**Figure 15-19**

Mechanisms of pulmonary edema formation. **A**, Fluid overload. **B**, Decreased serum and albumin. **C**, Lymphatic obstruction. **D**, Tissue injury. (From Black JM, Hawks JH, eds: *Medical-surgical nursing*, ed 7, St Louis, 2005, WB Saunders.)

decreasing the space available for gas exchange. Normally the lung is kept dry by lymphatic drainage and a balance among capillary hydrostatic pressure, capillary oncotic pressure, and capillary permeability.

Pulmonary edema develops as a result of (1) fluid overload, (2) decreased serum and albumin, (3) lymphatic obstruction, and (4) disruption of capillary permeability (tissue injury or immunoresponse) (Fig. 15-19). New studies show that loss of sodium transport capacity may be a factor in the development of some types of pulmonary edema.⁴⁴⁹

Fluid Overload. When the filling pressures on the left side of the heart increase, pulmonary capillary hydrostatic pressure increases. If it surpasses the oncotic pressure that holds fluid in the capillaries, fluid is drawn from capillaries in the lungs into the interstitial space. Normally, the lymphatic system removes this fluid from the lungs, but if the flow of fluid into the interstitium exceeds the ability of the lymphatic system to remove it, fluid

overload and consequently pulmonary edema develop.* When osmotic pressure in the venous end of the capillary exceeds interstitial pressure, fluid cannot return to the bloodstream and peripheral and pulmonary edema may result. Fluid overload may also occur from decreased

*A brief review of this concept may be necessary for an understanding of many pulmonary conditions. For an in-depth discussion the reader is referred to Guyton AC, Hall JE: *Textbook of medical physiology*, ed 11, Philadelphia, 2005, Saunders. Fluid movement in the lung (as in all vessels) is governed by vascular permeability and the balance of the hydrostatic and oncotic pressures across the capillary endothelium as described by Starling's equation. Hydrostatic forces favor fluid filtration, whereas oncotic pressure promotes reabsorption. Normally, filtration forces dominate and fluid continuously moves from the vascular space into the interstitium. Extravascular water does not accumulate because the lung lymphatics effectively remove the filtered fluid and return it to the circulation. When the capacity of the lymphatic system is exceeded, if the rate of fluid filtration exceeds its functional capabilities, water accumulates in the loose interstitial tissues around the airways, pulmonary arteries, and eventually, the alveolar walls (alveolar edema).

sodium and water excretion associated with renal disorders.

As the fluid pressure increases in the tissues, it also increases in the left ventricle, which increases pressure in the left atrium. The disturbed pressure gradient results in less forward flow, resulting in pulmonary edema. Pulmonary edema is commonly seen when the left side of the heart is distended and fails to pump adequately (e.g., myocardial ischemia or infarction or mitral or aortic valve damage).

In atrial fibrillation, the left atrium may be unable to efficiently pump blood into the left ventricle, resulting in fluid pooling and subsequent edema. If the right side of the heart fails, peripheral edema occurs through the same process. Left-sided heart failure leads to right-sided failure (and vice versa), so both pulmonary and peripheral edema may exist simultaneously.

Decreased Serum and Albumin. In the case of liver cirrhosis, the serum protein and albumin levels are reduced in the vascular fluids. Thus less fluid reabsorption from the tissue spaces occurs, which results in pulmonary and peripheral edema and ascites.

Lymphatic Obstruction. When lymphatic channels are obstructed, tissue oncotic pressure rises and results in edema. This obstruction can occur as a result of tumor infiltration but most often occurs in association with cardiogenic causes of pulmonary edema. When hemodynamic alterations (changes in the movement of blood and the forces involved) in the heart increase the perfusion pressure in the pulmonary capillaries, effective lymphatic drainage is blocked.

Tissue Injury. Disruption of capillary permeability is the cause of pulmonary edema in acute lung injury associated with ARDS, inhalation of toxic gases, aspiration of gastric contents, viral infections, and uremia. In these conditions, destruction of endothelial cells or disruption of the tight junctions between them alters capillary permeability (see Figs. 6-10 and 6-11). Transfusion reactions are due to leukocyte antibodies and result in increased capillary permeability.¹⁰⁰

Clinical Manifestations

Clinical manifestations of pulmonary edema occur in stages. During the initial stage, clients may be asymptomatic or they may complain of restlessness and anxiety and the feeling that they are developing a common cold. Other signs include a persistent cough, slight dyspnea, diaphoresis, and intolerance to exercise. As fluid continues to fill the pulmonary interstitial spaces, the dyspnea becomes more acute, respirations increase in rate, and there is audible wheezing. If the edema is severe, the cough becomes productive of frothy sputum tinged with blood, giving it a pinkish hue. If the condition persists, the person becomes hypoxic, less responsive, and may lose consciousness.

MEDICAL MANAGEMENT

PREVENTION. Prevention is a key component with persons at increased risk for the development of pulmonary edema. Preventive measures may be as simple as lowering salt intake or pharmacologic treatment such as the use of digoxin and diuretics.

DIAGNOSIS. Pulmonary edema is usually recognized by its characteristic clinical presentation. Cardiogenic pulmonary edema is differentiated from noncardiac causes by the history and physical examination; an underlying cardiac abnormality can usually be detected clinically or by the electrocardiogram (ECG), chest film, or echocardiogram. A chest film may show increased vascular pattern; increased opacity of the lung, especially at the bases; and pleural effusion.

There are no specific laboratory tests diagnostic of pulmonary edema; when the condition progresses enough to cause liver involvement the physician may observe the hepatojugular reflex (positional or palpatory pressure on the liver results in distention of the jugular vein). Auscultation reveals distinct abnormal breath sounds with crackles or rales. Blood gas measurements indicate the degree of functional impairment, and sputum cultures may indicate accompanying infection.

TREATMENT. Once pulmonary edema has been diagnosed, treatment is aimed at enhancing gas exchange, reducing fluid overload, and strengthening and slowing the heartbeat. Oxygen by mask or through ventilatory support is used along with diuretics, diet, and fluid restriction to remove excess alveolar fluid.

Morphine to relieve anxiety and reduce the effort of breathing may be used for people who do not have narcotic-induced pulmonary edema. Other pharmacologic-based treatment may be used to help dilate the bronchi and increase cardiac output, strengthen contractions of the heart, and increase cardiac output.

PROGNOSIS. The prognosis depends on the underlying condition. The presence of pulmonary edema is a medical emergency requiring immediate intervention to prevent further respiratory distress and death. It is often reversible with clinical management.

SPECIAL IMPLICATIONS FOR THE THERAPIST 15-19

Pulmonary Edema

PREFERRED PRACTICE PATTERNS

6B: Impaired Aerobic Capacity/Endurance Associated with Deconditioning

6C: Impaired Ventilation, Respiration/Gas Exchange, and Aerobic Capacity/Endurance Associated with Airway Clearance Dysfunction

6F: Impaired Ventilation and Respiration/Gas Exchange Associated with Respiratory Failure

Signs and symptoms of pulmonary edema that may come to the therapist's attention include engorged neck and hand veins (because of peripheral vascular fluid overload), pitting edema of the extremities, adventitious breath sounds, and of course, the paroxysmal nocturnal dyspnea so common with this condition. One of the first signs of dyspnea may be an increased difficulty breathing when lying down, relieved by sitting up (orthopnea). Pulmonary edema can become life-threatening within minutes, requiring

immediate action by the therapist to get medical assistance for this person.

Jugular vein distention may occur with liver involvement. Positional or palpatory pressure on the liver may result in right upper quadrant or right shoulder pain, as well as jugular vein distention. The distention may be best observed with the person positioned sitting 30 to 45 degrees up from a fully supine position.

Any liver involvement requires precautions when performing any soft tissue mobilization techniques to the anterior part of the abdomen, including the diaphragm. Indirect techniques or mobilization away from the liver is recommended.

When working with a client already diagnosed with pulmonary edema, the sitting (high Fowler's) position is preferred with legs dangling over the side of the bed or plinth. This facilitates respiration and reduces venous return. Monitor for decreased respiratory drive (less than 12 breaths per minute is significant), which should be documented and reported immediately. If oxygen is being administered, the therapist monitors the oxyhemoglobin saturation levels and titrates oxygen accordingly. It may be necessary to increase oxygen levels before exercise, but respiratory rate and breathing pattern must be monitored.

The client may be taking nitroglycerin sublingually, which will further increase vasodilation and decrease ventricular preload. Monitor blood pressure closely, and observe for signs of hypotension because nitroglycerin can drop blood pressure dangerously. The therapist should consult with nursing or respiratory staff for any special considerations for each individual client.

Gradual exercise intolerance usually occurs as the dyspnea progresses. The client may comment about weight gain or difficulty fastening clothes. Check for peripheral edema in the immobile or bedridden client. In this group of people, edema can occur in the sacral hollow rather than in the feet and legs because the sacrum is the lowest place on the trunk. Care must be taken to prevent pressure ulcers in this area.

Acute Respiratory Distress Syndrome

Definition

ARDS is a form of acute respiratory failure after a systemic or pulmonary insult. It is also called *adult respiratory distress syndrome*, *shock lung*, *wet lung*, *stiff lung*, *hyaline membrane disease (adult or newborn)*, *posttraumatic lung*, or *diffuse alveolar damage (DAD)*. It is often a fatal complication of serious illness (e.g., sepsis), trauma, or major surgery.

Incidence

ARDS has only been identified within the last 40 years, affecting a reported 150,000 people per year in the United States. This figure has been challenged, and part of the reason for the uncertainty of numbers is the lack of uniform definitions for ARDS and the heterogeneity of

Box 15-9

CAUSES OF ACUTE (ADULT) RESPIRATORY DISTRESS SYNDROME*

- Severe trauma (e.g., multiple bone fractures)
- Septic shock
- Pancreatitis
- Cardiopulmonary bypass surgery
- Diffuse pulmonary infection
- Burns
- High concentrations of supplemental oxygen
- Aspiration of gastric contents
- Massive blood transfusions
- Embolism: fat, thrombus, amniotic fluid, venous, air
- Near drowning
- Radiation therapy
- Inhalation of smoke or toxic fumes
- Thrombotic thrombocytopenic purpura
- Indirect: chemical mediators released in response to systemic disorders (e.g., viral infections, pneumonia)
- Drugs (e.g., aspirin, narcotics, lidocaine, phenylbutazone, hydrochlorothiazide, most chemotherapeutic and cytotoxic agents)

*Listed in order of decreasing frequency.

diseases underlying ARDS. The incidence has increased as improvements in intensive care have allowed more people to survive the catastrophic illnesses that precede ARDS. Any age can be affected, but often young adults with traumatic injuries develop ARDS.

Etiologic and Risk Factors

ARDS occurs as a result of injury to the lung by a variety of unrelated causes; the most common are listed in Box 15-9.

Pathogenesis

Alveolocapillary units, alveolar spaces, alveolar walls, and lungs are the site of initial damage (thus the name *diffuse alveolar damage*). Although the mechanism of lung injury varies with the cause, damage to capillary endothelial cells and alveolar epithelial cells is common in ARDS regardless of cause. Both necrosis (cell death by injury and swelling) and apoptosis (programmed cell death) play a role in this syndrome.²⁸⁰ Damage to the cell inactivates surfactant and allows fluids, proteins, and blood cells to leak from the capillary bed into the pulmonary interstitium and alveoli. The increased vascular permeability and inactivation of surfactant lead to interstitial and alveolar pulmonary edema and alveolar collapse. Fibroproliferation also occurs, thickening alveolar septa and impairing respiration (gas exchange).

Pulmonary edema decreases lung compliance and impairs gas exchange. The loss of surfactant leads to atelectasis and further impairment in lung compliance and hypoxia and hypercapnia. These are only the pulmonary manifestations of what is now recognized as a more systemic process called *multiple organ dysfunction syndrome (MODS)*, formerly called *multiple organ failure (MOF)*. See Chapter 5 for a discussion of MODS.

Clinical Manifestations

The clinical presentation is relatively uniform regardless of cause and occurs within 12 to 48 hours of the initiating event. The earliest sign of ARDS is usually an increased respiratory rate characterized by shallow, rapid breathing. Pulmonary edema, atelectasis, and decreased lung compliance cause dyspnea, hyperventilation, and the changes observed on chest radiographs (Fig. 15-20).

As breathing becomes increasingly difficult, the individual may gasp for air and exhibit intercostal, clavicular, or sternal retractions and cyanosis. Unless the underlying disease is reversed rapidly, especially in the presence of sepsis (toxins in the blood), the condition quickly progresses to full-blown MODS, involving kidneys, liver, gut, CNS, and the cardiovascular system.

MEDICAL MANAGEMENT

DIAGNOSIS. Since ARDS is a collection of symptoms rather than a specific disease, differential diagnosis is through a process of diagnostic elimination. Cardiogenic pulmonary edema and bacterial pneumonia must be ruled out because there are specific treatments for those disorders. By definition, respiratory failure in the proper clinical setting (history and physical findings) constitutes ARDS. Physical examination, blood gas analysis to assess the severity of hypoxemia, microbiologic cultures to identify or exclude infection, and radiographs may be part of the diagnostic process.

TREATMENT. Specific treatment is administered for any underlying conditions (e.g., sepsis or pneumonia). Otherwise, treatment is supportive and toward prevention of complications. Supportive therapy to maintain adequate blood oxygen levels may include administration of humidified oxygen by a tight-fitting face mask, allowing for CPAP. Traditional ventilator management of ARDS emphasized normalization of blood gases and promoted high rates of further lung damage. It is now known that overdistention and cyclic inflation of injured lung can exacerbate lung injury and promote systemic inflammation. Mechanical ventilation with PEEP can minimize these effects, but evidence for protective ventilation is still lacking.¹⁵⁶⁻¹⁶⁹ A technique called "open lung maneuver," which opens all alveoli and prevents them from collapsing, shows promise.¹⁸⁴

Other strategies for protective ventilation (e.g., low-volume ventilation, permissive hypercapnia, prone positioning combined with airway pressure release ventilation [APRV], and high-frequency percussive ventilation) have reduced ARDS morbidity or mortality in some cases.^{371,429,430}

Sedation to reduce anxiety and restlessness during ventilation is required in some cases. If tachypnea, restlessness, or respirations out of phase with the ventilator (bucking) cannot be managed by sedation, pharmacologic paralysis may be induced. Other pharmacologic agents have been ineffective in altering morbidity or mortality.^{5,215} Inhaled NO is a vasodilator and may be useful in life-threatening situations but has no advantage in changing the course of ARDS.¹⁷⁹

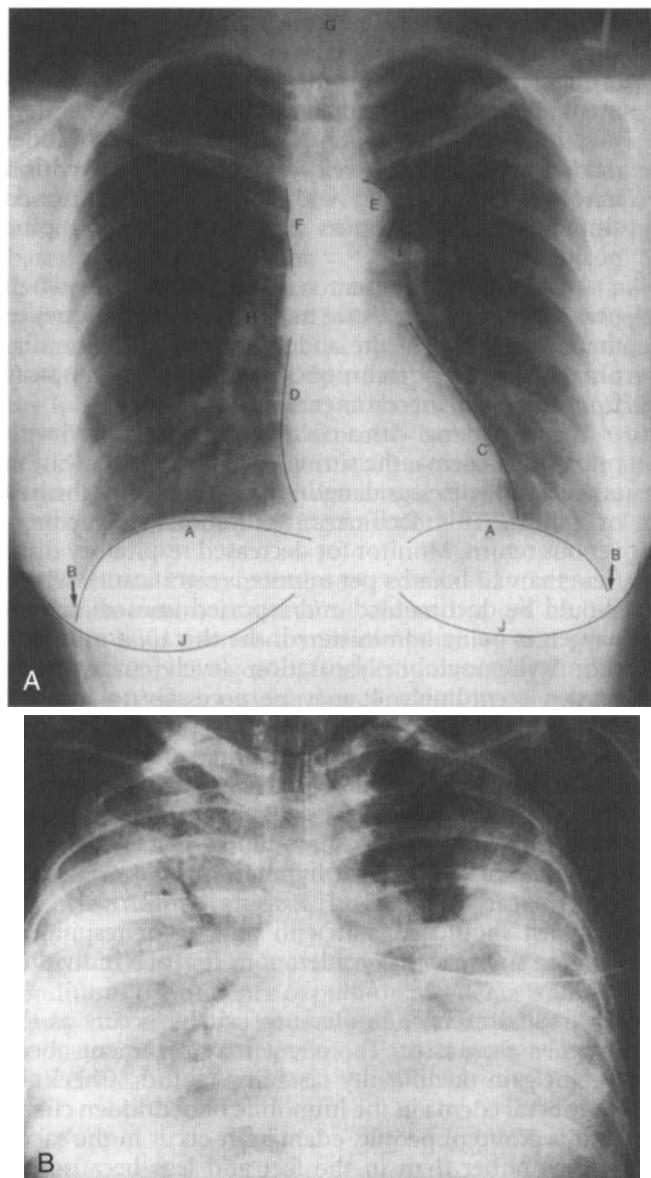


Figure 15-20

A, Normal chest film taken from a posteroanterior (PA) view. The backward L in the upper right corner is placed on the film to indicate the left side of the chest. Some anatomic structures can be seen on the x-ray study and are outlined: A, diaphragm; B, costophrenic angle; C, left ventricle; D, right atrium; E, aortic arch; F, superior vena cava; G, trachea; H, right bronchus; I, left bronchus; J, breast shadows. **B,** This chest film shows massive consolidation from pulmonary edema associated with acute (adult) respiratory distress syndrome (ARDS) after multisystem trauma. (A, from Black JM, Hokanson Hawks, J, editors: *Medical-surgical nursing*, ed 7, St Louis, 2005, WB Saunders; B, from Fraser RG, Paré JA, Paré PD, et al: *Diagnosis of diseases of the chest*, ed 3, Philadelphia, 1990, WB Saunders.)

Many studies are under way investigating new methods of prevention or treatment of ARDS, including intravascular oxygenators implanted in the vena cava to improve systemic oxygenation and extracorporeal membrane oxygenation, which fully replaces lung function.

Tracheal gas insufflation, an adjunct to mechanical ventilation, allows ventilation of the central airway while

carbon dioxide is cleared and may help reduce the amount of peak airway pressure required to maintain blood oxygen levels. High-frequency ventilation may have some benefits over conventional ventilation in children.⁴⁵⁵ No randomized trials have been conducted with this technique, and no commercial product is available.²³¹

Prophylactic immunotherapy, antibodies against endotoxin, and inhibition of various inflammatory mediators are among the possibilities being tested. (32-Agents have been proposed as treatment for reducing the pulmonary edema.²⁸⁷

PROGNOSIS. The final outcome is difficult to predict at the onset of disease, but associated multiorgan dysfunction and uncontrolled infection contribute to the mortality rate for ARDS of 50% to 70%. The major cause of death in ARDS is nonpulmonary MODS, often with sepsis. If ARDS is accompanied by sepsis, the mortality rate may reach 90%. Median survival in such cases is 2 weeks. The mortality rate increases with age, and clients older than 60 years of age have a mortality rate as high as 90%.

Most survivors are asymptomatic within a few months and have almost normal lung function 1 year after the acute illness. Lung fibrosis is the most common post-ARDS complication; the fibrosis may resolve completely; may result in respiratory dysfunction and in some cases, pulmonary hypertension; or may result in death.

Assess the client's respiratory status frequently, and observe for retractions on inspiration, the use of accessory muscles of respiration, and developing or worsening dyspnea. On auscultation, listen for adventitious (rales or rhonchi) or diminished breath sounds and report any clear, frothy sputum that may indicate pulmonary edema.

Closely monitor heart rate and blood pressure watching for arrhythmias (see Special Implications for the Therapist: Arrhythmias in Chapter 12) that may result from hypoxemia, acid-base disturbances, or electrolyte imbalance. With pulmonary artery catheterization, know the desired pulmonary capillary wedge pressure (PCWP)* level and check the readings; report any significant elevations (see Table 40-17) or changes in waveform that indicate the catheter has become wedged. Empty condensation from the tubing of the ventilator to ensure maximal oxygen delivery during therapy.

Critical illness polyneuropathy is a neurologic complication of ARDS, multiple organ failure, and other trauma. Therapists should be alert for signs of motor or sensory changes in clients with ARDS.⁶

V/Q mismatch is common in ARDS and can be altered by position changes that can facilitate lung expansion and redistribute fluid in the lungs. Oxygenation in clients with ARDS may sometimes be improved by turning them from the supine to the prone position, dramatically reducing pulmonary dead space and improving aeration.¹³⁰ This change takes the weight off (and improves ventilation in) the posterior regions of the lungs while promoting perfusion in the anterior aspects. The net result is improved oxygenation, expansion of atelectatic alveoli, and increased functional residual lung capacity.

Caregivers may be reluctant to use the prone position. The therapist can be very instrumental in providing education on proper technique and rationale. Selection criteria for this type of positioning may include individuals receiving ventilatory support at an oxygen concentration greater than 50%, with poor ABG levels and PEEP of 10 to 15 mm Hg or higher. Prone positioning should be considered if routine ventilator management has not been enough to improve the ventilatory status in an individual who is already pharmacologically immobilized or sedated (sedation is a requirement for prone positioning).

The client should be turned as far as possible on the abdomen; a 270-degree turn can improve oxygenation in some individuals, but ideally the full prone position is optimal. The person can be turned almost fully prone and supported with two or three pillows to help protect the airway, permit visualization, and allow suctioning as necessary. The better the person responds to

Continued.

* Pulmonary artery catheterization measures left ventricular pressure and diastolic pressure. PCWP can indicate left ventricular failure coinciding with the onset of pulmonary congestion and pulmonary edema. PCWP can also register insufficient volume and pressure in the left ventricle indicating hypovolemic shock in other conditions.

SPECIAL IMPLICATIONS FOR THE THERAPIST 15-20

Acute (Adult) Respiratory Distress Syndrome

PREFERRED PRACTICE PATTERNS

See also *Special Implications for the Therapist: Atelectasis* and *Special Implications for the Therapist: Pulmonary Edema* in this chapter.

6B: Impaired Aerobic Capacity/Endurance Associated with Deconditioning (pulmonary edema; progression to multi-system failure)

6C: Impaired Ventilation, Respiration/Gas Exchange, and Aerobic Capacity/Endurance Associated with Airway Clearance Dysfunction

6F: Impaired Ventilation and Respiration/Gas Exchange Associated with Respiratory Failure (pulmonary edema; atelectasis)

6G: Impaired Ventilation, Respiration/Gas Exchange, and Aerobic Capacity/Endurance Associated with Respiratory Failure in the Neonate

7A: Primary Prevention/Risk Reduction for Integumentary Disorders (pressure ulcers in the case of ventilatory support and/or prone positioning)

ARDS requires careful monitoring and supportive care; one case study even suggests 24-hour access to physical therapy intervention in acute respiratory failure as a means of avoiding invasive medical procedures. Timely physical therapy interventions improve gas exchange and reverse pathologic progression, thereby curtailing or avoiding artificial ventilation.⁴⁵²

the prone position, the longer that position can be maintained, although tolerance may build up with repeated use of the position. It is the repeated change from supine to prone positioning that redistributes pulmonary fluid and improves aeration and oxygenation overall.

Before turning, identify all invasive lines and bring them above the person's waist and over the head; lines inserted in the groin area can be moved over to the side that will remain nondependent. Taking these precautions will reduce the chances that the lines will get kinked or dislodged. One person should be in charge of the person's airway during the turning, supporting the client's head and watching the intravenous lines. Any side-port line of a pulmonary artery catheter must be monitored especially carefully because it is closest to the client and more likely to kink. When the turn is completed, this same clinician turns the client's head to one side, making sure the airway is visible and open. Extra pillows or foam/gel pads may be needed to make room for the airway and increase comfort level. The dependent shoulder should be positioned with the elbow directly to the side and the hand facing up toward the head to prevent dislocation. A pad around the mouth to absorb bronchial secretions will decrease the potential for eye contamination.

The prone position promotes secretion removal by propelling secretions toward the upper airways. It also makes it easy to perform back care and help maintain sacral and heel skin integrity. Disadvantages include the potential for facial skin irritation (especially on the forehead), loss of important vascular accesses, and difficulty performing CPR if required. Blood pressure may drop after the turn but should stabilize within a few minutes; unstable blood pressure will necessitate returning the person to the supine position. Other indicators of poor position tolerance include a decline in SaO_2 , SVo_2 , or the tidal volume over time.^{120,130}

Postoperative Respiratory Failure

Postoperative respiratory failure can result in the same pathophysiologic and clinical manifestations as ARDS but without the severe progression to MODS (see previous discussion of ARDS). Risk factors include surgical procedures of the thorax or abdomen, limited cardiac reserve, chronic renal failure, chronic hepatic disease, infection, period of hypotension during surgery, sepsis, and smoking, especially in the presence of preexisting lung disease. In the pediatric population, a difficult respiratory course may result in necrotizing enterocolitis, a postoperative gastrointestinal complication related to ischemia of the bowel. This condition occurs when oxygen depletion in the heart or brain causes blood to be shunted away from less vital organs, such as the intestine.

The most common postoperative pulmonary problems include atelectasis, pneumonia, pulmonary edema, and pulmonary emboli. Prevention of any of these prob-

lems involves frequent turning, deep breathing, humidified air to loosen secretions, antibiotics for infection as appropriate, supplemental oxygen for hypoxemia, and early ambulation.

If respiratory failure develops, mechanical ventilation may be required, and treatment is very similar to that for ARDS.

Sarcoidosis

Definition

Sarcoidosis is a systemic disease of unknown cause involving any organ that is characterized by granulomatous inflammation present diffusely throughout the body. Technically, this condition could be discussed earlier in this chapter in the Infectious and Inflammatory Diseases section but without a better sense of the underlying etiology, it remains here under diseases that affect the lung parenchyma. The granulomas consist of a collection of macrophages surrounded by lymphocytes taking a nodular form. In fact, granulomatous inflammation of the lung is present in 90% of clients with sarcoidosis. Secondary sites include the skin, eyes, liver, spleen, heart, and small bones in the hands and feet.

Incidence

Sarcoidosis occurs predominantly in the third and fourth decades (between the ages of 20 and 40 years) and has a slightly higher incidence in women than men. It is present worldwide with some interesting differences in prevalence among ethnic groups. It is three to four times more frequent in blacks than whites in the United States. Socioeconomic, environmental, and genetic factors appear to influence the occurrence.⁹⁷

Etiologic Factors and Pathogenesis

The etiologic factors and pathogenesis of sarcoidosis are unknown, but there appears to be an exaggerated cellular immune response on the part of the helper T lymphocytes to a foreign antigen whose identity remains unclear. Increasing evidence points to a triggering agent that may be genetic, infectious (bacterial or viral), immunologic, or toxic. Abnormalities of immune function, as well as autoantibody production, including rheumatoid factor and antinuclear antibodies, are seen in sarcoidosis and in connective tissue diseases, suggesting a common immunopathogenetic mechanism.

IFN- γ , TNF, and IL-12 and -18 all have a part in the granulomatous process.³²⁴ A series of interactions between the excessive accumulation of T lymphocytes and monocytes and macrophages leads to the formation of noncaseating (i.e., do not undergo necrotic degeneration) granulomas in the lung and other organs characteristic of the disease. Granuloma formation may regress with therapy or as a result of the disease's natural course but may also progress to fibrosis and restrictive lung disease.

Clinical Manifestations

Sarcoidosis can affect any organ, including bones, joints, muscles, and vessels. Lungs and thoracic lymph nodes are most often involved with acute or insidious respiratory

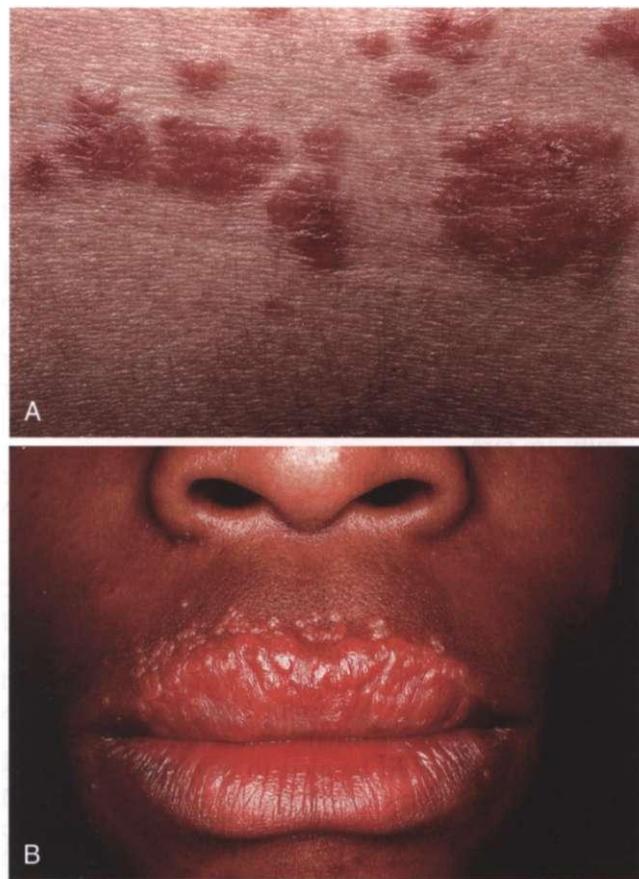


Figure 15-21

Sarcoidosis. **A**, Cutaneous sarcoidosis usually consists of papules and plaques with a typical reddish-brown color. **B**, Lesions often favor the lips and perioral region. (From Bolognia JL, Jorizzo JL, Rapini RP: *Dermatology*, St Louis, 2003, Mosby. Courtesy Jean Bolognia, MD. Used with permission.)

problems sometimes accompanied by symptoms affecting the skin, eyes, or other organs. The diverse manifestations of this disorder lend support to the hypothesis that sarcoidosis has more than one cause. The clinical impact of sarcoidosis is directly related to the extent of granulomatous inflammation and its effect on the function of vital organs.

Pulmonary sarcoidosis has a variable natural course from an asymptomatic state to a progressive life-threatening condition. Signs and symptoms may develop over a period of a few weeks to a few months and include dyspnea, cough, fever, malaise, weight loss, skin lesions (Fig. 15-21), and erythema nodosum (multiple, tender, nonulcerating nodules). This condition may be entirely asymptomatic, presenting with abnormal findings on routine chest radiographs. Respiratory symptoms of dry cough and dyspnea without constitutional symptoms (symptoms of systemic illness, including fatigue, weakness, malaise, weight loss, sweating, and fever) occur in over one-half of all people with sarcoidosis, and up to 15% develop progressive fibrosis. Chest pain, hemoptysis, or pneumothorax may be present.

