IX  DISORDERS OF THE PLEURA, HILA, AND MEDIASTINUM

Gerald W. Staton, Jr., m.d.
Roland H. Ingram, Jr., m.d.

Pleurisy

Pleurisy (also known as pleuritis) is characterized by chest pain that results from inflammation of the pleural surfaces from any cause. The pain originates from the parietal pleura, which derives most of its innervation from the intercostal nerves. The central portion of the diaphragmatic parietal pleura receives phrenic innervation, so that inflammation of the diaphragmatic surfaces causes referred pain to the ipsilateral shoulder. Inspiratory chest pain, however, is not uniquely pleural and may occur with pericarditis or chest wall disease.

Pleuritic chest pain may result from primary involvement of the pleura by neoplasia, infection, trauma, or inflammation or from secondary spread of one of these processes from subjacent lung tissue. Thus, a common cause of pleuritic chest pain is pneumococcal pneumonia, which typically begins at the lung periphery and spreads to the adjacent pleural surfaces. Many middle-aged and elderly persons who report having experienced pleurisy in the past probably suffered from pneumonia.

DIAGNOSIS

Pleuritic chest pain is typified by intensification on deep inspiration. It is usually sharp in quality, may be present continuously, and is characteristically made worse by movements of the thorax, as well as by coughing, sneezing, or other sudden respiratory movements. If the pain is severe, inability to take a deep breath without aggravating the pain may lead to the sensation of shortness of breath. Often, pleuritic chest pain must be differentiated from chest wall pain of musculoskeletal origin (e.g., localized muscle strain, costochondritis, or rib fracture) and from the pain associated with pericarditis. Superficial tenderness of the chest wall on light palpation favors chest wall pain, but tenderness on deep palpation does not reliably exclude pleuritis. A pleural friction rub heard on auscultation of the chest establishes the presence of a pleural disorder.

A chest radiograph can be useful in suggesting the underlying cause of pleuritic pain. If the chest radiograph shows the presence of effusions, the causes of pleuritic pain are limited to the processes that produce pleural effusion [see Pleural Effusion, below]. If the chest radiograph is normal, pleuritic chest pain has a relatively limited differential diagnosis. Major etiologic possibilities include pulmonary embolism, viral pleurisy, and serositis in association with collagen vascular disease, especially systemic lupus erythematosus (SLE). Less common causes of pleuritic chest pain include uremia, sickle cell crisis, and pleurepericarditis that occurs after myocardial infarction or pericardiectomy (Dressler syndrome). Some patients present with an acute illness characterized by low-grade fever, headache, and myalgia; in many such episodes, the cause cannot be determined but is presumed to be viral. These acute illnesses are usually self-limited, resolving within a few days to 1 to 2 weeks. Coxsackievirus B and other enteroviruses cause an epidemic form of viral pleuritis called epidemic pleureodynia, or Bornholm disease, which often affects multiple family members. Relapse may occur after the patient is asymptomatic for several days.

TREATMENT

Idiopathic or viral pleuritis can be treated effectively with nonsteroidal anti-inflammatory drugs and, if necessary, narcotic analgesics. However, the diagnosis is one of exclusion, and pulmonary embolism, a potentially lethal condition, is the most important cause to exclude.

Plural Effusion

Pleural effusion, the abnormal accumulation of liquid in the pleural space, may affect as many as 800,000 persons in the United States each year. The most common causes are congestive heart failure, malignancy, pneumonia, and pulmonary emboli.

PATHOPHYSIOLOGY

A number of factors favor pleural effusion, including (1) altered permeability of the pleural membranes; (2) decreased intravascular oncotic pressure and, once a pleural effusion has formed, increased pleural liquid oncotic pressure; (3) increased hydrostatic pressure in the pleural capillaries as a result of heart failure; (4) greater negativity of pressure in the pleural space (e.g., if the lung is unable to expand normally); (5) lymphatic obstruction; (6) migration of ascitic liquid across the diaphragm; and (7) migration of pulmonary edema liquid across the visceral pleura. Pleural effusion produces a restrictive defect that is correlated with the size of the effusion. Because both the air spaces and the pulmonary circulation are compressed and because of pulmonary hypoxic vasoconstriction, there is little shunting and only mild hypoxemia. Removal of a large effusion can result in modest improvement in lung function, but often, the underlying cause of the effusion (e.g., heart failure or lymphangitic carcinoma) causes persistent functional abnormalities. Various mediators are involved in the production of altered permeability and the evolution of pleural effusions.

CLASSIFICATION AND ETIOLOGY

Various types of liquid may accumulate in the pleural space. Accumulation of serous liquid is referred to as a hydrothorax. If blood accumulates, the condition is referred to as a hemothorax. An effusion composed of lymph is known as a chylothorax. Accumulation of pus is known as a pyothorax, or empyema. Although imaging studies can be helpful, the actual condition can be distinguished only by analysis of the liquid itself.

Hydrothoraces fall into two major categories on the basis of mechanisms of pleural liquid accumulation: transudation and exudation. Transudation of liquid into the pleural space occurs when there is an imbalance between the hydrostatic and the oncotic pressures governing the normal rates of pleural liquid formation and resorption. The most common cause of a transudative pleural effusion is congestive heart failure. Other causes are constrictive pericarditis, superior vena cava obstruction, and the hypoalbuminemic states associated with cirrhosis and the nephrotic syndrome [see Table 1]. Pulmonary arterial hypertension and right heart failure usually do not by themselves cause pleural effusions.

RESPIRATORY MEDICINE:IX  Disorders of the Pleura, Hila, and Mediastinum–1

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Exudation of liquid into the pleural space results from any process that disrupts the integrity of the endothelial membrane that lines the pleural capillaries and venules. Obstruction of lymphatic drainage from the pleural space is another mechanism that can cause a protein-rich effusion. Exudative effusions are associated with a broad range of disorders, including a variety of infectious, neoplastic, inflammatory, embolic, and vasculitic diseases. In addition, exudative effusions may be caused by the effects of certain drugs and physical agents [see Table 1].

**Table 1 Causes of Hydrothorax**

<table>
<thead>
<tr>
<th>Type</th>
<th>Causes</th>
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<tbody>
<tr>
<td>Transudative</td>
<td>Congestive heart failure</td>
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<tr>
<td></td>
<td>Constrictive pericardial disease</td>
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<td>Cirrhosis</td>
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<td>Nephrotic syndrome</td>
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<td>Superior vena cava obstruction</td>
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<td></td>
<td>Ascites (transudative)</td>
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<td>Peritoneal dialysis</td>
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<tr>
<td>Exudative or Transudative</td>
<td>Hypothyroidism</td>
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<td></td>
<td>Pulmonary embolism</td>
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<td></td>
<td>Trapped lung</td>
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<tr>
<td>Exudative</td>
<td>Infections (i.e., parapneumonic effusion, tuberculosis)</td>
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<td></td>
<td>Malignant disorders</td>
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<td>Primary lung cancer</td>
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<td>Cancer metastases to the lungs or pleura</td>
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<td>Lymphoma</td>
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<td>Mesothelioma</td>
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<td>Collagen vascular diseases and vasculitides</td>
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<td>Gastrointestinal diseases</td>
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<td>Pancreatitis and pancreatic pseudocyst</td>
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<td>Esophageal rupture</td>
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<td>Abdominal or retroperitoneal abscess</td>
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<td></td>
<td>Postabdominal surgery</td>
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<td>Postendoscopic variceal sclerotherapy</td>
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</table>

**Miscellaneous**

- Benign asbestos effusion
- Meigs syndrome
- Dressler syndrome (after myocardial infarction or pericardiectomy)
- Post-coronary artery bypass
- Uremia
- Sarcoidosis and necrotizing sarcoid granulomatosis
- Radiation therapy
- Drugs (e.g., nitrofurantoin, dantrolene, methysergide, all-trans-retinoic acid)
- Yellow nail syndrome

**Radiography**

When the patient is in the upright position, liquid collects first in the posterior sulcus, the most inferiorly located recess of the pleural space. Blunting of the normally sharp posterior costophrenic angle on a lateral chest radiograph indicates the presence of at least 25 to 50 ml of pleural liquid. As additional liquid accumulates (approximately 150 ml total), the lateral costophrenic angle on a posteroanterior radiograph becomes obliterated. Greater amounts of pleural liquid displace the lung centrally and produce a characteristic homogeneous opacity that forms a concave meniscus with the chest wall [see Figure 1].

A massive pleural effusion may opacify an entire hemithorax and displace mediastinal structures to the opposite side of the chest [see Figure 2]. Large effusions may reduce venous return and thus cardiac output, creating hemodynamic compromise. The displacement force that is exerted is proportional to the height of the effusion. A contralateral shift of the mediastinum in a patient with massive pleural effusion may go undetected if there is ipsilateral atelectasis of the lung or if the mediastinum is fixed by an invasive tumor or fibrosis. A mediastinal shift toward the side of the effusion indicates almost complete atelectasis of the underlying lung, most often resulting from an obstructing tumor of the mainstem bronchus.

When intense pleural inflammation leads to the formation of adhesions between the visceral and parietal surfaces, localized effusions may collect in the resultant pockets. These loculated effusions may form along any part of the pleural surface and at times may be mistaken for infiltrates or masses within the lung parenchyma [see Figure 3]. A radiographic sign that favors the diagnosis of pleural loculation is the oblique angle formed by the chest wall and the margin of the pleural density. A subpleural lung nodule, in contrast, usually forms an acute angle with the chest wall.

An atypical presentation of pleural effusion is the subpulmonary collection of liquid [see Figure 3]. For unknown reasons, sizable amounts of pleural liquid sometimes collect between the diaphragm and the base of the lung without significantly distorting the contour of the inferior lung margin. In a patient with a...
subpulmonary effusion, it is possible to mistake the superior border of the effusion for the diaphragmatic silhouette, prompting a needless search for causes of an elevated hemidiaphragm. Several radiographic findings suggest the correct diagnosis. First, the contour of the base of the lung is slightly altered by a subpulmonary effusion; the normal domelike curve formed by the diaphragm is replaced by a hockey stick–like shape, with lateralization of the apex of the dome. Second, on the left side, the distance between the base of the lung and the gastric gas bubble is increased. The diagnosis of a subpulmonary effusion is confirmed by a lateral decubitus chest radiograph, which will show layering of the effusion along the lateral chest wall.

