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CHAPTER

4 Respiratory Diseases

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A thorough knowledge of pulmonary anatomy and physiology is of paramount importance to the practicing anesthesiologist. Familiarity with common clinical conditions such as chronic obstructive lung disease (COPD) and asthma is presumed. In this chapter we present a comprehensive review of less common pulmonary conditions, organized in an anatomic manner, and discuss, in order, the pulmonary vasculature, conditions that obstruct the airways, the pulmonary interstitium, and conditions extrinsic to the lungs that affect pulmonary function, such as severe arthritic disorders. We then move to a discussion of drug-induced lung injury and conclude by discussing rare infectious pulmonary diseases, including severe acute respiratory syndrome (SARS).

Many of the conditions discussed in this chapter 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. In many cases, the evaluation necessary to arrive at an accurate diagnosis will be comprehensive and includes a detailed history and physical examination, a chest radiograph, and pulmonary function tests (PFTs), including spirometry, diffusing capacity, and lung volume determination, and perhaps even arterial blood gas (ABG) analysis. For some conditions bronchoscopy and biopsy will have been 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 clinical condition of the patient has changed in a substantial way. If a diagnosis has already been established, there is no evidence to suggest that repetition of a test such as spirometry and lung volume determination, which is the gold standard for the presence or absence of pulmonary disease but a poor predictor of who will go on to develop a pulmonary complication after surgery, is indicated before proceeding to surgery.[1] If a diagnosis has not been established in a patient who has symptoms consistent with one of the diseases discussed in this chapter, pulmonary consultation should be obtained preoperatively, because the patient's pulmonary disorder may well be a more pressing concern than an elective surgical procedure.

Unfortunately, pulmonary complications are common after many surgical procedures, particularly those involving the upper abdomen or thorax.[2-4] Preexisting lung disease, smoking, anesthetic time in excess of 180 minutes, and advanced age are also risk factors for pulmonary complications.[4,5] There is no standard definition of exactly what constitutes a pulmonary complication, but the most important complications are those that cause significant morbidity, such as postoperative pneumonia, or postoperative respiratory failure. Because all of the disorders discussed in this chapter constitute preexisting 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 for the individual diseases are discussed in the main body of this chapter. In the postoperative period aggressive treatment with mechanical measures such as incentive spirometry has been shown to minimize the frequency of the occurrence of pulmonary complications.[6,7]

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, as a consequence, a reduction in Pa_{O_2}. Many patients with pulmonary AV fistulas are asymptomatic, but associated signs and possible symptoms consistent with chronic hypoxemia are possible (Table 4-1).

There are several known causes of pulmonary AV fistula formation (Table 4-2). Many pulmonary AV fistulas are the result of congenital malformations and may be associated with hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu syndrome).[8] Hereditary hemorrhagic telangiectasia is transmitted in an autosomal dominant pattern and most commonly seen in middle-aged women, although diagnosis in early childhood is possible. Patients with this syndrome are more likely to have multiple fistulas and more severe symptoms.

TABLE 4–1 Signs and Symptoms of Arteriovenous Fistula

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

TABLE 4–2 Causes of Pulmonary Arteriovenous Fistulas

Congenital
Hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber 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 of fistula with resulting hemothorax and hemoptysis, which are potentially life threatening. Thrombus formation within the fistula may also occur, with the potential for embolization of clot to the brain, resulting in symptoms such as stroke or seizures. Embolization of other organ systems is also a possibility. 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 cardiac symptoms are more pronounced, significant respiratory symptoms are present, room air desaturation develops, or complications such as emboli with central nervous system (CNS) manifestations have occurred. Surgical preoperative evaluation requires chest computed tomography (CT) and pulmonary arteriography to localize the lesion. Pulmonary lobectomy, segmentectomy, or wedge resection via thoracotomy or video-assisted thoracoscopic surgery (VATS) are the most commonly performed surgical procedures. Embolization procedures are gaining wider acceptance and can be utilized preoperatively in the event of hemorrhage or as standalone therapy.[9]

Anesthetic evaluation focuses on the degree of shunt and hypoxemia. Analysis of an arterial blood gas sample will provide much of this information. 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 will revolve around avoiding increased pulmonary

vascular resistance and elevated levels of positive end-expiratory pressure (PEEP).

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 access is recommended in the event significant hemorrhage occurs. An arterial catheter is also indicated to monitor oxygenation and guide resuscitative efforts. 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 pulmonary vascular resistance (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 pulmonary AV 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 debris into the venous system, because such debris may bypass the pulmonary capillary bed and gain access into systemic arteries where end-organ embolization can occur. Preoperative evaluation should include assessment of neurologic function to rule out prior embolic stroke, and postoperative evaluation should include a neurologic check as well, to look for perioperative CNS embolization.

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.[10] 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. Symptoms associated with WG are vague, and diagnosis can be elusive (Table 4-3). Biopsy of a lesion is necessary to make the diagnosis.

If the disease process advances, there is the potential for significant respiratory and renal compromise, as well as hearing and vision loss (Table 4-4). Cardiac involvement is uncommon, although pericarditis, coronary arteritis, valvular involvement, and left ventricular hypertrophy have been reported. Current therapy with cyclophosphamide, corticosteroids, methotrexate, or azathioprine yields very good results, with long-term remission occurring in the majority of patients.

