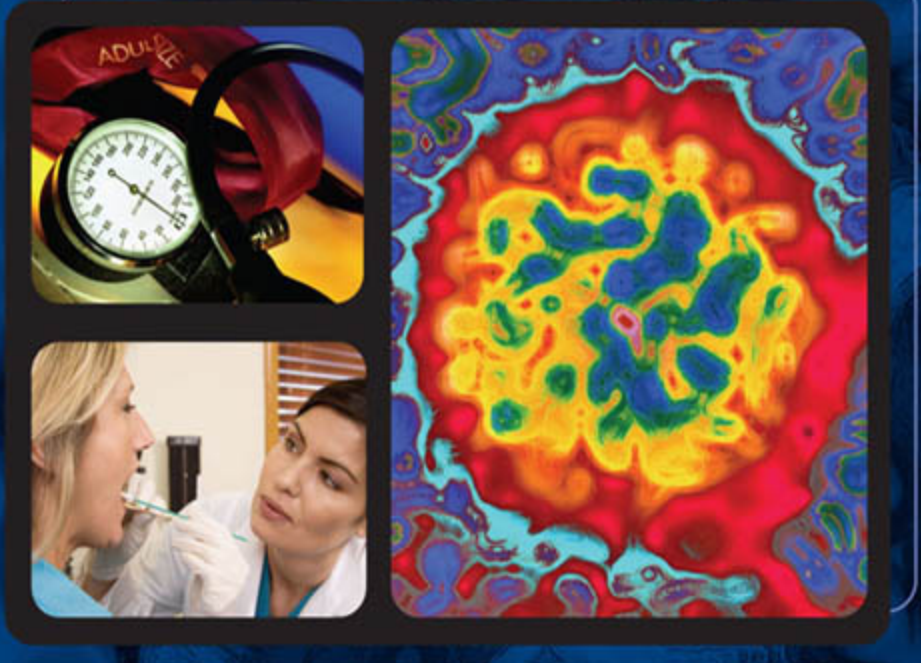
2008

CURRENT Medical Diagnosis & Treatment



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2008 CURRENT Medical Diagnosis & Treatment

FORTY-SEVENTH EDITION

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disseminated intravascular coagulation. These are distinguished from cardiogenic pulmonary edema by the clinical setting, the history, and the physical examination. Conversely, in most patients with cardiogenic pulmonary edema, an underlying cardiac abnormality can usually be detected clinically or by the ECG, chest radiograph, or echocardiogram.

The chest radiograph reveals signs of pulmonary vascular redistribution, blurriness of vascular outlines, increased interstitial markings, and, characteristically, the butterfly pattern of distribution of alveolar edema. The heart may be enlarged or normal in size depending on whether heart failure was previously present. Assessment of cardiac function by echocardiography is important, since a substantial proportion of patients has normal EFs with elevated atrial pressures due to diastolic dysfunction. In cardiogenic pulmonary edema, the PCWP is invariably elevated, usually over 25 mm Hg. In noncardiogenic pulmonary edema, the wedge pressure may be normal or even low.

Treatment

In full-blown pulmonary edema, the patient should be placed in a sitting position with legs dangling over the side of the bed; this facilitates respiration and reduces venous return. Oxygen is delivered by mask to obtain an arterial Po_2 greater than 60 mm Hg. Noninvasive pressure support ventilation may improve oxygenation and prevent severe CO_2 retention while pharmacologic interventions take effect. However, if respiratory distress remains severe, endotracheal intubation and mechanical ventilation may be necessary.

Morphine is highly effective in pulmonary edema and may be helpful in less severe decompensations when the patient is uncomfortable. The initial dosage is 2–8 mg intravenously (subcutaneous administration is effective in milder cases) and may be repeated after 2–4 hours. Morphine increases venous capacitance, lowering LA pressure, and relieves anxiety, which can reduce the efficiency of ventilation. However, morphine may lead to CO_2 retention by reducing the ventilatory drive. It should be avoided in patients with opioid-induced pulmonary edema, who may improve with opioid-antagonists, and in those with neurogenic pulmonary edema.

Intravenous diuretic therapy (furosemide, 40 mg, or bumetanide, 1 mg—or higher doses if the patient has been receiving long-term diuretic therapy) is usually indicated even if the patient has not exhibited prior fluid retention. These agents produce venodilation prior to the onset of diuresis.

Nitrate therapy accelerates clinical improvement by reducing both BP and LV filling pressures. Sublingual nitroglycerin or isosorbide dinitrate, topical nitroglycerin, or intravenous nitrates will ameliorate dyspnea rapidly prior to the onset of diuresis, and these agents are particularly valuable in patients with accompanying hypertension. Intravenous nesiritide (recombinant BNP), when given as a bolus followed by an infusion, improves dyspnea more rapidly than intravenous nitroglycerin, though this may reflect the cautious way in which nitroglycerin is up-titrated by many practitioners. This agent, as well as nitrates, may precipitate hypotension, especially since these agents are used in combination with multiple drugs that lower BP. In patients with low-output states—particularly when hypotension is present—positive inotropic agents are indicated. These approaches to treatment have been discussed previously.

Bronchospasm may occur in response to pulmonary edema and may itself exacerbate hypoxemia and dyspnea. Treatment with inhaled β-adrenergic agonists or intravenous aminophylline may be helpful, but both may also provoke tachycardia and supraventricular arrhythmias.

In most cases, pulmonary edema responds rapidly to therapy. When the patient has improved, the cause or precipitating factor should be ascertained. In patients without prior heart failure, evaluation should include echocardiography and in many cases cardiac catheterization and coronary angiography. Patients with acute decompensation of chronic heart failure should be treated to achieve a euvolemic state and have their medical regimen optimized. Generally, an oral diuretic and an ACE inhibitor should be initiated, with efficacy and tolerability confirmed prior to discharge. In selected patients, early but careful initiation of β-blockers in low doses should be considered.

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MYOCARDITIS & THE CARDIOMYOPATHIES

INFECTIOUS MYOCARDITIS

ESSENTIALS OF DIAGNOSIS

- Often follows an upper respiratory infection.
- May present with chest pain (pleuritic or nonspecific) or signs of heart failure.
- ECG may show sinus tachycardia, other arrhythmias, nonspecific repolarization changes, and intraventricular conduction abnormalities.
- Echocardiogram documents cardiomegaly and contractile dysfunction.
- Myocardial biopsy, though not sensitive, may reveal a characteristic inflammatory pattern.

General Considerations

Cardiac dysfunction due to primary myocarditis is presumed to be caused by either an acute viral infection or a postviral immune response. Secondary myocarditis is the result of inflammation caused by nonviral pathogens, drugs, chemicals, physical agents, or inflammatory diseases such as systemic lupus erythematosus. The list of infectious causes of myocarditis is extensive and includes viruses with DNA and RNA cores. The coxsackie virus is the predominant agent, but many others have been implicated. Rickettsial myocarditis occurs with scrub typhus, Rocky Mountain spotted fever, and Q fever. Diphtheritic myocarditis is caused by the exotoxin and is often manifested by conduction abnormalities as well as heart failure.