In patients with congestive heart failure, pleural liquid may collect between the two visceral pleural surfaces that line the interlobar fissures. Interlobar effusions, which may be mistaken for tumors of the lung parenchyma, disappear with effective treatment of the heart failure and thus have been called vanishing tumors, or pseudotumors. Interlobar effusions have a characteristic lenticular shape, with the tapered ends oriented in the plane of the fissure.

In some cases of pleural effusion, the only radiograph available for interpretation is an anteroposterior chest radiograph obtained with the patient in the supine position. In this position, a free-flowing pleural effusion spreads along the posterior costal surfaces. The radiograph shows a uniform increase in the opacity of the involved hemithorax, but normal lung markings are visible through the opacity.

On lateral decubitus radiographs, small amounts of pleural liquid can be identified if the patient is positioned carefully. Free-flowing effusions can be distinguished from loculated effusions or thickened pleural tissue by comparing the pleural density with its appearance on a radiograph taken with the patient in the upright position.

**Ultrasonography**  
Ultrasonography is also a very sensitive test for detecting pleural effusions. It is particularly effective in cases of loculated pleural effusions because it can identify the precise site on the chest wall where a needle can be introduced to aspirate a sample.

**Computed tomography**  
CT scanning is helpful in distinguishing a pleural mass from a loculated effusion and distinguishing a hydrothorax from a lung abscess. CT scanning performed with contrast usually shows parietal pleural thickening in patients with exudates and enhancement of the parietal pleura in patients with empyema.

**Laboratory Studies**

Examination of pleural liquid is useful for diagnosis. Thoracentesis should be performed in virtually all patients with pleural effusions of a significant size and of uncertain etiology. Pneumothorax is relatively common but rarely serious, so routine chest radiography is not necessary after uncomplicated thoracentesis. Occasionally, pulmonary edema develops acutely in the reexpanded lung after rapid removal of large pleural effusions, especially if they have been present for a long time.

![Figure 2](image1.jpg)  
*Figure 2 (a) A massive hydrothorax resulting from a subpleural adenocarcinoma of the lung with a malignant pleural effusion is present in this patient. The heart and mediastinum are deviated to the right. Compression of the heart and increased intrathoracic pressure cause a reduction in venous return and resulting tachycardia (heart rate, 120 beats/min). (b) The heart and mediastinum return to the midline after evacuation of liquid; heart rate falls to 80 beats/min.*

![Figure 3](image2.jpg)  
*Figure 3 This chest radiograph demonstrates two patterns of atypical pleural liquid accumulation. In the left pleural space, a loculated effusion has formed along the lateral chest wall; it is presumably trapped in this position by fibrous adhesions between adjacent areas of visceral and parietal pleurae, preventing free flow of the liquid to the most dependent portions of the pleural space. In the right pleural space, liquid has accumulated in a subpulmonic position, between the base of the lung and the superior surface of the diaphragm. The gas-liquid interface has a shape slightly different from the normal contour of the diaphragmatic silhouette: it is more flattened and curves inferiorly at a point more laterally displaced. A small meniscus sign at the lateral chest wall hints at the presence of this subpulmonic effusion.*
moving a limited amount of liquid (1,000 to 1,500 ml) during each drainage procedure or by terminating the procedure if highly negative pressures are required to remove additional liquid.24 The gross appearance of pleural liquid may occasionally provide useful diagnostic information. Gross pus or putrid-smelling liquid is diagnostic of infection. A highly viscous clear liquid reflects the presence of hyaluronic acid elaborated by a mesothelioma, whereas a chocolate-sauce or anchovy-paste appearance suggests a hepatopleural fistula caused by amebiasis.

Three general categories of laboratory tests have been distinguished: (1) those that provide specific information, such as cytoplogic studies and microbiologic cultures and stains; (2) certain tests that, if the results are abnormal, indicate a limited number of diagnostic possibilities, such as measurements of amylase, glucose, pH (measured by a pH meter, not by dipstick), triglycerides, and antinuclear antibody (ANA) titers and differential cell counts; and (3) those that are useful in distinguishing between transudates and exudates, such as measurements of lactate dehydrogenase (LDH), protein, and cholesterol. Routine laboratory studies pertinent to most cases include total and differential white cell counts, microbiologic stains and cultures, cytologic analysis, pH measurement, and determinations of protein, LDH, amylase, and glucose levels. Measurement of pleural liquid triglycerides or ANA titers may be appropriate in certain patients with pleural effusions. When pleural fluid appears sanguineous, red cell counts may be useful.

Clinical and radiographic findings may indicate whether a pleural effusion is transudative or exudative. Patients who have painful effusions, pleural rubs, loculation of effusion on chest radiograph, or conditions known to produce pleural inflammation (e.g., pneumonia or active lupus) are more likely to have pleural exudates. Patients with cirrhosis and ascites, heart failure, or hypoproteinemia with bilateral free effusions are likely to have transudates. Clinical information may be helpful in designing strategies for pleural liquid analysis [see Figure 6].

If a pleural effusion is not pus, chyle, or blood, it is the clinical context that allows categorization as an exudate or transudate. In fact, the gold standards that are used to assess the sensitivities and specificities of the various pleural liquid measurements for differentiating exudates from transudates are based solely on clinical data. Pleural effusions resulting from exudation or obstruction of lymphatic drainage typically have a high protein concentration, usually 3 g/dl or greater. However, four criteria differentiate exudative from transudative pleural effusions more effectively than the absolute protein concentration: (1) a ratio of pleural protein to serum protein greater than 0.5, (2) a ratio of pleural LDH to serum LDH greater than 0.6, (3) a pleural LDH concentration greater than two thirds the upper limit of normal for serum LDH, or (4) a pleural cholesterol level of 60 mg/dl or higher.25 If one or more of these criteria are met, the effusion is usually exudative or caused by lymphatic obstruction. If none of these characteristics are present, a transudative mechanism would be expected. Although these criteria are extremely useful, they are not absolute, and the results must be considered in the clinical context.

No additional information about the etiology of a transudative pleural effusion can be obtained by further testing of the pleural liquid. However, results of certain laboratory studies can be used to narrow the differential diagnosis of exudative pleural effusions.

**Amylase level** Determination of the pleural liquid amylase level is warranted in patients with unexplained left-sided pleural effusions, particularly in the presence of coexistent abdominal disease. In patients who have pleural effusions associated with acute pancreatitis or pancreatic pseudocysts, the pleural liquid amylase level typically exceeds serum levels and remains elevated long after the concentration of amylase in the serum has returned to normal. Elevated amylase levels are also commonly seen in patients with malignancy.26

**Red cell count** Most bloody pleural effusions in which the red cell count is greater than 100,000/mm³ are caused by malign-

![Figure 4](image-url)

This anteroposterior radiograph was made in a patient with congestive heart failure. The ovoid or lenticular opacity in the right upper lung zone is an interlobar effusion collected in the minor fissure; such effusions are sometimes mistaken for tumors of the lung parenchyma. Interlobar effusions resolve with treatment of the heart failure; hence, they are sometimes called vanishing tumors, or pseudotumors. The radiograph also demonstrates the presence of osteopenia and scoliosis in this patient.

![Figure 5](image-url)

In a chest radiograph obtained with the patient in the supine position, a pleural effusion may be apparent as only a diffusely increased opacity or haze over the affected hemithorax, as seen in the left pleural space of this patient. In this position, the effusion uniformly layers along the posterior chest wall; the x-ray beam penetrates perpendicular to the thin pleural liquid layer, producing a diffuse haze without a discrete meniscus or gas-liquid interface.
nant disorders, injuries to the chest, or pulmonary embolism. Other possible causes include tuberculous pleurisy, esophageal rupture, pancreatitis, and benign asbestos effusions. A pleural liquid hematocrit that exceeds half the simultaneous peripheral blood hematocrit can be used to distinguish between transudates and exudates. If there is a clinical suspicion of a specific diagnosis in a patient with an exudative pleural effusion, certain other tests can be performed to help confirm the diagnosis. Examples include amylase determination in patients with suspected pancreatitis and triglyceride measurement in patients with suspected lymphoma or thoracic duct injury. Repetition of thoracentesis and performance of a pleural biopsy increase the probability of achieving a specific diagnosis in patients with tuberculosis and pleural malignant disorders.

White cell count Total and differential white cell counts may further narrow the differential diagnosis. Pleural liquid white cell counts exceeding 50,000 to 100,000/mm³ are usually associated with grossly visible pus; such effusions are by definition pyothoraces or empyemas. Absolute white cell counts below this range cannot be used to differentiate infected pleural effusions from other inflammatory processes. Likewise, a predominance of polymorphonuclear leukocytes in the differential white cell count simply indicates an acute inflammatory process; the etiology may be empyema, parapneumonic effusion, pulmonary embolism, pancreatitis, viral pleuritis, benign asbestos effusion, malignant disease, early tuberculous effusion, or other, less common disorders.

More than 90% of patients with exudates containing a predominance of small lymphocytes have a malignant or tuberculous effusion. Pleural liquid eosinophilia is rarely the result of a fungal or parasitic infection. Much more commonly, the eosinophilia is a nonspecific finding; in some cases, it is thought to result from prior introduction of air or blood into the pleural space. The finding of more than 10% eosinophils in the pleural liquid is relatively uncommon in effusions associated with tuberculosis or malignant disease but does not exclude these diagnoses. Finally, the presence of mesothelial cells in an exudative pleural effusion may be of diagnostic utility because tuberculous pleural effusions, except perhaps at their very onset, almost never contain more than 5% mesothelial cells.
**pH level** In congestive heart failure, the pH of the pleural liquid is very close to that of the serum (7.35 to 7.45), and in patients who also have acidemia, the pleural liquid pH falls below 7.35 as the serum pH falls. Certain exudative pleural effusions are acidic (pH < 7.3), presumably because of metabolism of glucose to carbon dioxide and fixed acids (e.g., lactic acid). A pleural liquid pH of less than 7.3 in the absence of systemic acidosis suggests one of the following diagnoses: empyema, malignant disease (usually associated with a pleural effusion of several months’ duration), collagen vascular disease, tuberculosis, esophageal rupture, or hemothorax. In patients who have a pleural effusion associated with bacterial pneumonia (parapneumonic effusion), a pleural liquid pH of less than 7.0 is suggestive of an infected pleural space (empyema). A pH of 6.0 or less suggests esophageal rupture.

