PERICARDIAL DISEASE (PERICARDITIS)

PERSPETIVE

Our knowledge of pericardial function and disease has increased greatly since Hippocrates described the pericardium in 460 BC as “a smooth tunic that envelops the heart and contains a small amount of fluid resembling urine.” Galen provided the first description of a pericardial effusion and performed the first pericardial resection.1 Lancisi first described the appearance of constrictive pericarditis at autopsy in 1728. Also in the 18th century, Laennec said, “There are few diseases attended by more variable symptoms and more difficult to diagnose than [pericarditis].”1 In 1935, Beck described the clinical presentation of cardiac tamponade, known as Beck’s triad (hypotension, jugular venous distention, and muffled heart sounds).2 Despite the passage of time and the modern availability of many diagnostic tools, the diagnosis and treatment of pericardial disease still present a challenge.

ETIOLOGY

Each of the disorders listed in Box 82-1 can produce acute pericarditis, with or without pericardial effusion. In addition, most of these disorders can progress to cardiac tamponade or constrictive pericarditis.

Most cases of pericarditis in developed countries are idiopathic. Even exhaustive clinical testing identifies a specific cause in less than 20% of patients, with the remainder being idiopathic despite often being putatively of viral cause.

EPIDEMIOLOGY

Acute pericarditis is a syndrome caused by inflammation of the pericardium. Although the exact incidence is unknown, autopsy series show an incidence of pericarditis of approximately 5%. The incidence of pericarditis in the emergency department (ED) is not known.

PRINCIPLES OF DISEASE

Pericardial Anatomy and Physiology

The normal pericardium envelops the heart and attaches to the great vessels. It consists of parietal and visceral layers, with a narrow potential space between them. The visceral layer or epicardium adheres to the myocardium. It is separated from the parietal layer by a potential space. Each layer is 1 or 2 mm thick and is composed of elastic fibers. The position of the heart within the chest is stabilized by the attachment of the parietal pericardium to the sternum, the diaphragm, and the vertebral column. Its blood supply comes from the internal mammary artery, and its nerve supply from the phrenic nerve.3

An ultrafiltrate of plasma, 15 to 35 mL of fluid, is normally contained in the pericardial space. Abnormal amounts of pericardial fluid can accumulate when the venous or lymphatic drainage of the heart is obstructed. The pericardium serves several functions: it maintains the heart’s position, lubricates the heart’s surface, prevents the spread of infection, prevents cardiac overdistention, augments atrial filling, and maintains the normal pressure-volume relationships of the cardiac chambers. Patients with congenital absence (or surgical removal) of the pericardium, however, show few, if any, problems.

PATHOPHYSIOLOGY

The inflammation of pericarditis is characterized by a granulocytic and lymphocytic infiltration of the pericardium. There is an increase in the number of antibodies in the pericardial fluid.

IDIOPATHIC PERICARDITIS

Clinical Features

The classic symptoms of pericarditis include chest pain, pericardial friction rub, and electrocardiogram (ECG) abnormalities. A history of fever and myalgia is common. Pericarditis chest pain usually is sharp and pleuritic and varies with position. It is typically relieved by sitting forward and is worsened by lying down, deep inspiration, or swallowing. Pericarditis pain is usually retrosternal, can radiate to the trapezius muscles, and may manifest as isolated shoulder pain. Pain can also be felt in the area of the diaphragm.

The physical examination hallmark of acute pericarditis is the pericardial friction rub. The rub may be caused by friction between inflamed or scarred visceral and parietal pericardium or may result from friction between the parietal pericardium and adjacent pleura. It may be audible anywhere over the anterior chest wall but usually is best heard at the lower left sternal border. Friction rubs are best heard via the diaphragm of the stethoscope, with the patient leaning forward in full expiration. The rub also can be accentuated by a full inspiration, followed by a breath hold, during which auscultation is performed. The rub tends to be intermittent, migratory, and difficult to hear in a loud ED.

Diagnostic Strategies

There is no single test that is diagnostic for pericarditis. The ECG is the most reliable diagnostic tool. It evolves through stages that...
Etiology of Pericarditis

Infectious
- Viral
- Bacterial
- Fungal
- Parasite
- Rickettsia

Postinjury
- Trauma
- Surgery
- Myocardial infarction
- Radiation

Metabolic diseases
- Uremia
- Medications

Systemic diseases
- Rheumatoid arthritis
- Systemic lupus erythematosus
- Sarcoidosis
- Scleroderma
- Dermatomyositis
- Amyloidosis

Tumors
- Aortic dissection

Normal sinus rhythm with marked sinus arrhythmia
Acute pericarditis
Abnormal ECG

Occur over time. The first stage occurs in the first hours to days of illness. It includes diffuse ST segment elevation seen in leads I, II, III, aVL, aVF, and V2 through V6, and also reciprocal ST segment depression in aVR and V1. Most patients with acute pericarditis have concurrent PR segment depression (Fig. 82-1). In the next stages, the ST and PR segments normalize, but the T waves flatten, and then there is deep, symmetrical T wave inversion. At the last stage, the ECG reverts to normal, although the T wave inversions may become permanent.

The early ECG findings of acute pericarditis may be difficult to distinguish from acute myocardial infarction (MI), coronary artery spasm, or benign early repolarization. The differentiation of acute MI from acute pericarditis is essential. Thrombolytic therapy is contraindicated in pericarditis because its use may precipitate hemorrhagic cardiac tamponade. In contrast to the ECG in acute MI, the ST segment elevations in stage 1 acute pericarditis are concave rather than convex upward, and simultaneous T wave inversions are not seen. Subsequent tracings do not evolve through a typical MI pattern, and Q waves do not appear.

Differentiation of pericarditis from ST elevation MI is often difficult, especially if the history is atypical or the patient has a significant communication barrier, such as language. When the ECG pattern suggests ACS and the pain is not clearly pericarditic
in nature, often the best course is early diagnostic coronary angiography. Ventricular dysrhythmias are rare in pericardial disease. Patients with pericarditis who have ventricular dysrhythmias should be presumed to have concomitant myocarditis or another cardiac disease or to have been misdiagnosed.

Echocardiography facilitates the definitive diagnosis of pericarditis with effusion, although it will be normal in patients without significant effusion, and a normal echocardiogram cannot be used to exclude pericarditis. In addition, cardiac tamponade, increased pericardial thickness, pericardial tumors and cysts, constrictive pericarditis, and the congenital absence of the pericardium can all be diagnosed by echocardiography.

Some patients with acute pericarditis have elevated cardiac markers caused by myopericarditis, myocarditis, or MI. The white blood cell count and erythrocyte sedimentation rate (ESR) may be elevated or normal and are not sensitive or specific. Other laboratory studies should be directed at determining nonidiopathic causes of pericarditis.

**Management and Disposition**

If a specific cause of pericarditis is found, therapy should be specific for that cause. Otherwise, therapy for acute pericarditis is symptomatic. Anti-inflammatory therapy will reduce pain, and a nonsteroidal anti-inflammatory drug (NSAID) is the treatment of first choice. Ibuprofen has the best side effect profile, but other NSAIDs should be equally effective. The patient will often report significant pain relief from the analgesic effect of the ibuprofen while in the ED, even before onset of the anti-inflammatory effect. A dose of 600 mg four times a day for 1 week is a good initial therapy. If the chosen NSAID is not effective within 1 week, a different class of NSAIDs should be tried, such as indomethacin 25 mg three times a day for 1 week. Colchicine (1.2 initially then 0.6 mg daily for up to 6 months) is effective for recurrent pericarditis, and steroid therapy (1 mg/kg daily) has shown mixed results.5,6

**Complications**

The clinical course of pericarditis is variable: 60% of patients have complete recovery within 1 week, and almost 80% have complete recovery within 3 weeks. Patients with fever, pericardial effusion, a subacute course, or failure of initial NSAID treatment have a worse prognosis. Eighteen percent of patients can have recurrent pericarditis that may require serial echocardiography to exclude effusion or tumor.6

**UREMIC PERICARDIAL DISEASE**

**Perspective and Etiology**

Pericarditis may occur secondary to renal failure or dialysis. It occurs more frequently in hemodialysis patients than in those receiving peritoneal dialysis. Acute renal failure is also associated with pericarditis, and the cause is unknown. The evaluation of a chronic renal disease patient with pericarditis requires a diligent search for infectious causes.