Sarcoidosis may present with extrapulmonary symptoms referable to bone marrow, skin, eyes, cranial nerves

Box 15-10

CLINICAL MANIFESTATIONS OF SARCOIDOSIS

Pulmonary

Asymptomatic with abnormal chest film
Gradually progressive cough and shortness of breath (SOB)
Pulmonary fibrosis with pulmonary insufficiency
Laryngeal and endobronchial obstruction

Extrapulmonary

Löfgren's syndrome: fever, arthralgias, bilateral hilar adenopathy, erythema nodosum
Heerfordt's syndrome (uveoparotid fever): fever, swelling of parotid gland and uveal tracts, seventh cranial nerve palsy
Erythema nodosum
Peripheral lymphadenopathy/splenomegaly
Lymphoma
Eyes: excessive tearing, swelling, uveitis, iritis, glaucoma, cataracts
Skin: nodules or skin plaques (see Fig. 15-21); skin cancer
Central nervous system: cranial nerve palsies, subacute meningitis, diabetes insipidus
Joints: polyarticular and monarticular arthritis
Bones: punched-out cystic lesions in phalangeal and metacarpal bones
Heart: paroxysmal arrhythmias, conduction disturbances, congestive heart failure, sudden death
Kidney: hypercalcemia with nephrocalcinosis or nephrolithiasis
Liver: granulomatous hepatitis, liver cancer

or peripheral nerves (neurosarcoidosis), liver, or heart (Box 15-10). Neurosarcoidosis is an uncommon but severe and sometimes life-threatening manifestation of sarcoidosis occurring in 5% to 15% of cases. Sarcoidosis appears to be associated with a significantly increased risk for cancer in affected organs (e.g., skin, liver, lymphoma, or lung). Chronic inflammation is the mediator of this risk.²²

MEDICAL MANAGEMENT

DIAGNOSIS. There is no specific test other than history for sarcoidosis so diagnosis is based on clinical examination, radiographic, CT, pulmonary function and laboratory test findings, and biopsy of easily accessible granulomas (e.g., skin lesions, salivary gland, or palpable lymph nodes). When lung involvement is suspected, further testing may be required and new imaging techniques improve detection. Other granulomatous diseases (e.g., TB, berylliosis, lymphoma, carcinoma, or fungal disease) must be ruled out.

CNS involvement in sarcoidosis poses a difficult diagnostic problem. Although neurologic involvement may occur long before the onset of symptoms, contrast-enhanced CT does not always reveal parenchymal and meningeal involvement.

TREATMENT. Treatment may not be required, especially in those clients who are asymptomatic. Short-term (less than 6 months) use of inhaled steroids may improve symptoms especially in people who mainly have cough. The long-term use of corticosteroids is the treatment of

choice for those clients who have impaired lung function with pulmonary granulomas. Corticosteroids are quite effective in reducing the acute granulomatous inflammation as seen on radiograph, but their efficacy in improving lung function and altering the long-term prognosis is unproven. Oral steroids may be beneficial for stage 2 and 3 disease.^{324,333}

Other immunosuppressant and cytotoxic agents, such as methotrexate, chloroquine, cyclosporine, indomethacin, and azathioprine, have been used for symptomatic skin and eye involvement but have not been shown to be effective in pulmonary sarcoidosis.^{48,334} New drugs targeting TNF- α are being developed.

People with sarcoidosis who smoke are encouraged to quit because smoking aggravates impaired lung function and promotes osteoporosis. Management of osteoporosis in this population requires special attention because there is often an underlying disorder in calcium metabolism that results in hypercalciuria and hypercalcemia.

Prolonged exposure to direct sunlight should be avoided because vitamin D aids absorption of calcium, which can contribute to elevated serum and urinary calcium levels and the formation of kidney stones. Bronchoscopy may be required if fibrosis or swelling leads to stenosis of the airways.²⁵⁸

In cases of end-stage sarcoidosis, lung transplantation has been proven successful.²⁵⁸ Selection of clients with pulmonary sarcoidosis for transplantation requires that medical therapy, including the use of corticosteroids and alternative medications, has been exhausted and that other contraindicated variables are not present (see the section on Lung Transplantation in Chapter 21). Sarcoidosis frequently recurs in the allograft but rarely causes symptoms or pulmonary dysfunction.²³⁰

PROGNOSIS. The prognosis is usually favorable, with complete resolution of symptoms and chest radiographic changes within 1 to 2 years. Most clients do not manifest clinically significant sequelae. However, because sarcoidosis is a multisystem disease that can cause complex problems, it can have a variable prognosis ranging from spontaneous remissions to progressive lung disease with pulmonary fibrosis in active sarcoidosis. In such cases, respiratory insufficiency and cor pulmonale may eventually occur. In 65% to 70% of cases there are no residual manifestations, 20% are left with permanent lung or ocular changes, and 10% of all cases die. Active sarcoidosis responds well to the administration of corticosteroids.

SPECIAL IMPLICATIONS FOR THE THERAPIST 15-21

Sarcoidosis

PREFERRED PRACTICE PATTERNS

4A: Primary Prevention/Risk Reduction for Skeletal Demineralization (prolonged use of corticosteroids)

6E: Impaired Ventilation and Respiration/Gas Exchange Associated with Ventilatory Pump Dysfunction or Failure (progressive pulmonary fibrosis)

6F: Impaired Ventilation and Respiration/Gas Exchange Associated with Respiratory Failure (hemothorax)

6H: Impaired Circulation and Anthropometric Dimensions Associated with Lymphatic System Disorders

In the case of extrapulmonary manifestations of sarcoidosis (e.g., skin, cranial or peripheral nerve, heart involvement), other practice patterns may be identified.

There is a distinct arthritic component associated with sarcoidosis, variously reported in 10% to 35% of people who develop extrapulmonary involvement. The knees or ankles are the most common sites of acute arthritis. Distribution of joint involvement is usually polyarticular and symmetric, and the arthritis is commonly self-limiting after several weeks or months. Occasionally, the arthritis is recurrent or chronic, but even then, joint destruction and deformity are rare.

Treatment of arthritis in sarcoidosis is usually as for any other form of arthritis. The arthritic symptoms may develop early as the first manifestation of the disease or late in the disease and are usually accompanied by erythema nodosum. When further complicated by bilateral hilar adenopathy (enlargement of hilum or roots of the lung where the main bronchi enter the lungs), this triad of symptoms is called Lofgren's syndrome. Recurrent Lofgren's syndrome is extremely rare and is usually self-limiting.

Therapists should be alert to any presenting signs or symptoms of increased disease activity associated with sarcoidosis since medical vigilance with attention to new symptoms is important in the management of sarcoidosis. This disease presents in many and diverse patterns, but observe especially for exertional dyspnea that progresses to dyspnea at rest, chest pain, joint swelling, or increased fatigue and malaise, reducing the client's functional level or ability to participate in therapy. Muscle involvement and bone involvement are frequently underdiagnosed. Symptoms of muscle weakness, aches, tenderness, and fatigue, often accompanied by neurogenic atrophy, may indicate sarcoid myositis.²⁹

Cranial nerve palsies (especially facial palsy), multiple mononeuropathy, and less commonly, symmetric polyneuropathy may all occur. Symmetric polyneuropathy can affect either motor or sensory fibers solely or both disproportionately. An unusual combination of neurologic deficits affecting the CNS or peripheral nerves (or both) suggests sarcoidosis and should be evaluated medically. Improvement of neurologic function may occur with the use of corticosteroids.

For clients receiving steroid therapy, increased side effects of the medication should be reported to the physician. For example, long-term use of steroids lowers resistance to infection, may induce diabetes and myopathy, and is associated with weight gain, loss of potassium in the urine, and gastric irritation (see the section on Corticosteroids in Chapter 5 and Tables 5-4 and 5-5).

Table 15-12 Characteristics of Lung Cancer

Tumor Type	Incidence	Growth Rate	Metastasis	Treatment
Small Cell Lung Cancer (SCLC)				
Small cell (oat cell)	20%-25%	Very rapid	Very early; to mediastinum or distal area of lung	Combination chemotherapy; surgical resectability is poor
Non-Small Cell Lung Cancer (NSCLC)				
Squamous cell (epidermal)	17% (greater in men)	Slow	Localized metastasis not common or occurs late, usually to hilar lymph nodes, adrenals, liver	Surgical resectability is good if stage I or II. Chemotherapy and radiation therapy for all stages are under continued investigation.
Adenocarcinoma	35%-40%*	Slow to moderate	Early; metastasis throughout lung and brain or to other organs	Surgical resectability is good if localized stage I or II. Chemotherapy or chemoradiation and surgery may be combined for stage III.
Large cell (anaplastic)	10%-15%	Rapid	Early and widespread metastasis to kidney, liver, adrenals	Surgical resectability is poor if involvement is widespread; better prognosis if stage I or II. Chemotherapy of limited use, radiation therapy is palliative.

Statistical data from the U.S. Department of Health Services. Publication No. 96-691. Washington, D.C., 1996.

*A major histologic change has occurred over the last 3 decades as the most common cell type has shifted from squamous cell to adenocarcinoma. This shift appears to be the result of physiochemical changes in the late twentieth century smoke (e.g., increased levels of tobacco-specific nitrosamines).²³

Lung Cancer Overview

Lung cancer, a malignancy of the epithelium of the respiratory tract, is the most frequent cause of cancer death in the United States. The term *lung cancer*, also known as bronchogenic carcinoma, excludes other pulmonary tumors such as sarcomas, lymphomas, blastomas, hematomas, and mesotheliomas.

Types of Lung Cancer

At least a dozen different types of tumors are included under the broad heading of lung cancer. Clinically, lung cancers are classified as small cell lung cancer (SCLC), or 20% of all lung cancers, and non-SCLC (NSCLC), or 80% of all lung cancers. Within these two broad categories, there are four major types of primary malignant lung tumors: SCLC includes small cell carcinoma (oat cell carcinoma); NSCLC includes squamous cell carcinoma, adenocarcinoma, and large cell carcinoma. The characteristics of these four lung cancers are summarized in Table 15-12. *Adenocarcinoma*, the most common form of lung cancer in the United States, tends to arise in the periphery, usually in the upper lobes at different levels of the bronchial tree. An individual tumor may reflect the cell structure of any part of the respiratory mucosa from the large bronchi to the smallest bronchioles. Because of this, adenocarcinoma refers to a heterogeneous group of neoplasms that have in common the formation of glandlike structures. Adenocarcinoma is further subdivided into four categories: acinar, papillary, bronchioloalveolar, and solid carcinoma. Increasing incidence of adenocarcinoma cell type lung cancer is currently attributed to changes in smoking patterns (e.g., deeper and more intense inhalation) in response to reduced tar and nicotine in cigarettes. Presumably, the excess volume inhaled to satisfy addictive needs for nicotine delivers increased amounts of car-

cinogens and toxins to the peripheral areas of the lungs.³⁹⁹

Large cell carcinomas are so poorly differentiated that they cannot be classified with the other three categories above and require special diagnostic testing procedures to differentiate from other lung pathologic conditions.

Incidence

Lung cancer remains the leading cause of cancer death in the United States (estimated 167,050 deaths in 2006) and one of the world's leading causes of preventable death.²²¹ More people die of lung cancer than of colon, breast, and prostate cancer combined. In 1987, lung cancer overtook breast cancer to become the most common cause of death from cancer among women in the United States.

Among men and women, both incidence and mortality have slowed with the decline in cigarette smoking. Smoking among adolescents peaked in 1996 and has been on the decline, yet a survey in 2002 showed that 9.8% of middle school students and 22.5% of high school students reported that they currently smoke cigarettes.²⁷⁸ Deaths from lung cancer increase at ages 35 to 44 years, with a sharp increase between ages 45 and 55 years. Incidence continues to increase up until age 74 years, after which the incidence levels off and decreases among the very old. There are differences in mortality rates for racial and ethnic groups.

Black males have the highest death rate and Asian/Pacific Islanders, American Indian/Alaska natives, and Hispanic males have the lowest death rate. Among women, blacks and whites have the highest mortality, whereas Asian/Pacific Islander and Hispanic females have the lowest death rate from lung cancer.²²⁰ Women taking hormone replacement therapy have an earlier onset and greater mortality with lung cancer.¹⁵⁰

Risk Factors

Contributions to lung cancer include environment (smoking, secondhand smoke, occupational exposure, or air pollution), nutrition, genetic factors (enzymes for carcinogen metabolism, enzymes that detoxify, and the capacity to repair DNA damage).²⁴⁴ Age, family history, and medical history, especially lung disease, also influence the occurrence, morbidity, and mortality.

Cigarette Smoking. Cigarette smoking (more than 20 cigarettes per day) remains the greatest risk factor for lung cancer; 85% to 90% of all lung cancers occur in smokers, although remarkably, fewer than 20% of cigarette smokers develop lung cancer. The relative risk of lung cancer increases with the number of cigarettes smoked per day and the number of years of smoking history. The people at highest risk began smoking in their teens, inhale deeply, and smoke at least one-half pack per day.

The number of pack years is calculated by multiplying the packs of cigarettes consumed per day by the number of years of smoking. Lung cancer increases proportionately to the history of packs smoked per year and also depends on other variables such as time of breath holding, amount of cigarette smoked, and size of puff. The risk for dying of lung cancer is 20 times higher among people who smoke two or more packs of cigarettes per day than among those who do not smoke.

Smoking is a major cause of cancers of the oropharynx and bladder among women. Evidence is also strong that women who smoke have increased risks for liver, colorectal, and cervical cancer and cancers of the pancreas and kidney. There is also an increased risk for stroke, death from ruptured abdominal aortic aneurysm, and peripheral vascular disease among smokers compared to nonsmokers.¹⁹⁵ For other effects of smoking see the section on Tobacco in Chapter 3.

Former smokers have about one-half the risk for dying from lung cancer than do current smokers (see Table 3-4). Compared with current smokers, the risk for lung and bronchus cancer among former smokers declines as the duration of abstinence lengthens, but it takes over 20 years to reach the risk level of people who never smoked.²⁴⁴ These statistics support the fact that lung cancer is the most preventable of all cancers. The elimination of cigarette smoking would virtually eliminate SCLC. Smoking cessation also appears to slow the rate of progression of carotid atherosclerosis and other vascular disease.

There are approximately 50 known carcinogens and promoting substances found in tobacco smoke; the major causal agents of lung cancer are the polynuclear aromatic hydrocarbons (PAHs) and tobacco-specific N-nitrosamines (nicotine). Tobacco smoking also results in increased exposure to ethylene oxide, aromatic amines, and other agents that cause damage to DNA.³⁴⁰ For this reason, the risk of lung cancer is increased in a smoker who is also exposed to other carcinogenic agents, such as radioactive isotopes, polycyclic aromatic hydrocarbons and arsenicals, vinyl chloride, metallurgic ores, and mustard gas.

Marijuana. Marijuana contains many of the same organic and inorganic compounds that are carcinogens, co-carcinogens, or tumor promoters found in tobacco

smoke. Marijuana produces inflammation, edema, and cell injury in the tracheobronchial mucosa of smokers and contributes to oxidative stress, which is a precursor for DNA mutations.⁴¹⁰ However, cannabinoids modulate and minimize free radical production and inhibit tumor angiogenesis. In addition, cannabinoid receptors are not found in the lung epithelial cells.²⁹⁵ Cannabinoids have been shown to inhibit certain breast, lung, and brain cancers,²⁴⁶ although other studies have shown an increase in head, neck, and lung cancers.¹⁹⁰ Unfortunately, most studies do not examine the magnitude of exposure and concurrent tobacco use.

The risk of marijuana smoking does not appear to approach that of smoking tobacco and any increased risk may be associated with the route of delivery (the heat and particulate irritation of smoking) rather than the drug itself. Further studies are needed.

Environmental Tobacco Smoke. In 1992, the U.S. EPA declared secondhand smoke or ETS to be a group A human carcinogen. ETS increases the relative risk for lung cancer about 1.5-fold and there are 3000 lung cancer deaths each year from ETS.⁸¹ This exposure increases the risk for the children and partners of smokers and becomes an occupational hazard in individuals working in bars, restaurants, or other places that are not smoke-free. See previous section on Environmental Tobacco Smoke in this chapter.

Occupational Exposure. Studies on whether occupational factors increase the risk of cancer development in the nonsmoker are limited in number but confirm that certain occupational exposures are associated with an increased risk for lung cancer among both male and female nonsmokers.³⁴⁵ The inhalation of asbestos fibers is associated with higher cancer risks for both smokers and nonsmokers, although the rate is considerably higher for smokers.

The rate of lung cancer in people who live in urban areas is 2.3 times greater than that of those living in rural areas, possibly implicating air pollution as a risk factor in lung cancer. The exact role of air pollution is still unknown, but carcinogens with known genotoxicity continue to be released into outdoor air from industrial sources, power plants, and motor vehicles; epidemiologic research provides evidence for an association between air pollution and lung cancer.^{91,433}

Indoor exposure to radon, which is a colorless, odorless gas that is a product of uranium and radium produced from the decomposition of rocks and soil, is a known carcinogen and the second leading cause of lung cancer. Concentrations vary geographically (more in the northern United States), and radon gas levels are highest in basements, nearest the soil.¹⁴¹ Other sources of radon exposure include radioactive waste and underground mines; exposure to tobacco smoke multiplies the risk of concurrent exposure to radon.

Other occupational or environmental risk factors associated with lung cancer include diesel exhaust, benzopyrenes, silica, formaldehyde, copper, chromium, cadmium, arsenic, alkylating compounds, sulfur dioxide, and ionizing radiation.

Previous Lung Disease. The presence of other lung diseases, such as pulmonary fibrosis, scleroderma, and

sarcoidosis, may increase the risk of developing lung cancer. COPD or fibrosis of the lungs inhibits the clearance of carcinogens from the lungs, thereby increasing the risk of alteration of DNA with resultant malignant cell growth.

Nutrition. Other risk factors may include low consumption of fruits and vegetables, reduced physical activity, increased dietary fat (especially diets high in saturated or animal fat and cholesterol), and high alcohol intake. A recent prospective study demonstrated positive effects of fruit consumption, but not of vegetables.¹⁷¹

Studies have shown no beneficial effect of vitamin E (α -tocopherol), beta-carotene, and retinol, and several studies have determined that beta-carotene supplementation in smokers increases the risk for lung cancer. The mechanism for this carcinogenic action remains unknown.³⁶⁷

Genetic Susceptibility. Several published studies suggest that lung cancer can aggregate in some families, and it has been hypothesized that the defect in the body's ability to defend against the carcinogens in tobacco smoke may be inherited.⁴⁵³ A first-degree smoking relative of an individual with lung cancer has an increased risk of developing lung cancer. This predilection may be due to a genetic predisposition, but the trait (lung cancer) may be expressed only in the presence of its major predisposing factor (i.e., tobacco). Carcinogenic chemicals may induce genomic instability either directly or indirectly through inflammatory processes in the lung epithelial cells.

Lung cancer is used as a model for the study of the interplay between genetic factors and environmental exposure since the primary etiology is well established. Developments in molecular biology have led to the identification of biologic markers that may increase predisposition to smoking-related carcinogenesis. In the future, lung cancer screening may be possible by using specific biomarkers.²⁴³

Pathogenesis

As mentioned, there is a clear relationship between cigarette smoking and the development of SCLC. The effects of smoking include structural, functional, malignant, and toxic changes. DNA-mutating agents in cigarettes produce alterations in both oncogenes and tumor suppressor genes, as well as genes that detoxify and assist with DNA repair. Normal polymorphism (variations in genes) also plays a role in the development of or resistance to cancer.

Understanding of the molecular pathology of lung cancer is advancing rapidly, with several specific genes and chromosomal regions being identified. Lung cancer appears to require many mutations in both dominant and recessive oncogenes before they become invasive. Several genetic and epigenetic changes are common to all lung cancer histologic types, whereas others appear to be tumor-type specific. The sequence of changes remains unknown.²⁴⁴ There appears to be an interaction between estrogen receptors and epidermal growth factor in the lung that plays a role in women's susceptibility to lung

¹²⁴ cancer.

All lung cancers are thought to arise from a common bronchial precursor cell, with differentiation then proceeding along various histologic pathways from poorly differentiated small cell cancer to the more intermediate undifferentiated large cell tumors, to the more differentiated adenocarcinomas and squamous cell tumors. Perhaps the histologic changes (thickening of bronchial epithelium, damage to and loss of protective cilia, mucous gland hypertrophy and hypersecretion of mucus, and alveolar cell rupture) that occur more frequently in long-term smokers than nonsmokers predispose the lungs to changes. This results in a multistep process involving the development of hyperplasia, metaplasia, dysplasia, carcinoma in situ, invasive carcinoma, and metastatic carcinoma. As the details of the carcinogenic process are unraveled, one goal is to identify intermediate (preneoplastic) markers of exposure and inherent predisposition that will help assess the risk of lung cancer and allow for early detection.

Small Cell Lung Cancer. When the cells become so dense that there is almost no cytoplasm present and the cells are compressed into an ovoid mass, the tumor is called small cell carcinoma or oat cell carcinoma. SCLC develops most often in the bronchial submucosa, the layer of tissue beneath the epithelium, and tends to be located centrally, most often near the hilum of the lung. These tumors can produce hormones that stimulate their own growth and the rapid growth of neighboring cells causing bronchial obstruction and pneumonia with early intralymphatic invasion. Lymphatic and distant metastases are usually present at the time of diagnosis.

Non-Small Cell Lung Cancer. Squamous cell carcinomas arise in the central portion of the lung near the hilum, projecting into the major or segmental bronchi. Although these tumors tend to grow rapidly, they often remain located within the thoracic cavity, making curative treatment more likely compared with other NSCLC types. These tumors may be difficult to differentiate from TB or an abscess because they often undergo central cavitation (formation of a cavity or hollow space).

Clinical Manifestations

Symptoms of early stage localized lung cancer do not differ much from pulmonary symptoms associated with chronic smoking (e.g., cough, dyspnea, and sputum production), so the person does not seek medical attention. Women with lung cancer have lower incidence or severity of COPD, so symptoms may be fewer and diagnosis delayed.²⁶² Symptoms may depend on the location within the pulmonary system, whether centrally located, peripheral, or in the apices of the lungs. Systemic symptoms, such as anorexia, fatigue, weakness, and weight loss, are common, especially with advanced disease (metastases) and associated with poor prognosis.³⁶

Bone pain associated with bone metastasis is common; other symptoms resulting from metastases depend on the site of involvement (e.g., hepatomegaly and jaundice with liver metastasis and seizures, headaches, confusion, or focal neurologic signs with brain metastasis). Other signs and symptoms of disease include recurring bronchitis or pneumonia; productive cough with hemoptysis; wheezing; poorly defined persistent chest pain; difficulty

swallowing or hoarseness; orthopnea; nerve involvement (phrenic, laryngeal, brachial plexus, or sympathetic ganglion); and vascular (superior vena cava), cardiac, and esophageal compression as a result of local tumor invasion.^{36,142,347}

Small Cell Lung Cancer. Signs and symptoms of SCLC depend on the size and location of the tumor and the presence and extent of metastases. Because SCLCs most commonly arise in the central endobronchial location in people who are almost exclusively long-term smokers, typical symptoms are a result of obstructed air flow and consist of persistent, new, or changing cough, dyspnea, stridor, wheezing, hemoptysis, and chest pain.⁶¹

Intercostal retractions on inspiration and bulging intercostal spaces on expiration indicate obstruction. As obstruction increases, bronchopulmonary infection (obstructive pneumonitis) often occurs distal to the obstruction. Centrally located tumors cause chest pain with perivascular nerve or peribronchial involvement that can refer pain to the shoulder, scapula, upper back, or arm.

SCLC is (more often than NSCLC) associated with several paraneoplastic syndromes, including ectopic hormone production (adrenocorticotrophic hormone [ACTH]) with Cushing's syndrome, production of hormones by tumors of nonendocrine origin, or production of an inappropriate hormone (antidiuretic hormone) by an endocrine gland. Neuroendocrine cells containing neurosecretory granules exist throughout the tracheobronchial tree. This phenomenon is important because resulting signs and symptoms may be the first manifestation of underlying cancer. See Special Implications for the Therapist: Lung Cancer in this section; see also the section on Paraneoplastic Syndromes in Chapter 9.

Non-Small Cell Lung Cancer. The less common peripheral pulmonary tumors (large cell) often do not produce signs or symptoms until disease progression produces localized, sharp, and severe pleural pain increased on inspiration, limiting lung expansion; cough and dyspnea are present. Pleural effusion may develop and limit lung expansion even more.

Tumors in the apex of the lung, called *Pancoast's tumors*, occur both in squamous cell and adenocarcinomatous cancers. Symptoms do not occur until the tumors invade the brachial plexus (see Special Implications for the Therapist: Lung Cancer in this section). Destruction of the first and second ribs can occur. Paralysis, elevation of the hemidiaphragm, and dyspnea secondary to phrenic nerve involvement can also occur.

Other manifestations may include digital clubbing, skin changes, joint swelling associated with hypertrophic pulmonary osteoarthropathy (see previous discussion of this condition in the section on Cystic Fibrosis), decreased or absent breath sounds on auscultation, or pleural rub (inflammatory response to invading tumor).

Metastasis

The rich supply of blood vessels and lymphatics in the lungs allows the disease to metastasize rapidly.^{60b} Lung cancers spread by direct extension, lymphatic invasion, and blood-borne metastases. Tumors spread by direct

invasion in the bronchus of origin; others may invade the bronchial wall and circle and obstruct the airway. Intrapulmonary spread may lead to compression of lung structures other than airways such as blood or lymph vessels, alveoli, and nerves.

Direct extension through the pleura can result in spread over the surface of the lung, chest wall, or diaphragm. Carcinomas of the lung of all types metastasize most frequently to the regional lymph nodes, particularly the hilar and mediastinal nodes. Supraclavicular, cervical, and abdominal channels may also be invaded. Tumors originating in the lower lobes tend to spread through the lymph channels.

Lung cancer generally has a widespread pattern of hematogenous metastases. This is caused by the invasion of the pulmonary vascular system. After tumor cells enter the pulmonary venous system, they can be carried through the heart and disseminated systemically. Tumor emboli can become lodged in areas of organ systems where vessels become too narrow for their passage or where blood flow is reduced.

The most frequent site of extranodal metastases is the adrenal gland. Lung cancer can also metastasize to the brain, bone, and liver before presenting symptomatically. Brain metastases constitute nearly one-third of all observed recurrences in people with resected NSCLC of the adenocarcinoma type. Metastases to the brain usually result in CNS symptoms of confusion, gait disturbances, headaches, or personality changes.

Tumor spread intrathoracically to the mediastinum and beyond can produce superior vena cava (SVC) syndrome with swelling of the face, neck, and arms and neck and thoracic vein distention more common in the early morning or after being recumbent for several hours. SVC syndrome is usually a sign of advanced disease. If left untreated, SVC syndrome results in cerebral edema and possible death. Increased intracranial pressure, headaches, dizziness, visual disturbances, and alteration in mental status are signs of progressive compression. Cardiac metastasis can occur and results in arrhythmias, congestive heart failure, and pericardial tamponade.

As a form of secondary malignancy, the lungs are the most frequent site of metastases from other types of cancer. Any tumor cell dislodged from a primary neoplasm can find its way into the circulation or lymphatics, which are filtered by the lungs. Carcinomas of the kidney, breast, pancreas, colon, and uterus are especially likely to metastasize to the lungs.

MEDICAL MANAGEMENT

PREVENTION. Prevention is the key to eliminating or at least reducing the need for treatment of lung cancer. Targeted state and federal antitobacco programs have contributed to significant drops in cigarette consumption.

Healthy People 2010 has set a goal of reducing the lung cancer mortality rate from 57.6 per 100,000 population (1998 figure) to 44.9 per 100,000 population, representing a 22% improvement. *Healthy People 2010* has outlined a systematic approach to health improvement that includes methods for lung cancer prevention through prevention of tobacco use and tobacco addiction in all age, ethnic, and socioeconomic groups. *Healthy*

People 2010 is available on-line at www.health.gov/healthypeople/.

Other strategies for lung cancer prevention have included chemoprevention (i.e., administration of agents, usually drugs but also nutraceuticals or nutritional supplements, before the diagnosis of invasive cancer to absorb free oxygen radicals and to block or reverse carcinogenesis), adopting a diet high in fruits and vegetables, and reduction of ETS.

Although significantly lower levels of vitamin C and E are found in people with lung cancer, a review of eight prospective studies show no reduction of cancer risk from diet or vitamin supplements.^{4,86} Reduction or prevention of occupational exposure may be achieved through a combination of approaches, including toxicologic testing of new compounds before marketing them, application of industrial hygiene techniques, industry regulation, and epidemiologic surveillance.

DIAGNOSIS. Many lung cancers are detected on routine chest film in clients presenting for unrelated medical conditions without pulmonary symptoms, although 90% of the people with lung cancer are symptomatic at diagnosis. Unfortunately, chest radiograph is not sensitive enough to show tumors when they are small and operable and routine screening is not supported by the evidence.

A chest scan called low-dose spiral CT (LDCT) detects tumors too small to be seen on radiographs. There are some concerns with the LDCT (e.g., cost, false-positive findings, unnecessary biopsies of small benign tumors), although the availability of this type of diagnostic procedure may bring about annual screening for lung cancer for those at risk. However, mass screening for lung cancer with CT is not currently advocated because to date no randomized population trial has demonstrated a significant reduction in lung carcinoma mortality as a result of any screening intervention.^{25,274}

Lung imaging fluorescence endoscope (LIFE) can literally light up cancerous (and preinvasive cancerous) cells using intravenously administered radioactive tracer that attaches to these cells. When the person is imaged with a special camera, the cancer cells show up as bright spots. New endoscopy techniques that use white-light color images and tissue autofluorescence images have been used for early detection of lung lesions.⁴⁶⁴

Without the LDCT chest scan, diagnosis is usually established on sputum cytology for participants in a lung cancer detection program or on bronchoscopy in persons presenting with hemoptysis and a normal chest film. Localization of occult lung tumors is done by fiberoptic bronchoscopy that allows examination to the sixth or seventh branch of the bronchial tree. CT scans are routinely done to assess for metastasis to the mediastinum, liver, and adrenals. Other routine procedures include evaluation of serum chemistry values to look for electrolyte abnormalities (see Chapter 5), especially those associated with paraneoplastic syndrome (see Chapter 9), evaluation of renal and hepatic function, hematologic profiles, and ECG analysis.