**Glucose level** Low pleural liquid glucose values (60 mg/dl) are found in tuberculous effusions, parapneumonic effusions and empyemas, and large or highly cellular effusions associated with malignant disorders. In these conditions, consumption of glucose by microorganisms or by inflammatory or malignant cells is thought to be the cause of the low glucose concentrations. Glucose values are extremely low in effusions associated with rheumatoid arthritis caused by impaired transport of glucose into the pleural space.

**ANA and rheumatoid factor titer** Identification of lupus erythematosus cells or an ANA titer equal to or greater than that found in the serum is diagnostic of SLE as the cause of the pleural effusion. In contrast, latex fixation titers of rheumatoid factor as high as 1:160 may be found in the pleural liquid of patients who have a pleural effusion related to a variety of conditions other than rheumatoid arthritis.14

Repetition of pleural liquid analysis and pleural biopsies increases the probability of achieving a diagnosis in patients with tuberculosis or pleural malignant disorders. When tuberculosis or malignancy is still suspected, thoracocopy can be used to visualize the pleura and to obtain biopsies of visible lesions.22 Follow-up in the clinic is indicated in the minority of patients in whom exhaustive evaluation has failed to yield a specific diagnosis. In most of these patients, the disease will have a benign course, with resolution of the effusion occurring over several months.16

**HYDROTHERAX**

**Hydrothorax Caused by Congestive Heart Failure**

Pleural liquid accumulation may be a relatively early sign of congestive heart failure. A portion of the liquid comes directly from the lung into the pleural space.1 Radiographic evidence of pleural effusion (i.e., blunting of the costophrenic angles) will appear during the stage of interstitial pulmonary edema formation. Pulmonary venous hypertension, especially in combination with elevated systemic venous pressures, favors the development of transudative pleural effusions. However, at any given level of venous pressure elevation, the likelihood of pleural liquid formation varies widely among individuals; the reason for this variability remains unexplained.

Most often, pleural effusions caused by congestive heart failure form either bilaterally or on the right side only. Successful treatment of congestive heart failure usually leads to clearing of the associated effusions within hours to a few days. The protein concentration of these effusions increases slightly after diuresis, and the resultant protein concentration is occasionally in a range that would be confused with a pleural exudate.23 In most patients with heart failure, frankly exudative effusions are caused by a process other than congestive heart failure.10

**Ascites**

Liquid that collects in the abdomen from cirrhosis,19 ovarian tumors, or peritoneal dialysis may migrate into the pleural space. In all these conditions, ascitic liquid is usually evident clinically, and there is a preponderance (60% to 70%) of right-sided effusions. The pressure gradient between the peritoneal cavity (supra-atmospheric pressure) and the pleural cavity (sub-atmospheric pressure) favors this direction of flow. The transdiaphragmatic migration of liquid appears to occur via lymphatic vessels or physical openings in the diaphragm. Thoracocentesis is recommended to establish the diagnosis of hepatic hydrothorax, because a significant proportion of the patients with pleural effusion will have alternative diagnoses (e.g., infection, malignancy).20 Symptomatic liquid collection may be controlled by diuresis in cirrhosis and by the resection of benign ovarian tumors when these are associated with accumulations in the chest. Repetition of therapeutic thoracocentesis is discouraged because this procedure results in protein and volume depletion. A preferable approach to the management of hepatic hydrothorax is to use video-assisted thoracoscopy to close the defects in the diaphragm, which may result in the resolution of the effusions.21

**Hydrothorax Caused by Malignant Disease**

Neoplastic invasion of the pleura, usually involving both the visceral and the parietal surfaces, can cause a pleural effusion.21 The effusion most often has the characteristics of an exudate. Mediastinal obstruction of lymphatic channels by a tumor frequently contributes to the pathogenesis of pleural liquid formation.

The lung and breast are the most common primary sites from which pleural metastases arise; stomach and ovarian carcinomas are next in frequency. Breast, stomach, and ovarian cancers usually spread to the pleura indirectly from hepatic metastases, although contiguous spread through the chest wall occasionally occurs with breast cancer and spread across the diaphragm occasionally occurs with ovarian or stomach cancer. Virtually any carcinoma can metastasize to the pleura, and in some cases, pleural carcinomatosis is found with no identifiable primary site.23 Lymphomas can also cause pleural effusions; the mechanism usually involves infiltration of mediastinal lymph nodes and consequent obstruction of lymphatic drainage from the pleural cavity.

Pleural effusions are a common manifestation of primary pleural neoplasms, such as mesothelioma,24 a rare neoplasm that can be either localized and benign or diffuse and malignant. Risk factors for the malignant form include exposure to asbestos, zeolite (erionite), and therapeutic radiation. Survival of patients with malignant mesothelioma is poor with all forms of therapy.

**Diagnosis** Pleural effusions associated with malignant disease typically produce the following pleural liquid findings: (1) the pleural liquid is serosanguineous; (2) protein and LDH concentrations are elevated, characteristic of an exudative effusion; (3) the differential white cell count reveals more than 50% lymphocytes; (4) the pleural liquid glucose level is normal (> 60 mg/dl); and (5) the pleural liquid pH is greater than 7.3. However, none of these findings is consistently present.
Two clinical circumstances in which malignant disease is the likely cause of pleural effusion are (1) massive pleural effusions, in which the pleural liquid opacifies an entire hemithorax, and (2) effusions in which the etiology eludes thoracentesis and closed pleural biopsy.

In a majority of cases of malignant pleural effusion, the diagnosis can be made by cytologic examination. Routine studies include Papanicolaou stain of the centrifuged material and hematoxylin-eosin stain of the paraffin-embedded cell pellet (so-called cell block). When a lymphoma is suspected as the cause of a lymphocytic pleural effusion, special studies of cell surface markers can be of use in differentiating a monoclonal lymphocytic process from a polyclonal inflammatory reaction. Other immuno-histochemical studies can assist in the diagnosis of carcinoma or mesothelioma. The greater the amount of material provided for analysis, the higher the diagnostic yield of malignant cells; thus, the number of positive diagnoses increases with the second and third diagnostic thoracenteses. Closed pleural biopsy, which provides samples of parietal pleura 1 to 2 mm in diameter, will identify only an additional 7% of cases of pleural malignancy when repeated thoracenteses have been negative. Image-guided percutaneous biopsy may provide a better yield than traditional closed pleural biopsy. Fiberoptic bronchoscopy is useful in cases that present with clinical features suggestive of bronchogenic carcinoma, such as hemoptysis, a mass, an infiltrate, or atelectasis seen on radiographs. Thoracoscopy is needed for diagnosis in a minority of cases.

**Treatment**

Management of symptomatic pleural effusions should be directed at draining the pleural liquid and, when necessary, obliterating the pleural space. In terminally ill patients with slowly reaccumulating pleural effusions, repetitive thoracenteses may be sufficient to control dyspnea for a few weeks to months. Often, however, a longer-term solution to this problem is needed, in which case chemical pleurodesis may be indicated. This technique requires that the pleural space be drained by a chest tube until a minimal amount of liquid remains, allowing apposition of the visceral and parietal surfaces. Small (14 French) tubes can be used to drain the pleural space, and the procedure can be performed on selected ambulatory patients. In patients with multiloculated malignant effusions, use of an intrapleural fibrinolytic agent may help achieve adequate drainage. Once sufficient liquid is removed, a sclerosing agent (e.g., doxycycline, talc slurry, bleomycin, or iodopovidone) is introduced into the pleural space through the chest tube; during healing of the resultant inflammatory process, a fibrous bond forms between the two pleural surfaces.

Talc is the least costly sclerosing agent available for pleurodesis, and the results with talc are no different from those with doxycycline and bleomycin. When pleurodesis is successful, pleural sclerosis prevents further accumulation of pleural liquid or limits accumulation of liquid to small pockets between pleural adhesions, and the patient experiences remarkably little compromise of ventilatory function. However, pleurodesis will be ineffective if the pleural liquid pH is less than 7.3 or if the lung does not expand to fill the space when pleural liquid is removed. Talc poudrage performed during thoracoscopy is an alternative and possibly more effective technique than pleurodesis. In patients who do not respond to pleurodesis or talc poudrage, implantable catheters or pleuropertitoneal shunts may be useful in controlling pleural effusions.

**Hydrothorax Caused by Tuberculosis**

Pleural effusion is more often a manifestation of primary tuberculosis than of reactivation tuberculosis. Tuberculous effusions occur more commonly in young adults than in children. Typically, the effusion develops 3 to 6 months after initial exposure to *Mycobacterium tuberculosis*. A tuberculin skin test is positive at the time of clinical presentation in 70% of patients; in the remaining 30% of patients, the skin test becomes positive within 6 weeks after an initial negative result. In many cases, pleural effusion is the only abnormality detected on chest radiograph. Tuberculous pleural effusions are thought to be caused by the rupture of a small subpleural focus of infection into the pleural space, with the discharge of tuberculin protein and viable tubercle bacilli. Widespread granulomatous infection of the parietal and visceral pleurae ensues, as indicated by the high yield of closed pleural biopsy in this setting. In patients with primary tuberculosis, untreated pleural effusions resolve spontaneously in approximately 2 to 4 months. However, active tuberculosis develops in two thirds of such patients during the ensuing 5 years.

**Diagnosis**

Tuberculous pleuritis in patients with primary tuberculosis may present acutely as a febrile illness accompanied by pleuritic chest pain or subacutely as anorexia, weight loss, and dyspnea on exertion. The pleural liquid is usually serous or xerosanguineous. In most cases, the differential white cell count reveals a lymphocytosis. A finding of more than 10% eosinophils or more than 5% mesothelial cells suggests a diagnosis other than pleural tuberculosis. In approximately 20% of cases, the pleural liquid glucose level drops below 60 mg/dl and the pleural liquid pH below 7.3. Increased levels of adenosine deaminase and interferon gamma distinguish tuberculous effusions from those of other causes. Use of polymerase chain reaction techniques to analyze pleural liquid for detection of mycobacterial DNA may become the method of choice for identifying tuberculous effusions.

**Hydrothorax Caused by Pulmonary Embolism**

Pleural effusion may develop in patients with pulmonary embolism, even though pulmonary infarction (as manifested by a parenchymal infiltrate on chest radiograph) may not be present. In a large series of patients with emboli documented by angiography, 28% of the patients had radiographic evidence of pleural effusion at presentation. Spiral CT scans used for the diagnosis of pulmonary embolism detect pleural effusions in 57% of cas-
es. The precise pathogenetic mechanism for pleural liquid formation in the absence of lung infarction is not known, although increased capillary permeability in the lung and visceral pleura and systemic venous hypertension have been suggested as contributing factors.