**Clinical Features and Diagnostic Strategies**

Patients with uremic pericarditis have chest pain, unexplained fever, and possibly a coarse friction rub. They also may have significant effusions. The ECG in uremic pericarditis is often normal because little epicardial inflammation occurs.7 In a dialysis patient, cardiac enlargement on chest radiograph in the absence of signs of volume overload or congestive heart failure (CHF) should prompt consideration of pericardial effusion. An echocardiogram will provide the definitive answer. Pericardiocentesis may be needed to exclude infection.

**Management and Disposition**

Uremic pericarditis is initially treated with intensive dialysis. NSAIDs are ineffective and often are contraindicated by the patient’s underlying renal impairment. Systemic steroids (prednisone 1 mg/kg daily) may require 1 or 2 weeks of therapy in the few patients who do not respond to dialysis.

**Complications**

Uremic pericardial effusions are among the most common causes of cardiac tamponade. Uremic pericardial effusions may be locular and difficult to fully drain with a catheter, and surgical options should be considered.

**POST–MYOCARDIAL INFARCTION PERICARDITIS**

Approximately 20% of patients with transmural MIs experience a different quality of chest pain 2 to 4 days after infarction. This pain may represent early post-MI pericarditis. There is frequently low-grade fever and a transient pericardial friction rub. A large pericardial effusion is unusual. Early post-MI pericarditis is generally short-lived and disappears with 1 to 3 days with aspirin therapy (325 mg/day).

The ECG changes of pericarditis usually are masked by the acute MI changes. Patients with early post-MI pericarditis have more dysrhythmias and heart failure. Pericarditis in acute MI may be an indicator of greater myocardial damage and a worse outcome. Dressler reported a syndrome of fever, pleuritis, leukocytosis, pericardial friction rub, and chest radiograph evidence of new pericardial or pleural effusions in post-MI patients.8 Frequent relapses and a high incidence of friction rubs led Dressler to describe this syndrome as a delayed complication of MI in contrast to the well-known syndrome of early post-MI pericarditis. The cause of late post-MI pericarditis (Dressler’s syndrome) may be immunologic, but the syndrome may also occur with pulmonary embolus and after pericardiectomy. Anticoagulants should be discontinued to reduce the risk of hemorrhage. Delayed post-MI pericarditis is treated with NSAIDs such as ibuprofen 600 mg four times per day or indomethacin 25 mg three times per day.

**POSTINJURY PERICARDITIS**

**Perspective**

Postcardiac injury syndrome is defined as pericarditis after MI, cardiac surgery, or trauma. The incidence ranges from approximately 5% after MI to 30% after thoracic surgery or trauma. Pericarditis develops in 20% of patients with a penetrating cardiac injury, few of whom have cardiac tamponade. It can also occur after chest trauma that does not involve the heart or pericardium.

**Principles of Disease**

Injury to the pericardium in blunt trauma may range from contusion to laceration or rupture. Some degree of traumatic pericarditis is found during surgery or at autopsy in many patients sustaining severe blunt trauma of the chest. Penetrating wounds to the heart usually cause laceration of the pericardium and the myocardium, with secondary pericarditis
and pericardial infections. Although the exact incidence is unknown, infection, tamponade, myocarditis, and inflammatory pericarditis may occur.

An immune pathogenesis is suggested by the development of cardiac autoantibodies, although these autoantibodies are common after injury, even in patients who do not develop pericarditis. Constrictive pericarditis occurs secondary to trauma. This may be caused by pericardial blood, possibly secondary to the decreased resorptive power of damaged pericardium, with secondary fibrosis and constriction.

Clinical Features

Symptoms and signs of postcardiac injury syndrome include pericardial rub, fever, and chest pain. Although the diagnosis is usually established clinically, confirmation by echocardiography is helpful. The interval between injury and the onset of pericarditis ranges from 4 to 12 days. During hospitalization, purulent pericarditis should be considered as a possible source of febrile illness in a trauma patient with multisystem organ failure.

Management and Disposition

Most patients respond to aspirin (325 mg daily) or NSAIDs (ibuprofen 600 mg four times per day). Uncomplicated pericarditis secondary to blunt trauma usually resolves. The patient should be observed until other life-threatening disease processes have been excluded.

NEOPLASTIC PERICARDIAL DISEASE

Perspective

Malignant pericardial tumors typically manifest late, which complicates diagnosis and treatment. Malignant involvement of the pericardium is observed in 3.4% of general autopsies and 2 to 31% of cancer autopsies. The most common causes are lung cancer (30%), breast cancer (23%), lymphoma (17%) and leukemia (9%). Primary malignancies of the pericardium are rare.

Principles of Disease and Pathophysiology

The pattern of cardiac involvement by a malignant tumor is determined by the heart's lymphatic drainage system.

Malignant pericardial effusions contribute directly to the patient's death in most cases commonly from cardiac tamponade. Although the underlying disease process is often advanced when tamponade develops, the patient's quality of life can usually be improved if tamponade is treated promptly.

Clinical Features

Primary cardiac neoplasms, such as angiosarcoma and teratoma, can initially cause symptoms consistent with pericarditis. The typical course is that of an acute pericarditis that resolves and subsequently recurs. Malignant pericardial disease is difficult to diagnose. Most patients are asymptomatic or have nonspecific symptoms, such as shortness of breath, cough, palpitations, ill-defined chest pain, weakness, dizziness, hiccups, or fatigue.

Diagnostic Strategies

The diagnostic workup for malignant pericardial effusion includes an echocardiogram, computed tomography (CT), or magnetic resonance imaging (MRI). When a pericardial effusion is identified, pericardial fluid cytology is recommended if the underlying malignancy is undiagnosed.

Management and Disposition

Malignant pericardial effusion treatment may include pericardiocentesis, local instillation of sclerosing or chemotherapeutic agents, systemic chemotherapy, cardiac radiation, and pericardial window. The method chosen depends on the primary tumor and the patient's expected length of survival.

The prognosis for patients with malignant pericardial disease depends on the type and extent of the underlying cancer.

RADIATION-INDUCED PERICARDITIS

Fewer than 5% of patients treated with radiation therapy develop pericarditis. The incidence has decreased with improved radiation therapy techniques. The percentage of pericardial volume irradiated and the dosage determine which patients develop pericarditis. Radiation-induced pericarditis is seen most commonly in patients with Hodgkin's lymphoma or breast cancer. Pericardial effusion and constrictive pericarditis are common, and tumor recurrence should be considered.

PERICARDIAL DISEASE RELATED TO CONNECTIVE TISSUE DISORDERS

Pericarditis occurs in approximately one third of patients with rheumatoid arthritis (RA), usually within 3 years of the initial diagnosis. Rheumatoid pericardial disease is rarely clinically significant. Occasional patients develop effusions, constrictive pericarditis, or cardiac tamponade. These patients usually have rheumatoid nodules, elevated circulating rheumatoid factor levels, and valvular heart disease. Pericardial fluid may have rheumatoid factor or a low glucose level. Corticosteroid treatment is useful. Prednisone 1 mg/kg/day is the initial treatment, with close follow-up appointment.

Pericarditis is found at autopsy in more than 50% of patients with systemic lupus erythematosus (SLE). The effusion is usually thick and fibrinous. Either cardiac tamponade or constrictive pericarditis may develop. Lupus erythematosus cells may be identified in pericardial fluid specimens. Corticosteroid therapy is indicated.

Other connective tissue diseases that may cause pericarditis include Sjögren's syndrome, giant cell arteritis, ankylosing spondylitis, Reiter's syndrome, Behçet's disease, systemic sclerosis, and polyarteritis nodosa.