At this point, there is no evidence to support sputum-based cellular diagnostics for cancer screening. New tests

under development include the electronic nose that uses "smell prints" to identify individuals with cancer; blood tests for specific elevated proteins in serum; and testing for abnormal DNA in sputum.²²⁶

STAGING. NSCLC of the lung is staged at the time of initial presentation and used to estimate the person's prognosis and to determine intervention. The tumor, nodes, metastasis (TNM) staging system is used (see explanation in Chapter 9) and provides the basis for selecting cases for resection. Tumors confined to the lung without any metastases, regional or distant, are classified as stage I, and tumors associated with only hilar or peribronchial lymph node involvement (N1) are classified as stage II. Locally advanced tumors with mediastinal or cervical lymph node metastases and those with extension to the chest wall, mediastinum, diaphragm, or carina are classified as stage III tumors. Finally, tumors presenting with distant metastases (M1) are classified as stage IV.

SCLC is usually not considered a surgical disease requiring staging but rather is designated as limited or extensive disease. Limited disease is defined by involvement of one lung, the mediastinum, and either or both ipsilateral and contralateral supraclavicular lymph nodes (i.e., disease that can be encompassed in a single radiation therapy port). Spread beyond the lung, mediastinum, and supraclavicular lymph nodes is considered extensive disease.

TREATMENT. Awareness of the influence of growth factors, oncogenes, and tumor suppressor genes, as well as signal transduction and angiogenesis pathways on the natural history of cancer cells, has led to attempts to develop new molecular-based strategies directed at interrupting tumor cell growth. Treatments using monoclonal antibodies, inhibitors, antiangiogenic substances, and gene transfer and alteration are still under investigation.⁶⁸

In the meantime, current treatment with new agents used in combination, as well as when combined with radiation and hormones, has led to an improved response rate in the treatment of some lung cancers.⁶⁷ Photodynamic therapy is used successfully with tumors in the airways. Photochemical sensitization of the tumor precedes laser therapy that causes necrosis of the cancer.³⁰⁵ Chemotherapy approaches are numerous and address different targets. Newer agents that inhibit epidermal growth factor receptors are showing promise alone and in combination with other drugs.⁴²⁰

Small Cell Lung Cancer. Surgical resection in the treatment of SCLC is not usually considered and when used, seems most effective for clients in the early stages of SCLC, after combination chemotherapy, which is the cornerstone of treatment for all stages of this disease, resulting in high response rates (65% to 85%).²³⁸ For clients with more advanced disease, surgery causes unnecessary risk and stress, with no valid benefits. Laser therapy is a surgical treatment used when the tumor mass is causing nonresectable bronchial obstructions and when accessible by bronchoscope.

SCLC is quite sensitive to radiation therapy, which, in conjunction with chemotherapy, is now routinely administered to those with limited disease.⁴² Individuals with

extensive disease usually receive combination chemotherapy initially. Other treatment options depend on the clinical manifestations and client needs (e.g., radiation therapy may be administered to the brain, bone, spine, or other sites of metastasis). In the future, tumor growth may be halted by replacement or substitution of mutated tumor suppressor gene functions or biochemical modulation of oncogene products. New forms of immunotherapy may also be targeted specifically toward mutant oncogenes in cancer cells.

Non-Small Cell Lung Cancer. Options for palliative treatment of late obstructing NSCLC by photodynamic therapy, brachytherapy, electrocautery, cryotherapy, and laser therapy are currently being used as primary treatment of early disease with some success.²⁸⁶ Surgical resection by lobectomy or pneumonectomy for treatment of stage I carcinoma is recommended with curative intent.²⁷⁴ Postoperative radiation is considered harmful and is not recommended, particularly in early stage NSCLC.³⁴⁸ Concurrent chemoradiation reduces risk of death at 2 years by 14% and 7% compared to radiation alone.^{365b}

For stage III NSCLC, surgery is usually not warranted. Combinations of treatments appear to help, but optimal treatment techniques and dose are controversial and primarily directed to increasing survival time.^{223,358} Approach to stage IV disease is palliative and depends on location and extent of disease and clinical manifestations. For example, clients who develop spinal cord compromise secondary to metastatic disease can be palliated effectively with short-course external-beam radiotherapy.

SVC obstruction can also be ameliorated by chemotherapy and radiotherapy as well as the placement of stents.³⁶³ Short-term radiotherapy can also reduce some lung symptoms.²⁶⁷ Chemotherapy has also been useful in improving palliation and increasing survival in stage IV disease.³⁹⁴

PROGNOSIS. The curability of lung cancer remains poor because by the time lung cancer is detected, invasion and metastasis have already occurred. The prognosis is influenced by the stage of the disease at presentation, the cell type, the treatment that can be given, and the status of the client at the time of diagnosis (e.g., people who are ambulatory respond to treatment better than those who are confined to bed more than 50% of the time).

Other factors associated with poor prognosis include weight loss of more than 10% of body weight in 6 months and generalized weakness. Overall 5-year survival rate among older blacks with NSCLC is significantly lower compared with whites, largely explained by lower rates of surgical treatment.²⁴ Although women appear to be more susceptible to lung cancer, they have higher survival rates.¹⁴²

Currently, with treatment, only 14% of people with lung cancer survive beyond 5 years after diagnosis, but if caught early, lung cancer can be cured up to 70% of the time. Survival without treatment is rarely possible, and most untreated persons die within 1 year of diagnosis, with a median survival of less than 6 months. Curative treatment requires effective control of the primary tumor before metastasis occurs. Chemotherapy is usually com-

bined with surgery or irradiation for more advanced tumors.

Other factors thought to confer poor prognosis include male gender, age older than 70 years, prior chemotherapy, elevated serum lactic dehydrogenase levels, low serum sodium, and elevated alkaline phosphatase levels (see Tables 40-14 and 40-15).

SPECIAL IMPLICATIONS FOR THE THERAPIST 15-22

Lung Cancer

PREFERRED PRACTICE PATTERNS

Symptoms resulting from metastases and corresponding practice patterns depend on the site of involvement but may include musculoskeletal patterns for bone metastases, neuromuscular patterns for nerve disorders such as brachial plexus compression caused by local invasion, and lymphatic compression secondary to intrapulmonary spread.

4C: Impaired Muscle Performance (cachexia and treatment-induced muscle loss and impairment is classic in cancer)

6A: Primary Prevention /Risk Reduction for Cardiovascular/Pulmonary Disorders (tobacco disorder)

6B: Impaired Aerobic Capacity/Endurance Associated with Deconditioning

6C: Impaired Ventilation, Respiration/Gas Exchange, and Aerobic Capacity/Endurance Associated with Airway Clearance Dysfunction (asbestosis; obstructive disease)

6E: Impaired Ventilation and Respiration/Gas Exchange Associated with Ventilatory Pump Dysfunction or Failure (obstructive disease)

6F: Impaired Ventilation and Respiration/Gas Exchange Associated with Respiratory Failure (obstructive disease)

7A: Primary Prevention/Risk Reduction for Integumentary Disorders (skin breakdown; late-stage cancer)

The effective management of short- and long-term side effects from lung cancer and its treatment is essential for rehabilitation. The American College of Chest Physicians has developed recommendations for improving quality of life in end-of-life care.¹⁷⁸ Increasing the therapist's knowledge of psychosocial-spiritual effects in these cases assists the therapist in planning appropriate intervention programs and promoting the optimal use of resources. If clients and their families can overcome treatment barriers, they will be more motivated toward achieving increased and sustained independence and quality of life.

The therapist can be very helpful in teaching clients with lung cancer nonpharmacologic means of pain relief and energy conservation techniques while providing an optimal rest schedule and activity program in accordance with the degree of pulmonary involvement. Effective breathing and coughing techniques should be taught and reinforced. There is some evidence to support noninvasive treatment to improve quality of life for people with cancer, but more studies need to be conducted.³⁹⁶

Cigarette smoking should be discouraged. Numerous surveys have shown that the majority of current

smokers demonstrate a desire to stop smoking and that intervention through smoking-cessation programs can be successful. The Agency for Health Care Policy and Research (AHCPR), which is now called the Agency for Healthcare Research and Quality (AHRQ), has recommended specific guidelines with intervention strategies to assist health care providers in giving smokers consistent and effective smoking cessation guidelines. Every therapy and rehabilitation department should have information available about local smoking-cessation programs and a listing of local physicians willing to help anyone who expresses a desire to cease smoking.

Metastasis

Metastatic spread of pulmonary tumors to the long bones and to the vertebral column, especially the thoracic vertebrae, is common, occurring in as many as 50% of all cases. Local metastases by direct extension may involve the chest wall and may even erode the first and second ribs and associated vertebrae, causing bone pain and paravertebral pain associated with involvement of sympathetic nerve ganglia. Subsequently, chest, shoulder, arm, or back pain can be the presenting symptom but usually with accompanying pulmonary symptoms.

The client may not associate the musculoskeletal symptoms with the pulmonary symptoms, so the therapist must always remember to screen for medical disease. Cases of patients with lung cancer and shoulder pain for which no local cause could be found have been reported, and in each case, radiotherapy to the ipsilateral mediastinum eliminated symptoms. Pain referred from intrathoracic involvement of the phrenic nerve was the suspected underlying pain generator.²⁴¹ Anytime a mechanical cause is not found or the client fails to progress or improve in therapy, return to the physician is recommended for further diagnostic evaluation.

Spinal cord compression from extradural metastases of lung cancer usually occurs from direct extension of vertebral metastases. Back pain is often the first sign and may occur as progressive back pain 6 months before the diagnosis is made. The pain may be constant and aggravated by Valsalva maneuver, sneezing or coughing, movement, and lying down, and diminished by sitting up. Weakness, sensory loss, and a positive Babinski's reflex may be observed.

Radiation is usually the treatment of choice for epidural metastases from lung cancer. Neurosurgical intervention may be indicated if the area of compression has been previously irradiated to maximal tolerance. Surgical decompression may also be indicated if neurologic deterioration occurs during the initiation of radiation therapy. The treatment field extends two vertebral bodies above and below the level of blockage. Corticosteroids are prescribed to reduce swelling and inflammation around the cord.^{60b}

Apical (Pancoast's) tumors do not usually cause symptoms while confined to the pulmonary parenchyma, but once they extend into the surrounding structures, the brachial plexus (C8 to T1) may become

involved, presenting as a form of thoracic outlet syndrome. This nerve involvement produces sharp pleuritic pain in the axilla, shoulder (radiating in an ulnar nerve distribution down the arm), and subscapular area of the affected side, with atrophy and weakness of the upper extremity muscles. Invasion of the cervical sympathetic plexus may cause *Horner's syndrome* with unilateral miosis, ptosis, and absence of sweating on the affected side of the face and neck.

Treatment for these two conditions may combine surgery with radiation. Local anesthetics administered through an axillary catheter placed in the brachial plexus for intractable neuropathic pain have also been reported; this approach is reversible and may be preferable to destructive procedures, such as cordotomy.⁴³⁶ Therapy intervention for the thoracic outlet syndrome is an important part of the palliative treatment for this condition (see also the section on Thoracic Outlet Syndrome in Chapter 39).

Trigger points of the serratus anterior muscle also mimic the distribution of pain caused by C8 nerve root compression and must be ruled out by palpation, lack of neurologic deficits, and possible elimination with appropriate trigger point therapy. Pancoast's tumors may also masquerade as subacromial bursitis.

Paraneoplastic Syndrome

Paraneoplastic syndromes (remote effects of a malignancy; see discussion in Chapter 9) occur in 10% to 20% of lung cancer clients. These usually result from the secretion of hormones by the tumor acting on target organs producing a variety of symptoms, most commonly hypercalcemia, digital clubbing, osteoarthropathies, or rheumatologic disorders, such as polymyositis, lupus, and dermatomyositis.

Occasionally, symptoms of paraneoplastic syndrome occur before detection of the primary lung tumor or as the first sign of recurrence presenting as a neuromusculoskeletal condition. For example, hypertrophic osteoarthropathy with joint involvement may be diagnosed as arthritis without recognition of the underlying lung cancer.

Digital clubbing is almost always present (or developing), sometimes with neurovascular changes of the hands and feet and usually with a previous history of cancer to alert the therapist. Treatment of the underlying cancer provides the most significant improvement of these syndromes because the underlying cause of the hormone secretion is the carcinoma itself.

Chemotherapy and Radiation Treatment

Clients undergoing chemotherapy, radiation therapy, or a combination of both and their family members must work closely with members of the multidisciplinary health team to obtain the information and emotional support they need. It is important that therapists have knowledge of side effects associated with different antineoplastic interventions and anticipate toxicities.

For example, side effects of chemotherapy, including nausea and vomiting, require careful scheduling of

Continued.

therapy to optimize treatment success. Some chemotherapy is neurotoxic and the therapist should watch for peripheral neuropathies. In the presence of cancer pain, pain medication should be timed to allow maximal comfort during therapy (e.g., approximately 30 to 60 minutes before therapy).

Loss of appetite with accompanying weight loss may result in muscle weakness and decreased physical endurance requiring more frequent rest periods. The therapist may be able to assist the client with reduced functional status exhibiting other symptoms, such as dyspnea and fatigue, by teaching diaphragmatic breathing techniques, use of relaxation techniques for overused respiratory accessory muscles, and positioning for easing the WOB (e.g., sitting upright leaning forward slightly with elbows resting on knees).

Energy conservation (see Box 9-8) should be addressed by teaching the client to schedule strenuous activities at times of the day when energy levels are the highest, alternating strenuous tasks with easier ones, using frequent rest breaks, planning activities to minimize the use of stairs or walking long distances, and workload reduction (encourage the client to perform elective tasks, especially household chores, less often and in the sitting position whenever possible).

Monitoring platelet, hematocrit, and hemoglobin levels can help guide the therapist and client in establishing activity level (see Tables 40-8 and 40-9). Vital signs should be monitored before and after periods of increased activity; heart and lung sounds and oxygen saturation should be monitored during activity. Observe for signs of extreme fatigue, chest pain, or diaphoresis.

Other concerns addressed by the therapist may include regaining strength and endurance following chemotherapy or radiation therapy, mobility training for those clients with gait and balance disturbances, instruction for sleeping postures and bed mobility for clients with bone pain from metastasis, and in late-stage cancer, prevention or treatment of contractures or skin breakdown. Helping the client recognize short- and long-term side effects associated with treatment before these effects become life-threatening is essential (see Table 9-8).

DISORDERS OF THE PULMONARY VASCULATURE

Pulmonary Embolism and Infarction

Definition and Incidence

Pulmonary embolism (PE) is the lodging of a blood clot in a pulmonary artery with subsequent obstruction of blood supply to the lung parenchyma. Although a blood clot is the most common cause of occlusion, air, fat, bone marrow (e.g., fracture), foreign intravenous material, vegetations on heart valves that develop with endocarditis, amniotic fluid, and tumor cells (tumor emboli) can also embolize and occlude the pulmonary vessels.

PE is common, and in the United States the incidence is estimated at approximately 600,000 cases and 50,000 to 200,000 deaths annually.²⁵⁴ It is the most common cause of sudden death in the hospitalized population. The overall incidence of PE appears to be declining, probably because of better treatment of established deep vein thrombosis (DVT) and increased use of thromboprophylaxis.

Etiologic and Risk Factors

The most common cause of PE is DVT originating in the proximal deep venous system primarily of the lower extremity, but 20% come from the upper extremity. PE encompasses embolism from many sources, including air, bone marrow, arthroplasty cement, amniotic fluid, tumor, and sepsis. Before the introduction of routine prophylaxis with heparin (now low-molecular-weight heparin [LMWH]) or warfarin sodium (Coumadin), the incidence of DVT after hip fracture, total hip replacement, or other surgeries involving the abdomen, pelvis, prostate, hip, or knee was extremely high.

Three major physiologic risk factors linked with PE are (1) blood stasis (e.g., immobilization caused by prolonged trips including air travel or spinal cord injury; bed rest, such as with burn cases, pneumonia, or obstetric and gynecologic clients; fracture care with casting or pinning; and older or obese populations); (2) endothelial injury (local trauma) secondary to surgical procedures (as late as 1 month postoperatively), trauma, or fractures of the legs or pelvis; and (3) hypercoagulable states (e.g., oral contraceptive use, cancer, and hereditary thrombotic disorders).

Major clinical risk factors for PE (DVT) include immobility; abdominal/pelvic surgery; hip/knee replacement; late pregnancy; cesarean section; lower limb fractures; malignancy of pelvis or abdomen; and previous PE. Minor risk factors include congenital heart disease; congestive heart failure; hypertension; superficial venous thrombosis; indwelling catheter; COPD; oral contraceptives; hormone replacement therapy; neurologic disability; long distance travel; obesity; and smoking.²⁵⁴

Pathogenesis

In DVT, clots form in the popliteal or iliofemoral arteries (50%) and deep calf veins (5%) or subclavian vein (up to 20%). Part or all of the clot may embolize, traveling through the venous system, the right side of the heart, and into the lungs. Each embolus is a mass of fresh or organizing thrombus comprised of alternating bands of red cells, fibrin strands, and leukocytes with a rim of fibroblasts at the periphery. Any level of the pulmonary artery, from the main trunk to the distal branches, is a site for emboli to lodge. This causes an area of blockage and ischemic necrosis to the area perfused by that vessel.

PE ranges from peripheral and clinically insignificant to massive embolism and sudden death. PE may lead to V/Q mismatch, which leads to hypoxia. PE and DVT should be considered part of the same pathologic process, and in fact, studies showed that a large percentage of people with DVT but no symptoms of PE also had evidence of PE on lung scanning. Conversely, people with

PE often have abnormalities on ultrasonographic studies of leg veins.¹⁶⁷

In addition to the loss of capillary beds, pulmonary emboli cause vasoconstriction as a result of vasoactive mediators released by activated platelets, increased pulmonary vascular resistance, pulmonary hypertension, and right ventricular failure (in severe cases).

Clinical Manifestations

Clients may be asymptomatic in the presence of small thromboemboli or sustain cardiac arrest, depending on the size and location of the embolus and the individual's preexisting cardiopulmonary status. Common symptoms in people with PE include dyspnea (84%), pleuritic chest pain (74%), apprehension (59%), and cough (53%). Common signs include tachypnea greater than 16 breaths/minute (92%), rales (58%), accentuated S2 (53%), tachycardia (44%), and fever (43%). Other signs and symptoms may include hemoptysis, diaphoresis, S3 or S4 gallop, lower extremity edema, cardiac murmur, and cyanosis.²³⁴

A DVT may present up to 2 weeks postoperatively as tenderness, leg pain, swelling (a difference in leg circumference of 1.4 cm in men and 1.2 cm in women is significant), and warmth. One exception to this presentation is the person who has been immobilized for a prolonged period in a cast. Immobilization causes muscle atrophy in the involved leg, so equal leg circumference should be a clinical red flag for medical evaluation.

A positive Homans' sign (deep calf pain on slow dorsiflexion of the foot or gentle squeezing of the affected calf) is not specific for this condition and should not be relied on because it also occurs with Achilles tendinitis and gastrocnemius and plantar muscle injury. Only one-half of the people with DVT experience pain with this test in the presence of a thrombus. Other signs of DVT may include subcutaneous venous distention, discoloration, swelling, warmth, a palpable cord (superficial thrombus), and pain on placement of a blood pressure cuff around the calf (considerable pain with the cuff inflated to 160 to 180 mm Hg).

MEDICAL MANAGEMENT

DIAGNOSIS. PE is difficult to diagnose because the signs and symptoms are nonspecific. PE may mimic (and even coexist with) pneumonia, congestive heart failure, pericarditis, myocardial infarction, pneumothorax, anxiety, and even rib fractures. The physician must also differentiate conditions that can mimic thromboembolism to the calf such as cellulitis, muscle strain or rupture, lymphangitis, and rupture of a Baker cyst. Circumstances such as the onset of chest pain or dyspnea in hospitalized, postsurgical, or trauma cases are highly suspicious of PE.

Clinical screen and need for further testing are conducted using Wells, Wicki, or Charlotte criteria and non-imaging laboratory tests (especially D-dimer, which is a by-product of fibrin crosslinks). Negative clinical assessment and D-dimer test may limit the need for further testing.²³⁵ ABGs are not helpful in the physician's differential diagnosis.

Using combinations of additional tests to rule out or rule in PE to make the diagnosis is optimal. V/Q scans

can rule out PE if it is normal in the presence of normal x-ray and with no other cardiopulmonary disease.²³⁴

Alveolar dead space evaluation in combination with D-dimer created a false negative response of less than 1%. Echocardiogram can detect PE in 80% of cases. Conventional angiogram has potential for serious side effects and has poor reliability. Spiral CT scan has become the initial diagnostic tool and is useful to exclude PE.²⁰¹ The major disadvantage of spiral CT is its inability to visualize beyond fourth-order branches of the pulmonary artery so that small distal emboli are not seen. Compression ultrasonography is used for the detection of DVT, but a negative result should not rule out DVT.

PREVENTION AND TREATMENT. The management of DVT and PE has changed dramatically in the last few years. Given the mortality of PE and the difficulties involved in its clinical diagnosis, prevention of DVT and PE is crucial. Primary prevention of DVT through the prophylactic use of anticoagulants is important for persons undergoing total hip replacement, major knee surgery, abdominal or pelvic surgery, prostate surgery, and neurosurgery. In fact, anyone hospitalized should be evaluated for risk of PE and placed on prophylaxis as appropriate.

LMWH (anticoagulant now replacing unfractionated heparin) is the most common agent for prophylaxis because it prolongs the clotting time and allows the body time to resolve the existing clot, thereby preventing further development of the thrombus; it does not reduce the immediate embolic risk or enhance clot lysis. LMWHs have fewer major bleeding complications and do not require laboratory monitoring of coagulation tests to adjust medications. The U.S. FDA has approved outpatient treatment of DVT with the LMWH enoxaparin as a bridge to warfarin. Warfarin (Coumadin), an oral anticoagulant, is used simultaneously with heparin or during the transition from intravenous to oral anticoagulant with a targeted activated partial thromboplastin time of 1.5 to 2.5 times the baseline value and an international normalized ratio of 2 to 3 (see discussion in Chapter 40).

Prophylaxis and treatment with these medications for PE and DVT are different (see further discussion in the section on Thrombophlebitis in Chapter 12). Direct thrombin inhibitors, fondaparinux, idraparinux, and ximelagatran, have been shown to be at least as effective as LMWH and well tolerated.²¹³

Thrombolytic therapy (a controversial, expensive treatment used with massive embolism) to lyse pulmonary thromboemboli in situ is accomplished through the use of thrombolytic agents, such as streptokinase, urokinase, recombinant tissue plasminogen activator, and newer agents, such as reteplase, saruplase, and recombinant staphylokinase, that enhance fibrinolysis by activating plasminogen, generating plasmin.

Plasmin directly lyses thrombi both in the pulmonary artery and in the venous circulation and has a secondary anticoagulant effect. Successfully utilized, pulmonary embolism thrombolysis reverses right-sided heart failure rapidly and safely. There is limited evidence that thrombolytics are better than heparin for PE¹²² but moderate

evidence that they effective in reducing postthrombotic syndrome and maintaining vessel patency.^{443b}

Surgical implantation of a filter in the vena cava may be used to prevent PE in anyone who cannot tolerate anticoagulation therapy by filtering the blood and preventing clots from moving past the screen. There is an increased risk of caval occlusion and dependent edema as a result of obstruction of the filter with this procedure. As temporary measures, the filters are helpful, but permanent filters have not improved survival rates.³¹³ Other procedures used in the case of massive DVT or hemodynamically unstable PE may include thrombectomy and embolectomy performed surgically in an angiography laboratory.

Mechanical compression reduces the risk of DVT by two-thirds alone and by 50% when used with anticoagulants. There was also a risk reduction for PE by two-fifths.³⁵⁹

PROGNOSIS. PE is the primary cause of death for as many as 100,000 people each year (perhaps double that amount) and a contributory factor in another 100,000 deaths annually. About 10% of victims die within the first hour, but prognosis for survivors (depending on underlying disease and on proper diagnosis and treatment) is generally favorable. Clients with PE who have cancer, congestive heart failure, or chronic lung disease have a higher risk of dying within 1 year than do clients with isolated PE.

Small emboli resolve without serious morbidity, but large or multiple emboli (especially in the presence of severe underlying cardiac or pulmonary disease) have a poorer prognosis. PE may recur despite LMWH therapy, most commonly in people with massive PE or in whom anticoagulant therapy has been inadequate. PE is the leading cause of pregnancy-related mortality in the United States.

SPECIAL IMPLICATIONS FOR THE THERAPIST 15-23

Pulmonary Embolism and Infarction

PREFERRED PRACTICE PATTERN

6F: Impaired Ventilation and Respiration/Gas Exchange Associated with Respiratory Failure

Page-Schroetter syndrome is a DVT of the upper extremity primarily caused by weight lifting that results in compression and subsequent stenosis of the subclavian vein. Therapists should be aware of this syndrome because early detection can prevent PE and other complications.⁵⁹

A careful review of the client's medical history may alert the therapist to the presence of predisposing factors for the development of a DVT or PE. Frequent changing of position, exercise, the use of graduated-compression stockings, devices that provide intermittent pneumatic compression, and early ambulation are necessary to prevent thrombosis and embolism; sudden and extreme movements should be avoided. All postsurgical patients should be taught to do ankle pumps hourly. Under no circumstances should the

legs be massaged to relieve muscle cramps, especially when the pain is located in the calf and the person has not been up and about.

Restrictive clothing, crossing the legs, and prolonged sitting or standing should be avoided. Elevating the legs, bending the bed at the knees, or propping pillows under the knees can produce venous stasis and should be done with caution to avoid severe flexion of the hips, which will slow blood flow and increase the risk of new thrombi.

After a PE or in the case of total hip replacement, treatment with anticoagulation continues for those at high risk of recurrence. Anyone taking anticoagulants should be monitored carefully for signs of bleeding such as bloody stool, blood in urine, vaginal bleeding, bloody gums or nose, or large ecchymoses. If the person mentions any of these symptoms to the therapist, the client should be instructed to contact the physician immediately.

Medications should not be changed without the physician's approval; the use of additional medications, especially over-the-counter preparations for colds, headaches, rheumatic pain, and so on, must be approved by the physician. See also Special Implications for the Therapist: Peripheral Vascular Disease in Chapter 12.

Pulmonary Hypertension

Definition and Incidence

Pulmonary hypertension (PH) is high blood pressure in the pulmonary arteries defined as a rise in pulmonary artery pressure of 5 to 10 mm Hg above normal (normal is 15 to 18 mm Hg). There is no definitive set of values used to diagnose pulmonary hypertension, but the National Institutes of Health (NIH) requires a resting mean artery pressure of more than 25 mm Hg at rest and 30 mm Hg during exercise.

The World Health Organization (WHO) met in 1998 and established a classification of pulmonary hypertensive diseases. The classifications includes five major categories: (1) pulmonary artery hypertension (PAH), (2) pulmonary venous hypertension, (3) PAH associated with disorders of the respiratory system or hypoxemia, (4) PAH caused by chronic thrombotic or embolic disease, and (5) PAH caused by disorders directly affecting the pulmonary vasculature. There are several subcategories for each class.³⁸⁸

Primary PH (PPH) is rare, that is—1 or 2 cases per 1 million in the United States. PAH in neonates occurs in 1.9/1000 births from a variety of conditions.¹⁷⁷ PPH occurs most commonly in young and middle-aged women (pregnant women have the highest mortality). It may have no known cause (idiopathic), although familial disease (defects in the bone morphogenetic protein receptor type II gene and the transforming growth factor beta have been found)⁴¹³ accounts for approximately 10% of cases. An epidemic of PAH was caused by the appetite suppressant aminorex fumarate that was sold from 1965 to 1968. This drug produced the same vascular lesions

as those seen in PPH and was the stimulus for new research.¹³³

Pathogenesis

PPH is characterized by diffuse narrowing of the pulmonary arterioles caused by hypertrophy of smooth muscle in the vessel walls and formation of fibrous lesions in and around the vessels. The underlying cause of these changes is unknown, but looking beyond simple pulmonary vasoconstriction, it is now recognized that defects in endothelial function, pulmonary vascular smooth muscle cells, and platelets may all be involved in the pathogenesis and progression of PPH.

Endothelial-cell injury may result in an imbalance in endothelium-derived mediators (too many "bad" mediators). Impaired endothelium release may account for reduced production of NO , a vasodilator, from the airways resulting in vasoconstriction.

Defects in ion channel activity in smooth muscle cells in the pulmonary artery also may contribute to vasoconstriction and vascular proliferation.²¹¹ These changes create increased resistance to the right side of the heart, which can eventually cause heart failure (*cor pulmonale*).

Secondary pulmonary hypertension is caused by any respiratory or cardiovascular disorder that increases the volume or pressure of blood entering the pulmonary arteries; narrows, obstructs, or destroys the pulmonary arteries; or increases the pressure of blood leaving the heart (pulmonary veins).

Increased volume or pressure overloads the pulmonary circulation whereas narrowing or obstruction elevates the blood pressure by increasing resistance to flow within the lungs. For example, COPD destroys alveoli and associated capillary beds thus increasing pressure through the remaining vasculature. Left sided heart failure causes blood to "back up" and thus resistance is increased.

With persistent PAH, the result is right ventricular hypertrophy and eventual *cor pulmonale*.

Clinical Manifestations

Signs and symptoms of secondary pulmonary hypertension are difficult to recognize in the early stages when the symptoms of the underlying disease are more prominent.

The most common symptoms of primary or secondary pulmonary hypertension are atypical cardiorespiratory symptoms, such as fatigue, weakness, chest discomfort or pain, syncope, peripheral edema, abdominal distention, and unexplained SOB, beginning with exercise and later occurring with minimal activity or at rest.³¹

MEDICAL MANAGEMENT

DIAGNOSIS. PPH can be difficult to diagnose, and there is usually a delay of 1 to 2 years between onset of symptoms and diagnosis. Sometimes the first indication of pulmonary hypertension is seen incidentally on a chest radiograph or ECG. The x-ray study may show rib scalloping (erosion of the inferior aspect of the ribs) from dilation of the arteries supplying the ribs. Standard assessment should include a physical examination of heart and

lung auscultation and observation and palpation for jugular vein distention, hepatomegaly, and peripheral edema. Chest x-ray, electrocardiogram, and Doppler echocardiogram are also part of the screening.

