CARDIOMYOPATHIES:

The diagnosis of cardiomyopathy encompasses a wide spectrum of diseases, with divergent pathogenic mechanisms, which have as their final common pathway the syndrome of congestive heart failure (CHF). These heart muscle diseases may be primary or secondary—i.e., resulting from specific cardiac or systemic disorders. Etiologies associated with the development of cardiomyopathy are listed in Table 1. Endomyocardial biopsy is generally a low-yield procedure; however, in this group of diseases, it can be diagnostic (Table 2).

I DILATED: (MOST COMMON)

1. MYOCARDITIS

Myocardial dysfunction from viral myocarditis may result from viral injury, immunologic responses initiated by the virus, or apoptotic cell death. Multiple infectious etiologies (Table1) can cause myocarditis, the most common being viral, specifically, coxsackie B virus. The clinical manifestations of myocarditis are variable. The majority of patients are asymptomatic, as cardiac dysfunction is subclinical and self-limited. However, other patients present in cardiogenic shock. Antecedent flu-like symptoms occur in 60 percent of patients. Chest pain occurs in 35 percent of patients and may be typically anginal, atypical, or pericardial in character. Sudden death, syncope, and palpitations are other presentations. Complete atrioventricular (AV) block is common and generally transient; it rarely requires a permanent pacemaker. Sudden cardiac death can result from complete heart block or ventricular tachycardia. Systemic or pulmonary thromboembolic disease can also be seen.

Physical findings include fever, tachycardia, and signs of CHF. The first heart sound may be soft and a summation gallop may be present. An apical systolic murmur of functional mitral regurgitation may be auscultated. A pericardial friction rub can be heard. Laboratory findings are generally nondiagnostic. Some 60 percent of patients will have an elevated erythrocyte sedimentation rate (ESR) and 25 percent an elevated white blood cell (WBC) count. Elevated titers to cardiotropic viruses may be present. A fourfold rise in IgG titer over a 4-to 6-week period is required to document acute infection. Increase in the MB band of CPK is observed in 12 percent of patients and elevated troponin levels in 32 percent of patients. The electrocardiogram (ECG) frequently shows sinus tachycardia. Diffuse ST-T-wave changes, a prolonged QT interval, low voltage, an acute infarct pattern, and conduction delays also occur.

Echocardiography can reveal left ventricular systolic dysfunction in patients with a normal-sized left ventricular cavity. Segmental wall motion abnormalities may be observed. Wall thickness may be increased early in the disease, when inflammation is fulminant. Ventricular thrombi are seen in 15 percent of those studied. Endomyocardial biopsy confirms the diagnosis. As myocarditis can be focal, four to six fragments are obtained to reduce sampling error to <5 percent. Active myocarditis is defined pathologically as an inflammatory infiltrate with myocyte necrosis. Endomyocardial biopsy must be applied quickly to maximize the diagnostic yield. Resolution of myocarditis can occur within 4 days of initial biopsy.

Approximately 40 percent of patients with acute myocarditis fully recover. The prognosis depends somewhat on the causative agent, but if clinical CHF develops, 5-year mortality rates are 50 to 60 percent. Predictors of recovery include the degree of left ventricular dysfunction at presentation, shorter duration of disease, and less intensive conventional drug therapy. A recent study suggests that patients with “fulminant” myocarditis—defined as rapid onset of symptoms, fever, and severe hemodynamic compromise—have a better survival than patients with acute nonfulminant myocarditis.