MISCELLANEOUS INFECTIOUS CAUSES OF PERICARDITIS

Other causes of pericarditis include *Rickettsia conorii*, which causes Mediterranean spotted fever (treated with doxycycline), *Mycoplasma pneumoniae* (treated with a macrolide), *Nocardia asteroides* (treated with pericardectomy and long-term use of antibiotics such as sulfisoxazole), *Chlamydia trachomatis*, Epstein-Barr virus, cytomegalovirus infection, *Haemophilus influenzae* (treated with chloramphenicol), and coccidioidomycosis (endemic in the southwestern United States). Viral and bacterial causes of pericarditis can coexist, such as varicella-zoster infection superinfected with *Staphylococcus aureus*. These bacterial superinfections associated with varicella are more common in children.
PERICARDIAL EFFUSION

Etiology and Clinical Features

The most common causes of pericardial effusion are viral or idiopathic pericarditis, malignancy, uremia, trauma, and radiation therapy. Drug reactions and autoimmune diseases are less common causes.

Pericardial effusion is often asymptomatic. Patients with known associated conditions (e.g., cancer or renal failure) with cough, fever, chest pain, or dyspnea may have an effusion.

Diagnostic Strategies

Pericardial effusion may cause an enlarged cardiac silhouette on chest radiograph, usually with normal pulmonary vasculature. A minimum of 200 to 250 mL of pericardial fluid is necessary to produce cardiomegaly on a chest radiograph.

Echocardiography is the diagnostic modality of choice (Fig. 82-2). It easily differentiates pericardial fluid from cardiac chamber effusion. Echocardiography is technically unsatisfactory. MRI can also be diagnostic. Nuclear scans may be useful in detecting purulent pericardial effusions.

CT may be useful in diagnosing pericardial effusion when the echocardiogram is technically unsatisfactory. MRI can also be diagnostic. Nuclear scans may be useful in detecting purulent pericardial effusions.

Figure 82-2. A, Bedside ultrasound showing a pericardial effusion. The effusion is best seen superior to the left ventricle at the top of the image. B, The proper technique for emergency department ultrasound of pericardial effusion. (Courtesy Jessica Resnick, MD.)

CARDIAC TAMPOONADE

Etiology and Pathophysiology

Ten percent of all patients with cancer develop cardiac tamponade. Cardiac tamponade should be suspected in patients with penetrating chest wounds. It is also common in patients with uremic pericarditis.

Cardiac tamponade is the result of compression of the myocardium by the contents of the pericardium. This compression is usually caused by fluid, but it may be caused by gas, pus, blood, or a combination of factors.

Cardiac tamponade is a physiologic continuum reflecting the amount of fluid, the rate of accumulation, and the nature of the heart. The three stages necessary for tamponade to develop are fluid filling the recesses of the parietal pericardium, fluid accumulating faster than the rate of the parietal pericardium's ability to stretch, and accumulation that exceeds the body's ability to increase blood volume to support right ventricle filling pressure. The final result is increased pericardial pressure, which causes decreased ventricle compliance and decreased flow of blood into the heart. The reduction of blood inflow into the right ventricle results in decreased stroke volume that leads to decreased cardiac output. The most important factor in the development of tamponade is the rate of fluid accumulation.

The heart initially responds to tamponade by increasing heart rate to maintain cardiac output. This compensatory mechanism is maintained until late in the clinical course, followed by decompensation.

Symptoms and Signs

Cardiac tamponade symptoms are often nonspecific, but particularly include chest pain, cough, or dyspnea, any of which may be progressive and severe. The classic triad of cardiac tamponade signs described by Beck is hypotension, distended neck veins, and muffled heart sounds. These signs may not be present if tamponade develops quickly.

Diagnostic Strategies

The chest radiograph shows cardiomegaly only if there is a large accumulation of fluid (250 mL). The ECG classically shows decreased voltage or electrical alternans (Fig. 82-3), but the latter
Clinical Features and Diagnostic Strategies

Purulent pericarditis usually manifests as a febrile illness lasting 2 or 3 days. Common presenting signs include tachycardia, dyspnea, hepatomegaly, elevated central venous pressure, chest pain, friction rub, and leukocytosis. The most common presentation is a hospitalized patient with a serious underlying disease who initially improves after treatment of the primary process but later develops fever, dyspnea, and chest pain.

The diagnosis should be suspected in any febrile patient with multisystem illness who has a pericardial effusion. Pericardiocentesis is necessary to establish the diagnosis, obtain fluid for microbiologic studies, and relieve cardiac tamponade.

Management and Disposition

Pericardiectomy is the traditional treatment of choice. Indwelling catheters, coupled with lavage, antibiotics (such as vancomycin 1 g two times per day or ampicillin-sulbactam 3 g four times a day), and fibrinolytics, may avoid the need for surgery. Intravenous antibiotics or antifungals are also needed.

The overall survival rate for purulent pericarditis is approximately 30% with antibiotic therapy alone and 50% when combined with early surgical drainage. In addition to the initial complications related to sepsis and tamponade, long-term sequelae of purulent pericarditis include the development of constrictive pericarditis.

TUBERCULOUS PERICARDITIS

Tuberculous pericarditis is estimated to occur in 1 or 2% of patients with pulmonary tuberculosis. In Africa, it is the most common cause of pericarditis. In countries in which tuberculosis is not a major health problem, tuberculous pericarditis is most common in patients who are socioeconomically deprived or immunodeficient. In many patients the chest radiograph shows an enlarged cardiac silhouette without a pulmonary infiltrate. Pericardial fluid aspirates reveal acid-fast bacilli by smear or culture (which may require 4–6 weeks to become positive) in approximately 50% of cases. Diagnostic workup should include
assessment for human immunodeficiency virus (HIV). Patients with tuberculous pericarditis should be hospitalized and observed for evidence of cardiac tamponade. Triple-drug therapy should be started in the hospital and continued for at least 9 months. Patients with chronic pericardial effusions may benefit from oral prednisone therapy. The mortality rate is approximately 15% in HIV-negative patients and 20 to 35% in HIV-positive patients.12

OTHER CAUSES OF PERICARDITIS

Amyloid deposition can cause either restrictive cardiomyopathy (RCM) or constrictive pericarditis. Pericarditis can occur rarely as an extraintestinal complication of inflammatory bowel disease and is independent of the clinical course of the gut disorder.

Iatrogenic pericarditis can also occur as a complication of an implantable defibrillator or an atrial lead of a permanent pacemaker. A polymicrobial bacterial pericarditis can occur after transbronchial needle aspiration or as a complication of endoscopic variceal sclerotherapy. Rarely, pericarditis can also be caused by erosion of a foreign body, such as a sewing needle or toothpick, through the esophagus into the pericardium.

Less than 1% of patients with HIV develop acute pericarditis, but 40% have asymptomatic pericardial effusion. Pericardial effusion is more frequent in patients in the more advanced stages of HIV infection. The clinical features and diagnostic evaluation of patients with HIV-related pericarditis are the same as those in patients without acquired immunodeficiency syndrome (AIDS).

PNEUMOPERICARDIUM

Perspective and Etiology

Pneumopericardium and pyopneumopericardium are rare. Pneumopericardium may be caused by diseases that can lead to formation of fistulae between the pericardial and pleural space, bronchial tree, or upper gastrointestinal tract (e.g., peptic ulcer disease, carcinoma of the esophagus or stomach, and esophageal diverticulum). It may result from bronchial carcinoma or infection with gas-producing microorganisms, or it can be idiopathic. Pyopneumopericardium may result from trauma, foreign body, ingestion of caustic substances, or invasive procedures (e.g., esophagoscopy, thoracentesis, and endotracheal intubation).

Spontaneous pneumopericardium may complicate asthma, labor, barotrauma from positive-pressure ventilation, or Valsalva maneuvers, such as might occur during weightlifting. Cocaine inhalation from positive-pressure devices can also cause pneumopericardium.

Pathophysiology

Pneumopericardium is caused most commonly by an increase in intra-alveolar pressure above atmospheric pressure, resulting in rupture of alveoli. Air dissects into the hilum and mediastinum, through the pericardial reflection on the pulmonary vessels, and into the pericardium.

Clinical Features and Diagnostic Strategies

Physical findings depend on the quantity of fluid and gas in the pericardial space. Heart sounds can be of variable intensity, change depending on body position, and have a metallic quality that may be accompanied by splashing sounds. Hamman’s sign and mediastinal crunch are the terms used for a loud, crunching sound associated with pneumopericardium or pneumomediatinum. This is best heard with the patient in a left lateral recumbent position and is diagnostic for the presence of mediastinal air. The diagnosis of pneumopericardium is confirmed by chest radiograph, CT scan, or echocardiography. Tension pneumopericardium manifests with clinical findings of acute cardiac tamponade.