Preoperative assessment is directed toward evaluating any of the potential complications of WG that the patient may have acquired, with renal and pulmonary insufficiency being the most common. Blood urea nitrogen 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, which can be severe. Spirometry or other PFTs can help determine the severity of such disease. Bronchoscopy and a neck and chest CT may be necessary to fully evaluate subglottic stenosis and provide an indication of what size ETT 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 attendant 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,

TABLE 4–3 Common Signs and Symptoms of Wegener's Granulomatosis

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

TABLE 4–4 Complications of Wegener's Granulomatosis

Chronic renal insufficiency or renal failure
Hearing loss
Tracheal stenosis
Pulmonary insufficiency
Functional nasal deformities
Vision loss

owing to subglottic stenosis, and may require multiple laryngoscopies. If the patient is receiving corticosteroids at the time of surgery, stress dosing should be considered. In view of these concerns, it is best to proceed with a conservative plan for managing the airway in this population, with immediate availability of difficult airway equipment, multiple sizes of ETTs, and the means to obtain a surgical airway. If the patient is known to have significant tracheal or bronchial stenosis, care should be taken to prevent air-trapping and auto-PEEP by allowing sufficient time for exhalation.

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 it as a malignant B-cell lymphoma associated with immunosuppression and Epstein-Barr virus (EBV). Diagnosis requires histologic evaluation of a biopsy specimen. It was recently categorized as a lymphoma, although if diagnosed early (grade I angiocentric immunoproliferative lesions) it is considered benign, although premalignant.[11] Typically, it presents in the fifth or sixth decade, affecting males twice as often as females. The etiology of LYG is unknown, although the incidence of LYG in patient populations with immune dysfunction, such as human immunodeficiency virus (HIV) infection and organ transplant recipients, is significantly increased when compared with the general population. Based on this observation, speculation that LYG may result from an opportunistic infection has now been confirmed through laboratory investigation.

The disease process primarily involves the lungs, although the skin, kidneys, and central nervous system can also be affected. Signs and symptoms resulting from LYG are numerous, with an emphasis on the pulmonary system, and include an increased risk of pneumonia (Table 4-5). 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.[12] Corticosteroids 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, and vincristine and prednisone (CHOP) is often used. Radiation therapy may be indicated for localized disease. More recently, immunomodulation with interferon alfa-2b has played a role in treatment.

TABLE 4–5 Clinical Manifestations of Lymphomatoid Granulomatosis

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

In preparation for anesthesia, evaluation of the patient's pulmonary function is the primary concern. 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. The CHOP protocol's toxicities include peripheral neuropathy, cardiomyopathy, and myelosuppression.

Several issues should be considered when planning an anesthetic for a patient with LYG. The presence or potential for peripheral neuropathy in this patient population may deter many anesthesiologists from utilizing regional techniques (i.e., for fear that any subsequent neurologic dysfunction will be assigned to the regional anesthetic technique). 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 medications used for premedication or for monitored anesthesia care. If general anesthesia is chosen, the potential need for postoperative intubation and respiratory support should be addressed with the patient. The need for postoperative mechanical ventilation is more likely in cases of 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's comorbidities and surgical procedure. Long-term corticosteroid therapy in this population may result in adrenal suppression, and stress doses of corticosteroids should be considered.

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 the six following criteria: bronchospasm, eosinophil count greater than 10%, neuropathy (poly or mono), nonfixed pulmonary infiltrates, paranasal sinus abnormalities, and extravascular eosinophils (Table 4-6).[13] 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. CSS is treated with corticosteroids, which generally results in dramatic improvement or resolution of symptoms. The length of required therapy is proportional to the severity of symptoms and may be as long as 1 year.

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 or endocarditis. 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 principles applied to all asthmatics to minimize airway reactivity. If possible, avoidance of airway instrumentation and positive-pressure ventilation is desirable. A prolonged expiratory phase may be needed in patients with more advanced obstructive disease if positive-pressure ventilation is utilized, and preoperative spirometry will provide guidance in this area. β-Blockers should be avoided, if possible, because of the risk of bronchospasm and exacerbation of congestive heart failure (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.

TABLE 4–6 Clinical Manifestations of Churg-Strauss Syndrome

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

Primary Pulmonary Hypertension

Primary pulmonary hypertension (PPH) is an idiopathic disease and is a diagnosis of exclusion (Table 4-7). 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.[14] 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 pulmonary vascular resistance seen in this disease. Dyspnea is the most common presenting symptom, and syncope is a particularly poor prognostic sign. 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 pressures (PAP), and eventually right ventricular failure.[15]

Historically, treatment for PPH relied on oxygen and calcium channel blockers in an effort to decrease pulmonary vascular resistance (PVR) (Table 4-8). 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 right

TABLE 4–7 Symptoms and Signs of Primary Pulmonary Hypertension

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

TABLE 4–8 Current Therapies for Primary Pulmonary Hypertension

Therapy	Advantages	Disadvantages
Nitric oxide	Pulmonary circulation selective vasodilation; increases Pa_{O_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 nitric oxide therapy	
Endothelin receptor antagonist (Bosentan)	Recently approved by FDA	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
Coumadin	Improved long-term survival; decreases risk of intrapulmonary thrombosis	Increased bleeding risk
Magnesium	Vasodilation through blockage of Ca^{2+} channels; enhance nitric oxide synthase activity; releases prostaglandin I	Risk of magnesium toxicity: weakness, sedation, ECG changes

ventricular failure ensues. More recently, promising results have been achieved with prostaglandins (PGI_2, PGE_1; alprostadil) and nitric oxide to induce pulmonary vasodilation with minimal systemic effects. These may be used separately or in combination.[14] Currently, prostacyclins must be delivered by continuous intravenous infusion owing to their short half-life. Nitric oxide is delivered by inhalation and requires a tank and delivery system. Phosphodiesterase-5 inhibitors such as sildenafil and dipyridamole potentiate the pulmonary vasodilation resulting from nitric oxide and can be used separately or in a combined fashion.[14] Unfortunately, cost and unwieldy delivery systems have limited the use of these therapies to the short term or the most severe of cases. New approaches to delivering PGI_2 are under development, including the inhaled, subcutaneous, and oral routes. Another new agent is bosentan, an oral endothelin receptor antagonist that is thought to inhibit smooth muscle vasoconstriction and proliferation and has been approved by the U.S. Food and Drug Administration (FDA) to treat PPH.[14]

