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Pleura: Anatomy, Physiology, and Disorders

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Disorders of the pleura and pleural space reflect some of the oldest diseases encountered in surgical history. Hippocrates described the symptoms of empyema, 2400 years ago: "Empyema may be recognized by the following symptoms: In the first place the fever is constant, less during the day and greater at night, and copious sweats supervene. There is a desire to cough and the patient expectorates nothing worth mentioning." He also described an open drainage procedure: "When the fifteenth day after rupture has appeared, prepare a warm bath, set him upon a stool, which is not wobbly, someone should hold his hands, then shake him by the shoulders and listen to see on which side a noise is heard. And right at this place, preferably on the left, make an incision, then it produces death more rarely."[1,2] Beyond providing less wobbly stools, few advances were made for more than 2000 years that allowed surgeons to routinely enter the pleural cavity, the fear being a potentially fatal pneumothorax. With the advent of positive pressure ventilation in the early 1900s, pneumothorax was no longer a prohibitive risk and the era of surgical intervention in the pleural cavity had begun.[3]

Empyema represents just one of many disorders of the pleural space that the practicing surgeon may encounter. Disorders of the pleural space may result from a pathological change in the pleura itself or may reflect disease in adjacent or distant organs. The problems span the spectrum from a benign effusion of cardiac origin to mesothelioma, a deadly primary malignancy of the pleura. Despite vastly different etiologies, the presentation and radiographic images of these two conditions may appear very similar. Thus, it is important for the clinician to be familiar with the normal anatomy and physiology of this space as well as the numerous disorders thereof. The goal of this chapter is to provide such a background and to also give a review of the diagnostic and therapeutic procedures currently employed for pleural diseases.

Anatomy

Embryology and Microscopic Anatomy

Embryologically, the pleural cavity is created during a month, starting in the third week of gestation. Initially, the lateral plate forms two layers, the splanchnopleura and the somatopleura, which subsequently develop into the visceral and parietal pleura, respectively. Eventually, it is the visceral pleura that surrounds the lung and the parietal pleura that lines the remainder of the chest cavity. The different embryological origins of the visceral and parietal pleura are responsible for the separate vascular, lymphatic, and neural supplies of these two structures as seen in the adult. By the end of the seventh week of gestation, the diaphragm has separated the thoracic cavity from the peritoneal cavity, and by the third month of gestation the two pleural cavities have expanded sufficiently to encase the pericardium.[4]

In the adult, both pleural surfaces are approximately 30 to 40 μm thick and are composed of a single layer of mesothelial cells with an underlying layer of connective tissue. Depending on their location, the mesothelial cells may be flat, cuboidal, or columnar.[5] Mesothelial cells characteristically have numerous microvilli that play a role in phagocytosis as well as contributing to the lubricious nature of the pleural surfaces. Surfactant molecules, produced by the mesothelium, line the pleural surfaces and, secondary to similar electrical charge, repulse each other and facilitate sliding, analogous to the lubrication achieved with graphite. It is these apposing layers of mesothelial cells that form the potential space of the pleural cavity and which glide over each other during respiration.[5–7]

The connective tissue layer contains the neurovascular and lymphatic supply of the pleura. There are certain important differences in this layer between the visceral and parietal pleura. For the visceral pleura, the connective tissue layer

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is functionally continuous with the fibroelastic network of the lung itself. Functionally, it is this relationship that prevents the visceral pleura from being surgically separated from the surface of a normal lung. Pathological disruption of this connection, however, may result in subpleural air collections known as blebs.[8] The connective tissue layer for the parietal pleura may also be tightly adherent to the underlying structures, as is characteristic of the diaphragmatic pleura. Around the skeletal portion of the thorax, however, the pleura is bound to the underlying tissue by another connective tissue layer called the endothoracic fascia, which forms a natural cleavage plane. It is this plane that the surgeon develops when performing an "extrapleural" dissection.[8,9]

The blood supply to the visceral pleura in humans is thought to reflect that of the lung itself, with a dual arterial supply from both the pulmonary and bronchial arteries and singular venous drainage into the pulmonary veins. The blood supply to the parietal pleura is from systemic arteries only and drains, predominantly, into peribronchial and intercostal veins, but it may also drain directly into the azygous vein and vena cava.[10–12]

The visceral pleura is innervated by vagal and sympathetic fibers, but has no somatic innervation and is therefore insensate. The parietal pleura is also innervated with sympathetic and parasympathetic fibers, but it is also somatically innervated. Thus, the parietal pleura is capable of sensing and transmitting the sensation of pain. "Pleurisy" from inflammation and pain from chest tubes, during insertion and subsequently as well, are attributable to the somatic intervention of the parietal pleura.

There are also differences in the lymphatic drainage between the two pleural layers. The visceral pleura drains through a lymphatic network into the pulmonary lymphatics, which eventually flow toward the pulmonary hilum. This lymphatic system is richer in the lower lobes than the upper lobes. The parietal pleural lymphatics drain to different locations. The mediastinal pleura drains to the mediastinal and tracheobronchial nodes. The chest wall drains anteriorly to the internal thoracic chain and posteriorly toward the intercostal nodes near the heads of the ribs. The diaphragmatic pleura drains to the parasternal, middle phrenic, and posterior mediastinal lymph nodes.[10] There are also transdiaphragmatic lymphatic communications that allow some degree of lymphatic flow from the peritoneum to the pleural space.

The parietal pleura also differs from the visceral pleura by virtue of the presence of Kampmeier foci and stomata. Kampmeier foci are collections of activated mesothelial and lymphoreticular cells, centered about a lymphatic core, that augment the pleura defensive capabilities. They are concentrated in the lower mediastinal region of the parietal pleura.[4–7,13–15] Stomata are 2- to 6-μm pores that communicate directly with the parietal pleural lymphatics. During inspiration these pores have the capacity to stretch, and their architecture is such that they form functional one-way valves. Thus, they provide for a very effective system for draining both fluid and particles, including both red blood cells and macrophages. It is the presence of these pores on the parietal pleural surface that makes it predominantly, if not exclusively, responsible for clearance of cells and particulate matter from the pleural space.[12,14] It should be noted that although stomata are well studied and characterized in sheep and other mammals, the definitive presence of stomata in humans is less well established.[16,17]

Gross Anatomy

In each hemithorax, the visceral pleura is a continuous surface that completely envelops the entire lung, including the fissures. At the pulmonary hilum, it continues on as the parietal pleura to line the mediastinum, chest wall, diaphragm, and cupola of the chest cavity. In humans the pleural cavities are completely separate, coming into contact with each other for a short distance behind the upper half of the body of the sternum (Fig. 56.1). It is this pleural separation of the right and left chest cavities that prevents bilateral pneumothoraces from occurring as the result of a unilateral chest injury. At the costophrenic and costomediastinal sinuses the parietal pleural folds back on itself, providing a potential space into which the lungs can expand during inspiration.

Superiorly, the pleura extends above the bony thorax into the base of the neck (Fig. 56.2). This fact explains why pneumothorax may complicate internal jugular central line placement as well as subclavian central line placement.[18] Anteriorly the pleura extends to the sixth rib, to the ninth rib laterally, and to the twelfth rib posteriorly (Fig. 56.2). In the living patient the lung can fill the entire posterior recess. In a review of 100 chest radiographs, 80% of patients were found to have lung present at or below the level of the twelfth rib and in 18% it was seen at the level of the first lumbar vertebra.[19] These external landmarks of the pleural space are of practical clinical significance, particularly when evaluating a patient with penetrating trauma.

The pulmonary ligament is a double fold of the mediastinal pleura that tapers down from the root of the lung, where it is in continuity with the visceral pleura, to the caudal mediastinum. This ligament is one of the structures that must be divided to perform a pneumonectomy or lower lobectomy. It is also routinely divided to its superior border, the

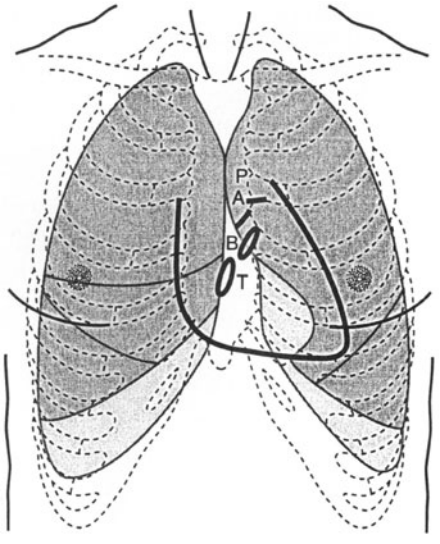


FIGURE 56.1. Relationship of the thoracic skeleton to the heart (line), pleura (light gray), and lungs (dark gray). (Adapted with permission from Gray's Anatomy, 36th edition, ©1980 W.B. Saunders Co.)

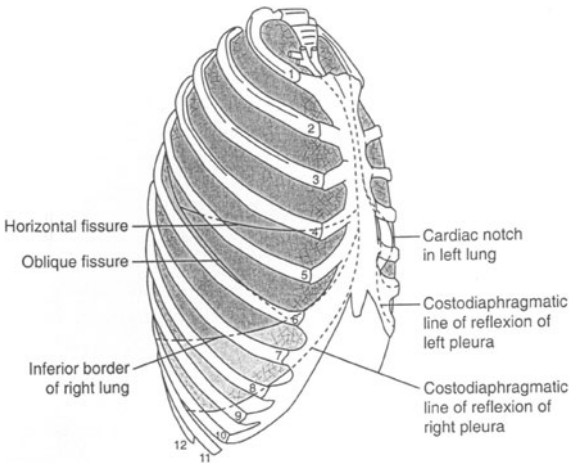


FIGURE 56.2. Relationship of the lung (dark gray) and the parietal pleural envelope, which extends down beyond the edge of the lung (light gray). (Reprinted with permission from Gray's Anatomy, 36th edition, ©1980, W.B. Saunders Co.)

inferior pulmonary vein, when attempting to provide mobility to the lower lobe after resecting the upper and/or middle lobes. The lymph nodes within the pulmonary ligament are the level 9 nodes, which are N2 lymph nodes, and are routinely harvested when performing a resection for lung cancer.

Physiology

The pleura has both mechanical and physiological functions. It transmits negative pressure from the thorax to the lung, thereby opposing the lung's natural elastic recoil and maintaining pulmonary expansion. During respiration, this function is performed in an environment of very low friction, thereby allowing the lungs to glide smoothly over the internal thoracic surfaces as they expand and contract. The pleura also controls the environment of the chest cavity by maintaining fluid homeostasis, preventing or removing air collections and keeping the space sterile.