Management

Stable patients with uncomplicated spontaneous pneumopericardium can usually be observed. After all other life-threatening injuries and complications have been excluded, no long-term sequelae are expected. Tension pneumopericardium should be treated with emergency pericardiocentesis.

CONSTRUCTIVE PERICARDITIS

Perspective and Etiology

Constrictive pericarditis may be a late consequence of acute pericarditis of virtually any cause. There is an increased incidence of constrictive pericarditis as a result of improved survival in patients with chronic renal disease. Other predisposing conditions include radiation, trauma, purulent pericarditis, actinomycosis, and post-pericardiotomy adhesions. Tuberculosis is still the leading cause of constrictive pericarditis in some countries.

Principles of Disease and Pathophysiology

Constrictive pericarditis usually results from fibrous reaction of the pericardium. The key pathophysiologic feature is impaired diastolic filling from external cardiac compression caused by the thickened pericardium. In advanced cases the visceral and parietal pericardial layers may be adherent.

Because the pericardium limits volume, ventricular filling is rapid and completed within the first third of diastole, after which left ventricular volume and pressure remain unchanged. Early ventricular filling followed by a period of unchanging pressure yields a corresponding dip and plateau pattern or square root sign on the left ventricular diastolic pressure curve, which suggests the diagnosis of constrictive pericarditis.

Clinical Features

The symptoms and signs of constrictive pericarditis are identical to those of CHF. Dyspnea, fatigue, and weight gain are the most common complaints. Hepatomegaly, marked pitting lower extremity edema, and ascites can be seen on physical examination. The characteristic auscultatory finding of constrictive pericarditis is a pericardial knock in early diastole. A friction rub may also be heard.

Diagnostic Strategies

The diagnosis is considered in a patient with right-sided heart failure symptoms. Heart size on the chest radiograph is typically small but may be increased by atrial enlargement. Pericardial calcification is suggestive when present on CT or MRI. Liver function tests are consistent with passive congestion. ECG findings include low QRS voltage, nonspecific ST–T wave abnormalities, and atrial dysrhythmias.

Doppler echocardiography may help differentiate constrictive pericarditis from RCM or cardiac tamponade.13 Cardiac catheterization and simultaneous measurement of right ventricular and left ventricular end-diastolic pressures or endomyocardial biopsy may be necessary.
**Differential Considerations and Management**

Constrictive pericarditis is often confused with CHF. The diagnosis should also be considered with signs of elevated venous pressure but no history of myocardial dysfunction. Pericardiectomy is the therapy of choice.

**MYOCARDIAL DISEASES (MYOCARDITIS)**

**Perspective**

The term *myocarditis* was coined initially by Sobernheim in 1837. Romberg reported the association with scarlet fever and typhus in 1891, and “isolated idiopathic interstitial myocarditis” was described by Fiedler in 1899.

**Epidemiology and Etiology**

Some degree of myocarditis is detected in almost 10% of routine autopsies but is often not recognized clinically. The overall incidence is unknown and probably underdiagnosed. The Coxsackie B virus was originally named as the causative organism, but the predominant agents in the 1990s were the adenoviruses, followed by parvovirus 19 and human herpesvirus 6 since 2000. In reality, any infectious agent can cause myocarditis (Box 82-2). The etiology varies by patient age and region. Cytomegalovirus and *Toxoplasma gondii* have emerged as potential causes of myocarditis in cardiac transplant patients. Of patients who have died of AIDS, 67% have myocarditis on autopsy. Worldwide, Chagas’ disease is a leading cause of myocarditis, especially in South America. Mortality from myocarditis has not changed since before 1990. The mortality rate is approximately 20% at 1 year and 50% at 5 years.

**Principles of Disease and Pathophysiology**

Myocarditis occurs by (1) necrosis from direct invasion of an offending infectious agent and its replication within or near myocytes, (2) destruction of cardiac tissue from infiltration of host cellular immune components or from cytotoxic effects of host immunity activated by the infectious agent, or (3) the toxic effect of exogenous or endogenous chemicals produced by a systemic pathogen. Three stages are proposed: acute (early after infection), with viral cytoxicity and focal necrosis; subacute, in which there is an increase in humoral factors leading to autoimmune injury; and chronic, in which there is diffuse myocardial fibrosis and cardiac dysfunction that may lead to dilated cardiomyopathy (DCM). In neonates, the pathologic changes are more often related to direct viral damage, whereas adults are more often injured by immunologic damage.

Isolation of a Coxsackievirus adenovirus receptor shows how these two types of viruses, one RNA and one DNA, may enter the heart.

Cardiac autoantibodies develop after myocarditis. There is also a higher concentration of immunoglobulin G (IgG) anti-β-myosin antibodies in patients with myocarditis and DCM than in controls. Because myocarditis is linked to the development of DCM, idiopathic DCM after myocarditis may be predominantly autoimmune in origin, resulting from either shared antigens or molecular mimicry. The amino acid sequences of the Coxsackie B virus and β-myosin heavy chain protein are similar. An immune response to the former yields damage to the latter (molecular mimicry).

**Clinical Features**

Flulike complaints, including fever, fatigue, myalgias, vomiting, and diarrhea, are usually the first symptoms and signs of myocarditis. The most common presentation in children is dyspnea. In adults, it is dyspnea, chest pain, and dysrhythmias. Altered vital signs include fever, tachycardia, tachypnea, and, uncommonly, hypotension. Tachycardia disproportionate to the temperature or apparent toxicity may occur but is a nonspecific finding. No symptom or sign is sensitive or specific. Cardiac examination is often unremarkable. When chest pain or CHF occurs at initial presentation, there is a worse prognosis.

In children, prominent physical findings include grunting respirations and intercostal retractions. Although the lungs are clear to auscultation in most patients, approximately 10 to 15% have rhonchi. This may be related to infection with respiratory syncytial virus (RSV), which can cause these symptoms with or without associated myocarditis. Infants often have a fulminant syndrome characterized by fever, cyanosis, respiratory distress, tachycardia, and cardiac failure. When children have ventricular dysrhythmias, myocarditis and idiopathic DCM are commonly seen on endomyocardial biopsy, despite findings of a structurally normal heart by noninvasive studies. Long-term prognosis in children correlates with the severity of their initial presentation.

**Diagnostic Strategies**

Common ECG changes include sinus tachycardia, a widened QRS, and low electrical activity. There may be a prolonged corrected QT interval, atrioventricular block, or acute MI pattern abnormalities.

Cardiac troponin may be elevated although when in the course of the disease is unknown. The prognostic significance of elevation is not known, although one can assume that a higher level correlates with more myocardial damage. The white blood cell count and ESR may be elevated or normal and so are not of diagnostic value. The echocardiographic features of myocarditis, although nonspecific, include reduced left ventricular ejection fraction, global hypokinesis, and regional wall motion abnormalities. Contrast-Enhanced MRI may be diagnostic. Indium-111 antimony antibodies bind specifically to exposed myosin in damaged myocardial cells, providing a noninvasive approach for identification of myocarditis.
the diagnosis of myocardial necrosis. Acute and convalescent viral titers are positive in less than 40% of cases. A rise in viral titers or a high titer of viral-specific IgM may help establish a viral cause, although not in the ED.

Endocardial biopsy, the historical gold standard, has variable sensitivity and specificity owing to sampling error when the tissue taken is different from the tissue involved (Fig. 82-4). Histologic criteria for myocarditis are present in only 5 to 30% of patients with clinically suspected myocarditis and up to half of patients with DCM. Molecular genetic probes, such as polymerase chain reaction assays, are used to supplement standard histologic analysis. In addition, polymerase chain reaction analysis of tracheal aspirates of intubated patients with myocarditis shows a correlation with endocardial biopsy. Because of the limitations of biopsy, magnetic imaging may become the diagnostic test of choice and the next gold standard.

DIFFERENTIAL DIAGNOSIS

Myocarditis can masquerade as acute MI with severe chest pain, ECG changes, elevated cardiac markers, and heart failure. Patients with myocarditis are usually young and have few risk factors for coronary artery disease. ECG abnormalities may extend beyond the distribution of a single coronary artery, or there may be global, rather than segmental, wall motion abnormalities on echocardiography. In myocarditis, chest pain continues, but there are no further ischemic ECG changes. The diagnosis of myocarditis should also be considered in an otherwise healthy patient with symptoms and signs of new CHF or dysrhythmias.