Preoperative studies focus on the severity of the patient's pulmonary hypertension, the degree of hypoxia, and the effects of these on the heart (Table 4-9). ABG analysis will elucidate 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 due to right ventricular hypertrophy or right atrial dilation. An electrocardiogram 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 right ventricular filling. Preoperative echocardiography is helpful in determining the extent of right ventricular hypertrophy and function, right atrial enlargement, pulmonic or tricuspid valve dysfunction, and patency of the foramen ovale. Pulmonary systolic

TABLE 4–9 Suggested 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 radiograph	Enlarged pulmonary arterial root; enlarged right heart
Electrocardiography	Dysrhythmias; signs of right-sided heart strain
Echocardiography	Assess right ventricle function and hypertrophy; valvular dysfunction and right atrial enlargement; patency of foramen ovale; estimate pulmonary artery pressure

pressures may be estimated by Doppler techniques. A more reliable method of measuring pulmonary pressures, gauging response to therapies, and detecting a patent foramen orale is right-sided heart catheterization. This procedure should only be considered if other studies have not provided an adequate assessment of disease severity and is not typically needed for preanesthetic evaluation. If the patient is being treated with digoxin, serum potassium and digoxin levels should be measured.

It is essential to keep the high morbidity and mortality of this disease in mind when preparing to deliver an anesthetic to a PPH patient and not assume the risk of perioperative complications is low even if the patient is undergoing a "minor" procedure. Regional anesthetic techniques do not preclude the need for 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 will need to be discontinued and replaced with a heparin infusion preoperatively. The risk of a thromboembolic event and the possibility of a 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 cause a rise in PVR.

Intraoperative management should emphasize maintenance of cardiac output and systemic blood pressure while minimizing further increases in pulmonary artery pressures and the risk of right ventricular failure. Invasive monitors, used selectively, including an arterial catheter, pulmonary artery catheter, and transesophageal echocardiography, may be helpful in the management of these patients. These invasive monitors allow for sampling of arterial blood, pharmacologic manipulation of pulmonary artery pressures and cardiac output, and detection of right ventricular failure, while maintaining adequate ventricular preload. Many different anesthetic techniques have been used successfully in patients with PPH. Regional, epidural, and general anesthesia with controlled ventilation are all reasonable options. Spinal anesthesia may result in a significant reduction in systemic vascular resistance 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 right ventricular ischemia and failure. Drugs commonly used in the provision of anesthesia are safe in patients with PPH. An exception is nitrous oxide, which has been implicated in raising PVR in several studies. Another exception is ketamine, which has sympathomimetic properties and may cause unintended increases in pulmonary vascular resistance.

In the event that an increase in PVR does occur, every effort must be made to avoid right ventricular ischemia and possible right ventricular failure. Helpful maneuvers include hyperventilation and maximizing Pa_{O_2} to decrease PVR. Inhaled drugs such as nitric oxide, 20 to 40 ppm, and prostacyclin (inhaled; IV) can selectively decrease pulmonary artery pressure with minimal decreases in systemic blood pressure. Milrinone and amrinone are excellent choices when a decrease in PVR and increase in cardiac contractility is desired, although a decrease in systemic vascular resistance will also occur. Dobutamine will increase contractility and may decrease PVR. In the event that an increase in systolic blood pressure is desired to avoid right ventricular ischemia, norepinephrine may have a slight advantage over phenylephrine.[16]

OBSTRUCTIVE DISEASE

Cystic Fibrosis

Cystic fibrosis (CF) is a genetic disease that follows an autosomal-recessive pattern and that affects chloride channels. With an incidence of 1:2000 to 1:4500 in whites, 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. CF is a universally fatal disease, although advances in therapy have resulted in significant gains in quality of life and longevity. There are a wide variety of clinical manifestations seen in CF (Table 4-10).

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.[17] 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 cross-sectional area results in pulmonary hypertension. Chronic hypoxemia also develops.

Patients with more advanced disease 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 positive-pressure ventilation can increase the risk of spontaneous pneumothorax. In the event of pneumothorax, surgical pleurodesis

TABLE 4–10 Clinical Manifestations of Cystic Fibrosis

Sign or Symptom	Cause
Nasal sinusitis and polyps	Abnormal mucus production and secretion; chronic infections
Chronic bronchitis	Hypersecretion of viscid mucus and impaired host defenses
Obstructive pulmonary disease	Due to chronic pulmonary infections and airway plugging from excessive mucus secretion
Pneumothorax	Rupture of subpleural blebs through the visceral pleura
Failure to thrive	Chronic infection and 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

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.[18]

The chronic hypoxia seen in this population causes an increase in pulmonary vascular resistance and pulmonary hypertension. Ventilation-perfusion inequality results in hypoxemia. Loss of pulmonary arteriole cross-sectional area causes increased pulmonary vascular resistance 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 therapy effective in treating pulmonary hypertension and improving right ventricular performance in this population is oxygen.[19]

The primary gastrointestinal manifestation of CF is malabsorption and steatorrhea due to pancreatic dysfunction from obstruction of pancreatic ducts with viscous exocrine secretions. 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 due to pancreatic dysfunction (impaired endocrine function) is also common and may require insulin therapy. An increased incidence of gastroesophageal reflux disease (GERD) has also been reported in this population.[20]

Preparation for anesthesia should focus on evaluation of the patient's pulmonary status. Significant deterioration due to 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.[18] 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, owing to the risk of exacerbating the preexisting respiratory compromise, and 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.

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 positive-pressure ventilation will decrease the incidence of perioperative pneumothorax formation. If a long-acting or continuous regional technique is chosen, postoperative opioid requirements will decrease. 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. Positive-pressure ventilation is usually preferable to spontaneous ventilation in advanced cases of CF, owing to the risk of respiratory fatigue and marginal tidal volumes. CF is an obstructive process, and prolonged expiratory

times may be necessary, as will 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 necessary. Nitrous oxide should be used with caution because of the increased risk of pneumothorax formation with positive-pressure ventilation, as well as the likely presence of multiple blebs.