**Diagnosis** In many cases of pleural effusion caused by pulmonary embolism, pleural liquid analysis reveals an exudative effusion that is serosanguineous in appearance (> 10,000 red cells/mm³). A differential white cell count typically reveals a predominance of polymorphonuclear leukocytes. However, the characteristics of such an effusion are highly variable. The pleural liquid may be serous, may have a low protein concentration and meet the diagnostic criteria for a transudate, and may contain more than 50% lymphocytes. In addition, the total white cell count may vary from less than 100/mm³ to more than 50,000/mm³. Thus, none of the findings on routine pleural liquid analysis can be used to exclude a diagnosis of pulmonary embolism.

**Treatment** Management of pulmonary embolism need not be modified because of the presence of a pleural effusion, even if the effusion is bloody. In this setting, pleural effusions are maximal at their onset and gradually resorb with time, although resolution often requires more than 7 days if the effusion is large and associated with pulmonary consolidation. An enlarging effusion or the subsequent development of a contralateral effusion should raise suspicion of recurrent embolization or another complication, such as empyema.

**HEMOTHORAX**

Direct hemorrhage into the pleural space most commonly results from trauma to the thorax. The trauma may be either blunt (e.g., sustained in a motor vehicle accident), in which case rib fractures are usually present, or penetrating (e.g., a knife or bullet wound). In a majority of cases, air or alveolar gas enters the pleural space along with blood, causing a hemopneumothorax. Hemothorax may also complicate invasive diagnostic or therapeutic procedures that lacerate pleural or mediastinal blood vessels; such procedures include thoracentesis, pleural biopsies, and cannulation of the subclavian or internal jugular veins. In rare instances, abnormal vascular structures in the mediastinum or lung periphery rupture into the pleural space; examples include hemothorax associated with arteriovenous malformation, pleural endometriosis, and thoracic aortic aneurysm. Rare causes of nontraumatic hemothorax include pleural metastasis and iatrogenic or disease-related coagulopathy.

**Diagnosis**

When hemothorax is suspected, the hematocrit of the pleural liquid should be measured. It is important to remember that the pleural liquid may appear bloody even when its hematocrit is less than 1%. However, in true hemothorax, the pleural liquid hematocrit exceeds 50% of the peripheral blood hematocrit. Hemothorax, even if it is sterile, may be a cause of transient fever.

**Treatment**

In a large or rapidly accumulating hemothorax, blood should be promptly drained from the pleural space with a wide-bore chest tube. If rapid bleeding (100 to 200 ml/hr) continues, a thoracoscopy or thoracotomy will be necessary. After bleeding has stopped, intrapleural fibrinolytic therapy to lyse clots not removed by the chest tube may obviate thoracotomy. Potential adverse consequences of undrained pleural blood include empyema and fibrothorax. Empyema may develop because blood provides a rich culture medium for growth of bacteria. Fibrothorax is a late sequela of moderate or large hemothoraces and results from organization of clotted blood into a dense fibrous peel surrounding the lung. A small, self-limited hemothorax associated with minor trauma such as a rib fracture will resolve without drainage or surgery.

**CHYLOTHORAX AND PSEUДOCHYLOTHORAX**

Chyle is the lipid-rich liquid transported from small intestinal villi—the so-called lacteals—to systemic veins in the thorax via the thoracic duct. Disruption or compression of the thoracic duct may lead to leakage of chyle first into the posterior mediastinum and then into the pleural space. Alternatively, an atretic or obstructed thoracic duct may cause reversal of lymph flow through dilated collateral channels. Rupture of these lymphatic channels may also produce chylothorax.

The thoracic duct follows a variable course through the mediastinum. Commonly, it crosses the diaphragm to the right of the vertebral column, entering the chest cavity through the aortic hiatus. It then crosses to the left of the vertebral column between the seventh and fifth thoracic vertebrae, arches above the level of the clavicle, and enters the systemic venous circulation in the region of the left jugular and subclavian veins. Depending on the particular anatomy of a given patient and the level at which the thoracic duct is disrupted, chylous effusions may be left sided, right sided, or, occasionally, bilateral.

**Chylothorax**

**Etiology** Various conditions can cause chylothorax. Mediastinal tumors are the most common cause, with lymphomas exceeding metastatic carcinomas in frequency. Trauma is the other major cause of chylothorax in adults. In some cases, major chest trauma has been sustained. In other cases, seemingly minor actions, such as hyperextension of the back, are the only identifiable antecedent events. Thoracic and cardiovascular surgery occasionally results in transection of the thoracic duct and the subsequent development of chylothorax. In addition, chylothorax frequently occurs as a complication of the rare disease lymphangiomyomatosis. Other conditions producing mediastinal lymphatic disruption or obstruction may cause chylothorax. Such conditions include congenital lymphangectasis, mediastinal irradiation, fibrosing mediastinitis, granulomatous mediastinitis, left subclavian vein thrombosis, and esophageal sclerotherapy.

**Diagnosis** Chylothorax is usually not suspected until thoracentesis reveals a milky-white pleural liquid. Identification of chylomicrons by lipoprotein analysis establishes the diagnosis of chylothorax and distinguishes it from other causes of an opalescent pleural liquid. However, several less expensive screening tests also may be useful. For example, a chylous effusion remains opaque after centrifugation, whereas the supernatant in empyema is clear. Furthermore, if a chylous effusion sample is allowed to remain undisturbed for 12 to 24 hours, a creamy layer of chylomicrons floats to the top, and the addition of a few drops of ethyl ether rapidly causes the liquid to clear. In most cases of chylothorax, the triglyceride concentration exceeds 110 mg/dl; exceptions usually are limited to patients in whom feedings have been withheld, such as postoperative patients. A CT scan of the chest is indicated in most patients with chylothorax to de-
Chylous effusions elicit little pleural inflammation and are only very rarely complicated by empyema because of the bacteriostatic properties of chyle. The major consequence of chylous effusions is the rapid and recurrent accumulation of liquid in the pleural space. Normally, the thoracic duct transports chyle at a rate of 1.5 to 2.5 L/day. In patients with chylothorax, much or all of this liquid may enter the pleural space.

**Treatment** Repeated thoracenteses or chest tube drainage can avert lung compression caused by pleural liquid buildup. However, these procedures may result in large losses of protein, fat, and circulating lymphocytes, rapidly leading to malnutrition and possible immunosuppression.

Definitive treatment of chylothorax varies with the specific etiology. Radiation therapy, with or without chemotherapy, is frequently effective for patients with mediastinal malignant disease, especially lymphomas. Thoracotomy, with oversewing of the thoracic duct leak or ligation of the duct below the leak, is curative in cases of accidental or intraoperative trauma. Pleurodesis [see Hydrothorax Caused by Malignant Disease, above] may prevent reaccumulation of chyle in patients with unresponsive malignant disease or in other poor operative candidates.

**Pseudochylothorax**

Occasionally, in patients with long-standing pleural effusions, cholesterol crystals collect in the pleural liquid, causing a milky-white appearance that is indistinguishable from chylothorax on gross inspection. Such pseudochylous, or chyliform, effusions can usually be readily differentiated from true chylothorax on the basis of the clinical setting. Pseudochylous effusions typically occur as a complication of rheumatoid or tuberculous effusions that have been present for several years and are associated with extensive pleural thickening. Chyliform effusions have been reported with paragonimiasis. These effusions should be drained and the underlying process treated.

**Parapneumonic Effusions and Empyema**

Thoracic empyema most often results from contiguous spread of infection from an underlying region of pneumonia and occasionally from a lung abscess or bronchiectasis. Bacteria are the most common pathogens, although any microorganism capable of causing pneumonia may also cause empyema. In a report from an inner-city municipal hospital, as many as 7% of patients admitted with acute pneumonia had empyema on presentation. The pleural space may also become infected as a result of seeding of pathogens after thoracic surgery, penetrating trauma, thoracostesis, or tube thoracostomy. Direct spread of infection from a subdiaphragmatic site, hematogenous spread of infection during septicemia, and embolic spread during septic thrombophlebitis are other mechanisms by which the pleural space may become infected. Finally, empyema may occur as a complication of spontaneous pneumothorax, mediastinitis, or esophageal rupture.

**Etiology** Microorganisms causing empyema have changed considerably during the past 50 years, largely because of the introduction and increasingly widespread use of potent broad-spectrum antibiotics. In the 1930s and 1940s, *Streptococcus pneumoniae* (pneumococcus) and hemolytic streptococci were the pathogens most frequently isolated from empyemas. In the 1950s and 1960s, *Staphylococcus aureus* and gram-negative bacilli (e.g., *Escherichia coli*, *Haemophilus influenzae*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*) became the predominant pathogens found in empyemas. Some series, employing modern techniques for culturing anaerobic bacteria, have found a preponderance of anaerobes, either alone or in combination with aerobic bacteria. Fungi have been isolated from empyemas more frequently in recent years, particularly in hospitalized patients with significant comorbidities who are immuno-compromised.

**Diagnosis** The most common presenting symptoms of empyema are fever, chest pain, cough, and dyspnea. These symptoms, however, are not specific enough to distinguish patients who have pneumonia and empyema from those who have pneumonia alone. Patients with anaerobic empyema are more likely to have an indolent presentation, characterized by low-grade fever, anorexia, weight loss, or anemia. Between 10% and 15% of patients with empyema do not have fever or an elevated white cell count.

In patients with pneumonia and pleural effusion, it is important to determine whether the effusion is a typical parapneumonic effusion (formerly known as a sympathetic effusion), a complicated parapneumonic effusion, or an empyema. These three types of effusion can be distinguished on the basis of the radiographic appearance and characteristics of the pleural liquid obtained at thoracentesis [see Table 2].