If the differentiation of myocarditis from MI is unclear, cathe terization may be necessary. Coronary angiography is usually normal in myocarditis, which should prompt consideration of endomyocardial biopsy.

MANAGEMENT

Treatment is supportive and aimed at preserving left ventricular function. The type of supportive care necessary is determined by the patient’s clinical presentation and the stage and severity of disease. This may extend from simple limitation of activity to rhythm and CHF treatment, extracorporeal membrane oxygenation, ventricular assist devices (VADs), and eventual cardiac transplantation.

Therapy is stage specific, given the three distinct phases of the disease. In the first phase, demonstration of replicating virus suggests that early antiviral agents, such as pleconaril or ribavirin, may be effective. Unfortunately, the diagnosis is often made after the initial viral phase. Agents active at the Coxsackievirus-adenovirus receptor present an intriguing theoretic approach.

Multicenter trials of immunosuppressive therapy for the subacute phases of myocarditis have shown no benefit. Efforts to identify patient and treatment subsets in which immunosuppressive therapy may be beneficial are ongoing. High-dose gamma globulin therapy has been studied in a pediatric population. High-dose intravenous immunoglobulin may be associated with improved recovery of left ventricular function and better survival during the first year after presentation.

In the chronic stage, CHF symptoms predominate and standard pharmacologic treatment for CHF is indicated. In some cases the deterioration of cardiac function is reversible with the aid of a VAD. These devices have been used successfully over extended periods, including up to 70 days. Their use should be considered before transplantation.

DISPOSITION

All patients should be monitored, and those with persistent hemodynamic instability require intensive care. Paradoxically, patients with fulminant myocarditis have the best prognosis. Complications of myocarditis include ventricular dysrhythmias, left ventricular aneurysm, and cardiac failure.

The mortality rate is 20% at 1 year and 50% at 5 years, despite optimal medical management. Ejection fraction and right ventricular function 1 year after initial presentation may be the best predictors of subsequent survival. The long-term prognosis in survivors is variable.

Patients who undergo transplantation because of myocarditis heart failure have decreased 1-year survival compared with patients who undergo transplantation for other reasons. They also have higher allograft rejection rates than other recipients. The overall 5-year survival rate for children is 70%.

CHAGAS’ DISEASE

Chagas’ disease is one of the leading causes of myocardial disease in many countries in Latin America, particularly in Central America. Chagas’ disease is caused by the protozoan Trypanosoma cruzi with transmission by insect vectors.

Approximately 75% of seropositive patients with Chagas’ disease never have symptoms. Systemic symptoms include fever, hepatic or splenic enlargement, and unilateral periportal edema. Cardiac manifestations include angina-like chest pain, dysrhythmias, embolic episodes, heart failure, conduction abnormalities, multifocal ventricular premature contractions, and abnormal ST segment and T wave abnormalities. Ventricular tachycardia is common. Syncope or near-syncope episodes occur in nearly two thirds of patients.

Serum parasites establish the diagnosis, as does measuring anti-IgG for T. cruzi. Chagas’ disease should be included in the differential diagnosis for patients with new cardiac symptoms and a Latin American travel or immigration history. Echocardiography may show a left ventricular apical aneurysm or scar, which is a reliable marker of the disease.

Chagas’ disease is treated with the antitrypanosomal drugs benznidazole (5 mg/kg/day divided into two daily doses for 60 days) and nifurtimox (15-20 mg/kg/day for patients younger than 10 years, 12.5-15 mg/kg/day for patients aged 10-18 years, and 8-10 mg/kg/day for patients older than 18 years, divided into four doses for 90 days). These medications are available from the Center for Disease Control and Prevention. Amiodarone may be useful to treat ventricular tachycardia. An angiotensin-converting enzyme inhibitor may be useful for CHF. Increased world attention, with elimination of the vector and improved blood donation screening, especially for platelet transfusions, is decreasing the incidence of this disease in Latin America.
TRICHINOSIS

Trichinosis is caused by ingestion of the cysts of Trichinella spiralis in undercooked meat. Historically, pork was the most commonly implicated meat, but Trichinella has been eradicated from commercial domestic pork for many decades in the United States. Trichinosis in the United States is most likely caused by wild game. Hunters, immigrants who home raise pork, and international travelers are at risk. Larvae may be deposited in the muscles, which incite an inflammatory reaction and necrosis of muscle fibers. The acute illness consists of fever, myalgias, muscle tenderness, neck stiffness, and a characteristic periorbital edema. Laboratory studies reveal an eosinophilia and often elevated creatine phosphokinase CPK or lactate dehydrogenase (LDH).

Myocardial involvement is present in approximately 20% of clinically diagnosed cases and appears in the second or third week of illness, when other symptoms are declining. Cardiac manifestations include chest pain, dyspnea, cardiomegaly, dysrhythmias, and CHF. ECG findings, such as nonspecific ST-T wave abnormalities and conduction blocks, may appear transiently, even in the absence of cardiac symptoms.

The diagnosis is usually established with serologic studies or biopsy of any symptomatic muscle group. Treatment usually involves corticosteroids (1 mg/kg/day) together with anthelminthic drugs such as albendazole (400 mg twice a day for 14 days) and mebendazole (400 mg four times per day for 14 days).21

DIPHTHERIA

Diphtheria presentation, diagnosis, and treatment are discussed in Chapter 129. Myocardial involvement is clinically evident in 10 to 25% of cases and is the major cause of death.22 Early signs of myocarditis are tachycardia and faint heart sounds. Cardiac enzymes are often elevated. Prolongation of the PR interval and ST-T wave abnormalities occur early in the course of the disease. Bundle branch block or complete heart block, when they occur, precede total circulatory collapse and are associated with a poor prognosis. Treatment with oral carnitine, a cofactor in the transport of fatty acids to mitochondria, is associated with a lower incidence of mortality, heart failure, and severe conduction blocks.22

LYME DISEASE

Epidemiology and Clinical Features

Lyme disease is caused by infection with the spirochete Borrelia burgdorferi and is discussed in Chapter 141.134 Lyme disease–related carditis occurs weeks to months after the onset of erythema migrans. Cardiac complications occur in 4 to 10% of patients. Such complications most commonly is a conduction delay, usually a reversible effect on the AV node. Pericarditis and CHF also occur.

Lyme disease–related carditis should be suspected in otherwise healthy persons with unexplained heart block and potential exposure to ticks in an endemic area. Lyme disease is diagnosed by identification of the spirochete with serologic testing. A screening ECG should be performed whenever the diagnosis of Lyme disease is suspected.

Temporary placement of a pacemaker is often required in unstable patients. Antibiotic therapy with intravenous penicillin (2 million units four times per day) or oral doxycycline (100 mg twice per day for 21 days) is effective and can reverse atrioventricular block. Erythromycin (250 mg four times per day for 21 days) should be prescribed in place of tetracycline in young children. Ceftriaxone (500 mg twice per day for 21 days) is also effective. Most patients recover completely, and a permanent pacemaker is rarely needed.

OTHER CAUSES OF MYOCARDITIS

The cardiac manifestations of AIDS are diverse and cause death in at least 6% of patients with HIV (HIV is discussed in Chapter 132). The prevalence of left ventricular dysfunction in adult AIDS patients is approximately 20%. Myocarditis is described in approximately 46% of AIDS patients undergoing postmortem examination. Cardiac involvement increases as the disease worsens. HIV treatment may also lead to cardiac toxicity. Pentamidine can cause torsades de pointes ventricular tachycardia. Zidovudine and dideoxynosine also can lead to cardiac dysfunction.

Cardiac involvement with Legionella pneumophila is uncommon, although the heart may be the only affected organ. Clinical symptoms resemble pericarditis and myocarditis, including dysrhythmias and conduction blocks. After treatment with erythromycin, normal cardiac function may return.

Cardiac Toxoplasma infection may lead to clinically significant disease. Infection is well described in recipients of bone marrow and cardiac transplantation. Immunocompromised patients with toxoplastic myocarditis may have bundle branch block, CHF, pericarditis, and dysrhythmias as a result of lesions in the conducting system. Untreated toxoplastic myocarditis is fatal.