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.[21] BOOP has not been conclusively determined to be more than an incidental finding. It results from the formation of granulation tissue, which obstructs the lumens 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 flu-like 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 owing to the preservation of lung architecture.[21]

Corticosteroids are commonly 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 as treatment, although their efficacy is not well established. In the event that cyclophosphamide has been used, the risk of leukopenia and, more rarely, thrombocytopenia or anemia should be kept in mind.

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.

Because of the high success rate in treating BOOP and the fact that dramatic improvement is typically seen after a few weeks of therapy with prednisone, it is unlikely that many patients will 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, will 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 positive-pressure ventilation unless appropriate reductions in tidal volume are made. Rapid arterial hypoxemia can occur with apnea. The use of low levels of PEEP will improve functional residual capacity and assist in maintaining Pa_{O_2}. Continuation of PEEP or continuous positive airway pressure in the postoperative period may be necessary to maintain functional residual capacity.

Idiopathic Pulmonary Hemosiderosis

Idiopathic pulmonary hemosiderosis (IPH) is a rare disorder of unknown etiology characterized by diffuse alveolar hemorrhage and is a diagnosis of exclusion. The disease 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, 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 later) 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 4-11).

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.[22]

TABLE 4–11 Sequelae of Idiopathic Pulmonary Hemosiderosis

	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

Evaluation of ongoing alveolar hemorrhage and quantification of the extent of any fibrotic changes is essential to 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 owing to 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 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, owing to absorption by intra-alveolar hemoglobin. Anemia frequently develops from ongoing alveolar hemorrhage, and measuring the amount of serum hemoglobin is essential.

If intubation 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 a decreased tidal volume is selected. The risk of pneumothorax is increased. Corticosteroids or other therapies for IPH should be continued throughout the perioperative period.

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, there must be no identifiable cause for the pneumonia such as infection or sarcoidosis. CEP is more likely to occur in women and is frequently preceded by the development of adult-onset asthma. Common presenting symptoms include constitutional complaints such as night sweats, weight loss, fevers, and a cough. Progression to dyspnea may occur if not treated. Chest radiographs may show dense peripheral infiltrates, which have been described as a "photographic negative of pulmonary edema."[23] 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 used in the treatment of CEP and are very effective. Improvement of symptoms is frequently seen in 1 to 3 days, with radiographic resolution occurring 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. It has been suggested that this may be due to the use of inhalation corticosteroids as part of the management of asthma in this population.[24] Because of the effectiveness of corticosteroid therapy, the prognosis for CEP is excellent.

If at all possible, surgery should be delayed until CEP patients have received corticosteroid therapy and experienced resolution of symptoms. Typically, 7 to 14 days are needed for complete resolution. In the event of emergency surgery, the pathophysiologic alterations seen in CEP are similar to those of any other pneumonia. Fever may result in reduced intravascular volume and an 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 due to perfusion of inflamed alveoli will increase the speed of desaturation on induction if apnea developes. Excellent preoxygenation and expeditious securing of the airway is therefore essential. Intraoperative ventilator management must be individualized with an effort 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 of these patients are receiving long-term corticosteroid therapy and the use of perioperative corticosteroid dosing should be considered.

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 progressing glomerulonephritis that is frequently accompanied by vasculitis and pulmonary hemorrhage. The incidence is approximately 1:100,000, 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 concentrations of oxygen increase the odds that pulmonary hemorrhage will occur.[25,26] 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.[26] Onset of the disease is dramatic, with sudden hemoptysis, dyspnea, and renal failure (Table 4-12). 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 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 the disease, and renal transplantation may be necessary. Early diagnosis and treatment has a strong correlation with better outcomes.

If at all 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 blood urea nitrogen and creatinine determinations and urinalysis to assess renal function. The patient's symptoms and medical condition at the time of operation will dictate the extent of the required pulmonary evaluation. This may include a chest radiograph, ABG analysis, spirometry, and diffusing capacity to quantify the extent and significance of pulmonary hemorrhage.[27] 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.

TABLE 4–12 Symptoms and Signs Seen in Goodpasture's Syndrome

Dyspnea
Fatigue and weakness
Hematuria
Oliguria
Hemoptysis
Anemia
Hypertension
Azotemia
Proteinuria

Oxygenation is the primary challenge of the anesthetic management of patients who have active GS. With ongoing alveolar hemorrhage, patients will not only have impaired gas exchange at the alveolar level but will most likely be anemic. These will contribute to decreased oxygen delivery to the tissues. Exposure of the lungs to an increased oxygen tension and high airway pressures may exacerbate alveolar hemorrhage. These stresses, along with overly aggressive 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 anything more than mild disease. For major operations in patients with significant pulmonary impairment, placement of a pulmonary artery catheter or transesophageal echocardiography 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 creatine clearance.

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, which presents in infancy, is caused by mutations in the genes coding for surfactant proteins. There is a defect in surfactant-associated protein B (SP-B), which results in accumulation of surfactant-like material in alveoli.[28] The secondary form involves decreased alveolar macrophage activity, either functional impairment or decreased number, which may be related to immunosuppression, myeloid disorders, and hematologic malignancies, infection, or inhalation of noxious fumes. There is also an idiopathic categorization, which does not fit into either of the above categories and accounts for 90% of the cases.[29] Idiopathic PAP is thought to be due to 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.[30] The appearance of the chest radiograph may be out of proportion to the severity of the symptoms the patient is experiencing. High-resolution CT findings tend to more closely correlate with the clinical picture. PFTs frequently reveal a mild restrictive pattern with a severe reduction in diffusing capacity. ABG analysis demonstrates hypoxemia and an increased alveolar-arterial gradient due to interpulmonary shunting.[29]

Therapy for congenital PAP is supportive, with lung transplantation being 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 recently there have been reports of lobar lavage through fiberoptic bronchoscopes in the treatment of PAP.[31] This latter approach is very 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 due to PAP should be evaluated for the need for 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 oxygen 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.