Under normal conditions, the pleura cavity is a potential space with a thickness ranging from 10 to 20 μm. The lung is maintained in an expanded state by the maintenance of a negative pressure in the pleural space; this allows the expandable chest cavity to overcome the opposing forces exerted by the natural elastic recoil of the lung. The resting pressure in the pleural space, when the lung is at its functional residual capacity, is slightly negative at -2 to -5 cm H_2O. When measured in an upright posture, there is more negative pressure in the apex of the chest than at the diaphragm, likely a gravitational effect. The negative pressure continues to increase through inspiration with the pressure ranging from -25 to -35 cm H_2O at the vital capacity. Disorders that decrease the compliance of the lung or increase airway resistance further increase the negative pressure in the pleural space with inspiration.[8,20]

Initially it would seem curious that gas is not drawn out of solution into the pleural space by the negative pressure in the space. It is the lower partial pressure of gases on the venous side of the pleural circulation, as opposed to the arterial side, that prevents spontaneous pneumothorax from occurring under normal conditions. This difference in partial pressures between the two sides of the circulation is mainly a result of oxygen absorption. Unless the pressure in the pleural space decreases to significantly less than -50 cm H_2O, the sum total of the forces under normal conditions favors absorption of gas out of the pleural space.[8,10]

This diffusion gradient also accounts for reabsorption of gas that is introduced into the pleural space. The clearance rate of gases introduced into the pleural space is dependent upon the concentrations of those gases with respect to their partial pressures in the pleural circulation. As the partial pressure of nitrogen is the greatest in the air we breathe, it therefore constitutes the highest partial pressure of the gases that form a pneumothorax. Nitrogen also has the highest partial pressure of the gases in our circulation; this can be decreased by altering the composition of inspired gases. Thus, administration of supplemental oxygen decreases the partial pressure of nitrogen in the bloodstream and thereby steepens the nitrogen pressure gradient between the circulation and the pneumothorax, favoring more rapid reabsorption of the trapped gas. This relationship serves as the rationale for placing a patient on supplemental oxygen to facilitate reabsorption of a pneumothorax that is not being externally evacuated.[10,21]

Under normal conditions the pleural space contains very little fluid, estimated at approximately 0.3 ml/kg. The fluid is generally hypooncotic with a protein content of approximately 1 g/dl. The mechanisms of fluid production and reabsorption are complicated and not completely understood. Numerous forces interact from both the parietal and visceral pleura, including their respective hydrostatic and oncotic pressures. Respiratory movement and gravity are both thought to have roles in maintaining the fluid dynamics of the pleural cavity. The predominant factor, however, is thought to be the uptake of fluid into the parietal pleural lymphatics. These lymphatics tend to be concentrated in the dependent portions of the chest cavity. Under normal conditions, this flow rate has been estimated at 0.1 to 0.15 ml/kg/h. The lymphatic flow rate has the capacity to increase and has been estimated to reach as high as 30 ml/h, approximately 700 ml/day in an average-size individual. When the dynamics of this equilibrium are unbalanced beyond the rate at which the lymphatics are able to compensate, pleural effusion accumulates.[6,7,15,20,22,23]

It is interesting to note that the exact purpose of the pleura is still not fully understood. Empirically, it is clear that the pleura maintains fluid and gas homeostasis, mechanically couples the lungs to the bellows mechanism for respiration, and maintains sterility in its described space. To accomplish this, however, it is not clear how important it is to have the configuration of two opposing layers with a small amount of intervening fluid. It has been observed, for instance, that there is little change in pulmonary function tests in patients before and after fusion of the pleural space.[10,24,25] Studies in sheep have suggested that the pleura may be important in maintaining fluid homeostasis within the lung itself, but applicability of this information to human physiology remains uncertain.[26–28] Finally, it is interesting to note that some mammals do not have a pleural space, similar to patients who have undergone pleurodesis, but that these animals clearly function normally.[29] Thus, the exact necessity for having two pleural membranes defining a potential space remains somewhat of a mystery.

Disorders of the Pleura

There are a large number of pleural disorders. The majority lead to symptoms as a result of mechanical compression of the lung, although many may be asymptomatic or may present with constitutional symptoms or pain. In most cases, the pathology results from the presence of something in the pleural space, which, as previously described, is normally a potential space. Therefore, in an effort to organize this large number of disorders, they are grouped according to what abnormal phase of material is occupying the pleural space; that is, gas, liquid, or solid. When gas enters the pleural space, it is referred to as a pneumothorax. When liquid enters the pleural space, it may sometimes be broadly referred to as an exudative or transudative effusion but is frequently classified according to the type of liquid, such as hemothorax, chylothorax, or empyema. Last, solid masses may occupy the pleural space. Most benign masses are pleural plaques, but there are also rare benign tumors of the pleura, some of which may reach enormous size. Malignant masses of the pleura are usually cancers that have metastasized to the pleura, but there are also some rare primary tumors, most commonly mesothelioma. Sometimes the groups may overlap with more than one abnormal phase of material filling the pleural space. Such examples include air and blood, a hemopneumothorax, after trauma or air and pus, a hydropneumothorax, which may be seen with empyemas resulting from a bronchopleural fistula. Frequently, however, there is a predominant, if not sole, etiology for the abnormal accumulation and thus the following subsections review disorders of the pleura according to the state of matter that is abnormally occupying the space—gas, liquid, or solid.

Gas-Phase Disorders of the Pleural Space

Pneumothorax

Pneumothorax is defined as air in the pleural space. It may occur traumatically, iatrogenically, or spontaneously. Spontaneous pneumothorax may be subclassified as primary or secondary, with primary spontaneous pneumothorax arising in an otherwise healthy patient and secondary spontaneous pneumothorax arising as a complication in a patient with known underlying pulmonary disease. Essentially any pneumothorax resulting from pleural disruption can present as a tension pneumothorax. This condition represents a true emergency and is discussed separately.

Pneumothorax Presentation and Diagnosis

Pneumothorax may cause pain or dyspnea, or it may be asymptomatic, depending on its size and the underlying pulmonary function of the patient. Physical findings may range from none to the classic findings seen with a tension pneumothorax: contralateral tracheal deviation, ipsilateral absent breath sounds, and percussive hyperresonance. Electrocardiographic changes may be present, including diminished voltage, right-axis deviation, or T-wave changes that may mimic a subendocardial myocardial infarction.[30]

Except for tension pneumothorax, most cases require an upright chest radiograph to establish the diagnosis. As the pneumothorax occupies a greater proportion of the chest cavity at expiration than inspiration, the former is more sensitive for detecting the diagnostic pleural line.[31] Although rarely indicated for a patient able to obtain an upright chest X-ray, a CT scan of the chest is the most sensitive test and may demonstrate a small amount of air in the pleural space that is not visible on the plain radiograph.[32,33]

Pneumothorax Treatment Options

For all pneumothoraces, the common goal is removal of air from the pleural space. Depending upon the etiology, however, prevention of recurrence may also be an objective of the treatment. Options for treatment range from observation to thoracotomy. Selection of the appropriate modality depends on a number of factors including, but not limited to, presentation, previous history, comorbidities, need for positive pressure ventilation, associated effusion, and even the patient's lifestyle. In addition, the size of the pneumothorax can also play a significant role in determining the appropriate treatment.

In practice, many physicians estimate the size of a pneumothorax by the area of the hemithorax that it appears to occupy in an anteroposterior radiograph of the chest. This practice generally underestimates the size of the pneumothorax. There are a number of formulas to better estimate the size of a pneumothorax, the simplest of which estimates the fractional volume occupied by a pneumothorax to be approximately equal to three times the fractional decrease in the linear dimensions of the lung.[34–36] The most accurate noninvasive estimate, however, is likely obtained by chest CT scan with the appropriate interpretive software.[37]

The following sections review the basic technique and indications for the different treatment options that are available with specific recommendations for different pneumothoraces to be described in the following section.

Pneumothorax Treatment Options: Observation

Observation is generally reserved for patients who are asymptomatic and are diagnosed with a small primary spontaneous pneumothorax or a simple iatrogenic pneumothorax. In such situations, the patient is followed with serial radiographs to ensure that the pneumothorax is decreasing in size. When a patient is breathing room air, gas is absorbed from the pleural cavity at approximately 1.25% of the pleural volume/day, approximately 50 to 70 ml/day.[38] Supplemental oxygen, by mechanisms reviewed in the physiology section, can increase this rate up to 4.2%/day.[39,40] As it is a minimal intervention, it is reasonable to place all hospitalized patients on supplemental oxygen if they are being observed for a pneumothorax.

There are several factors to weigh when considering observation alone for a patient with a pneumothorax. The first is that deaths have been reported in patients with pneumothorax who were being observed. Development of unrecognized tension pneumothorax was believed to have played a role in these cases.[41] This fact highlights the selectivity and judgment required to simply follow these patients, particularly on an outpatient basis. Another consideration is that a lung that has not fully expanded by 2 weeks is at risk for fibrous peel deposition and subsequent entrapment. Correction of this situation commits the patient to a surgical procedure that might have been avoided by initial evacuation of the pneumothorax.[8]

It is recommended that observation be considered only for patients with a simple pneumothorax less than approximately 15%.[42] If the pneumothorax has not resolved within 1 to 2 weeks, intervention to achieve full expansion should be instituted. Another factor to consider, particularly with primary spontaneous pneumothorax, is that observation alone does nothing to decrease the chance of recurrence. Last, in this age of economic constraints, it may be more cost-effective to definitively treat a pneumothorax upon presentation.

Pneumothorax Treatment Options: Simple Aspiration

Simple aspiration can be considered in the case of a simple pneumothorax in which there is no suspicion of an ongoing air leak and the patient is not on positive pressure ventilation. Some authors believe that in select situations aspiration is the treatment of choice.[43] The goal of aspiration is to remove air from the pleural space. It conveys no protection from an ongoing leak or recurrence in the future. The procedure is performed in a manner similar to that used for decompressing a tension pneumothorax. After sterilely preparing the skin and infiltrating with a local anesthetic, a 16-gauge intravenous catheter is placed into the pleural space in the midclavicular line over the superior surface of the second rib. The needle is then withdrawn and the catheter is connected to a short length of intravenous tubing capped with a three-way stopcock. A 60-ml syringe is then used to aspirate air from the chest cavity. When air can no longer be aspirated, the catheter is withdrawn and the first chest X-ray is obtained. If 4 l of air is aspirated and no resistance is met, there is an ongoing air leak and a chest tube should be placed.[10]

Pneumothorax Treatment Options: Percutaneous Tube Thoracostomy

Percutaneous tube thoracostomy is a good option for a simple pneumothorax. Some authors consider this the procedure of choice for simple pneumothoraces. Cited advantages are therapeutic- and cost-effectiveness as well as less trauma compared to standard tube thoracostomy. Depending upon the size and etiology of the pneumothorax, success rates for these catheters are reported in the 85% to 90% range.[44–47] The catheters range in size from 9 to 16 French and are placed using a catheter-over-needle or Seldinger technique. The kits (e.g., Arrow Pneumothorax Kit, Arrow International, Reading, PA, USA) are usually equipped with all the necessary supplies to insert the catheters and an adapter such that the catheter can be connected to a Heimlich valve or a standard suction device such as PleurEvac (DSP Worldwide, Fall River, MA).

These tubes are limited by their size and would be a poor choice for a patient with a large air leak. The principal factor in determining the flow rate through a tube is the diameter of the tube. Thus, a patient with a massive air leak, especially on positive pressure ventilation, should have a standard chest tube placed. As a general guide, it takes at least a 28-Fr. tube to accommodate approximately 15 l/min of flow at -10 cm of H_2O suction.[48]

Pneumothorax Treatment Options: Tube Thoracostomy

A standard chest tube should be placed for failure of a percutaneous tube, a pneumothorax associated with a significant fluid collection, or a pneumothorax where the leak is expected to overwhelm a small-caliber tube, more likely in the setting of positive pressure ventilation. Such tubes are generally placed under local anesthesia and sedation, employing sterile technique. Apical tubes, as employed for drainage of air, are best placed in the mid- or anterior axillary line in the third or fourth intercostal space.[49] It is generally recommended to tunnel the tube subcutaneous up one interspace before entering the pleural cavity. The tunnel serves two purposes. First, it forms a flap valve that helps prevent entrance of air into the chest after the tube is removed. Second, the tunnel allows the surgeon to control the direction of the tube, anteriorly when placed for air or posteriorly when placed to drain fluid. The tube can then be placed for passive or active drainage. Passive drainage may be achieved by connecting the tube to a Heimlich flutter valve or waterseal on a PleurEvac. For active drainage, most surgeons use a three-bottle system (Fig. 56.3), generally unified as a commercially available unit such as PleurEvac. Active drainage expedites and facilitates full expansion of the lung. Although also reported with passive drainage, the rare complication of reexpansion pul-

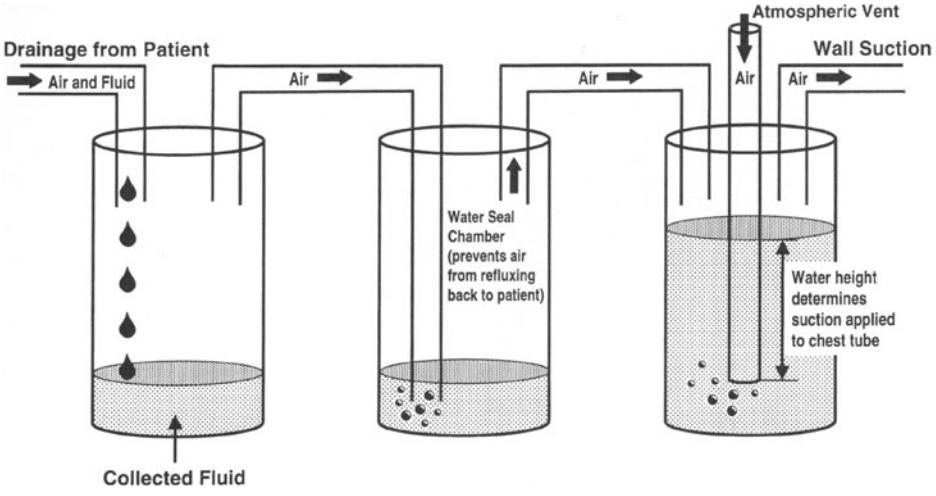


FIGURE 56.3. Three-bottle suction setup for pleural drainage.

monary edema appears to be more common with active suction.[50,51]

Generally viewed as a "floor procedure," chest tube placement should be given all the consideration of a major operation. Although it can be performed with minimal discomfort, utilizing intravenous sedation and strategic local anesthesia, it is not uncommon to hear patients state that chest tube placement was an uncomfortable ordeal. In addition to the discomfort, chest tube placement is accompanied by a number of complications including empyema, lung injury and bleeding, and death.[52] Therefore, coagulation profiles and immunocompetency should be taken into consideration for all patients being considered for this procedure.

