epoprostenol, treprostinil, iloprost)	Potent vasodilation; inhibits platelet aggregation and smooth muscle cell proliferation	Not selective for pulmonary circulation; systemic hypotension; headaches; expensive; requires continuous infusion or inhalation
Phosphodiesterase-5 inhibitors (dipyridamole, sildenafil)	Possible synergy with NO therapy inhibitors	—
Endothelin receptor antagonist (Bosentan)	FDA approval	Limited data available
Calcium channel blockers	High efficacy; inexpensive	Less effective in severe cases; negative inotropic effects can worsen right ventricular failure
Oxygen	Directly reduces pulmonary vascular resistance in cases of hypoxia	None
Warfarin (Coumadin)	Improved long-term survival; decreases risk of intrapulmonary thrombosis	Increased bleeding risk
Magnesium	Vasodilation through blockage of Ca^{2+} channels; enhance NO synthase activity; releases prostaglandin I	Risk of magnesium toxicity: weakness, sedation, ECG changes

ECG, Electrocardiographic; *Pao_2,* arterial oxygen tension (partial pressure).

and nitric oxide (NO), alone or in combination, have been used to induce pulmonary vasodilation, with minimal systemic effects.[24,26] Currently, prostacyclins must be delivered by continuous IV infusion because of their short half-life. NO is delivered by inhalation and requires a tank and delivery system. Phosphodiesterase-5 inhibitors such as sildenafil and dipyridamole potentiate the NO-induced pulmonary vasodilation and can be used separately or in combination.[24] Unfortunately, cost and unwieldy delivery systems have limited the use of these therapies to the short term or the most severe cases. New approaches to delivering PGI_2 are under development, including the inhaled, subcutaneous, and oral routes. A newer agent, bosentan, an oral endothelin receptor antagonist thought to inhibit smooth muscle vasoconstriction and proliferation, is now approved by the U.S. Food and Drug Administration (FDA) to treat PPH.[24,27] Adjunctive therapy with bosentan has demonstrated promise when combined with prostacyclin therapy.[26,27]

Preoperative studies focus on the severity of PPH, degree of hypoxia, and resulting effects on the heart (Table 4-2). ABG analysis elucidates the level of hypoxia and acidemia, both of which exacerbate pulmonary hypertension. A chest radiograph may reveal enlarged main pulmonary arteries or an enlarged heart caused by RV hypertrophy or right atrial dilation. An electrocardiogram (ECG) may also reveal changes consistent with pulmonary hypertension (e.g., right atrial enlargement), as well as the presence of abnormal cardiac rhythm (e.g., atrial fibrillation). Sinus rhythm is essential to adequate RV filling. Preoperative echocardiography is helpful in determining the extent of RV hypertrophy and function, right atrial enlargement, pulmonic or tricuspid valve dysfunction, and patency of the foramen ovale. Pulmonary systolic pressures may be estimated by Doppler techniques. A more accurate but much more invasive method of measuring pulmonary pressures, gauging response to therapies, and detecting a PFO is right-sided heart catheterization. This procedure should be considered only if other studies have not provided an adequate assessment of disease severity and is not typically needed for preanesthetic evaluation. The patient treated with digoxin should have serum potassium and digoxin levels measured.

TABLE 4-2 ■ Preoperative Studies to Assess Pulmonary Hypertension

Study	Possible Significant Findings
Arterial blood gas analysis	Level of hypoxemia and acidosis; assess relative value of supplemental oxygen.
Chest radiography	Enlarged pulmonary arterial root; enlarged right side of heart
Electrocardiography	Dysrhythmias; signs of right-sided heart strain
Echocardiography	Assess right ventricular function and hypertrophy, valvular dysfunction and right atrial enlargement, and patency of foramen ovale; estimate pulmonary artery pressure.

ANESTHETIC MANAGEMENT

The increased perioperative morbidity and mortality of this disease must be considered when preparing to deliver an anesthetic to the PPH patient, and not assume the risk of perioperative complications is low with a "minor" procedure

(see Box 4-3). Regional anesthetic techniques do not preclude the need for possible invasive monitoring and vasoactive therapy. Each patient's needs should be considered individually. All medications being used to treat the patient's PPH and resulting right-sided heart failure should be continued in the perioperative period. Warfarin should be discontinued and replaced with a heparin infusion preoperatively. The risk of a thromboembolic event and a possible right-to-left shunt justify a preoperative hospital admission to administer heparin. Sedation must be carefully titrated; oversedation may lead to hypoxia, whereas not adequately addressing a patient's anxiety may also increase PVR.

Intraoperative management of PPH patients should emphasize maintenance of cardiac output and systemic blood pressure (BP) while minimizing further increases in PAP and the risk of RV failure. Invasive monitors, used selectively, including an arterial catheter, PAC, and transesophageal echocardiography (TEE), allow for sampling of arterial blood, pharmacologic manipulation of PAP and cardiac output, and detection of RV failure, while maintaining adequate ventricular preload.

Many different anesthetic techniques have been used successfully in patients with PPH; regional, epidural, and general approaches with controlled ventilation are all reasonable options. Spinal anesthesia may result in a significant reduction in systemic vascular resistance (SVR) and may precipitate a drop in preload with no change in pulmonary vascular pressures. This may result in inadequate coronary flow to perfuse the right side of the heart, with consequent RV ischemia and failure. Drugs typically used in the provision of anesthesia are safe in patients with PPH. An exception is nitrous oxide (N_2O), which has been implicated in raising PVR in several studies. Another exception is ketamine, which has sympathomimetic properties and may cause unintended PVR increase.

If PVR does increase, every effort must be made to avoid RV ischemia and possible RV failure. Helpful maneuvers include hyperventilation and maximizing Pao_2 to decrease PVR. Inhaled drugs such as NO (20-40 ppm), and prostacyclin (inhaled/IV) can selectively decrease PAP with minimal decreases in systemic BP. Milrinone and amrinone are excellent choices to decrease PVR and increase cardiac contractility, although SVR will also be decreased. Dobutamine will increase contractility and may decrease PVR. To increase systolic BP and avoid RV ischemia, norepinephrine may have a slight advantage over phenylephrine.[27] Maintenance of adequate intravascular volume and RV preload is also important.

OBSTRUCTIVE DISEASE

Cystic Fibrosis

Cystic fibrosis (CF) is an autosomal recessive genetic disease that affects chloride channels. With an incidence of 1 per 2000 to 4500 Caucasians, CF is one of the more common inherited conditions. It results in a significant reduction in life expectancy and quality of life. The responsible gene is found on the long arm of chromosome 7 and codes for a protein known as *cystic fibrosis transmembrane* (conductance) *regulator* (CFTR), which functions as a chloride channel. This defect decreases the water content of various secretions throughout the body, resulting in increased viscosity. Diagnosis is based on sweat chloride measurements, genetic testing for the CFTR gene, and clinical symptoms.[28] CF is a universally fatal disease, although advances in therapy have resulted in significant gains in quality of life and longevity. A wide variety of clinical manifestations are seen in CF patients (Table 4-3).

Pulmonary manifestations result from the inability to clear thickened and inspissated mucus from the airways. This causes airway obstruction and impaired defense against bacterial infection, which results in the majority of deaths related to CF. Recurrent bacterial infections result in dilation of the conducting airways, leading to bronchiectasis.[29] Although CF is a chronic progressive disease, the extent of current pulmonary infection fluctuates, creating significant daily variability in a patient's pulmonary function. Eventually, as the disease progresses, there is destruction of parenchyma and conduction airways. Loss of pulmonary arterial vascular cross-sectional area results in pulmonary hypertension. Chronic hypoxemia also develops.

TABLE 4-3 ■ Cystic Fibrosis: Clinical Manifestations

Sign/Symptom	Cause
Nasal sinusitis, polyps	Abnormal mucus production and secretion; chronic infection
Chronic bronchitis	Hypersecretion of viscid mucus; impaired host defenses
Obstructive pulmonary disease	Chronic pulmonary infections and airway plugging from excessive mucus secretion
Pneumothorax	Rupture of subpleural blebs through visceral pleura
Failure to thrive	Chronic infection; malabsorption
Recurrent pancreatitis	Obstruction of pancreatic ducts with viscous exocrine secretions
Gastroesophageal reflux disease	Unknown
Maldigestion	Biochemically abnormal intestinal mucins impair absorption of specific nutrients; abnormal bile secretion and absorption
Fat-soluble vitamin deficiencies	Abnormal bile secretion and absorption
Obstructive azoospermia	Atretic or absent vas deferens
Salt-loss syndromes	Inability to create hypotonic sweat

Patients with more advanced CF may develop spontaneous *pneumothorax.* The etiology of pneumothorax is unknown but presumably involves rupture of subpleural blebs through the visceral pleura. This becomes more likely in advanced disease. Over a lifetime, the incidence of pneumothorax may be as high as 20% in adult CF patients. Application of PPV can increase the risk of spontaneous pneumothorax. In the event of pneumothorax, surgical pleurodesis is the treatment of choice for CF patients who have a low anesthetic risk; higher-risk patients frequently receive talc pleurodesis as a safer, yet less effective, alternative.[30] Ventilation/perfusion inequality results in hypoxemia. The chronic hypoxia seen in this population causes an increase in PVR and pulmonary hypertension. Loss of pulmonary arterial vascular cross-sectional area also causes increased PVR and pulmonary hypertension, which is exacerbated by chronic hypoxemia. The severity of pulmonary hypertension correlates with the severity of CF. Chronic pulmonary vasoconstriction (from hypoxia) results in a muscularization of the pulmonary arterial vascular tree, which results in cor pulmonale, although the initial enlargement of the right ventricle is considered a beneficial adaptation to the increased resistance to pulmonary blood flow. The only medical therapy effective in treating pulmonary hypertension and improving RV performance in this population is supplemental oxygen.[31] Although lung transplantation has been successful with a 2-year survival of greater than 50%, about 40% of patients do not survive awaiting the transplant due to organ shortage.[28]

The primary gastrointestinal manifestation of CF is malabsorption and steatorrhea caused by pancreatic dysfunction from obstruction of pancreatic ducts with viscous exocrine secretions, usually requiring pancreatic enzyme replacements as well as multivitamins. Malnutrition and deficiencies of fat-soluble vitamins such as vitamin K can increase the patient's risk of bleeding if this issue is not addressed. Glucose intolerance resulting from pancreatic dysfunction (impaired endocrine function) is also common and may require insulin therapy. CF patients also have an increased incidence of gastroesophageal reflux disease (GERD).[32]

Preparation for anesthesia should focus on evaluation of the CF patient's pulmonary status. Significant variation in symptoms and disease severity from increased respiratory secretions or infection can be seen in a patient from one day to the next. Surgery should be postponed, if possible, unless the patient is at a baseline level of health. Preoperative testing should include a recent chest radiograph to diagnose pneumothorax, pneumonic processes, or bullous disease. In one series of patients with CF, 16% had an asymptomatic pneumothorax. Thus, chest radiography is essential in these patients.[30] Coagulation studies such as prothrombin time and partial thromboplastin time can provide information regarding coagulopathy resulting from vitamin K deficiency or general malnutrition. Sedating premedications should be given only if absolutely necessary, because of the risk of exacerbating pre-existing respiratory compromise, and only then under close observation with administration of supplemental oxygen to minimize the risk of desaturation. All CF patients should be questioned regarding symptoms consistent with GERD. If present, appropriate premedications and aspiration precautions such as a rapid-sequence induction should be considered, although CF patients may desaturate rapidly when apneic.

ANESTHETIC MANAGEMENT

Choice of anesthetic technique will be primarily determined by the scheduled procedure, although regional techniques offer some advantages. Avoidance of airway instrumentation will decrease the risk of bronchospasm and aspiration. Avoiding PPV will decrease the incidence of perioperative pneumothorax formation. If a long-acting or continuous regional technique is chosen, postoperative opioid requirements will be less. The risk of postoperative respiratory insufficiency may be less with regional anesthetic techniques, although this has not been rigorously studied.

The plan for general anesthesia should take into account the increased risk of aspiration (from GERD) and bronchospasm. The likelihood of chronic sinusitis and the presence of paranasal sinus polyps are reasons to avoid nasal instrumentation, if possible. A rapid-sequence induction proceeded by nonparticulate antacids and H_2 antagonists may help minimize the likelihood and consequences of pulmonary aspiration of gastric contents. However, use of rapid-sequence induction may result in uncontrolled systemic and pulmonary hemodynamics, and its use must balance airway risks with the risk of cardiovascular instability. PPV is usually preferable to spontaneous ventilation in advanced cases of CF, because of the risk of respiratory fatigue and marginal tidal volumes. CF is an obstructive process, and prolonged expiratory times may be necessary, as well as humidification of inspired gases and minimization of peak airway pressures to reduce the risk of barotrauma and pneumothorax. Low respiratory rates and smaller-than-usual tidal volumes may be required. Nitrous oxide should be used with caution because of the increased risk of pneumothorax formation with PPV, as well as the likely presence of multiple blebs. Meticulous attention to pulmonary toilet and suctioning of secretions is also advisable (Box 4-9).