BPL requires a general anesthetic and placement of a double-lumen ETT. A rapid decrease in oxygen saturation on induction is common, making excellent preoxygenation and expedient placement of the double-lumen ETT critical. 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 appropriate. Testing for leaks that would allow contamination of the ventilated lung by spillage of lavage fluid is essential. Then the nonventilated lung is lavaged repeatedly with saline while the ipsilateral chest wall is mechanically percussed. The procedure is repeated until the drained saline is nearly clear, indicating removal of the majority of the lipoproteinaceous material. The fluid used for the lavage should be warmed to decrease the risk of hypothermia; additionally, the volume of the drainage as well as the presence of bubbles should be 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 due to the dramatic drop in alveolar pressure. Significant hemodynamic changes can also occur during the infusion of the saline into the lung. Hypotension, as well as an increase in central venous pressure and pulmonary capillary wedge pressure, is not unusual. Use of transesophageal echocardiography has suggested that these changes were due to impaired venous return to the left side of the heart.[32] Presumably, saline infusion compresses alveolar capillaries, increasing pulmonary vascular resistance and resulting in an increase in central venous pressure, while also causing decreased left-sided heart output owing to decreased blood flow to the left ventricle. In some cases the contralateral lung can be lavaged during the same anesthetic, although it is not uncommon to wait several days 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, with a higher incidence in African-Americans, people of Northern European decent, and females. The annual mortality rate of a patient with sarcoid is low but is increased by symptomatic cardiac[33] or neurologic[34] involvement. The initial presentation of sarcoid will vary depending on the organ systems affected. 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 volumes and diffusion capacity. In some cases an obstructive pattern may also be present owing to

airway narrowing. In more advanced cases ABG analysis reveals hypoxemia and an increased alveolar-arterial gradient. Cardiac symptoms occur in a significant number of sarcoid patients. Some are the result of myocardial granulomas, and others are secondary to respiratory system disease. Possible findings include conduction abnormalities (complete heart block, bundle branch block, or first-degree AV block), ventricular arrhythmias, congestive heart failure, pericarditis, supraventricular tachycardia, ventricular aneurysms, and sudden death.[33]

Neurologic findings in sarcoid are uncommon, although all of 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.[34]

There is also the potential for airway involvement. This occurs in approximately 5% of patients with sarcoidosis.[35] 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.[36] These lesions may result in airway compromise and, rarely, the need for tracheostomy. Vocal cord paralysis has also been reported and is due to recurrent laryngeal neuropathy caused by sarcoid mediastinal lymphadenopathy.[37] Encountering a pregnant patient with a history of sarcoid is not unusual, because sarcoid occurs with an increased frequency in women of childbearing age. However, in general, pregnancy tends to improve sarcoid-related symptoms. This is presumably owing to increased cortisol levels during pregnancy.[38]

Corticosteroids are often required to treat sarcoid. Systemic corticosteroids appear to improve or shorten the length of most symptoms related to sarcoidosis. Owing to the relapsing and remitting nature of the disease it is difficult to verify the efficacy of this treatment. As is often the case, early diagnosis and treatment appears to improve the likelihood of successful treatment. Radiation therapy and immunosuppressants such as cyclophosphamide and azathioprine may also be used as treatment. 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 occur as a result of 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 a on review of other organ systems known to have been affected in that particular patient. A review of recent chest radiographs along with PFTs is recommended. If a history of significant dyspnea is present, an ABG analysis is warranted. Screening for airway involvement can be accomplished by inquiring about dysphagia, hoarseness, or throat pain. If suspected, an evaluation by indirect 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 electrocardiography and echocardiography 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 presence of significant restrictive lung disease will require altered ventilator management and consideration of the need for postoperative ventilatory support. An intra-arterial catheter will be helpful in managing oxygenation and ventilation and allows close observation and early detection of any hemodynamic instability. In caring for patients with significant pulmonary fibrosis, placement of a pulmonary artery catheter or use of transesophageal echocardiography may help guide resuscitation and hemodynamic management. Sarcoid patients with an implantable cardiac defibrillator may need to have these devices inactivated for fear of interference from electrocautery units, although modern units are less susceptible to this issue. In this event, 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 may occasionally be 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 commonly afflicts women of childbearing age. Its incidence is estimated at 40 per 100,000 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 all possible hematologic sequelae. Renal involvement, in the form of glomerulonephritis, has a highly variable course. Neurologic findings include cognitive dysfunction, migraine-like headaches, and seizures. Pericarditis, small pericardial effusions, valvular abnormalities, and endocarditis represent the majority of the cardiac manifestations of SLE. Congestive heart failure may occur but is typically not the result of cardiomyopathy.[39] Treatment is typically directed at specific symptoms. Examples include 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 numerous (Table 4-13). These conditions are the direct result of autoantibody reactions in the lung vasculature, lung parenchyma, and pleura. Histopathologic findings include alveolar wall damage, inflammatory cell infiltration, hemorrhage, and hyaline membranes. Some of these manifestations are thought to occur primarily in SLE patients with antiphospholipid antibodies. The presence of these antibodies is referred to as antiphospholipid syndrome (APS), with 50% of cases of APS being in patients with SLE although only a minority of SLE patients have APS.[40] The primary defect in APS is recurrent arterial and venous thrombosis,[41] although there is an association with pulmonary hypertension and diffuse alveolar hemorrhage. Alveolar hemorrhage and pulmonary hypertension are particularly dire manifestations and predict a higher mortality.[42]

TABLE 4–13 Pulmonary Manifestations of Systemic Lupus Erythematosus

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	Due to 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. Data from references 40 to 42.