**Treatment** In general, very small pleural effusions (maximum thickness < 10 mm as measured on lateral decubitus chest radiograph) in the setting of acute pneumonia will resolve with

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**Table 2** Classification and Treatment of Parapneumonic Effusions and Empyema

<table>
<thead>
<tr>
<th>Type of Effusion</th>
<th>Radiographic and Laboratory Findings</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical parapneumonic pleural effusion</td>
<td>&gt; 10 mm maximum thickness on lateral decubitus chest radiograph; glucose level and pH are normal; Gram stain and culture are negative</td>
<td>Antibiotics alone</td>
</tr>
<tr>
<td>Complicated parapneumonic pleural effusion</td>
<td>May be nonloculated or multiloculated; no obvious pus; glucose level and pH are low and/or Gram stain and culture are positive</td>
<td>Tube thoracostomy plus antibiotics; if loculated, use intrapleural fibrinolytics; surgery rarely required</td>
</tr>
<tr>
<td>Empyema</td>
<td>Free-flowing single loculus or multiloculated; obvious pus present</td>
<td>Tube thoracostomy plus antibiotics; if loculated, use intrapleural fibrinolytics; may require thoracoscopy or decortication</td>
</tr>
</tbody>
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appropriate antibiotic treatment of the pneumonia and do not require further investigation by thoracentesis. However, most larger effusions require thoracocentesis. Loculations on radiographic studies, low pleural liquid pH and glucose concentrations, high LDH, or positive Gram stain and cultures indicate the presence of a complicated parapneumonic effusion (in cases in which there is no obvious presence of pus) or empyema (in cases in which there is obvious presence of pus). A pleural liquid pH of 7.2 or higher favors the diagnosis of typical parapneumonic effusion. Pleural liquid pH values between 7.0 and 7.2 are considered to be indeterminate (borderline complicated pleural effusion) and necessitate repeated thoracenteses, often from different sites, to determine whether a parapneumonic effusion is typical or complicated.

Systemic antibiotic therapy and prompt drainage of the pleural space are key. In general, antibiotics penetrate the pleural space well and should be given systemically rather than intrapleurally. The choice of antibiotics should be guided by the results of a Gram stain and culture of pleural samples, blood samples, sputum samples, or a combination of these. For anaerobic empyema, clindamycin is the drug of choice because as many as 10% to 15% of the anaerobic isolates are penicillin-resistant Bacteroides fragilis.

Pleural drainage usually requires prompt placement of a chest tube because complicated parapneumonic effusions and empyema liquid reaccumulate rapidly after thoracentesis. In addition, continuous drainage is required to sterilize the pleural space, and drainage prevents the formation of loculi. In some patients with complicated parapneumonic effusions and empyema that do not resolve radiographically after placement of a chest tube, intrapleural streptokinase or urokinase may allow adequate drainage and obviate the use of multiple chest tubes or surgical drainage, although the evidence for this approach is not strong. Urokinase may be preferred over streptokinase because urokinase is associated with less frequent febrile reactions. Use of intrapleural fibrinolytic agents may also allow small-bore pigtail catheters to be placed into loculi with CT or fluoroscopic guidance. This approach may be unsuccessful with thick pleura, multiple loculi, or both. Early thoracoscopic therapy may be more cost-effective than attempts at drainage and the use of fibrinolytic agents in such cases.

With appropriate treatment, most patients will become afebrile within 4 days, and peripheral white cell counts will return to normal within a week. In a minority of cases, adequate pleural drainage cannot be achieved, and fever and leukocytosis persist; in such cases, a surgical procedure, either video-assisted thoracoscopy (early stage) or thoracotomy (late stage), is usually required. Stripping the adherent inflammatory peel from the pleural surfaces and removing the purulent exudate from the pleural cavity (i.e., decortications and empyemectomy) is a demanding surgical procedure. In elderly or severely debilitated patients, a more conservative surgical procedure may be used in which a partial rib resection is performed to create an open pleuropulmonary tract. The chronic empyema cavity that is formed can then be managed in the same way as any other chronic open wound and eventually may close spontaneously or can be closed by reconstructive surgery.

If left untreated, empyema can lead to septic shock. Other complications of untreated empyema include localized dissection of infection and consequent rupture through the skin (empyema necessitatis) or into the bronchial tree (bronchopleural fistula).

**Figure 7**  (a) Dense, white linear opacity along the left diaphragm (arrow) represents calcification of the parietal pleura in a patient with long-standing asbestos exposure. (b) CT scan shows area of dense calcification along the central dome of the diaphragm (arrow).
Radiograph reveals a so-called trapped lung, which was caused by marked thickening of the visceral pleura from a chronic empyema. Despite the application of a highly negative pressure to the pleural space, the right lung does not expand. A pyopneumothorax is present in the right thorax because evacuated pus has been replaced by air. There is no bronchopleural fistula (air leak from the lung). Obstruction of the mainstem bronchus may also cause a trapped lung.

Pleural thickening develops when pleural inflammation of any cause heals with the formation of fibrous tissue involving the visceral or parietal pleural surfaces. The costophrenic angle is most frequently involved, causing blunting of the normal recess. Localized pleural thickening over the apex of the lung—the so-called apical pleural cap—usually involves fibrous scarring of the apical lung merging into the adjacent visceral pleura. Although apical pleural thickening was once thought to be indicative of granulomatous disease from tuberculosis, more recent studies have documented the absence of any correlation with tuberculosis. The etiology of this asymptomatic finding is unknown.

Pleural thickening may be bilateral or unilateral. Extensive bilateral pleural thickening, extending along the lateral margins of the chest and even to the apex of the lung, is frequently the result of exposure to inorganic fibers—most often asbestos and, occasionally, talc. Other causes of bilateral pleural thickening include uremia and collagen vascular diseases, especially SLE and rheumatoid arthritis. Diffuse unilateral pleural thickening usually results from one of three causes: hemothorax, bacterial empyema, or tuberculosis.

Diffuse pleural thickening may be sufficiently dense to entrap the underlying lung, preventing its full expansion and impairing gas exchange [see Figure 8]. This condition is referred to as fibrothorax. During the months immediately after hemothorax or empyema, inflammatory pleural thickening may gradually regress. However, once an organized fibrous peel has formed, surgical decortication is the only available therapy. If the underlying lung tissue is relatively normal, resection of a thick pleural peel may result in significant improvement in ventilatory function.

In rare cases, localized or diffuse pleural thickening can entrap a small region of lung, producing a masslike lesion termed rounded atelectasis. It can be difficult to differentiate such lesions from other, more serious mass lesions (e.g., neoplasm).

**PLEURAL CALCIFICATION**

Diffuse, sheetlike calcification may develop in patients with hemothorax, bacterial empyema, or tuberculous pleurisy. Unlike the pattern of calcification that is observed in asbestos-related pleural plaques, calcium deposition after these conditions always takes place along the visceral pleura, thereby outlining the inner margin of the pleural thickening. In addition, calcification is generally found at the level of the midthorax, sparing the diaphragmatic pleural surface.

**Pneumothorax**

**ETIOLOGY**

Pneumothorax, the presence of gas within the pleural space, indicates that disruption of the visceral or parietal pleura has occurred. The gas that enters the pleural space may come from various sources. For example, in a penetrating injury involving the chest wall and parietal pleura, the gas enters from the outside environment. Alternatively, the gas may come from a gas-filled gastrointestinal structure; this situation might arise as a result of a ruptured esophagus, or it could arise from a ruptured intra-abdominal viscus and subsequent escape of gas across the diaphragm from a pneumoperitoneum. Most commonly, the source of the gas is the lung—after alveolar or tracheobronchial injury, after blunt or penetrating trauma, or as a complication of invasive diagnostic and therapeutic procedures, such as thoracentesis, attempted percutaneous cannulation of a central vein, acupuncture, or intercostal nerve block.

Pneumothorax caused by disruption of the visceral pleura may also result from focal pulmonary processes. Focal destructive processes may involve the visceral pleura as a primary site or may extend to the pleura from adjacent lung tissue. Examples of focal pulmonary processes that cause pneumothorax include bronchogenic carcinoma, rheumatoid lung nodule, thoracic endometriosis, necrotizing pneumonia, and pulmonary infarct. In the past, tuberculosis was frequently implicated as a cause of pneumothorax. *Pneumocystis carinii* pneumonia, a complication of AIDS, has become a common cause of pneumothorax, particularly in patients receiving aerosolized pentamidine, those who smoke cigarettes, and those with pneumatoceles seen on chest radiograph or CT scan.
Diffuse diseases of the lung parenchyma can also cause pneumothorax. Such diseases can greatly distort the lung architecture, resulting in an uneven distribution of ventilation within the lung. In this setting, localized alveolar overdistention, along with weakened alveolar walls, leads to an increased incidence of associated pneumothorax. The most common of these diffuse processes are the obstructive lung diseases, specifically emphysema, asthma, and cystic fibrosis. Rarer conditions that also carry an increased risk of pneumothorax include pulmonary lymphangiomatosis, tuberous sclerosis, eosinophilic granuloma, scleroderma, and congenital disorders of connective tissue. In some cases, the visceral pleura remains intact but alveolar gas gains entry to the pleural space via the mediastinum. When perivascular alveoli rupture, alveolar gas can dissect centripetally along the bronchovascular interstitium to the mediastinum, entering the pleural space through the mediastinal parietal pleura.

**Classification of Pneumothorax**

A commonly used classification of pneumothorax recognizes traumatic pneumothorax and iatrogenic pneumothorax as distinct clinical entities and lumps all other causes of pneumothorax under the somewhat misleading label of spontaneous pneumothorax. When spontaneous pneumothorax occurs in patients with underlying pleural or parenchymal disease, it is called secondary spontaneous pneumothorax. When no underlying lung disease is evident, it is called idiopathic spontaneous pneumothorax. Although patients with idiopathic spontaneous pneumothorax are otherwise healthy, most have subpleural apical blebs, frequently associated with more diffuse centrilobular emphysema detectable by CT scan; during surgery, the blebs are often found to have ruptured into the pleural space. These abnormalities may have a genetic etiology. Secondary spontaneous pneumothorax is a more serious problem than idiopathic spontaneous pneumothorax because patients with secondary spontaneous pneumothorax typically have impaired lung function.

**Epidemiology**

**Secondary Spontaneous Pneumothorax**

The incidence of secondary spontaneous pneumothorax depends on the underlying disease process. The incidence of pneumothorax in patients with chronic obstructive lung disease is approximately 26 per 100,000 per year, and the incidence is directly related to the severity of obstruction. Pneumothorax will develop in 5% to 8% of cystic fibrosis patients at some point in their lifetime; however, it occurs in 16% to 20% of cystic fibrosis patients older than 18 years. Pneumothorax occurs in 2% to 6% of HIV patients and is almost always associated with P. carinii pneumonia. Twenty-five percent of patients with eosinophilic granuloma and 80% of patients with pulmonary lymphangiomatosis have pneumothorax at some point in their disease course, and pneumothorax can be a presenting manifestation in both diseases.

For most underlying lung diseases, the rate of recurrent pneumothorax is similar to that of idiopathic spontaneous pneumothorax (39% to 47%), although patients with cystic fibrosis have a much higher recurrence rate (68% to 90%).