BOX 4-9 ■ ANESTHESIA CONCERNS WITH CYSTIC FIBROSIS PATIENTS

Assess cardiopulmonary function.
Aspiration precautions should be considered secondary to association with gastroesophageal reflux disease.
Avoid airway instrumentation if possible.
Avoid positive-pressure ventilation if possible.
Consider regional techniques when applicable and appropriate.
Avoid nasal instrumentation.
May need to prolong expiratory times.

INFILTRATIVE AND INTERSTITIAL DISEASES

Bronchiolitis Obliterans Organizing Pneumonia

Bronchiolitis obliterans organizing pneumonia (BOOP) is an inflammatory lung disease of unknown etiology. It has been associated with bone marrow transplantation, although there is a very low incidence of BOOP in this population;[33] it has not been conclusively determined to be more than an incidental finding. BOOP results from the formation of granulation tissue, which obstructs the lumen of small airways and extends into the alveoli. The formation of the granulation tissue is associated with connective tissue proliferation, fibrinous exudates, and inflammation of alveolar and airway walls. These changes yield a clinical picture that presents as a flulike illness with cough and dyspnea. BOOP shares many characteristics of idiopathic pulmonary fibrosis, with the most significant difference being the reversibility of the fibrinous changes in BOOP as a result of the preservation of lung architecture.[33]

Corticosteroids are often used, although some cases resolve spontaneously. Typically, therapy lasts for 1 year, with resolution of symptoms by the end of the third month of treatment. Symptoms may recur, particularly if the course of corticosteroids is not completed. Other agents such as erythromycin and cyclophosphamide have been used, although their efficacy is not well established. Patients who received cyclophosphamide are at risk of leukopenia and, more rarely, thrombocytopenia or anemia.

Radiologic evaluation is consistent with an organizing pneumonia with patchy consolidation in a diffuse peripheral distribution. Effusions are a rare finding. Spirometry typically demonstrates a restrictive pattern, although it is possible to find an obstructive component. Decreased diffusion capacity and an increased alveolar-arterial oxygen gradient are common. Definitive diagnosis requires lung biopsy, typically performed thoracoscopically. BOOP occurs in 25% to 50% of long-term survivors of lung transplants, and 10% of all lung transplant recipients, indicating a poor prognosis.[34] It is a manifestation of chronic rejection treated, usually unsuccessfully, with steroids and immunosuppressive agents.[34]

Because of the high success rate in treating cases of BOOP unrelated to lung transplant, and because dramatic improvement is typically seen after a few weeks of therapy with prednisone, patients are unlikely to present for surgery with respiratory compromise. These factors also suggest that it may be prudent to defer all but the most emergent surgery in patients just beginning treatment for BOOP. A review of recent radiographs and spirometry, along with a history and physical examination, typically provide enough information as to whether the patient's pulmonary function has been optimized for elective procedures.

In the event surgery is emergent and cannot be postponed, the primary anesthetic issues relate to ventilator management. As in other restrictive lung diseases, high peak pressures may occur with PPV unless appropriate reductions in tidal volume are made. Rapid arterial hypoxemia can occur with apnea because of a decreased functional residual capacity (FRC). The use of low levels of PEEP will improve FRC and assist in maintaining Pao_2. Continuation of PEEP or continuous positive airway pressure (CPAP) in the postoperative period may be necessary to maintain functional residual capacity (Box 4-10).

Idiopathic Pulmonary Hemosiderosis

Idiopathic pulmonary hemosiderosis (IPH) is a rare disorder of unknown etiology characterized by diffuse alveolar hemorrhage. A diagnosis of exclusion, IPH is primarily seen in infants and children. There is an association with cow's milk hypersensitivity, celiac disease, autoimmune hemolytic anemia, and several other autoimmune disorders, such as lupus, periarteritis nodosa, and WG (see previous WG section), which suggests an immunologic basis for IPH, but no firm relationship has been established. Clinically, IPH is similar to the immune-mediated alveolar hemorrhage seen in syndromes such as Goodpasture's syndrome (see Goodpasture's syndrome section) and WG, although extrapulmonary involvement is not present as it is in these disorders. Hemoptysis, anemia, and pulmonary infiltrates on chest radiograph are the common presenting signs and symptoms. The clinical course of IPH is variable, with some reports of spontaneous remission. Other patients will die suddenly of severe alveolar hemorrhage or more gradually from respiratory insufficiency within 3 years of initial presentation. As a result of recurrent hemorrhage, pulmonary fibrosis with restrictive lung disease and eventually pulmonary hypertension and cor pulmonale will ensue (Table 4-4).

Corticosteroids are the cornerstone of therapy for IPH. Although the long-term efficacy of corticosteroid therapy for IPH is unclear, it is still the best option currently available. Long-term, if not lifelong, therapy is usually required, and complications arising from corticosteroid therapy are a concern, which leads physicians to minimize doses. This increases the risk of recurrence. Treatments with plasmapheresis, azathioprine, and cyclophosphamide have been attempted with some success, but these therapies are generally reserved for patients refractory to corticosteroid therapy. Definitive therapy is offered by double-lung transplantation, although there is a case report of recurrence of IPH 40 months after transplantation.[35]

Evaluation of ongoing alveolar hemorrhage and quantification of the extent of any fibrotic changes is essential for a complete preoperative assessment. The presence of dyspnea or hemoptysis provides a starting point. Gas exchange is impaired by ongoing alveolar hemorrhage, and there is an increased need for transfusion in the perioperative period because of the acute and chronic loss of red blood cells. It is prudent to postpone elective surgery until active alveolar hemorrhage resolves. Evaluating recent chest radiographs for bilateral alveolar infiltrates or new or changing infiltrates will help identify ongoing alveolar hemorrhage. These infiltrates usually resolve 1 to 2 weeks after the bleeding has stopped. “Honeycombing” may be observed if pulmonary fibrosis has

BOX 4-10 ■ ANESTHESIA CONCERNS FOR PATIENTS WITH INFILTRATIVE AND INTERSTITIAL DISEASE

Bronchiolitis Obliterans Organizing Pneumonia
Assess pulmonary function.
Tailor anesthetic plan for each patient.

Idiopathic Pulmonary Hemosiderosis
Assess pulmonary function.
Evaluate for coagulopathy.
Plan for possible bronchoscopy and pulmonary toilet (use large ETT when possible).
May require stress-dose steroids.
Avoid high airway pressures and tidal volumes.

Chronic Eosinophilic Pneumonia
Assess pulmonary function.
Delay surgery until steroid therapy implemented.
May need intraoperative bronchodilators.
Utilize PEEP cautiously and at low levels, if needed at all; minimize intrathoracic pressures to decrease shunt.

Goodpasture's Syndrome
Assess cardiopulmonary and renal function (BUN/creatinine, urinalysis, ABGs, ECG, echocardiography, spirometry).
Maintain oxygenation but limit supplemental O_2 to lowest level consistent with arterial saturation >90%.
Consider invasive monitors.
Arterial catheter used for all but the mildest disease; consider TEE or PAC if assessment of volume status or adequacy of cardiac output unclear.

Pulmonary Alveolar Proteinosis
Assess pulmonary function (level of dyspnea, baseline O_2 saturation, time since last BPL, ABGs, chest radiograph).
Double-lumen ETT required for BPL.
Invasive monitoring (PAC, TEE) may facilitate intraoperative management for higher-risk procedures.

Sarcoidosis
Assess all organ system involvement (PFTs, ECG, echocardiography, BUN/creatinine).
Evaluate airway to rule out lesions by indirect laryngoscopy or CT.
Possible postoperative ventilatory support.
Consider invasive monitors.
May require perioperative stress-dose steroids.

Systemic Lupus Erythematosus
Assess all organ system involvement (chest radiograph, PFTs, ABGs, BUN/creatinine, LFTs).
Invasive monitors may be indicated if cardiac or pulmonary involvement and for type of surgery (arterial catheters).
Minimize airway manipulation secondary to risk of inflammation and potential laryngeal involvement.
Refrain from nitrous oxide use secondary to bone marrow suppression.
Ensure thorough evaluation of medications:
- Echocardiography may be indicated for cardiac function with high-dose cyclophosphamide or hydroxychloroquine.
- LFTs should be evaluated for hepatotoxicity (azathioprine, methotrexate).
- May require stress-dose steroids.
- May require increased doses of neuromuscular blockers if taking azathioprine.
- Cyclophosphamide may prolong effects of succinylcholine.

Idiopathic Pulmonary Fibrosis
Assess cardiopulmonary function, (PFTs/spirometry, ECG, echocardiography).
Evaluate for pulmonary hypertension/cor pulmonale.
Aspiration precautions should be considered secondary to association with gastroesophageal reflux disease.

Acute Respiratory Distress Syndrome
Assess cardiopulmonary function.
Lung protective ventilation: low tidal volumes (~6 mL/kg predicted body weight); PEEP to maintain arterial saturation >90%; <30 cm H_2O plateau pressures.
Utilize permissive hypercapnia as needed.
Consider invasive monitors (arterial/central venous catheters, TEE).
Provide supportive care, with carefully guided fluid resuscitation.
Ensure postoperative ventilatory support.

Pulmonary Histiocytosis X
Assess cardiopulmonary function.
Tailor anesthetic management to progression of disease.
Give special attention to possible pathologic fractures.

Lymphangioleiomyomatosis
Assess cardiopulmonary function.
May need enteral/parenteral nutrition perioperatively.
Consider postoperative ventilation support.

BPL, bronchopulmonary lavage; BUN, blood urea nitrogen; CT, computed tomography; ETT, Endotracheal tube; LFTs, liver function tests; PAC, pulmonary artery catheter; PEEP, positive end-expiratory pressure; TEE, transesophageal echocardiography.

developed. Preoperative spirometry is recommended, because a restrictive pattern develops over the course of the disease. If active bleeding is present, the diffusion capacity will be artificially elevated because of absorption by intra-alveolar hemoglobin. Anemia frequently develops from ongoing alveolar hemorrhage, and measuring the amount of serum hemoglobin is essential.

If intubation of the trachea is part of the anesthetic plan, the largest possible ETT should be placed to facilitate bronchoscopy, if needed, and adequate pulmonary toilet. As with other restrictive processes, higher airway pressures will occur unless either a decreased tidal volume is selected or the inspiratory phase of ventilation is lengthened. The risk of pneumothorax is increased. Corticosteroids or other therapies for IPH should be continued throughout the perioperative period (see Box 4-10).

Chronic Eosinophilic Pneumonia

Chronic eosinophilic pneumonia (CEP) is a rare disorder of unknown etiology characterized by subacute respiratory symptoms caused by infiltration of the alveoli and interstitium by an eosinophil-rich inflammatory process. For the diagnosis to be made, the pneumonia must have no identifiable cause (e.g., infection, sarcoidosis). CEP is more likely to occur in women and is frequently preceded by adult-onset asthma. Common presenting symptoms include constitutional

TABLE 4-4 ■ Sequelae of Idiopathic Pulmonary Hemosiderosis

Sequela	Etiology
Recurrent hemoptysis	Active alveolar bleeding; very young children may not be able to expectorate heme.
Anemia	Chronic iron deficiency anemia related to sequestration of hemosiderin within alveolar macrophages
Pulmonary fibrosis	Scar tissue and clot formation at the sites of alveolar hemorrhage
Restrictive lung disease	Pulmonary fibrosis
Pulmonary hypertension	Obstruction of pulmonary blood flow in interstitial fibrosis
Cor pulmonale	Pulmonary fibrosis and hypertension

complaints such as night sweats, weight loss, fever, and cough. Progression to dyspnea may occur if not treated. Chest radiographs may show dense peripheral infiltrates, described as a "photographic negative of pulmonary edema."[36] Spirometry in a symptomatic, untreated patient typically reveals a restrictive pattern. Diffusion capacity is reduced. If bronchospasm is also present, the picture may be mixed with a reversible obstructive component.