Treatment of acute myocarditis consists of supportive care. Diuretics, angiotensin-converting-enzyme inhibitors, beta-blockers and aldosterone antagonists should be given in the proper clinical context. Digoxin can increase the expression of inflammatory cytokines and should be used cautiously and only in low doses. Immunosuppressive therapies have not been shown to be effective. The Multicenter Myocarditis Treatment Trial randomized patients with biopsy-proven myocarditis to conventional medical therapy versus steroid/azathioprine or steroid/cyclosporine immunosuppression. Treatment assignment was not predictive of improvement in left ventricular ejection fraction, attenuation of clinical disease, or mortality. The IMAC trial (Intervention in Myocarditis and Acute Cardiomyopathy with Immune Globulin) used a single infusion of high-dose immunoglobulin (2 g/kg) to treat presumed inflammatory cardiomyopathies. Improvement in left ventricular ejection fraction and symptoms were similar in both groups. Patients with ongoing myocarditis and increased HLA expression in biopsy samples may be more likely to respond to immunosuppression, but no uniform methodology yet exists to identify them.

Human Immunodeficiency Virus

Human immunodeficiency virus (HIV) is increasingly recognized as a cause of dilated cardiomyopathy. This cardiomyopathy may result from infection of myocardial cells with HIV, coinfection with other viruses, post-viral autoimmune response, or cardiotoxicity from illicit drugs or therapy. Asymptomatic HIV-positive patients develop cardiomyopathy with an annualized incidence of 16 cases per 1000 patients. A CD4 count <400 cells per mililiter predisposes to the development of cardiomyopathy. Symptoms of CHF and HIV can be similar (fatigue and wasting), so careful follow-up is needed to detect left ventricular dysfunction in these patients.

Chagas' Disease

American trypanosomiasis, or Chagas' disease, is the most common cause of CHF in the world and is endemic to rural South and Central America. It results from the bite of the reduviid bug, leading to infection with *Trypanosoma cruzi*. In the acute phase, hematogenous spread of the parasite is accompanied by an intense inflammatory reaction. Patients experience fever, sweating, and myalgias. Most patients recover from the acute illness and enter an asymptomatic latent phase. Twenty to 30 percent of patients develop chronic disease up to 20 years after the initial infection. The gastrointestinal tract and the heart are the most commonly involved sites, with cardiac disease the primary cause of death. Fibrosis of the myofibrils and Purkinje fibers leads to cardiomegaly, CHF, heart block, and arrhythmia. Parasites are found in about a quarter of the patients on endomyocardial biopsy. The acute disease is diagnosed with the discovery of trypomastigotes in the blood. Chronic disease may be confirmed with complement-fixation, immunofluorescence or enzyme-linked immunosorbent assays. Echocardiography shows segmental wall motion abnormalities—specifically apical aneurysms. ECG findings include complete heart block, atrioventricular block, or right bundle branch block. The treatment of chronic Chagas' disease includes a pacemaker for complete heart block, an implantable cardioverter/defibrillator for recurrent ventricular arrhythmia, and standard CHF therapy. Antiparasitic agents such as nifurtimox and benzimidazole eradicate parasitemia during the acute phase and are curative. They should be administered if the disease has not been treated and may be used as prophylaxis if there is a high likelihood of recurrence. Heart transplantation is effective for end-stage cardiac disease.

Lyme Carditis

Lyme disease may result from infection with the spirochete *Borrelia burgdorferi,* introduced by a tick bite. Patients who develop cardiac involvement frequently experience complete heart block. Left ventricular dysfunction may be seen but is unusual. Endomyocardial biopsy may show active myocarditis and rarely spirochetes. Treatment consists of tetracycline and corticosteroids.