**Idiopathic Spontaneous Pneumothorax**

Idiopathic spontaneous pneumothorax has an incidence of approximately 4.3 cases per 100,000 patient-years. The peak incidence is in persons between 20 and 30 years of age, and the male-to-female ratio is approximately 5:1. Patients often have a tall, thin stature and very frequently are cigarette smokers. The precise mechanism whereby male sex, asthenic habitus, and cigarette smoking predispose to apical pleural bleb formation or rupture is unknown. One study detected anomalies of the bronchial tree in the majority of patients with spontaneous pneumothorax, suggesting associated congenital abnormalities of lung structure. How these anomalies may relate to the occurrence of pneumothorax is unclear. Common misconceptions are that strenuous physical activity is frequently a trigger for the development of pneumothorax and that patients are at increased risk during airplane travel. In fact, most studies have found that the onset of symptoms of pneumothorax usually occurs at rest or during light activity, and a study of pneumothoraces among pilots in the United States Air Force found that very few episodes occurred during flight.

**Diagnosis**

The most common symptoms of pneumothorax are chest pain and dyspnea. The pain may be a dramatic, severe, stabbing unilateral chest pain with a sudden, explosive onset, sometimes radiating to the ipsilateral shoulder or scapular area. In other cases, the discomfort may be more modest and more easily tolerated. Often, patients will recall previous transient episodes of pain that were similar to, although milder in degree or shorter in duration than, the one that finally caused them to seek medical attention. Dyspnea develops in most patients. The dyspnea is more severe when the pneumothorax is large and when there is significant underlying lung disease (i.e., secondary spontaneous pneumothorax).

**Secondary Spontaneous Pneumothorax**

In a patient with secondary spontaneous pneumothorax associated with underlying emphysema, the diagnosis is particularly difficult to make on the basis of physical findings. Decreased lung elastic recoil and residual hyperinflation keep the lung from fully collapsing and limit changes in the size of the thoracic cage. In addition, in patients with emphysema, physical findings such as hyperresonance and diminished breath sounds may be found over the contralateral lung. In a patient with chronic airflow obstruction, the sudden onset of chest pain and worsened dyspnea should raise the suspicion of pneumothorax. Confirmation of the diagnosis of pneumothorax usually requires a chest radiograph.

**Idiopathic Spontaneous Pneumothorax**

Characteristic physical findings on the involved side include expansion of the hemithorax (caused by release of the ipsilateral chest wall from the recoil forces of the lung), hyperresonance, diminished fremitus, diminished transmission of voice sounds, and distant or absent breath sounds.

As gas collects in the pleural space, the lung recoils from the chest wall toward the hilum. The presence of a pneumothorax can be identified on a chest radiograph by visualization of a thin (=1 mm) linear shadow made by the visceral pleura as it passes along a plane tangential to the x-ray beam. This linear shadow, marking the outer rim of the lung, follows the contour of the inner aspect of the chest wall, and no lung markings (i.e., bronchovascular shadows) can be seen peripheral to it. In cases in which the pneumothorax is small and gas collects over the apex of the lung, it may be difficult to distinguish the visceral pleural line from superimposed rib margins. When the chest radiograph
is taken with the patient in the supine position, a pneumothorax will collect along the costophrenic sulcus rather than along the apex of the lung. This so-called deep sulcus sign may be useful in identifying occult pneumothorax in hypotensive patients in whom upright chest radiographs are inadvisable. Chest radiographs taken during full expiration have not been shown to enhance the detection of pneumothorax. Pitfalls in the radiographic diagnosis of pneumothorax include confusion regarding two other causes of curvilinear shadows in the chest: (1) extrathoracic skin folds and (2) intrapulmonic cysts or bullae.

It is difficult to accurately estimate the size of a pneumothorax relative to the size of the hemithorax by casual inspection of the chest radiograph. As a rough indicator, a collection of gas around the lung that has an average thickness of 1 in. represents a 30% pneumothorax. When collapse of the lung is complete (100% pneumothorax), the lung forms a fist-sized opacity near the hilum, and the mediastinum may shift slightly toward the contralateral lung; the diagnosis is obvious on x-ray [see Figure 9].

A small pleural effusion is commonly present in pneumothorax. It is detected on radiograph by blunting of the costophrenic sulcus. The pleural liquid is usually bloody. The effusion is probably formed as a result of the rupture of small blood vessels within pleural adhesions.

TREATMENT

Secondary Spontaneous Pneumothorax

Because initial or recurrent episodes of secondary spontaneous pneumothorax can be life threatening, aggressive treatment is required. Patients should be hospitalized and a chest tube placed for drainage; observation and simple aspiration are not adequate treatment. The methods for preventing recurrence of secondary spontaneous pneumothorax are the same as those of idiopathic spontaneous pneumothorax (e.g., thoracotomy, video-assisted thoracotomy, pleurodesis) (see below), although many experts feel that application of such methods should be utilized on the first occurrence of secondary spontaneous pneumothorax.

Idiopathic Spontaneous Pneumothorax

Treatment of idiopathic spontaneous pneumothorax is directed in part at allowing the collapsed lung to expand fully again and in part at preventing recurrences. In mildly symptomatic patients with moderate pneumothorax, simple aspiration of the pneumothorax may be successful in 60% to 70% of cases. A patient with a small (15% to 20%) pneumothorax who is asymptomatic or minimally symptomatic can be safely observed, and the pneumothorax can be allowed to resorb spontaneously. Complete resolution of a pneumothorax usually requires approximately 10 days, provided there is no further air leak. Resolution can be accelerated by the administration of supplemental oxygen. Supplemental oxygen lowers the nitrogen content of blood, thereby increasing the pressure gradient for nitrogen that favors transfer of gas from the pleural space into the venous end of the pleural capillaries. Strict bed rest does not hasten resolution and is not necessary. A large pneumothorax in a symptomatic patient should be evacuated promptly with an intercostal small-bore (14 French) or large-bore (28 French or greater) chest tube passed cephalad into the apex of the chest. The air leak from the lung may seal immediately or may persist for 3 to 5 days until the tear in an apical bleb heals. An air leak from the lung that persists for more than 7 days is considered by many physicians to be an indication for surgical intervention; at thoracoscopy or thoracotomy, the blebs can be oversewn or excised by wedge resection and the pleura abraded or pleurodesis performed.

Incidence of recurrence

Idiopathic spontaneous pneumothorax often recurs. At least 20% to 30% of patients with idiopathic spontaneous pneumothorax will experience an ipsilateral recurrent pneumothorax within the ensuing 5 years; most recurrences occur within a year after the initial event. According to some reports, the rate of initial recurrence may be as high as 50%. Recurrences are more common in women and taller men and are reduced by smoking cessation. Ninety percent or more of recurrences are ipsilateral, despite the fact that the underlying abnormality (i.e., apical subpleural blebs) is bilateral in more than half the cases. Simultaneous bilateral idiopathic spontaneous pneumothoraces are fortunately infrequent, occurring in approximately 1% of cases; surprisingly, when they do occur, they are rarely fatal. After the first ipsilateral recurrence of a pneumothorax, subsequent recurrences become increasingly likely.

Management of recurrence

There is debate regarding the best method of preventing recurrences and the optimal timing for such an intervention. Because half or more of patients with idiopathic spontaneous pneumothorax will never suffer a recurrence, it seems reasonable to withhold preventive treatment until after a recurrence. At that point, the probability of further recurrences is quite high, and the discomfort and inconvenience associated with recurrent pneumothoraces would have become increasingly apparent to the patient. Traditional and definitive treatment for prevention of recurrences involves thoracotomy: apical blebs are oversewn or excised by wedge resection, and adhesions are induced between the lung and chest wall by abrasion of the pleural surface with dry gauze or by partial parietal

Figure 9 This chest radiograph of a patient with pneumothorax demonstrates virtually complete collapse of the right lung. There has been a slight shift of the mediastinum toward the contralateral side. The visceral pleura (arrows) can be clearly identified because gas is present on both sides.
pleurectomy. Recurrent pneumothorax occurs after this procedure in 0% to 2% of patients. Video-assisted thoracoscopic surgery has allowed these procedures to be performed without thoracotomy, resulting in less pain and shorter hospital stays.\textsuperscript{69} Attempts have also been made to achieve pleurodesis without thoracotomy via a chest tube. This technique is the same as that used for the management of pleural effusions in patients with malignant disease [\textit{see Hydrothorax Caused by Malignant Disease, above}]. Recurrence of spontaneous pneumothorax is reduced after doxycycline administration or talc pleurodesis.

**TENSION PNEUMOTHORAX**

Occasionally, gas enters the pleural space during the inspiratory phase and is prevented from escaping during expiration, presumably because an airway or tissue flap acts as a one-way valve. Under these circumstances, there is a progressive increase in the amount of pleural gas, and the pleural gas is under increased pressure (i.e., tension). This situation is referred to as tension pneumothorax. Tension pneumothorax occurs in only 1\% to 2\% of the cases of idiopathic spontaneous pneumothorax. However, it is a more common manifestation of the barotrauma that may occur as a complication of positive pressure mechanical ventilation.

**Diagnosis**

Tension pneumothorax is a medical emergency. Patients are often dyspneic at rest and gasping for breath. Cyanosis and hypotension are common. The diagnosis cannot be established by a plain chest radiograph, although a marked contralateral shift of the mediastinum and depression or inversion of the ipsilateral hemidiaphragm are suggestive.

**Treatment**

If there is acute distress, immediate action must be taken to remove gas from the pleural space. Introduction of a small-bore plastic catheter together with a needle through an intercostal space may suffice for emergency relief if delay in placing a full-sized chest tube is anticipated. In patients with tension pneumothorax, the gas that is under pressure will rush out of the chest through the open catheter. If a Heimlich flutter valve, which allows one-way passage of gas, is attached to the catheter, a series of coughs or Valsalva maneuvers will allow almost complete evacuation of the remainder of the pneumothorax that is not under tension. Because of the life-threatening nature of tension pneumothorax, a procedure to prevent recurrence should be undertaken after the first such event in cases involving idiopathic spontaneous pneumothorax.

**Hilar and Mediastinal Disorders**

**NORMAL ANATOMY OF THE HILA AND MEDIASTINUM**

The mediastinum is the intrathoracic compartment situated between the two lungs. It is bordered anteriorly by the sternum, posteriorly by the vertebral column, and laterally by parietal pleura. It extends from the thoracic inlet to the superior surface of the diaphragm. Several important structures are contained within or pass through the mediastinum, including the heart and great vessels, the esophagus, the trachea and mainstem bronchi, lymphatic vessels and nodes, and nerves.