Chagas' disease, caused by the insect-borne protozoan *Trypanosoma cruzi*, is a common form of myocarditis in Central and South America; the major clinical manifestations appear after a latent period of more than a decade. At this stage, patients present with cardiomyopathy, conduction disturbances, and sudden death. Associated gastrointestinal involvement (megaesophagus and megacolon) is the rule. Toxoplasmosis causes myocarditis that is usually asymptomatic but can lead to heart failure. Among parasitic infections, trichinosis is the most common cause of cardiac involvement. The potential for the HIV virus to cause myocarditis is now well recognized, though the prevalence of this complication is not known and it appears related to the level of viral load and CD4 count. In addition, other infectious causes of myocarditis are more common in patients with AIDS. A complete list of infectious causes of myocarditis is shown in Table 10–11.

Table 10–11. Major causes of infectious myocarditis.

Viral	Adenovirus, arbovirus (dengue fever, yellow fever), arenavirus (Lassa fever), coxsackie virus, cytomegalovirus, echovirus, encephalomyocarditis virus, Epstein–Barr virus, hepatitis B, herpesvirus, HIV-1, influenza virus, mumps virus, poliomyelitis virus, rabies, respiratory syncytial virus, rubella and rubeola virus, vaccinia virus, varicella virus, variola virus
Bacterial	Brucellosis, clostridia, diphtheria, *Francisella* (tularemia), gonococcus, *Haemophilus*, *Legionella*, meningococcus, *Mycobacterium*, *Mycoplasma*, *Pneumococcus*, psittacosis, *Salmonella*, *Staphylococcus*, *Streptococcus*, Whipple's disease
Fungal	*Actinomyces, Aspergillus, Blastomyces, Candida, Cryptococcus, Histoplasma, Nocardia, Sporothrix*
Rickettsial	Rocky Mountain spotted fever, Q fever, scrub typhus, typhus
Spirochetal	*Borrelia* (Lyme disease and relapsing fever), *Leptospira*, syphilis
Helminthic	*Cysticercus, Echinococcus, Schistosoma, Toxocara* (visceral larva migrans), *Trichinella*
Protozoal	*Entamoeba, Leishmania, Tryponosoma* (Chagas' disease), toxoplasmosis

Modified, with permission, from Pisani B et al. Inflammatory myocardial disease and cardiomyopathies. Am J Med. 1997 May;102(5):459–69.

Giant cell myocarditis is a rare idiopathic disorder characterized by giant cell and lymphocyte infiltration of the heart muscle. Patients usually die of ventricular arrhythmias or heart failure but occasionally respond to immunosuppressive therapy or early transplantation.

Clinical Findings

A. Symptoms and Signs

Patients may present several days to a few weeks after the onset of an acute febrile illness or a respiratory infection or with heart failure without antecedent symptoms. The onset of heart failure may be gradual or may be abrupt and fulminant. Emboli may occur due to the procoagulant effect of cytokines combined with decreased myocardial contractility and blood pooling. Pleural-pericardial chest pain is common. Examination reveals tachycardia, gallop rhythm, and other evidence of heart failure or conduction defect. Many acute infections are subclinical, though they may present later as idiopathic cardiomyopathy or with ventricular arrhythmias. At times, the presentation may mimic an acute myocardial infarction with ST changes, positive cardiac markers, and regional wall motion abnormalities despite normal coronaries. Microaneurysms may also occur and may be associated with serious ventricular arrhythmias. Patients may present in a variety of ways with fulminant, subacute, or chronic myocarditis.

B. ECG and Chest Radiography

Nonspecific ST–T changes and conduction disturbances are common. Ventricular ectopy may be the initial and only clinical finding. Chest radiograph is nonspecific, but cardiomegaly is frequent, though not universal. Evidence for pulmonary venous hypertension is common and frank pulmonary edema may be present.

C. Diagnostic Studies

There is no specific laboratory study that is consistently present, though the white blood cell count is usually elevated and the sedimentation rate may increase. Troponin I levels are elevated in about one-third of patients, but CK-MB is elevated in only 10%. Echocardiography provides the most convenient way of evaluating cardiac function and can exclude many other processes. Gallium-67 scintigraphy may reveal increased cardiac uptake in acute or subacute myocarditis, but it is not very sensitive. MRI with gadolinium enhancement reveals spotty areas of injury throughout the myocardium. Paired serum viral titers and serologic tests for other agents may indicate the cause.

D. Endomyocardial Biopsy

Pathologic examinations may reveal a lymphocytic inflammatory response with necrosis, but the patchy distribution of abnormalities makes this relatively insensitive. By biopsy, the diagnosis of myocarditis has been established by the 1986 "Dallas" criteria. The diagnosis is dependent on describing the severity of an inflammatory infiltrate with necrosis and degeneration of adjacent myocytes. The

type of infiltrate is dependent on the causal agent; usually this is lymphocytic in viral disease, but it may be neutrophilic, eosinophilic, giant cell, granulomatous, or mixed.

Treatment & Prognosis

Patients with fulminant myocarditis may present with acute cardiogenic shock. Their ventricles are usually not dilated, but thickened (possibly due to myoedema). There is a high death rate, but if the patients recover, they are usually left with no residual cardiomyopathy. Patients who present with subacute disease have a dilated cardiomyopathy and generally make an incomplete recovery. Those who present with chronic disease tend to have only mild dilation of the LV and eventually present with a more restrictive cardiomyopathy.

Specific antimicrobial therapy is indicated when an infecting agent is identified. All patients should receive standard heart failure therapy and have arrhythmias suppressed. Exercise should be limited during the recovery phase. Some believe digoxin should be avoided. Immunosuppressive therapy with corticosteroids and intravenous immunoglobulins may improve the outcome when the process is acute (< 6 months) and if the biopsy suggests ongoing inflammation. However, controlled trials have not been positive, so the value of routine myocardial biopsies in patients presenting with an acute myocarditic picture is uncertain; immunosuppressive therapy without histologic confirmation is clearly unwise, and there are few data to support its use. Patients with fulminant myocarditis require aggressive short-term support including an intra-aortic balloon pump or an LV assist device. Ongoing studies are addressing whether patients with giant cell myocarditis may be responsive to immunosuppressive agents, as a special case. Overall, if improvement does not occur, many patients may be eventual candidates for cardiac transplantation.

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Brady WJ et al. Myocarditis: emergency department recognition and management. Emerg Med Clin North Am. 2004 Nov;22 (4):865–85. [PMID: 15474774]

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DRUG-INDUCED & TOXIC MYOCARDITIS

A variety of medications, illicit drugs, and toxic substances can produce acute or chronic myocardial injury; the clinical presentation varies widely. Doxorubicin and other cytotoxic agents, emetine, and catecholamines (especially with pheochromocytoma) can produce a pathologic picture of inflammation and necrosis together with clinical heart failure and arrhythmias; toxicity of the first two is dose related. The phenothiazines, lithium, chloroquine, disopyramide, antimony-containing compounds, and arsenicals can also cause ECG changes, arrhythmias, or heart failure. Hypersensitivity reactions to sulfonamides, penicillins, and aminosalicylic acid as well as other drugs can result in cardiac dysfunction. Radiation can cause an acute inflammatory reaction as well as a chronic fibrosis of heart muscle, usually in conjunction with pericarditis.