Rheumatic Carditis

The incidence of rheumatic myocarditis has declined dramatically in the United States but remains high in developing countries. Rheumatic fever (RF) follows group A streptococcal pharyngitis. The major manifestations are carditis, polyarthritis, chorea, erythema marginatum, subcutaneous nodules, and evidence of preceding streptococcal infection. Minor criteria are nonspecific findings such as fever, arthralgia, previous rheumatic fever or rheumatic heart disease, elevated ESR or C-reactive protein, and prolonged PR interval. Clinical diagnosis is made using the Jones criteria (two major criteria or one major and two minor criteria). Two-thirds of patients present with pharyngitis followed by symptoms of RF in 1 to 5 weeks (mean, 19 days). Severe carditis resulting in death is unusual. CHF is generally mild and is observed in 5 to 10 percent of cases. The physical examination is notable for fever and heart murmurs with the mitral valve being involved three times as often as the aortic valve. ECG findings include PR prolongation and nonspecific ST-T-wave changes. Endomyocardial biopsy demonstrates the pathognomonic Aschoff body which is a persistent focal inflammatory lesion. Laboratory tests suggestive of rheumatic fever include antibodies to antistreptolysin O and anti-DNAase B, an elevated ESR, and C-reactive protein. Aspirin and penicillin are the mainstays of therapy. Corticosteriods can provide symptomatic relief. Once the condition has been diagnosed, antibiotic prophylaxis using monthly injections of 1.2 million units of benzathine penicillin G is recommended until age 21.

2. NONINFECTIVE MYOCARDITIS

Giant-Cell Myocarditis

Giant-cell myocarditis is a rare, but aggressive form of myocarditis. This disease is most prevalent in young adults, and is associated with other autoimmune disorders in 20 percent of cases. Diagnosis is made by endomyocardial biopsy. Widespread or multifocal necrosis with a mixed inflammatory infiltrate including lymphocytes and histiocytes is required for histologic diagnosis. Eosinophils are often seen, as are multinucleated giant cells in the absence of granuloma. The clinical course is characterized by progressive CHF and is often associated with refractory ventricular arrhythmia. It is almost uniformly and rapidly fatal. Rare reports of response to immunosuppressive regimens have been described. Cardiac transplant is the best treatment option, although Giant-cell myocarditis may recur.

Peripartum Cardiomyopathy

Peripartum cardiomyopathy has a reported incidence varying from 1 in 1300, to 1 in 15,000 pregnancies. Predisposing factors include black race, age >30 years, obesity, cesarean delivery, multiple gestations, preeclampsia, and chronic hypertension. Patients present with CHF in the last trimester of pregnancy or in the first 5 months postpartum. Absence of a demonstrable cause of CHF and structural heart disease is required to make the diagnosis. Proposed mechanisms include myocarditis due to a viral illness or autoimmune etiology, nutritional deficiencies, genetic disorders, hormonal imbalances, volume overload, alcohol, physiologic stress of pregnancy, or unmasking of latent idiopathic dilated cardiomyopathy. Patients present with CHF, syncope, thromboemboli or sudden death. The ECG frequently shows left ventricular

hypertrophy. Echocardiographic findings are non-specific. Endomyocardial biopsy may reveal myocarditis in as many as fifty percent of women. Serial echocardiograms have been used to predict prognosis. Patients with higher ejection fractions and smaller ventricular diastolic dimensions at the time of diagnosis have a better long-term prognosis. If the congestive cardiomyopathy persists for more than 6 months, it is likely to be irreversible and to be associated with a worse prognosis. Patients with stable heart failure or those who have recovered are at high risk for recurrence in subsequent pregnancies.

Hypersensitivity Myocarditis

Hypersensitivity myocarditis due to an allergic reaction to drugs (Table 34-1) is characterized by peripheral eosinophilia and infiltration into the myocardium of eosinophils, multinucleated giant cells, and leukocytes. Resolution is reported with stopping of the offending agent and treatment with corticosteroids. Unfortunately, the presence of this condition often goes unnoticed, with the initial manifestation being sudden death.

3. ENDOCRINE DISORDERS

Thyroid hormone deficiency or excess can produce cardiomyopathy. Thyroid hormone metabolism is frequently abnormal in patients with CHF. Low T3 levels may be an adaptive mechanism to decreased catabolism. Thyroid hormone replacement increases cardiac output, decreases peripheral vascular resistance, and improves exercise performance. Thyroid toxicity initially produces high-output CHF. Prolonged tachycardia and the high-output state caused by thyrotoxicosis may ultimately result in left ventricular dilatation and a decline in systolic function. This process can be reversed by reduction of excess hormone levels.