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 operation. A review of serum creatinine and blood urea nitrogen 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 if bronchiolitis is present there will be 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.[43] 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 it must be kept in mind that patients with APS are at increased risk of thrombosis, and appropriate precautions must be taken. Perioperative corticosteroid dosing may be required for patients with adrenal insufficiency due to chronic corticosteroid administration.

Idiopathic Pulmonary Fibrosis

Idiopathic pulmonary fibrosis (IPF), also referred to as cryptogenic fibrosing alveolitis, is an interstitial lung disease of uncertain etiology. It is a progressive illness with a median survival time of 3 to 4 years. This rare condition has a prevalence rate of about 5 per 100,000 and is more common in current or former smokers. A typical patient is a middle-aged man. Diagnosis is based on the presence of 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 radiograph or high-resolution CT consistent with the diagnosis.[44]

There is also an increased incidence of pulmonary malignancy in IPF patients. Unfortunately, it is unclear if resection of these lesions adds to life expectancy in this population.[45] There is no effective treatment currently available, although therapy with corticosteroid and cytotoxic agents is frequently attempted. There are currently many novel therapies in development intended to block fibrogenic pathways that may be of benefit (Table 4-14).[46] Lung transplantation is the only therapeutic option available for IPF. Although thought to be effective, there is still only a 49% survival rate 5 years post transplantation.[47]

IPF patients presenting for surgery will typically be tachypneic and cyanotic and will 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. There appears to be a very high incidence of GERD in IPF patients.[48] It is appropriate to consider premedicants 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.

Patients with IPF are most likely to present to the operating room for lung biopsy to establish the diagnosis, for lung transplant in a curative effort, or for resection of a pulmonary neoplasm. These procedures commonly 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.

TABLE 4–14 Experimental Idiopathic Pulmonary Fibrosis Therapies

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

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

Acute Respiratory Distress Syndrome

Acute respiratory distress syndrome (ARDS) is a severe form of acute lung injury that occurs as a result of an underlying illness or lung injury. It may occur in as many as 10 to 20 per 100,000 individuals.[49] Several disorders have been implicated as risk factors for developing ARDS, some through direct lung injury, others by a systemic inflammatory response (Table 4-15). The underlying lesion is injury to the alveolar-capillary membrane and increased alveolar-capillary permeability. Proteinaceous edema fluid accumulates in the alveoli, resulting in impaired oxygenation and poorly compliant (stiff) lungs. ARDS develops acutely over a 1- to 2-day period. If a patient is alert and spontaneously 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 very 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 $Pa_{O_2}/F_{I}O_2$ 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.[50] ARDS has a high mortality rate, which is in the range of 35% to 40%. Patients who do survive generally return to a pulmonary function near their baseline. If a defect does remain it is likely to be a restrictive defect or decreased diffusion capacity, and more disabling sequelae are possible.[51]

Intraoperative management of ARDS is an extension of the care the patient is receiving in the intensive care unit. Many patients will have a severe underlying injury or illness, which will also require significant attention in the perioperative period. The approach to ventilator management plays a significant role in the mortality rate

TABLE 4–15 Clinical Disorders Associated with ARDS

Direct Lung Injury	Indirect Lung Injury
Aspiration of gastric contents	Sepsis
Inhalation of toxic fumes	Major trauma
Near-drowning	Reperfusion injury
Pulmonary contusions	Massive transfusion
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 (eds): Fishman's Pulmonary Diseases and Disorders. New York, McGraw-Hill, 1998, p 2550.

from ARDS. Instituting low tidal volume ventilation on the order of 4 to 6 mL/kg (predicted body weight) and maintaining plateau pressures of less than 30 cm H_2O were found to reduce the mortality from ARDS by almost 20%.[52] This approach may result in hypercapnia and respiratory acidosis, which can be treated with sodium bicarbonate. There are currently no data to suggest a particular level of respiratory acidosis, which is dangerous.[53] 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. There is no set level of PEEP that has been shown to be superior.[54] Other maneuvers such as sigh breaths and periodic rotation of the patient to the prone position may result in improved oxygenation but are not associated with an improvement in outcomes. Invasive monitors will frequently be in place when the patient arrives in the operating room; if not, an intra-arterial catheter should be inserted. For procedures involving major fluid shifts, placement of a pulmonary artery catheter or use of transesophageal echocardiography may be helpful in guiding resuscitation and avoiding overzealous fluid administration, which might adversely impact the patient's respiratory status. 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.

Pulmonary Histiocytosis X

Pulmonary histiocytosis X (PHX) is also called pulmonary Langerhans cell granulomatosis and is an uncommon interstitial lung disease that has an association with cigarette smoking. Related disorders are Hand-Schüller-Christian disease and Letterer-Siwe disease. 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; there is equal representation of men and women. Presenting symptoms are nonspecific and include nonproductive cough, dyspnea, fatigue, fever, and weight loss (Table 4-16). The presence of reticulonodular infiltrates, of upper and middle lobe cysts, and of stellate nodules with sparing of the costophrenic angle on chest radiography is highly suggestive of PHX. Diagnosis is confirmed by bronchoalveolar lavage (BAL) or biopsy. Results of spirometry in this population may yield an obstructive, restrictive, mixed, or normal pattern. A decrease in diffusion capacity appears to be the most consistent finding. Physical limitation in this population is frequently out of proportion to the results of spirometry, and the presence of pulmonary hypertension may play a significant role in contributing to diminished exercise capacity.