The incidence of cocaine cardiotoxicity has increased markedly. Cocaine can cause coronary artery spasm, myocardial infarction, arrhythmias, and myocarditis. Because many of these processes are believed to be mediated by cocaine's inhibitory effect on norepinephrine reuptake by sympathetic nerves, β-blockers have been used therapeutically. In documented coronary spasm, calcium channel blockers and nitrates may be effective.

Floyd JD et al. Cardiotoxicity of cancer therapy. J Clin Oncol. 2005 Oct 20;23(30):7685–96. [PMID: 16234530]

Gharib MI et al. Chemotherapy-induced cardiotoxicity: current practice and prospects of prophylaxis. Eur J Heart Fail. 2002 Jun;4(3):235–42. [PMID: 12034146]

Yeh ET et al. Cardiovascular complications of cancer therapy: diagnosis, pathogenesis, and management. Circulation. 2004 Jun 29;109(25):3122–31. [PMID: 15226229]

DILATED CARDIOMYOPATHY

ESSENTIALS OF DIAGNOSIS

- Symptoms and signs of heart failure.
- Examination often reveals cardiomegaly, elevated JVP, S_3, S_4, mitral and tricuspid regurgitation, low systemic BP and pulse width, occasionally pulsus alternans.
- ECG may show low QRS voltage, nonspecific repolarization abnormalities, intraventricular conduction abnormalities.
- Radiograph shows cardiomegaly.
- Echocardiogram confirms LV dilation, thinning, and global dysfunction.

General Considerations

The cardiomyopathies are a heterogeneous group of entities affecting the myocardium primarily and not associated with the major causes of cardiac disease, ie, ischemic heart disease, hypertension, pericardial disease, valvular disease, or congenital defects. Recently, two additional entities have been added to the list: a transient cardiomyopathy due to high catecholamine discharge (Tako-Tsubo cardiomyopathy) and an embryologic defect resulting in massive trabeculation in the LV (ventricular noncompaction). Although some have specific causes, many cases are idiopathic. The classification of cardiomyopathies is based on features of presentation and pathophysiology (Table 10–12).

Dilated cardiomyopathies cause about 25% of all cases of CHF. It usually presents with symptoms and signs of CHF (most commonly dyspnea). Occasionally, symptomatic ventricular arrhythmias are the presenting event. LV dilation and systolic dysfunction (EF < 50%) are essential for diagnosis. Dilated cardiomyopathy occurs more often in blacks than whites and in men more than women. A growing number of cardiomyopathies due to genetic

Table 10–12. Classification of the cardiomyopathies.

	Dilated	Hypertrophic	Restrictive
Frequent causes	Idiopathic, alcoholic, major catecholamine discharge, myocarditis, postpartum, doxorubicin, endocrinopathies, genetic diseases	Hereditary syndrome, possibly chronic hypertension	Amyloidosis, post-radiation, post-open heart surgery, diabetes, endomyocardial fibrosis
Symptoms	Left or biventricular congestive heart failure	Dyspnea, chest pain, syncope	Dyspnea, fatigue, right-sided congestive heart failure
Physical examination	Cardiomegaly, S_3, elevated jugular venous pressure, rales	Sustained point of maximal impulse, S_4, variable systolic murmur, bisferiens carotid pulse	Elevated jugular venous pressure, Kussmaul's sign
Electrocardiogram	ST–T changes, conduction abnormalities, ventricular ectopy	Left ventricular hypertrophy, exaggerated septal Q waves	ST–T changes, conduction abnormalities, low voltage
Chest radiograph	Enlarged heart, pulmonary congestion	Mild cardiomegaly	Mild to moderate cardiomegaly
Echocardiogram, nuclear studies, MRI	Left ventricular dilation and dysfunction	Left ventricular hypertrophy, asymmetric septal hypertrophy, small left ventricular size, normal or supranormal function, systolic anterior mitral motion, diastolic dysfunction	Small or normal left ventricular size, normal or mildly reduced left ventricular function
Cardiac catheterization	Left ventricular dilation and dysfunction, high diastolic pressures, low cardiac output	Small, hypercontractile left ventricle, dynamic outflow gradient, diastolic dysfunction	High diastolic pressure, "square root" sign, normal or mildly reduced left ventricular function

abnormalities are being recognized, and these may represent up to 25–30% of cases. Often no cause can be identified, but chronic alcohol abuse and unrecognized myocarditis are probably frequent causes. Chronic tachycardia may also precipitate a dilated cardiomyopathy. Amyloidosis, sarcoidosis, hemochromatosis, and diabetes may rarely present as dilated cardiomyopathies, as well as the more classic restrictive picture. The RV may be primarily involved in arrhythmogenic RV dysplasia, an unusual cardiomyopathy with displacement of myocardial cells by adipose tissue, or in Uhl's disease, in which there is extreme thinning of the RV walls. Intraventricular thrombus is not uncommon. Histologically, the picture is one of extensive fibrosis unless a specific diagnosis is established. Myocardial biopsy is rarely useful in establishing the diagnosis, though occasionally the underlying cause (eg, sarcoidosis, hemochromatosis) can be discerned.

Clinical Findings

A. Symptoms and Signs

In most patients, symptoms of heart failure develop gradually. Cardiomyopathy may be recognized because of asymptomatic cardiomegaly or ECG abnormalities, including arrhythmias. The initial presentation may be severe left or biventricular failure. The physical examination reveals rales, an elevated JVP, cardiomegaly, S_3 gallop rhythm, often the murmurs of functional mitral or tricuspid regurgitation, peripheral edema, or ascites. In severe CHF, Cheyne-Stokes breathing, pulsus alternans, pallor, and cyanosis may be present.

B. ECG and Chest Radiography

The major findings are listed in Table 10–12. Sinus tachycardia is common. Other common abnormalities include left bundle branch block and ventricular or atrial arrhythmias. The chest radiograph reveals cardiomegaly, evidence for left and/or right heart failure, and pleural effusions (right > left).

C. Diagnostic Studies

An echocardiogram is indicated to exclude unsuspected valvular or other lesions and confirm the presence of dilated cardiomyopathy and reduced systolic function (as opposed to diastolic heart failure). Mitral Doppler inflow patterns also help in the diagnosis of associated diastolic dysfunction. Color flow Doppler can reveal tricuspid or mitral regurgitation, and continuous Doppler can help define PA pressures. Exercise or pharmacologic stress myocardial perfusion imaging may suggest the possibility of underlying coronary disease. Radionuclide ventriculography provides a noninvasive measure of the EF and both RV and LV wall motion. Cardiac MRI is particularly helpful in infiltrative processes, such as sarcoidosis or hemochromatosis, and is the diagnostic study of choice for RV dysplasia. MRI can also help define an ischemic etiology by noting gadolinium enhancement consistent with myocardial scar. Cardiac catheterization is seldom of specific value unless myocardial ischemia or LV aneurysm is suspected. The serum ferritin is an adequate screening study for hemochromatosis. The erythrocyte sedimentation rate may be low due to liver congestion. The serum level of BNP or pro-BNP can be used to help quantitate the severity of CHF.