Diabetic patients face a fivefold increased risk of developing CHF. The metabolic abnormalities associated with diabetes may contribute to myocyte dysfunction and produce a diabetes-induced cardiomyopathy. Typically, interstitial fibrosis and arteriolar hyalinization are present. Both systolic and diastolic dysfunction can occur; the severity of the dysfunction is related to the degree of metabolic control.

4. TOXINS:

ALCOHOL

Chronic alcohol abuse accounts for up to 45 percent of all dilated cardiomyopathies. Cardiac damage results from direct toxic effects of alcohol or its metabolites in addition to nutritional deficiencies, sympathetic stimulation, or coexistent hypertension. The disease occurs most frequently in patients with a >10-year history of heavy alcohol use. Atrial fibrillation is common. Sudden death may be the initial presentation. Both the ECG and echocardiogram are frequently abnormal, but changes are non-specific. Histologic findings of endomyocardial biopsies are not pathognomonic. The mainstay of treatment is abstinence from alcohol. Cessation of drinking in the early stages of the disease has a favorable prognosis, but those who continue to consume alcohol face a 43 percent chance of dying within 42 months. Abstinence from alcohol is not effective in reversing the disease once structural histologic abnormalities have occurred.

COCAINE

Cocaine blocks the reuptake of norepinephrine producing tachycardia, vasoconstriction, hypertension, and ventricular arrhythmias. Cardiomyopathy may result from secondary changes in the heart due to tachycardia or sustained increased ventricular afterload. Cocaine may also be directly toxic to myocytes. The risk of toxicity in any given individual are unpredictable, and the duration or amount of cocaine use does not predict disease. There are no clinical or histologic features specific for cocaine-induced myocardial damage. Treatment is aimed at abstinence and

treatment of heart failure. Beta-blockers may potentiate coronary spasm and should probably be avoided.

CHEMOTHERAPEUTIC AGENTS

The anthracyclines (doxorubicin) and cyclophosphamide are the most common agents associated with CHF. Doxorubicin is frequently prescribed for hematologic malignancies. Its cardiotoxicity may be due to increased oxidative stress from the generation of free radicals. Risk factors for the development of doxorubicin cardiomyopathy include age >70 years, combination chemotherapy, mediastinal irradiation, prior cardiac disease, hypertension, and liver disease. Cardiac toxicity may become apparent early or late. Early cardiotoxicity manifests as a pericarditis-myocarditis syndrome and is not dose-related. Left ventricular dysfunction is rarely seen, but arrhythmias, abnormalities of conduction, decreased QRS voltage, and nonspecific ST-segment and T-wave abnormalities are observed in 40 percent of patients. Discontinuation of therapy results in a quick resolution of symptoms and has a favorable prognosis. In contrast, the late cardiotoxicity is due to a dose-dependent degenerative cardiomyopathy. This syndrome occurs at doses >550 mg/m^2. Serial assessment of ejection fractions is useful to monitor for toxicity. However, histopathologic grading delineates best the safety of continued doxorubicin administration. Cardiotoxicity may occur during therapy, within a year of the last dose or up to 10 years after cessation of chemotherapy. Therefore prolonged cardiac surveillance is necessary. Prognosis depends on the severity at time of presentation, but overall the mortality is high. The best management of anthracycline cardiotoxicity is prevention. Heart failure due to doxorubicin is typically refractory to conventional therapy. Diminished symptoms and improved left ventricular function have been described in patients on beta blockers.

Cyclophosphamide produces an acute cardiotoxicity that is not dose-related. Pericarditis, systolic dysfunction, arrhythmias, and myocardial edema can occur. Prior left ventricular dysfunction is a risk factor for the development of cardiomyopathy. Mortality is not trivial, but survivors regain normal cardiac function.