Corticosteroids are effective treatment for CEP patients, with symptoms often improving in 1 to 3 days and radiographic resolution over several months. Unfortunately, recurrence is common once corticosteroid therapy is discontinued, and thus treatment may be needed for life. CEP patients with concurrent asthma seem to have a lower recurrence rate, possibly because inhalation corticosteroids are used as part of the management of their asthma.[37] The prognosis for CEP is excellent because of the effectiveness of corticosteroid therapy. If possible, surgery should be delayed until CEP patients have received corticosteroids and experienced resolution of symptoms, typically 7 to 14 days.

In the event of emergency surgery, the pathophysiologic alterations seen in CEP are similar to those of other pneumonias. Fever may result in reduced intravascular volume and increased metabolic rate. Fluid resuscitation to restore euvolemia before induction will decrease the risk of hemodynamic instability. The increased metabolic rate and increased shunt fraction caused by perfusion of inflamed alveoli (which have impaired gas exchange) will increase the speed of desaturation on induction if apnea develops. Adequate preoxygenation and expeditious securing of the airway are therefore essential. Intraoperative ventilator management must be individualized, attempting to minimize airway pressures while delivering adequate volumes. If an obstructive component is present, bronchodilator therapy may be helpful, and expiratory times may need to be prolonged. PEEP should be used with caution because it may divert blood flow from ventilated alveoli and increase the shunt fraction. Adrenal suppression may exist because many CEP patients are receiving long-term corticosteroid therapy, and perioperative corticosteroids should be considered (see Box 4-10).

Goodpasture's Syndrome

Goodpasture's syndrome (GS) is an autoimmune disorder that affects the lungs and the kidneys. It is caused by circulating anti–glomerular basement membrane (anti-GBM) antibodies that bind to the vascular basement membrane in the lung and kidneys, resulting in an autoimmune reaction. The end result is rapidly progressive glomerulonephritis that is frequently accompanied by vasculitis and pulmonary hemorrhage. The incidence is approximately 1 per 100,000 population, with both genders being affected equally. Genetic factors are thought to increase the likelihood of developing GS, although environmental factors such as smoking, infection, inhalation injury, volume overload, and exposure to high oxygen (O_2) concentrations increase the risk of pulmonary hemorrhage.[38,39] The genetic component of GS is poorly defined. However, there is increased occurrence (88%) of HLA-DR2 in patients with anti-GBM disease compared with controls (30%). There is also an increased incidence of disease in twins, siblings, and cousins of those with GS. Inheritance of certain allelic variants of immunoglobulin heavy chain also increases susceptibility to anti-GBM disease.[39] Onset of the disease is dramatic, with sudden hemoptysis, dyspnea, and renal failure (Box 4-11). New-onset hypertension may also be part of the presentation. Renal biopsy is necessary to make the diagnosis and distinguish GS from collagen vascular diseases such as WG.

Because of the sudden onset and severity of the disease, initial treatment frequently requires hemodialysis and mechanical ventilation. If the GS patient survives the acute phase, high-dose corticosteroids and cyclophosphamide induce immunosuppression, and plasmapheresis is used to clear anti-GBM antibodies and complement. Therapy usually lasts 3 to 6 months, with resolution of symptoms occurring within the first 2 months. End-stage renal disease is a common complication of GS, and renal transplantation may be necessary. Early diagnosis and treatment has a strong correlation with better outcomes.

BOX 4-11 ■ SYMPTOMS AND SIGNS SEEN IN GOODPASTURE'S SYNDROME

Dyspnea
Fatigue and weakness
Hematuria
Oliguria
Hemoptysis
Anemia
Hypertension
Azotemia
Proteinuria

If possible, surgery should be delayed until medical management is underway and pulmonary involvement has resolved. In all likelihood, some renal insufficiency, if not failure, will still be present. Preoperative evaluation should include BUN/creatinine determinations and urinalysis to assess renal function. The patient's symptoms and medical condition at surgery will dictate the extent of pulmonary evaluation. This may include a chest radiograph, ABG analysis, spirometry, and diffusing capacity to quantify the extent and significance of pulmonary hemorrhage.[40] If pulmonary involvement is ongoing, hypoxemia and a restrictive defect on spirometry are common. A chest radiograph in a typical patient shows diffuse bilateral alveolar infiltrates from the pulmonary hemorrhage. Microcytic anemia from ongoing hemorrhage is also typical.

Oxygenation is the primary challenge of the anesthetic management of patients who have active GS. With ongoing alveolar hemorrhage, patients not only will have impaired gas exchange at the alveolar level, but also will most likely be anemic. These will contribute to decreased O_2 delivery to the tissues. Exposure of the lungs to an increased O_2 tension and high airway pressures may exacerbate alveolar hemorrhage. These stresses, along with overaggressive fluid resuscitation, should be avoided in all patients with GS to minimize the risk of further anti-GBM–mediated lung injury. An intra-arterial catheter is indicated when caring for patients with more than mild disease. For major procedures in patients with significant pulmonary impairment, placement of a PAC or TEE may be helpful in guiding resuscitation and hemodynamic management. When selecting anesthetic agents and other medications, renal function must be considered, and any potentially nephrotoxic drugs should be avoided. Dosing of medications that rely on renal excretion should be altered based on the patient's creatinine clearance (see Box 4-10).

Pulmonary Alveolar Proteinosis

Pulmonary alveolar proteinosis (PAP) is a rare disorder characterized by accumulation of a lipoprotein-rich substance in the alveoli. There appear to be three distinct forms of PAP. *Congenital* PAP presents in infancy and is caused by mutations in the genes coding for surfactant proteins; a defect in surfactant-associated protein B (SP-B) results in accumulation of surfactant-like material in alveoli.[41] The *secondary* form of PAP involves decreased alveolar macrophage activity, either functional impairment or decreased number, which results in decreased clearance of surfactant products and may be related to immunosuppression, myeloid disorders, hematologic malignancies, infection, and inhalation of noxious fumes or toxic mineral dusts. *Idiopathic* PAP does not fit into either of the two previous categories and accounts for 90% of cases.[42] Idiopathic PAP may also be caused by reduced clearance of surfactant. The proteinaceous material found in the lungs of patients with PAP is surfactant.

Patients typically present with gradual onset of cough and worsening dyspnea with exertion. Chest pain, fever, and hemoptysis may also be present. Patients may also have clubbing, cyanosis, and rales. Definitive diagnosis of PAP requires transbronchial or open-lung biopsy. The clinical course of PAP is variable. Some patients have spontaneous improvement or remission; others experience persistent but stable symptoms. The other possible clinical course is steady progression of the disease with worsening hypoxia and increased risk of infection.

Chest radiographs typically have bilateral perihilar infiltrates extending into the periphery in a "butterfly" or "bat wing" distribution suggestive of pulmonary edema.[43] The appearance of the chest radiograph may be out of proportion to the severity of the patient's symptoms. High-resolution CT findings tend to correlate more closely with the clinical picture. Spirometry frequently reveals a mild restrictive pattern. A severe reduction in diffusing capacity is also observed. ABG analysis demonstrates hypoxemia and an increased alveolar-arterial gradient from interpulmonary shunting.[44]

Therapy for congenital PAP is supportive; lung transplantation is the only definitive therapy currently available. Secondary PAP will typically resolve with treatment of the underlying disorder. Whole-lung lavage, also known as *bronchopulmonary lavage* (BPL), has been used in the treatment of acquired PAP for 40 years and is still the current standard of care. More recent reports detail lobar lavage through fiberoptic bronchoscopes in PAP treatment.[44] This latter approach is time-consuming and uncomfortable for the patient and may be most useful in patients who cannot tolerate whole-lung lavage or the required general anesthetic.

A patient with moderate to severe disability caused by PAP should be evaluated for the need to have BPL before any elective surgical procedure. Caring for patients receiving BPL is significantly easier if the contralateral lung has been recently lavaged, because this will dramatically improve oxygenation during one-lung ventilation, which is required to perform the procedure. Preoperative testing should be directed by the patient's level of dyspnea, baseline O_2 saturation, and time since the last BPL was performed. In patients with more severe symptoms, preoperative ABG analysis or measurement of room-air, resting, arterial saturation analysis is indicated. Chest radiography is unlikely to be useful in evaluating the extent of disease (see Box 4-10).

BRONCHOPULMONARY LAVAGE

A general anesthetic and placement of a double-lumen ETT are required for BPL. A rapid decrease in O_2 saturation on induction is common, making excellent preoxygenation and expeditious placement of the double-lumen ETT essential. An intra-arterial catheter is useful in monitoring the patient's oxygenation and hemodynamic response to the procedure. Confirmation of correct positioning of the ETT by fiberoptic visualization is essential. Testing for leaks that would allow contamination of the ventilated lung by spillage of lavage fluid is critical. The nonventilated lung is then lavaged repeatedly with saline while the ipsilateral chest wall is mechanically percussed. The procedure is repeated until the drained saline is almost clear, indicating removal of the majority of

the lipoproteinaceous material. The BPL fluid should be warmed to decrease the risk of hypothermia and the volume of the drainage and presence of bubbles closely monitored, to ensure isolation of the contralateral lung. Oxygenation may improve during the instillation of fluid as alveolar pressure increases. This results in decreased perfusion to the lavaged lung (which is not being ventilated) and thus improves overall ventilation/perfusion matching. Hypoxia is most likely to occur during the drainage phases of the procedure, when an increase in intrapulmonary shunting occurs because of the dramatic drop in alveolar pressure. Significant hemodynamic changes can also occur during the infusion of saline into the lung. Hypotension and an increase in central venous pressure or pulmonary capillary wedge pressure may be seen. TEE suggests these changes are caused by impaired venous return to the left side of the heart.[45] Presumably, saline infusion compresses alveolar capillaries, increasing PVR and resulting in increased central venous pressure, while also causing decreased left-sided heart output because of decreased blood flow to the left ventricle. In some patients the contralateral lung can be lavaged during the same anesthesia, although several days may pass between treatments. BPL may result in improvement lasting 12 to 18 months before it is again required.

Sarcoidosis

Sarcoidosis is a chronic granulomatous disease of unknown etiology that can involve almost any organ system. The diagnosis is usually made in the first half of adult life, with an occurrence in the United States of 20 to 50 per 100,000 population, with a higher incidence in African-Americans, people of Northern European descent, and females. The annual mortality rate of a patient with sarcoid is low but is increased by symptomatic cardiac[46] or neurologic[47] involvement. The initial presentation of sarcoid will vary depending on the organ systems affected. Sarcoidosis commonly involves the skin, eyes, lungs, heart, and CNS. Frequently, abnormal chest radiographs in asymptomatic individuals raise suspicion. The lesions responsible for sarcoidosis are noncaseating granulomas, which may spontaneously resolve or proceed to fibrosis.

The vast majority of sarcoid patients have pulmonary involvement. Many are asymptomatic, whereas others will have nonspecific complaints such as chest pain, dyspnea, and nonproductive cough. Radiographic abnormalities progress from bilateral hilar adenopathy to diffuse pulmonary infiltration, and in severe cases, pulmonary fibrosis. PFTs frequently demonstrate restrictive disease with decreased lung volumes and diffusion capacity. In some cases an obstructive pattern may also be present because of airway narrowing. In more advanced cases, ABG analysis reveals hypoxemia and an increased alveolar-arterial gradient. A significant number of sarcoid patients have cardiac symptoms resulting from myocardial granulomas or the effects of respiratory system disease on the heart. Possible findings include conduction abnormalities (complete heart block, bundle branch block, or first-degree AV block), ventricular arrhythmias, CHF, pericarditis, supraventricular tachycardia, ventricular aneurysms, and sudden death.[46]

Neurologic findings in sarcoid patients are uncommon, although all the nervous system is at risk. Possible manifestations of neurologic involvement include seizures, progressive dementia, diabetes insipidus, hydrocephalus, and acute mononeuropathy. Facial nerve neuropathy is the most common of the neurologic lesions and usually has a benign course.[47]

The airways are involved in approximately 5% of patients with sarcoidosis.[48] Symptoms may include dyspnea, dysphagia, throat pain, hoarseness, a weak voice, or stridor. Most lesions are supraglottic and involve the epiglottis, aryepiglottic folds, and arytenoids.[49] These lesions may result in airway compromise and, rarely, the need for tracheostomy. Vocal cord paralysis has also been reported, from recurrent laryngeal neuropathy caused by sarcoid mediastinal lymphadenopathy.[50] Encountering a pregnant patient with a history of sarcoid is not unusual, because sarcoid occurs with an increased frequency in women of childbearing age. In general, however, pregnancy tends to improve sarcoid-related symptoms, presumably because of increased cortisol levels during pregnancy.[51]

Corticosteroids are often required to treat sarcoid and, regardless of the lack of correlative data, remain the standard of care. Systemic corticosteroids appear to improve or shorten the length of most symptoms related to sarcoidosis. The relapsing, remitting nature of the disease makes it difficult to verify the efficacy of this treatment. Data are limited correlating oral steroids and improved lung function.[52,53] Remission occurs within 3 years from diagnosis for more than half of patients with sarcoidosis.[54] As is often the case, early diagnosis and treatment appear to improve the likelihood of successful treatment. Radiation therapy and immunosuppressants such as cyclophosphamide and azathioprine may also be used. Anti-inflammatory agents, such as anti–tumor necrosis factor (anti-TNF) therapy (adalimumab) currently are in clinical trials.[54]

Serial chest radiographs, PFTs, and serum angiotensin-converting enzyme (ACE) levels can be used to follow the progress of a patient. Serum ACE appears to be synthesized within sarcoid granulomas. High levels are associated with more severe pulmonary infiltration, and lower levels are seen with disease inactivity. Trends within a given patient are more important than the absolute level of ACE. Cardiac rhythm abnormalities can result from sarcoid heart disease and may necessitate placement of a pacemaker or implantable cardiac defibrillator, as well as other treatment for arrhythmias, cardiomyopathy, and heart failure.