Treatment

Standard therapy for heart failure should include ACE inhibitor, β-blockers, diuretics, and an aldosterone antagonist. Digoxin is a second-line drug but remains favored as an adjunct by some clinicians. Calcium channel blockers should generally be avoided. Sodium restriction is helpful, especially in acute cardiomyopathy. When atrial fibrillation is present, heart rate control is important if sinus rhythm cannot be established or maintained. Many patients may now be candidates for cardiac synchronization therapy with biventricular pacing and an implantable defibrillator. Few cases of cardiomyopathy are amenable to specific therapy for the underlying cause. Alcohol use should be discontinued. There is often marked recovery of cardiac function following a period of abstinence in alcoholic cardiomyopathy. Endocrine causes (thyroid dysfunction, acromegaly, and pheochromocytoma) should be treated. Immunosuppressive therapy is not indicated in chronic dilated cardiomyopathy. The management of CHF is outlined in the section on heart failure.

Prognosis

The prognosis of dilated cardiomyopathy without clinical heart failure is variable, with some patients remaining stable, some deteriorating gradually, and others declining rapidly. Once heart failure is manifest, the natural history is similar to that of other causes of heart failure, with an annual mortality around 11–13%. Arterial and pulmonary emboli are more common in dilated cardiomyopathy than in ischemic cardiomyopathy. Suitable candidates may benefit from long-term anticoagulation, and all patients with atrial fibrillation should be so treated. Some patients may be candidates for cardiac transplantation.

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Burkett EL et al. Clinical and genetic issues in familial dilated cardiomyopathy. J Am Coll Cardiol. 2005 Apr 5;45(7):969–81. [PMID: 15808750]

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TAKOTSUBO CARDIOMYOPATHY

ESSENTIALS OF DIAGNOSIS

- Occurs after an episode that results in major catecholamine discharge.
- Acute chest pain or shortness of breath.
- Predominately affects postmenopausal women.
- Presents as an acute anterior myocardial infarction, but coronaries normal at cardiac catheterization.
- ECG often with deep anterior T wave inversion.
- Imaging reveals apical left ventricular ballooning due to anteroapical stunning of the myocardium.

General Considerations

LV apical ballooning can follow a high catecholamine stress. The resulting shape of the LV suggests a rounded ampulla form similar to an octopus pot (takotsubo pot). The acute myocardial injury that occurs is more common in postmenopausal women. It has been described following some stressful event, such as hypoglycemic, lightning strikes, earthquakes, postventricular tachycardia, during alcohol withdrawal, following surgery, during hyperthyroidism, and following emotional stress.

Clinical Findings

A. Symptoms and Signs

The symptoms are similar to any acute coronary syndrome. Typical angina and dyspnea is usually present. Syncope is rare.

B. ECG and Chest Radiography

The ECG reveals ST segment elevation consistent with an acute myocardial infarction. The chest radiograph is either normal or reveals pulmonary congestion.

C. Diagnostic Studies

The echocardiogram reveals LV apical dyskinesia. The urgent cardiac catheterization reveals the LV apical ballooning in association with normal coronaries.

Treatment

Immediate therapy is similar to any acute myocardial infarction. Initiation of long-term therapy depends on whether LV dysfunction persists. Most patients receive aspirin, β-blockers, and ACE-inhibitors until the LV fully recovers.

Prognosis

Prognosis is good unless there is a serious complication (such as mitral regurgitation, ventricular rupture, ventricular tachycardia). Recovery is expected in most cases after a period of weeks to months. At times, the LV function recovers in days.

Valente AM et al. Unusual cardiomyopathies: ventricular noncompaction and takotsubo cardiomyopathy. Rev Cardiovasc Med. 2006 Summer;7(3):111–8. [PMID: 17088856]

HYPERTROPHIC CARDIOMYOPATHY

ESSENTIALS OF DIAGNOSIS

- May present with dyspnea, chest pain, syncope.

- Though LV outflow gradient is classic, symptoms are primarily related to diastolic dysfunction.
- Examination shows sustained apical impulse, S_4, systolic ejection murmur that increases with Valsalva.
- ECG shows LVH, occasionally septal Q waves in the absence of infarction.
- Echocardiogram shows septal hypertrophy, which is usually asymmetric, and enhanced contractility. Systolic anterior motion of the anterior mitral valve is present if there is outflow tract obstruction.

General Considerations

Myocardial hypertrophy unrelated to any pressure or volume overload reduces LV systolic stress, increases the EF, and can result in an "empty ventricle" at end-systole. The interventricular septum may be disproportionately involved (asymmetric septal hypertrophy), but in some cases the hypertrophy is localized to mid ventricle or to the apex. The LV outflow tract is often narrowed during systole between the bulging septum and an anteriorly displaced anterior mitral valve leaflet, causing a dynamic obstruction. The obstruction is worsened by factors that increase myocardial contractility (sympathetic stimulation, digoxin, postextrasystolic beat) or that decrease LV filling (Valsalva maneuver, peripheral vasodilators). The amount of obstruction is preload and afterload dependent and can vary from day to day. The consequence of the hypertrophy is elevated diastolic pressures rather than systolic dysfunction. Rarely, systolic dysfunction develops late in the disease. The LV is usually more involved than the RV and the atria are frequently significantly enlarged. It has been increasingly appreciated that hypertrophic obstructive cardiomyopathy (HOCM) is inherited as an autosomal dominant trait with variable penetrance and is caused by mutations of a number of genes, most of which code for myosin heavy chains or proteins regulating calcium handling. The prognosis is related to the specific gene mutation. These patients usually present in early adulthood. Elite athletes may demonstrate considerable hypertrophy that can be confused with HOCM, but generally diastolic dysfunction is not present. The apical variety is particularly common in those of Asian descent. A hypertrophic cardiomyopathy in the elderly (usually in association with hypertension) has also been defined as a distinct entity. Mitral annular calcification is often present.

Clinical Findings

A. Symptoms and Signs

The most frequent symptoms are dyspnea and chest pain (Table 10–12). Syncope is also common and is typically postexertional, when diastolic filling diminishes and outflow obstruction increases. Arrhythmias are an important problem. Atrial fibrillation is a long-term consequence of chronically elevated LA pressures and is a poor prognostic sign. Ventricular arrhythmias are also common, and sudden death may occur, often in athletes after extraordinary exertion.

Features on physical examination are a bisferiens carotid pulse, triple apical impulse (due to the prominent atrial filling wave and early and late systolic impulses), and a loud S_4. The JVP may reveal a prominent a wave due to reduced RV compliance. In cases with outflow obstruction, a loud systolic murmur is present along the left sternal border that increases with upright posture or Valsalva's maneuver and decreases with squatting. These maneuvers help differentiate the murmur of HOCM from that of aortic stenosis. Mitral regurgitation is frequently present as well.

B. ECG and Chest Radiography

LVH is nearly universal in symptomatic patients, though entirely normal ECGs are present in up to 25%, usually in those with localized hypertrophy. Exaggerated septal Q waves inferolaterally may suggest myocardial infarction. The chest radiograph is often unimpressive. Unlike aortic stenosis, the ascending aorta is not dilated.