5. IDIOPATHIC

The term *idiopathic cardiomyopathy* describes a group of myocardial diseases of unknown cause. Idiopathic dilated cardiomyopathy probably represents the end result of a number of disease processes that lead to myocyte dysfunction, loss, hypertrophy, and fibrosis. It is a diagnosis of exclusion. Surreptitious alcohol use and undiagnosed and untreated hypertension represent other etiologies of cardiomyopathy in many of these cases. The incidence of IDC has been estimated at 0.005 to 0.006 percent, increasing with age and male gender. Mortality for untreated cardiomyopathy approaches 50 percent at 5 years.

II. INFILTRATIVE CARDIOMYOPATHIES (RARE)

1. Amyloidosis

Amyloidosis is the most common infiltrative cardiomyopathy . AL amyloid results from the overproduction of immunoglobulin light chains by a monoclonal population of plasma cells. Secondary or reactive amyloidosis (AA type) is associated with chronic infectious or inflammatory disease. Familial amyloidosis results from the overproduction of transthyretin. Senile amyloidosis occurs with aging. The frequency of cardiac involvement varies. With primary amyloidosis, 33 to 50 percent of patients have cardiac involvement and >25 percent have symptomatic CHF. The rigid amyloid fibrils lead to relaxation abnormalities and diastolic dysfunction; however, when myocardial replacement occurs, systolic dysfunction becomes

prominent. The clinical presentation is predominately that of right-sided CHF. Sudden death and myocardial infarction may result from vascular involvement. Atrial and ventricular arrhythmias are common. Diagnosis is made by characteristic echocardiographic features and endomyocardial biopsy. Echocardiography demonstrates symmetrical thickening of the left ventricular wall with a diffuse hyper-refractile, granular, sparkling appearance of the myocardium. The ECG typically demonstrates low voltage despite marked hypertrophy on echocardiography. A pseudoinfarct anterior wall pattern is often present. Amyloid is detected on endomyocardial biopsy using Congo red staining.

2. Sarcoidosis

Sarcoidosis is a systemic granulomatous disease of unknown etiology characterized by enhanced cellular immune responses. The pathologic hallmark of this disease is the noncaseating granuloma. Less than 10 percent of patients with sarcoid have cardiac symptoms; however, cardiac involvement is more common than recognized. Because of the varied extent and location of the myocardial granulomas, presenting signs and symptoms range from first-degree heart block to fulminant CHF. Frequently, the initial presentation is sudden death. Heart failure can present as a cardiomyopathy with restrictive hemodynamics or systolic dysfunction. Some 25 percent of the deaths due to cardiac sarcoid are from CHF and 33 to 50 percent from sudden cardiac death. In diagnosing cardiac sarcoid, evidence of other organ system involvement is sought. In cases where the heart is predominantly involved, little or no evidence of extracardiac sarcoidosis may be found. CXR, ECG, and echocardiography findings depend on the extent and location of involvement. Due to the scattered location of the granulomas, endomyocardial biopsy lacks sensitivity and seldom makes the diagnosis despite high specificity. Magnetic resonance imaging is useful in diagnosing myocardial lesions. While no controlled trials have been performed, high-dose corticosteroids are usually given. Corticosteroids can improve cardiac symptoms and reverse ECG changes in >50 percent of treated patients. Antiarrhythmic drugs are used as necessary, although drug therapy of ventricular tachycardia is associated with a high rate of arrhythmia recurrence. Automatic internal cardioverter/defibrillators have been advocated to prevent sudden death. Prognosis is generally poor with survival of 41 percent at 5 years. Transplantation is a successful treatment, as the recurrence of sarcoid in the allograft is low.

3. Hemochromatosis

Primary hemochromatosis is an inborn error of metabolism leading to iron deposition in a variety of organs including the heart. Both restrictive and dilated presentations can occur. Treatment with phlebotomy is highly effective. In secondary forms of hemochromatosis due to multiple blood transfusions for blood dyscrasias, chelation therapy is highly effective. Diagnosis is made by symptom constellation in the presence of an elevated serum iron and ferritin. Endomyocardial biopsy is diagnostic.