Preparation for anesthesia in a patient with a history of sarcoidosis should focus on the airway and pulmonary function, as well as on evaluation of other organ systems known to have been affected in the individual patient. A review of recent chest radiographs along with PFTs is recommended. A history of significant dyspnea warrants an ABG analysis. Screening for airway involvement can be accomplished by inquiring

about dysphagia, hoarseness, or throat pain. If suspected, an evaluation by indirect or direct laryngoscopy and, if necessary, head and neck CT will provide the necessary anatomic data. Swelling of supraglottic structures may increase the difficulty of intubation and increase the risk of postoperative respiratory compromise. Delaying surgery to allow for adequate corticosteroid therapy may be appropriate. Other preoperative testing is guided by the patient's history and may include ECG and echocardiogram if cardiac involvement or advanced pulmonary fibrosis is present. All ongoing cardiac therapy should be continued perioperatively. Because of the sporadic nature of neurologic symptoms, a thorough neurologic examination is advisable during preoperative evaluation to help differentiate between existing deficits and those resulting from anesthetic interventions, surgery, or positioning for surgery. Renal involvement also occurs, making review of recent electrolyte and renal function data advisable.

Intraoperative management of an asymptomatic patient should be uneventful and require little change in the anesthetic plan when compared with a healthy individual undergoing the same procedure. The patient with significant restrictive lung disease will require altered ventilator management and possible postoperative ventilatory support. An intra-arterial catheter facilitates oxygenation and ventilation management and allows close observation and early detection of any hemodynamic instability. In caring for patients with significant pulmonary fibrosis, placement of a PAC or use of TEE may help guide resuscitation and hemodynamic management. Sarcoid patients with an implantable cardiac defibrillator may need to have these devices inactivated because of interference from electrocautery units, although modern units are less susceptible. In patients with deactivated devices, defibrillator pads should be placed during the period of inactivation to allow for external pacing and defibrillation, if needed. Airway management will be dictated by the preoperative evaluation; awake fiberoptic intubation or elective tracheostomy is occasionally necessary. Continuation of corticosteroid therapy with consideration of stress dosing is encouraged.

Systemic Lupus Erythematosus

Systemic lupus erythematosus (SLE) is a connective tissue disease resulting from autoantibodies directed at cellular nuclei antigens found in multiple organ systems. The cause of SLE is unknown. SLE can occur in anyone but most often affects women of childbearing age. Its incidence is estimated at 40 per 100,000 population in North America.

Arthritis is the most common clinical manifestation of SLE. Other common signs and symptoms include cutaneous lesions such as butterfly malar erythema, Raynaud's phenomenon, oral ulcers, and recurrent noninfectious pharyngitis. Anemia, thrombocytopenia, leukopenia, and an increased incidence of thrombus formation are possible hematologic sequelae. Renal involvement, in the form of glomerulonephritis, has a highly variable course. Neurologic findings with SLE include cognitive dysfunction, migraine-like headaches, and seizures. Pericarditis, small pericardial effusions, valvular abnormalities, and endocarditis represent the majority of the cardiac manifestations. CHF may occur, although usually not the result of cardiomyopathy.[55]

Treatment is typically directed at specific symptoms, including nonsteroidal anti-inflammatory drugs (NSAIDs) for arthritic pain, glucocorticoids for anemia and thrombocytopenia, anticonvulsants for seizures, anticoagulants for thrombosis, and dialysis for end-stage renal disease. Other treatments may include plasmapheresis, azathioprine, and cyclophosphamide.

Pulmonary manifestations of SLE are the direct result of autoantibody reactions in the lung vasculature, lung parenchyma, and pleura (Table 4-5).[56–59] Laryngeal complications in SLE have an incidence of 0.3% to 30% and range from mild inflammation to vocal cord paralysis, subglottic stenosis, and acute obstruction from edema.[56] Therefore, thorough airway evaluation and history is crucial preoperatively. Histopathologic findings include alveolar wall damage, inflammatory cell infiltration, hemorrhage, and hyaline membranes. Some manifestations are thought to occur primarily in SLE patients with antiphospholipid antibodies, the presence of which is known as *antiphospholipid syndrome* (APS); 50% of APS cases occur in patients with SLE, although only a minority of SLE patients have APS.[57] The primary defect in APS is recurrent arterial and venous thrombosis.[58] However, APS is also associated with pulmonary hypertension and diffuse alveolar

TABLE 4-5 ■ Systemic Lupus Erythematosus (SLE): Pulmonary Manifestations

Finding	Comment
PRIMARY MANIFESTATIONS	
Lupus pneumonitis	Mimics acute infectious pneumonia
Diffuse alveolar hemorrhage	Rare; may be associated with APS
Lupus pleuritis	Pleurisy and pleural effusion are common in SLE
Interstitial pneumonia	Includes lymphocytic and BOOP variants
Pulmonary hypertension	Resembles PPH; associated with APS
Bronchiolitis	Rare and unexplained
Chronic interstitial lung disease	Resembles idiopathic pulmonary fibrosis
SECONDARY MANIFESTATIONS	
Pulmonary embolism	Caused by recurrent thrombosis associated with APS
Respiratory muscle dysfunction	Subsegmental atelectasis; elevated diaphragm; "shrinking lung" syndrome

APS, Antiphospholipid syndrome; *BOOP,* bronchiolitis obliterans organizing pneumonia; *PPH,* primary pulmonary hypertension.

hemorrhage, particularly dire manifestations that predict a higher mortality.[59] The majority of these patients respond to immunosuppressive therapy and rarely require emergency airway intervention.[56]

Preoperative testing should be directed toward the affected organ systems. Many SLE patients have mild disease and require little deviation from the routine perioperative evaluation and care required for a given procedure. A review of serum BUN/creatinine levels is reasonable to rule out any occult renal involvement. Pulmonary evaluation may include chest radiography, ABG analysis, and PFTs if current symptoms and history suggest pleuropulmonary involvement. A restrictive pattern is frequently seen on PFTs, although patients with bronchiolitis will have obstruction as well. The diffusing capacity is reduced when interstitial disease is present. Diffusing capacity is normal when corrected for diminished lung volumes if respiratory muscle dysfunction is the sole cause of underlying restrictive lung disease.[60] Patients with significant pulmonary involvement may require postoperative ventilation. Ventilator management should be tailored to their specific disease process: diaphragmatic weakness or interstitial fibrosis. During the perioperative period, patients with APS are at increased risk of thrombosis, and appropriate precautions must be taken. Perioperative corticosteroids may be required for patients with adrenal insufficiency because of chronic corticosteroid administration (see Box 4-10).

Idiopathic Pulmonary Fibrosis

Idiopathic pulmonary fibrosis (IPF), also referred to as "cryptogenic fibrosing alveolitis," is an interstitial lung disease of uncertain etiology. IPF is a progressive illness with a median survival of 3 to 4 years. This rare condition has a prevalence of about 5 per 100,000 population and is more common in current or former smokers. A typical patient is a middle-aged man. Diagnosis is based on the histologic pattern of usual interstitial pneumonia and exclusion of other causes of this histologic pattern. Extrapulmonary involvement does not occur. The presentation is insidious and typically involves dyspnea and a nonproductive cough. Physical examination frequently reveals fine crackles at the lung bases, expanding upward as the disease progresses. Clubbing, cyanosis, peripheral edema, and cor pulmonale are later findings. There must be a restrictive pattern on spirometry and radiologic changes on chest radiography or high-resolution CT consistent with the diagnosis.[61]

Patients with IPF also have an increased incidence of pulmonary malignancy. Unfortunately, it is unclear if resection of these lesions adds to life expectancy in this population.[62] No effective treatment is currently available, although corticosteroid and cytotoxic agents are frequently used. Many novel therapies attempt to block fibrogenic pathways and may be of benefit (Table 4-6).[63] Lung transplantation is the only therapeutic option available for IPF patients. Although thought to be effective, there is still only a 49% survival rate 5 years after transplantation.[64] The median survival time is 2 to 3 years from time of diagnosis.[65]

TABLE 4-6 ■ Idiopathic Pulmonary Fibrosis: Experimental Therapies

Therapy	Action
Interferon-γ 1b	Inhibition of fibroblast proliferation and collagen synthesis
Pirfenidone	Inhibits synthesis of collagen and tumor necrosis factor alpha
Acetylcysteine	Stimulates glutathione synthesis

Data from Selman M, Thannickal VJ, Pardo DA, et al: Idiopathic pulmonary fibrosis: pathogenesis and therapeutic approaches, *Drugs* 64:405-430, 2004.

Patients with IPF presenting for surgery typically are tachypneic and cyanotic and appear to be in poor health. Preoperative evaluation should include a review of recent spirometry and other PFTs. A decrease in lung volumes with a reduction in diffusion capacity is expected. Ventilation/perfusion inequality and impaired diffusion result in hypoxemia. In patients with advanced disease, echocardiography may reveal pulmonary hypertension and cor pulmonale. IPF patients seem to have a very high incidence of GERD.[66] It is appropriate to consider premedication to reduce gastric volume and acidity, as well as an anesthetic technique to minimize the risk of pulmonary aspiration of gastric contents. An aspiration event in such a patient could easily be fatal. Placement of an intra-arterial catheter is advised for all but the most vigorous of these patients undergoing minor surgery (see Box 4-10).

Patients with IPF are most likely to present to the operating room (OR) for lung biopsy to establish the diagnosis, for lung transplant in a curative effort, or for resection of a pulmonary neoplasm. These procedures usually require one-lung ventilation, a challenge in patients with advanced disease. Placement of a double-lumen ETT will provide the added ability to provide passive oxygenation to the nonventilated lung in an effort to minimize hypoxemia. Patients with advanced disease may require postoperative care in an intensive care unit (ICU) and possible mechanical ventilation.

Acute Respiratory Distress Syndrome

Acute respiratory distress syndrome (ARDS) is a severe form of acute lung injury resulting from an underlying illness or lung injury. ARDS may occur in as many as 10 to 20 per 100,000 individuals.[67] Several disorders are implicated as risk factors for developing ARDS, through direct lung injury or a systemic inflammatory response (Table 4-7). The underlying lesion is injury to the alveolar-capillary membrane and increased membrane permeability. Proteinaceous edema fluid accumulates in the alveoli, resulting in impaired oxygenation and poorly compliant (stiff) lungs. ARDS develops acutely over 1 to 2 days. If a patient is alert and spontaneously

TABLE 4-7 ■ Acute Respiratory Distress Syndrome: Associated Clinical Disorders

Direct Lung Injury	Indirect Lung Injury
Aspiration of gastric contents	Sepsis
Inhalation of toxic fumes	Major trauma
Near-drowning	Reperfusion injury
Pulmonary contusions	Massive transfusions
Diffuse pulmonary infection	Drug overdose

Data from Hudson LD, Steinberg KP: Acute respiratory distress syndrome: clinical features, management and outcome. In Fishman AP, et al, editors: *Fishman's pulmonary diseases and disorders,* New York, 1998, McGraw-Hill, p 2550.

ventilating, anxiety and dyspnea will be the earliest signs. As inflammatory changes occur, tachypnea and increased work of breathing will be noted.