If PAH is suspected, then additional testing is done to determine severity and to choose appropriate treatment. Essential testing should include pulmonary function tests; oximetry; V/Q scan; blood tests, including complete blood count (CBC), HIV, and antinuclear antibody (ANA) tests; test for exercise capacity (usually 6-minute walk test); and right heart catheterization (with and without vasodilator).³¹ Additional tests, such as spiral CT or angiography, may be needed. Right heart catheterization is needed to confirm the diagnosis.

TREATMENT. Synthetic prostacyclin and prostacyclin analogues (vasodilators) are effective in improving tolerance to exercise and hemodynamics. Intravenous administration of the synthetic prostacyclin, epoprostenol (Flolan), is the only treatment that has improved survival. Inhaled prostacyclins have shown some promise with short-term improvement and may be beneficial in early stages of PAH.¹⁰⁶

Endothelin-1 receptor antagonists work to counteract the vasoconstriction caused by overproduction of endothelin-1. Investigational oral drug therapy used to treat pulmonary hypertension (e.g., Sitaxsentan or Ambrisentan) has shown promise in improving exercise capacity and hemodynamics. The PDE5 inhibitor, Sildenafil, causes vasodilation and improvement of symptoms, although more research needs to be done with this medication.^{149,234}

Inhaled nitrous oxide (N_2O , not nitric oxide, which is NO), a vasodilator, has not been shown to be effective in treatment of PAH in children and has potential toxicity.⁴³ Calcium channel blockers have been effective in children in high doses. There are no controlled studies to support use of diuretics, digoxin, and oxygen in routine treatment of PAH. Anticoagulants are used with success in appropriate individuals, although guidelines need to be clarified.²⁶³ Balloon atrial septostomy and lung transplantation are used in end-stage PAH, and heart-lung transplants may be more beneficial because of *cor pulmonale*.

Other treatment approaches under investigation include gene therapy and focus on pathogenetic factors outside the pulmonary endothelium (e.g., potassium channel defect favoring vasoconstriction and cell proliferation, role of elastase, and circulating blood factors contributing to blood thrombosis). In secondary PH, it is essential to treat the underlying cause.

PROGNOSIS. The progression of PPH varies for each affected individual, but prognosis is poor without heart-lung transplantation. Some individuals may live 5 to 6 years from the time of diagnosis, but most people have a downhill course over a shorter period of time (2 to 3 years) with a fatal outcome.

The cause of death is usually right ventricular failure or sudden death; sudden death occurs late in the disease process. Mortality in the United States has increased notably since 1979, although survival has improved in PPH with the advent of treatment with prostacyclin.

Some portion of this reported increase may be related to improvements in diagnostic recognition, and some data suggest that the disease may be more common in the older population than has been previously recognized and reported.²⁶⁰

Secondary PH can be reversed if the underlying disorder is successfully treated. If the hypertension has persisted long enough for the medial smooth muscle layer to hypertrophy, secondary PH is no longer reversible.

SPECIAL IMPLICATIONS FOR THE THERAPIST 15-24

Pulmonary Hypertension

PREFERRED PRACTICE PATTERN

6D: Impaired Aerobic Capacity/Endurance Associated with Cardiovascular Pump Dysfunction or Failure

Impairment of exercise performance is associated with PH because pulmonary vascular resistance and pulmonary artery pressure increase dramatically with exercise. There may be impaired heart rate kinetics during exercise with corresponding impaired cardiac output response and slow recovery of the heart.³⁵⁶ For these reasons, clients with PH must be closely monitored when participating in activities or therapy that requires increased physical stress. See Appendix B and Table 40-17.

Maintenance of adequate systemic blood pressure is essential, and the therapist must be familiar with the medications used and potential side effects, especially if blood pressure is altered pharmacologically. A drop in blood pressure can indicate heart failure. Inhaled N₂O or prostacyclin, which are endogenous vasodilators, increase oxygen consumption at the same workload during exercise, thereby improving exercise capacity. N₂O use is diminishing as a result of its toxicity and cost.²⁶⁵

Secondary PH may occur in clients with connective tissue diseases, such as scleroderma, because the disease affects the vasculature of several organs, including the lungs (pulmonary fibrosis) and kidneys. The arterioles usually demonstrate intimal proliferation with progressive luminal occlusion. The development of hypertension often indicates the onset of an accelerated scleroderma renal crisis. Medical treatment is toward control of the blood pressure.

Cor Pulmonale

Definition and Incidence

Cor pulmonale, also called *pulmonary heart disease*, is the enlargement of the right ventricle secondary to pulmonary hypertension that occurs in diseases of the thorax, lung, and pulmonary circulation. It is a term that describes the pathologic effects of lung dysfunction as it affects the right side of the heart. Right-sided heart dysfunction secondary to left-sided heart failure, vascular dysfunction, or

congenital heart disease is excluded in the definition of cor pulmonale.

Chronic cor pulmonale occurs most frequently in adult male smokers, although the incidence in women is increasing as heavy smoking in females becomes more prevalent. The actual prevalence of cor pulmonale is difficult to determine because cor pulmonale does not occur in all cases of chronic lung disease and because routine physical examination and laboratory tests are relatively insensitive to the presence of pulmonary hypertension. It has been estimated that cor pulmonale accounts for 5% to 10% of organic heart disease.

Etiologic and Risk Factors

Pulmonary vascular diseases and respiratory diseases (e.g., emphysema or chronic bronchitis) are the primary causes of cor pulmonale. Emphysema and chronic bronchitis cause over 50% of cases of cor pulmonale in the United States. When a PE has been sufficiently massive to obstruct 60% to 75% of the pulmonary circulation, acute cor pulmonale can occur. Cor pulmonale is frequently the cause of death in COPD.⁴⁴⁵

Cor pulmonale can also develop under conditions of sustained elevations in intrathoracic pressure associated with mechanical ventilation (and PEEP). The intrathoracic vessels narrow, leading to reduced cardiac output and possible cor pulmonale. Chronic widespread vasculitis, such as occurs in association with the collagen vascular disorders (e.g., rheumatoid arthritis, SLE, dermatomyositis, polymyositis, Sjogren's syndrome, CREST [calcinosis cutis, Raynaud's phenomenon, esophageal dysfunction, sclerodactyly, and telangiectasis] syndrome accompanying scleroderma), can also cause chronic cor pulmonale. Occasionally, widespread radiation pneumonitis can be the underlying cause of cor pulmonale.

Other (uncommon) causes include pneumoconiosis, pulmonary fibrosis, kyphoscoliosis, pickwickian syndrome, lymphangitic infiltration from metastatic carcinoma, and obliterative pulmonary capillary changes that cause vasoconstriction and later, hypertension. The feature common to all these conditions that predisposes to cor pulmonale is hypoxia, which leads to vasoconstriction.⁴⁴⁵

Pathogenesis

Sustained elevation in pulmonary arterial hypertension can be mediated through persistent vasoconstriction, abnormal vascular structural remodeling, or vessel obliteration (see Pulmonary Hypertension in this chapter). Cor pulmonale develops as these factors increase pulmonary vessel pressure and overload in the right ventricle. Normally, the ventricle is a thin-walled (heart) muscle able to meet an increase in volume and pressure, but long-term pressure overload from hypertension causes the tissue to hypertrophy. In the case of acute cor pulmonale caused by emboli from DVT, the thrombus breaks loose and lodges at or near the bifurcation of the main pulmonary artery. Whether caused by vascular abnormalities or embolic obstruction, there is a marked fall in pressure necessary to drive blood through the compromised vascular bed since the right ventricle is compromised.

Clinical Manifestations

Evidence of cor pulmonale may be obscured by primary respiratory disease and appear only during exercise testing. The heart appears normal at rest, but with exercise, cardiac output falls and the ECG shows right ventricular hypertrophy. The predominant symptoms are related to the pulmonary disorder and include chronic productive cough, exertional dyspnea, wheezing respirations, easy fatigability, and weakness.

With a large pulmonary embolus, sudden severe, central chest pain can occur caused by acute dilation of the root of the pulmonary artery and secondary to ischemia. The person may collapse, often with loss of consciousness, and death may occur within minutes if the thrombus is large and does not dislodge. If the thrombus is small or moves more peripherally in response to pounding on the chest or chest compression during resuscitation, acute cor pulmonale develops rather than sudden death.

Low cardiac output causes pallor, sweating, hypotension, anxiety, impaired consciousness, and a rapid pulse of small amplitude. The specific signs associated with cor pulmonale include exercise-induced peripheral cyanosis, clubbing (see Fig. 15-4), distended neck veins, and bilateral dependent edema. Hypoxia can cause pulmonary vasoconstriction and worsen symptoms.

MEDICAL MANAGEMENT

DIAGNOSIS. Diagnosis is made on the basis of physical examination, radiologic studies, and ECG or echocardiogram, sometimes both. Echocardiogram can be performed at bedside and can effectively and efficiently detect right ventricular enlargement, as well as excessive right ventricular afterload.²¹⁹ Pulmonary function tests usually confirm the underlying lung disease. Laboratory findings may include polycythemia present in cor pulmonale secondary to COPD. ECG and chest film may not be diagnostic in the early stages of cor pulmonale.

TREATMENT. The primary goal of medical treatment is to reduce the workload of the right ventricle. This is accomplished by lowering pulmonary artery pressure, as in the treatment of pulmonary hypertension (see section in this chapter on Pulmonary Hypertension). Oxygen administration, salt and fluid restriction, and diuretics are essential, as well as treatment of the underlying chronic pulmonary disease, while at the same time relieving the hypoxemia, hypercapnia, or acidosis.

Surgical removal of embolic material is a controversial procedure performed only when a confirmed diagnosis of massive PE with accessible thrombus in the main pulmonary artery or its branches is available. There is no specific surgical treatment available for most causes of chronic cor pulmonale. Heart-lung transplantation for clients with PPH is valuable in late-stage disease.

PROGNOSIS. Since cor pulmonale generally occurs late during the course of COPD and other irreversible disease, the prognosis is poor. Once congestive signs appear, the average life expectancy is 2 to 5 years, but survival is significantly longer when uncomplicated emphysema is the

cause. Although cor pulmonale can be caused by obstructive and restrictive lung diseases, restrictive lung diseases have a lower life expectancy once they reach the stage of cor pulmonale.

SPECIAL IMPLICATIONS FOR THE THERAPIST 15-25

Cor Pulmonale

PREFERRED PRACTICE PATTERNS

6B: Impaired Aerobic Capacity/Endurance Associated with Deconditioning

6D: Impaired Aerobic Capacity/Endurance Associated with Cardiovascular Pump Dysfunction or Failure

7A: Primary Prevention/Risk Reduction for Integumentary Disorders

Those people who are bedridden must be repositioned frequently to prevent atelectasis (and skin breakdown). Breathing exercises should be carried out frequently throughout the day. Diaphragmatic and pursed-lip breathing exercises should be reviewed for anyone with COPD and used with appropriate individuals; more details about this are available.⁷¹

Teach the client (or family member) how to detect edema in the lower extremities, especially the ankles, by pressing the skin over the shins for 1 to 2 seconds, looking for a lasting finger impression. Watch for signs of digitalis toxicity (see Table 12-5) such as complaints of anorexia, nausea, vomiting, or yellow halos around visual images.

Since pulmonary infection exacerbates COPD and cor pulmonale, all health care workers must practice careful handwashing and follow standard precautions. Early signs of infection (e.g., increased sputum production, change in sputum color, chest pain or chest tightness, or fever) must be reported to the physician immediately. Watch for signs of respiratory failure such as change in pulse rate; deep, labored respirations; and increased fatigue produced by exertion.

Collagen Vascular Disease

Collagen vascular diseases, now more commonly referred to as diffuse connective tissue diseases (see Box 12-17), are often associated with pulmonary manifestations, including exudative pleural effusion, pulmonary nodules, rheumatoid nodules in association with coal workers' pneumoconiosis (Caplan's syndrome), interstitial fibrosis, and pulmonary vasculitis. All of these pulmonary conditions have been associated with rheumatoid arthritis; all except the nodules and pleural effusion have been seen with SLE; and pleuritis and pneumonitis have been observed in Sjogren's syndrome, polymyositis, and dermatomyositis.

Pulmonary fibrosis or PH, or both, are commonly part of the clinical picture associated with scleroderma. Polymyalgia rheumatica and temporal arteritis may demonstrate granulomatous inflammation of the pulmonary

parenchyma. Approximately one-half of clients with SLE develop lung disease, primarily pleuritis, pleural effusion, or acute pneumonitis. Pulmonary involvement may not be evident clinically, but pulmonary function tests reveal abnormalities in many persons with SLE.

Lupus pneumonitis causes recurrent episodes of fever, dyspnea, and cough. Interstitial pneumonitis leading to fibrosis occurs in a small proportion of people with SLE; the inflammatory phase may respond to treatment, whereas the fibrosis does not. Occasionally, PH develops. Rarely are ARDS and massive intraalveolar hemorrhage fatal pulmonary complications.

Interstitial lung disease can develop before joint involvement becomes evident in rheumatoid arthritis, particularly in men. People with rheumatoid arthritis who are receiving treatment with methotrexate or gold may develop interstitial lung disease that represents a drug hypersensitivity. Penicillamine therapy in clients with rheumatoid arthritis has been implicated in causing bronchiolitis obliterans.

Bilateral upper lobe fibrosis may develop late in ankylosing spondylitis. Lung involvement varies in systemic sclerosis, but there is radiographic evidence of pulmonary disease in a majority of clients. Cutaneous scleroderma can involve the anterior chest wall and abdomen, causing restrictive lung function.

General dryness and lack of airway secretions cause the major problems of hoarseness, cough, and bronchitis in Sjogren's syndrome, and interstitial lung disease is possible. Only 5% to 10% of clients with polymyositis and dermatomyositis develop interstitial lung disease, but weakness of respiratory muscles contributing to aspiration pneumonitis is common.

DISORDERS OF THE PLEURAL SPACE

Pneumothorax

Definition

Pneumothorax is an accumulation of air or gas in the pleural cavity caused by a defect in the visceral pleura or chest wall. The result is collapse of the lung on the affected side. Pneumothorax is classified as spontaneous or traumatic. Primary spontaneous pneumothorax (PSP) develops with no underlying lung pathology. Secondary spontaneous pneumothorax (SSP) is typically a result of blebs or bullae that occur in COPD, CF, or other lung disorders. Traumatic pneumothoraces are iatrogenic or noniatrogenic³⁴ (Fig. 15-22).

Incidence and Risk Factors

Spontaneous pneumothorax may affect up to 20,000 people per year in the United States. Although pneumothorax can develop at any age, spontaneous pneumothorax is especially common in tall, slender boys and men between the ages of 20 and 40 years. Smoking appears to increase the risk of primary spontaneous pneumothorax in men by as much as a factor of 20 in a dose-dependent manner (i.e., chances increase as number of cigarettes smoked increases).³⁶⁹

The most common causes of iatrogenic pneumothorax are transthoracic needle lung biopsy, subclavian vein

catheterization, thoracentesis, transbronchial lung biopsy, and positive pressure ventilation. Surgical procedures that involve the chest wall and abdomen also can precipitate pneumothorax. Pneumothorax can occur with a variety of primary or metastasized lung tumors, but this is an uncommon cause. A single case of CPR training causing a minimally symptomatic pneumothorax has been reported.⁴⁰⁸ Catamenial pneumothorax is a rare, recurring form that occurs in women who are menstruating and is associated with thoracic endometriosis.²⁴⁸

Pathogenesis

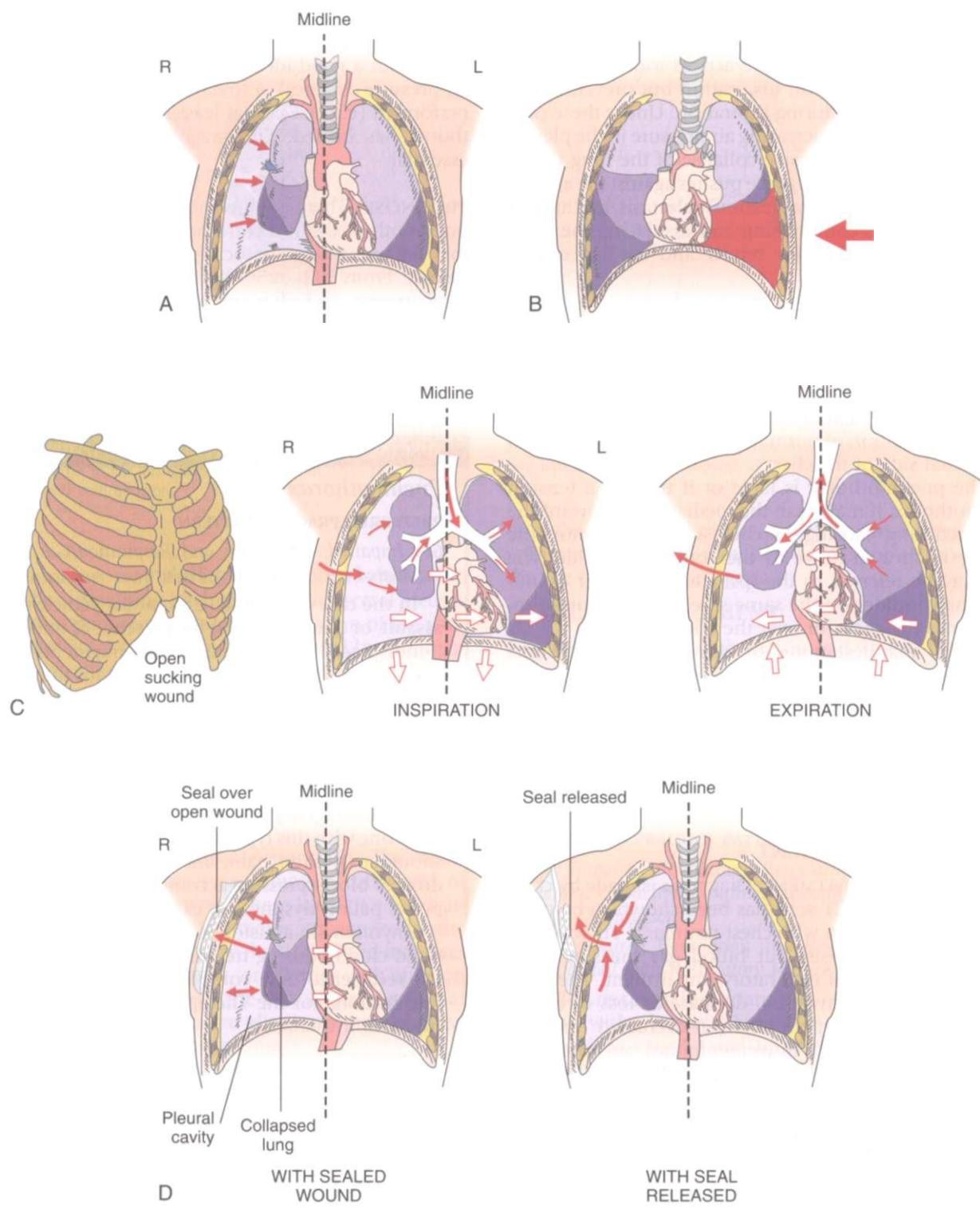
When air enters the pleural cavity the lung collapses and a separation between the visceral and parietal pleurae (see Fig. 15-3) occurs, destroying the negative pressure of the pleural space. This disruption in the normal equilibrium between the forces of elastic recoil and the chest wall causes the lung to recoil by collapsing toward the hilum. Depending on the individual's overall lung function, a loss of 40% may be present before symptoms appear.³⁶⁹ The result is SOB and mediastinal shift toward the unaffected side, compressing the opposite lung. The causative pleural defect may be in the lung and visceral pleura (lung lining) or the parietal pleura (chest wall lining). After chest trauma, both air and blood are likely to escape into the pleural space. This is called *hemopneumothorax*.

Spontaneous pneumothorax occurs when there is an opening on the surface of the lung allowing leakage of air from the airways or lung parenchyma into the pleural cavity. Most often this happens when an emphysematous bleb (blisterlike formation) or bulla (larger vesicle) or other weakened area on the lung ruptures. The majority of people with spontaneous pneumothorax have subpleural bullae that are most likely induced by the degradation of elastic fibers in the lung caused by the smoking-related influx of neutrophils and macrophages. Spontaneous pneumothorax can occur during sleep, at rest, or during exercise and can progress to become a tension pneumothorax. Other causes of this type of pneumothorax include TB, sarcoidosis, lung abscess, ARDS, and PCP.

Traumatic pneumothorax is a secondary pneumothorax with the entry of air directly through the chest wall or by laceration of the lung caused by penetrating or nonpenetrating chest trauma, such as a rib fracture, stab, or bullet wound that tears the pleura.

Open pneumothorax is a type of traumatic pneumothorax occurs when air pressure in the pleural space equals barometric pressure because air that is drawn into the pleural space during inspiration (through the damaged chest wall and parietal pleura or through the parietal pleura and damaged visceral pleura) is forced back out during expiration. This can rapidly lead to hypoventilation and hypoxia.

Iatrogenic pneumothorax develops as a result of direct puncture or laceration of the visceral pleura during attempts at central line placement, percutaneous lung aspiration, thoracentesis, or closed pleural biopsy. Direct alveolar distention can occur with anesthesia, CPR, or mechanical ventilation with PEEP.

**Figure 15-22**

A, Pneumothorax. Lung collapses as air gathers in the pleural space between the parietal and visceral pleurae. **B**, Massive hemothorax, blood in the pleural space (arrow) below the left lung, causing collapse of lung tissue. **C**, Open pneumothorax (sucking chest wound). Air movement (solid arrows) and structural movement (open arrows). A chest wall wound connects the pleural space with atmospheric air. During inspiration, atmospheric air is sucked into the pleural space through the chest wall wound. Positive pressure in the pleural space collapses the lung on the affected side and pushes the mediastinal contents toward the unaffected side. This reduces the volume of air in the unaffected side considerably. During expiration, air escapes through the chest wall wound, lessening positive pressure in the affected side and allowing the mediastinal contents to swing back toward the affected side. Movement of mediastinal structure from side to side is called mediastinal flutter. **D**, Tension pneumothorax. If an open pneumothorax is covered (e.g., with a dressing), it forms a seal, and tension pneumothorax with a mediastinal shift develops. A tear in lung structure continues to allow air into the pleural space. As positive pressure builds in the pleural space, the affected lung collapses, and the mediastinal contents shift to the unaffected side. Tension pneumothorax is corrected by removing the seal (i.e., dressing), allowing air trapped in the pleural space to escape.

Tension pneumothorax can result from any type of pneumothorax and is life-threatening. In tension pneumothorax, the site of pleural rupture acts as a one-way valve, permitting air to enter on inspiration but preventing its escape by closing up during expiration. Under these conditions, continuously increasing air pressure in the pleural cavity may cause progressive collapse of the lung tissue. Air pressure in the pleural space pushes against the already recoiled lung, causing compression atelectasis, and against the mediastinum, compressing and displacing the heart and great vessels. Venous return and cardiac output decrease.⁴⁵⁷

Clinical Manifestations

Dyspnea is the first and primary symptom of pneumothorax, but other symptoms may include a sudden sharp pleural chest pain, fall in blood pressure, weak and rapid pulse, and cessation of normal respiratory movements on the affected side of the chest.

If the pneumothorax is large or if there is a tension pneumothorax, it may push the mediastinum toward the unaffected lung, causing the chest to appear asymmetric and the trachea to move to the contralateral side. The pain may be referred to the ipsilateral shoulder (corresponding shoulder on the same side as the pneumothorax), across the chest, or over the abdomen.

Clinical manifestations of tension pneumothorax include severe hypoxemia, dyspnea, and hypotension (low blood pressure) in addition to the other signs and symptoms of pneumothorax already mentioned. Increased intrathoracic pressure from a tension pneumothorax may result in neck vein distention. Untreated tension pneumothorax may quickly produce life-threatening shock and bradycardia.

MEDICAL MANAGEMENT

DIAGNOSIS AND TREATMENT. Diagnosis is made by chest film at inspiration. CT scan has been shown to be more sensitive in the person with chest trauma.³⁰¹ There are no specific laboratory tests, but blood gas measurements indicate the degree of respiratory impairment. The presence of dyspnea, tachycardia, decrease or loss of breath sounds, percussive hyperresonance, decreased fremitus, asymmetric chest wall movement, and subcutaneous emphysema (swelling and crepitus with palpation) will assist in the diagnosis.

Depending on the size of the pneumothorax, no specific treatment is required for PSP less than 20% beyond rest and the administration of oxygen to relieve dyspnea.⁴²⁸ However, recurrences are frequent and associated with increased mortality in SSP.

Thoracoscopic procedures of pleurodesis (pleural abrasion, talc poudrage, and pleurectomy) are recommended to prevent further recurrence in SSP and catamenial pneumothorax. Placement of a chest tube is standard procedure for traumatic pneumothoraces.³⁴ Surgical repair is sometimes warranted, particularly with major trauma. In catamenial pneumothorax, hormonal suppression of menses may be required.

Pneumothorax is an unwanted sequela to respiratory distress syndrome in premature infants. The use of pro-

phylactic surfactant significantly reduces the incidence of pneumothorax in this population.³⁹⁶

It is not a good idea to travel by airplane (because of air pressure changes) or to have pulmonary function tests performed (e.g., CF) for at least 2 weeks after a pneumothorax has healed. Encouraging smoking cessation is essential.

PROGNOSIS. There is a low mortality rate with idiopathic pneumothorax, but a corresponding 15% mortality rate for pneumothorax associated with underlying lung disease. From 30% to 50% of affected persons experience a recurrence, and after one recurrence, subsequent episodes are much more likely. The physiologic events associated with tension pneumothorax are life-threatening, requiring immediate treatment.

SPECIAL IMPLICATIONS FOR THE THERAPIST 15-26

Pneumothorax

PREFERRED PRACTICE PATTERN

6F: Impaired Ventilation and Respiration/Gas Exchange Associated with Respiratory Failure

In the case of trauma (e.g., motor vehicle accident, assault, or traumatic falls) the presence of undiagnosed nondisplaced rib fractures or rib fragments must be considered when getting a person up for the first time. The client's movements and the action of parasternal intercostal muscles can displace the rib, causing puncture of the lung or penetrating aortic injury.

When getting someone up for the first time, monitor vital signs, especially blood pressure and pulse, and request emergency medical help immediately anytime someone with this type of history demonstrates sudden shoulder or chest pain, altered breathing pattern, or drop of blood pressure accompanied by weak and fast pulse, pallor, dyspnea, or extreme anxiety.

Anyone with a history of SSP should also be monitored closely during treatment because of the chance for recurrence and complications. See also Special Implications for the Therapist: Chest Wall Disease or Injury in this chapter.

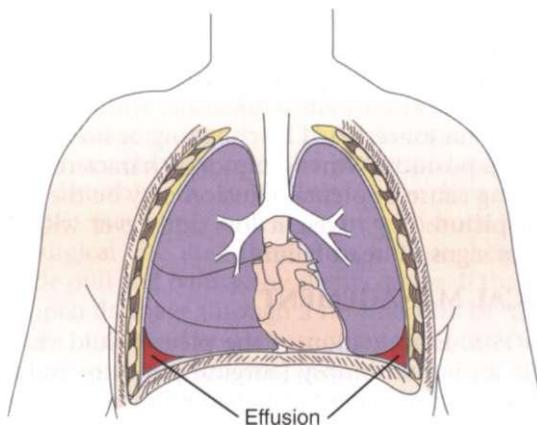
Pleurisy

Definition and Etiologic Factors

Pleurisy (pleuritis) is an inflammation of the pleura caused by viral or bacterial infection, injury (e.g., rib fracture), or tumor (particularly malignant pleural mesothelioma). It may be a complication of lung disease, particularly of pneumonia, but also of TB, lung abscesses, influenza, SLE, rheumatoid arthritis, or pulmonary infarction.

Clinical Manifestations

The symptoms develop suddenly, usually with a sharp, sticking chest pain that is worse on inspiration, coughing, sneezing, or movement associated with deep inspiration.

**Figure 15-23**

Pleural effusion, a collection of fluid in the pleural space between the membrane encasing the lung and the membrane lining the thoracic cavity, as seen on upright x-ray examination. Pleurisy (pleuritis) is an inflammation of the visceral and parietal pleurae. When there is an abnormal increase in the lubricating fluid between these two layers, it is called pleurisy with effusion.

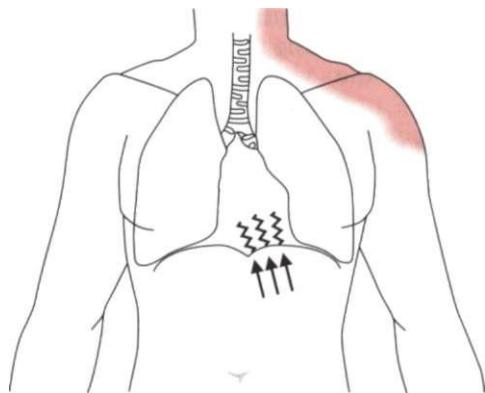
Other symptoms may include cough, fever, chills, and rapid shallow breathing (tachypnea). The visceral pleurae is insensitive; pain results from inflammation of the parietal pleurae. Because the latter is innervated by the intercostal nerves, chest pain is usually felt over the site of the pleuritis, but pain may be referred to the lower chest wall, abdomen, neck, upper trapezius muscle, and shoulder. On auscultation, a pleural rub can be heard (sound caused by the rubbing together of the visceral and costal pleurae).

Pathogenesis

There are two types of pleurisy: wet and dry. The membranous pleura that encases each lung is composed of two close-fitting layers; between these layers is a lubricating fluid. If the fluid content remains unchanged by the disease, the pleurisy is said to be dry. If the fluid increases abnormally, it is a wet pleurisy, or pleurisy with effusion (Fig. 15-23). Inflammation of the part of the pleura that covers the diaphragm is called diaphragmatic pleurisy and occurs secondary to pneumonia.

When the central portion of the diaphragmatic pleura is irritated, sharp pain may be referred to the neck, upper trapezius, or shoulder. Stimulation of the peripheral portions of the diaphragmatic pleura results in sharp pain felt along the costal margins, which can be referred to the lumbar region by the lower thoracic somatic nerves (Fig. 15-24).