4. Carcinoid

Carcinoid heart disease typically produces a restrictive cardiomyopathy. Its apparent predilection for right sided structures results from the inactivation of serotonin and bradykinin by the lungs and sparing of the mitral and aortic valves. Cardiac involvement responds to control of the tumor with chemotherapy or catheter embolization. Tricuspid valve replacement and/or pulmonary valvulotomy and outflow tract enlargement have been recommended when hemodynamically indicated. Alternatively, balloon valvuloplasty for tricuspid or pulmonary stenoses has been used successfully.

5. Eosinophilic Heart Disease

Hypereosinophilic syndromes (Loeffler's disease) are characterized by peripheral eosinophilia and endocardial disease with eosinophilic infiltration, fibrosis, and eventual occlusion of the ventricular cavity by scar and thrombus. This leads to severe restrictive disease known as *obliterative myocardial disease*. It is an immunologic disorder caused by clones of abnormal eosinophils infiltrating the heart. It occurs primarily in men in their forties from temperate climates. Diffuse organ involvement may be observed (lungs, bone marrow, brain), with cardiac involvement in >75 percent of patients. Clinical presentation includes weight loss, fever, cough, skin rash, and CHF. Overt CHF occurs in 50 percent of patients and is the leading cause of death. Echocardiography demonstrates localized thickening of the left ventricle with valvular leaflet abnormalities and atrial enlargement. In advanced endomyocardial fibrosis, there may be apical obliteration by thrombus but normal systolic function. Diagnosis is by endomyocardial biopsy and echocardiogram. Early therapy with corticosteroids and cytotoxic drugs may substantially improve survival. Surgical therapy offers palliation once the later fibrotic stages have been reached.

III HYPERTROPHIC CARDIOMYOPATHY

Hypertrophic cardiomyopathy accounts for approximately 5% of cardiomyopathies and presents with marked myocardial hypertrophy in the absence of an extrinsic cause (i.e. obstructive valvular disease, hypertension) . Cardiac mass is increased due to left ventricular wall thickening which can be asymmetric with marked septal involvement. It may also present with predominantly apical or mid-ventricular involvement. This is a genetic disorder with autosomal dominant inheritance. 50% of the mutations are inherited. 50% are spontaneous mutations. Mutations in genes encoding myofibillar proteins result in the cardiomyopathy (myosin, troponin, actin). Several mutations have been described with varying severity, disease penetrance and prognosis. Histopathology reveals pathognomonic feature of myocyte disarray. Diagnosis is made by 2 D echocardiography which reveals striking hypertrophy in the LV with usually preserved or supranormal LV function. Clinical presentation is variable. Dyspnea, chest pain, sudden death or atrial or ventricular arrhythmias are all observed. Sudden death is a major lifelong concern. In the US, unrecognized hypertrophic cardiomyopathy is the leading cause of sudden death in young athletes. Age of onset is variable . Best predictor of outcome may be the molecular defect. Risk factors for sudden death are age, syncope, family history of sudden death, sustained ventricular tachycardia on electrophysiology testing or monitoring. Sub-aortic or mid ventricular obstruction can occur from the ventricular hypertrophy and change in the coaptation of the mitral valve.

Symptoms are primarily from diastolic dysfunction resulting in myocardial stiffness. The presence of obstruction has important therapeutic implications. Treatment primarily involves use of beta blockers and calcium channel blockers. Myomectomy (surgical excision of excess tissue), non surgical septal reduction (i.e. septal infarct using alcohol), and dual chamber pacing for patients with obstructive disease. Placement of implantable defibrillators for the prevention of sudden death is advocated.