Mechanical ventilation is required to maintain oxygenation. Chest radiographs typically reveal diffuse bilateral alveolar infiltrates similar to the findings of pulmonary edema. There is no laboratory test to diagnose ARDS. As a clinical diagnosis, criteria for diagnosing ARDS are acute onset of respiratory distress requiring intubation and mechanical ventilation; a Pao_2/Fio_2 ratio of less than 200, a chest radiograph with bilateral infiltrates suggestive of pulmonary edema, and no evidence of CHF or, if measured, a pulmonary artery wedge pressure less than 18 mm Hg.[68] Although it has declined over the past 10 years, ARDS still has a high mortality rate of 25% to 35%. Patients who do survive generally return to a pulmonary function near their baseline. Any remaining defect is likely restrictive or involving decreased diffusion capacity, and more disabling sequelae are possible.[69]

Intraoperative management of ARDS is an extension of the patient's ICU care. Many patients have a severe underlying injury or illness, which also requires significant perioperative attention. The approach to ventilator management plays a significant role in ARDS mortality. Instituting low–tidal volume ventilation of 6 mL/kg (predicted body weight) and maintaining plateau pressures of less than 30 cm H_2O were found to reduce mortality by almost 20%.[70,71] This approach may result in hypercapnia and respiratory acidosis, which can be monitored and treated with sodium bicarbonate. Permissive hypercapnia is usually well tolerated and may reduce mortality from lung injury.[72] There is no clear evidence to support that pressure-cycled ventilation is superior to volume-cycled ventilation.

Administration of PEEP is necessary and results in recruitment of alveoli and better ventilation/perfusion matching. No set level of PEEP has been shown to be superior.[71] Other maneuvers, such as sigh breathing and periodic rotation of the patient to the prone position, may result in improved oxygenation but are not associated with improved outcomes. Invasive monitors will frequently be in place when the patient arrives in the OR; if not, an intra-arterial catheter should be inserted. For procedures involving major fluid shifts, placement of a PAC or use of TEE may be helpful in guiding resuscitation and avoiding overzealous fluid administration, which might adversely impact the patient's respiratory status. However, ARDS patients in an ICU do not have better outcomes when managed with a PAC as opposed to a central venous catheter.[73] Neutral fluid balance can also benefit patients with ARDS, although appropriate fluid resuscitation and maintenance of vital organ perfusion usually preclude such an intraoperative fluid management strategy. Colloids such as albumin and hetastarch offer no advantage over crystalloid solutions because impaired alveolar-capillary membranes allow both classes of fluid to reach the extravascular space (see Box 4-10).

Pulmonary Histiocytosis X

Pulmonary histiocytosis X (PHX), also called "pulmonary Langerhans cell granulomatosis," is an uncommon interstitial lung disease associated with cigarette smoking. Related disorders are Hand-Schüller-Christian and Letterer-Siwe diseases. The primary defect appears to be the pathologic accumulation of Langerhans cells around bronchioles and the pulmonary vasculature, leading to the formation of granulomas and fibrosis. Most PHX patients present in early adulthood and have a history of cigarette smoking, with men and women equally affected.

Presenting symptoms are nonspecific and include nonproductive cough, dyspnea, fatigue, fever, and weight loss (Table 4-8). Reticulonodular infiltrates, upper-lobe and middle-lobe cysts, and stellate nodules with sparing of the costophrenic angle on chest radiography highly suggest PHX; bronchoalveolar lavage (BAL) or biopsy confirms the diagnosis. Results of spirometry may yield an obstructive, restrictive, mixed, or normal pattern. A decrease in diffusion capacity appears to be the most consistent finding. Physical limitation in PHX patients is frequently out of proportion to spirometry results, and pulmonary hypertension

TABLE 4-8 ■ Pulmonary Histiocytosis X: Associated or Causal Comorbidities

Condition	Issues
Spontaneous pneumothorax	May be recurrent
Hemoptysis secondary to aspergillosis	Rare
Primary lung tumors	Causative relationship is unclear.
Secondary pulmonary hypertension	Common, may result in cor pulmonale
Central diabetes insipidus	Occurs with central nervous system involvement
Cystic bone lesions	Cause bone pain and pathologic fractures

may play a significant role in contributing to diminished exercise capacity. In advanced disease, pulmonary artery pressures in the range of 60 mm Hg are not unusual.[74]

The course of PHX is unpredictable. Improvement or complete remission may occur spontaneously or as the result of smoking cessation. A minority of patients progress to pulmonary fibrosis. Age at presentation (>26 years), forced expiratory volume in 1 second/forced viral capacity (FEV_1/FVC) ratio less than 0.66, and right ventricular/total lung capacity (RV/TLC) ratio greater than 0.33 are cited as predictors of advanced disease and increased mortality.[75] Corticosteroids and chemotherapeutic agents are used in attempts to treat PHX, but the disease is frequently refractory to treatment. Lung transplantation has been performed with success, although PHX has recurred in the transplanted lungs of patients who had extrapulmonary involvement and had resumed smoking.[76]

Patients who are in remission or have only mild symptoms do not require special preoperative evaluation or intraoperative management beyond that warranted by the scheduled procedure. In patients with more advanced disease, a review of PFT results and ABG analysis and evaluation of pulmonary pressures by echocardiography or direct measurement are recommended. Based on these results, intraoperative management should be tailored to avoid increases in pulmonary artery pressure. Placement of a PAC may be necessary to help achieve this goal. The risk of pneumothorax in this population warrants an effort to minimize peak airway pressures. If diabetes insipidus is present, treatment with desmopressin should be continued perioperatively. The potential for pathologic fractures from cystic bone lesions requires special attention to patient positioning and padding. As in all patients with pulmonary disability preoperatively, the potential for postoperative ventilatory support should be factored into the anesthetic plan and discussed in advance with the patient (see Box 4-10).

Lymphangioleiomyomatosis

Lymphangioleiomyomatosis (LAM) is a rare, progressive interstitial lung disease of unknown origin that frequently leads to deteriorating lung function and death secondary to respiratory failure. LAM occurs in women of reproductive age and is exacerbated by pregnancy. It also occurs in male and female patients with tuberous sclerosis. The condition results from the proliferation of interstitial smooth muscle and formation of cysts, which obliterate and obstruct the airways. Complaints of dyspnea are the typical presenting symptom. Individuals with LAM develop hyperinflated lungs with an increased total lung capacity. They also develop an obstructive pattern on spirometry. Spontaneous pneumothorax caused by cyst rupture is common. Obstruction and eventual rupture of the thoracic duct, resulting in chylothorax, is another manifestation of LAM. Hemoptysis occurs infrequently. Chest radiographs are normal appearing early in the disease but resemble those of end-stage emphysema in advanced disease. Reticulonodular opacities may also be seen. An obstructive or occasionally a mixed pattern is present on spirometry, along with a significant decrease in diffusion capacity. Exercise capacity will be severely decreased because of ventilation/perfusion inequality and increased work of breathing.[77] ABG analysis typically reveals a decrease in Po_2 and Pco_2, although pH is normal.[78]

Estrogen is thought to play a role in the development of LAM because of its almost exclusive occurrence in women of childbearing age, its exacerbation by pregnancy, and presence of estrogen receptors on biopsy tissue. Recently, rapamycin (sirolimus) has been suggested as a therapeutic option for LAM. The results are not consistent, and some studies show significant reduction in size of angiomyolipomas and improvement of lung function.[79] Corticosteroids are ineffective. Modalities to block the molecular effects of estrogen (e.g., doxycycline) have been somewhat more successful. These approaches include oophorectomy, progesterone, and tamoxifen. Lung transplantation is offered to patients with advanced disease, although this is frequently complicated by disease-associated problems such as pleural adhesions, postoperative chylothorax, pneumothorax, and recurrent LAM.[79] Lung transplant may be considered as an option for end-stage pulmonary LAM. Survival after lung transplant is 79% at 1 year and 73% at 3 years.[80]

Preoperative evaluation should include a review of recent PFTs and chest radiographs, as well as ABG analysis in advanced cases. Elective surgery should be postponed until after significant chylothorax, if present, can be drained and chest tubes inserted to resolve existing pneumothoraces. Recurrent leakage of lymph results in an impaired immune response and nutritional wasting, which increase the patient's risk of perioperative complications and should be addressed before surgery by enteral or parenteral nutritional support. For patients with advanced disease, ventilator management should be similar to that for a patient with severe emphysema, including prolonged expiratory time and avoidance of high inspiratory pressure. Postoperative ventilatory support may be required if the patient has severe underlying disease and is undergoing major or extensive surgery. Placement of an intra-arterial catheter is helpful in obtaining serial ABGs to guide ventilator management (see Box 4-10).

ARTHRITIC DISEASES CREATING UPPER AIRWAY AND RESPIRATORY PROBLEMS

Ankylosing Spondylitis

Ankylosing spondylitis (AkS) is a chronic inflammatory process of unknown etiology that primarily deforms the axial skeleton, resulting in fusion. The disease is predominantly diagnosed in young adults, with men more likely to be affected than women. Prevalence in the United States is about 1 in 1000 individuals. AkS apparently has a genetic component, because most affected individuals are HLA-B27 positive.

As a result of chronic inflammatory changes at the ligamentous insertions onto bone, the vertebrae begin to grow into each other, forming outgrowths known as *syndesmophytes*. These changes result in the appearance of a "bamboo spine"

in radiologic evaluation and decreased mobility of the spine. This process generally begins in the sacral and lumbar regions, with cervical involvement occurring much later in the disease course. Extraskeletal manifestations of AkS may occur, particularly peripheral joint manifestations; although generally uncommon, these include aortic insufficiency, cardiac conduction abnormalities, iritis, upper-lobe fibrobullous disease, and pleural effusions. Risk of aspergilloma and hemoptysis is high if fibrobullous disease develops.[81]

Involvement of the sternocostal, costovertebral, and thoracic spine results in decreased mobility of the thoracic cage and a restrictive ventilatory pattern. Although common in AkS patients, decreased exercise tolerance is thought to be caused by deconditioning as opposed to a primary pulmonary defect.[82] The limitation in thoracic cage movement is almost totally compensated for by increased diaphragmatic excursion.[83] As the disease progresses, exercise tolerance also is decreased because of the restrictive lung process.

Historically, treatment for AkS was symptom based and relied on NSAIDs and physical therapy to reduce back pain and stiffness. Using NSAIDs for long-term therapy poses an increased risk of peptic ulcers and gastritis in this population. For this reason, cyclo-oxygenase (COX-2) inhibitors have been increasingly used as an alternative. The controversy regarding the cardiovascular safety of COX-2 inhibitors indicates careful consideration of the risks and benefits. Sulfasalazine, methotrexate, and corticosteroids are used in severe cases. Most recently, more than a third of AkS patients were in remission after 5 years of continuous TNF inhibitors therapy.[84,85]

ANESTHESIA MANAGEMENT

A patient with advanced AkS presents a significant challenge to the anesthesiologist, frequently needing orthopedic procedures on the hips and knees (Box 4-12). Preoperative evaluation should include radiographs of the lower and cervical spine to assess the extent of fusion. Caution should be exercised when instrumenting the airway because of involvement of the cervical spine. Decreased range of motion and poor mouth opening can make direct laryngoscopy difficult, and excess force applied to the neck can result in cervical fracture. Atlantoaxial subluxation is also present in a subset of these patients.[86] If advanced disease is present, an alternative and conservative approach to airway management (including an awake intubation) is strongly recommended, preferably one that maintains spontaneous ventilation. Adjuncts such as a laryngeal mask airway (LMA), videolaryngoscope, and fiberoptic bronchoscope should be readily available. Neuraxial anesthesia is very challenging in AkS patients. The ossification of spinal ligaments significantly narrows or even closes the intervertebral space and prevents optimal positioning. Alternatives reported as successful include a lateral approach to spinal placement[87] and placement of caudal catheters.[88]

Intraoperative management must include special attention to positioning because of the inflexibility of the AkS patient's spine. Diaphragmatic function should be optimized during spontaneous ventilation because of a restrictive thoracic cage. This can be accomplished by avoiding the Trendelenburg position and using large-diameter ETTs when possible. Interscalene blocks can result in short-term ipsilateral diaphragmatic paralysis and should be avoided. Higher peak pressures may occur with PPV and are expected. Adequate ventilation during laparoscopic surgery may not be possible, and hypercarbia may develop; if not excessive, it can be tolerated until the end of the procedure. Strictest extubation criteria should be observed in patients with AkS, because their heavy reliance on diaphragmatic function increases their risk of postoperative respiratory insufficiency, and emergent reintubation carries a significant risk of morbidity and failure.