It is convenient to divide the mediastinum into three parts on the basis of imaginary coronal sections [\textit{see Figure 10}]. The anterior or mediastinum (i.e., the portion anterior and superior to the anterior surface of the pericardium) contains the thymus, lymph nodes, and mesenchymal tissue. The middle mediastinum consists of the heart and pericardium, the major vessels as they enter and leave the heart, the trachea and main bronchi, lymph nodes, and portions of the phrenic and vagus nerves. Between the posterior aspect of the pericardium and the vertebral column lies the posterior mediastinum, which contains the descending aorta, the esophagus, the thoracic duct, lymph nodes, and a portion of the vagus nerve. The sympathetic nerve chain, which runs in the costovertebral gutter, is conventionally included in the posterior mediastinum.

As blood vessels, airways, and nerves leave the mediastinum and pass into the lungs, they form the pulmonary hila. On chest radiographs, the hilar shadows are composed primarily of branches of the pulmonary arteries. The right pulmonary artery bifurcates just before entering the hilum as the truncus anterior artery (superior branch) and the right interlobar artery (inferior branch). The left pulmonary artery divides within the hilum into superior branches and the larger left interlobar artery. In 97\% of normal persons, the left hilum is positioned superior to the right hilum; displacement from this normal position may be caused by mass lesions or lobar atelectasis. Central bronchopulmonary lymph nodes that are important for drainage of the lung parenchyma are situated within the pulmonary hila along the bronchial tree, especially within bifurcations.

**HILAR ENLARGEMENT**

The most common causes of enlargement of the hilar shadows on chest radiographs are vascular engorgement and adenopathy.
Enlargement Caused by Vascular Engorgement

Vascular engorgement may result from increased blood flow in the pulmonary circulation, as in atrial septal defect with left-to-right intracardiac shunt, or from pulmonary arterial hypertension of any cause. The caliber of the pulmonary arteries can be assessed by measurement of the transverse diameter of the right interlobar artery on a posteroanterior radiograph; in normal persons, this value is usually less than 16 mm. In rare cases, localized aneurysmal dilatation of the pulmonary arteries occurs; this condition is referred to as the Hughes-Stovin syndrome.

On plain chest radiographs, it is sometimes difficult to distinguish vascular from nodal enlargement of the hila. Pulmonary angiography was formerly needed to make this distinction. Currently, however, contrast-enhanced CT scanning of the chest can effectively identify vascular structures in the hila without the need for invasive procedures. Occasionally, there is a strong contraindication to the use of intravenous contrast agents in some patients; in such cases, magnetic resonance imaging, which does not require the use of contrast agents, can be used.

Enlargement Caused by Adenopathy

Hilar lymph node enlargement may be unilateral or bilateral. Unilateral lymphadenopathy may accompany virtually any pneumonia, although it is most characteristic of granulomatous infections (e.g., tuberculosis and atypical mycobacteriosis, histoplasmosis, and coccidioidomycosis) and certain atypical pneumonias (e.g., Mycoplasma infections, tularemia, pertussis, and psittacosis). Neoplastic enlargement of hilar lymph nodes usually results from spread of bronchogenic carcinoma; extrathoracic cancers that metastasize to the hilar and mediastinal lymph nodes include cancers of renal cell origin, which are implicated especially often, and cancers of the breast and GI tract. Hodgkin disease and other lymphomas may also cause unilateral or asymmetrical hilar adenopathy. Finally, about 1% to 3% of patients with sarcoidosis have unilateral hilar adenopathy.

A common diagnostic challenge is the evaluation of a patient with bilateral hilar adenopathy. This condition is often found in association with mediastinal adenopathy and sometimes in association with parenchymal infiltrates. Nonspecific symptoms of cough, chest pain, dyspnea, or malaise may have prompted the chest radiograph, or bilateral hilar adenopathy may have been detected incidentally on a chest radiograph obtained for unrelated reasons. The most common etiology, especially in patients between 20 and 40 years of age, is sarcoidosis. The differential diagnosis of bilateral hilar adenopathy includes the following: (1) lymphoma, which is usually accompanied by extrathoracic manifestations, such as systemic symptoms, peripheral adenopathy, and anemia; (2) metastatic cancer, in which the primary malignant disease is most often known; (3) chronic granulomatous infections, such as tuberculosis or histoplasmosis, in which the adenopathy is more commonly unilateral; and (4) berylliosis, which can precisely mimic sarcoidosis but which can be readily diagnosed with a careful occupational history.

In a retrospective analysis of 100 cases of bilateral hilar adenopathy not caused by infection, it was found that patients who were asymptomatic and had a normal physical examination or those who had erythema nodosum or uveitis as the only manifestation of their disease invariably had sarcoidosis. On the other hand, it was found that patients who were symptomatic or patients with other abnormal physical findings (e.g., peripheral adenopathy, hepatomegaly, or splenomegaly) in some cases had sarcoidosis and in other cases had neoplastic node involvement. The approach to diagnosis in patients with bilateral hilar adenopathy depends on the relative likelihood of the various diagnostic probabilities, as determined by clinical assessment. Patients strongly suspected of having sarcoidosis may be observed with serial chest radiographs or may undergo transbronchial lung biopsy via the fiberoptic bronchoscope for tissue confirmation (i.e., identification of noncaseating granulomas). In patients with granulomatous infection, CT scanning can indicate the presence of active infection when areas of low attenuation (necrosis), peripheral rim enhancement, and larger nodes are seen, whereas inactive infection is suggested by smaller nodes, homogeneous density, and calcification. When lymphoma is suspected, lymph node biopsy by mediastinoscopy should provide diagnostic material. In patients suspected of having carcinoma of the lung, an increase in the uptake of fluorodeoxyglucose by the thoracic lymph nodes, as shown through use of positron emission tomography, indicates high risk of malignancy. The definitive diagnosis of cancerous lymph nodes can be determined with a high yield by needle aspiration of the hilar mass under fluoroscopic, CT, or transesophageal endosonographic guidance. It should be noted, however, that direct histologic analysis of hilar lymph nodes, which might be necessary in cases of lymphoma in which there is no mediastinal involvement, requires at least a limited anterior thoracotomy to obtain a tissue sample of adequate size.

Enlargement Caused by Calcified Lymph Nodes

Calcified hilar lymph nodes most often indicate previous granulomatous infection, especially tuberculosis or histoplasmosis. Hilar and mediastinal lymph node calcification in patients with silicosis may appear in a highly characteristic pattern referred to as eggshell calcification, in which calcium outlines only the perimeter of the lymph nodes. Sarcoidal lymph nodes rarely become calcified.

Acute Mediastinitis

Acute bacterial mediastinitis usually occurs as the consequence of esophageal perforation and the subsequent release of acidic gastric juices, often along with anaerobic bacteria, into the mediastinum. Rupture of the lower esophagus from violent vomiting is referred to as Boerhaave syndrome; free gas in the mediastinum (i.e., pneumomediastinum) and pleural effusion or pneumothorax (which is usually left sided) are common manifestations of this syndrome. Esophageal rupture may also occur as a complication of foreign-body ingestion, esophageal carcinoma, penetrating or blunt chest trauma, and medical procedures that dilate the esophagus. Occasionally, infection spreads to the mediastinum from adjacent sites; empyema, lung abscess, pericarditis, and retropharyngeal abscess may all be complicated by acute mediastinitis. Mediastinitis can also be a complication of sternotomy for cardiac or thoracic surgery. Finally, a mediastinal bronchogenic cyst may become infected and discharge its contents into the mediastinum.

Patients who have acute mediastinitis are usually acutely and severely ill. Symptoms of the disorder include fever, dysphagia, and a lancinating chest pain. The chest radiograph may reveal, in addition to mediastinal widening, such abnormalities as the presence of pneumomediastinum and pleural effusions. Treatment consists of the administration of broad-spectrum antibiotics, including antibiotics that are effective against anaerobic bacteria, because the infections are usually polymicrobial. In addition, open surgical drainage is required in most cases.
cutaneous catheter drainage may be successful in some cases of limited esophageal leakage.

**MEDIASTINAL WIDENING AND MASS LESIONS**

A great diversity of benign and malignant lesions may cause the mediastinum to have an abnormal appearance on the chest radiograph. Occasionally, a specific set of findings may prompt a search for a mediastinal lesion. For example, the muscle weakness of myasthenia gravis may prompt a search for associated thymomas. Alternatively, the constellation of abnormalities suggesting the superior vena cava syndrome (e.g., headaches, jugular venous distention, engorgement of the head and neck, and a prominent collateral venous pattern across the upper thorax) may prompt a search for an obstructing lesion [see *12:VIII Lung Cancer* and *12:XII Oncologic Emergencies*]. In some patients, the mediastinal disorder induces nonspecific symptoms referable to the thorax, such as cough, dyspnea, chest pain or pressure, hemoptysis, dysphagia, hoarseness, or wheezing. Most often, however, diagnostic evaluation is prompted by an asymptomatic radiographic finding.

The differential diagnosis of abnormal radiographic opacities within the mediastinum includes benign and malignant neoplasms, cysts, vascular abnormalities, ectopic thyroid tissue, granulomatous diseases, and several other disorders. It is useful to distinguish abnormalities that cause diffuse widening of the mediastinum from those in which the abnormality is confined primarily to the anterior, middle, or posterior mediastinum [see Table 3]. Selected examples of each category will be presented.

With the use of intravenous contrast agents, CT scanning can distinguish vascular structures, fat density, cysts, and calcifications from soft tissue density. Often, benign mediastinal lesions can be identified with reasonable certainty by the CT image alone; nonneoplastic lesions include those associated with mediastinal lipomatosis, congenital cysts, vascular aneurysms, diaphragmatic hernias, and intrathoracic goiters. In other cases, CT scanning can be used with a high degree of sensitivity and specificity to guide the biopsy of suspected malignant lesions. MRI may provide advantages over CT in cases suspected to be vascular.

**Diffuse Mediastinal Widening**

Diffuse mediastinal widening may occur acutely or chronically. Acute widening of the mediastinal shadows may result from an acute mediastinitis or from mediastinal hemorrhage. Important causes of chronic mediastinal widening include mediastinal lipomatosis and mediastinal granuloma and fibrosis.