Intravenous analgesia or a short-acting benzodiazepine or both should be used for an elective chest tube placement. Proper use of local anesthesia is critical for patient comfort during the procedure. The amount of local anesthetic that can be administered is limited by toxicity. A small amount of anesthetic is injected for the skin incision, and the remainder is accurately injected along the course of the tunnel that will be created to place the tube. This step allows the surgeon to both locate the superior surface of the rib and, by aspirating, to identify the parietal pleura. A small bolus of anesthesia can be injected at the level of the parietal pleura and, if adequate time is allowed after injection of the pleura, the discomfort of the tube placement can be limited to "pressure" and not sharp pain. As with all procedures under local anesthesia, it is also important to prepare the patient for any anticipated sensations, particularly the entrance into the pleural space as well as the possibility for triggering severe coughing if a collapsed lung is rapidly reexpanded.

Pneumothorax Treatment Options: Surgery

With the exception of those with a large open pneumothorax, essentially all patients being considered for surgical treatment for a pneumothorax already have a chest tube in place. With a progressive air leak, tension physiology is imminent once positive pressure ventilation is instituted unless there is a pathway for egress of air from the pleural space or intubation is performed directly with a double-lumen endotracheal tube such that the leaking lung can be immediately isolated. Specific surgical procedures are discussed under the appropriate sections, but it is worth noting that there are two surgical approaches available, video-assisted thoracoscopic surgery (VATS) or standard thoracotomy.

General indications for surgical intervention for a pneumothorax are failure of less invasive therapy or occurrence of the pneumothorax in the context of additional indications for chest exploration. A VATS approach can be employed, at least initially, for most pneumothoraces. Examples of contraindications to a VATS approach are a pneumothorax secondary to an esophageal perforation, major airway disruption, or a pneumothorax accompanied by significant ongoing bleeding or concomitant trauma to other thoracic organs.

Types of Pneumothorax

Pneumothoraces can be broadly grouped as spontaneous or traumatic. Spontaneous pneumothoraces can be further subclassified as primary or secondary, with primary arising in patients with no known underlying pulmonary disease and secondary spontaneous pneumothoraces arising as a complication of known underlying pulmonary disease. Traumatic pneumothoraces can be subclassified as those that are the result of blunt or penetrating trauma to the chest or those which are iatrogenically induced secondary to an invasive procedure or barotrauma from positive pressure ventilation. In this chapter, the former are referred to as traumatic pneumothoraces and the latter as iatrogenic pneumothoraces.

Primary Spontaneous Pneumothorax

Primary spontaneous pneumothorax most commonly occurs in tall young men, but may occur in anyone at any age. The peak incidence has been reported to occur for both men and women age 25 to 34 years old. It is approximately six times more common in men than women, with approximately 10,000 new cases per year in the United States.[10,53,54]

It is thought that the final common pathway for most primary spontaneous pneumothoraces is rupture of subpleural blebs.[55,56] It is also thought that inflammation of the distal airways plays a significant role in the pathogenesis of this disorder. The lack of communication between these blebs and the distal airways, and hence the inability to rapidly decompress, may explain the increased incidence of primary spontaneous pneumothorax associated with significant drops in atmospheric pressure.[57,58] The role of inflammation may explain why spontaneous pneumothorax is much more common in smokers.[59,60] In fact, there appears to be a dose–response relationship, with light smokers (fewer than 13 cigarettes/day) running a risk 7 times that of nonsmokers and those smoking more than 22 cigarettes/day at least 100 times more likely to have a spontaneous pneumothorax than nonsmokers.[61]

It is generally accepted that recurrent spontaneous pneumothoraces become increasingly likely with each successive occurrence. The exact statistics vary, but it is estimated that the risk of recurrence in the absence of aggressive preventive measures is in the range of 25% after the first recurrence and 50% after the second recurrence.[56,62] The chance of recurrence is very much related to the treatment undertaken for the initial spontaneous pneumothorax. Cessation of smoking also decreases the risk of recurrence. Although the literature reports many different recurrence rates, a reasonable estimation of recurrence following different treatments is observation alone, 30%; aspiration, 20% to 50%, tube thoracostomy drainage, 20% to 50%; tetracycline pleurodesis, 10% to 25%; talc pleurodesis, 7%; and surgical treatment, 0% to 2%.[8,63]

Selection of treatment remains an area of controversy. Observation alone should be reserved for the initial presentation of a small asymptomatic primary pneumothorax without any associated comorbidities. It should be reserved for patients who have no barotrauma risks and have ready access to medical help. This treatment may be particularly appropriate for patients who present with heavy cigarette abuse and are willing to stop smoking.

Aspiration is another option, but confers no significant protection from recurrence. Once the decision has been made to violate the pleura for aspiration, it is probably worthwhile leaving a catheter through which air can be continuously aspirated and subsequent pleurodesis can be performed. Some authors maintain that percutaneous catheter placement with subsequent pleurodesis should be the treatment of choice for a simple, primary spontaneous pneumothorax.[10,62] This has become the strategy I have adopted in the majority of these cases (for discussion of chemical sclerosants, please see "Ex-

udative Effusions: Malignant"). If a large air leak is anticipated or if there is significant effusion associated with the pneumothorax, then a standard 28-Fr. chest tube should be placed. Neither technique, without pleurodesis, seems to convey significant protection from recurrence.

Surgical treatment remains the gold standard in preventing recurrence of spontaneous pneumothorax. Some of the indications for surgical treatment of a spontaneous pneumothorax include a second pneumothorax (ipsilateral recurrence or a new pneumothorax on the contralateral side), tension physiology, synchronous bilateral pneumothoraces (rare but reported[64]), associated hemothorax (likely secondary to a torn adhesion and complicating approximately 5% of spontaneous pneumothoraces[65]), failure of tube thoracostomy, and lifestyle factors. Surgery should be considered if a leak persists for more than 3 to 4 days because most leaks seal within 48 h of instituting tube decompression and only a small additional fraction seal with further tube treatment, even after another week.[66] Lifestyle issues that are accepted indications for surgical therapy at the initial presentation of a primary spontaneous pneumothorax include occupational exposure to barotrauma (scuba diving or flying) and poor accessibility to medical care.[8]

The surgical procedure for spontaneous pneumothorax is resection of the blebs that are usually present, most commonly located in the apex of the upper lobe or the superior segment of the lower lobe. Resection of the blebs is performed with a pulmonary stapling device. Most surgeons also perform a mechanical pleurodesis of the pleural, utilizing an abrasive material such as a Bovie scratch pad. My practice is to perform all these procedures videoscopically and to perform a parietal pleurectomy of the entire chest wall and mechanical abrasion of the diaphragmatic and mediastinal pleura. Currently, VATS is considered by many thoracic surgeons to be the preferred surgical approach.[67–70]

A standard triad of video ports can be employed in most cases (Fig. 56.4). Use of a 30° degree thoracoscope facilitates visualization at the apex of the chest. The thoracoscope is introduced through the inferior port with a grasping device and thoracoscopic stapler introduced through the two superior ports. A sponge stick or folded Bovie scratch pad can be used for the pleurodesis. At the conclusion of the operation, a single 28-Fr. chest tube can be placed posteriorly to the apex of the chest. Additional suction ports can be cut in the tube, measuring to ensure the most proximal hole remains in the chest cavity and taking care to cut that hole through the radiopaque line for X-ray identification.

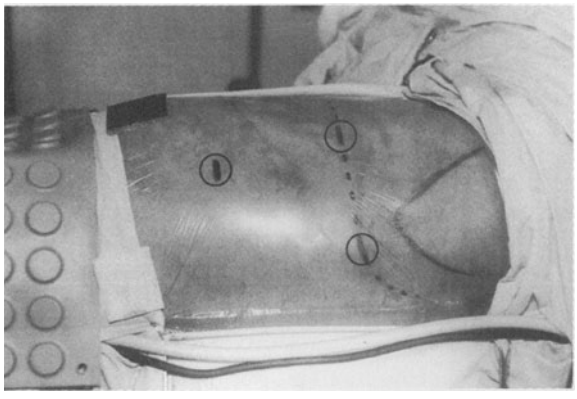


FIGURE 56.4. Typical arrangement of video thoracoscopy ports. The camera, and eventually the chest tube, are introduced through the lowest port (on the *left*). The remaining two incisions (on the *right*) are placed along a potential thoracotomy incision. Outline of the scapula is seen on the *right*. (Reprinted with permission from Friedberg and Kniger in Minimal Access Surgical Oncology, ©1998 Greenwich Medical Media Ltd.)

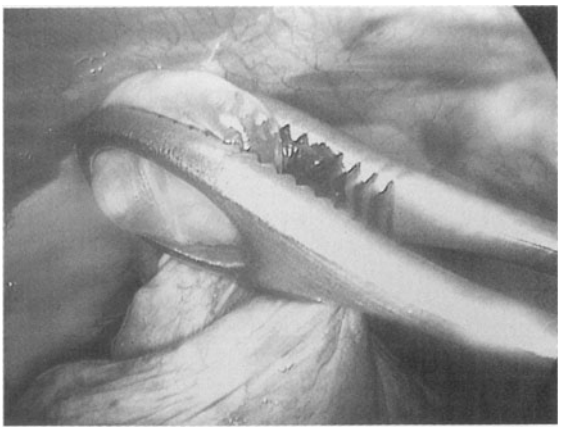


FIGURE 56.5. Intraoperative photograph taken through the video thoracoscope demonstrates an apical bleb (*within the grasping forceps*) in a patient presenting with a recurrent primary spontaneous pneumothorax. The bleb was then resected with a thoracoscopic stapling device, introduced through the third port incision. Subsequently, a parietal pleurectomy of the entire chest wall pleura and a mechanical pleurodesis of the mediastinal and diaphragmatic pleura were performed. A single chest tube was then inserted through the lowest incision, which had been used for the video thoracoscope during the procedure.

In skilled hands, particularly with the 30° thoracoscope, the entire lung can be well visualized and mobilized for stapler application, mechanical pleurodesis, and, if necessary, pleurectomy (Fig. 56.5). For most of these cases, thoracotomy offers little advantage with respect to visualization or performance of the bleb resection and pleurodesis.

Secondary Spontaneous Pneumothorax

Secondary spontaneous pneumothorax is a more serious condition than primary spontaneous pneumothorax because of its occurrence in patients who likely have significantly less pulmonary reserve than the typical patient presenting with a primary spontaneous pneumothorax. As opposed to primary spontaneous pneumothoraces, secondary spontaneous pneumothoraces are associated with a significant mortality.[71] Historically, the most common cause of secondary spontaneous pneumothorax has been chronic obstructive pulmonary disease (COPD). More recently, at least in urban centers, there is an increase in secondary pneumothoraces presenting as complications of *Pneumocystis carinii* infections in patients with acquired immunodeficiency syndrome AIDS.[72,73] There are many other causes of secondary spontaneous pneumothorax including, but not limited to, cystic fibrosis, asthma, cancer, many types of infection, sarcoid, collagen vascular diseases, and catamenial.