Wet pleurisy is less likely to cause pain because there usually is no chafing. The fluid may interfere with breathing by compressing the lung. If the excess fluid of wet pleurisy becomes infected with formation of pus, the condition is known as *purulent pleurisy* or *empyema*. Pleurisy causes pleurae to become reddened and covered with an exudate of lymph, fibrin, and cellular elements and may lead to pleural effusion. In dry pleurisy, the two layers of membrane may become congested and swollen and rub against each other, which is painful. Although

**Figure 15-24**

Diaphragmatic pleurisy. Irritation of the peritoneal (outside) or pleural (inside) surface of the central area of the diaphragm refers sharp pain to the neck, supraclavicular fossa, and upper trapezius muscle. The pain pattern is ipsilateral to the area of irritation. Irritation to the peripheral portion of the diaphragm refers sharp pain to the costal margins and lumbar region (not shown).

only the outer layer causes pain (the inner layer has no pain nerves), the pain may be severe enough to require the use of a strong analgesic.

MEDICAL MANAGEMENT

Treatment is usually with aspirin and time or if the pleurisy is severe and unresponsive, NSAIDs. Antibiotics may be prescribed for a specific infection. Sclerosing therapy for chronic or recurrent pleurisy may be recommended.

SPECIAL IMPLICATIONS FOR THE THERAPIST 15-27

Pleurisy

PREFERRED PRACTICE PATTERNS

6C: Impaired Ventilation, Respiration/Gas Exchange, and Aerobic Capacity/Endurance Associated with Airway Clearance Dysfunction

6F: Impaired Ventilation and Respiration/Gas Exchange Associated with Respiratory Failure

Bed rest is an important part of the care plan for the client with pleurisy. Therapy in the acute care setting should be coordinated to provide as much uninterrupted rest as possible. Breathing and coughing exercises are important but often avoided because of the pain these respiratory movements cause. To minimize discomfort, apply firm pressure with hands or a pillow to the site of the pain during deep breathing and coughing.

Pleural Effusion

Definition

Pleural effusion is the collection of fluid in the pleural space (between the membrane encasing the lung and the membrane lining the thoracic cavity) where there is normally only a small amount of fluid to prevent friction as the lung expands and deflates (see Fig. 15-23). Pleural

fluid normally seeps continually into the pleural space from the capillaries lining the parietal pleura and is then reabsorbed by the visceral pleural capillaries and lymphatics.

Incidence and Etiologic Factors

The causes of pleural effusions are best considered in terms of the underlying pathophysiology: transudates caused by abnormalities of hydrostatic or osmotic pressure (e.g., congestive heart failure, cirrhosis with ascites, nephrotic syndrome, or peritoneal dialysis) and exudates resulting from increased permeability or trauma (e.g., infection, primary or secondary malignancy, PE, trauma including surgical trauma [e.g., cardiotomy]).

An exudate is a fluid with a high content of protein and cellular debris that has escaped from blood vessels and has been deposited in tissues or on tissue surfaces, usually as a result of inflammation. A transudate is a fluid substance that has passed through a membrane or has been forced out from a tissue; in contrast to an exudate, a transudate is characterized by high fluidity and a low content of protein, cells, or solid matter derived from cells. (See discussion in Chapter 6 and Figs. 6-8 and 6-9.)

Any condition that interferes with either the secretion or drainage of this fluid will lead to pleural effusion. Pleural effusion is common with heart failure and lymphatic obstruction caused by neoplasm. Less common causes include drug-induced effusion, pancreatitis, collagen vascular diseases (SLE or rheumatoid arthritis), intraabdominal abscess, or esophageal perforation. A person of any age can be affected, but it is more common in the older adult because of the increased incidence of heart failure and cancer.

Pathogenesis

The most common mechanism of pleural effusion is migration of fluids and other blood components through the walls of intact capillaries bordering the pleura. When stimulated by biochemical mediators of inflammation, junctions in the capillary endothelium separate slightly, enabling leukocytes and plasma proteins to migrate out into affected tissues. Rupture of a blood vessel or leakage of blood from an injured vessel causes a form of pleural effusion called hemothorax (see Fig. 15-23).

Malignancy effusion is usually a local effect of the tumor such as lymphatic obstruction or bronchial obstruction with pneumonia or atelectasis. Lymphatic blockage from any cause can result in drainage of the contents of lymphatic vessels into the pleural space. It can also be a result of systemic effects of tumor elsewhere, but in either case, malignant cells in the pleural effusion of a person with lung cancer indicate an inoperable situation.

Clinical Manifestations

Clinical manifestations of pleural effusion will depend on the amount of fluid present and the degree of lung compression. A small amount of effusion may be discovered only by chest x-ray examination. Large effusions cause clinical manifestations related to their volume and the rate at which they accumulate in the pleural space

causing restriction of lung expansion. Clients usually present with dyspnea on exertion that becomes progressive. They may develop nonspecific chest discomfort; sometimes the chest pain is pleuritic, which is a sharp, stabbing pain exacerbated by coughing or breathing and changes in position. Other symptoms characteristic of the underlying cause of pleural effusion may be the primary clinical picture (e.g., weight loss and fever with TB or cancer or signs of heart failure).³⁸⁰

MEDICAL MANAGEMENT

DIAGNOSIS. Examination of the pleural fluid via transthoracic aspiration biopsy (surgical puncture and drainage of the thoracic cavity) includes analysis of pH; specific gravity; protein; stains and cultures for bacteria, TB, and fungi; eosinophilia count; and glucose concentration to aid in the differential diagnosis.³⁸⁰

Some markers, such as neutrophil-derived enzymes, may be indicators for necessity of chest tubes for drainage. Chest pain must be differentiated from pain of pericardial or musculoskeletal origin. Chest radiographs and physical examination with possible CT scan are necessary components of the diagnostic process.

TREATMENT. Treatment may not be required when the individual is asymptomatic, or if the client is only mildly symptomatic, transthoracic aspiration may be all that is necessary. In the case of an underlying disease process (e.g., congestive heart failure or renal pathologic findings associated with transudates), treatment is aimed toward that condition.

Drainage of the fluid for exudate-caused effusion provides symptomatic improvement but does not significantly alter lung volumes or gas exchange. Removal of fluid associated with malignancy is considered only if the individual is symptomatic and could benefit from aspiration. Repeated aspiration is avoided since significant protein loss can occur and the fluid reaccumulates in 1 to 3 days.

Some (exudate) pleural effusions resolve with antibiotic therapy. Recurrent (exudate) pleural effusions may be treated by pleurectomy (surgically stripping the parietal pleura away from the visceral pleura) and pleurodesis (sclerosing substance introduced into the pleural space to create an inflammatory response that scleroses tissues together). Both of these procedures have negative effects that must be taken into consideration.

PROGNOSIS. Prognosis depends on the underlying disease; in cancer, recurrent pleural effusion may be associated with the terminal stage of disease. Tumor-related effusion generally implies a poor prognosis.

SPECIAL IMPLICATIONS FOR THE THERAPIST 15-28

Pleural Effusion

PREFERRED PRACTICE PATTERN

6F: Impaired Ventilation and Respiration/Gas Exchange Associated with Respiratory Failure

After transthoracic aspiration, encourage deep-breathing exercises to promote lung expansion and

watch for respiratory distress or pneumothorax (sudden onset of dyspnea or cyanosis). In the presence of a chest tube, prevent kinking by carefully coiling the tubing on top of the bed and securing it to the bed linen, leaving room for the client to turn.

Position changes must be performed carefully to avoid disturbing the surgical site or the chest tube. The therapist may apply firm support with both hands to the surgical site and chest tube area to help lessen muscle pull and pain as the client coughs. If the person has open drainage through a rib resection or intercostal tube, use hand and dressing precautions.

Small pleural effusions (greater than 500 ml) frequently have minimal findings on physical exam. Effusions with 500 to 1500 ml demonstrate dullness to percussion, diminished breath sounds, and reduced tactile and vocal fremitus over the involved hemithorax. Effusions greater than 1500 ml will present with concomitant atelectasis, demonstrate bronchial or tracheal breath sounds, and sound like the bleating of a goat on auscultation (referred to as egophony) with inspiratory lag on the affected side.

Pleural Empyema

Pleural empyema (infected pleural effusion) is an accumulation of pus that occurs occasionally as a complication of pleurisy or some other respiratory disease, usually pneumonia. It is a normal response to infection but may also occur after external contamination (penetrating trauma, chest tube placement, or other surgical proce-

dure) or esophageal perforation. Symptoms include dyspnea, coughing, ipsilateral pleural chest or shoulder pain, malaise, tachycardia, cough, and fever. In addition to chest films, transthoracic aspiration biopsy may be done to confirm the diagnosis and determine the specific causative organism.

The condition is treated with intercostal chest tube drainage, rest, and sedative cough mixtures. Long-term antibiotics are generally needed and attention must be paid to the person's nutritional status.⁸⁴ Intrapleural fibrinolytic agents may have some use reducing need for surgery in patients with empyema.⁴²² See Special Implications for the Therapist: Pleural Effusion in this chapter.

Pleural Fibrosis

Pleural fibrosis may follow inflammation (especially from asbestos), hemorrhagic effusion, and infection of the pleurae. It can present as localized plaques or diffuse. There appears to be a complex interaction of inflammatory cells, coagulation, profibrotic mediators, and growth factors in this process.³¹⁶ Early use of corticosteroids may decrease the incidence but is not effective in reducing established fibrosis. Surgical decortication can be effective in resolving symptoms.²⁰⁷

References

To enhance this text and add value for the reader, all references are included on the companion Evolve site that accompanies this textbook. The reader can view the reference source and access it on-line whenever possible. There are a total of 466 cited references and other general references for this chapter.

CHAPTER 16

The Gastrointestinal System

CATHERINE C. GOODMAN

The gastrointestinal (GI) tract consists of upper and lower segments with separate functions. The upper GI tract includes the mouth, esophagus, stomach, and duodenum and aids in the ingestion and digestion of food. The lower GI tract includes the small and large intestines (Fig. 16-1). The small intestine accomplishes digestion and absorption of nutrients, whereas the large intestine absorbs water and electrolytes, storing waste products of digestion until elimination.

The enteric nervous system has become the focus of new research and discoveries in a new area of study referred to as *psychoneuroimmunology* with a subspecialty of clinical gastroenterology called *neurogastroenterology*. There are as many nerve cells in the human small intestine as there are in the human spinal cord, and the enteric nervous system can function completely independently of the central nervous system. The enteric nervous system is sometimes referred to as the "brain in the bowel."

Insight into the connections among emotions, brain function, and GI function have revolutionized our thinking about the so-called mind-body connection. New information is being discovered about the sensory functions of the intestine and how neural, hormonal, and immune signals interact. More than 30 chemicals of different classes (neuropeptides, neurotransmitters) transmit instructions to the brain, and all these chemicals are represented in the enteric nervous system.

Representatives of all the major categories of immune cells are found in the gut or can be recruited rapidly from the circulation in response to an inflammatory stimulus. The constant presence of these neurotransmitters and neuromodulators in the bowel suggests that emotional expression or active coping generates a balance in the neuropeptide-receptor network and physiologic healing beginning in the GI system. In fact, it has been suggested that since the enteric nervous system can function on its own, it is possible that the brain in the bowel can have its own psychoneuroses such as the functional bowel syndromes discussed later in this chapter.⁵⁹

Scientists continue to study influences of the nervous system on immune and inflammatory responses in the mucosal surfaces of the intestines along with the innervation of the immune system and the molecular communication pathways as these relate to emotions and thoughts and the GI system.⁷⁰

The gut immune system has 70% to 80% of the body's immune cells, and the protective blocking action of the secretory response in the gut is crucial to the integrity of the GI tract immune function and host defense. Studies suggest that the development and expression of the regional immune system of the GI tract is independent of systemic immunity. Nutrients have fundamental and regulatory influences on the immune response of the GI tract and therefore on host defense.

Reduction of normal bacteria in the gut after antibiotic treatment or in the presence of infection may interfere with the nutrients available for immune function in the GI tract. New understanding of intestinal disorders and new approaches to the management of these disorders are expected in the next decade.

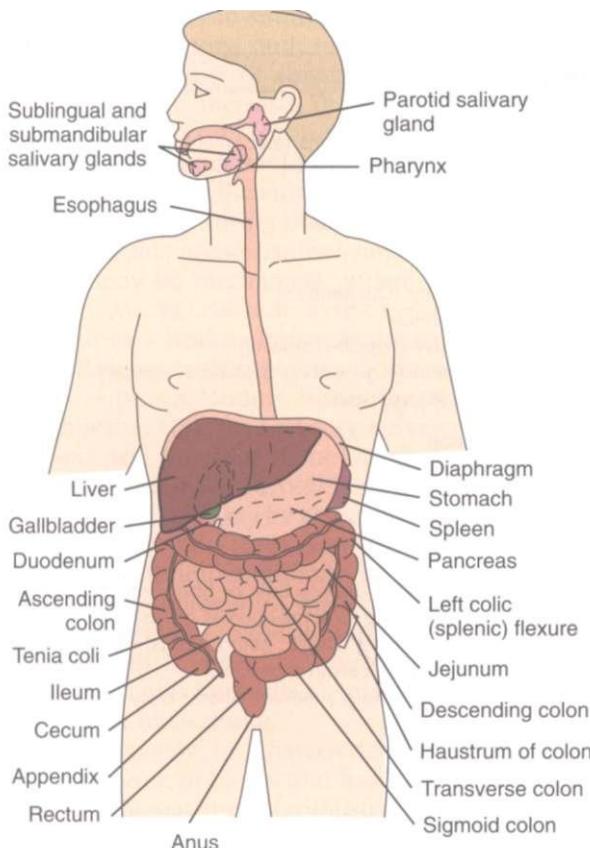
SIGNS AND SYMPTOMS OF GASTROINTESTINAL DISEASE

Clinical manifestations of GI disease can be caused by a variety of underlying conditions or disorders. The primary condition may be of GI origin, but some GI symptoms are part of a collection of systemic symptoms called *constitutional symptoms* and may be associated with any systemic condition (Table 16-1).

Nausea occurs when nerve endings in the stomach and other parts of the body are irritated and usually precedes vomiting. Intense pain in any part of the body can produce nausea as a result of the nausea-vomiting mechanism of the involuntary autonomic nervous system. Nausea can be caused by strong emotions and may accompany psychologic disorders, a variety of systemic disorders (e.g., acute myocardial infarction, diabetic acidosis, migraine, hepatobiliary and pancreatic disorders, Meniere's syndrome, and GI disorders), and drugs such as morphine, codeine, excess alcohol, anesthetics, and anticancer drugs.

Vomiting may be caused by anything that precipitates nausea. Complications of vomiting include fluid and electrolyte imbalances, pulmonary aspiration of vomitus, gastoesophageal mucosal tear (Mallory-Weiss syndrome), malnutrition, and rupture of the esophagus.

Diarrhea (abnormal frequency or volume of stools) results in poor absorption of water and nutritive elements

**Figure 16-1**

The digestive system.

and electrolytes, fluid volume deficit, and acidosis as a result of bicarbonate depletion (see Chapter 5). Other systemic effects of prolonged diarrhea are dehydration, electrolyte imbalance, and weight loss. The causes of diarrhea are many and varied (Table 16-2). Drug-induced diarrhea, most commonly associated with antibiotics, may not develop until 2 to 3 weeks after first ingestion of an antibiotic, but if the onset of diarrhea coincides with the use of drugs, it may resolve when the drug is discontinued.

Anorexia, diminished appetite or aversion to food, is a nonspecific symptom often associated with nausea, vomiting, and sometimes diarrhea. It may be associated with disorders of other organ systems, including cancer, heart disease, and renal disease. It is the major component of eating disorders such as *anorexia nervosa*.

Anorexia-cachexia, a systemic response to cancer, occurs as a result of increased metabolic rate caused by the tumor cells and metabolites produced and released by tumor cells into the bloodstream. These effects of tumor cells stimulate the satiety center in the hypothalamus and produce appetite loss, gross alterations of metabolic patterns, and a profound systemic condition referred to as *anorexia-cachexia*. A downward spiral of symptoms occurs with appetite loss leading to malnutrition, weight loss, muscular weakness, and a negative nitrogen balance that contributes to the development of cachectic wasting.

Table 16-1 Clinical Manifestations of Gastrointestinal (GI) Disease

GI Signs and Symptoms	Constitutional Symptoms	GI Signs and Symptoms Associated with Strenuous Exercise
Nausea and vomiting	Nausea	Fecal urgency; diarrhea
Diarrhea	Vomiting	Abdominal cramps
Anorexia	Diarrhea	Belching
Constipation	Malaise	Nausea and vomiting
Dysphagia	Fatigue	Heartburn
Achalasia	Fever	
Heartburn	Night sweats	
Abdominal pain	Pallor	
Gastrointestinal bleeding	Diaphoresis	
Hematemesis	Dizziness	
Melena		
Hematochezia		
Fecal incontinence		

Constipation is a common condition affecting up to one quarter of the American population, especially prevalent in women and people over the age of 65 years.⁶⁸ Constipation occurs when fecal matter is too hard to pass easily or when bowel movements are so infrequent that discomfort and other symptoms interfere with daily activities.

Constipation may occur as a result of many factors such as diet, dehydration (including lack of fluid intake), side effects of medication, acute or chronic diseases of the digestive system, inactivity or prolonged bed rest, emotional stress, personality, and lack of exercise (see Table 16-2).

Although constipation often is described as a condition of old age, it is probably multifactorial, caused more often by lifestyle factors than by physiologic decline. Life-long bowel habits, current diet, lack of fluid intake, and immobility are likely causes of constipation in the older adult (older than 65 years).⁴³ Constipation may be the result of underlying organic disease or may be caused by lesions or structural abnormalities within the colon that narrow the intestines and/or rectum, slow-transit alimentary canal, and defecatory disorders.⁶⁴

People with mechanical low back pain may develop constipation as a result of muscle guarding and splinting that causes reduced bowel motility. Pressure on sacral nerves from stored fecal content may cause an aching discomfort in the sacrum, buttocks, or thighs.⁶⁰

Constipation associated with defecatory disorders can be the result of pelvic floor or anal sphincter dysfunction, including pelvic floor dyssynergia, spastic pelvic floor syndrome, and anismus. In these disorders, the external anal sphincter contracts and tightens rather than relaxing and opening during defecation. Individuals with this type of constipation often strain to defecate and experience incomplete bowel emptying.⁸⁹

Dysphagia (difficulty swallowing) produces the sensation that food is stuck somewhere in the throat or chest

Table 16-2 Causes of Diarrhea and Constipation

	Diarrhea	Constipation
Neurogenic	Irritable bowel syndrome Diabetic enteropathy Hyperthyroidism Caffeine	Irritable bowel syndrome Central nervous system lesions (e.g., multiple sclerosis, Parkinson's) Dementia Spinal cord tumors or lesions Atony
Muscular	Muscular incompetence Electrolyte imbalance Endocrine disorder	Muscular dystrophy (Duchenne's) Electrolyte imbalance Endocrine disorder (hypothyroidism) Severe malnutrition (e.g., eating disorders, cancer) Inactivity; back injury/pain
Mechanical	Incomplete obstruction (e.g., neoplasm, adhesions, stenosis) Postoperative effect (e.g., gastrectomy, ileal bypass, intestinal resection, cholecystectomy) Diverticulitis	Bowel obstruction Extraalimentary tumors Pregnancy Colostomy
Other	Diet (including food allergy, lactose intolerance, food additives) Medications (including antibiotics, over-the-counter drugs, and laxative abuse) Supplements (creatine) Malabsorption Infectious/inflammatory disorders (including pelvic inflammatory disease) Strenuous exercise	Diet (especially lack of dietary bulk or fiber, iron compounds) Medications* (including over-the-counter drugs) Rectal lesions (e.g., anal fissure, hemorrhoids, abscess, rectocele, stenosis, ulcerative proctitis) Psychologic variables (e.g., mental illness, busy lifestyle or ignoring the urge)

*Many drugs commonly prescribed, especially for older adults, can cause constipation, including α -adrenergic blocking agents, angiotensin-converting enzyme inhibitors, antiarrhythmics, anticholinergic antiseizure drugs, antihistamines, antilipidemics, antiparkinson drugs, antipsychotics, benzodiazepines, calcium channel blockers, nonsteroidal antiinflammatory agents, opioids, and antidepressants.

(esophagus). Dysphagia may be a symptom of many other disorders, including neurologic conditions (e.g., stroke, Alzheimer's disease, Parkinson's disease), local trauma and muscle damage (including physical assault), or mechanical obstruction. Obstruction may be *intrinsic*, originating in the wall of the esophageal lumen (e.g., tumors, strictures, outpouchings called *diverticula*), or *extrinsic*, outside the esophageal lumen, such as a tumor or swelling that prevents the passage of food. Dysphagia caused by swelling can occur as a side effect of certain types of drugs such as antidepressants, antihypertensives, and asthma medications.

Achalasia is a failure to relax the smooth muscle fibers of the GI tract. This especially occurs as a result of failure of the lower esophageal sphincter (LES) to relax normally with swallowing. The affected person reports a feeling of fullness in the sternal region and progressive dysphagia.

Although the cause of achalasia is not known, the loss or absence of ganglion cells in the myenteric plexus of the esophagus appears to be a part of the cause. The myenteric plexus is the nerve plexus lying in the muscular layers of the esophagus, stomach, and intestines. Anxiety and emotional tension aggravate the condition and pre-

cipitate the attacks. Progression of the condition results in dilation of the esophagus and loss of peristalsis in the lower two thirds of the esophagus.

Heartburn, dyspepsia, pyrosis, or indigestion, a burning sensation in the esophagus usually felt in the midline below the sternum in the region of the heart, is often a symptom of gastroesophageal reflux and occurs when acidic contents of the stomach move backward or regurgitate into the esophagus. The presence of a hiatal hernia, drugs such as alcohol and aspirin, and movements such as lifting, stooping, or bending over after a large meal may bring on heartburn. Indigestion also may be a potential manifestation of angina associated with coronary artery disease.

Certain foods act as muscle relaxants and can also bring on heartburn. For example, chocolate contains four substances that can relax the LES: caffeine, theobromine, theophylline, and fat. Fat-rich foods lower sphincter muscle pressure by release of cholecystokinin from the upper intestinal mucosa. Fat also delays emptying of the stomach, giving more opportunity for this effect to occur. Other implicated foods include spicy and highly seasoned foods, onions, alcohol, peppermint, and spearmint.

Emotional stress can stimulate the vagus nerve, which controls the secretory and motility functions of the stomach. Stimulation of this cranial nerve causes the stomach to churn, increases the flow of various gastric juices, and causes contraction and spasm of the pylorus (opening of the stomach into the duodenum). Heartburn can occur if some of the stomach contents are displaced into the esophagus during this nervous activity.

Abdominal pain accompanies a large number of GI diseases and may be mechanical, inflammatory, ischemic, or referred. *Mechanical pain* occurs because of stretching of the wall of a hollow organ or the capsule of a solid organ. *Inflammatory pain* occurs via the release of mediators such as prostaglandins, histamine, and serotonin or bradykinin that stimulate sensory nerve endings.

Ischemic pain occurs as tissue metabolites are released in an area of diminished blood flow. *Referred pain* usually is well localized and may be associated with hyperalgesia and muscle guarding. Pain from the spine also can be referred to the abdomen, usually as a result of nerve root irritation or compression. This type of neuromusculoskeletal pain referred to the abdomen is characteristically associated with hyperesthesia over the involved spinal dermatomes and is intensified by motions such as coughing, sneezing, or straining.

GI bleeding may be characterized by coffee-ground emesis (vomiting of blood that has been in contact with gastric acid), hematemesis (vomiting of bright red blood), melena (black, tarry stools), or hematochezia (bleeding from the rectum, or maroon-colored stools), depending on the location of the lesion. Bleeding may not be clinically obvious to the client and may be diagnosed only by further testing.

The major causes of upper GI bleeding in the therapy population are erosive gastritis common in (1) severely ill people with major trauma or systemic illness, burns, or head injury; (2) peptic ulcers; (3) use of nonsteroidal antiinflammatory drugs (NSAIDs) such as aspirin or ibuprofen; and (4) chronic alcohol use. Drugs such as warfarin, heparin, and aspirin used as anticoagulants in the treatment of pulmonary emboli, venous thrombus, or valvular abnormalities can contribute to or exacerbate gastric erosion and subsequent bleeding.

Accumulation of blood in the GI tract is irritating and increases peristalsis, causing nausea, vomiting, or diarrhea with possible referred pain to the shoulder or back. The digestion of proteins originating from massive upper GI bleeding is reflected by an increase in blood urea nitrogen (BUN) (see Table 40-2). Other complications include fatigue, postural hypotension, tachycardia, weakness, or shortness of breath on exertion. Slow, chronic blood loss may result in iron deficiency anemia.

Fecal incontinence (inability to control bowel movements) has both psychologic and physiologic contributing factors. Psychologic factors include anxiety, confusion, disorientation, and depression. The most commonly observed physiologic causes seen in a therapy practice are neurologic sensory and motor impairment (e.g., stroke and spinal cord injury); anal distortion secondary to traumatic childbirth, sexual assault, hemorrhoids, and hemorrhoidal surgery; altered levels of consciousness; and severe diarrhea.

SPECIAL IMPLICATIONS FOR THE THERAPIST

16-1

Signs and Symptoms of Gastrointestinal Disease

Fluid and Electrolyte Imbalance

Body fluid loss associated with weight loss, excessive perspiration, or chronic diarrhea and vomiting may cause an imbalance in the body chemistry (electrolyte imbalance) and may cause orthostatic changes in blood pressure (i.e., postural drops in blood pressure).

Electrolyte changes often include decreased potassium, which alters the sodium-potassium pump necessary for normal muscle function (contraction and relaxation). Muscle cramping occurs, which increases a person's risk for musculoskeletal injury during exercise.

In anyone with chronic diarrhea taking antidiarrheal agents containing bismuth subsalicylate, such as Pepto-Bismol, Bismatrol, Pink Bismuth, or Kaopectate, the client may report darkened or black stools. The tongue may also appear black.

Significant postural hypotension often reflects extracellular fluid volume depletion as occurs with excessive body fluid loss. The maintenance of arterial pressure during upright posture depends on adequate blood volume, an unimpaired venous return, and an intact sympathetic nervous system. Monitoring vital signs and observing for accompanying symptoms promote safe and effective exercise for anyone with the potential for electrolyte imbalance. See Chapter 5 and Appendix B: Guidelines for Activity and Exercise.

In a screening interview, the therapist should always ask clients if there are any other symptoms of any kind to report. Remember to ask about the use of nutritional or other supplements (especially among athletes) as these can have adverse GI effects on some people. For example, creatine used to improve athletic performance can cause loss of appetite, diarrhea, dizziness, and cramps, presumably from dehydration.

Pelvic Floor Rehabilitation

The physical therapist can assist individuals with constipation associated with defecatory disorders involving the soft tissues of the pelvic floor. Pelvic floor muscle strength and tone and breathing patterns during pelvic floor contraction/relaxation can be assessed. Retraining pelvic floor muscle function during evacuation is a key part of the rehabilitation process.⁶⁴

Clients can be trained to relax their external anal sphincter and learn to coordinate abdominal contractions to assist stool propulsion into the rectum. Toileting techniques to avoid straining during a bowel movement may help decrease the risk of developing pudendal nerve dysfunction. The therapist can be helpful in identifying ways to incorporate scheduled toileting with transfer, strength, and balance training.⁶⁴ Bathroom and safety modifications can also be made.

Continued.

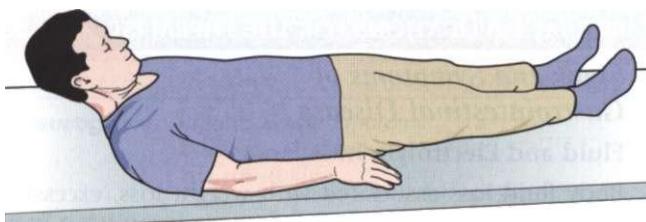


Figure 16-2

The Shaker head-lifting exercise to strengthen the upper esophageal sphincter muscle. The affected person lies in the supine position keeping the feet, back, and shoulders and arms down. The person raises the head until the toes can be seen, pauses but does not hold the head lift, then lowers the head back down. This movement is repeated 30 times (isokinetic exercise) using a relatively constant speed of movement. The person rests for 1 minute, then raises the head and looks at the feet for 1 minute, pauses 1 minute, and repeats the long look and long rest twice more (isometric exercise). The entire sequence should be completed three times daily. These exercises can be used by anyone with dysphagia or other swallowing problems in addition to hiatal hernia and gastroesophageal reflux disease (GERD). (Exercise developed by R. Shaker, MD, Medical College of Wisconsin, Milwaukee, 1998.)

Exercise and Gastrointestinal Function

Slow-transit constipation as a result of decreased neuromuscular function of the colon can be improved with aerobic exercise.⁵⁸ Strengthening exercises can also decrease GI transit time.⁵⁹ The therapist has a key role in client education helping people understand the benefit of exercise and activity in promoting better bowel transit time and potentially relieving constipation. Older adults who are constipated do not want to exercise or engage in activity. They must understand that refusal to increase activity can aggravate the constipation.

During an upper quadrant screening, the therapist usually inquires whether the client has difficulty swallowing. Forward head posture or anterior disk protrusion may be a possible cause of difficulty swallowing, but a pathologic condition of the esophagus may also be the cause.

The therapist can instruct anyone with dysphagia who does not have cervical disk disease in an isometric/isotonic head lift exercise that may restore normal swallowing, thereby helping some individuals to eat normally and keep food or liquids from being aspirated into the lungs (Fig. 16-2).

This exercise strengthens muscles that open the upper esophageal sphincter, the "gate" that allows food or drink to slide down the esophagus to the stomach. This exercise works best for people with weak or ineffective upper esophageal sphincter but may prove useful for other types of swallowing problems. How long the exercise must be continued once the swallowing function returns remains under investigation.⁵³

Studies have documented the physiologic changes in the GI system and the onset of GI symptoms during and after strenuous exercise. Intensity and duration of exercise are important factors, and lower GI symptoms predominate.¹⁵² On the other hand, GI bleeding can

be reduced with regular exercise, and people with limited physical activity (e.g., physical disability) are at greater risk for ulceration and GI bleeding.