C. Diagnostic Studies

The echocardiogram is diagnostic, revealing asymmetric LVH, systolic anterior motion of the mitral valve, early closing followed by reopening of the aortic valve, a small and hypercontractile LV, and delayed relaxation and filling of the LV during diastole. The septum is usually 1.3–1.5 times the thickness of the posterior wall. Septal motion tends to be reduced. Doppler ultrasound reveals turbulent flow and a dynamic gradient in the LV outflow tract and, commonly, mitral regurgitation. Abnormalities in the diastolic filling pattern are present in 80% of patients. Myocardial perfusion imaging may suggest septal ischemia in the presence of normal coronary arteries. Cardiac MRI confirms the hypertrophy and contrast enhancement frequently reveals evidence for scar at the junction of the RV attachment to the septum. Cardiac catheterization confirms the diagnosis and assesses the presence of CAD. Frequently, coronary arterial bridging (squeezing in systole) occurs, especially of the septal arteries. Alcohol in small doses can be injected into these septal perforators to create a septal infarction that reduces the outflow tract gradient.

Treatment

β-Blockers should be the initial drug in symptomatic individuals, especially when dynamic outflow obstruction is noted on the echocardiogram. The resulting slower heart rates assist with diastolic filling of the stiff LV. Dyspnea, angina, and arrhythmias respond in about 50% of patients. Calcium channel blockers, especially verapamil, have also been effective in symptomatic patients. Their effect is due primarily to improved diastolic function, but their vasodilating actions can also increase outflow obstruction and cause hypotension. Disopyramide (Norpace) is also used because of its negative inotropic effects; it is usually used in addition to the other therapies. Diuretics are frequently necessary due to the high diastolic pressure and PCWP. Patients do best in sinus rhythm, and atrial fibrillation should be aggressively treated with antiarrhythmics. Dual-chamber pacing may prevent the progression of hypertrophy and obstruction. Nonsurgical septal ablation has been performed by injection of alcohol into septal branches of the left coronary artery with good results in small series of patients. Patients with malignant ventricular arrhythmias and unexplained syncope in the

presence of a positive family history for sudden death are probably best managed with an implantable defibrillator. Excision of part of the outflow myocardial septum (myotomy–myomectomy) by surgeons experienced with the procedure has been successful in patients with severe symptoms. Some experts advocate mitral valve replacement, as this results in resolution of the gradient as well, and prevents associated mitral regurgitation.

Prognosis

The natural history of HOCM is highly variable. Several specific mutations are associated with a higher incidence of early malignant arrhythmias and sudden death, and definition of the genetic abnormality provides the best estimate of prognosis. Some patients remain asymptomatic for many years or for life. Sudden death, especially during exercise, may be the initial event. The highest risk patients are those with a family history of sudden death, those with marked hypertrophy, and those that do not increase their systemic blood pressure with exercise. HOCM is the pathologic feature most frequently associated with sudden death in athletes. Pregnancy is generally well tolerated. Endocarditis prophylaxis is indicated. A final stage may be a transition into dilated cardiomyopathy in 5–10% of patients.

Harris KM et al. Prevalence, clinical profile and significance of LV remodeling in the end-stage phase of hypertrophic cardiomyopathy. Circulation. 2006 Jul 18;114(3):216–25. [PMID: 16831987]

Ho CY et al. A contemporary approach to hypertrophic cardiomyopathy. Circulation. 2006 Jun 20;113(24):e858–62. [PMID: 16785342]

Sherrod MV. Pathophysiology and treatment of hypertrophic cardiomyopathy. Prog Cardiovasc Dis. 2006 Sep–Oct;49(2):123–51. [PMID: 17046437]

RESTRICTIVE CARDIOMYOPATHY

ESSENTIALS OF DIAGNOSIS

- Right heart failure tends to dominate over left heart failure.
- Pulmonary hypertension present.
- Amyloidosis is the most common cause.
- Echocardiography is key to diagnosis.
- MRI and cardiac catheterization are helpful. Myocardial biopsy can confirm.

General Considerations

Restrictive cardiomyopathy is characterized by impaired diastolic filling with preserved contractile function. The diastolic filling pattern in restrictive cardiomyopathy reveals that early diastolic filling is accentuated (rapid E wave on the echocardiogram/Doppler). The LV systolic function may be mildly depressed and the atria are generally enlarged; if present, hypertrophy of the interatrial septum is a helpful additional finding diagnostically. The condition is relatively uncommon, with the most frequent causes being amyloidosis. In Africa, endomyocardial fibrosis, a specific entity in which there is severe fibrosis of the endocardium, often with eosinophilia (Löffler's syndrome), is seen. Other causes of restrictive cardiomyopathy are infiltrative cardiomyopathies (eg, hemochromatosis, carcinoid syndrome) and connective tissue diseases (eg, scleroderma).

Amyloidosis results from deposition of various proteins within the myocardium. Primary amyloidosis is caused by deposition of immunoglobulin light chains (AL) by monoclonal plasma cells, often as a consequence of multiple myeloma. The heart may be the only organ involved at times. Systemic amyloidosis is due to production of AA light chains. Familial amyloidosis results from production of a carrier protein called transthyretin. Systemic amyloidosis may affect any organ but is particularly associated with significant pulmonary and renal involvement and with a peripheral neuropathy (that often results in orthostatic hypotension).

Clinical Findings

A. Symptoms and Signs

Restrictive cardiomyopathy must be distinguished from constrictive pericarditis (Table 10–12). The key feature is that ventricular interaction is accentuated with respiration in constrictive pericarditis, and that interaction is absent in restrictive cardiomyopathy. Pulmonary pressure is invariably elevated in restrictive cardiomyopathy and is normal in uncomplicated constrictive pericarditis.

B. Diagnostic Studies

Conduction disturbances are frequently present. Low voltage on the ECG combined with ventricular hypertrophy revealed by echocardiography are suggestive. Cardiac MRI presents a distinctive pattern in amyloidosis and is a useful screening test. The echocardiogram reveals a small thickened LV with bright myocardium, rapid early diastolic filling revealed by Doppler, and biatrial enlargement. Atrial septal thickening may be evident. Rectal, abdominal fat, or gingival biopsies can confirm systemic involvement, but myocardial involvement may still be present if these are negative, and requires biopsy for confirmation. Demonstration of tissue infiltration on biopsy specimens using special stains followed by immunohistochemical studies and genetic testing is essential to define which specific protein is involved.

Treatment

Unfortunately, little useful therapy is available for either the causative conditions or the restrictive cardiomyopathy itself. Diuretics can help, but excessive diuresis can produce worsening symptoms. As with most patients with severe right heart failure, loop diuretics, thiazides, and aldosterone antagonists are all useful. Digoxin may precipitate arrhythmias and generally should not be used. β-Blockers help slow heart rates and improve filling. Corticosteroids may be helpful in sarcoidosis but relieve conduction abnormalities more often than heart failure. In amyloidosis, the therapeutic strategy depends on the characterization of the type of

amyloid protein and extent of disease and may include chemotherapy, stem cell transplantation, and liver transplantation. Cardiac transplantation is a potential option in patients with primary cardiac amyloidosis.

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ACUTE RHEUMATIC FEVER & RHEUMATIC HEART DISEASE

ESSENTIALS OF DIAGNOSIS

- Uncommon in the United States (approximately 2 cases/100,000 population); more common (100 cases/100,000 population) in developing countries.
- Peak incidence ages 5–15 years.
- Diagnosis based on Jones criteria and confirmation of streptococcal infection.
- May involve mitral and other valves acutely, rarely leading to heart failure.