The recurrence rates for secondary primary pneumothoraces have been reported to be similar or slightly greater than those that are seen with primary spontaneous pneumothoraces.[74,75] Thus, the principal factor affecting choice of treatment in this setting is the more serious nature of a pneu-

mothorax in a patient with underlying pulmonary disease. If the patient is symptomatic, which is far more likely with this patient population, then there is no role for observation. Furthermore, an increase in the pneumothorax could possibly place the patient's life in jeopardy. Therefore, observation of a secondary spontaneous pneumothorax is recommended only in very select and highly monitored situations. There is some evidence indicating that simple aspiration is less effective in patients with secondary pneumothoraces than primary pneumothoraces.[76] As a result, simple aspiration should also be employed in very select situations. Tension physiology is frequently unnecessary to cause clinical decompensation in these patients. Any consideration of employing positive pressure ventilation in a patient with a secondary pneumothorax should be considered an automatic indication for thoracostomy tube placement.

Earnest consideration should be given to sclerosis for prevention in most of these cases. An important exception is the patient who is awaiting lung transplantation because adhesions resulting from sclerosis can significantly complicate explantation of the native lung at the time of transplantation and may lead to significant bleeding. Another consideration is the nature of the underlying pulmonary disease. If the pneumothorax occurs in the setting of a disease, such as certain malignancies or infections, it may not be possible to staple the lung or to achieve total lung expansion. In these cases, particularly if the patient is terminally ill, consideration should be given to sending the patient home with a chest tube and a Heimlich valve if this provides adequate palliation.

Traumatic Pneumothorax

Please refer to Chapter 54 on thoracic trauma.

Iatrogenic Pneumothorax

Iatrogenic pneumothorax may be the most common cause of pneumothorax.[77] The most common causes include transthoracic needle biopsy, subclavian central line placement, thoracentesis, transbronchial pulmonary biopsy, and positive pressure ventilation. The management of an iatrogenic pneumothorax must take into account a number of factors including the etiology, symptoms, and size of the pneumothorax and ventilatory status of the patient. It is logical to consider those patients with pneumothorax secondary to positive pressure ventilation, barotrauma, separately from those who developed pneumothorax secondary to violation of the visceral pleura.

The development of a pneumothorax as a result of barotrauma is an indication for immediate placement of a standard chest tube.[78–80] This indication is also true for a procedure-induced pneumothorax in a ventilated patient because positive pressure ventilation could rapidly lead to a tension pneumothorax. The clinician should always consider pneumothorax as a cause for instability in a ventilated patient who recently underwent thoracentesis or central line placement.

The majority of iatrogenic pneumothoraces are procedure induced. These pneumothoraces differ from spontaneous pneumothoraces in that the patient is not at an increased risk for recurrence. For small asymptomatic pneumothoraces, observation is appropriate and thoracostomy tube placement and sclerosis are not indicated. For larger pneumothoraces or symptomatic pneumothoraces in ambulatory patients, simple aspiration or temporary placement of a small percutaneous catheter is the preferred approach of many clinicians.[76,81–83]

Last, it is worth remembering that an esophageal perforation, most commonly from endoscopy or dilatation, can present with a pneumothorax, usually accompanied by a pleural effusion. As with traumatic pneumothorax, if the diagnosis is seriously entertained, then it must be investigated with a contrast study or endoscopy.

Tension Pneumothorax

Any closed pneumothorax arising from visceral pleural disruption has the potential to develop into a tension pneumothorax. Tension pneumothorax occurs when air accumulates in the pleural space in excess of atmospheric pressure and actively compresses the ipsilateral lung. This tension physiology will eventually lead to contralateral mediastinal shift and, in addition to pulmonary embarrassment, can severely limit venous return and compromise cardiac output. Untreated, tension pneumothorax may lead to cardiopulmonary arrest and, for this reason, is a life-threatening emergency.

Tension pneumothorax is believed to occur when a pleural disruption forms a functional one-way valve allowing air to escape from the lung but not reenter. Such physiology is occasionally well tolerated in a healthy adult and can await chest tube placement under urgent, but controlled, conditions.

If, however, the patient is in distress and the diagnosis is suspected, placement of a 16-gauge intravenous catheter through the second interspace, in the midclavicular line, will convert the tension pneumothorax to an open pneumothorax. After decompression has been achieved, a chest tube can then be placed in the usual manner. This procedure should always be performed immediately in any patient who is decompensating and for whom tension pneumothorax is in the differential diagnosis. It is a mistake to wait for a confirmatory chest X-ray in such a situation.

Blebs and Bullae

Although pneumothorax is a disorder of air that has entered into the pleural space, blebs and bullae are also disorders of abnormal air collections, but still contained within the lung. Only blebs can be considered a true pleural disorder. Blebs arise when air escapes from the pulmonary parenchyma and is trapped in the visceral pleura. Simply stated, blebs are subpleural collections of air.[84] They are usually small, less than 2 cm, and tend to occur at the apex of the upper lobe or the apex of the superior segment. The significance of blebs is uncertain. By themselves, it is doubtful that they cause any significant effect on pulmonary function. Their primary clinical significance lies in the fact that they appear to be involved in the pathogenesis of spontaneous pneumothorax.

No specific treatment is indicated for the finding of pulmonary blebs in the absence of pneumothorax. Cessation of smoking, as always, is recommended.

Bullae are air collections measuring at least 1 cm, but may become so large as to occupy the greater part of the hemithorax. As opposed to blebs, bullae are formed by destruction and coalescence of alveoli. They may demonstrate trabeculated lumens formed by the residual structural elements from the lung parenchyma they replaced. Blebs may be an incidental finding in patients with otherwise normal lungs, but bullae

TABLE 56.1. Differential Diagnoses of Pleural Effusion.

- Transudative Pleural Effusions
  - Congestive heart failure
  - Cirrhosis
  - Nephrotic syndrome
  - Superior vena cava obstruction
  - Fontan procedure
  - Urinothorax
  - Peritoneal dialysis
  - Glomerulonephritis
  - Myxedema
  - Pulmonary emboli
  - Sarcoidosis
- Exudative Pleural Effusions
  - Neoplastic disease
    - Metastatic disease
    - Mesothelioma
  - Infectious diseases
    - Bacterial infections
    - Tuberculosis
    - Fungal infections
    - Parasitic infections
    - Viral infections
  - Pulmonary embolization
  - Gastrointestinal disease
    - Pancreatic disease
    - Subphrenic abscess
    - Intrahepatic abscess
    - Intrasplenic abscess
    - Esophageal perforation
    - After abdominal surgery
    - Diaphragmatic hernia
    - Endoscopic variceal sclerosis
    - After liver transplant
  - Collagen vascular diseases
    - Rheumatoid pleuritis
    - Systemic lupus erythematosus
    - Drug-induced lupus
    - Immunoblastic lymphadenopathy
    - Sjögren's syndrome
    - Familial Mediterranean fever
    - Churg-Strauss syndrome
    - Wegener's granulomatosis
  - Drug-induced pleural disease
    - Nitrofurantoin
    - Dantrolene
    - Methysergide
    - Bromocriptine
    - Amiodarone
    - Procarbazine
    - Methotrexate
  - Miscellaneous diseases and conditions
    - Asbestos exposure
    - Postpericardiectomy or postmyocardial infarction syndrome
    - Meig's syndrome
    - Yellow nail syndrome
    - Sarcoidosis
    - Pericardial disease
    - After coronary artery bypass surgery
    - After lung transplant
    - Fetal pleural effusion
    - Uremia
    - Trapped lung
    - Radiation therapy
    - Ovarian hyperstimulation syndrome
    - Postpartum pleural effusion
    - Amyloidosis
    - Electrical burns
    - Iatrogenic injury
  - Hemothorax
  - Chylothorax

Source: Reprinted with permission from Pleural Diseases, edited by RW Light, © 1995 Lippincott, Williams & Wilkins.

are likely to be associated with some form of pulmonary disease, most likely emphysema.[84]

Bullous disease is also frequently asymptomatic. In such cases, cessation of smoking and annual chest X-rays are sufficient. In the setting of known underlying lung disease, treatment of that disorder is the priority. Pneumothorax, infection, or hemoptysis can prompt surgical intervention. Surgical intervention can also be indicated for compression of normal lung tissue to improve pulmonary function. Generally, very good results can be anticipated if the bulla is occupying more than 50% of the hemithorax, compressing well-perfused parenchyma.[84]

Liquid-Phase Disorders of the Pleural Space

Pleural effusions are a very common disorder encountered by the clinician. There are many potential causes of effusions (Table 56.1). Occasionally it is possible to deduce the etiology in the context of the patient's chest radiograph and concurrent morbidities. Frequently, however, the fluid must be sampled to yield a diagnosis. There is a normal composition of pleural fluid (Table 56.2) and a host of tests that can be performed on the fluid in pursuit of a diagnosis (Table 56.3). Once the fluid is sampled, it will fall into one of two categories, transudative or exudative, and 99% of exudative effusions will demonstrate at least one of the following characteristics: pleural fluid protein/serum protein ratio greater than 0.5, pleural fluid LDH/serum LDH greater than 0.6, or pleural fluid LDH more than two-thirds of the upper normal limit for serum LDH.[85]

Transudative effusions result from a perturbation in the hydrostatic or oncotic forces that affect fluid formation and turnover in the pleural space, as described in the physiology section. This imbalance results in fluid accumulation in the pleural space. For transudative effusions the goal is to drain the effusion for symptomatic relief, if necessary, but to focus on the systemic disease.

TABLE 56.2. Normal Composition of Pleural Fluid.

Volume	0.1–0.2 ml/kg
Cells/mm^3	1000–5000
% mesothelial cells	3%–70%
% monocytes	30%–75%
% lymphocytes	2%–30%
% granulocytes	10%
Protein	1–2 g/dl
% albumin	50%–70%
Glucose	≈ plasma level
LDH	<50% plasma level
pH	≥ plasma

Data from humans and animals.

Source: Reprinted with permission from Pulmonary Diseases and Disorders, Alfred P. Fishman, editor. ©1998 McGraw Hill.

TABLE 56.3. Useful Tests in the Evaluation of Pleural Effusion.

Test	*Abnormal value*	*Frequently associated condition*
Red blood cells/mm^3	>100,000	Malignancy, trauma, pulmonary embolism
White blood cells/mm^3	>10,000	Pyogenic infection
Neutrophils, %	>50	Acute pleuritis
Lymphocytes, %	>90	Tuberculosis, malignancy
Eosinophilia, %	>10	Asbestos effusion, pneumothorax, resolving infection
Mesothelial cells	Absent	Tuberculosis
Protein, PF/S[a]	>0.5	Exudate
LDH, PF/S	>0.6	Exudate
LDH, IU[b]	>200	Exudate
Glucose, mg/dl	<60	Empyema, TB, malignancy, rheumatoid arthritis
pH	<7.20	Complicated parapneumonic effusion, empyema, esophageal rupture, TB, malignancy, rheumatoid arthritis
Amylase, PF/S	>1	Pancreatitis
Bacteriological	Positive	Cause of infection
Cytology	Positive	Diagnostic of malignancy

[a]PF/S, pleural fluid to serum ratio.

[b]IU, concentration in International Units.

Exudative effusions result from diseases that involve the pleura and may be broadly grouped as benign or malignant. The treatment of an exudative effusion is disease specific.

Pleural effusions may be asymptomatic or may cause the patient to present with shortness of breath, secondary to compression of pulmonary parenchyma, as well as other symptoms. A nonspecific sign that is compatible with an effusion is the presence of a nonproductive cough. If the disorder causing the effusion has provoked an inflammatory response in the parietal pleura, the patient may complain of pain, known as pleuritic chest pain.