**Mediastinal Lipomatosis**

Mediastinal lipomatosis is a consistently asymptomatic condition in which excess fat tissue is deposited between and around mediastinal structures; it is found in some patients with Cushing disease, iatrogenic Cushing syndrome, or obesity. The only significance of mediastinal lipomatosis is that it must be distinguished from other, more serious causes of mediastinal widening. CT scanning of the thorax readily establishes the diagnosis by identifying material of fat density deposited diffusely through the mediastinum.

**Mediastinal Granuloma and Fibrosis**

Mediastinal lymph node involvement is common in patients with chronic granulomatous infections, such as histoplasmosis and tuberculosis. Infrequently, an excessive fibrotic response develops around a caseous focus within lymph nodes. In some cases, fibrosis causes a capsule 2 cm or greater in thickness to form around a caseous focus, giving rise to a mediastinal mass that is usually situated in a subcarinal or right paratracheal location. In other patients, the fibrosis invades or compresses adjacent structures and at times extends diffusely through the mediastinum. The latter condition, called fibrosing mediastinitis, is the most common nonmalignant cause of superior vena cava syndrome.

Depending on which structures the fibrosis impinges, patients may also exhibit bronchial obstruction, pulmonary arterial or venous obstruction, or esophageal obstruction.

In some cases of fibrosing mediastinitis, histologic examination of a surgical or postmortem specimen reveals only dense fi-
brosis. In other cases, a small caseous focus of infection can be identified, almost always caused by infection with *Histoplasma capsulatum*.39 The presumed mechanism in all cases is rupture of caseous material into the mediastinum, leading to an intense inflammatory reaction that heals with fibrosis.

Even when viable fungal organisms can be identified, the therapeutic response to amphotericin B is poor, and corticosteroids are generally ineffective as well. Some studies have suggested that ketocanazole may be helpful.52 In some patients, surgical extirpation of the fibrotic mass is possible. Endovascular balloon angioplasty and placement of stents have been successful in the management of superior vena cava and pulmonary artery obstructions. In general, progression of the fibrosis is slow, and long-term survival is possible.

**Anterior Mediastinal Masses**

In addition to lymphomas, common causes of masses found in the anterior mediastinum are thymomas, teratomas, dermoid cysts, and retrosternal goiters.88

**Thymomas** Thymomas may be found in adults of any age. They may arise from epithelial or lymphocytic cell lines. Most thymomas are benign, but some behave as malignant lesions and exhibit local invasion into adjacent structures. Reports of distant metastases are rare. Calcification may be present at the perimeter of or throughout the thymoma, but its presence does not necessarily signify that the lesion is benign. As many as one quarter to one third of patients with thymomas have myasthenia gravis, and some of these patients will experience a remission of symptoms after removal of the tumor. Other rare paraneoplastic syndromes that are associated with thymomas include red cell aplasia, Cushing syndrome, Graves disease, carcinoid syndrome, and hypogammaglobulinemia. Because of their malignant potential, suspected thymomas should be surgically excised in most cases. Other thymic lesions include thymic carcinoma, thymic carcinoid, thymolipoma, and thymic cysts.

**Dermoid cysts and teratomas** Germ cell tumors are most common in young adults 18 to 25 years of age. They originate from germ cell rests that were deposited in the mediastinum during embryogenesis. Dermoid cysts are usually benign cystic tumors composed of epidermal and dermal tissue; on occasion, hair, bone, or teeth form within these lesions. Teratomas consist of cells from all three embryonic origins (i.e., ectodermal, mesodermal, and endodermal) and may be cystic (usually benign) or solid (usually malignant). As with thymomas, calcification may be present along the periphery of the tumor. A potential complication of dermoid cysts and cystic teratomas is rupture and subsequent discharge of the cyst contents into the mediastinum or tracheobronchial tree. Surgical excision is the treatment of choice. Other germ cell tumors of the mediastinum include seminoma and nonseminomatous malignant tumors.

**Goiters** Cervical goiters may extend inferiorly into the thorax.60 On occasion, masses within the mediastinum, usually located anteriorly, that have no palpable cervical connection prove to be intrathoracic goiters. These lesions are usually nodular colloid goiters that arise from the lower pole or isthmus of the thyroid gland and extend down into the chest; occasionally, such lesions prove to be adenomas or malignant tumors.

Most patients with nodular colloid goiters are asymptomatic, but some lesions grow sufficiently large to compress the trachea, causing dyspnea and stridor. Dysphagia, vascular compression, and vocal cord paresis or paralysis are other potential presenting manifestations. Uptake of radiolabeled iodine by a mediastinal mass on thyroid scan is diagnostic, but this is a relatively infrequent finding because most of these lesions are nonfunctioning goiters. Certain characteristic features of the CT image, including anatomic continuity with the cervical thyroid gland and particular patterns of calcification, have proved useful in identifying intrathoracic goiters. Patients with small, asymptomatic intrathoracic goiters can be observed or possibly given suppressive thyroid therapy; however, symptomatic patients require thyroidectomy, which can usually be achieved with a suprasternal incision.

**Middle Mediastinal Masses**

Mediastinal bronchogenic cysts usually originate near the main carina of the tracheobronchial tree, but they may extend into any of the three mediastinal compartments.90 They are lined with respiratory epithelium and contain a milky-white or brown mucoid material. Direct communication with the tracheobronchial tree is rare, although the potential exists for infection within the cyst and subsequent rupture into the airways or mediastinum. Bronchogenic cysts are usually discovered during childhood or early adulthood; in the latter age group, related symptoms are uncommon. Surgical excision is warranted for infected bronchogenic cysts or for cysts communicating with the tracheobronchial tree.

**Posterior Mediastinal Masses**

Neurogenic tumors are the most common primary neoplasms of the posterior mediastinum.90 They are round or oval masses in the paravertebral sulcus. Most patients are asymptomatic, although in some patients, chest or back pain or symptoms of bronchial compression develop. Tumors that arise from the nerve sheath (schwannomas) are usually benign; tumors derived from nerve cells may be benign (ganglioneuromas) or malignant (neuroblastomas or ganglioneuroblastomas). Neurofibromas derive from all nerve elements, including axons, sheath cells, and connective tissue; most are benign. Mediastinal neurofibromas may represent an isolated finding or may be part of generalized neurofibromatosis (von Recklinghausen disease). A rare tumor arising from paraganglionic cells is a mediastinal pheochromocytoma, which may be hormonally active.

Even benign neurogenic tumors may erode into an adjacent rib or cause pleural effusion. Some neurogenic tumors, most commonly neurofibromas, may extend into the spinal canal, causing widening of the intervertebral foramen; as a result, such tumors may assume a dumbbell shape. CT and MRI have for the most part supplanted myelography in the assessment of spinal extension of these so-called dumbbell tumors, which often require a coordinated thoracic and neurosurgical approach for resection.

**Pneumomediastinum**

Gas outside of normal GI structures may enter the mediastinum by several routes. First, it may collect in the mediastinum after esophageal or tracheobronchial rupture. Second, it may dissect into the mediastinum along fascial planes from the neck or oropharynx (e.g., after dental extraction or tracheotomy) or from the retroperitoneum below (e.g., after colonic rupture or duodenal perforation). Third, after alveolar rupture,
gas may track along the perivascular interstitium in the lung and enter the mediastinum at the pulmonary hilum. This third pathway is the likely route of gas entry in patients subjected to barotrauma from mechanical positive pressure ventilation or in those who suffer pneumomediastinum as a complication of bronchoscopy. Pneumomediastinum occurring in the setting of mechanical ventilation may be associated with the more serious complications of barotrauma, which include pneumothorax, gas embolization, and pneumopericardium. Most often, however, pneumomediastinum occurs independently of traumatic or iatrogenic causes, in which case it is referred to as spontaneous pneumomediastinum.

**Etiology**

Spontaneous pneumomediastinum occasionally occurs as a complication of pneumonia or asthma, but most often, it is found in young and otherwise healthy individuals. Symptoms are typically abrupt in onset and usually follow exaggerated respiratory efforts. Presumably, distended marginal alveoli rupture into the interstitium when the transpulmonary pressure is high; the elevated transpulmonary pressure would occur, for example, when a person inhales deeply or when a scuba diver holds his or her breath during ascent from an underwater depth. Thus, events that commonly precede spontaneous pneumomediastinum include parturition, cough, emesis, and straining at stool. In addition, numerous reports have appeared describing spontaneous pneumomediastinum after cocaine or marijuana use.

**Diagnosis**

Typical symptoms are retrosternal chest pain and dyspnea. The chest pain mimics that of pericarditis in that it is improved by sitting up and leaning forward; coughing, swallowing, and deep inspiration generally aggravate the pain. Because the free mediastinal gas often escapes cephalad into the subcutaneous tissues of the neck and supraclavicular area, patients may also complain of neck pain and sore throat, dysphagia, or a peculiar swelling and crepitation in the upper chest and neck. Physical findings may include a crunchlike sound heard in synchrony with the heartbeat (Hamman mediastinal crunch), diminished dullness on percussion of the heart, and subcutaneous emphysema. The last finding, which is detected by palpation of crepitations resulting from the formation of gas bubbles just below the surface of the skin, may in extreme cases of pneumomediastinum extend as far down as the arms, abdominal wall, and genitals. Gas in the mediastinum may also decompress into the pleural space, leading to a concomitant pneumothorax, usually on the left side.

The diagnosis is established with chest radiography. On posteroanterior view, a lucent zone of up to a few centimeters in width separates the cardiac silhouette from the medial border of the parietal and visceral pleurae. Gas may be seen outlining the aortic knob and extending in linear streaks up into the neck. On lateral view, gas collects between the sternum and the anterior border of the heart and outlines the aorta and other mediastinal soft tissue structures. In more subtle cases, lateral views of the neck reveal gas in the pretracheal fascia. In mild cases, CT may be necessary to detect the air in the mediastinum.

**Treatment**

Spontaneous pneumomediastinum in spontaneously breathing adults resolves without specific therapy within a few days, and recurrences are uncommon. In contrast to spontaneous pneumothoraces, spontaneous pneumomediastinum is not recurrent. Thus, other than treating any underlying lung disease, management consists of reassurance, avoidance of strenuous activities, and use of analgesics if needed. Breathing-enhanced concentrations of oxygen may accelerate the rate of gas resorption. In adults, it is exceedingly rare that gas within the mediastinum is of sufficient pressure to compress vascular structures; therefore, surgical decompression of the mediastinal space by techniques such as tracheotomy is not indicated.

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