Myocarditis associated with M. pneumoniae may be caused by direct invasion of the myocardium, an autoimmune mechanism, or intravascular coagulation. Miliary tuberculosis, including tuberculosis myocarditis, can produce granulomas within the myocardial conduction system that can precipitate fatal dysrhythmias. Sudden death can also occur secondary to Chlamydia pneumoniae myocarditis. In addition, myocarditis, presumably mediated by exotoxin, is associated with Shigella infection. Cardiac involvement of the conduction system and the pericardium also may occur in dermatomyositis and polymyositis. Patients are usually asymptomatic, but pericarditis, myocarditis, and dysrhythmias can occur.

COCAINE CARDIOTOXICITY

Cocaine has various cardiac effects in addition to ischemia, including myocarditis and DCM. Myocarditis is a common autopsy finding in patients with cocaine abuse. The mechanism responsible for the cardiotoxic effects of cocaine is largely unknown. Theories include the following: (1) cocaine may have a direct effect on lymphocyte activity; (2) intravenous cocaine can increase natural killer cell activity in blood, which may be cytotoxic to myocardial cells; (3) there is a cocaine-related eosinophilic infiltrate that suggests a hypersensitivity reaction; and (4) catecholamine administration can induce a focal myocarditis. Cocaine has a direct, negative inotropic effect on cardiac muscle.

Patients who die with detectable cocaine levels have myocarditis and myocardial constriction bands more often than controls. The severity of contraction-band necrosis correlates with the serum and urine concentrations of cocaine. Catecholamine excess caused by cocaine use may contribute to contraction-band necrosis, which may supply the anatomic substrate for ventricular dysrhythmias.

Lastly, acute and chronic cardiotoxicity occur secondary to the use of doxorubicin. Manifestations of acute cardiotoxicity include dysrhythmias, pericarditis, myocarditis, and left ventricular dysfunction.

KAWASAKI DISEASE

Kawasaki disease, or mucocutaneous lymph node syndrome, is of unknown cause and primarily affects children. This self-limited vasculitis affects many organ systems. Twenty-five percent of all patients develop coronary artery abnormalities, usually several
When injury occurs, common pathophysiologic pathways are activated, which eventually leads to clinical pathology. There are many of these diseases result from genetic mutations. The diseases included are listed in Box 82-3.

A variety of pathologic processes may initiate myocyte injury. When injury occurs, common pathophysiologic pathways are activated. These pathways involve neurohumoral factors, immune factors, and cytokines that cause myocyte dysfunction and subsequent remodeling. At the organ level the remodeling is hypertrophy or dilation. There is also an increase in interstitial fibrosis, which impairs ventricular filling; this leads to increased metabolic demands on the myocardium. At a cellular level, the pathophysiologic derangement may be the troponin complex, intracellular concentration of calcium, myocardial subproteins, or the sarcoplasmic reticulum. These lesions lead to alteration in the cardiac muscle's ability to contract, which eventually leads to clinical pathology. There is also change in the cardiac microvascular circulation that is an independent predictor of morbidity and mortality. Although traditionally defined by organ level pathology, the classification of cardiomyopathies may evolve into a unified theory that shows all types of cardiomyopathy to be variations of a common genetic, anatomic, and humoral pathophysiologic process.

Mutations of genes for myocardial protein components lead to molecular changes in the myocardium that eventually lead to clinical disease. Mutations have been found for abnormalities in cytoskeleton force transmission, impaired force production, and cell junction regulation. The exact correlation between genotype, phenotype, and clinical presentation is unknown, as is the point when molecular level changes transition from compensatory to pathologic.

**DILATED CARDIOMYOPATHY**

**Epidemiology and Etiology**

DCM is a spectrum of disorders that have in common a dilated and failing heart. The incidence of DCM is estimated to be 1 case per 2500 adults and 0.57 cases per 100,000 children. The true incidence is probably underestimated because many asymptomatic cases remain undiagnosed. DCM is estimated to affect 5.5 million adults and 500,000 children in the United States, costing $10 billion annually. Many cases previously thought to be of unknown cause may be secondary to infection. Myocarditis is the most common cause of DCM in children. It is now known that 30 to 40% of DCM cases have a genetic cause, with more than 35 gene mutations discovered, primarily coding for cytoskeleton or sarcomere proteins.

DCM affects men more often than women, affects African Americans more often than whites, and may occur in any age group, with middle age (40-65 years old) being the most common. Risk factors include ethanol and tobacco abuse, pregnancy, hypertension, and infection.

**Pathophysiology**

There are both primary and secondary causes for DCM. Possible pathophysiologic causes include myocardial inflammation mediated by cytokines, macrophages, and natural killer cells; local inflammation caused by the release of cytokines by infiltrating lymphocytes; direct reaction of antibodies with receptors on myocardial muscle; toxins, such as ethanol, impairing myocardial biochemical processes; and loss or dysfunction of myocardial matrix proteins. Myocardial damage initiates a vicious cycle of hypertrophic cell death that increases the burden of the remaining cells; this leads to signaling, more work, and cell death.

**Clinical Features**

Symptoms of DCM have an insidious onset. Left-sided heart failure occurs as the initial manifestation in 75% of adults, with dyspnea (usually with exertion or while supine) being the major symptom. Exacerbation of heart or renal disease, dietary indiscretion, and medication noncompliance are key contributors. CHF symptoms are the most common presentation in children. Chest pain on exertion is the initial symptom in 10% of adults, and systemic or pulmonary emboli are the initial manifestation in 4%. Right-sided heart failure is a late and ominous sign.

**Diagnostic Strategies**

ECG findings are nonspecific and may include poor R wave progression, intraventricular conduction delay, or a left bundle branch block pattern. Holter monitoring may show frequent premature ventricular contractions and occasional ventricular tachycardia. Sudden death is uncommon. The chest radiograph reveals cardiomegaly.

Echocardiography shows left ventricular dilation, reduced systolic function, and variable wall motion abnormalities. Abnormal ventricular contractility defines DCM, and an ejection fraction less than 45% is required for diagnosis. End-diastolic and systolic volumes are increased, as are pulmonary capillary wedge pressure and central venous pressure.

Endomyocardial biopsy may also be necessary, although histologic abnormalities are nonspecific. New histochemical, immunologic, and molecular biologic techniques improve the diagnostic yield, especially for infectious causes. MRI may help diagnose cardiomyopathy. Right-side failure should have occult atrial septal defect ruled out.

As many as one third of patients may have a genetic defect as the underlining cause. Obtaining a family history and genetic counseling may be indicated.

**Management and Disposition**

Therapy includes supportive measures, such as adequate rest, weight control, abstinence from tobacco, moderate salt and ethanol consumption, and reduced physical activity. Medical treatment includes standard measures for CHF. Angiotensin-converting enzyme inhibitors reduce morbidity and mortality. Other afterload-reducing agents, such as isosorbide dinitrate and hydralazine, also prolong survival in patients with...
heart failure. Spironolactone and the angiotensin receptor-blocking agents also prolong survival. Implantable defibrillators improve survival and should be considered in patients with an ejection fraction less than 30% or symptoms for more than 9 months. Short-term statin therapy may help. Antidysrhythmics are not usually effective.

Beta-blockers can reduce symptoms and improve left ventricular function, functional capacity, and survival. In addition, the improvement in cardiac function associated with beta-blockers is also associated with changes in expression of genes encoding for α- and β-myosin heavy chain and sarcoplasmic reticulum calcium adenosine triphosphate.

**Outcome**

Because medical therapy usually fails, DCM is the leading indication for cardiac transplantation in adults and children. Mortality from DCM is 18% by 1 year, 35% by 5 years, and 50% by 10 years. Patients with DCM show progressive deterioration, with 75% of patients dying within 5 years of diagnosis. The clinical course for children is variable, with a better prognosis in young children. Most deaths occur within the first 2 years. Some children show delayed, spontaneous, and unexplained improvement.

**HYPERTROPHIC CARDIOMYOPATHY**

**Perspective**

Hypertrophic cardiomyopathy (HCM), formerly called idiopathic hypertrophic subaortic stenosis (IHSS), is a complex disorder with variable clinical manifestations. The prevalence is estimated to be 1 in 500 persons in the general population. It affects all races, men and women equally, and can manifest at any age.