Restricted chest wall movement or change in the contour of the hemithorax may be evident, depending on the nature of the effusion and its effect on pleural pressure. If the effusion is unilateral and massive, the trachea may deviate to the contralateral side. Absence of vocal fremitus, dullness to percussion, and decreased breath sounds are all characteristic findings on physical exam. If the pleura is inflamed there may be an audible rub. A rub is likely to precede a significant effusion that will separate the roughened pleural surfaces and diminish or resolve the rub. In the case of a hydropneumothorax there may be an audible "splash," as originally described by Hippocrates.[86]

Plain radiographs of the chest remain the most common test obtained to evaluate a suspected effusion.[87] If the effusion is free flowing, the lateral costophrenic angle may be blunted on an upright posteroanterior radiograph if the effusion is greater than 175 ml. Sometimes more than 500 ml is required to achieve this effect.[88] The lateral radiograph is more sensitive than the posteroanterior view, but neither is as sensitive as the lateral decubitus projection, which can detect as little as 25 to 50 ml of fluid.[84]

For a free-flowing effusion that layers on a lateral decubitus film, additional radiographic studies are seldom indicated. Additional studies that are commonly used to obtain more information about a suspected effusion include ultrasound and CT scan. Ultrasound is very helpful in distinguishing pleural thickening from pleural fluid, determining if an effusion is complex or simple, and has the advantage of being portable. It can be used to help direct the clinician to the best area to perform a thoracentesis at the bedside. CT scans give the most information with respect to exact location of an effusion and may be particularly helpful in distinguishing effusion from pleural disease or parenchymal disease.[33,87] At this time, magnetic resonance imaging (MRI) scans are rarely indicated in the diagnosis or assessment of pleural effusions.

If the clinical scenario warrants diagnosis of the effusion, then the next step is to perform a thoracentesis to obtain a specimen for analysis and, possibly, to drain the effusion for relief of symptoms. The decision to perform such a procedure should be taken very seriously, for the complications can be significant and include pneumothorax, hemothorax, and conversion of a sterile effusion into an empyema. Thus, it is important to make sure the patient is not coagulopathic and, if there is any question as to the appropriate site to insert the needle, a bedside ultrasound should be performed.

Sterile technique must be observed. The procedure is most easily accomplished with the patient in the sitting position and leaning over a bedside table that has been padded with one or two pillows. For a diagnostic tap, a long 25-gauge needle can be used to infiltrate with lidocaine and can be used as a finder needle. A 22-gauge needle is then used to perform the aspiration.

If a therapeutic tap is indicated, a similar technique is employed, except that a catheter is placed into the chest cavity and connected via tubing to a three-way stopcock that is, in turn, connected to a syringe or a vacuum bottle. A number of commercial kits are available for this purpose, or the clinician can use a long 16-gauge intravenous catheter. It is this author's practice to place a triple-lumen catheter into the pleural space, using a Seldinger technique, and to connect each of the ports, via intravenous tubing, to a suction bottle. The different orientation of the ports appears advantageous in accessing the fluid and not occluding against tissue.

Regardless of the technique, it is generally recommended that not more than 1 l of fluid should be aspirated at one time

as this increases the chances of developing reexpansion pulmonary edema.[10] The exact etiology of this syndrome is not fully understood and may be accompanied by a 20% mortality.[50] Treatment for reexpansion edema is similar to treatment for other causes of pulmonary edema; upright posture, diuresis, supplemental oxygen and, if necessary, intubation.

Transudative Effusions

If the effusion is transudative, then it is most likely to be secondary to congestive heart failure, hepatic insufficiency, or renal insufficiency. Pleural effusions secondary to congestive failure are the most common transudative effusions.[89] Most of these effusions are bilateral. The presence of a unilateral effusion or bilateral effusions of significantly different sizes does not exclude this diagnosis, but would be unusual. The disorder is thought to result from increased pressure at the pulmonary capillary level secondary to left heart failure.[90] The treatment is the same as for other transudative effusions and is directed at the underlying cause, in this case, congestive failure. If the etiology is unclear or if the effusion remains unchanged after the congestive heart failure has improved, a diagnostic thoracentesis should be performed. Occasionally it is necessary to perform a therapeutic tap.

Approximately 5% of patients with hepatic cirrhosis will develop pleural effusions as a result of their disease.[91] Two-thirds of cirrhotic pleural effusions are right sided. The remainder is equally distributed between bilateral and left-sided effusions.[10,92] Usually, but not always, the patient will have ascites in addition to the pleural effusion. The pleural effusion is thought to result from a one-way communication and fluid flow from the peritoneum, across the diaphragm, to the pleural space; this can be demonstrated with radionuclide studies.[91,93–95] The treatment should be directed at the liver failure and ascites, with diuresis and salt restriction as the initial steps in management. Decompression of the portal circulation, percutaneously or surgically, may be indicated to treat the underlying disease.[96,97] If the pleural effusion is unresponsive to these measures, or if pulmonary symptoms necessitate intervention, the options include drainage and pleurodesis. Sometimes surgical intervention is indicated, combining closure of a demonstrated peritoneal–pleural communication with pleurodesis; this has been accomplished using VATS techniques as well as thoracotomy.[10,98] Shunting ascites to venous system is another option; however, these patients are generally poor surgical candidates unless their liver failure is corrected.

Nephrotic syndrome is another disorder associated with pleural transudates. These effusions tend to be bilateral and result from decreased plasma oncotic pressure. Again, treatment should be aimed at the primary disorder. In severely symptomatic patients, drainage and sclerosis can be considered. Other conditions that may provoke a transudative effusion include, but are not limited to, pulmonary embolism, superior vena cava obstruction, peritoneal dialysis, myxedema, glomerulonephritis, Meigs' syndrome, and sarcoidosis.[10,84]

Exudative Effusions

Exudative effusions can be broadly grouped into benign and malignant effusions. The malignant effusions arise most commonly from metastatic disease, but can also herald the presence of a primary malignancy of the pleura. The benign causes of exudative effusion include a very long list of conditions including but not limited to infectious diseases, pulmonary embolism, collagen vascular diseases, drug-induced disorders, bleeding, chyle leak, subdiaphragmatic infections, pancreatitis, and esophageal perforation. If the cause is not obvious, then a thoracentesis should be the next step in diagnosing the etiology of the effusion. The following sections discuss the conditions most likely to be encountered by the surgeon.

Exudative Effusions: Malignant

Malignant effusions represent one of the most common indications for chest tube placement. The tumors most frequently associated with a pleural effusion include lung cancer, breast cancer, and lymphoma. These three tumors account for approximately 75% of malignant effusions, with ovarian cancer, sarcoma, and melanoma accounting for the greater part of the remaining 25%.[10] A number of effects are likely to be responsible for the accumulation of malignant pleural effusions. These include blocking the normal uptake mechanism of the pleura, increasing the permeability of the pleura, thereby allowing more fluid into the space, blocking downstream lymphatic drainage of the pleura, and possibly by increasing negative intrathoracic pressure in cases of lung cancer where atelectasis has occurred.[10]

Dyspnea from pulmonary compression is the most common symptom produced by a malignant effusion. Malignant effusions are exudative and frequently sanguinous in appearance. The diagnosis can frequently be established by cytological demonstration of cancer cells in the fluid although up to 40% of effusions yield nondiagnostic cytology.[99,100] Thus, if malignancy is suspected and the fluid cytology is nondiagnostic, a closed pleural biopsy should be considered. Generally, closed pleural biopsy yields a diagnosis less commonly than fluid cytology, but it may be diagnostic when the cytology is negative.[10] Depending on the patient's surgical risk and the expertise available, it may be in the patient's best interest to proceed to thoracoscopy if the thoracentesis is nondiagnostic. If such services are not readily available then closed pleural biopsy is clearly indicated. If, after both closed biopsy and thoracentesis, a diagnosis remains elusive, a surgical biopsy is the only remaining option.

VATS is the approach of choice if surgery is required to establish a diagnosis. Depending on their surgical risk, patients may be well served by going to the operating room early in their course for diagnosis and drainage. Under general anesthesia, a single chest tube incision can be created through which the effusion can be drained and the thoracoscope introduced for examination and photodocumentation of the pleural cavity. Pleural biopsies can then be performed through the same incision by sliding the camera port out of the incision onto the proximal scope and sliding a biopsy forceps alongside the scope, through the same incision. The 30° thoracoscope is particularly helpful for this procedure as it allows the surgeon to look over the surfaces of the lung and to move the scope off to the side, which facilitates manipulation of the biopsy forceps. If the lung demonstrates the ability to fully expand and a malignant diagnosis is confirmed, intraoperative talc poudrage can be considered. All this can be accomplished through a single 10- to 15-mm incision.

Once the etiology of the malignant effusion is established, a treatment strategy can be formulated. Surgical debulking of metastatic pleural tumor is generally not part of the treat-

ment algorithm outside an experimental protocol. Most patients are relegated to chemotherapy and/or radiation therapy, or palliative measures directed at preventing further fluid accumulation. Some tumors, such as small cell lung cancer, breast cancer, ovarian cancer, and lymphoma, may respond very well to chemotherapy, including resolution of the pleural effusion.[101] Mediastinal radiation therapy may also be indicated in treatment of the patient's tumor, especially if the tumor has involved the thoracic duct and resulted in a chylothorax.[10]

If the patient is not receiving treatment for the underlying malignancy, or reaccumulates the effusion in spite of treatment, an alternative strategy must be considered if the effusion is causing symptoms. The options include chemical or surgical pleurodesis to prevent fluid accumulation or to provide a route for continuous drainage. Drainage may be accomplished by internal shunting of the fluid from the pleural cavity to the peritoneum or external drainage with a catheter connected to a collection bag.

Pleurodesis. If the lung expands completely when fluid has been drained, then pleurodesis is an option. If the lung does not expand, pleural apposition cannot occur and injection of a sclerosant will not work. In fact, the sclerosant may further hinder the absorptive mechanisms of the pleura, thereby making the effusion worse. Another factor to consider is the pH of the pleural effusion. One study reported a 43% failure of thorascopic talc pleurodesis if the pH of the effusion was less than 7.20, but only 9% if it was above 7.20.[102] Low pH is not a contraindication to attempting pleurodesis, if the lung expands, but it is a factor to be considered when considering treatment options.

The literature does not support the belief that the pleural drainage must be less than 150 ml/day to achieve effective sclerosis. Equal results and greater cost-effectiveness appear to occur if the sclerosis is performed as soon as the lung is fully expanded, regardless of the volume of drainage.[103]

Unless there is air in the chest cavity, the patient does not have to roll into different positions as there is likely to be rapid dispersion of the sclerosant through the chest cavity in a very short period of time without any change in position. If there are loculations or a pneumothorax component to the effusion, positional changes do seem to facilitate agent dispersion.[104] After instillation, the chest tube is clamped for 2 h and subsequently opened and placed to suction for at least 24 h. Therefore, the tube should stay on suction until the drainage is less than 150 ml/day. At that point, the chest tube can be removed.

Choice of Sclerosant. The most popular agents for chemical pleurodesis currently in use are talc, doxycycline, and bleomycin. The greatest experience with these agents is in the setting of sclerosis for malignant effusions. In this setting, there are numerous reports citing greater efficacy of one agent over the others[105–109]; however, randomized trials have demonstrated similar efficacy of these three agents.[110–113] There are fewer reports on the use of sclerosants for treating pneumothorax, but significant efficacy is reported for both doxycycline and talc.[105,114–116] There are currently no series reported for bleomycin sclerosis for pneumothorax. Each agent has relative advantages and disadvantages.

Talc is likely the most popular chemical sclerosant and is generally considered to be safe, well tolerated, and effective.[10] Few patients complain of significant discomfort associated with talc pleurodesis; however, a significant proportion develop a transient fever.[117] Talc can be administered via chest tube as a slurry or insufflated into the chest cavity at the time of surgery. The most common dose is 2 to 5g,[10] but doses up to 10 g have been reported.[118] In our institution, the routine is to use 2 g when insufflating intraoperatively, and 5 g mixed in 100 ml sterile saline and 100 mg of lidocaine when it is introduced as a slurry. Despite its relative safety, however, talc has been associated with a number of significant complications, including acute respiratory distress syndrome (ARDS). The incidence of ARDS was thought to be a dose- or route-related phenomenon,[10,117] but this has recently been disputed.[119] Empyema is another reported complication, thought to result from contamination of the talc, that can be avoidable with new sterilization techniques used to prepare the talc.[117] Of the three most common agents, talc is the only one that remains as a permanent foreign body, a factor that can significantly complicate the management of an empyema. The potential carcinogenic effects of intrapleurally administered talc remain controversial.[120,121] This effect is of little concern in the setting of a malignant pleural effusion. It is, however, of potential concern when being used in the setting of benign conditions, such as spontaneous pneumothorax, which predominantly present in young healthy patients. However, some still maintain that purified talc is a safe and effective treatment for spontaneous pneumothorax.[105,106]

Doxycycline is the cheapest of the three agents. It is also the one that most commonly causes significant discomfort. It is administered via chest tube, dissolved in 50 to 100 ml sterile saline and 200 mg lidocaine.[116]

Bleomycin generally causes little if any discomfort, but is the most expensive agent. In many institutions, an intrapleural dose (60 units) costs approximately $1000.[10,110] It is administered via chest tube, dissolved in 100 ml of sterile saline. Although generally very well tolerated, intrapleural bleomycin is absorbed systemically and is, therefore, not recommended for patients who are receiving chemotherapy, are immunosuppressed, or have renal failure.[122] Some authors contend that bleomycin should not be used for benign conditions, on the basis of experimental observations in a rabbit model.[123] This finding conflicts with the demonstrated efficacy for sclerosing malignant effusions in humans.