BOX 4-12 ■ ANESTHESIA CONCERNS FOR PATIENTS WITH ARTHRITIC DISEASE

Ankylosing Spondylitis

Assess cardiopulmonary function.
Review radiographic imaging to determine the significance of cervical spine disease before airway management and positioning that necessitate movement of the neck.
Use cautious manipulation of the neck because of instability and mobility limitations.
These patients should be regarded as having a "difficult airway."
Neuroaxial anesthesia is very challenging.
Give special attention to positioning.

Kyphosis and Scoliosis

Assess cardiopulmonary and neurologic function.
May have significant blood loss during surgery to correct either condition.
May have one-lung ventilation.
Deliberate hypotension may be requested intraoperatively.
Take special care with positioning.
Consider intraoperative neurophysiologic monitoring (SSEP, MEP).

Kyphosis and Scoliosis

Scoliosis is a lateral and rotational deformity of the spine that also results in deformity of the rib cage. *Kyphosis* is an exaggerated anterior flexion of the spine resulting in a rounded or humpbacked appearance. These disorders are frequently seen together and are referred to as *kyphoscoliosis.* The vast majority of cases can be classified as idiopathic, congenital, or neuromuscular. The *idiopathic* form is the most common and is more likely to occur in women than men. Corrective surgery is performed for scoliosis when spinal angulation, also known as the Cobb angle, exceeds 50% in the thoracic or 40% in the lumbar spine.[89]

Preoperative assessment should focus on any cardiovascular, respiratory, or neurologic impairment related to the deformity. Restrictive lung disease is common, the result of a narrowed chest cavity. Although patient history will provide significant insight into the level of disability, PFTs and ABG analysis are crucial in evaluating the extent of restriction and hypoxemia. This information will guide decisions regarding postoperative ventilatory support. PFTs are likely to demonstrate a reduced vital capacity and total lung capacity, as well as a normal residual volume. Hypoxemia results from ventilation/perfusion inequality. Patients may

also hypoventilate. Cor pulmonale resulting from chronic hypoxemia and pulmonary hypertension may be present in advanced cases. These concerns make electrocardiography, echocardiography, and, in some situations, an exercise stress test reasonable components of preoperative testing. A history and physical examination is sufficient to evaluate the patient's neurologic status. It is important to document any pre-existing neurologic deficits so as to differentiate between baseline deficits and those resulting from surgery. This is also helpful in minimizing further injury secondary to positioning or airway management.

Corrective spinal surgery is the procedure most likely to bring these patients to the OR. The many variations include anterior, posterior, and combined approaches, as well as lumbar and thoracic level repairs. A combined anterior/posterior approach under a single anesthetic has a higher rate of major complications than a staged procedure and is best avoided if possible.[90] Many elements of the anesthetic plan, such as positioning and the need for one-lung ventilation, will be dictated by the specific procedure.

ANESTHESIA MANAGEMENT

Despite differences in the types of spinal surgery, several concerns apply to all. These procedures frequently involve significant blood loss, possible one-lung ventilation, and the need for deliberate hypotension. The patients have underlying pulmonary restrictive disease. All of these factors make arterial line placement and ABG analysis critical to effective perioperative management. The presence of restrictive lung disease combined with prone or lateral positioning can make oxygenation and ventilation with acceptable peak airway pressures challenging. The use of an anesthesia machine or ventilator capable of pressure control ventilation may be helpful. Based on the level of preoperative disability, the need for postoperative ventilation should be discussed with the patient and family. Of note, adequate oxygenation during one-lung ventilation for anterior thoracic approaches may be difficult. Placement of a double-lumen ETT instead of a bronchial blocker offers the advantage of delivering passive oxygenation to the nonventilated lung. However, such tubes have the disadvantage of needing to switch to a single-lumen ETT at the end of the procedure if postoperative ventilation is required. Improvement in the patient's pulmonary function does not occur immediately after surgery, and any improvement may take months to several years, depending on the procedure.[91]

Large-bore venous access, central or otherwise, is needed to ensure rapid replacement of intraoperative blood loss. Central venous pressure monitoring is of limited usefulness in these procedures because of the effects of positioning on the values obtained and possible pulmonary hypertension or cor pulmonale, which reduces the value of central venous pressure monitoring in determining the adequacy of intravascular volume. TEE is a reasonable choice to monitor intravascular volume status and cardiac contractility, if available and if the patient's position allows.

Spinal cord monitoring such as *somatosensory evoked potentials* (SSEPs) and, to a lesser extent, motor evoked potentials (MEPs) are frequently used to detect direct trauma or vascular compromise to the spinal cord. Data obtained by TEE and venous oxygen saturation (SvO_2) monitoring suggest that spinal cord ischemia that results from distraction of the spine is the result of both direct compression of the spinal cord as well as decreased cardiac output and decreased BP caused by compression of vena cava or the heart.[92] Intraoperative neurologic monitoring has become the standard of care for procedures involving significant distraction of the spine. Patient temperature, pH, and adequate BP must all be maintained within narrow limits to maximize the effectiveness of SSEP monitoring. Controversy surrounds the preferred anesthetic agents with SSEP monitoring. The literature is frequently contradictory, and institutional preferences vary greatly, although propofol infusions and nitrous oxide are popular. The most important factor does appear to be administration of a stable anesthetic, with minimal bolus dosing and close communication with the clinician monitoring the evoked potentials (see Box 4-12).

DRUG-INDUCED LUNG INJURY

Bleomycin Toxicity

Bleomycin is an antineoplastic antibiotic used in combination chemotherapy for a number of malignancies, including Hodgkin's lymphoma, Wilms' tumor, and testicular cancer. Although effective in treating bacterial and fungal infections, bleomycin is not used for these purposes because of its cytotoxicity. The appeal of bleomycin in combination chemotherapy protocols is its lack of a myelosuppressive effect. This avoids adding to the bone marrow toxicity common to other antineoplastic agents.

Unfortunately, bleomycin carries the risk of inducing pulmonary toxicity, which can result in pulmonary fibrosis and can be life threatening. Total dose received relates to the extent of pulmonary toxicity in animals, but this is less clear in humans. There is no consensus on a cumulative dose that increases risk, although more than 300,000 IU is the suggested threshold.[93] Intravascular administration may be a risk factor compared with intramuscular dosing.[94] Chest irradiation in conjunction with bleomycin therapy appears to increase the risk of bleomycin-induced pulmonary fibrosis, as does advanced age, a history of smoking, and treatment with other chemotherapeutic agents that have pulmonary toxicities, such as busulfan, carmustine, semustine, and lomustine. Impaired renal function increases the risk of toxicity by reducing the elimination of bleomycin from the body.

Pulmonary toxicity caused by bleomycin results in a similar pulmonary fibrosis as seen in IPF. Patients usually present with a nonproductive cough accompanied by dyspnea. Chest radiographs initially reveal bibasilar infiltrates, but as the process continues, the radiograph will take on a "honeycomb lung" appearance. PFTs will have a restrictive pattern in symptomatic patients but are of little predictive value in asymptomatic patients who have been exposed to bleomycin.

Evaluation of the bleomycin patient for anesthesia focuses on pulmonary function, symptoms (e.g., dry cough, dyspnea, decreased exercise tolerance), and risk factors (e.g., large cumulative dose, chest radiation, smoking). If the patient

denies symptoms, chest radiographs, PFTs, and ABG analysis are not likely to be useful. Symptomatic patients require testing to quantify their disability, plan appropriate perioperative care, and determine the need for postoperative ventilatory support.

ANESTHESIA MANAGEMENT

A landmark study has guided the anesthetic management of bleomycin patients for 35 years. Goldiner et al.[95] implicated hyperoxia and fluid overload as increasing the risk of perioperative pulmonary morbidity and mortality in patients who received bleomycin. Although subsequent studies have questioned these guidelines, there is no reason to believe that providing a higher fraction of inspired oxygen (Fio_2) than that needed to maintain adequate oxygenation is of any benefit to these patients. The one exception to this is during preoxygenation, which is relatively brief, before induction of general anesthesia.[94] When adequate oxygenation does require an Fio_2 greater than 30%, use of PEEP may facilitate oxygen action without necessitating higher levels of Fio_2. Fluid therapy should be conservative, with the goal of maintaining adequate intravascular volume and avoiding excess fluid administration. There is no evidence to support the use of colloid instead of crystalloid in bleomycin patients. When significant blood loss or significant fluid shifts are expected in surgery, intraarterial and central venous catheters may be helpful. There is no clear answer as to how long after completion of therapy with bleomycin a patient continues to be at risk for pulmonary fibrosis, although minimizing Fio_2 for 1 to 2 years would seem prudent (Box 4-13).

In patients with documented pulmonary bleomycin toxicity, higher-than-normal peak pressures are expected with PPV, although this may be necessary for adequate oxygenation and ventilation. Strict extubation criteria should be observed because these patients are at increased risk of postoperative pulmonary complications; sedating medications decrease respiratory effort and should be minimized postoperatively. If the surgery permits, the use of regional techniques with minimal sedation and opioids may be helpful. Good postoperative pulmonary toilet, including deep breathing and coughing, must be encouraged to reduce the risk of postoperative pulmonary complications.

INFECTIOUS DISEASES

Influenza A

Although outbreaks of influenza are common, the strain and severity vary significantly. Influenza pandemics occur every few decades and are devastating. More than 40 million people died during the pandemic in Spain in 1918, and 1 million died in Hong Kong in 1968.[96] Both were the result of an influenza A strain variant (H1N1). Influenza viruses undergo continual antigenic drift, aiding in their ability to resist the host's immunity. This contributes to the continued pandemics of viruses, particularly influenza A strains. Most recently, the H1N1 strain led to catastrophic mortality, particularly in the infant and young population. First identified in Mexico in 2009, H1N1 quickly spread worldwide. This variant is composed of swine, bird, and human strains of influenza A. The rates of transmission are higher than for the seasonal influenza. The main route of transmission is human-to-human exposure through large respiratory droplets or contaminated surfaces.

Patients present with a combination of flulike symptoms, including fever, cough, shortness of breath, fatigue, diarrhea, and vomiting. Associated comorbidities include asthma, obesity, and diabetes mellitus. Infants and children are at increased risk, as are patients with chronic health conditions, those receiving renal replacement therapy, and pregnant women. Concomitant complications include myocarditis, encephalitis, ARDS, refractory hypoxemia, and secondary bacterial infections (e.g., sepsis).

A few diagnostic tests are available for influenza A, but treatment should not be delayed awaiting results. Patients with a high index of suspicion should be treated without a confirmatory test. A provisional diagnosis can be established within 30 minutes to 1 hour by the rapid influenza diagnostic test (RIDT). However, both RIDT and direct immunofluorescent assay (DFA) are unable to differentiate between pandemic and seasonal influenza variants and have lower sensitivity than real-time reverse-transcriptase polymerase chain reaction (rRT-PCR) and viral culture. Confirmation of pandemic virus can be determined only by rRT-PCR or viral culture (Table 4-9).

Prophylactic treatment is of no benefit and increases the risk of resistance to antiviral medication such as neuraminidase inhibitors (e.g., oseltamivir phosphate). Early treatment in high-risk patients with antiviral medication within 48 hours of onset of symptoms may reduce morbidity and mortality. Older patients are less susceptible to the recent pandemic strain, but if infected and they develop disease, the clinical manifestations are more severe. Vaccination is one of the most effective methods to reduce morbidity and mortality associated with influenza. Specific vaccinations do not provide protection against other influenza viruses. The vaccine is effective 14 days after vaccination.

Most deaths result from rapidly progressive respiratory failure, ARDS, and refractory shock. These patients deteriorate 3 to 5 days after onset of symptoms. They present with resistant hypoxia and frequently require respiratory rescue therapies such as neuromuscular blockade, inhaled NO, prone positioning, and high-frequency oscillatory ventilation (HFOV). Extracorporeal membrane oxygenation (ECMO) may be beneficial in patients with severe infection, but it is unclear whether it decreases mortality.

ANESTHESIA MANAGEMENT

The anesthesiologist is at high risk of exposure to influenza virus (Box 4-14). Therefore, full contact precautions are indicated, including disposable fluid-resistant gowns, goggles, face

BOX 4-13 ■ ANESTHESIA CONCERNS FOR PATIENTS WITH BLEOMYCIN TOXICITY

Assess cardiopulmonary function.
Use conservative fluid resuscitation.
Minimize fraction of inspired oxygen (Fio_2).
Ensure aggressive postoperative pulmonary care.