Referred Pain Patterns

An acute ulcer can present as thoracolumbar junction pain. Back pain and/or shoulder pain caused by GI bleeding and perforation associated with an ulcer of long standing may cause painful biomechanical changes in muscular contractions and spinal movement.^{60,123} The clinical presentation may be one with objective musculoskeletal findings to support a diagnosis of back or shoulder dysfunction when, in fact, the symptoms may be associated with GI bleeding. See also Special Implications for the Therapist: Anemias in Chapter 13.

Pain in the left shoulder caused by free air or blood in the abdominal cavity is called *Kehr's sign* and may occur with perforation of viscus (e.g., stomach ulcer, diverticular disease), after laparoscopy (lasting 24 to 48 hours), or after rupture of the spleen. Any precipitating trauma or injury, such as a sharp blow during an athletic event, fall, assault, or automobile accident, may elicit Kehr's sign. Laparoscopy, the visual inspection of the peritoneal cavity using an instrument called an *endoscope*, and other abdominal surgical procedures that introduce air into the abdominal cavity can place pressure on the diaphragm, causing shoulder pain.

AGING AND THE GASTROINTESTINAL SYSTEM

Age-related changes in GI function begin before the age of 50 years. Constipation, incontinence, and diverticular disease are the GI problems most commonly seen in older adults, but each of these disorders has many different underlying causes, and the specific pathogenesis dictates treatment.

Oral changes may include tooth enamel and dentin wear and increasing tooth decay, causing periodontal disease and subsequent tooth loss. Sensory changes may include decreased taste buds and diminished sense of smell resulting in altered sense of taste. These oral and sensory changes eventually depress the appetite and make eating less pleasurable. Salivary secretion decreases, contributing to dry mouth, and when it is complicated by tooth decay or loss, chewing food and swallowing become more difficult.

The alimentary organs (esophagus, stomach, small intestine, and colon), like all muscular structures, lose some tone with age but still manage to perform almost as well in age as in youth. Changes within the alimentary tract include decreases in gastric motility, blood flow, nutrient absorption, and volume and acid content of gastric juice. These changes slow gastric digestion and emptying but usually not enough to be noticeable. Proteins, fats, minerals including iron and calcium, and vitamins are absorbed more slowly and in lesser amounts, and carbohydrates are absorbed more slowly.

A decline in the production of intrinsic factor (IF), a substance that promotes vitamin B12 absorption in the stomach, frequently occurs after middle age. B12 is required to produce blood cells and to maintain the integrity of the nervous and GI systems. B12 deficiency can lead to pernicious anemia with its hematologic and neurologic manifestations and GI symptoms (e.g., diarrhea, constipation, weight loss).

In advanced age, the prevalence of such problems associated with B12 deficiency increases to 90% for those aged 90 and older. Other causes of B12 deficiency with aging include low dietary intake of B12, gastric atrophy (gradual loss of stomach lining with decreased hydrochloric acid), and atrophic gastritis. As these conditions progress, IF is lost and, with it, the ability to extract B12 from food.

Atrophic gastritis may be the result of many possible variables, including normal aging, nutritional deficiency (e.g., iron, folate, ascorbate), autoimmune mechanisms, endocrine insufficiency (e.g., thyroid, adrenal, pancreatic), or infection (usually with *Helicobacter pylori*).¹⁴ *H. pylori* is a gram-negative spiral bacterium that lives in the gastric mucosal layer of humans and induces a chronic inflammatory response that can result in both peptic ulceration and gastric neoplasms.

Further research is needed regarding the basic mechanisms in neuromuscular dysfunction with aging, including studies of physical characteristics of the colonic wall, pelvic floor function, and neurohormonal control of motility and sensation. Insights on the pathophysiology and mechanisms of neural injury and aging may lead to more specific treatments in the future (e.g., serotonergic agents and neurotrophins).¹⁵

In addition to the effects of aging on the GI system, changes in other organ systems (e.g., endocrine, cardiovascular, and nervous systems) also can affect GI structure and function, producing many variations in presentation of illness. Extraintestinal disorders, such as diabetes and the neurologic and vascular changes that occur with age, have a greater effect on the GI tract than the natural process of aging.

THE ESOPHAGUS

Hiatal Hernia

Definition and Incidence

A hiatal or diaphragmatic hernia occurs when the cardiac (lower esophageal) sphincter becomes enlarged, allowing the stomach to pass through the diaphragm into the thoracic cavity (Fig. 16-3). Hernias are either *congenital*, resulting from a failure of formation or fusion of the multiple developmental components of the diaphragm, or *acquired*, as a result of penetrating wounds, particularly stab wounds and gunshot wounds; blunt trauma, as occurs in motor vehicle accidents; and less commonly as a result of surgical trauma, empyema, and subphrenic abscess.

Hiatal hernia (symptomatic or asymptomatic) is common, and the incidence has been estimated as 5 per 1000. The incidence increases with age and may be as high as 60% in people over 60 years of age. Women are

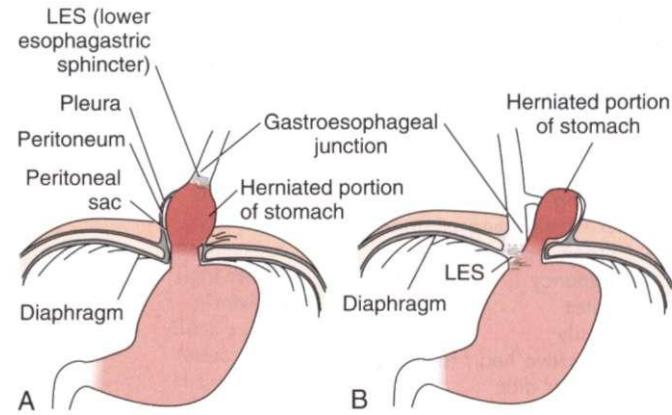


Figure 16-3

Hiatal hernia. **A**, Sliding hiatal hernia. Approximately 90% of esophageal hiatal hernias are sliding hernias. The stomach and gastroesophageal junction are displaced upward into the thorax (i.e., the stomach and gastroesophageal junction slide up into the thoracic cavity, following the usual path of the esophagus through an enlarged hiatal opening in the diaphragm). **B**, Rolling hiatal hernia. The remaining hiatal hernias are rolling or paraesophageal hernias. The gastroesophageal junction stays below the diaphragm, but all or part of the stomach pushes through into the thorax.

affected more often than men, and children may have the sliding type but do not usually exhibit symptoms until they reach middle age.

Etiologic and Risk Factors

As an acquired condition, multiple causes and risk factors exist for the development of hiatal hernia. Anything that weakens the diaphragm muscle or alters the hiatus (the opening in the diaphragm for the passage of the esophagus) and increases intraabdominal pressure can predispose a person to hiatal hernia. Muscle weakness can be congenital or caused by aging, trauma, surgery, or anything that increases intraabdominal pressure (Box 16-1).

Pathogenesis and Clinical Manifestations

As part of the stomach herniates through a weakness in the diaphragm, regurgitation and motor impairment cause the major clinical manifestations associated with this type of hernia. There is evidence for its origin in esophageal longitudinal muscle dysfunction, indicating that this condition could originate from alterations in nerve innervation, alteration in the viscoelastic properties of distal esophagus, or increased strength of unopposed longitudinal muscle layers.^{27,28}

Symptoms vary depending on the type of hernia present and increase in the presence of tight, constrictive clothing or if the person is in a recumbent position. A sliding hernia may produce heartburn 30 to 60 minutes after a meal, especially if the person is lying down or sleeping in the supine position. Large sliding hernias with reflux may be associated with substernal pain. Rolling hernias are not subject to altered pressure or the resulting reflux, but the person may complain of difficult and painful swallowing.

Box 16-1**CAUSES OF INCREASED INTRAABDOMINAL PRESSURE**

- Lifting
- Straining
- Bending over
- Prolonged sitting or standing
- Chronic or forceful cough
- Pregnancy
- Ascites
- Obesity
- Congestive heart failure
- Low-fiber diet
- Constipation (see Table 16-2)
- Delayed bowel movement
- Vigorous exercise

MEDICAL MANAGEMENT

DIAGNOSIS, TREATMENT, AND PROGNOSIS. Hiatal hernias may be diagnosed by ultrasonography or barium swallow with fluoroscopy showing the position of the stomach in relation to the diaphragm. These tests may both be necessary to confirm the diagnosis, because the hernia may slide down when the person is placed in the upright position for the radiograph.

The primary treatment remains symptomatic control through the use of antacids and elevating the head of the bed. Treatment is essentially the same for gastroesophageal reflux disease (see the section on Gastroesophageal Reflux Disease in this chapter). The prognosis is good overall with recurrences expected.

SPECIAL IMPLICATIONS FOR THE THERAPIST**16-2****Hiatal Hernia**

For any client with a known hiatal hernia, the flat supine position and any exercises requiring the Valsalva maneuver (which increases intraabdominal pressure) should be avoided during therapy intervention. Before discharge, the client must be warned against activities that cause increased intraabdominal pressure and given safe lifting instructions.

A slow return to function over the next 6 to 8 weeks is advised. Postoperatively (after surgical repair of the hernia using the thoracic approach), the client may have chest tubes in place requiring careful observation of the tubes during turning and repositioning and chest physical therapy to prevent pulmonary complications.

Gastroesophageal Reflux Disease**Definition**

Gastroesophageal reflux disease (GERD), or esophagitis, may be defined as an inflammation of the esophagus, which may be the result of reflux (backward flow) of infectious agents, chemical irritants, physical agents such

as radiation and nasogastric intubation, or gastric juices. *Heartburn* or *acid indigestion* is not just another term for GERD; it is the most common symptom of GERD, a complex disease with potentially serious complications.

Reflux esophagitis is the most common type of esophagitis, with backward or return flow of the stomach and duodenal contents into the esophagus. Other types of esophagitis, such as infectious esophagitis, may occur with immunosuppression resulting from viral, bacterial, fungal, or parasitic organisms. Chemical esophagitis is usually a result of accidental poisoning in children or attempted suicide in adults. External irradiation for the treatment of thoracic cancers may include portions of the esophagus and lead to esophagitis and stricture.

Incidence and Etiologic Factors

Although any age can be affected, this condition has an increasing incidence with increasing age; older people are more likely to develop severe disease.¹¹⁵

It is estimated that 15% or more of the population has daily symptoms of GERD and as much as one third of the population has monthly symptoms. A reduction in the pressure of the LES, increased gastric pressure, or gastric contents located near the gastroesophageal junction can contribute to the development of esophageal reflux. A wide range of foods and lifestyle factors can contribute to GERD¹¹⁶ (Table 16-3).

Reflux is often associated with a sliding hiatal hernia, also called a *diaphragmatic hernia* (see Fig. 16-3). Smooth muscle relaxants used for cardiac conditions, such as (3-adrenergics, aminophylline, nitrates, and calcium channel blockers, may contribute to incompetence of the LES.

Pathogenesis

Normally, a high-pressure zone exists around the gastroesophageal sphincter, which permits the passage of food and liquids but prevents reflux. Any of the predisposing factors listed in Table 16-3 may alter the pressure around the LES, resulting in reflux.

Hydrochloric acid or gastric and duodenal contents containing bile acid and pancreatic juice coming in contact with the walls of the esophagus cause inflammation and mucosal ulcerations that may bleed. Subsequent granulation tissue causes scarring that frequently develops into esophageal strictures that narrow the esophagus, making swallowing difficult.

Clinical Manifestations

Heartburn, reflux, belching, dysphagia, and painful swallowing are the primary symptoms of esophagitis in younger adults. Pain usually is described as a burning sensation that moves up and down and may radiate to the back, neck, or jaw. Heartburn most often occurs 30 to 60 minutes after a meal and is produced by contact of regurgitated contents with the inflamed esophageal mucosa.

Children can be affected by GERD. Symptoms are similar to those experienced by adults. Persistent GERD is linked to developmental problems. Neurologic disorders and GERD can have overlapping symptoms, such as irritability associated with arching, neck extension, and abnormal muscle tone with spastic movements.

Table 16-3 Causes of Gastroesophageal Reflux Disease

Decreased Pressure of Lower Esophageal Sphincter	Increased Gastric Pressure	Gastric Contents Near Junction
Foods: chocolate, peppermint, fatty foods, citrus products (including tomatoes), spicy foods, garlic, onions	Food (protein)	Recumbency
Beverages: coffee (including decaf), carbonated drinks, alcohol	Pregnancy (increased abdominal pressure)	Increased intraabdominal pressure
Caffeine	Obesity	
Nicotine or cigarette smoke	Ascites	
Central nervous system depressants (e.g., morphine, diazepam)	Tight clothing; Spandex; pantyhose	
Other medications (e.g., calcium channel blockers, dopamine, theophylline, tricyclic antidepressants)	Back supports	
Estrogen therapy	Antacids	
Nasogastric intubation	Histamines	
Scleroderma		
Prolonged vomiting		
Surgical resection (destroys sphincter)		
Position (right side lying; sitting)		
Pregnancy (last trimester: increased progesterone relaxes sphincter)		

Asthma may be associated with GERD in both children and adults, although the relationship is not well understood at this time. Reflux exacerbates asthma, potentially by the acid's triggering a vagal response. Aspiration of gastric acid contents can cause bronchorestriction; acid reflux medications can actually help reduce asthma symptoms.

Older adults (older than 70 years) are more likely to have atypical symptoms such as dysphagia, vomiting, respiratory difficulties, weight loss, anemia, and anorexia with or without heartburn or acid regurgitation. Dysphagia is an indication of narrowing of the lumen, usually as a result of edema, spasm, or esophageal strictures. Pathophysiologic changes in esophageal function associated with age are also contributing factors in the development of dysphagia.¹¹⁵ Aggravating factors include recumbency, bending, and meals; relief is obtained with antacids or baking soda, standing and walking, fluids, and avoidance of predisposing factors.

Although GERD is more serious and potentially more damaging than simple heartburn, its symptoms are not necessarily more severe. Reflux in the absence of esophagitis may be asymptomatic or accompanied by a sour taste in the mouth; severe reflux may reach the pharynx and mouth and result in laryngitis and morning hoarseness. Pulmonary aspiration can occur in people who are incapacitated (e.g., neurologically impaired); recurrent pulmonary aspiration can cause aspiration pneumonia, pulmonary fibrosis, or chronic asthma.

Complications of chronic heartburn include reflux esophagitis, strictures, and Barrett's esophagus. Reflux esophagitis is an inflammation of the lining of the esophagus caused by chronic exposure to stomach acid. Esophageal ulcers that can bleed and cause severe pain can develop. When the ulcers heal, scar tissue forms, creating fibrous strictures that can narrow the lumen of the esophagus.

Persistent GERD may cause a more serious complication known as Barrett's esophagus. Barrett's esophagus is a condition that occurs when a damaged esophagus heals abnormally, so that the lining develops a type of cell

normally found in the intestine rather than in the esophagus. The intestine-type cells are more resistant to acid but can become cancerous.

MEDICAL MANAGEMENT

DIAGNOSIS. Diagnostic tools include history, endoscopy, barium radiography, and *H. pylori* and esophageal pH testing. A full diagnostic evaluation is not always required when history and current symptoms clearly point to esophagitis; a therapeutic trial of treatment in mild cases may be diagnostic in itself.

Ironically, some individuals who think they have excess stomach acid may actually suffer from indigestion from deficient stomach acid. Taking antacids when stomach acid is already chronically deficient can lead to nutritional deficiencies such as vitamin B12 deficiency. The end result can be even more complications from anemia and dementia. Proper medical evaluation is always advised before self-treating for what may seem like indigestion.

Response to nitroglycerin may help the physician differentiate between esophagitis and angina pectoris, but the response is not always diagnostic because nitroglycerin also can relieve esophageal spasm and some women with angina improve with antacids rather than nitroglycerin.

TREATMENT. The goals of treatment are to alleviate symptoms, heal esophagitis if present, maintain remission of the disease, and manage any complications.

MEDICATIONS. The first-line treatment is acid-suppressing inhibitors called proton pump inhibitors (PPIs) (e.g., Prilosec, Aciphex, Prevacid, Nexium) for the healing of erosive GERD and maintenance of healed erosive GERD (Table 16-4).

These medications shut off the chemical pump that transports acid into the stomach, cutting acid production to zero. This usually brings fast relief and healing of burns and erosions in the esophagus. The individual treated with these drugs must digest foods without the benefit of stomach acid.

Table 16-4 Common Types of Medications Used for Gastroesophageal Reflux Disease

Medication	Common Examples	Mechanism	Common Side Effects
Proton pump inhibitor (PPI)	Lansoprazole (Prevacid) Omeprazole (Prilosec) Esomeprazole (Nexium) Rabeprazole (Aciphex)	Shuts off acid pump; blocks stomach acid production	Headache Constipation or diarrhea Abdominal pain
Histamine 2 receptor blocker	Cimetidine (Tagamet) Ranitidine (Zantac) Famotidine (Pepcid)	Reduces acid production by the stomach	Headache Nausea Constipation or diarrhea Dizziness Abdominal pain
Antacid	Calcium carbonate (Tums) Calcium carbonate/magnesium hydroxide (Mylanta, Rolaids) Magnesium-aluminum hydroxide (Maalox)	Neutralizes and reduces stomach acid	Loss of appetite Constipation or diarrhea

Long-term suppression of stomach acid is not advised unless recurrence cannot be controlled or esophageal healing cannot be maintained. Doctors usually administer PPIs for a limited time to allow healing but avoid adverse effects of chronic use. The long-term effects of PPIs remain unknown. Researchers are looking for a way to restore the natural mechanisms that prevent gastric acid reflux.

Uncomplicated cases of esophagitis and typical symptoms of heartburn and regurgitation may be treated with two types of over-the-counter drugs: histamine 2 blockers (H_2 -blockers) such as Tagamet, Zantac, or Pepcid AC and antacids (Tums, Rolaids, Mylanta, Maalox). Antacids neutralize stomach acid, whereas histamine blockers prevent acid secretion. The goal of antacids is quick symptom relief, whereas the goal of histamine blockers is long-term cure. Drinking fluids between meals (not with meals) helps reduce the likelihood of reflux.

Individuals should avoid prolonged and regular use of antacids as this can reduce the body's phosphate levels, with resultant fatigue and loss of appetite. Aluminum hydroxide tends to produce constipation, whereas magnesium hydroxide can cause loose stools or diarrhea in some individuals.

LIFESTYLE MODIFICATIONS. Lifestyle modifications also may be recommended, including wearing loose clothing; avoiding caffeine, nicotine, alcohol, salicylates, and NSAIDs; remaining upright at least 3 hours after meals; avoiding meals near bedtime or nap time; losing weight, if obese (this last recommendation has not been confirmed by clinical studies).

Elevation of the head of the bed at least 6 inches to reduce nocturnal reflux and enhance esophageal acid clearance may help. Some people find it helpful to sleep on their left side. This may help keep the acidic contents of the stomach below the juncture of the lower esophagus.

Some people find it helpful to avoid vigorous activities for 1 to 3 hours after eating. Avoiding large meals that can distend the stomach and avoiding foods that decrease pressure in the LES (e.g., chocolate, peppermint, alcohol, caffeine, fried and fatty foods), thereby causing reflux, may be helpful. Acidic foods such as orange juice, wine,

and tomatoes may irritate an already inflamed esophagus. Keeping a food diary and recording any symptoms may help each individual determine personal triggers.

Chewing sugarless gum after a meal helps promote salivation and aids in neutralizing acid. Greater saliva production also soothes the esophagus by washing acid back down to the stomach. Avoiding peppermint flavors and quitting the use of tobacco products will also increase saliva production.

SURGERY. Minimally invasive endoscopic surgical procedures (e.g., antireflux therapy) to tighten up the LES are being developed. These procedures may eventually allow the majority of people to stop taking all GERD medications, including PPIs.⁷²

Endoscopic or luminal delivered techniques for the treatment of GERD include endoscopic radiofrequency therapy, endoscopic injection or implantation of a liquid polymer directly into the weakened esophageal sphincter, and plication. Data to establish long-term efficacy of these techniques have not been reported yet, but the results of short-term studies have been favorable for some individuals. Not everyone is a good candidate for surgical intervention.¹⁴⁹

Suturing or gastroplication is done endoscopically so that the surgeon can see where to place the stitches. A special suturing device called an EndoCinch is inserted into the esophagus, allowing the surgeon to place a stitch in the upper stomach about 1 cm below the LES. Another stitch is placed next to the first and the two stitches are tied or clipped together to form a pleat. More than one pleat may be needed. Fundoplication is another antireflux surgical procedure. It involves wrapping the fundus of the stomach around the lower esophagus, creating either a 360-degree wrap or an incomplete wrap.

An implantable product called Enteryx has been removed from the market due to reported complications. Enteryx was a liquid injected into the lower esophagus through an endoscope, which then solidified into a spongy material to reinforce the sphincter.²²

PROGNOSIS. The prognosis is good for reflux esophagitis with complete symptom resolution, but often variable for the chemical type and poor for infectious esophagitis.

GERD can contribute to asthma and vocal cord inflammation, and people who have uncontrolled acid reflux are at increased risk of developing esophageal cancer, which has a very poor prognosis.^{50,63}

SPECIAL IMPLICATIONS FOR THE THERAPIST 16-3

Gastroesophageal Reflux Disease

Clients with GERD are often treated in a therapy practice or rehabilitation setting for orthopedic and other conditions. Occasionally, GERD presents with atypical head and neck symptoms (e.g., sensation of a lump in the throat) without heartburn.

Exercise and Gastroesophageal Reflux Disease

Exercise is important for anyone with GERD who is overweight. Excess abdominal fat puts pressure on the stomach; even moderate weight loss can reduce symptoms. However, people with GERD may have trouble exercising because some types of physical activity can worsen symptoms. In fact, GERD induced by strenuous exercise is extremely common among athletes. The degree of reflux is greater in activities with more body agitation (e.g., running, aerobics) than in swimming or biking.

Strenuous exercise inhibits both gastric and small intestinal emptying, which may contribute to GERD. This, combined with the potential for relaxation of the gastroesophageal sphincter, suggests the importance of avoiding high-calorie meals or fatty foods (or other triggers) immediately before exercising to avoid or minimize exercise-related GERD.¹⁵²

The therapist can be instrumental in providing education and encouragement, essential to the lifestyle modifications necessary to this condition, and assist the person to implement changes related to diet and exercise.

Positioning

Any intervention requiring a supine position should be scheduled before meals and avoided just after eating. Modification of position toward a more upright posture may be required if symptoms persist during therapy. Consider a trial of the exercises to strengthen the muscles around the esophageal sphincter (see Fig. 16-2).

For nocturnal reflux, encourage the individual to sleep on the left side with a pillow in place to maintain this position. Right side lying makes it easier for acid to flow into the esophagus because of the effect of gravity on the esophagus (the lower esophagus bends to the left and this straightens out with right side lying).⁷⁹ See Special Implications for the Therapist: Hiatal Hernia in this chapter. Activities that increase intraabdominal pressure; constipation, which often accompanies back pain and other conditions (see Table 16-2); and tight clothing must be avoided.

The presence of GERD requires careful positioning to promote drainage of secretions without causing reflux. This is more readily accomplished when the

stomach is empty. Positioning clients with GI dysfunction for breathing control and coughing maneuvers requires special attention to minimize the risk of aspiration. Although head-up positions minimize reflux by reducing intraabdominal pressure, they can promote aspiration of pharyngeal contents. Side-lying positions (especially left side lying) prevent regurgitation and aspiration and promote oropharyngeal accumulations and ease of suctioning.⁴⁴

Other Considerations

Polypharmacy (the use of multiple medications for a single disorder or for comorbidities) can result in significant toxicity and drug interactions when taken with medications for acid-related diseases. Any new or unusual symptoms reported to the therapist should be documented with physician notification. In addition, anyone with GI dysfunction is at risk for impaired metabolism due to evacuation of medicine, improper absorption, or both. Monitoring GI status and medication responses, in conjunction with the individual's response to therapy intervention, is essential.⁴⁴

With postoperative complications, chest physical therapy may be indicated. In addition, coughing and bronchospasm can result from a vagally mediated reflex secondary to refluxed acid contents in the esophagus. The therapist also may observe reflux in clients who have chronic bronchitis, asthma, and pulmonary fibrosis.

Mallory-Weiss Syndrome

Mallory-Weiss syndrome is mucosal laceration of the lower end of the esophagus accompanied by bleeding. The most common cause is severe retching and vomiting as a result of alcohol abuse, eating disorders such as bulimia, or in the case of a viral syndrome.

Other conditions such as pregnancy, migraine, hiatal hernia, gastric ulcer, biliary disease, and various medications have been associated with Mallory-Weiss syndrome. Any event that suddenly raises transabdominal pressure in exercise or lifting can cause such a tear. Diagnosis is made on endoscopy, and when treatment is necessary, fluid replacement and blood transfusion and H₂-receptor antagonists may be administered. Endoscopic ligation may be required if bleeding cannot be brought under control.

Scleroderma Esophagus

Esophageal involvement is common in people with progressive systemic sclerosis caused by the CREST syndrome (calcinosis, Raynaud's phenomenon, esophageal motility disorder, sclerodactyly, and telangiectasia; see the section on Systemic Sclerosis in Chapter 10).

The esophageal lesions in systemic sclerosis consist of muscular atrophy of the smooth muscle portion, with weakness of contraction in the lower two thirds of the esophagus and incompetence of the LES.

Symptoms include dysphagia to solids and to liquids in the recumbent position. Heartburn and regurgitation occur in the presence of gastroesophageal reflux and esophagitis. Currently, no effective treatment exists for the motor difficulty, but reflux esophagitis and its complications are treated aggressively as described earlier.

Neoplasm

Overview and Incidence

Histologically, two types of esophageal cancer exist: squamous cell and adenocarcinoma. Worldwide, more than 90% of all esophageal cancers are squamous cell carcinomas. In the West, however, there has been a decline in the frequency of squamous cell carcinoma and a dramatic rise in the frequency of adenocarcinoma of the esophagus.

Esophageal cancer is relatively uncommon, but the incidence of adenocarcinoma is rising, possibly as a result of *H. pylori* eradication in GERD. Evidently, although *H. pylori* predisposes individuals to peptic ulceration and gastric neoplasms, it also has a protective effect against esophageal cancer. The mechanism by which this works remains unclear.

Barrett's esophagus, which is a precursor of esophageal adenocarcinoma, may be more common in older adults (over age 65) than previously thought. Screening for Barrett's esophagus in patients undergoing a colonoscopy has revealed the presence of Barrett's esophagus in up to 22% of men and 11% of women.¹⁵³

Risk Factors

Esophageal cancer is known for its marked variation by geographic region, ethnic background, and gender. In the United States, adenocarcinoma of the esophagus most frequently affects middle-aged white men, whereas squamous cell cancer is much more common in blacks and is associated with alcohol and tobacco use.¹⁵³

The presence of other esophageal disease such as hiatal hernia, reflux, Barrett's esophagus, rings, webs, diverticula, stricture from lye ingestion, achalasia, and other head and neck cancers increases the risk of developing esophageal cancer. Gastroesophageal reflux is highly correlated with an increased risk of esophageal adenocarcinoma (but not squamous cell carcinoma of the esophagus).⁶³

Etiologic Factors

Chronic inadequate nutrition can impair both the structure and function of the esophagus. Nutritional deprivation, particularly deficiencies of vitamins C, E, and B6, niacin, selenium, and zinc, results in mucosal changes, increasing the vulnerability of esophageal mucosa to neoplastic changes. Obesity has been established as a strong risk factor for esophageal adenocarcinoma.¹⁴⁰

Any change in esophageal function that permits food and drink to remain in the esophagus for prolonged periods of time can result in ulceration and metaplasia. Chronic exposure to irritants such as alcohol and tobacco (inhaled or chewed) also can cause neoplastic transformation. Nitrosamines are powerful carcinogens involved as causative agents of cancers of the lung, oral cavity,

esophagus, and pancreas associated with the use of tobacco products. Chronic stimulation of nicotinic receptors by nicotine and nitrosamines in smokers is one of the molecular events responsible for stimulation of cell proliferation and ultimately neoplasms.

Tumors may be obstructive, causing circumferential compression or ulceration with bleeding. Distant metastases also may occur, most commonly involving the liver and lung, but almost any organ can be involved.

Barrett's esophagus is a premalignant condition in which the normal squamous epithelium of the esophagus that is damaged by GERD is replaced by metaplastic epithelium, predisposing the individual to esophageal adenocarcinoma.

The progression of Barrett's metaplasia to adenocarcinoma is associated with several changes in gene structure, gene expression, and protein structure. Researchers are identifying some of the molecular alterations in hopes of finding markers for early cancer detection or prognostication.¹⁵⁸

Pathogenesis

Adenocarcinoma of the esophagus is thought to develop through a stepwise process termed the *metaplasia-dysplasia-carcinoma* sequence. The replacement of reflux-damaged esophageal epithelium by metaplastic intestine-type epithelium results in Barrett's esophagus. The metaplastic epithelia may be predisposed to deoxyribonucleic acid (DNA) damage that causes dysplasia and carcinoma.¹⁴⁰

Underlying these changes in cell phenotype are sequential genetic alterations that bring the normal epithelial cells closer to malignancy. Many of the molecular alterations that occur during carcinogenesis of the upper GI tract affect genes whose protein products regulate the cell cycle (see Fig. 9-3) clock apparatus, the key nuclear mechanism that controls whether a cell will proliferate, differentiate, or die. There is a molecular switch that helps the cell "decide" which phase it will enter. The exact sequence of molecular changes necessary to alter this switching and produce adenocarcinoma remains obscure.¹⁴⁰

Clinical Manifestations

Dysphagia with or without pain is the predominant symptom of this condition and may not occur until the diameter of the lumen of the esophagus is reduced 30% to 50%. Pain associated with dysphagia usually is described as pressurelike and may radiate posteriorly between the scapulae.

Heartburn initiated by lying down is the most common type of pain. Constant retrosternal chest pain that radiates to the back may occur in the presence of mediastinal extension or spinal nerve compression. Other signs and symptoms include anorexia and weight loss, hoarseness resulting from laryngeal nerve compression, and tracheoesophageal fistula causing cough and recurrent pneumonia.