Support can be found in the literature for using any of these agents in nearly any situation. My approach is to use talc for pleurodesis of malignant effusions. For benign conditions, I use doxycycline if the patient can safely tolerate significant sedation with intravenous narcotics and benzodiazepines or if they already have an epidural catheter in place. My experience has been that patients who receive intrapleural doxycycline, even with lidocaine, frequently describe it as the most painful experience of their lives. I have used bleomycin as the sclerosing agent for the remaining patients with benign conditions. The experimental data notwithstanding, during the past 3 years I have used bleomycin in this setting and have noted no difference compared to doxycycline.

Other Options

If the patient's lung does not expand, or if pleurodesis has failed, then drainage becomes the next option. There are three techniques currently available: intermittent thoracentesis, placement of a long-term drainage catheter, or internal

drainage with a pleuroperitoneal shunt. Intermittent thoracentesis may be the best for a patient who is minimally symptomatic or has a very short life expectancy. Indwelling catheter placement for repeat thoracentesis or continuous external drainage has been reported to provide good palliation for as long as 10 months.[124,125]

Internal drainage can be accomplished by implanting a shunt, such as the Denver Shunt (Denver Biomaterials, Evergreen, CO), which has a pumping chamber that the patient can press to transfer fluid across the negative pressure gradient from the pleural cavity to the peritoneal cavity. There are a number of downsides to this option. Placement requires an operation, usually under general anesthesia, a small percentage of the shunts will obstruct, and the patient must actively pump the shunt to transfer fluid. These shunts, however, are very effective at controlling symptoms and may result in a shorter hospital stay than a typical admission for chemical pleurodesis.[126,127]

The role of thoracoscopy for treatment of malignant effusion is currently under investigation. It remains to be determined if thoracoscopy with insufflation of talc is superior to installation of a talc slurry through a chest tube.[128,129] A reasonable approach is to perform intraoperative talc insufflation if the patient requires thoracoscopy for diagnosis or drainage of a complex effusion. Otherwise, if the patient already has a diagnosis and a chest tube that has adequately drained the effusion, pleurodesis can be performed at the bedside.

Thoracotomy with decortication, in the presence of a malignant effusion, is rarely indicated. Although highly variable, the average survival of a patient with a malignant effusion from lung cancer is of the order of 4 months, whereas for breast or ovarian cancer it may be more in the range of 7 to 9 months.[102] Thus, recovery from such an operation is likely to result in decreased quality of life for a significant portion of the patient's remaining time.

Exudative Effusions: Benign

Effusions associated with pneumonia (parapneumonic effusions) are the most common cause of benign exudative effusions. They result from visceral pleural inflammation that alters the normal fluid balance of the pleural space.[10] These effusions may initially be sterile, but if the parenchymal infection spreads to the effusion, an empyema results.

There is a continuum that reflects the natural history of untreated parapneumonic effusions, from a thin, clear sterile collection to an infected fibrous peel encasing the lung. The first stage is the "exudative stage" characterized by fluid exuding from the lung into the pleural space, likely from the pulmonary interstitial space. This stage should resolve with antibiotic therapy and generally does not require drainage. Normal pH and glucose with a low LDH and white blood cell count are characteristic of the fluid at this stage.

Untreated, the effusion is likely to progress to the "fibropurulent stage," characterized by increased fluid that is heavily laden with white blood cells, microorganisms, and cellular debris. Fibrin is deposited on the pleural surfaces and the stage is set for pulmonary entrapment. At this point, the fluid pH and glucose fall and the LDH rises. Chest tube drainage is indicated, but becomes more difficult as the effusion loculates. The final stage is the "organizational stage" during which fibroblasts grow into the effusion, laying down a thick fibrous peel that encases the lung and results in entrapment. The remaining effusion is thick and infected and may necessitate through the chest wall or into the lung.[10,130]

The presentation of a parapneumonic effusion or empyema depends, to a certain extent, on the organism causing the infection. For aerobic organisms the presence of the effusion has little impact on the clinical picture, which is that of a bacterial pneumonia: fever, chest pain, and a productive cough. An anaerobic infection, frequently as a result of aspiration, is more likely to present in a subacute manner. A patient with an anaerobic empyema may have symptoms for more than a week before seeking medical help, and significant weight loss may be a chief component of their presentation.[10]

Exudative Effusions: Benign, Diagnosis

True empyema thoracis is simply defined as pus in the pleural space, a clear indication for drainage. For a small simple parapneumonic effusion, in a patient being treated with and responding to appropriate antibiotics, there is no indication for drainage. The issue is how to identify the effusion that is not yet frankly purulent but will require drainage to resolve. If the patient with a pneumonia continues to have a large or increasing effusion, then a thoracentesis should be performed.

The fluid from the tap should be sent for glucose, pH, LDH, amylase, protein, complete blood count with differential analysis, Gram stain, aerobic/anaerobic bacterial cultures, and, if indicated, special microorganism cultures and stains. If malignancy is suspected, cytology should also be sent. A pH below 7.0, a glucose less than 60 mg/dl, or an LDH greater than 1000 IU/l are frequently used as indications to drain an effusion in the setting of a negative microbiological evaluation.[10] These remain, however, only guidelines as it has been shown that complicated pleural effusions can resolve without drainage.[131]

Exudative Effusions: Benign, Treatment

Once the decision has been made to drain the fluid collection, a number of options are available: aspiration, chest tube drainage, VATS drainage, limited thoracotomy and open drainage, or full thoracotomy with drainage and decortication.

For diagnosis and initial treatment of a free-flowing pleural effusion, aspiration is an appropriate initial step. If the clinical situation mandates further drainage, then the clinician has several options. If the effusion is free flowing, then placement of a standard chest tube is a reasonable option. If the effusion is loculated, ultrasound guidance may be helpful either for marking the ideal location for thoracentesis or thoracostomy tube placement or for placement of a percutaneous drainage catheter.[132]

The use of intrapleural streptokinase or urokinase has been advocated if drainage fails due to loculations.[133] In several well-constructed studies, however, it has been shown that enzymatic treatment will increase the volume of chest tube output but not affect the clinical course. Furthermore, use of these agents is inferior to early videoscopic surgical drainage with respect to treatment efficacy, length of hospital stay, and cost of treatment.[134,135] A reasonable case can be made to reserve fibrinolysis for patients who are extremely high-risk surgical candidates.

There are several surgical options for patients with an empyema. The goals of surgical therapy are to establish

drainage and, depending upon the situation, to eliminate space in the pleural cavity. Space elimination can be accomplished by decortication to allow the lung to expand, collapsing the chest wall with a thoracoplasty or by transposing muscle flaps to fill the space. A critical component is to always establish drainage. The least invasive option is to thoracoscopically explore the chest cavity, disrupt loculations, debride the visceral pleura, and strategically place chest tubes. Frequently it is possible to accomplish this procedure utilizing the patient's already existing chest tube sites as video ports. This option is most likely to be successful if performed in the exudative or early fibrinopurulent stages.[136]

Once in the organizational stage, the lung is encased in a fibrous peel that most often requires an open thoracotomy to adequately remove. If the patient is able to tolerate such a procedure, then this represents the most effective treatment of the problem. The goal in such a situation is to drain the infection and obliterate any space with reexpanded lung tissue. If a portion of the lung has already been removed or if the infection has rendered portions nonviable, mandating resection, then space may become an issue. The favored option is to transpose muscle flaps into the chest cavity to obliterate any residual space that exists after the lung has been decorticated and reexpanded. The commonly used muscle flaps are serratus, latissimus, and pectoralis. Omentum is also a good option. A good approach in these cases is to enter the chest through a vertically oriented muscle-sparing thoracotomy such that both serratus and latissimus are spared and can be harvested if necessary.

After a drainage procedure the clinician is faced with the management of the chest tubes. The classic treatment of a chest tube placed into an empyema is to leave it to closed suction drainage for 2 to 3 weeks. Thereafter, the tubes are taken off suction and converted to open drainage, slowly withdrawing them over the course of several more weeks.[8] Another option is to leave the tubes in place for approximately 1 week on suction. If the lung is fully expandable, drainage is minimal (<50 ml/day), and the patient has no further signs of infection, then the tubes may be removed.[84] The critical point is that the lung must be fully expanded. Cases in which this strategy is safe and effective usually demonstrate full expansion of the lung on the chest X-ray and "walling off" of the chest tube, characterized by essentially no drainage and lack of respiratory variation in the waterseal chamber of the PleurEvac.

For patients with chronic empyema, empyema with bronchopleural fistula, or patients unable to tolerate thoracotomy, an open drainage procedure may represent the best option. These procedures involve localizing the most dependent portion of the empyema cavity and resecting a portion of the overlying rib. The cavity is then entered, the pleural space debrided, and, if possible, the lung decorticated. The chest wall defect can be made just big enough to allow placement of a large-bore silastic "empyema tube," or it can be converted into a pleurocutaneous fistula large enough to permit intracavitary dressing changes. These procedures fulfill the single greatest priority, drainage of pus, and permit the patient to recover from their infectious process. Depending on the size of the cavity, it may close spontaneously or may require reconstruction, usually with a muscle flap. In an elderly or infirmed patient, the cavity may be left open.

Exudative Effusions: Benign, Other Causes

Infectious, Nonbacterial

Almost any organism can cause an infection with which a pleural effusion is associated. Tuberculosis may cause a pleural effusion that tends to be unilateral and of moderate size. They can be difficult to diagnose based on chemical and microbiological evaluation of the pleural fluid, but usually demonstrate granulomatous pleuritis on closed pleural biopsy if the diagnosis is in doubt. The effusion usually responds to appropriate antibiotic therapy and, unless symptomatic or part of a mixed empyema, usually does not require drainage or surgery.

Viral effusions usually elude diagnosis and are self-limited. Human immunodeficiency virus (HIV) does not appear to cause pleural effusions, but patients with HIV are more likely to develop pleural complications associated with a bacterial pneumonia.

Effusions may accompany any of a number of fungal pulmonary infections. The primary treatment is appropriate antibiotic therapy and, depending upon the infection, drainage. Of note, *Aspergillus* empyemas are almost always associated with a bronchopleural fistula, or a history of previous treatment of tuberculosis with artificial pneumothorax, and almost always require surgical evacuation as part of their treatment.

Although relatively uncommon in the United States, the clinician should be aware that pleural effusions commonly accompany a number of parasitic infections. Again, appropriate drug therapy is essential. Of note, rupture of pleural or hepatic cysts into the pleural space can present with acute symptoms and, as in the case of *Echinococcus*, may represent an indication for urgent thoracotomy to debride and drain the pleural space and to drain the original cyst.[10,84]

Pulmonary Emboli

Pleural effusions may accompany pulmonary emboli in 30% to 50% of cases. Although the majority of these effusions are exudative, approximately one-quarter may be transudative. This is likely to be determined by the relative contribution to the effusion by the two mechanisms thought to be primarily responsible for the effusion. Transudative effusions are thought to exude from the parietal pleura secondary to right heart failure. Exudative effusions are thought to arise from the visceral pleural secondary to release of local factors from the emboli that increase capillary permeability. The treatment for pulmonary emboli with effusion is the same as for pulmonary emboli without effusion and, as always, the key factor is to consider the diagnosis in a patient with any of the symptoms suggestive of pulmonary embolus.