**Principles of Disease**

**Anatomy**

HCM is a disease involving abnormalities of heart muscle at anatomic, cellular, and genetic levels. Specifically, it is a genetic disease of sarcomere proteins. The defining anatomic feature of HCM is a hypertrophied left ventricle in the absence of another cause of left ventricular hypertrophy. The thickening is usually asymmetrical and involves the septum more than the free ventricular wall. The extent of hypertrophy at any given site can vary greatly and bears significantly on the manifestation of the disease. The dimensions of the left ventricular and right ventricular cavities are small or normal. Atrial dilation is another feature.

Histologically, individual muscle cells are hypertrophied, with a disorganized, characteristic whorled pattern. Sarcomere disarray is the histologic hallmark. Abnormal fibrous tissue is often found in the left ventricle, and the scarring mimics a healed MI.

**Pathophysiology**

HCM is an autosomal dominant disease caused by mutations in genes that encode for sarcomere contractile proteins. Ten genes encoding for cardiac sarcomere proteins and more than 200 different mutations of these genes have been identified. Half the mutations involve three genes: those for β-myosin heavy chain (which constitutes 30% of myocardial protein), myosin-binding protein C, and troponin T. The hypertrophy in HCM may be a compensatory response to the cardiac protein abnormalities. In vitro studies show that mutant β-myosin heavy chain protein exhibits impaired contractility and disrupts formation of the normal sarcomere. The usual cardiac response to physiologic stress is hypertrophy, dilation, or a combination of both. A gene mutation may lead to mutant protein that impairs cellular structure and function owing to fibrous changes in the sarcomere. This causes compensatory tissue hypertrophy manifests as HCM.

Clinically, patients with HCM have asymmetrical left ventricular hypertrophy. They have an abnormal echocardiogram or cardiac magnetic resonance image that shows hyperdynamic ventricles. There may be an outflow obstruction, although this usually occurs with exertion. The thickness of the ventricle and degree of outflow obstruction correlate with disease severity. The pathophysiology involves impaired ventricular filling during diastole.

Genetic studies of families with HCM identify specific mutations that correlate with sudden cardiac death. In families with Arg403Gln mutation, less than half of affected family members survive past 45 years of age. Genetics alone does not account for the clinical manifestation of HCM, because patients with the same genotype differ in phenotypic expression and clinical course. This indicates that modifier genes and environmental factors are also important.

**Clinical Features**

Although HCM occurs at all ages, the average age at diagnosis is 30 to 40 years. Approximately 2% of cases are diagnosed in children younger than age 5 years, and 7% are diagnosed before 10 years of age. HCM gained notoriety after the press coverage of the sudden deaths of several young athletes. There is advocacy for large-scale ECG screening of young athletes, but no studies demonstrate an appropriate strategy for effective screening. The presentation of HCM varies widely, and it may be discovered by screening relatives of patients who have HCM.

In many patients the initial event is sudden death, which usually occurs during exertion. Ninety percent of patients have shortness of breath. Other symptoms include chest pain, syncope, near-syncope, and palpitations.

Physical examination may reveal a loud S4 gallop and a harsh crescendo-decrescendo mid-systolic murmur. This murmur is accentuated by the Valsalva maneuver or changing from a standing to a squatting position. Such position interventions change preload and afterload, which accentuates the murmur. Other physical findings may include a bifid arterial pulse, paradoxical splitting of the second heart sound, and, rarely, a mitral leaflet septal contact sound. Many dysrhythmias are seen in HCM, including premature atrial and ventricular contractions, multifocal ventricular ectopy, and ventricular and supraventricular tachydysrhythmias. In the ED, the diagnosis should be suspected in anyone with a family history, characteristic murmur, and cardiopulmonary symptoms (i.e., chest pain, dyspnea, and dysrhythmia) not explained by other life-threatening conditions.

**Diagnostic Strategies**

Patients with suspected HCM should have an ECG, chest radiograph, and echocardiogram. The ECG is abnormal in approximately 90% of patients. The most common abnormalities are left ventricular hypertrophy, ST segment alterations, T wave inversion, left atrial enlargement, abnormal Q waves, and diminished or absent R waves in the lateral leads. The chest radiograph may be normal or may show left ventricular or atrial enlargement.

Echocardiography is the most important clinical diagnostic strategy. Findings include asymmetrical left ventricular hypertrophy, left ventricular outflow tract narrowing, a small left ventricular cavity, and reduced septal motion. The dynamic characteristic of HCM distinguishes it from the discrete forms of obstruction to ventricular flow. Doppler techniques help assess
the severity of this obstruction at rest and with provocative maneuvers. Magnetic resonance is helpful when the echocardiogram is not. Nuclear studies can be used to assess systolic and diastolic ventricular function and ventricular scarring. Electrophysiologic studies may show dysrhythmias but are not more predictive of sudden death than clinical factors. Genetic screening may be helpful to predict other family members at risk.

**Differential Diagnosis**

HCM mimics many disorders. In individuals who have a gradient and a loud systolic murmur, HCM may be confused with valvular diseases or a ventricular septal defect. In the absence of a murmur, symptoms may suggest mitral valve prolapse, primary pulmonary hypertension, or coronary artery disease. ECG changes, without a history of preceding MI, may also suggest HCM. Echocardiography is often helpful, but ultimately cardiac catheterization may be necessary to confirm the diagnosis.

**Management**

Long-term beta-blocker therapy is the mainstay of therapy, and modulates the effect of catecholamines on the outflow gradient. This prolongs diastole, increases ventricular filling, and results in symptomatic improvement (primarily dyspnea and chest pain) and exercise tolerance. Calcium channel blockers are also useful. Verapamil reduces obstruction, decreases contractility, and improves diastolic relaxation and filling. This improves exercise capacity, and the negative effects on heart rate and blood pressure. Decrease oxygen consumption and the incidence of angina. Verapamil is contraindicated when conduction blocks are present but should be considered when there is no response to beta-blockers. Another option is disopyramide.

Nitroglycerin, the traditional initial ED management for chest pain, is avoided in HCM-associated chest pain because it decreases ventricular volume. Amiodarone is the drug of choice for treatment of ventricular dysrhythmias in HCM. Amiodarone may also control atrial fibrillation. Automatic implantable cardioverter defibrillators are indicated for patients with sudden death or a history of a sudden death risk factor. Updated American Heart Association guidelines do not recommend prophylactic antibiotics in patients with HCM.

Surgical treatment is reserved for patients with large (>50 mm Hg) systolic gradients, severe symptoms, and poor quality of life who do not respond to drug therapy. The most common procedure is septal myomectomy. Dual-chamber pacing decreases outflow gradient and improves symptoms, but it does not improve outcome.

**Disposition**

The natural history of HCM is variable and probably reflects the many different genetic causes. The annual mortality rate is 1%. The onset of atrial fibrillation in patients with HCM may precipitate marked hemodynamic compromise and severe CHF. Cardioversion is indicated, as is rate control and anticoagulation to prevent thrombembolism.

Risk factors for sudden death include malignant genotype, unexplained syncope, sudden death in first-degree relatives, abnormal hemodynamic response to exercise, and greater than 30-mm ventricular thickening.

Patients with HCM initially diagnosed in the ED should have strenuous physical activity specifically proscribed until they have been evaluated by a cardiologist. Patients with HCM who have angina, syncope, near-syncope, dysrhythmias, and abrupt changes in cardiopulmonary status should be hospitalized.

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**RESTRICTIVE CARDIOMYOPATHY**

**Perspective**

The hallmark of RCM is a gradual and progressive limitation of ventricular filling secondary to myocardial infiltration. RCM is the least common type of cardiomyopathy, accounting for less than 5% of all cases. The most common cause is amyloidosis in the United States. Other causes include sarcoidosis, hemochromatosis, scleroderma, neoplastic cardiac infiltration, glycogen storage disorders, Fabry’s disease, Gaucher’s disease, and mutations related to myocardial muscle proteins.

The most common cause of RCM worldwide is tropical endomyocardial fibrosis, which is endemic to India, Africa, and Latin America. Symptoms include an initial viral-like illness followed by persistent fever, malaise, and the development of severe right-sided heart failure.