MEDICAL MANAGEMENT

PREVENTION. Preventing GERD and Barrett's esophagus is the major method of reducing rates of esophageal adenocarcinoma. Despite this knowledge, the rates of

esophageal adenocarcinoma remain unchanged.¹⁵³ There are many possible reasons for this, but the exact reason(s) remains unclear. It is possible that GERD is underreported and undertreated in many adults, especially those over age 65. Many people with GERD may have few or no symptoms, so that progression of the condition to Barrett's disease and transformation to adenocarcinoma goes unnoticed until it is too late.¹⁵³

Whereas early screening and detection can reveal dysplasia (a potentially curable form of neoplasia), there is no proof that such screening programs actually reduce morbidity or mortality associated with this condition.¹⁴⁰

Studies suggest that 40% of individuals with esophageal adenocarcinoma have no history of GERD symptoms.⁷¹ This means that screening only individuals with known GERD will leave out a significant portion of adults who may be affected. And there are reports of incurable malignancies developing despite endoscopic surveillance programs.¹⁴⁵

Researchers are continuing to study the strategy that early treatment of individuals with GERD might prevent the first step in the metaplasia-dysplasia-carcinoma sequence. Some day it may be possible to use a biomarker to identify individuals with GERD who are predisposed to develop Barrett's esophagus. Aggressive acid suppression and screening might be appropriate for this group of people.

DIAGNOSIS. Diagnosis is made by endoscopy with cytology and biopsy. After diagnosis, staging of the disease is performed with chest and abdominal computed tomographic (CT) scanning or, if available, endoscopic ultrasonography to determine the most appropriate treatment.

TREATMENT. Neoplasms are classified as resectable with curative intent, resectable but not curable, and not resectable and not curable. The presence of distant metastases, invasion of the mediastinal muscularis or pleural invasion, or distant lymph node involvement excludes a curative resection. Curative surgery is esophageal reconstruction, which may improve the ability to eat and may prevent local tumor complications.

The use of preoperative chemotherapy with radiation is under investigation. Patients with unresectable disease or poor operative candidates may receive radiation therapy, which provides short-term relief of symptoms. Combinations of esophageal brachytherapy, external beam radiation, and multidrug combination chemotherapy are under clinical investigation; the use of brachytherapy appears to be associated with severe toxicity and the development of fistulas.⁵⁶

PROGNOSIS. Endoscopic surveillance can detect esophageal adenocarcinomas when they are early and curable, but most of these neoplasms are detected at an advanced stage. Carcinoma of the esophagus has one of the lowest possibilities of cure, with 5-year survival rates estimated to be approximately 10% overall and a median survival of less than 10 months.

The first symptoms of esophageal cancer are not usually apparent until the tumor involves the entire esophageal circumference. More importantly, the tumor by that time

has often invaded the deeper layers of the esophagus and adjacent structures and is unresectable. Esophageal cancer metastasizes rapidly, and given the continuous nature of lymphatic vessels in the area, removal of lymph nodes with the tumor is impossible, contributing to the poor prognosis.

SPECIAL IMPLICATIONS FOR THE THERAPIST

16-4

Esophageal Cancer

PREFERRED PRACTICE PATTERN

6H: Impaired Circulation and Anthropometric Dimensions Associated with Lymphatic System Disorders

Lymphatic vessels of the esophagus are continuous with mediastinal structures and drain to the lymph nodes from the neck of the celiac axis. Metastasis is via this lymphatic drainage, with tumors of the upper esophagus metastasizing to the cervical, internal jugular, and supraclavicular nodes. During an upper quarter screening examination the therapist may identify changes in lymph nodes, requiring medical referral.

The usual precautions regarding clients with cancer apply to those with neoplasms of the GI system. The primary concern is the side effects of chemotherapy-induced bone marrow suppression. An exercise regimen including aerobic exercise at a minimal level enhances the immune system and is incorporated whenever possible. See also the section on Cancer and Exercise in Chapter 9.

Radical surgery for thoracic esophageal cancer is highly invasive and often leads to respiratory complications; thoracoscopic surgery is a less invasive alternative but may still result in respiratory decline. Airway clearance techniques discussed in Chapter 15 may be needed postoperatively for anyone undergoing surgery for this condition.¹⁰⁸

Esophageal Varices

Esophageal varices are dilated veins in the lower third of the esophagus immediately beneath the mucosa. Dilatation occurs in the presence of portal hypertension, usually secondary to cirrhosis of the liver. All the blood from the intestine drains via the portal vein to the liver before passing into the general circulation. Therefore, any disease of the liver or portal vein that obstructs the flow of blood will cause expanding force pressure.

The normal anatomic reaction to this condition is to decompress the portal venous system by opening up bypass veins (collaterals), most commonly around the lower esophagus and stomach. When blood flow can no longer be counterbalanced by the variceal wall tension, the dilated veins (varices) rupture and bleed. Rupture and hemorrhage are common when portal pressure causes the varices to reach a size greater than 5 mm in diameter.

Variceal bleeding usually presents with painless but massive hematemesis with or without melena. Associated

signs range from mild postural tachycardia to profound shock, depending on the extent of blood loss and degree of hypovolemia (decreased amount of blood in the body). The clinical picture is frequently consistent with chronic liver disease.

Diagnosis requires differentiation from peptic ulcer, gastritis, and other bleeding sources, often concurrent conditions in people with cirrhosis secondary to alcoholism. Diagnosis is made by fiberoptic endoscopy. Bleeding varices constitute one of the most common causes of death in people with cirrhosis and other disorders associated with portal hypertension; therefore, prevention and treatment are very important to prevent and replace blood loss and maintain intravascular volume.

About half of all episodes of variceal hemorrhage cease without intervention, although a high risk of rebleeding exists. Various prophylactic and therapeutic approaches to management include pharmacologic agents and endoscopic interventions such as band ligation or sclerotherapy (the injection of hardening agents).

For bleeding not controlled with these methods, a stent may be placed between the hepatic vein and the intrahepatic portion of the portal vein (transjugular intrahepatic portosystemic shunt [TIPS]).⁶⁰ This procedure provides a means of lowering portal pressure. Liver transplantation may be considered in cases unresponsive to treatment.⁶²

SPECIAL IMPLICATIONS FOR THE THERAPIST 16-5

Esophageal Varices

PREFERRED PRACTICE PATTERN

7A: Primary Prevention/Risk Reduction for Integumentary Disorders

The primary concerns in therapy are to avoid causing rupture of varices and proper handling of clients with known GI bleeding. Carefully instruct the client in proper lifting techniques and avoid any activities that will increase intraabdominal pressure (see Box 16-1). See also Special Implications for the Therapist: The Anemias in Chapter 14 and the section on Portal Hypertension in Chapter 17.

For the client with known esophageal varices, observe closely for signs of behavioral or personality changes. Report increasing stupor, lethargy, hallucinations, or neuromuscular dysfunction. Watch for asterixis (involuntary jerking movements), a sign of developing hepatic encephalopathy.

To assess fluid retention, inspect the ankles and sacrum for dependent edema. To prevent skin breakdown associated with edema and pruritus, caution the client and family members caring for that person to avoid using soap when bathing the client and to use moisturizing cleansing agents instead. Precautions must be taken to handle the client gently, turning and repositioning often to keep the skin intact. Rest and good nutrition will conserve energy and decrease metabolic demands on the liver.

Congenital Conditions

Tracheoesophageal Fistula

Overview. Tracheoesophageal fistula (TEF) is the most common esophageal anomaly and one of the most common congenital defects, occurring in approximately 1 in 4000 live births with equal gender distribution. In this disorder, the esophagus fails to develop as a continuous passage and abnormal communication between the lower portion of the esophagus and trachea occurs, often combined with some form of esophageal atresia, a condition in which the esophagus ends in a blind pouch (Fig. 16-4). Other associated conditions include congenital heart disease, prematurity, and the VATER complex

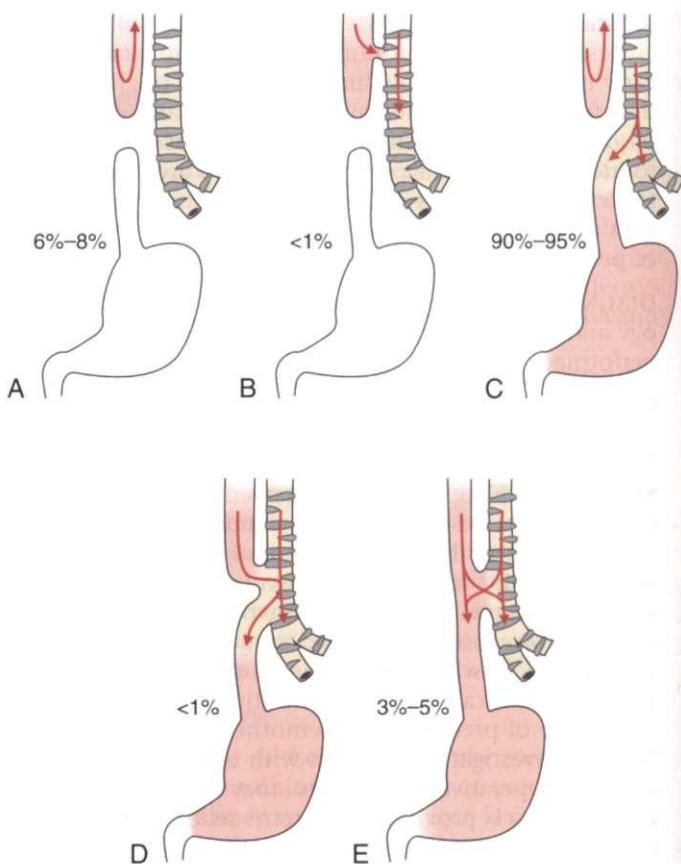


Figure 16-4

Five types of esophageal atresia and tracheoesophageal fistula. **A**, Simple esophageal atresia. Proximal and distal esophagus end in blind pouches. Nothing enters the stomach; regurgitated food and fluid may enter the lungs. **B**, Proximal and distal esophageal segments end in blind pouches, and a fistula connects the proximal esophagus to the trachea. Nothing enters the stomach; food and fluid enter the lungs. **C**, Proximal esophagus ends in a blind pouch, and a fistula connects the trachea to the distal esophagus. Air enters the stomach; regurgitated gastric secretions enter the lungs through the fistula. **D**, Fistula connects both proximal and distal esophageal segments to the trachea. Air, food, and fluid enter the stomach and lungs. **E**, Simple tracheoesophageal fistula between otherwise normal esophagus and trachea. Air, food, and fluid enter the stomach and lungs. Between 90% and 95% of esophageal anomalies are type C; 6% to 8% are type A; 3% to 5% are type E; and less than 1% are type B or D.

(vertebral defects, imperforate anus, tracheoesophageal fistula, and radial and renal dysplasia).

Etiologic Factors and Pathogenesis. Because TEF is a congenital malformation, the cause is unknown, but abnormalities are postulated to arise from defective differentiation as the trachea separates from the esophagus during the fourth to sixth weeks of embryonic development. Defective growth of endodermal cells leads to atresia (closure or absence of a normal body opening or tubular structure). In 90% of cases, the esophagus ends in a blind pouch with communication between the distal esophagus and the trachea. Less often, the proximal esophagus communicates with the trachea, or the esophagus is continuous in an H-type fistula.

Clinical Manifestations. The blind end of the proximal esophagus has a capacity of only a few milliliters, so as the infant with esophageal atresia swallows oral secretions, the pouch fills and overflows into the pharynx, resulting in excessive drooling and, occasionally, aspiration.

If a fistula connects the trachea with the distal esophagus, the abdomen fills with air and becomes distended, which may interfere with breathing. If the fistula connects the proximal esophagus to the trachea, the first feeding after birth will signal a problem.

As the infant swallows, the blind end of the esophagus and the mouth fill with fluid that is aspirated into the lungs when the infant tries to take a breath. This triggers a protective cough and the choke reflex with intermittent cyanosis. Coughing, choking, and cyanosis are called the three Cs of TEF and may occur especially with the H-type fistula, which may not be diagnosed for weeks to months after birth.

MEDICAL MANAGEMENT

DIAGNOSIS, TREATMENT, AND PROGNOSIS. Esophageal anomalies are usually diagnosed at birth on the basis of clinical manifestations, but new technology is making in utero diagnosis more readily available. Occasionally this condition escapes detection until adulthood, when recurrent pulmonary infections call attention to it. Confirmation of the non-H type is made by passing a catheter into the esophagus with radiographs of the chest and abdomen taken with the tube in place to show the level of the blind pouch. Fluoroscopy using radiopaque fluid also may be used to establish the diagnosis.

Surgical treatment to restore esophageal continuity and eliminate the fistula usually is performed shortly after birth. Surgical procedures may be performed in stages for infants who are premature, have multiple anomalies, or are in poor health. Antibiotics are instituted early owing to the certainty of aspiration pneumonia.

Without early diagnosis and treatment this condition is rapidly fatal. Early detection prevents feedings until the problem is corrected; feeding can cause aspiration and its complications. The survival rate is nearly 100% in full-term infants without severe respiratory distress or other anomalies. In premature, low-birth-weight infants with associated anomalies, the incidence of complications is high.

THE STOMACH

Gastritis

Definition and Incidence

Gastritis, inflammation of the lining of the stomach (gastric mucosa), is not a single disease but represents a group of the most common stomach disorders. Gastric erosions by definition are limited to the mucosa and do not extend beneath the muscularis mucosae. Based on clinical features, gastritis can be classified as *acute* or *chronic*.

Other classifications may be made according to clinical, endoscopic, radiographic, or pathologic criteria. *Acute gastritis* may be hemorrhagic or acute erosive, reflecting the presence of bleeding from the gastric mucosa. Gastric erosions and sites of hemorrhage may be distributed diffusely throughout the gastric mucosa or localized to the body of the stomach.

Chronic gastritis has two forms classified as types A and B. Type A gastritis is the less common form of chronic gastritis, associated with pernicious anemia, and is possibly an autoimmune disorder. The most severe type of chronic gastritis, chronic fundal gastritis, occurs in association with autoimmune diseases such as diabetes, Addison's disease, and thyroid disease, also suggesting an autoimmune mechanism.

Type B, the more common form of chronic gastritis, is caused by chronic bacterial infection by *H. pylori*. *H. pylori* is a gram-negative bacterium infecting half the world's population and causing chronic active gastritis in virtually all infected individuals.¹²²

Etiologic Factors

Acute erosive gastritis may develop without apparent cause but is more likely to occur in association with serious illness or with various medications such as aspirin or other NSAIDs that can produce acute gastric mucosal erosions.

GI complications occur only in a small percentage of people taking NSAIDs, but the widespread use of these agents results in a substantial number of people affected. Most susceptible persons are those 65 years of age or older, especially those who have a history of ulcer disease.

Other risk factors include taking NSAIDs longer than 3 months, taking high-dose or multiple NSAIDs, and concurrent corticosteroid or anticoagulation therapy. Use of NSAIDs combined with selective serotonin uptake inhibitors is also linked with upper GI bleeding.^{105,134,156}

Acute erosive gastritis associated with physiologic stress, often referred to as *stress-induced gastritis*, is associated with hospitalization for severe life-threatening disease, central nervous system injury, or trauma (particularly burns but also renal failure, mechanical ventilation, sepsis, and hepatic failure).

No persuasive evidence exists that acute gastric mucosal injury associated with stress, alcohol, aspirin, or other NSAIDs progresses to chronic gastritis. *H. pylori* is a primary risk factor in the development of chronic gastritis and the gastritis-associated diseases (e.g., gastric ulcer, duodenal ulcer, gastric cancer, gastric B-cell lymphoma/

mucosa-associated lymphoid tissue [MALT] lymphoma), but other risk factors include aging, vitamin deficiencies, abnormalities of the gastric juice, hiatal hernia, or a combination of any of these.

Pathogenesis

Agents known to injure the gastric mucosa (e.g., *H. pylori*, aspirin or other NSAIDs, bile acids, pancreatic enzymes, alcohol) alter the mucosal defense mechanism, leading to *acute gastritis*. The mechanism of mucosal injury is unclear and probably multifactorial. The most commonly accepted theory for agent-induced mucosal injury is the suppression of endogenous prostaglandins that normally stimulate the protective secretion of mucus.

The progression of *chronic gastritis* has three phases. Superficial gastritis is the initial stage with inflammation limited to the upper epithelial half of the gastric mucosa. Atrophic gastritis, the second stage, takes place as the inflammatory process extends to the deep portions of the mucosa with progressive distortion and destruction of the gastric glands.

Pepsinogen, hydrochloric acid, and IF are diminished, and the feedback mechanism that normally inhibits gastrin secretions is impaired, causing elevated plasma levels of gastrin. As mentioned under Aging and the Gastrointestinal System, IF is a glycoprotein secreted by the gastric glands that plays an important role in the absorption of vitamin B12. IF deficiency resulting in vitamin B12 deficiency may lead to pernicious anemia. The final stage, gastric atrophy, involves a profound loss of the glandular structures with thinning of the mucosa.

Clinical Manifestations

The most noticeable symptom of acute gastritis is epigastric pain with a feeling of abdominal distention, loss of appetite, and nausea. Pain is much less common with erosive gastritis than with ulcer disease; painless GI hemorrhage is frequently the only clinical manifestation.

Additional symptoms may include heartburn, low-grade fever, and vomiting. Occult (no visible evidence) GI bleeding commonly occurs, especially in cases of trauma and in people taking aspirin or other NSAIDs. Chronic gastritis may be asymptomatic, or pain may occur after eating accompanied by indigestion.

MEDICAL MANAGEMENT

DIAGNOSIS, TREATMENT, AND PROGNOSIS. The diagnosis of gastritis may be made by a careful history, but confirmation is made by upper endoscopic examination, possibly including biopsy, because epigastric pain may be due to peptic ulcer, gastroesophageal reflux, gastric cancer, biliary tract disease, food poisoning, and viral gastroenteritis.

Noninvasive tests such as the urea breath test or stool antigen test can be used to confirm the presence of *H. pylori* within the stomach. Antimicrobial therapy along with antisecretory drugs are used to eradicate *H. pylori*.

Management of gastritis requires avoidance of identified irritating substances (e.g., caffeine, nicotine, alcohol) combined with the use of PPIs, antacids, and/or H₂-blocking agents to block or reduce gastric acid secretion and minimize stomach acidity.

Vitamin B12 is administered to correct pernicious anemia when it develops secondary to chronic gastritis. Because people taking NSAIDs and those in intensive care units have a high incidence of erosive gastritis, preventive therapy may be used to reduce mucosal injury.

Prognosis is good for both acute and chronic gastritis, especially with removal of the predisposing factors for acute gastritis. The risk of gastric cancer is known to be high in people with chronic gastritis and particularly in those with atrophic gastritis.

SPECIAL IMPLICATIONS FOR THE THERAPIST 16-6

Gastritis

Half of all clients receiving NSAIDs on a long-term basis have acute gastritis (often asymptomatic). The therapist should continue to monitor clients for any symptoms of GI involvement indicating need for medical referral. For the client with known chronic GI bleeding, urge the client to seek immediate attention for recurring symptoms such as hematemesis, nausea, or vomiting.

Urge the client to take prophylactic medications as prescribed by the physician. Steroids should be taken with milk, food, or antacids to reduce gastric irritation; antacids can be taken between meals and at bedtime. Aspirin-containing compounds should be avoided unless specifically recommended by the physician. See also Special Implications for the Therapist: Signs and Symptoms of Gastrointestinal Disease in this chapter and Special Implications for the Therapist: The Anemias in Chapter 14.

Peptic Ulcer Disease

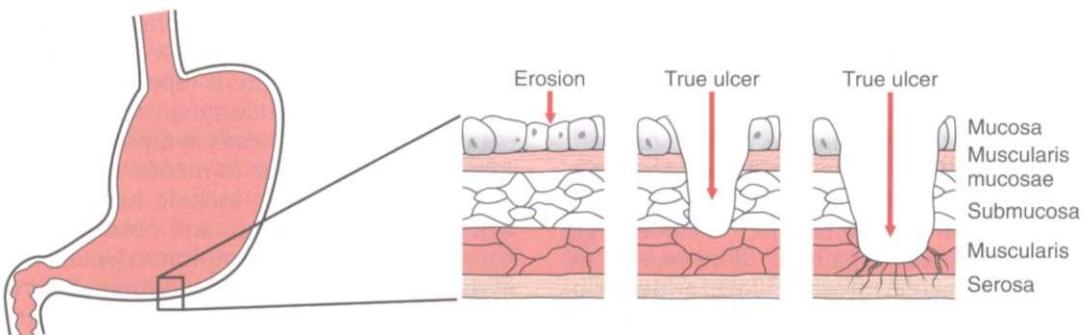
Definition and Overview

An ulcer is a break in the protective mucosal lining exposing submucosal areas to gastric secretions. The word *peptic* refers to pepsin, a proteolytic enzyme, the principal digestive component of gastric juice, which acts as a catalyst in the chemical breakdown of protein.

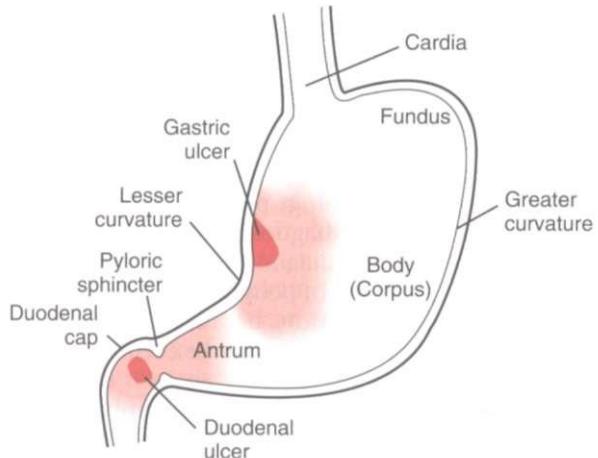
Acute lesions of the mucosa that do not extend through the muscularis mucosae are referred to as *erosions*. Chronic ulcers involve the muscular coat, destroying the musculature and replacing it with permanent scar tissue at the site of healing. Ulcers extending to the muscularis mucosae damage blood vessels, causing hemorrhage (Fig. 16-5).

Two kinds of peptic ulcer exist: the *gastric ulcer* (GU), which affects the lining of the stomach, and the *duodenal ulcer* (DU), which occurs in the duodenum. DUs are two to three times more common than GUs, although these ulcers can coexist. About 95% of DUs occur in the duodenal bulb or cap. About 60% of benign GUs are located at or near the lesser curvature and most frequently on the posterior wall (Fig. 16-6).

Stress ulcers, or secondary ulcers, occur in response to prolonged psychologic or physiologic stress (e.g., severe

**Figure 16-5**

Lesions caused by peptic ulcer disease.

**Figure 16-6**

Most common sites of peptic ulcers.

trauma, surgery, extensive burns, brain injury), causing an upset in the aggressive-defensive balance. For example, gastric mucosal changes develop within 72 hours in 80% of clients with burns over more than 35% of the body. The mechanism causing stress ulcers is unknown but probably involves ischemia of the gastric mucosa, which has large oxygen requirements and low gastric pH (high acidity). Stress ulcers differ pathologically and clinically from peptic ulcers with very few symptoms and are painless until perforation and hemorrhage occur.

Incidence

In the United States there are about 500,000 new cases of peptic ulcer and 4 million ulcer recurrences per year. Up to 10% of the American population will develop an ulcer at some time in their lives.

Older age groups, especially middle-aged and older adults, are more likely to develop GUs; the peak incidence for GUs is in the sixth decade. Approximately 10% to 20% of people with GUs also have DUs.

DUs are the most common, with an average age at onset in the mid-thirties, although DUs can occur at any time (including infancy). In the past, men were more likely than women to develop gastric and duodenal ulcers, but now equal distribution exists between the

genders. The overall frequency of DU has been decreasing in the United States, especially in males.

Etiologic and Risk Factors

In 90% of all ulcers (as well as for chronic gastritis), *H. pylori* bacterial infection is an important risk factor for and cause of the condition. Although *H. pylori* has been identified as a major cause of ulcer disease, not all infected people develop ulcers. This may be because certain *H. pylori* strains are more virulent than others. Some people naturally produce more stomach acid than others, which may explain some of the differences.

The majority of recent studies have not found tobacco use or alcohol consumption to be risk factors for *H. pylori* infection, although adequate nutritional status, especially frequent consumption of fruits and vegetables and vitamin C, appears to be protective.¹⁷

Lifestyle and psychologic stress are still considered as potential factors in the development of ulcers in some people. The presence of recurrent ulcers in individuals with multiple stressors, poor coping skills, and persistent anxiety and depression lends support to the hypothesis that physiologic changes leading to ulcer can occur secondary to psychologic stress. The mechanism of this association remains unknown.⁶¹⁻¹¹¹

The long-term use of NSAIDs has deleterious effects on the entire GI tract, from the esophagus to the colon, although the most obvious clinical effect is on the gastroduodenal mucosa. The exact mechanism remains unknown, but theoretically these drugs break down the mucous membrane that protects the GI tract by inhibiting the synthesis of gastric mucosal prostaglandins.

Prostaglandins have two types of actions: inhibition of acid secretion and enhancement of mucosal resistance to injury by mechanisms independent of acid-secretion inhibition, the latter phenomenon being called *cytoprotection*. This interference with normal mucosal protective mechanisms leads to local injury by allowing stomach acids to dissolve the intestine (for further discussion of the systemic effects of NSAIDs, see Chapter 5; see also Table 5-1 for a list of commonly used NSAIDs).

Pathogenesis

The mechanisms of injury differ between duodenal and gastric ulcers. DU is essentially an *H. pylori*-related disease

and is caused mainly by an increase in acid and pepsin load with gastric metaplasia occurring in the duodenal cap.

GU is most commonly associated with NSAID ingestion, although *H. pylori* might also be present. In both conditions, ulcer is associated with an imbalance between protective and aggressive factors, with inflammation being a major cause in this imbalance.¹⁶¹ Cholinergic hypersensitivity and parasympathetic dominance are related to the stimulation of hydrochloric acid and pepsin, which is a cofactor in the development of erosive injury to the gastric mucosa.

Psychologic stress, cigarette smoking, alcohol consumption, use of NSAIDs (including aspirin), oral bisphosphonates, potassium chloride, immunosuppressive medications, and an age-related decline in prostaglandin levels have all been shown to contribute to peptic ulcer disease. It was, however, the discovery that *H. pylori* is a significant factor in the development of peptic ulcer disease that led to the understanding of the role that inflammation and its associated cytokine cascade plays in gastric acid secretion.¹⁶¹

The presence of the *H. pylori* infection induces various humoral and cellular immunities in the gastric mucosa, but the exact mechanism of *H. pylori*-induced gastroduodenal diseases remains unknown. Prolonged impaired and excessive immunoinflammatory responses with destruction of the mucosal barrier system appear to be the underlying mechanism for tissue injury.¹⁶⁷ *H. pylori* evades attack by the host immune system and causes chronic inflammation by several mechanisms (e.g., reducing the thickness of the mucus gel layer, decreasing blood flow to the mucosal layer).¹⁶¹

In the case of emotional stress, an increase in gastric secretion, blood supply, and gastric motility by irritation of the vagal nerve stimulates the thalamus. The sympathetic nervous system then causes the blood vessels in the duodenum to constrict, making the mucosa more vulnerable to trauma from gastric acid and pepsin secretion. Multiple chemical, neural, and hormonal factors participate in regulation of gastric acid secretion, making ulcer development a multifactorial process in such cases.

Clinical Manifestations

No specific symptom differentiates *H. pylori*-induced ulcers from NSAID-associated ulcers. The classic symptom of peptic ulcer is epigastric pain described as burning, gnawing, cramping, or aching near the xiphoid, coming in waves that last several minutes. Distention of the duodenal bulb produces epigastric pain, which may radiate to the back.

Perforation of the posterior duodenal wall causes steady midline pain in the thoracic spine from T6 to T10 with radiation to the right upper quadrant. The daily pattern of pain is related to the secretion of acid and the presence of food in the stomach (e.g., the presence of food may cause GU pain, whereas pain occurs 1 to 3 hours after meals with DUs).

Other symptoms include nausea, loss of appetite, and sometimes weight loss. Symptoms may occur for 3 or 4 days or weeks, subsiding only to reappear weeks or months later.

Many people report symptoms outside the classic presentation of DU. Some people are asymptomatic until complications occur; this is especially typical in the older adult as weakened abdominal muscles and diminished pain perception mask early symptoms or present as non-specific indicators such as mental confusion.

Complications may include hemorrhage with resultant anemia, perforation, and obstruction accompanied by unremitting pain. Symptoms depend on the severity of the hemorrhage. In mild bleeding, slight weakness and diaphoresis may be the only symptoms. Signs of bleeding include bright red blood in the vomitus, coffee-ground vomitus, and melena (black, tarry stools).

MEDICAL MANAGEMENT

DIAGNOSIS. Ulcers are diagnosed on the basis of symptoms and history, although the history is not as characteristic for GU as it is for DU. Appropriate use of one of the many tests to diagnose *H. pylori* (e.g., serology, urease breath testing, saliva test, biopsy, and culture) can identify those individuals likely to benefit from antimicrobial treatment.

Breath testing and serology have comparable sensitivity and specificity, but serology provides faster results and is preferred for the initial diagnosis. Breath testing is more useful than serology in diagnosing failure of *H. pylori* eradication or reinfection in people who were previously treated for *H. pylori* infection, because serologic results will remain positive for several months even after successful treatment.⁵²

Other tests may include barium radiographic examination and gastroscopy (endoscope passed into the stomach) used to determine the site of bleeding and to differentiate between benign and malignant ulcerations.

PREVENTION AND TREATMENT. The primary goals of medical treatment of peptic ulcers are (1) relief of symptoms, (2) promotion of healing, (3) prevention of complications, and (4) prevention of recurrences. Each person responds differently to different treatment modalities, requiring individual treatment planning. In general, GUs tend to heal more slowly than DUs.

Antimicrobials (antibiotics) are 85% effective in the treatment of *H. pylori*, along with antisecretory drugs such as PPIs, antacids, and H₂-blocking agents (stomach acid suppressors or blockers; see Table 16-4) to allow the ulcer to heal completely.

Antibiotic resistance with increasing eradication failure rates is becoming increasingly common and has led to studies of new regimens for primary therapy of GERD to eliminate the acid-hypersecretory state that predisposes the person to peptic ulcer disease. Issues of dosage and timing remain under investigation.