Subdiaphragmatic Pathology

Inflammation or malignancy below the diaphragm can cause exudative pleural effusions as well as transudative effusions secondary to hepatic or renal dysfunction, as discussed in the transudative effusion section. Acute pancreatitis generally leads to a left-sided effusion, likely as a result of transdiaphragmatic transfer of exudative ascites arising from pancreatic inflammation. The fluid almost always has an elevated amylase, and that amylase is frequently higher than the serum amylase. The fluid generally resolves with resolution of the pancreatic inflammation. Pancreatic abscess can also

cause a pleural effusion and, again, the treatment is the usual treatment of a pancreatic abscess. A pancreatic pseudocyst can decompress into the pleural space, forming a pancreaticopleural fistula. These effusions tend to be large, usually left sided, very high in amylase, and are usually accompanied by chest, not abdominal, symptoms. This finding is thought to be secondary to decompression of the pseudocyst into the thorax. Treatment of this disorder is conservative, the same as the initial treatment of any pancreatic pseudocyst. The role of drainage of the effusion remains controversial, and the clinician should be aware of the risk of infection and the fact that the drainage is likely to be massive and with rapid reaccumulation until the fistula has closed. Should conservative treatment fail, a percutaneous or surgical drainage procedure should be planned.

Subphrenic abscess from any number of intraabdominal sources can lead to an exudative effusion. The effusions rarely are culture positive and tend to have a very high WBC, yet the pH is usually above 7.20 and the glucose is usually greater than 60 mg/dl. Treatment of the effusion should be symptomatic, as the approach is treatment of the abscess and its underlying cause. The effusion usually resolves with these measures.

The clinician is advised to always consider esophageal perforation in the diagnosis of a pleural effusion, particularly after instrumentation of the esophagus or retching. Iatrogenic injury accounts for two-thirds of these injuries, and the patient frequently complains of chest pain. The condition usually presents with a left-sided effusion, but it may be either side or bilateral, and accompanied by, or replaced with, a pneumothorax. The fluid is almost always high in amylase from saliva that has leaked into the pleural space. The mortality rate is high, up to 60%, which underscores the imperative of prompt diagnosis. If the diagnosis is being entertained, a contrast swallow study should be obtained. Treatment depends upon how early the disruption is diagnosed, and ranges from primary repair to esophageal exclusion. Pleural drainage and antibiotics are almost always necessary components of the treatment strategy.

Chylothorax

Chylothorax is an exudative effusion caused by disruption of the thoracic duct and subsequent drainage of chyle into the pleural space. The initial presentation of a chylothorax is determined by the size of effusion and its mechanical effects within the hemithorax. Once a chest tube is in place, the symptoms are determined by the persistence of the drainage. The longer the drainage continues, the more dangerous it becomes with the consequences being dehydration, nutritional depletion, and immunocompromise.[137] More than 50% of chylothoraces are secondary to ductal obstruction and disruption by tumor, with lymphoma accounting for 75% of these cases. Approximately 25% of chyle leaks are traumatic, with iatrogenic trauma being the most common. Of the iatrogenic causes, esophageal resection appears to be the leading cause, more common with transhiatal esophagectomies than transthoracic esophagectomies. The remainders are idiopathic and thought to be related to minor trauma.[84]

The diagnosis is established by analysis of the fluid. Although classically viewed as milky in appearance, chyle may frequently appear serosanguinous, particularly in the fasting state. A triglyceride level in the fluid greater than 110 mg/dl is highly suggestive of chyle whereas a level below 50 mg/dl essentially excludes the diagnosis of chylothorax. Intermediate values require a lipoprotein analysis to prove the presence of chylomicrons to establish the diagnosis.[138] Some believe that the most reliable test is to give an oral challenge of cream and to observe the tube drainage for gross changes.[137]

The treatment of chylothorax remains controversial; some authors advocate a generous period of conservative treatment while others recommend early intervention.[139–141] All authors agree that a prolonged, high-output leak can be devastating and most authors agree that an initial trial of conservative therapy should be instituted. Conservative therapy involves pleural drainage and a no-fat diet or total parenteral nutrition. Oral administration of medium-chain triglycerides is thought to be acceptable.[137] If the leak is secondary to a malignancy, then chemotherapy and/or radiation therapy may be the treatment of choice. For other chylothoraces, surgical intervention is indicated when conservative measures have failed. The timing of such intervention is debatable, but most authors agree it is unwise to wait more than 1 to 2 weeks in the setting of an unremitting leak. Up to 50% of leaks that are going to close spontaneously do so within 2 weeks.[8] It is important not to wait until the patient is immunocompromised and nutritionally depleted before deciding to operate as this would unnecessarily increase the risk of the surgery.

At the time of surgery, heavy cream is administered via nasogastric tube immediately after intubation; this makes the duct more visible and may also identify the area of leak. A number of surgical options are available, including parietal pleurectomy, direct ligation of the leak, and mass ligation of the duct. Mass ligation offers at least an 80% chance of resolving the leak.[8,139] Many advocate performing a ligation of the duct on the right side, just as it emerges from the diaphragm, regardless of the side of the chylothorax. This ligation has traditionally been performed through a small thoracotomy incision in the sixth or seventh interspace. This procedure is readily accomplished thoracoscopically, utilizing three 1.0- to 1.5-cm port incisions (Fig. 56.6). This proce-

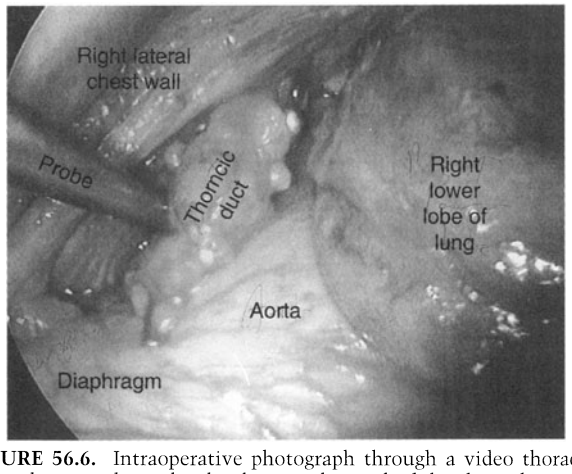


FIGURE 56.6. Intraoperative photograph through a video thoracoscope shows probe under the thoracic duct, which has been dissected free at the level of the diaphragm on the *right side*. Note thoracic duct, aorta, lung, and diaphragm. This duct was clipped and ligated via this VATS (video-assisted thoracoscopic surgery) approach through three 10-mm incisions that resulted in immediate and complete resolution of the patient's chyle leak.

dure seems to offer less morbidity and equal efficacy to the open procedure. In cases where surgery fails or the patient is at prohibitive risk for a major procedure, other options include pleuroperitoneal shunting or sclerosis. Last, at the University of Pennsylvania, some patients have been successfully treated using interventional radiologic techniques to percutaneously occlude the thoracic duct. It is too soon to know if this will become a standard treatment option.

Hemothorax

The overwhelming majority of hemothoraces are caused by trauma, including iatrogenic trauma. There are other, significantly less common, causes including bleeding from metastatic tumors involving the pleura, hemorrhage during anticoagulation therapy for pulmonary emboli, and catamenial hemothorax. The potential consequences of an undrained hemothorax include conversion to an empyema, provocation of a pleural effusion, and conversion to a fibrothorax with lung entrapment. The initial treatment of any hemothorax should be pleural drainage with a large-bore (32- or 36-French) chest tube. If the tube becomes clogged or is inadequate, additional tubes should be strategically placed.

Up to 4% of hemothoraces will become infected. The incidence of this complication can be reduced, at least in the setting of hemothorax caused by isolated chest trauma, by routine administration of prophylactic antibiotics.[142] This complication is more common in patients admitted in shock, with gross contamination of the pleura at the time of injury, with prolonged chest tube drainage, and with concomitant abdominal injuries.[10]

The pleural effusion associated with hemothoraces may occur after the blood has been evacuated and the chest tubes are removed. If the fluid is infected, it should be treated accordingly. If not, these effusions tend to be self-limited and require no further intervention.[10]

Rarely does hemothorax progress to fibrothorax.[143] Thus, there is no absolute indication to evacuate all sterile clot from a chest cavity if tube thoracostomy is not completely successful. The recommendation has been to consider surgical evacuation of residual blood if it occupies more than 30% of the hemithorax.[10] It should be noted, however, that this recommendation was proposed before the current era of thoracoscopy.

VATS has been shown to be a safe and effective way to evacuate blood from the chest cavity.[144–146] In a prospective randomized trial, early VATS drainage of retained hemothorax was found to decrease duration of tube drainage, hospital stay, and cost.[147] The earlier clot evacuation is attempted, the more likely VATS evacuation will be completely successful. In addition, if intervention is instituted early, the entire operation can frequently be performed through the existing chest tube incisions, occasionally requiring one additional videoscopic port incision.

There is also support in the literature for intrapleural instillation of thrombolytic agents for dissolution of formed clot and subsequent enhanced chest tube drainage.[148] Caution should be exercised, however, because fibrinolytic agents may cause rebleeding and also respiratory failure caused by the products of fibrinolysis.[149,150]

Miscellaneous

Collagen vascular disorders may be associated with pleural effusions. In each case, the treatment of the effusion is symptomatic with the primary goal being treatment of the underlying disorder. The two most common diseases are rheumatoid arthritis and systemic lupus erythematous. Rheumatoid disease may involve the pulmonary parenchyma as well as the pleura. The fluid of a rheumatoid effusion characteristically has a glucose less than 30 mg/dl, pH less than 7.2, LDH greater than 700 IU, and a very high rheumatoid factor. Lupus effusions tend to have a glucose greater than 60 mg/dl, pH greater than 7.2, LDH less than 500 IU, and a high antinuclear antibody titer.[10,84]

Although many drugs can cause pleural effusions, it is not a common cause. Some of the more commonly used drugs that may cause an effusion include amiodarone, methotrexate, nitrofurantoin, dantrolene, and metronidazole. Frequently there is a parenchymal abnormality or a pleural or systemic eosinophilia. The onset of the effusion may be acute or insidious and should be considered early, because prolonged administration of the offending agent may produce a chronic condition that may include permanent parenchymal changes, persistent effusions, or fibrothorax. Early discontinuation of the offending agent usually results in resolution of the syndrome.[10,84]

There are numerous other causes of exudative effusions. These include but are not limited to cardiac surgery, lung transplantation, asbestos exposure, Dressler's syndrome, Meigs' syndrome, yellow nail syndrome, sarcoid, postpartum state, trapped lung, radiation exposure, ovarian hyperstimulation, amyloidosis, ARDS, electrical burns, and uremia.[10]

Solid Disorders of the Pleural Space

A limited number of benign and malignant solid disorders affect the pleura. The most common benign conditions are fibrothorax, pleural plaques, diffuse pleural thickening, and benign fibrous tumors of the pleura. The most common malignancies are tumors metastatic to the pleura. The primary malignancy of the mesothelium is mesothelioma, and numerous cancers, such as liposarcoma and fibrosarcoma, may arise from any of the elements forming the connective tissue layer of the pleura.