TABLE 4-9 ■ Diagnostic Testing for Influenza A

Diagnostic Test	Typical Processing Time	Sensitivity for H1N1 2009	Method
Rapid influenza diagnostic test (RIDT)	0.5-1 hour	10%-70%	Antigen detection
Direct immunofluorescent assay (DFA)	2-4 hours	47%-93%	Antigen detection
rRT-PCR*	48-96 hours	86%-100%	RNA detection
Viral culture†	2-10 days	—	Virus isolation

Data from Fartoukh M, Humbert M, Capron F, et al: Severe pulmonary hypertension in histiocytosis X, *Am J Respir Crit Care Med* 161:216-223, 2000.
*Real-time reverse-transcriptase polymerase chain reaction.
†Differentiate among other influenza A viruses.

BOX 4-14 ■ ANESTHESIA CONCERNS FOR PATIENTS WITH INFECTIOUS DISEASE

Influenza A (H1N1)
Assess cardiopulmonary function.
May have ARDS presentation.
Severe cases may require postoperative ventilatory support.
Restrict steroid use.
Anesthesiologist is at high risk of exposure.
Use full contact precautions.
Take special care to avoid contamination of equipment and surfaces.
Provide supportive management.

Severe Acute Respiratory Syndrome
Assess cardiopulmonary function.
Anesthesiologist is at high risk of exposure.
Use full contact precautions.
Take special care to avoid contamination of equipment and surfaces.
Ensure supportive management.

Echinococcal Disease of Lung
Assess pulmonary function.
Large cysts may cause respiratory compromise.
May have one-lung ventilation.
Provide supportive management.

shields, gloves, and handwashing. Personal protection systems may be advisable for personnel caring for such patients (see SARS). Treatment and perioperative management of those with clinically severe disease is mainly supportive and similar to that of patients with ARDS who require ventilatory management. Intraoperative invasive monitors, such as arterial and central catheters, may be useful for cardiopulmonary management. Corticosteroids should be restricted to patients with adrenal suppression because these drugs have been associated with increased mortality in H1N1-infected patients, increasing viral shedding time and the risk of coinfection.[97]

Severe Acute Respiratory Syndrome

Severe acute respiratory syndrome (SARS) is a highly infectious disease transmitted by a coronavirus (SARS-CoV). It results in atypical pneumonia, which may progress to respiratory distress syndrome. First recognized in 2002 with cases in Southeast Asia, SARS had made its way to North America during 2003, with hundreds of cases in Ontario, Canada. More than 8000 reported cases of SARS worldwide resulted in over 700 deaths. Whether, when, or where another outbreak may occur is unknown, but familiarity with the syndrome and how to contain the spread are the responsibility of all health care professionals.

Otherwise healthy individuals can be infected by contact or droplet spread, which may be person to person or indirectly through contact with contaminated surfaces, because the coronavirus can live in the environment for 24 to 48 hours. The virus enters the body through mucosal surfaces in the respiratory tract and eyes. The incubation period is 2 to 7 days. Presenting symptoms are vague and include high fever, dry cough, malaise, myalgia, and shortness of breath, which typically progresses to pneumonia and in severe cases to ventilator-dependent respiratory distress syndrome. Diagnosis is based on clinical and epidemiologic data, because no laboratory test reliably detects infection early in the clinical course.[98] Treatment of infected patients is primarily supportive and similar to that of any other atypical pneumonia. None of the currently available antiviral drugs has been shown to be effective against SARS-CoV.

ANESTHESIA MANAGEMENT

The anesthesiologist's contact with SARS patients occurs primarily during airway management for patients in respiratory distress (see Box 4-14). The anesthesiologist will be close to the patient's upper airway and thus at high risk of exposure to the virus. Full contact precautions are recommended, including disposable fluid-resistant gowns, goggles, face shields, double gloving, handwashing, and N95 (or equivalent) fit-tested masks.[99] Standard surgical face masks and gowns are inadequate. Removal and disposal of equipment so as not to contaminate the wearer or others is as important as using the proper protection. Some institutions have taken the added precaution of using a personal protection system (PPS) for personnel involved in high-risk procedures with SARS patients. These PPS units consist of belt-mounted, powered air purifiers with high-efficiency particulate air (HEPA) filters and a lightweight headpiece. Use of this equipment requires training as well as adequate donning time. The noise generated by the system makes communication and auscultation of breath and

cardiac sounds difficult.[99,100] Attention must also be directed to avoiding contamination of anesthesia workstations and equipment. This includes placing HEPA filters on the inspiratory and expiratory limbs of ventilators and anesthesia machines. Providers must be mindful of everything they touch or that comes into contact with the patient and ensure appropriate cleaning or disposal of these materials. Maintaining separate clean and dirty work areas may be helpful in this regard.[100]

Echinococcal Disease of Lung

Echinococcal disease or hydatid disease occurs when a human is infected with *Echinococcus granulosus,* a canine tapeworm. The eggs of the worm are passed in the feces of infested dogs. Humans acquire the infection by unintentionally ingesting the eggs. Larvae then migrate to the liver, with some eventually arriving in the lungs and other tissues. The parasites then mature to form hydatid cysts. The lung forms a protective granulomatous layer around the cyst, which over time becomes fibrotic. It is estimated that hydatid cysts grow 1 to 2 cm a year.[101] As a result of the fecal-oral transmission, echinococcal lung disease is more common in children than adults. Overall it is rare in North America but common in other parts of the world.

These cysts are frequently asymptomatic, and pulmonary cysts are often detected on routine chest radiographs. The most likely symptoms are cough, dyspnea, and chest pain. Rupture of a cyst can occur spontaneously or on surgical manipulation. This may result in an anaphylactic reaction or spread the disease to other organs. For this reason, transthoracic needle aspiration should never be attempted. Chest radiographs will reveal a cystic lesion, which may be rather large, accompanied by an area of pneumonitis or atelectasis. There is no effective medical treatment for hydatid cyst of the lung, and surgical removal is the preferred therapeutic option.

Patients with small, asymptomatic cysts require no preoperative evaluation beyond the routine. Larger cysts may result in respiratory compromise, typically presenting as dyspnea. Spirometry may reveal decreased volumes because of the space-occupying lesion. Respiratory acidosis and hypoxemia may also be present. In advanced disease, the patient may not tolerate surgery or anesthesia. In these rare circumstances, removal of the cyst has been performed under thoracic epidural anesthesia with success.[102]

ANESTHESIA MANAGEMENT

For patients considered reasonable candidates for general anesthesia, one-lung ventilation may be requested to optimize surgical exposure for resection of the cyst. Isolation of the contralateral lung field has the added benefit of decreasing the risk of contamination should the cyst rupture during surgery. The patient with only unilateral disease should have little difficulty tolerating one-lung ventilation, because the unaffected side is primarily responsible for gas exchange if the cyst is clinically significant. An arterial catheter is appropriate when one-lung ventilation is planned. Close communication between surgeon and anesthesiologist during drainage and delivery of the cyst is essential to avoid spillage. In the event of contamination, anaphylaxis may occur, and the anesthesiologist should be prepared by having large-bore IV access, as well as immediate availability of epinephrine, diphenhydramine, and corticosteroids (see Box 4-14).

CONCLUSION

Clinical interactions with patients who have uncommon pulmonary conditions may range from a simple excisional biopsy for asymptomatic pulmonary sarcoid, to a hip replacement in ankylosing spondylitis, to a double-lung transplant for end-stage cystic fibrosis. The spectrum of procedures therefore extends from the routine to the extraordinarily complicated. Successful management of patients with respiratory disorders is often challenging in both the conceptual and technical realms. An understanding of the pathophysiology and treatment of the uncommon pulmonary disorder will allow the anesthesiologist to anticipate likely clinical problems and tailor anesthetic management to minimize the chance of intraoperative and postoperative complications.

REFERENCES

1. Lawrence VA, Dhanda R, Hilsenbeck SG, et al: Risk of pulmonary complications after elective abdominal surgery, *Chest* 110:744–750, 1996.
2. Ferguson M: Preoperative assessment of pulmonary risk, *Chest* 115: 58S–63S, 1999.
3. Passannante A, Rock P: When should pulmonary function tests be performed preoperatively? In Fleisher LA, editor: *Evidence-based practice of anesthesiology*, Philadelphia, 2004, Saunders.
4. Rock P, Passannante A: Assessment: pulmonary, *Anesthesiol Clin North America* 22:77–91, 2004.
5. Qaseem A, Snow V, Fitterman N, et al: Risk assessment for and strategies to reduce perioperative pulmonary complications for patients undergoing noncardiothoracic surgery: a guideline from the American College of Physicians, *Ann Intern Med* 144:575–580, 2006.
6. Wightman J: A prospective survey of the incidence of postoperative pulmonary complications, *Br J Surg* 55:85–91, 1968.
7. Johnson D, Kaplan L: Perioperative pulmonary complications, *Curr Opin Crit Care* 17:362–369, 2011.
8. Lawrence V, Dhanda R, Hilsenbeck S, et al: Risk of pulmonary complications after elective abdominal surgery, *Chest* 110:744–750, 1996.
9. Smetana G, Lawrence V, Cornell J: Preoperative pulmonary risk stratification for noncardiothoracic surgery: systematic review for the American College of Physicians, *Ann Intern Med* 144:581–595, 2006.
10. Celli B: What is the value of preoperative pulmonary function testing? *Med Clin North Am* 77:309–325, 1993.
11. Stock M, Downs J, Gauer P, et al: Prevention of postoperative pulmonary complications with CPAP, incentive spirometry, and conservative therapy, *Chest* 87:151–157, 1985.
12. Lawrence V, Cornell J, Smetana G: Strategies to reduce postoperative pulmonary complications after noncardiothoracic surgery: systematic review for the American College of Physicians, *Ann Intern Med* 144: 596–608, 2006.
13. Smetana G: Clinician's corner: a 68-year-old man with COPD contemplating colon cancer surgery, *JAMA* 297:2121–2130, 2007.
14. Dines D, Arms R, Bernatz P, et al: Pulmonary arteriovenous fistulas, *Mayo Clin Proc* 49:460–465, 1974.
15. Litzler PY, Douvrin F, Bouchart F, et al: Combined endovascular and video-assisted thoracoscopic procedure for treatment of a ruptured pulmonary arteriovenous fistula: case report and review of the literature, *J Thorac Cardiovasc Surg* 126:1204–1207, 2003.