There does not appear to be lifelong immunity from *H. pylori* once infected; researchers are working on vaccine development.¹⁴⁷ Researchers are actively seeking ways to prevent ulcer development and ulcer recurrence in NSAID users and the best means to treat non-NSAID, non-*H. pylori*-associated peptic ulcers.¹⁶¹

NSAID-induced injury with resultant ulceration is a separate issue from *H. pylori*-induced ulcers. Whether or not anyone who has had an ulcer or chronic indigestion

should be tested and treated for *H. pylori* before starting long-term NSAID therapy remains a point of controversy. Using a protective agent with the NSAID may be recommended, especially if long-term use of the NSAID is needed. The smallest effective dose of NSAIDs is recommended, and clients must be warned against adding over-the-counter NSAIDs to a prescription dose.

No substantial evidence supports dietary modifications as a treatment approach to peptic ulcers, although adequate nutrition may be preventive.¹⁷ Bland diets, soft diets, milk and cream diets, and diets free of spices or fruit juices have no known effect in reducing gastric acid secretion, relieving symptoms, or promoting ulcer healing.

Foods that seem to aggravate a person's symptoms most likely should be avoided. Coffee, caffeinated or not, stimulates gastric acid secretion and should be avoided. Researchers have reported that exercise at least three times a week greatly reduces the risk of GI bleeding. More strenuous forms of exercise such as swimming and bicycling do not provide greater protection from GI bleeding than do more moderate exercises such as walking.^{25,112}

Surgical intervention is required for perforation, because gastric and intestinal contents spilling into the peritoneal cavity can cause chemical peritonitis, bacterial septicemia, and hypovolemic shock. Peristalsis diminishes, and paralytic ileus can develop. Outlet obstruction caused by scarring of the duodenum or caudal portion of the stomach may also require surgery.

PROGNOSIS. Prognosis is usually good and medical management can adequately control ulcers unless massive hemorrhage or perforation occurs, which carries a high mortality. Both duodenal and gastric ulcers tend to have a chronic course with remissions and exacerbations.

Benign GUs should heal completely within 3 months of treatment. Well-controlled, double-blind studies have shown that curing *H. pylori* usually results in curing DU disease; however, antimicrobial resistance is largely responsible for treatment failure.

should be encouraged to report these findings to his or her physician.

Referred Pain Patterns

Peptic ulcers located on the posterior wall of the stomach or duodenum can perforate and hemorrhage, causing back pain as the only presenting symptom. Occasionally ulcer pain radiates to the midthoracic back and right upper quadrant, including the right shoulder. Right shoulder pain alone may occur as a result of blood in the peritoneal cavity from perforation and hemorrhage.

When back pain appears to be the only presenting symptom, a careful history may reveal alternating or concomitant GI symptoms such as vomiting of bright red blood or coffee-ground vomitus. Back pain relieved by antacids is an indication of GI involvement and must be reported to the physician, as well as any other indication of shoulder or back pain with accompanying GI involvement.

Musculoskeletal symptoms may recur after discontinuing the NSAIDs, owing to the masking effects of these drugs. Once the drug is discontinued, painful symptoms may return in the presence of continued underlying ulcer disease. Medical follow-up is required in such situations.

Exercise and Peptic Ulcer Disease

For the competitive athlete, during the acute episode, anxiety and nervousness may increase gastric secretions. This effect in combination with poor nutrition (often the athlete has not eaten at all) requires careful monitoring and maximizing the use of medications and food intake with the performance schedule. For the average adult uninvolved in competitive sports, regular exercise as part of stress reduction is essential during remission.

Gastric Cancer

Primary Gastric Lymphoma

The GI system, including the stomach, is a common site for extranodal disease associated with lymphoma; primary lymphoma of the stomach is relatively uncommon. Occurring most often during the sixth decade of life, it is characterized by epigastric pain, early satiety, and fatigue.

Clinically, primary gastric lymphoma does not differ significantly in its presentation from adenocarcinoma. Management of primary gastric lymphoma remains somewhat controversial; controlled clinical trials to evaluate different therapeutic methods, schedules, and prognostic factors have not been done.

Treatment is based on the staging of disease and may include surgery alone, surgery with radiotherapy, surgery with chemotherapy, and chemotherapy alone. Some experts recommend chemotherapy rather than surgery as the first treatment of choice for primary gastric lymphoma.⁹

SPECIAL IMPLICATIONS FOR THE THERAPIST 16-7

Peptic Ulcer Disease

Monitoring Symptoms and Vital Signs

Ulcer presentation without pain occurs more frequently in older, aging adults and in persons taking NSAIDs for painful musculoskeletal conditions, especially arthritis. Anyone with this type of medical history should be monitored for signs and symptoms of bleeding. Observe color (pallor), activity or exercise tolerance, and fatigue level.

Vital signs should be monitored for systolic blood pressure under 100 mm Hg, pulse rate greater than 100 beats/min, or a 10-mm Hg or more drop in diastolic blood pressure with position changes accompanied by increased pulse rate, which may signal bleeding. Any client complaining of GI symptoms

Gastric Adenocarcinoma

Definition and Incidence. Adenocarcinomas, malignant neoplasms arising from the gastric mucosa, constitute more than 90% of the malignant tumors of the stomach. In 2007, 21,260 new cases of stomach cancer were diagnosed in the United States and 11,210 Americans died from this disease.⁷³

For a long time there has been a downward trend in incidence, most likely attributable to improved sanitation and drinking water that has decreased transmission of the *H. pylori* bacteria. However, a recent increase in cancer of the gastric cardia has been reported in the United States and European countries. The reason(s) for this are under investigation.⁹⁷

Men over the age of 40 years are most likely to develop this disease, with a sharp increase in incidence after 50 years.

Etiologic and Risk Factors. Chronic gastritis with intestinal metaplasia, possibly secondary to chronic *H. pylori* infection, is a strong risk factor for gastric cancer, especially when combined with family history of gastric cancer.

Other nonenvironmental risk factors include individual susceptibility; pernicious anemia, which causes atrophy of the gastric mucosa in the same locations where gastric tumors arise; type A blood; gastrectomy; gastric polyps; dietary factors such as consumption of smoked fish and meat containing benzopyrene; and nitrosamines produced endogenously in chronic gastritis.

Pathogenesis. Development of gastric carcinoma is a multistep and multifactorial process beginning with *H. pylori* in most cases, but the underlying mechanisms remain to be defined. The most common site for adenocarcinoma appears to be the glands of the stomach mucosa located in the distal portion of the stomach on the lesser curvature of the prepyloric antrum (see Fig. 16-6).

Duodenal reflux and insufficient acid secretion may contribute to intestinal metaplasia. The reflux contains caustic bile salts that destroy the normally protective mucosal barrier in the stomach. Insufficient acid secretion by the atrophic mucosa creates an alkaline environment that permits bacteria to multiply and act on nitrates. The resulting increase in nitrosamines damages the DNA of mucosal cells further, promoting metaplasia and neoplasia.

Clinical Manifestations. The clinical presentation of gastric carcinoma depends on a variety of factors, including the morphologic characteristics of the tumor (e.g., infiltrating versus ulcerating), size of the tumor, presence of gastric outlet obstruction, and metastatic versus nonmetastatic disease. Early stages of gastric cancer may be asymptomatic or present with vague symptoms of indigestion, anorexia, and weight loss similar to peptic ulcer, because ulceration can occur with gastric carcinoma.

MEDICAL MANAGEMENT

PREVENTION. At the present time, the best advice for reducing the risk of stomach cancer is to eat at least five 1/2-cup servings of fruits and vegetables daily, combined

with regular physical activity, maintaining a healthy weight, and reducing salt-preserved foods.⁸⁶

DIAGNOSIS. Diagnosis may be delayed by the fact that symptomatic relief can be obtained from early GI symptoms using over-the-counter medications. The choice of diagnostic tests depends on the clinical manifestation at the time of presentation. Endoscopy with cytologic brushings and biopsies of suspicious lesions are highly sensitive for detecting gastric carcinoma.

In areas of high incidence, screening upper endoscopy is performed to detect early gastric carcinoma. Once the diagnosis has been made, staging to determine the local extent of disease and the presence of nodal or distant metastases must be done. Staging is accomplished through the use of liver chemistry tests, abdominal imaging studies (e.g., CT scan), and biopsy of suspected lymph nodes.

TREATMENT. Surgical therapy is still the treatment of choice for primary gastric adenocarcinoma. Despite many attempts, the postoperative strategies of adjuvant chemotherapy have been ineffective. Multimodality treatment consisting of preoperative chemotherapy and surgery may provide improved results if endoscopic ultrasonography and staging laparoscopy provide early identification of locally advanced tumors. Prevention through eradication of *H. pylori* is recommended only in individuals with high risk of cancer at this time.

PROGNOSIS. Prognosis depends on the degree of gastric wall penetration, the presence of lymph node metastases, and the location of the primary site. Screening programs in other countries detect approximately 40% of tumors early with a 5-year survival rate of more than 60%.

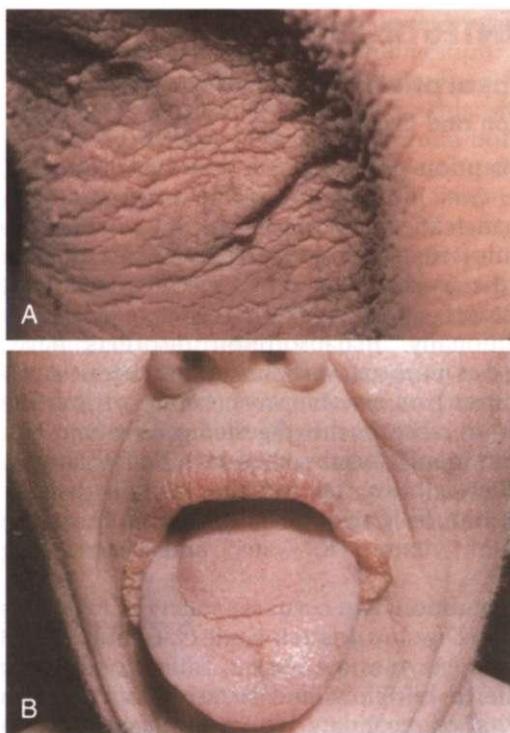
Without screening, the prognosis is poor, because symptoms do not occur until the tumor has penetrated muscle layers of the stomach, spread to local tissue by direct extension in the abdominal cavity, metastasized via the lymphatic system, or created a paraneoplastic manifestation.

Paraneoplastic syndromes are discussed in greater depth in Chapter 9. When these syndromes are associated with stomach cancer, affected individuals may present with any of the following:

- Trouseau's syndrome (spontaneous peripheral venous thrombosis of the upper and lower extremities that occurs in association with visceral carcinoma)
- Dermatomyositis
- Acanthosis nigricans

Acanthosis nigricans is a skin condition associated with an internal carcinoma characterized by diffuse thickening of the skin with grey, brown, or black pigmentation, usually in body folds such as the axillae (Fig. 16-7).

Metastatic gastric carcinoma is currently incurable. Surgical resection is only possible in one third of gastric cancers. Of those people in whom surgical resection is a possibility, 20% survive 10 years.

**Figure 16-7**

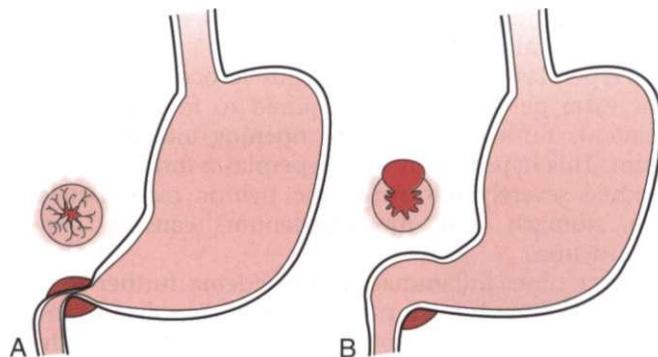
A, Paraneoplastic acanthosis nigricans with a velvety hyperpigmented rash in the axilla in an individual with gastric cancer. **B**, Acanthosis nigricans of the oral mucosa. This pattern of involvement is almost always associated with cancer. (From Goldman L: Cecil textbook of medicine, ed 22, Philadelphia, 2004, Saunders. Courtesy of Dr. Timothy Berger, Professor of Clinical Dermatology, University of California, San Francisco.)

SPECIAL IMPLICATIONS FOR THE THERAPIST 16-8

Gastric Cancer

Epigastric or back pain, possibly relieved by antacids, is a frequent complaint that the physician must differentiate from peptic ulcer disease. Generally the first manifestations of carcinoma are caused by distant metastasis when the condition is quite advanced. The therapist may palpate the left supraclavicular (Virchow's) lymph node, or the client may point out an umbilical nodule.

After surgery, position changes every 2 hours, deep breathing, coughing, and incentive spirometry (use of a handheld device to provide visual feedback for voluntary maximal inspiration) may be used to prevent pulmonary complications. The semi-Fowler position (head of the bed raised 6 to 12 inches with knees slightly flexed) facilitates breathing and drainage after any type of gastrectomy.

**Figure 16-8**

Hypertrophic pyloric stenosis. **A**, Enlarged muscular area nearly obliterates the pyloric channel. **B**, Longitudinal surgical division of muscle down to the submucosa or the placement of an expandable stent (not shown) establishes an adequate passageway.

Congenital Conditions

Pyloric Stenosis

Definition and Overview. Pyloric stenosis (PS) is an obstruction at the pyloric sphincter (the sphincter at the distal opening of the stomach into the duodenum). The pyloric sphincter is a ring of muscles that serve to close the opening from the stomach into the intestine (Fig. 16-8). Obstruction occurs as a congenital condition, or in adults the most common cause is ulcer disease. When present as a congenital condition, it is known as *hypertrophic PS* caused by hypertrophy of the sphincter and is one of the most common surgical disorders of early infancy.

Incidence and Etiologic Factors. The cause of congenital hypertrophy of the pyloric sphincter is unknown. White males are affected more commonly than females in a 4:1 ratio. It is more likely to occur in a full-term infant than in a premature infant, especially the first-born child. Siblings, offspring of affected persons, and fathers and sons are at increased risk of developing PS (genetic predisposition). Prophylactic administration of erythromycin to newborns exposed to neonatal pertussis has been reported to have a possible causal role in infantile PS.^{23,94} The role of *H. pylori* as a cause of infantile hypertrophic PS is under investigation.^{40,113,136}

Increased third-trimester maternal gastric secretion associated with maternal stress-related factors increases the likelihood of PS in the infant. PS may also be associated with other congenital conditions such as Turner's syndrome, trisomy 18, intestinal malrotation, esophageal and duodenal atresia, and anorectal anomalies.

The incidence of adult idiopathic PS is unknown, but it is considered rare. Although many physicians believe this condition is secondary to local disease, others think the condition in adults is the same entity as that observed in infants and children, but in a milder form and later in appearance.

Pathogenesis. The histologic and anatomic abnormalities in adult PS are indistinguishable from those in the infantile form. Individual fibers of the pyloric

sphincter thicken or hypertrophy, so the entire sphincter is grossly enlarged and inelastic.

Hyperplasia of the pyloric muscle occurs because of the extra peristaltic effort required to force the gastric contents through the narrow opening into the duodenum. This hypertrophy and hyperplasia form a palpable nodule severely narrowing the pyloric canal between the stomach and the duodenum, causing partial obstruction.

Over time, inflammation and edema further reduce the size of the lumen, progressing to complete obstruction preventing food from passing from the stomach to the small intestine. Progressive obstruction results in complications of malnutrition and fluid and electrolyte abnormalities.

Clinical Manifestations. Projectile vomiting is the most common and dramatic early symptom and may occur at birth. *Projectile vomiting* describes forcible vomiting that ejects vomitus 1 foot or more when in a supine position and 3 to 4 feet when in an upright or side-lying position.

Overall, the age of onset and pattern of vomiting vary, but usually regurgitation or occasional projectile vomiting develops around the second to fourth week after birth. Projectile vomiting quickly leads to dehydration and lethargy with rapid progression to complete obstruction and the accompanying complications of malnutrition, weakness, wasting, weight loss, and fluid and electrolyte imbalances.

The palpable nodule is firm, movable, about the size of an olive, and felt in the right upper quadrant in approximately 80% of all infants with PS. Persistent or episodic symptoms in some adults may extend from infancy with nausea and vomiting, epigastric pain, weight loss, and anorexia most commonly present. In contrast to congenital PS in the infant, the abdominal mass that occurs in adult PS is too small to be palpable.

MEDICAL MANAGEMENT

DIAGNOSIS, TREATMENT, AND PROGNOSIS. In infancy, diagnosis is usually by history and recognition of the clinical presentation. Ultrasound imaging is so accurate for the diagnosis of PS that it has replaced the upper GI series in most institutions.

Some infants are treated with antispasmodic drugs to relax the pylorospasm and nutritional management, including refeeding the infant after vomiting, waiting to see if the pylorus spontaneously opens by 6 to 8 months of age. Surgical repair, including endoscopic balloon dilatations, pyloromyotomy (local resection of the involved region of the pylorus), and pyloroplasty, is the standard medical treatment with a very high success rate for the infant and the adult. Placement of a stent at the site of obstruction is gaining popularity as an alternative intervention procedure.

Postoperative vomiting is not uncommon in the pediatric population, especially during the first 24 to 48 hours. Complications include persistent pyloric obstruction; partial, superficial, or total wound separation (dehiscence); or in the case of stent implantation, stent migration.

THE INTESTINES

Malabsorption Syndrome

Definition and Overview

Malabsorption syndrome is a group of disorders (celiac disease, cystic fibrosis, Crohn's disease, chronic pancreatitis, pancreatic carcinoma, pernicious anemia, short-gut syndrome) characterized by reduced intestinal absorption of dietary components and excessive loss of nutrients in the stool.

Traditionally, malabsorption disorders have been classified as *maldigestion* (failure of the chemical processes of digestion) or *malabsorption* (failure of the intestinal mucosa to absorb the digested nutrients). Nutrients most commonly malabsorbed include fat, fatty acids or bile salts, calories (fat, protein, carbohydrates), iron, vitamin B12, folic acid, calcium, vitamin D, magnesium, potassium, vitamin K, water, and lactose (sugar in milk).

The conditions can occur separately or together simultaneously. *Digestive defects* include cystic fibrosis, in which pancreatic enzymes are absent; biliary or liver diseases with altered bile flow; and lactase deficiency, in which congenital or secondary lactose intolerance occurs with lactose malabsorption.

Absorptive defects may be primary, such as celiac disease, or secondary to inflammatory disease of the bowel with the concomitant accelerated bowel motility and impaired absorption (e.g., ulcerative colitis, Crohn's disease).

Recent studies suggest that the prevalence of celiac disease, in particular, is much higher in the United States than previously thought, with rates equal to those in Europe. In fact, celiac disease may be more common than other better-known GI problems such as Crohn's disease and ulcerative colitis. Risk is highest for individuals of European ancestry; about 70% of reported cases occur in women.⁵¹

Celiac disease is an immune-mediated enteropathic condition triggered in genetically susceptible individuals by the ingestion of gluten, a protein found in wheat, rye, barley, and oats, that prompts an inflammatory response in the small intestine.

Etiologic Factors and Pathogenesis

Clients in a therapy practice affected by malabsorption most often include people who develop gastroenteritis secondary to NSAID use, fibrosis caused by progressive systemic sclerosis or radiation injury, drug-induced malabsorption, exocrine deficiency of the pancreas caused by diabetes mellitus, and short-gut syndrome.

Short-gut syndrome (short-bowel syndrome) is the malabsorptive state that often follows extensive resection of the small intestine or, more rarely, congenital shortening of the bowel structures. Hyperabsorption of substances (e.g., vitamin D, calcium) also can occur with the intake of excessive amounts of calcium carbonate (e.g., Turns) for acid indigestion.

Generally, maldigestion is caused by deficiencies of enzymes (e.g., pancreatic lipase) and specific defects (e.g., poor digestion, lactose intolerance). Inadequate secretion of bile salts (e.g., advanced liver disease, obstruction of

the common bile duct) and inadequate reabsorption of bile in the ileum also contribute to maldigestion.

In the case of inadequate absorption, food is fully digested but not adequately absorbed. This situation occurs when the absorptive surface is normal but inadequate, or adequate but not functioning normally. This problem occurs within the mucosal cell and may be highly specific owing to a gene defect. Malabsorption syndrome also can be caused by a digestive defect, a mucosal abnormality, or lymphatic obstruction and can be a generalized malabsorption or an isolated malabsorption of a particular nutrient.

In the case of celiac disease, human leukocyte antigen (HLA) appears to promote an inflammatory response to gliadin, a protein fragment of gluten. This autoimmune response attacks and destroys the small, fingerlike projections in the intestinal wall known as villi, where most nutrient absorption takes place. Impaired nutrient absorption is the outcome.

Clinical Manifestations

Early manifestations of malabsorption are progressive and not easily noticed by the person affected. Although symptoms often start in childhood, they may not appear or be recognized until much later in life. In the case of celiac disease, stress, surgery, infection, emotional crises, or some other event can precipitate the sensitivity reaction.

Weight loss, fatigue, depression, and abdominal bloating are early symptoms. A change in bowel habits may occur with production of bulky, malodorous oil-covered stools (steatorrhea) that are difficult to flush. Excessive nocturnal reabsorption of intestinal fluids may cause nocturia. A gluten-related skin disorder, dermatitis herpetiformis (Fig. 16-9), also maybe present. Other gluten-induced non-GI symptoms include joint pain, fatigue, depression, and weight loss (or gain from abdominal bloating).

Other common signs and symptoms include explosive diarrhea, chronic diarrhea, abdominal cramps and bloating, indigestion, and flatulence. Late manifestations caused by nutritional deficiencies secondary to the malabsorption may include muscle wasting owing to diminished muscle mass; changes in bone mineral density with the development of osteoporosis secondary to impaired absorption of calcium, phosphate, and/or vitamin D; low blood pressure; infertility; and abdominal distention with active bowel sounds.

Any cause of decreased IF can result in decreased absorption of vitamin B12, resulting in pernicious anemia. Other clinical findings are dependent on the particular condition or specific nutrient involved. The therapist is most likely to see the symptoms listed in Table 16-5.

Food-induced symptoms may appear within a few minutes of ingesting foods interpreted by the body as allergens. Or it may be several hours or even days before noticeable symptoms occur. In some cases it depends on the amount consumed, the other foods eaten with it, and the way it was prepared (fresh, cooked, peeled, unpeeled).

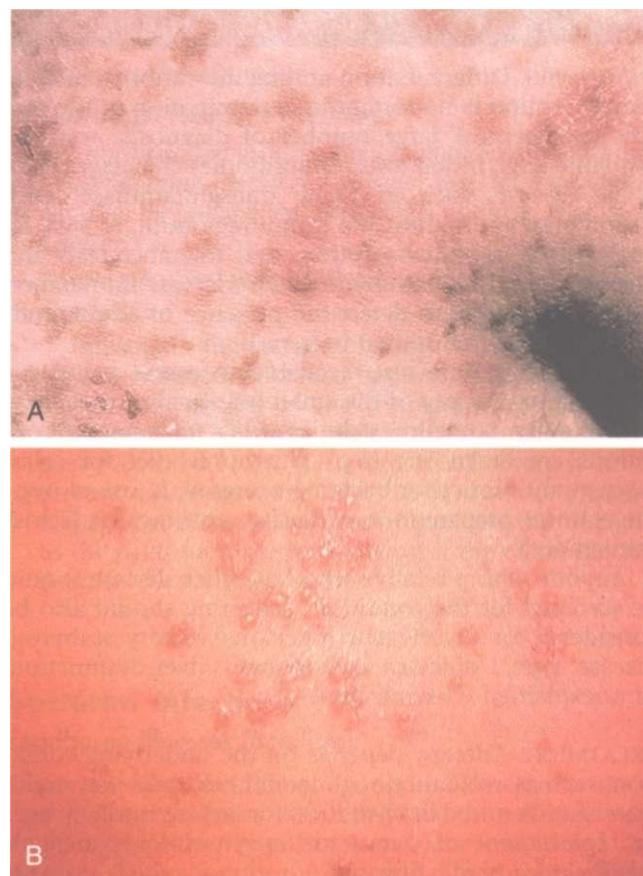


Figure 16-9

A and **B**, Dermatitis herpetiformis. Typical grouped pruritic papulovesicles associated with skin reaction from gluten sensitivity. This skin manifestation usually appears on the buttocks, elbows, or knees. It can affect children but is more common in adults between the ages of 30 and 40. It is almost always a sign of celiac disease and will usually resolve in 3 to 6 months with a gluten-free diet. (A, from Feldman M: *Sleisenger and Fordtran's gastrointestinal and liver disease*, ed 8, Philadelphia, 2006, Saunders. Courtesy of Dr. Timothy Berger, San Francisco. B, from Noble J: *Textbook of primary care medicine*, ed 3, St Louis, 2001, Mosby. Courtesy James C. Shaw, MD.)

Table 16-5 Symptoms Associated with Malabsorption

Symptoms	Malabsorbed Nutrients
Muscle weakness, muscle wasting, paresthesias Osteomalacia	Generalized malnutrition; fat, protein, carbohydrates Fat, protein, carbohydrates, iron, water; vitamins A, D, K Calcium, vitamin D, magnesium, potassium
Tetany, paresthesias, Troussseau's sign, Chvostek's sign Numbness and tingling; neurologic damage	Vitamin B12, vitamin B complex Vitamin B12, vitamin B complex
Bone pain, fractures, skeletal deformities	Calcium, vitamin D, protein
Muscle spasms	Electrolyte imbalance, calcium, pregnancy
Easy bleeding or bruising Generalized swelling Dermatitis herpetiformis	Vitamin K Protein Gluten

MEDICAL MANAGEMENT

DIAGNOSIS. Differentiation among the various causes of malabsorption is important in determination of the specific treatment. A large number of diagnostic tests are available (e.g., blood tests for antibodies characteristic in celiac disease, such as tissue transglutaminase, anti-endomysial antibodies, and immunoglobulin A; fecal fat analysis for fat malabsorption; oral tolerance tests and measurement of breath hydrogen for lactose intolerance; other breath tests to detect the presence of compounds produced by intraluminal bacteria).

Specific tests are also available to assess pancreatic insufficiency. Biopsy of the small intestinal mucosa may be necessary. Sometimes clinical trials for treatable conditions are diagnostic (e.g., gluten-free diet for celiac disease, antibiotics for bacterial overgrowth, use of over-the-counter preparations of lactase enzyme for lactose intolerance).

Anyone with a relative who has celiac disease should be screened for the condition. Screening should also be considered for anyone with a personal history of thyroid disease, type 1 diabetes, osteoporosis, liver dysfunction, or unexplained GI symptoms.

TREATMENT. Therapy depends on the underlying condition, such as avoidance of gluten for celiac disease, exclusion of milk and dairy products for lactose intolerance,⁹⁹ or replacement of pancreatic enzymes for pancreatic insufficiency (cystic fibrosis).

Probiotics, live microbial food supplements that beneficially affect the host by improving intestinal microbial balance, alleviating lactose intolerance, and enhancing immune function, may be beneficial in the treatment of malabsorption syndromes (and other GI-related conditions).^{26,118}

Muscular twitching and tetany are treated with calcium phosphate or gluconate administered orally or intravenously. In severe cases total parenteral nutrition (TPN) may be the only treatment option, as in the case of reduced absorptive surface (e.g., short-gut syndrome). Parenteral nutrition (sometimes called *hyperalimentation*) is a technique for meeting a person's nutritional needs by means of intravenous feedings, allowing bowel rest. Nutrition by intravenous feeding is administered via a central venous catheter, usually inserted into the superior vena cava, and may be TPN or supplemental. TPN also may be given peripherally for short periods of time.

PROGNOSIS. The prognosis is good for any of these conditions if the underlying defect can be corrected. About 95% of people with celiac disease or other food-related GI dysfunction who follow a corrective (usually gluten-free) diet recover completely. Full recovery can take up to 6 months if treatment begins before permanent damage occurs; otherwise, recovery is much longer for longstanding cases. In some cases, symptoms can be managed with proper diet and probiotics but complete recovery does not occur.

A higher incidence of non-Hodgkin's lymphoma in adult life may occur with untreated gluten-sensitive enteropathy. Anyone who develops GI symptoms while in

remission on a gluten-free diet should be evaluated for cancer.¹³⁷

People with celiac disease have a greater risk of developing other related immune system disorders. Genes that make a person more susceptible to celiac disease also are known to be connected with autoimmune disorders, including type 1 diabetes, systemic lupus erythematosus, Sjogren's syndrome, scleroderma, autoimmune chronic active hepatitis, Graves' disease, Addison's disease, and myasthenia gravis.

There is also a possible link between celiac disease and liver dysfunction, which may explain the lack of response to a gluten-free diet that some individuals experience. Evidence of increased incidence of mild, asymptomatic hepatitis and primary biliary cirrhosis in association with celiac disease has been reported.⁴⁶

SPECIAL IMPLICATIONS FOR THE THERAPIST 16-9

Malabsorption Syndrome

PREFERRED PRACTICE PATTERNS

4A: Primary Prevention /Risk Reduction for Skeletal Demineralization

4C: Impaired Muscle Performance (decreased muscle mass; muscle atrophy)

5E: Impaired Motor Function and Sensory Integrity Associated with Progressive Disorders of the Central Nervous System

5F: Impaired Peripheral Nerve Integrity and Muscle Performance Associated with Peripheral Nerve Injury (carpal tunnel syndrome associated with vitamin B12 deficiency)

In the rehabilitation setting or for the acute care client who has not been eating solid foods, diarrhea may develop when the person begins to reestablish a normal diet. Prolonged viral conditions can wash out the enzymes normally present in the columnar epithelial cells. Reestablishing normal eating may require additional time to restore the enzymatic homeostasis in the intestines.

Paresthesias, muscle weakness, and muscle wasting accompanied by fatigue and weight loss can be signs of malnutrition (e.g., eating disorders) or malabsorbed fat, protein, or carbohydrates. Malabsorption of calcium, vitamin D, magnesium, and potassium can cause paresthesias, tetany, and positive Troussseau's and Chvostek's signs (see Figs. 5-8 and 5-9).

Troussseau's sign is an indication of tetany seen as carpal spasm elicited by compressing the upper arm (as occurs when taking a blood pressure measurement). Chvostek's sign is a spasm of the facial muscles elicited by tapping the facial nerve in the region of the parotid gland; it is seen in tetany.

Other effects of malabsorption syndrome possibly seen in a therapy setting include muscle spasms caused by electrolyte imbalance (especially low calcium) and pregnancy, easy bleeding or bruising as a result of a vitamin K deficiency, and generalized swelling caused by protein depletion (see Table 16-5).