Benign Disorders

Fibrothorax results from deposition of a thick fibrous layer along the pleural surface. This layer may cause entrapment of the lung as well as contraction and immobility of the skeletal hemithorax. The most common causes of fibrothorax are hemothorax, tuberculosis, and bacterial pneumonia. Other causes include pancreatitis, collagen vascular diseases, and uremia.[10]

The treatment of fibrothorax is decortication, which in this setting is generally a major operation requiring a full thoracotomy. Patients who are being considered for decortication should be low-risk surgical candidates and should have pulmonary parenchyma that is anticipated to be able to expand upon release. Generally, the indication is significant pulmonary compromise in a patient whose fibrothorax is stable or worsening for at least several months (Fig. 56.7).[10]

The pathogenesis of pleural plaques remains unclear. They are thought to be predominantly caused by asbestos, perhaps secondary to release of local factors in response to the foreign body after macrophage phagocytosis.[151–155] Pleural plaques are hard, raised discrete areas involving the parietal

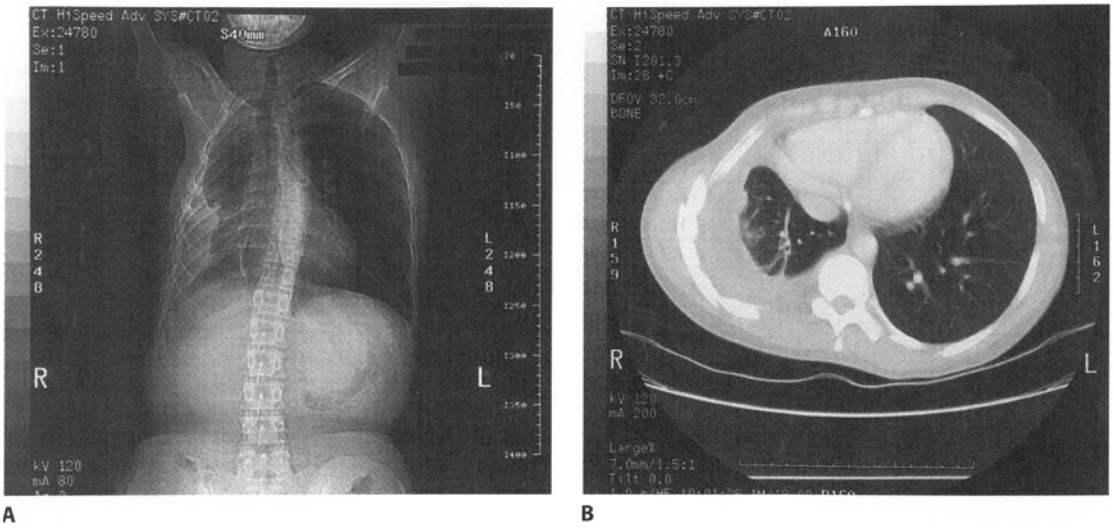
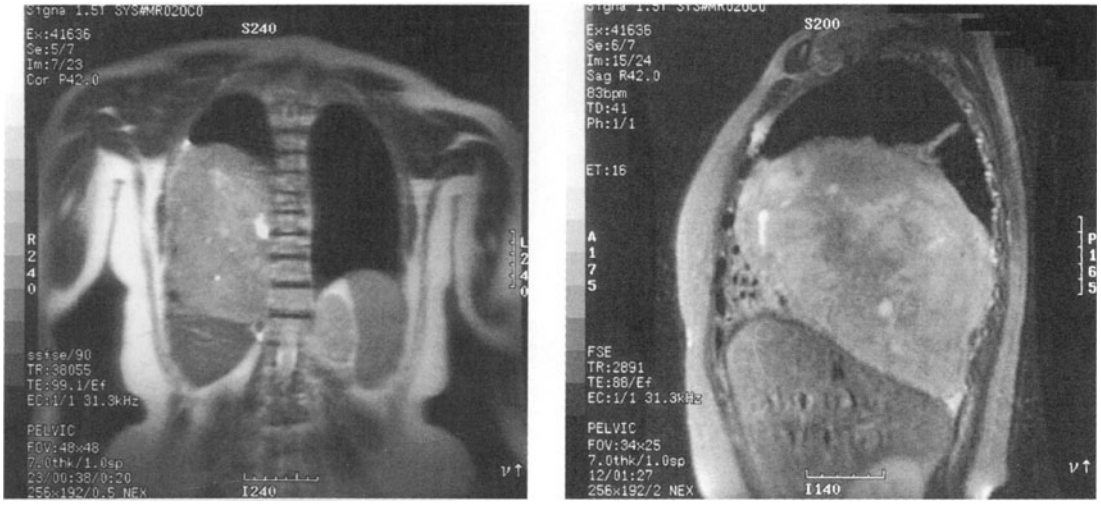


FIGURE 56.7. Anteroposterior radiograph of the chest (**A**) demonstrates scoliosis and volume loss resulting from a fibrothorax caused by a tuberculous empyema. CT cross section (**B**) demonstrates the thick parietal pleural peel entrapping healthy lung parenchyma. Notice contraction and overlapping of ribs in both radiographs. The patient underwent a decortication with dramatic improvement of her scoliosis and pulmonary function.



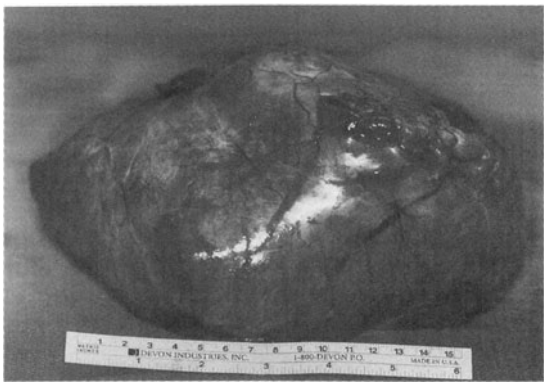


FIGURE 56.8. Coronal (**A**) and sagittal (**B**) MRI images demonstrate a large benign fibrous tumor of the pleura occupying the greater part of the right hemithorax. This patient presented with complaints of bilateral lower-extremity swelling that proved secondary to inferior vena cava compression. Photograph (**C**) shows the resected mass that arose from the visceral pleura of the right middle lobe and which was readily separated from the remainder of the lung with a small wedge resection of the affected area.

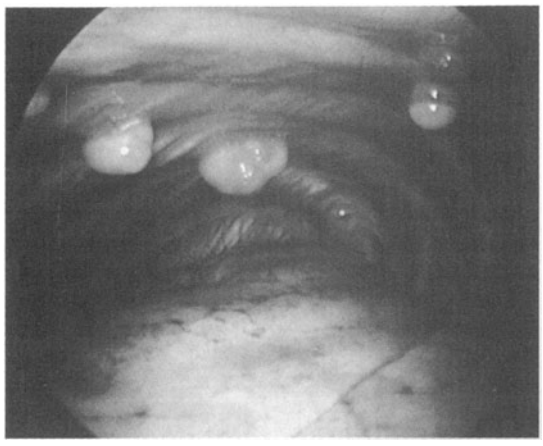


FIGURE 56.9. Intraoperative photograph through a video thoracoscope shows metastatic cancer implants on the parietal pleura on the chest wall. (Reprinted with permission from Friedberg and Kniger in Minimal Access Surgery in Oncology, ©1998 Greenwich Medical Media, Ltd.)

pleura, particularly in the lateral, posterior portion of the hemithorax; 80% of pleural plaques that are due to asbestos are bilateral, with the majority of unilateral plaques thought to be secondary to other causes such as previous trauma, tuberculosis, or collagen vascular disorders.[84] Generally, there is no therapy indicated for pleural plaques. Pleural plaques do not appear to be predecessors of mesothelioma.[10]

Of note, however, because asbestos is a risk factor for lung cancer, presence of pleural plaques may serve as an indicator of patients at increased risk for lung cancer.[156] Therefore, it is recommended that patients with pleural plaques have serial radiographs as part of their routine medical care.[84]

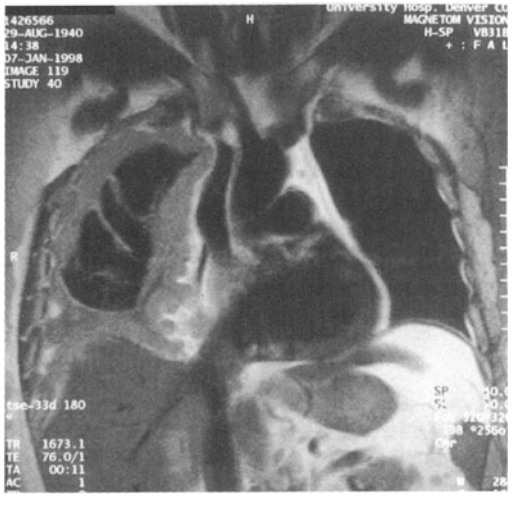
Diffuse pleural thickening, like pleural plaques, appears to be predominantly related to asbestos exposure. Other causes such as drug reaction, hemothorax, and tuberculosis have been reported. Unlike pleural plaques, however, diffuse pleural thickening affects the visceral pleura. Its exact etiology also remains unclear, but it is thought that inflammatory factors are likely to play a major role, particularly in the setting of a resolving asbestos-induced pleural effusion. There appears to be an initial decrease in pulmonary function associated with diffuse pleural thickening that tends to remain stable over time. Again, there is no specific treatment recommended, just routine surveillance. In severe cases, pleurectomy has been performed, the results of which were poor secondary to concomitant pulmonary fibrosis.[10,84,157,158]

A rare primary, benign tumor of the pleura is the benign fibrous tumor of the pleura, previously called benign mesothelioma. These tumors arise from the visceral pleura, are not associated with asbestos, and are frequently discovered incidentally on chest X-ray. These tumors may reach enormous size, thereby causing symptoms by virtue of compression of other structures (Fig. 56.8). Surgery is the treatment of choice and is almost always curative.[84]

Solid Malignancies of the Pleura

The most common malignancies of the pleura are metastatic, predominantly from lung, breast, or colonic carcinomas (Fig. 56.9). There are extremely rare primary sarcomas arising from the connective tissue elements of the pleura. The most common primary malignancy of the pleura is mesothelioma.

That being stated, however, it is a rare tumor, with only 1500 to 3000 cases per year in the United States. Mesothelioma is thought to be primarily related to asbestos exposure, although other causes such as chemicals and radiation have been implicated. There is a 20- to 40-year-lag period between exposure to asbestos and formation of the tumor. The tumor usually presents with dyspnea secondary to a pleural effusion, but may also present with chest pain or constitutional symp-



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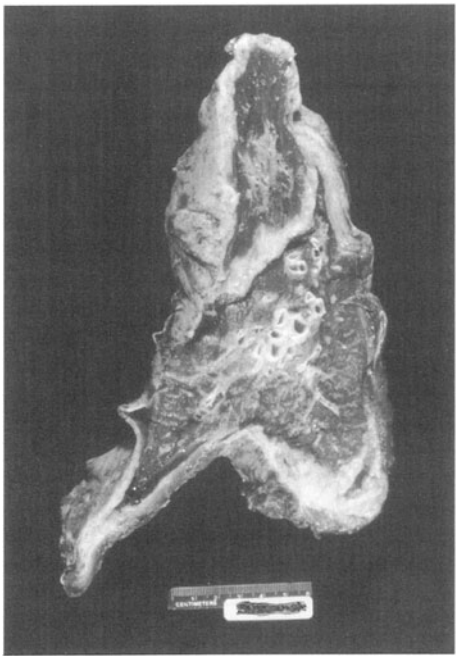

B

FIGURE 56.10. Coronal MRI image (**A**) demonstrates typical appearance of a mesothelioma. Note the thick rind lining the right hemithorax and invaginating between the lobes of the lung. Photograph (**B**) is a section through an extrapleural pneumonectomy specimen of a resected mesothelioma showing the same pathology as seen on the scan.

toms. The cancer tends to line the chest cavity as a thick, plaque-like mass, fusing the two pleural layers and invaginating between the lobes of the lung (Fig. 56.10). It progresses inexorably in a locoregional manner, invading lung, diaphragm, pericardium, and chest wall.[159,160] Contrary to popular belief, the disease also has the capacity to metastasize.[84]

The tumor is almost always unilateral and is diagnosed either by cytology or pleural biopsy. From the time of diagnosis, the median survival is 4 to 12 months. The incidence of the disease has increased during the past decade, likely because legislation to curb asbestos exposure has only recently been widely adopted.[159–161]

Another epidemiological factor of great concern is the recent link between the simian vacuolating virus 40 (SV40) and mesothelioma. The virus has been demonstrated in human mesotheliomas and is capable of inducing mesothelioma, by itself, in animal models. It has been identified as a contaminant in millions of vaccines administered in the United States and is under investigation as a predisposing factor to mesothelioma formation in humans.[162–165]

Currently, mesothelioma continues to defy any single treatment modality including surgery, chemotherapy, and radiation therapy. There are three cell type classifications: epithelial, sarcomatous, and mixed (demonstrating features of both sarcomatous and epithelial). Patients with epithelial tumors without chest wall, pericardial, or diaphragmatic transgression and with negative lymph nodes have the best prognosis. Utilizing a trimodality approach of surgery, chemotherapy, and radiation therapy, survivals up to 39% at 5 years have been reported.[160] The surgery employed for this protocol is an extrapleural pneumonectomy that entails en bloc resection of the parietal pleura, lung, pericardium, and diaphragm, with subsequent Gore-Tex patch reconstruction of the diaphragm and pericardium. Other treatment modalities, including new chemotherapies, immunotherapy, photodynamic therapy, and gene therapy, are being explored.[159,166,167]

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