Disease	Etiologies	Comment
Infectious Myocarditis: Viral	<u>Viruses</u> Coxsackie, Echovirus, HIV, Epstein-Barr virus, Influenza, Cytomegalovirus, Adenovirus, Hepatitis (A&B), Mumps, Poliovirus, Rabies, Respiratory Synctial Virus, Rubella, Vaccinia, Varicella-Zoster, Arbovirus	The most common etiology of infectious myocarditis in North America is viral infection by coxsackie or echo viruses. Most episodes are self-limited and asymptomatic. In patients with symptoms of CHF, acute and chronic viral titers are needed along with endomyocardial biopsy to confirm the diagnosis. In South American, the most common cause of myocarditis is Chagas' disease caused by the bite of the reduviid bug carrying the parasite T cruzi
Bacterial	<u>Bacteria</u> Cornyebacterium diptheriae, Streptococcus pyogenes, Staphylococcus aureus, Haemophilus pneumoniae, Salmonella spp., Neisseria gonorrhea, Leptospirosis, Lyme disease, Syphilis, Brucellosis, Tuberculosis, Actinomycosis, Chlamydia spp., Coxiella burnetti, Myocoplasma pneumoniae, Rickettsia spp.	
Fungal	<u>Fungi</u> Candida spp., Aspergillus spp, Histoplasmosis, Blastomycosis, Cryptococcosis, Cocciodiomyocosis	
Parasitic	<u>Parasites</u> Trypanosoma cruzii, Toxoplasmosis, Schistosomiasis, Trichinosis	
Dilated cardiomyopathy	Unknown	May represent prior undiagnosed episode of myocarditis, untreated hypertension or occult alcohol use
Infiltrative	Amyloid Sarcoid Hemochromatosis Carcinoid Hypereosinophilic (Loefflers) Glycogen Storage	Myocardial inflammation may be present on biopsy. Routine and special stains are extremely valuable in confirming these diagnoses
Hypersensitivity/ Eosinophilic	<u>Antibiotics :</u> sulphonamides, penicillins, cefaclor chloramphenicol, amphotericin B,	Treatment is discontinuation of the offending agent with or

	tetracycline, streptomycin Antituberculous : isoniazide, paraaminosalicylic acid Anticonvulsants : phenindione, phenytoin, carbemazepine, Phenobarbital, Antidepressants: Amitriptyline, Desipramine Anti-inflammatories : indomethcin, phenylbutazone, Oxyphenylbutazone, Diuretics : acetazolamide, chlorthalidone, hydrochlorothiazide, spironolactone Others : methyldopa, sulphonylureas, interleukin-2, interleukin-4, tetanus toxoid	without steroids. Potentially reversible
Toxins	Cocaine, cyclophosphamide, emetine, lithium, methysergide, phenothiazines, interferon alpha, interleuken-2, doxorubicin, cobalt, lead, chloroquine, hydrocarbons, carbon monoxide, anabolic steroids	Potentially reversible for some toxins
Radiation	Past history of lymphoma	
Giant cell myocarditis	Unknown	Generally a fulminant disease with a high mortality. May recur after transplant
Post-Partum Cardiomyopathy	Unknown	CHF onset in last trimester or first 5 months post delivery in patient with no structural heart disease or known cause of CHF.
Genetic	Fabry, Kearns-Sayre Sndrome, Right Ventricular Dysplasia	Patients with RV dysplasia present with ventricular arrhythmias.
Endocrine	Hypothyroidism, Hyperthyroidism, Pheochromocytoma, Acromegaly, Diabetes	
Metabolic	Hypocalcemia, Hypophatemia, Uremia Carnitine	

Table 2: Diseases diagnosed by endomyocardial biopsy:

1. Myocarditis
    - Giant Cell
    - Cytomegalovirus
    - Toxoplasmosis
    - Chagas
    - Rheumatic
    - Lyme

2. Infiltrative
    - Amyloid
    - Sarcoid
    - Hemochromatosis
    - Carcinoid
    - Hypereosinophilic
    - Glycogen Storage
    - Cardiac Tumors

3. Toxins
    - Doxorubicin
    - Chloroquine
    - Radiation Injury

4. Genetic
    - Fabry
    - Kearns-Sayre Sndrome
    - Right Ventricular Dysplasia