TABLE 287-1 PRESENTATION WITH SYMPTOMATIC CARDIOMYOPATHY

	Dilated	Restrictive	Hypertrophic
Ejection fraction (normal >55%)	Usually <30% when symptoms severe	25–50%	>60%
Left ventricular diastolic dimension (normal <55 mm)	≥60 mm	<60 mm (may be decreased)	Often decreased
Left ventricular wall thickness	Normal or decreased	Normal or increased	Markedly increased
Atrial size	Increased, may also be primarily affected	Increased; may be massive	Increased; related to elevated filling pressures
Valvular regurgitation	Related to annular dilation; mitral appears earlier during decompensation; tricuspid regurgitation with right ventricular dysfunction	Related to endocardial involvement; frequent mitral and tricuspid regurgitation, rarely severe	Related to valve-septum interaction; mitral regurgitation
Common first symptoms	Exertional intolerance	Exertional intolerance, fluid retention early, may have dominant right-sided symptoms	Exertional intolerance; may have chest pain
Congestive symptoms[a]	Left before right, except right prominent in young adults	Right often dominates	Left-sided congestion at rest may develop late
Arrhythmias	Ventricular tachyarrhythmia; conduction block in Chagas' disease, and some families. Atrial fibrillation.	Ventricular uncommon except in sarcoidosis, conduction block in sarcoidosis and amyloidosis. Atrial fibrillation.	Ventricular tachyarrhythmias; atrial fibrillation

[a]Left-sided symptoms of pulmonary congestion: dyspnea on exertion, orthopnea, paroxysmal nocturnal dyspnea. Right-sided symptoms of systemic venous congestion: hepatic and abdominal distention, discomfort on bending, peripheral edema.

TABLE 287-2 INITIAL EVALUATION OF CARDIOMYOPATHY

Clinical Evaluation
Thorough history and physical examination to identify cardiac and noncardiac disorders[a]
Detailed family history of heart failure, cardiomyopathy, skeletal myopathy, conduction disorders, tachyarrhythmias, and sudden death
History of alcohol, illicit drugs, chemotherapy or radiation therapy[a]
Assessment of ability to perform routine and desired activities[a]
Assessment of volume status, orthostatic blood pressure, body mass index[a]
Laboratory Evaluation
Electrocardiogram[a]
Chest radiograph[a]
Two-dimensional and Doppler echocardiogram[a]
Magnetic resonance imaging for evidence of myocardial inflammation and fibrosis
Chemistry:
Serum sodium,[a] potassium,[a] calcium, [a] magnesium[a]
Fasting glucose (glycohemoglobin in diabetes mellitus)
Creatinine,[a] blood urea nitrogen[a]
Albumin,[a] total protein,[a] liver function tests[a]
Lipid profile
Thyroid-stimulating hormone[a]
Serum iron, transferrin saturation
Urinalysis
Creatine kinase isoforms
Cardiac troponin levels
Hematology:
Hemoglobin/hematocrit[a]
White blood cell count with differential,[a] including eosinophils
Erythrocyte sedimentation rate
Initial Evaluation When Specific Diagnoses Are Suspected
Titers for infection in the setting of clinical suspicion:
Acute viral (coxsackie, echovirus, influenza)
Human immunodeficiency virus
Chagas' (*Trypanosoma cruzi*), Lyme (*Borrelia burgdorferi*), toxoplasmosis
Catheterization with coronary angiography in patients with angina who are candidates for intervention[a]
Serologies for active rheumatologic disease
Endomyocardial biopsy including sample for electron microscopy when suspecting specific diagnosis with therapeutic implications
Screening for sleep-disordered breathing

[a]Level I recommendations from ACC/AHA Practice Guidelines for Chronic Heart Failure in the Adult.

and the intercalated disks between muscle cells. Desmin mutations impair the transmission of force and signaling for both cardiac and skeletal muscle and may cause combined cardiac and skeletal myopathy.

Sarcolemmal membrane protein defects are associated with dilated cardiomyopathy. The best known is dystrophin, encoded by the X chromosome gene *DMD*, abnormalities of which cause Duchenne's and Becker's muscle dystrophy. (Interestingly, abnormal dystrophin can be acquired when the coxsackie virus cleaves dystrophin during viral myocarditis.) This protein provides a network that supports the sarcolemma and also connects to the sarcomere. The progressive functional defect in both cardiac and skeletal muscle reflects vulnerability to mechanical stress. Dystrophin is associated at the membrane with a complex of other proteins, such as metavinculin, abnormalities of which also cause dilated cardiomyopathy. Defects in the sarcolemmal channel proteins (*channelopathies*) are generally associated with primary arrhythmias, but mutations in *SCN5A*, distinct from those that cause the Brugada or long-QT syndromes, have been implicated in dilated cardiomyopathy with conduction disease.

Nuclear membrane protein defects in cardiac and skeletal muscle occur in either autosomal (lamin A/C) or X-linked (emerin) patterns. These defects are associated with a high prevalence of atrial arrhythmias and conduction system disease, which can occur in some family members without or before detectable cardiomyopathy.

Intercalated disks contribute to intracellular connections, allowing mechanical and electrical coupling between cells and also connections to desmin filaments within the cell. Mutations in proteins of the desmosomal complex compromise attachment of the myocytes, which can become disconnected and die, to be replaced by fat and fibrous tissue. These areas are highly arrhythmogenic and may dilate to form aneurysms. Although more often noted in the right ventricle (arrhythmogenic right ventricular dysplasia), this condition can affect both ventricles and has also been termed "arrhythmogenic cardiomyopathy."

Owing to the conservation of signaling pathways in multiple systems, we may expect to discover more extracardiac manifestations of genetic abnormalities initially considered to manifest exclusively in the heart. In contrast, the monogenic disorders of metabolism that affect the heart are already clearly recognized to affect multiple organ systems. Currently, it is most important to diagnose defective enzymes for which specific enzyme replacement therapy can now ameliorate the course of disease, such as with alpha-galactosidase A deficiency (Fabry's disease). Abnormalities of mitochondrial DNA (maternally transmitted) impair energy production with multiple clinical manifestations, including impaired cognitive function and skeletal myopathy. The phenotypic expression is highly variable depending on the