TABLE 4–16 Comorbidities Related to or Caused by Pulmonary Histiocytosis X

Symptom	Notes
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

In advanced disease, pulmonary artery pressures in the range of 60 mm Hg are not unusual.[55]

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 (older than 26 years), an FEV_1/FVC ratio less than 0.66, and a right ventricular/total lung capacity ratio greater than 0.33 have been suggested as predictors of advanced disease and increased mortality.[56] Corticosteroids and chemotherapeutic agents are utilized in attempts to treat PHX, but the disease is frequently refractory to treatment. Lung transplantation has been performed with success, although there are reports of recurrence of PHX in the transplanted lungs of patients who had extrapulmonary involvement and resumed smoking.[57]

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 cases in which more advanced disease is present, a review of results of PFTs and ABG analysis and an evaluation of pulmonary pressures by echocardiography or direct measurement are advisable. Based on these results, intraoperative management should be tailored to avoid increases in pulmonary artery pressure. Placement of a pulmonary artery catheter 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 in the perioperative period. The potential for pathologic fractures due to cystic bone lesions requires special attention to positioning and padding of the patient. As in all cases where pulmonary disability exists preoperatively, the potential for postoperative ventilatory support should be factored into the anesthetic plan and discussed in advance with the patient.

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. The disease occurs in women of reproductive age and is exacerbated by pregnancy. It also occurs in males and females with tuberous sclerosis. The condition results from the proliferation of interstitial smooth muscle and formation of cysts, which obliterate 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 due to cyst rupture is common. Obstruction and eventual rupture of the thoracic duct, resulting in chylothorax, is another manifestation of the disease. Hemoptysis may occur but is uncommon. 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 owing to ventilation-perfusion inequality and increased work of breathing.[58] ABG analysis typically reveals a decrease in P_{O_2} and P_{CO_2} although pH is normal.[59]

Estrogen is suspected of playing a role in the development of LAM. This notion arises from the almost exclusive occurrence of the disease in women of childbearing age, its exacerbation by pregnancy, and the presence of estrogen receptors on biopsy tissue. Effective treatment of LAM is difficult. Corticosteroids are ineffective. Modalities aimed at blocking the effects of estrogen 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.[60]

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 used for a patient with severe emphysema, including prolonged expiratory times and avoidance of high inspiratory pressures. 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.

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 predominately diagnosed in young adults, with men more likely to be affected than women. Prevalence in the United States is in the range of 1 in 1000. There does appear to be a genetic component to AkS, because most affected individuals are HLA-B27 positive.

Owing to chronic inflammatory changes that occur 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 they are for the most part uncommon. These include aortic insufficiency, cardiac conduction abnormalities, iritis, upper lobe fibrobullous disease, and pleural effusions. If fibrobullous disease does develop, the risk of aspergilloma and hemoptysis is very high.[61]

Involvement of the sternocostal, costovertebral, and thoracic spine results in decreased mobility of the thoracic cage and a restrictive ventilatory pattern. Although decreased exercise tolerance is common in AkS, it is thought to be due to deconditioning as opposed to a primary pulmonary defect.[62] The limitation in thoracic cage movement is almost totally compensated for by increased diaphragmatic excursion.[63] As the disease progresses, decreased exercise tolerance also is caused by 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, COX-2 inhibitors have been increasingly utilized as an alternative. The recent controversy regarding the cardiovascular safety of COX-2 inhibitors, suggests careful consideration of the risks and benefits of such therapy. Sulfasalazine, methotrexate, and corticosteroids are used in severe cases. The FDA has granted approval for the use of tumor necrosis factor-α inhibitors in the treatment of AkS. This promising new treatment may be the first therapy that will increase range of motion in AkS patients.

A patient with advanced AkS presents a significant challenge to the anesthesiologist. Frequently these patients will

present for orthopedic procedures on the hips and knees. 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.[64] If advanced disease is present, an alternative approach to airway management, such as LMA placement or awake fiberoptic intubation, is recommended. Neuraxial anesthesia is very challenging in AkS patients. The ossification of spinal ligaments significantly narrows or closes altogether the intervertebral space and prevents optimal positioning. Alternatives that have been reported to be successful include a lateral approach to spinal placement[65] and placement of caudal catheters.[66]

Intraoperative management must include special attention to positioning owing to the inflexibility of the patient's spine. Diaphragmatic function should be optimized during spontaneous ventilation because of the presence of a restrictive thoracic cage. This can be accomplished by avoiding the Trendelenburg position and using large ETTs when possible. Interscalene blocks, which can result in short-term ipsilateral diaphragmatic paralysis, should be avoided. Higher peak pressures may occur with positive-pressure ventilation 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 this population, 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.

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 hunchbacked 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 spine angulation, also known as the Cobb angle, exceeds 50% in the thoracic or 40% in the lumbar spine.[67]

Preoperative assessment should focus on any cardiovascular, respiratory, or neurologic impairment related to the deformity. The frequent presence of restrictive lung disease is 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 preexisting 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 spine surgery is the procedure that is most likely to bring these patients to the operating room. There are many variations to such procedures, including anterior, posterior, and combined approaches, as well as lumbar and/or thoracic level repairs. A combined anterior and posterior approach under a single anesthetic has a higher rate of major complications when compared with a staged procedure and is best avoided if at all possible.[68] Many elements of the anesthetic plan, such as positioning and the need for one-lung ventilation, will be dictated by the specific procedure.

Despite differences in the types of spine surgery there are several concerns that 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 a disadvantage, which is the need 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 if any improvement does occur it may take a few months to several years depending on the procedure.[69] 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 owing to the effects of positioning on the values obtained and to the possible presence of pulmonary hypertension and cor pulmonale, which reduces the value of central venous pressure monitoring in determining the adequacy of intravascular volume. Transesophageal echocardiography is a reasonable choice to monitor intravascular volume status and cardiac contractility if the patient's position allows and if it is available.