General Considerations

Rheumatic fever is a systemic immune process that is a sequela to β-hemolytic streptococcal infection of the pharynx. Pyodermic infections are not associated with rheumatic fever. Signs of rheumatic fever usually commence 2–3 weeks after infection but may appear as early as 1 week or as late as 5 weeks. In recent years, the disease has become quite uncommon in the United States, except in immigrants; however, there have been reports of new outbreaks in several regions of the United States. The peak incidence is between ages 5 and 15 years; rheumatic fever is rare before age 4 years or after age 40 years. Rheumatic carditis and valvulitis may be self-limited or may lead to slowly progressive valvular deformity. The characteristic lesion is a perivascular granulomatous reaction with vasculitis. The mitral valve is attacked in 75–80% of cases, the aortic valve in 30% (but rarely as the sole valve), and the tricuspid and pulmonary valves in under 5% of cases.

Clinical Findings

The diagnostic criteria first described by Jones were updated in 1992. The presence of two major criteria—or one major and two minor criteria—establishes the diagnosis.

A. Major Criteria

1. Carditis—Carditis is most likely to be evident in children and adolescents. Any of the following suggests the presence of carditis: (1) pericarditis; (2) cardiomegaly, detected by physical signs, radiography, or echocardiography; (3) CHF, right- or left-sided—the former perhaps more prominent in children, with painful liver engorgement due to tricuspid regurgitation; and (4) mitral or aortic regurgitation murmurs, indicative of dilation of a valve ring with or without associated valvulitis. The Carey–Coombs short mid-diastolic mitral murmur may be present.

In the absence of any of the above definitive signs, the diagnosis of carditis depends on the following less specific abnormalities: (1) ECG changes, including changing contour of P waves or inversion of T waves; (2) changing quality of heart sounds; and (3) sinus tachycardia, arrhythmia, or ectopic beats.

2. Erythema marginatum and subcutaneous nodules—Erythema marginatum begins as rapidly enlarging macules that assume the shape of rings or crescents with clear centers. They may be raised, confluent, and either transient or persistent.

Subcutaneous nodules are uncommon except in children. They are small (≤ 2 cm in diameter), firm, and nontender and are attached to fascia or tendon sheaths over bony prominences. They persist for days or weeks, are recurrent, and are indistinguishable from rheumatoid nodules.

3. Sydenham's chorea—Sydenham's chorea—involuntary choreoathetoid movements primarily of the face, tongue, and upper extremities—may be the sole manifestation; only 50% of cases have other overt signs of rheumatic fever. Girls are more frequently affected, and occurrence in adults is rare. This is the least common (3% of cases) but most diagnostic of the manifestations of rheumatic fever.

4. Polyarthritis—This is a migratory polyarthritis that involves the large joints sequentially. In adults, only a single joint may be affected. The arthritis lasts 1–5 weeks and subsides without residual deformity. Prompt response of arthritis to therapeutic doses of salicylates or nonsteroidal agents is characteristic.

B. Minor Criteria

These include fever, polyarthralgias, reversible prolongation of the PR interval, and an elevated erythrocyte sedimentation rate or CRP. Supporting evidence includes positive throat culture or rapid streptococcal antigen test and elevated or rising streptococcal antibody titer.

C. Laboratory Findings

There is nonspecific evidence of inflammatory disease, as shown by a rapid sedimentation rate. High or increasing titers of antistreptococcal antibodies (antistreptolysin O and anti-DNase B) are used to confirm recent infection; 10% of cases lack this serologic evidence.

Differential Diagnosis

Rheumatic fever may be confused with the following: rheumatoid arthritis, osteomyelitis, endocarditis, chronic meningococcemia, systemic lupus erythematosus, Lyme disease, sickle cell anemia, "surgical abdomen," and many other diseases.

Complications

CHF occurs in severe cases. In the longer term, the development of rheumatic heart disease is the major problem. Other complications include arrhythmias, pericarditis with effusion, and rheumatic pneumonitis.

Treatment

A. General Measures

The patient should be kept at strict bed rest until the temperature returns to normal (without the use of antipyretic medications) and the sedimentation rate, plus the resting pulse rate, and the ECG have all returned to baseline.

B. Medical Measures

1. Salicylates—The salicylates markedly reduce fever and relieve joint pain and swelling. They have no effect on the natural course of the disease. Adults may require large doses of aspirin, 0.6–0.9 g every 4 hours; children are treated with lower doses.

2. Penicillin—Penicillin (benzathine penicillin, 1.2 million units intramuscularly once, or procaine penicillin, 600,000 units intramuscularly daily for 10 days) is used to eradicate streptococcal infection if present. Erythromycin may be substituted (40 mg/kg/d).

3. Corticosteroids—There is no proof that cardiac damage is prevented or minimized by corticosteroids. A short course of corticosteroids (prednisone, 40–60 mg orally daily, with tapering over 2 weeks) usually causes rapid improvement of the joint symptoms and is indicated when response to salicylates has been inadequate.

Prevention of Recurrent Rheumatic Fever

The initial episode of rheumatic fever can usually be prevented by early treatment of streptococcal pharyngitis. (See Chapter 33.) Prevention of recurrent episodes is critical. Recurrences of rheumatic fever are most common in patients who have had carditis during their initial episode and in children, 20% of whom will have a second episode within 5 years. Recurrences are uncommon after 5 years following the first episode, and in patients over 25 years of age. Prophylaxis is usually discontinued after these times except in groups with a high risk of streptococcal infection—parents or teachers of young children, nurses, military recruits, etc. Secondary prevention of rheumatic fever depends on whether carditis has occurred. If there is no evidence for carditis, preventive therapy can be stopped at age 21 years. If carditis has occurred but there is no residual valvular disease, it can be stopped at 10 years after the episode. If carditis has occurred with residual valvular involvement, it should be continued for 10 years after the last episode or until age 40 years if the patient is in a situation in which reexposure would be expected.

A. Penicillin

The preferred method of prophylaxis is with benzathine penicillin G, 1.2 million units intramuscularly every 4 weeks. Oral penicillin (200,000–250,000 units twice daily) is less reliable.

B. Alternatives for Penicillin-Allergic Patients

If the patient is allergic to penicillin, sulfadiazine (or sulfisoxazole), 1 g daily, or erythromycin, 250 mg orally twice daily, may be substituted. The macrolide azithromycin is similarly effective against group A streptococcal infection. If the patient has not had an immediate hypersensitivity (anaphylactic-type) reaction to penicillin, then cephalosporin may also be used.

Prognosis

Initial episodes of rheumatic fever may last months in children and weeks in adults. The immediate mortality rate is 1–2%. Persistent rheumatic carditis with cardiomegaly, heart failure, and pericarditis implies a poor prognosis; 30% of children thus affected die within 10 years after the initial attack. After 10 years, two-thirds of patients will have detectable valvular abnormalities (usually thickened valves with limited mobility), but significant symptomatic valvular heart disease or persistent cardiomyopathy occurs in less than 10% of patients with a single episode. In developing countries, acute rheumatic fever occurs earlier in life, recurs more frequently, and the evolution to chronic valvular disease is both accelerated and more severe.