**Pathophysiology**

Restriction of ventricular filling results in low ventricular volumes, high end-diastolic ventricular pressures, and decreased cardiac output. Systolic function is maintained. Grossly, there is atrial enlargement with small ventricles. As the disease progresses the ventricular cavities may become obliterated by fibrous tissue, scarring, or thrombus.

**Clinical Features and Diagnostic Strategies**

Symptoms are those of worsening diastolic dysfunction and include exercise intolerance (cardiac output cannot be increased because ventricular filling is compromised), elevated central venous pressure, peripheral edema, pulmonary edema, and $S_3$ and $S_4$ gallops. Children can demonstrate failure to thrive. Differentiation from constrictive pericarditis requires CT, MRI, or Doppler echocardiography. Pericardial calcification favors a diagnosis of constrictive pericarditis over the diagnosis of RCM. Myocardial biopsy may be necessary.

**Management and Disposition**

Most of the underlying causes of RCM are untreatable. The exception is hemochromatosis. Symptomatic treatment with vasodilators and diuretics may help in all patients. Patients with RCM should be maintained in sinus rhythm, because loss of the “atrial kick” is devastating. Transplantation is a possibility in some patients with better survival than controls. RCM is relentless, with 90% of patients dying within 10 years of diagnosis. Patients with hemochromatosis are treated with phlebotomy.

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**PERIPARTUM CARDIOMYOPATHY**

**Perspective**

Peripartum cardiomyopathy (PPCM) is uncommon and represents less than 1% of the cardiovascular problems associated with pregnancy. PPCM is a form of DCM with symptoms and signs of heart failure that appear initially during the last 3 months of pregnancy or the first 5 months postpartum. The diagnosis is made if there is no previous heart disease and no other cause for the heart failure.

**Etiology and Epidemiology**

The cause of PPCM is unknown. Risk factors include myocarditis, excessive use of tocolytics, preeclampsia, advanced maternal
age, multiparity, twins, and genetic predisposition. The incidence is estimated to be 1 case of PPCM per 13,000 to 15,000 live births.39

Clinical Features and Diagnostic Strategies

PPCM is clinically identical to DCM. Patients usually have symptoms of CHF but may also have chest pain, palpitations, or thromboembolism. Physical examination often reveals tachycardia, tachypnea, pulmonary rales, an enlarged heart, and an S3 heart sound.

The ECG may show left ventricular hypertrophy or non-specific ST-T wave changes. On echocardiography, all four chambers are enlarged with reduction in left ventricular systolic function.

Management and Disposition

Treatment of PPCM includes limitation of physical activity, beta-blockers, alteration of preload with nitrates and diuretics, increase in ventricular contractility, and afterload reduction.40 Angiotensin-converting enzyme inhibitors are teratogenic and should be avoided, if possible, in pregnancy. Hydralazine and labetalol are effective choices.

Mortality for PPCM in the United States is approximately 2%.39 Half of the survivors have complete or near-complete recovery of cardiac function within the first 6 months. Patients who do not recover completely show either continuous clinical deterioration or persistent left ventricular dysfunction. Subsequent pregnancies may be associated with a high risk of maternal mortality. In the ED, patients with signs of hemodynamic instability or failure to maintain oxygenation should be admitted for treatment and fetal monitoring.

TAKOTSUBO CARDIOMYOPATHY

Perspective

Takotsubo cardiomyopathy (TCM), also known as stress cardiomyopathy, broken heart syndrome, or tako-tsubo cardiomyopathy, was first reported from Japan in 1991.41 In Japanese, tako-tsubo means octopus trap. The term was used because the cardiac abnormality observed in this disease resembles that of the device used to catch octopi.42 There have been hundreds of cases reported in the medical literature since that time (Box 82-4). The pathophysiology of TCM is a sudden temporary myocardial weakening. The exact mechanism is unknown. Speculated causes include stress hormones, microvascular spasm, focal myocarditis, and cellular level muscle changes.

Clinical Features and Diagnostic Strategies

The clinical presentation is usually chest pain, although dyspnea occurs, especially on exertion. Almost 90% of cases involve women.43 There is uniformly a significant stressful incident that precedes the onset of symptoms. ECG is often consistent with an anterior MI. There are transient Q waves and ST elevation. Later, the ECG shows T wave inversion and a prolonged QT interval. Cardiac enzymes are elevated slightly and resolve to normal levels quickly. Coronary artery angiography shows no—or very little—disease. The diagnosis is made by left ventricular angiography or echocardiography that shows a ballooning of the apex during the acute phase of the disease. The involved area does not match a coronary artery anatomic distribution.

Management and Disposition

In the ED, TCM is not distinguishable from acute MI. Patients should be treated the same as any patient with acute MI. Treatment is supportive care. Beta-blockers and angiotensin-converting enzymes are the mainstay of therapy. Almost all patients show complete resolution of symptoms and reversal to normal of their left ventricular apex ballooning and contractile function.

ION CHANNELOPATHIES

Several uncommon dysrhythmic diseases are caused by mutations of genes for ionic channel proteins, which are cell membrane transport proteins for sodium and potassium. These include long QT syndrome, short QT syndrome, Brugada’s syndrome, and catecholaminergic polymorphic ventricular tachycardia.

SPECIFIC HEART MUSCLE DISEASES

Amyloidosis

Massive amyloid deposition results in an increased cardiac weight and the diastolic dysfunction of RCM. CHF occurs in most cases of cardiac amyloidosis. Treatment involves standard CHF and antidysrhythmic therapy, although the dysrhythmias in amyloid heart disease are often refractory to treatment. The prognosis is poor, with death often resulting from progressive heart failure within 1 year of symptom onset.31

Sarcoidosis

Cardiac granulomas occur in approximately 25% of cases of systemic sarcoidosis. Granulomas located in the septum cause severe conduction defects, those in the papillary muscles cause
mitral regurgitation, and those in the ventricular walls produce scarring and wall motion abnormalities. Complete heart block is the most common conduction block. Ventricular dysrhythmias are often refractory to therapy. Myocardial involvement in sarcoidosis is an indication for systemic corticosteroid therapy. Refractory cardiac failure and dysrhythmias are indications for heart transplantation.

**Connective Tissue Disorders and Disease of the Myocardium**

Myocarditis associated with various connective tissue diseases occurs more often than is recognized clinically. Cardiac abnormalities occur in RA, juvenile RA, mixed connective tissue disease, and primary Sjögren’s syndrome. SLE is the connective tissue disease most commonly associated with cardiac abnormalities. Cardiac involvement in SLE includes pericarditis, endocarditis, and myocarditis.

Primary myocardial involvement is a major complication of diffuse scleroderma and develops as scleroderma worsens. Estimates of the frequency of myocardial involvement in scleroderma vary widely. The clinical presentation includes CHF, angina, and dysrhythmias. Pericardial disease can also occur. Although prognosis is poor, azathioprine may be a beneficial adjunct to steroid therapy.45

**Sudden Death**

Approximately 25% of sudden deaths in patients younger than age 21 years can be attributed to disease of the myocardium. Cardiac causes include myocarditis, HCM, and anomalous coronary artery circulation. In patients with sudden death attributed to cardiac causes, prodromal symptoms are reported in more than half of the patients, most commonly chest pain (25%) in patients older than age 20 years and dizziness (16%) in patients younger than age 20 years. The distribution of sudden death causes by age is as follows:

- Age younger than 20 years—myocarditis 22% and HCM 22%
- Age 20 to 29 years—myocarditis 22% and HCM 13%
- Age 30 to 39 years—myocarditis 11% and HCM 2%

Coronary artery disease becomes the leading cardiac cause (58%) in sudden death in people ages 30 to 39 years. HCM is the cardiac disease most commonly found on postmortem diagnosis of athletes with sudden death. HCM and anomalous coronary arteries are seen more often in sports-related deaths.

*The references for this chapter can be found online by accessing the accompanying Expert Consult website.*
References

33. Dickinson MG, et al: Statin use was associated with reduced mortality in both ischemic and nonischemic cardiomyopathy and in patients with implantable defibrillators: Mortality data and mechanistic insights from the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT). *Am Heart J* 2007; 153:573.