Spinal cord monitoring such as somatosensory evoked potentials (SSEPs) and, to a lesser extent, motor evoked potentials (MEPs) are frequently utilized to detect direct trauma or vascular compromise to the spinal cord. Data obtained by transesophageal echocardiography and $S\bar{v}O_2$ 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 blood pressure caused by compression of vena cava or the heart.[70] Intraoperative neurologic monitoring has become the standard of care for procedures involving significant distraction of the spine. Patient temperature, pH, and adequate blood pressure must all be maintained within narrow limits to maximize the effectiveness of SSEP monitoring. There is a great deal of debate regarding which anesthetic agents are preferred when SSEP monitoring is used. The literature is frequently contradictory, and institutional preferences vary greatly, although propofol infusions and nitrous oxide are popular. It does appear that the single most important factor is administration of a stable anesthetic with minimal bolus dosing and close communication with the individual monitoring the evoked potentials. The use of MEP monitoring would clearly prevent the use of neuromuscular blockade during the procedure.

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, it is not used for these purposes because of its cytotoxicity. The appeal of utilizing bleomycin in combination chemotherapy protocols is that it does not have 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. The risk of a patient developing pulmonary toxicity due to bleomycin therapy appears to be related to several factors. Total dose received has been shown to relate to the extent of pulmonary toxicity in animals, but this relationship is less clear in humans and there is no consensus on a cumulative dose that acts as a threshold for increased risk, although more than 300,000 IU has been suggested.[71] Some studies have suggested intravascular administration as a risk factor when compared with intramuscular dosing.[72] 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 due to bleomycin results in pulmonary fibrosis, similar to what is seen in IPF. Patients will 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.

When evaluating a patient for anesthesia who has received bleomycin, focused questioning regarding their pulmonary function, presence of symptoms such as a dry cough, dyspnea, or decreased exercise tolerance, and presence of risk factors such as large cumulative dose, chest radiation, or smoking is essential. 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.

A landmark study by Goldiner and colleagues has guided the anesthetic management of bleomycin patients for 25 years. This study implicated hyperoxia and fluid overload as factors that increase the risk of perioperative pulmonary morbidity and mortality in patients who have received bleomycin in the past.[73] Although there have been subsequent studies that question these guidelines, there is no reason to believe that providing a higher F_IO_2 than what is 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.[72] In cases in which adequate oxygenation does require an F_IO_2 greater than 30%, the use of PEEP is advisable, because it may facilitate oxygen action without necessitating higher levels of F_IO_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 this population. For operations in which significant blood loss or significant fluid shifts are expected, intra-arterial and central venous

catheters are recommended. 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 an interval of 1 to 2 years would seem prudent.

In patients with documented pulmonary bleomycin toxicity, higher than normal peak pressures are expected with positive-pressure ventilation, although this may be necessary for adequate oxygenation and ventilation. Strict extubation criteria should be observed, because the patients are at increased risk of postoperative pulmonary complications; and the use of sedating medications, which decrease respiratory effort, 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 in an attempt to minimize the occurrence of postoperative pulmonary complications.

INFECTIOUS DISEASES

Severe Acute Respiratory Syndrome (SARS)

Severe acute respiratory syndrome (SARS) is a highly infectious disease thought to be transmitted by a coronavirus (SARS-CoV). It results in atypical pneumonia, which may progress to respiratory distress syndrome. Recognition of this syndrome occurred in 2002, with the initial cases occurring in Southeast Asia. During 2003 SARS had made its way to North America, with hundreds of cases occurring in the Ontario province of Canada. All told there were over 8000 reported cases of SARS worldwide, resulting in over 700 deaths. There is no way of knowing if, when, or where another outbreak may occur, but familiarity with the syndrome and how to contain the spread is the responsibility of all health care professionals.

SARS is capable of infecting otherwise healthy individuals 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 there is no laboratory test available to reliably detect infection early in the clinical course.[74] 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.

The majority of the anesthesiologist's contact with SARS patients will occur during airway management for patients in respiratory distress. Because the anesthesiologist will be in close proximity to the patient's upper airway, there is a high risk of exposure to the virus. Full contact precautions, including wearing disposable fluid-resistant gowns, goggles, face shields, double gloving, hand washing, and use of N95 (or equivalent) masks that have been fit tested, are advised.[75] Standard surgical face masks and gowns are completely inadequate. It is just as important to wear correct protective equipment as it is to remove and dispose of it in a way that will not contaminate the wearer or others. Some institutions have taken the added precaution of using personal protection systems (PPS) for personnel involved in high-risk procedures with SARS patients. These PPS units consist of belt-mounted powered air purifiers with HEPA filters and a lightweight headpiece. Use of this equipment requires training as well as adequate time to put it on. The noise generated by the system makes communication difficult.[75,76] Attention must also be directed to avoiding contamination of anesthesia workstations and equipment. This includes placing high-efficiency 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 have these materials appropriately cleaned or disposed of. Maintaining a separate clean and a separate dirty work area may be helpful in this regard.[76]

Echinococcal Disease of the Lung

Echinococcal or hydatid disease occurs when a human is infected with *Echinococcus granulosus,* which is 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.[77] Due to the fecal-oral transmission, this 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, or 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 do not require any preoperative evaluations beyond the routine. Larger cysts may result in respiratory compromise, typically presenting as dyspnea. Spirometry may reveal decreased volumes due to the space-occupying lesion. Respiratory acidosis and hypoxemia may also be present. In advanced disease, there is the possibility that the patient may not tolerate surgery and anesthesia. In these very rare circumstances, removal of the cyst has been performed under thoracic epidural anesthesia with success.[78] 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. In cases in which there is only unilateral disease, there is little reason for the patient to have difficulty tolerating one-lung ventilation, as 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 for this by having large-bore intravenous access, as well as immediate availability of epinephrine, diphenhydramine, and corticosteroids.

CONCLUSION

We have reviewed a heterogeneous panoply of rare pulmonary conditions. Clinical interactions with patients with these disorders may range from a simple excisional biopsy in a patient with asymptomatic pulmonary sarcoid, to a hip replacement in a patient with ankylosing spondylitis, to a double-lung transplant for a patient with end-stage cystic fibrosis. The spectrum of possible procedures therefore extends from the routine to the extraordinarily complicated. Successful management of patients with these 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.

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