Rheumatic Heart Disease

Chronic rheumatic heart disease results from single or repeated attacks of rheumatic fever that produce rigidity and deformity of valve cusps, fusion of the commissures, or shortening and fusion of the chordae tendineae. Stenosis or insufficiency results, and the two often coexist. The mitral valve alone is affected in 50–60% of cases; combined lesions of the aortic and mitral valves occur in 20%; pure aortic lesions are less common. Tricuspid involvement occurs in about 10% of cases but only in association with mitral or aortic disease and is thought to be more common when recurrent infections have occurred. The pulmonary valve is rarely affected. A history of rheumatic fever is obtainable in only 60% of patients with rheumatic heart disease.

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DISEASES OF THE PERICARDIUM

ACUTE INFLAMMATORY PERICARDITIS

ESSENTIALS OF DIAGNOSIS

- Anterior pleuritic chest pain that is worse supine than upright.
- Pericardial rub.
- Fever common.
- Erythrocyte sedimentation rate usually elevated.
- ECG reveals diffuse ST segment elevation with associated PR depression.

General Considerations

Acute (< 2 weeks) inflammation of the pericardium may be infectious in origin or may be due to systemic diseases (autoimmune syndromes, uremia), neoplasm, radiation, drug toxicity, hemopericardium, postcardiac surgery, or contiguous inflammatory processes in the myocardium or lung. In many of these conditions, the pathologic process involves both the pericardium and the myocardium.

Viral infections (especially infections with coxsackieviruses and echoviruses but also influenza, Epstein–Barr, varicella, hepatitis, mumps, and HIV viruses) are the most common cause of acute pericarditis and probably are responsible for many cases classified as idiopathic. Males—usually under age 50 years—are most commonly affected. The differential diagnosis is primarily with myocardial infarction. **Tuberculous pericarditis** has become rare in developed countries but remains common in other areas. It results from direct lymphatic or hematogenous spread; clinical pulmonary involvement may be absent or minor, although associated pleural effusions are common. **Bacterial pericarditis** has become rare and usually results from direct extension from pulmonary infections. Pneumococci can cause a primary pericardial infection. *Borrelia burgdorferi,* the organism responsible for Lyme disease, can also cause myopericarditis. **Uremic pericarditis** is a common complication of renal failure. The pathogenesis is uncertain; it occurs both with untreated uremia and in otherwise stable dialysis patients. Spread of adjacent lung cancer as well as invasion by breast cancer, renal cell carcinoma, Hodgkin's disease, and lymphomas are the most common **neoplastic processes** involving the pericardium and have become the most frequent causes of pericardial tamponade in many countries. Pericarditis may occur 2–5 days after infarction due to an inflammatory reaction to transmural myocardial necrosis (**postmyocardial infarction or postcardiotomy pericarditis (Dressler's syndrome). Radiation** can initiate a fibrinous and fibrotic process in the pericardium, presenting as subacute pericarditis or constriction. Radiation pericarditis usually follows treatments of more than 4000 cGy delivered to ports including more than 30% of the heart.

Other causes of pericarditis include connective tissue diseases, such as lupus erythematosus and rheumatoid arthritis, drug-induced pericarditis (minoxidil, penicillins), and myxedema.

Clinical Findings

A. Symptoms and Signs

The presentation and course of inflammatory pericarditis depend on its cause, but all syndromes are often (not always) associated with chest pain, which is usually pleuritic and postural (relieved by sitting). The pain is substernal but may radiate to the neck, shoulders, back, or epigastrium. Dyspnea may also be present and the patient is often febrile. A pericardial friction rub is characteristic, with or without evidence of fluid accumulation or constriction (see below). The presentation of **tuberculous pericarditis** tends to be subacute, but nonspecific symptoms (fever, night sweats, fatigue) may be present for days to months. Pericardial involvement develops in 1–8% of patients with pulmonary tuberculosis. Symptoms and signs of **bacterial pericarditis** are similar to those of other types of inflammatory pericarditides, but patients appear toxic and are often critically ill. **Uremic pericarditis** can present with or without symptoms; fever is absent. Often **neoplastic pericarditis** is painless, and the presenting symptoms relate to hemodynamic compromise or the primary disease. **Postmyocardial infarction or postcardiotomy pericarditis (Dressler's syndrome)** usually presents as a recurrence of pain with pleural-pericardial features. A rub is often audible, and repolarization changes on the ECG may be confused with ischemia. Large effusions are uncommon, and spontaneous resolution usually occurs in a few days. Dressler's syndrome occurs weeks to several months after myocardial infarction or open heart surgery, may be recurrent, and probably represents an autoimmune syndrome. Patients present with typical pain, fever, malaise, and leukocytosis. Occasionally, the syndrome will occur within days of surgery. Rarely, other symptoms of an autoimmune disorder, such as joint pain and fever, may occur. Tamponade is rare with Dressler's syndrome after myocardial infarction but not when it occurs postoperatively. The clinical onset of **radiation pericarditis** is usually within the first year but may be delayed for many years.

B. Laboratory Findings and Diagnostic Studies

The diagnosis of **viral pericarditis** is usually clinical, and leukocytosis is often present. Rising viral titers in paired sera may be obtained for confirmation. Cardiac enzymes may be slightly elevated, reflecting a myocarditic component. The echocardiogram is often normal or reveals only a trivial amount of fluid during the acute inflammatory process. The diagnosis of **tuberculous pericarditis** can be inferred if acid-fast bacilli are found elsewhere. The tuberculous pericardial effusions are usually small or moderate but may be large.

The yield of organisms by pericardiocentesis is low; pericardial biopsy has a higher yield but may also be negative, and pericardiectomy may be required. If **bacterial pericarditis** is suspected on clinical grounds, diagnostic pericardiocentesis may be of value. In **uremic patients** not on dialysis, the incidence of pericarditis correlates roughly with the level of blood urea nitrogen (BUN) and creatinine. The pericardium is characteristically "shaggy" in uremic pericarditis, and the effusion is hemorrhagic and exudative. The diagnosis of **neoplastic pericarditis** can occasionally be made by cytologic examination of the effusion or by pericardial biopsy, but it may be difficult to establish clinically if the patient has received mediastinal radiation within the previous year. Neoplastic pericardial effusions develop over a long period of time and may become quite huge (> 2 L). The sedimentation rate is high in **postmyocardial infarction or postcardiotomy pericarditis.** Large pericardial effusions and accompanying pleural effusions are frequent. Myxedema pericardial effusions due to hypothyroidism usually are characterized by the presence of cholesterol crystals.

C. Other Studies

The ECG usually shows generalized ST and T wave changes and may manifest a characteristic progression beginning with diffuse ST elevation, followed by a return to baseline and then to T wave inversion. Atrial injury is often present and manifested by PR depression especially in the limb leads. The chest radiograph is frequently normal, but may show cardiac enlargement if fluid has collected, as well as signs of related pulmonary disease. Mass lesions and enlarged lymph nodes may suggest a neoplastic process. MRI and CT scan can visualize neighboring tumor in neoplastic pericarditis.