16. Khurshid I, Downie G: Pulmonary arteriovenous malformations, *Postgrad Med J* 78:191–197, 2002.
17. Lake CL: Anesthesia and Wegener's granulomatosis: case report and review of the literature, *Anesth Analg* 57:353–359, 1978.
18. Erickson V, Hwang P: Wegener's granulomatosis: current trends in diagnosis and management, *Curr Opin Otolaryngol Head Neck Surg* 15:170–176, 2007.
19. Pietra G, Salhany K: *Lymphoproliferative disorders*, New York, 1998, McGraw-Hill.
20. Katzenstein AL, Carrington CB, Liebow AA: Lymphomatoid granulomatosis: a clinicopathologic study of 152 cases, *Cancer* 43:360–373, 1979.
21. Katzenstein A, Doxtader E, Narendra S: Lymphomatoid granulomatosis: insights gained over 4 decades, *Am J Surg Pathol* 34:e35–e48, 2010.
22. Masi AT, Hunder GG, Lie JT, et al: The American College of Rheumatology 1990 criteria for the classification of Churg-Strauss syndrome (allergic granulomatosis and angiitis), *Arthritis Rheum* 33: 1094–1100, 1990.
23. Gross W: Churg-Strauss syndrome: update on recent developments, *Curr Opin Rheumatol* 14:11–14, 2002.
24. Blaise G, Langleben D, Hubert B: Pulmonary arterial hypertension: pathophysiology and anesthetic approach, *Anesthesiology* 99:1415–1432, 2003.
25. Fischer LG, Van Aken H, Burkle H: Management of pulmonary hypertension: physiological and pharmacological considerations for anesthesiologists, *Anesth Analg* 96:1603–1616, 2003.
26. Galie N, Manes A, Negro L, et al: A meta-analysis of randomized controlled trials in pulmonary artery hypertension, *Eur Heart J* 30:394–403, 2009.
27. Humbert M, Sitbon O, Simonneau G: Treatment of pulmonary artery hypertension, *N Engl J Med* 351:1425–1436, 2004.
28. Rocca G: Anaesthesia in patients with cycstic fibrosis, *Curr Opin Anaesthesiol* 15:95–101, 2002.
29. Gibson RL, Burns JL, Ramsey BW: Pathophysiology and management of pulmonary infections in cystic fibrosis, *Am J Respir Crit Care Med* 168:918–951, 2003.
30. Flume PA: Pneumothorax in cystic fibrosis, *Chest* 123:217–221, 2003.
31. Bright-Thomas RJ, Webb AK: The heart in cystic fibrosis, *J R Soc Med* 95(Suppl 41):2–10, 2002.
32. Scott RB, O'Loughlin EV, Gall DG: Gastroesophageal reflux in patients with cystic fibrosis, *J Pediatr* 106:223–227, 1985.
33. Epler GR: Bronchiolitis obliterans organizing pneumonia, *Arch Intern Med* 161:158–164, 2001.
34. Chaparro C, Chamberlain D, Maurer J, et al: Bronchiolitis obliterans organizing pneumonia (BOOP) in lung transplant recipients, *Chest* 110:1150–1154, 1996.
35. Calabrese F, Giacometti C, Rea F, et al: Recurrence of idiopathic pulmonary hemosiderosis in a young adult patient after bilateral single-lung transplantation, *Transplantation* 74:1643–1645, 2002.
36. Carrington CB, Addington WW, Goff AM, et al: Chronic eosinophilic pneumonia, *N Engl J Med* 280:787–798, 1969.
37. Marchand E, Etienne-Mastroianni B, Chanez P, et al: Idiopathic chronic eosinophilic pneumonia and asthma: how do they influence each other? *Eur Respir J* 22:8–13, 2003.
38. Turner AN, Rees AJ: Goodpasture's disease and Alport's syndromes, *Annu Rev Med* 47:377–386, 1996.
39. Kelly PT, Haponik EF: Goodpasture syndrome: molecular and clinical advances, *Medicine (Baltimore)* 73:171–185, 1994.
40. Ewan PW, Jones HA, Rhodes CG, et al: Detection of intrapulmonary hemorrhage with carbon monoxide uptake. Application in Goodpasture's syndrome, *N Engl J Med* 295:1391–1396, 1976.
41. Nogee L, de Mello D, Dehner L, et al: Brief report: deficiency of pulmonary surfactant protein B in congenital alveolar proteinosis, *N Engl J Med* 328:406–410, 1993.
42. Trapnell BC, Whitsett JA, Nakata K: Pulmonary alveolar proteinosis, *N Engl J Med* 349:2527–2539, 2003.
43. Mazzone P, Thomassen MJ, Kavuru M: Our new understanding of pulmonary alveolar proteinosis: what an internist needs to know, *Cleve Clin J Med* 68:977–978, 2001.
44. Cheng SL, Chang HT, Lau HP, et al: Pulmonary alveolar proteinosis: treatment by bronchofiberscopic lobar lavage, *Chest* 122:1480–1485, 2002.
45. Swenson JD, Astle KL, Bailey PL: Reduction in left ventricular filling during bronchopulmonary lavage demonstrated by transesophageal echocardiography, *Anesth Analg* 81:634–637, 1995.
46. Shammas RL, Movahed A: Sarcoidosis of the heart, *Clin Cardiol* 16: 462–472, 1993.
47. Heck AW, Phillips LH Jr: Sarcoidosis and the nervous system, *Neurol Clin* 7:641–654, 1989.
48. Wills MH, Harris MM: An unusual airway complication with sarcoidosis, *Anesthesiology* 66:554–555, 1987.
49. Neel HB 3rd: McDonald TJ: Laryngeal sarcoidosis: report of 13 patients, *Ann Otol Rhinol Laryngol* 91(pt 1):359–362, 1982.
50. Jaffe R, Bogomolski-Yahalom V, Kramer MR: Vocal cord paralysis as the presenting symptom of sarcoidosis, *Respir Med* 88:633–636, 1994.
51. Euliano TY, White SE, Aleixo L: Sarcoidosis in a pregnant woman, *J Clin Anesth* 9:78–86, 1997.
52. Paramothayan N, Lasserson T, Jones P: Corticosteroids for pulmonary sarcoidosis (review), *Cochrane Database Syst Rev* CD001114, 2000.
53. Paramothayan S, Jones P: Corticosteroid therapy in pulmonary sarcoidosis, *JAMA* 287:1301–1307, 2002.
54. Iannuzzi M, Fontana J: Sarcoidosis: clinical presentation, immunopathogenesis and therapeutics, *JAMA* 305:391–397, 2011.
55. Ben-Menachem E: Systemic lupus erythematosus: a review for anesthesiologists, *Anesth Analg* 111:665–676, 2010.
56. Mills J: Systemic lupus erythematosus, *N Engl J Med* 330:1871–1879, 1994.
57. Menon G, Allt-Graham J: Anaesthetic implications of the anti-cardiolipin antibody syndrome, *Br J Anaesth* 70:87–90, 1993.
58. Glueck HI, Kant KS, Weiss MA, et al: Thrombosis in systemic lupus erythematosus: relation to the presence of circulating anticoagulants, *Arch Intern Med* 145:1389–1395, 1985.
59. Orens J, Martinez F, Lynch J: Pleuropulmonary manifestations of systemic lupus erythematosus, *Rheum Dis Clin North Am* 20:159–193, 1994.
60. Chick T, DeHoratius R, Skipper B, et al: Pulmonary dysfunction in systemic lupus erythematosus without pulmonary symptoms, *J Rheumatol* 3:262–268, 1976.
61. American Thoracic Society: Idiopathic pulmonary fibrosis: diagnosis and treatment. International consensus statement. American Thoracic Society (ATS), European Respiratory Society (ERS), *Am J Respir Crit Care Med* 161(pt 1):646–664, 2000.
62. Fujimoto T, Okazaki T, Matsukura T, et al: Operation for lung cancer in patients with idiopathic pulmonary fibrosis: surgical contraindication? *Ann Thorac Surg* 76:1674–1678; discussion, 1679, 2003.
63. Selman M, Thannickal VJ, Pardo A, et al: Idiopathic pulmonary fibrosis: pathogenesis and therapeutic approaches, *Drugs* 64:405–430, 2004.
64. Thabut G, Mal H, Castier Y, et al: Survival benefit of lung transplantation for patients with idiopathic pulmonary fibrosis, *J Thorac Cardiovasc Surg* 126:469–475, 2003.
65. Lee J, McLaughlin S, Collard H: Comprehensive care of the patient with idiopathic pulmonary fibrosis, *Curr Opin Pulm Med* 17:2011.
66. Raghu G: The role of gastroesophageal reflux in idiopathic pulmonary fibrosis, *Am J Med* 115(Suppl 3A):60–64, 2003.
67. Goss C, Brower R, Hudson L, et al: Incidence of acute lung injury in the United States, *Crit Care Med* 31:1607–1611, 2003.
68. Bernard GR, Artigas A, Brigham KL, et al: The American-European Consensus Conference on ARDS: definitions, mechanisms, relevant outcomes, and clinical trial coordination, *Am J Respir Crit Care Med* 149(pt 1):818–824, 1994.
69. Herridge M, Cheung A, Tansey C, et al: One-year outcomes in survivors of the acute respiratory distress syndrome, *N Engl J Med* 348:683–693, 2003.

70. Acute Respiratory Distress Syndrome Network: Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome, *N Engl J Med* 342:1301–1308, 2000.
71. Brower R, Lanken P, MacIntyre N, et al: Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome, *N Engl J Med* 351:327–336, 2004.
72. Chonghaile M, Higgins B, Lafey J: Permissive hypercapnia: role in protective lung ventilatory strategies, *Curr Opin Crit Care* 11:56–62, 2005.
73. National Heart, Lung and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network: Pulmonary artery versus central venous catheter to guide treatment of acute lung injury, *N Engl J Med* 354:2213–2224, 2006.
74. Fartoukh M, Humbert M, Capron F, et al: Severe pulmonary hypertension in histiocytosis X, *Am J Respir Crit Care Med* 161:216–223, 2000.
75. Delobbe A, Durieu J, Duhamel A, et al: Determinants of survival in pulmonary Langerhans' cell granulomatosis (histiocytosis X). Groupe d'Etude en Pathologie Interstitielle de la Societe de Pathologie Thoracique du Nord, *Eur Respir J* 9:2002–2006, 1996.
76. Etienne B, Bertocchi M, Gamondes JP, et al: Relapsing pulmonary Langerhans cell histiocytosis after lung transplantation, *Am J Respir Crit Care Med* 157:288–291, 1998.
77. Carrington CB, Cugell DW, Gaensler EA, et al: Lymphangioleiomyomatosis: physiologic-pathologic-radiologic correlations, *Am Rev Respir Dis* 116:977–995, 1977.
78. Corrin B, Liebow AA, Friedman PJ: Pulmonary lymphangiomyomatosis: a review, *Am J Pathol* 79:348–382, 1975.
79. Boehler A, Speich R, Russi EW, et al: Lung transplantation for lymphangioleiomyomatosis, *N Engl J Med* 335:1275–1280, 1996.
80. Taille C, Borie R, Crestani B: Current management of lymphangioleiomyomatosis, *Curr Opin Pulm Med* 17:2011.
81. Rosenow E, Strimlan CV, Muhm JR, et al: Pleuropulmonary manifestations of ankylosing spondylitis, *Mayo Clin Proc* 52:641–649, 1977.
82. Carter R, Riantawan P, Banham SW, et al: An investigation of factors limiting aerobic capacity in patients with ankylosing spondylitis, *Respir Med* 93:700–708, 1999.
83. Grimby G, Fugl-Meyer AR, Blomstrand A: Partitioning of the contributions of rib cage and abdomen to ventilation in ankylosing spondylitis, *Thorax* 29:179–184, 1974.
84. Woodward L, Kam P: Ankylosing spondylitis: recent developments and aneaesthetic implications, *Anaesthesia* 64:540–548, 2009.
85. Braun J, Sieper J: Ankylosing spondylitis, *Lancet* 369:1379–1390, 2007.
86. Ramos-Remus C, Gomez-Vargas A, Guzman-Guzman J, et al: Frequency of atlantoaxial subluxation and neurologic involvement in patients with ankylosing spondylitis, *J Rheumatol* 22:2120–2125, 1995.
87. Kumar CM, Mehta M: Ankylosing spondylitis: lateral approach to spinal anaesthesia for lower limb surgery, *Can J Anaesth* 42:73–76, 1995.
88. DeBoard JW, Ghia JN, Guilford WB: Caudal anesthesia in a patient with ankylosing spondylitis for hip surgery, *Anesthesiology* 54:164–166, 1981.
89. Winkler M, Marker E, Hetz H: The peri-operative management of major orthopaedic procedures, *Anaesthesia* 53(Suppl 2):37–41, 1998.
90. McDonnell MF, Glassman SD, Dimar JR Jr, et al: Perioperative complications of anterior procedures on the spine, *J Bone Joint Surg Am* 78: 839–847, 1996.
91. Raw DA, Beattie JK, Hunter JM: Anaesthesia for spinal surgery in adults, *Br J Anaesth* 91:886–904, 2003.
92. Bernard JM, Le Penven-Henninger C, Passuti N: Sudden decreases in mixed venous oxygen saturation during posterior spinal fusion, *Anesth Analg* 80:1038–1041, 1995.
93. O'Sullivan JM, Huddart RA, Norman AR, et al: Predicting the risk of bleomycin lung toxicity in patients with germ-cell tumours, *Ann Oncol* 14:91–96, 2003.
94. Waid-Jones MI, Coursin DB: Perioperative considerations for patients treated with bleomycin, *Chest* 99:993–999, 1991.
95. Goldiner P, Carlon G, Cvitkovic E, et al: Factors influencing postoperative morbidity and mortality in patients treated with bleomycin, *BMJ* 1:1664–1667, 1978.
96. Michaelis M, Doerr H, Cinatl J: An influenza A H1N1 virus revival: pandemic H1N1/09 virus, *Infection* 37:381–389, 2009.
97. Patel M, Dennis A, Flutter C, et al: Pandemic (H1N1) 2009 influenza, *Br J Anaesth* 104:128–142, 2010.
98. Centers for Disease Control and Prevention: *Severe acute respiratory syndrome (SARS)*, 2004. http://wwwcdcgov/ncidod/sars/clinicalguidancehtm.
99. Kamming D, Gardam M, Chung F: Anaesthesia and SARS, *Br J Anaesth* 90:715–718, 2003.
100. Peng PW, Wong DT, Bevan D, et al: Infection control and anesthesia: lessons learned from the Toronto SARS outbreak, *Can J Anaesth* 50: 989–997, 2003.
101. Balikian J, Mudarris F: Hydatid disease of the lungs: a roentgenologic study of 50 cases, *Am J Roentgenol Radium Ther Nucl Med* 122:692–707, 1974.
102. Dyer RA, Gordon PC, De Groot KM, et al: Excision of a giant hydatid cyst of the lung under thoracic epidural anaesthesia, *Anaesth Intensive Care* 29:181–184, 2001.