Treatment

Treatment of **viral pericarditis** is generally symptomatic. Aspirin (650 mg every 3–4 hours) or other nonsteroidal agents (eg, indomethacin, 100–150 mg daily in divided doses) are usually effective. Corticosteroids may be beneficial in unresponsive cases. In general, symptoms subside in several days to weeks. The major early complication is tamponade, which occurs in less than 5% of patients. There may be recurrences in the first few weeks or months. Rare patients will continue to experience recurrences chronically. These patients may require long-term anti-inflammatory medications, either corticosteroids or colchicine. Rarely, acute pericarditis may lead to constrictive pericarditis, when pericardial resection may be necessary (see below). Standard antituberculous drug therapy is usually successful for **tuberculous pericarditis** (see Chapter 9), but constrictive pericarditis can occur. **Uremic pericarditis** usually resolves with the institution of—or with more aggressive—dialysis. Tamponade is fairly common, and partial pericardiectomy (pericardial window) may be necessary. Whereas anti-inflammatory agents may relieve the pain and fever associated with uremic pericarditis, indomethacin and systemic corticosteroids do not affect its natural history. The prognosis with **neoplastic effusion** is dismal, with only a small minority surviving 1 year. If it is compromising the clinical comfort of the patient, the effusion is initially drained percutaneously. Early attempts at ballooning the pericardium from a subxiphoid approach have been mostly abandoned in favor of surgical approaches. A pericardial window, either by a subxiphoid approach or via video-assisted thoracic surgery, allows for partial pericardiectomy. Instillation of chemotherapeutic agents or tetracycline may occasionally be used to reduce the recurrence rate. Aspirin or other nonsteroidal anti-inflammatory agents in dosages given for viral pericarditis above for 2–4 weeks are usually effective for the treatment of **postmyocardial infarction or postcardiotomy pericarditis (Dressler's syndrome).** In more severe cases, corticosteroids should be given in rapidly tapering doses. Relapses do occur and may require slow withdrawal of anti-inflammatory therapy over several months. Colchicine may be required for months to help prevent recurrences. Symptomatic therapy is the initial approach to **radiation pericarditis,** but recurrent effusions and constriction often require surgery.

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PERICARDIAL EFFUSION

Pericardial effusion can develop during any of the processes previously discussed. The speed of accumulation determines the physiologic importance of the effusion. Because the pericardium stretches, large effusions (> 1000 mL) that develop slowly may produce no hemodynamic effects. Smaller effusions that appear rapidly can cause tamponade. Tamponade is characterized by elevated intrapericardial pressure (> 15 mm Hg), which restricts venous return and ventricular filling. As a result, the stroke volume and pulse pressure fall, and the heart rate and venous pressure rise. Shock and death may result.

Clinical Findings

A. Symptoms and Signs

Pericardial effusions may be associated with pain if they occur as part of an acute inflammatory process or may be painless, as is often the case with neoplastic or uremic effusion. Dyspnea and cough are common, especially with tamponade. Other symptoms may result from the primary disease.

A pericardial friction rub may be present even with large effusions. In cardiac tamponade, tachycardia, tachypnea, a narrow pulse pressure, and a relatively preserved

systolic pressure are characteristic. Pulsus paradoxus—a greater than 10 mm Hg decline in systolic pressure during inspiration due to further impairment of LV filling—is the classic finding, but it may also occur with obstructive lung disease. Central venous pressure is elevated and there is no evident *y* descent in the RA, RV, or LV hemodynamic tracings. Edema or ascites are rarely present; these signs favor a more chronic process.

B. Laboratory Findings

Laboratory tests tend to reflect the underlying processes (see causes of pericarditis above).

C. Diagnostic Studies

Chest radiograph can suggest chronic effusion by an enlarged cardiac silhouette with a globular configuration but may appear normal in acute situations. The ECG often reveals nonspecific T wave changes and low QRS voltage. Electrical alternans is present uncommonly but is pathognomonic. It is due to the heart swinging within the large effusion. Echocardiography is the primary method for demonstrating pericardial effusion and is quite sensitive. If tamponade is present, the high intrapericardial pressure may collapse lower pressure cardiac structures, such as the RA and RV. In tamponade, the normal inspiratory reduction in LV filling is accentuated due to RV/LV interaction and there is a > 25% reduction in maximal mitral inflow velocities. Cardiac CT and MRI also demonstrate pericardial fluid and any associated contiguous lesions. Diagnostic pericardiocentesis or biopsy is often indicated for microbiologic and cytologic studies; a pericardial biopsy may be performed relatively simply through a small subxiphoid incision. Unfortunately, the quality of the pericardial fluid rarely leads to a diagnosis, and any type of fluid (serous, serosanguinous, bloody, etc) can be seen in most diseases.

Treatment

Small effusions can be followed clinically by careful observations of the JVP and by testing for a paradoxical pulse. Serial echocardiograms are indicated if no intervention is immediately contemplated. When tamponade is present, urgent pericardiocentesis is required. Because the pressure–volume relationship in the pericardial fluid is curvilinear and upsloping, removal of a small amount of fluid often produces a dramatic fall in the intrapericardial pressure and immediate hemodynamic benefit; but complete drainage with a catheter is preferable. Continued or repeat drainage may be indicated, especially in malignant effusions. Pericardial windows via video-assisted thorascopy have been particularly effective in preventing recurrences.

Additional therapy is determined by the nature of the primary process. Recurrent effusion in neoplastic disease and uremia, in particular, may require partial pericardiectomy as noted earlier.

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CONSTRICTIVE PERICARDITIS

ESSENTIALS OF DIAGNOSIS

- Evidence of right heart failure with an elevated JVP, edema, hepatomegaly, and ascites.
- No fall or an elevation of the JVP with inspiration (Kussmaul's sign).
- Echocardiographic evidence for septal bounce and reduced mitral inflow velocities with inspiration.
- Catheterization evidence for RV-LV interaction, a "square root" sign, equalization of diastolic pressures, and normal pulmonary pressure.

General Considerations

Inflammation can lead to a thickened, fibrotic, adherent pericardium that restricts diastolic filling and produces chronically elevated venous pressures. In the past, tuberculosis was the most common cause of constrictive pericarditis, but the process now more often occurs after radiation therapy, cardiac surgery, or viral pericarditis; histoplasmosis is another uncommon cause.

Clinical Findings

A. Symptoms and Signs

The principal symptoms are slowly progressive dyspnea, fatigue, and weakness. Chronic edema, hepatic congestion, and ascites are usually present. Ascites often seems out of proportion to the degree of peripheral edema. The examination reveals these signs and a characteristically elevated jugular venous pressure with a rapid *y* descent. This can be detected at bedside by careful observation of the jugular pulse and noting an apparent increased pulse wave at the end of systole (due to accentuation of the *v* wave by the rapid *y* descent). Kussmaul's sign—a failure of the JVP to fall with inspiration—is also a frequent finding. The apex may actually retract with systole and a pericardial "knock" may be heard in early diastole. Pulsus paradoxus is unusual. Atrial fibrillation is common.

B. Diagnostic Studies

The chest radiograph may show normal heart size or cardiomegaly. Pericardial calcification is best seen on the lateral view and is uncommon. It rarely involves the LV apex, and finding of calcification at the LV apex is more consistent with LV aneurysm. Echocardiography rarely demonstrates a thickened pericardium. A septal "bounce" reflecting the rapid early