TABLE 287-4 MAJOR CAUSES OF DILATED CARDIOMYOPATHY (WITH COMMON EXAMPLES)

Inflammatory Myocarditis
Infective
Viral (coxsackie,[a] adenovirus,[a] HIV, hepatitis C)
Parasitic (*T. cruzi*—Chagas' disease, trypanosomiasis, toxoplasmosis)
Bacterial (diphtheria)
Spirochetal (*Borrelia burgdorferi*—Lyme disease)
Rickettsial (Q fever)
Fungal (with systemic infection)
Noninfective
Granulomatous inflammatory disease
Sarcoidosis
Giant cell myocarditis
Eosinophilic myocarditis
Polymyositis, dermatomyositis
Collagen vascular disease
Peripartum cardiomyopathy
Transplant rejection
Toxic
Alcohol
Catecholamines: amphetamines, cocaine
Chemotherapeutic agents (anthracyclines, trastuzumab)
Interferon
Other therapeutic agents (hydroxychloroquine, chloroquine)
Drugs of misuse (emetine, anabolic steroids)
Heavy metals: lead, mercury
Occupational exposure: hydrocarbons, arsenicals
Metabolic[a]
Nutritional deficiencies: thiamine, selenium, carnitine
Electrolyte deficiencies: calcium, phosphate, magnesium
Endocrinopathy
Thyroid disease
Pheochromocytoma
Diabetes
Obesity
Hemochromatosis
Inherited Metabolic Pathway Defects[a]
Familial[a] (See Table 287-3)
Skeletal and cardiac myopathy
Dystrophin-related dystrophy (Duchenne's, Becker's)
Mitochondrial myopathies (e.g., Kearns-Sayre syndrome)
Arrhythmogenic ventricular dysplasia
Hemochromatosis
Associated with other systemic diseases
Susceptibility to immune-mediated myocarditis
Overlap with Nondilated Cardiomyopathy
"Minimally dilated cardiomyopathy"
Hemochromatosis[a]
Amyloidosis[a]
Hypertrophic cardiomyopathy[a] ("burned-out")
"Idiopathic"[a]
Miscellaneous (Shared Elements of Above Etiologies)
Arrhythmogenic right ventricular dysplasia (may also affect left ventricle)[a]
Left ventricular noncompaction[a]
Peripartum cardiomyopathy
Tachycardia-related cardiomyopathy
Supraventricular arrhythmias with uncontrolled rate
Very frequent nonsustained ventricular tachycardia or high premature ventricular complex burden
Left bundle branch block (LBBB) has been implicated as a cause of dilated cardiomyopathy appearing late after idiopathic LBBB and responding with near-normal left ventricle size and function after cardiac resynchronization therapy.

[a]Some specific cases can be linked now to specific genetic mutation in a familial cardiomyopathy; others with similar phenotypes that appear to be acquired or idiopathic may represent genetic factors not yet identified.

The secondary acquired immune response is more specifically addressed against the viral proteins and can include both T-cell infiltration and antibodies to viral proteins. If unchecked, the acquired immune response can perpetuate secondary cardiac damage. Ongoing cytokine release activates matrix metalloproteinases that can disrupt the collagen and elastin scaffolding of the heart, potentiating ventricular dilation. Stimulation of profibrotic factors leads to pathologic interstitial fibrosis. Some of the antibodies triggered through co-stimulation or molecular mimicry also recognize targets within the host myocyte, such as the β-adrenergic receptor, troponin, and Na^+/K^+ ATPase, but it remains unclear whether these antibodies contribute actively to cardiac dysfunction in humans or merely serve as markers of cardiac injury.

It is not known how long the viruses persist in the human heart, whether late persistence of the viral genome continues to be deleterious, or how often a dormant virus can again become pathogenic. Genomes of common viruses have frequently been detected in patients with clinical diagnoses of myocarditis or dilated cardiomyopathy, but there is little information on how often these are present in patients without cardiac disease (see below). Further information is needed to understand the relative timing and contribution of infection, immune responses, and secondary adaptations in the progression of heart failure after viral myocarditis (Fig 287-5).

Clinical Presentation of Viral Myocarditis *Acute viral myocarditis* often presents with symptoms and signs of heart failure. Some patients present with chest pain suggestive of pericarditis or acute myocardial infarction. Occasionally, the presentation is dominated by atrial or ventricular tachyarrhythmias, or by pulmonary or systemic emboli from intracardiac thrombi. Electrocardiographic or echocardiographic abnormalities may also be detected incidentally during evaluation for other diagnoses. The typical patient with presumed viral myocarditis is a young to middle-aged adult who develops progressive dyspnea and weakness within a few days to weeks after a viral syndrome that was accompanied by fever and myalgias.

A small number of patients present with fulminant myocarditis, with rapid progression from a severe febrile respiratory syndrome to cardiogenic shock that may involve multiple organ systems, leading to renal failure, hepatic failure, and coagulopathy. These patients are typically young adults who have recently been dismissed from urgent care settings with antibiotics for bronchitis or oseltamivir for viral syndromes, only to return within a few days in rapidly progressive cardiogenic shock. Prompt triage is vital to provide aggressive support with high-dose intravenous catecholamine therapy and sometimes with temporary mechanical circulatory support. Recognition of patients with this fulminant presentation is potentially life-saving as more than half can survive, with marked improvement demonstrable within the first few weeks. The ejection fraction function of these patients often recovers to near-normal, although residual diastolic dysfunction may limit vigorous exercise for some survivors.

Chronic viral myocarditis is often invoked, but rarely proven, as a diagnosis when no other cause of dilated cardiomyopathy can be identified. However, some cases of otherwise unexplained cardiomyopathy will later be recognized to have a genetic basis, or ultimately found to have resulted from excess alcohol consumption or illicit drugs. There are likely many other causes that cannot yet be identified. The prevalence of previous or persistent viral infection as the cause for chronic dilated cardiomyopathy remains highly controversial.

Laboratory evaluation for myocarditis The initial evaluation for suspected myocarditis includes an ECG, an echocardiogram, and serum levels of troponin and creatine phosphokinase fractions. Magnetic resonance imaging is increasingly used for the diagnosis of myocarditis, which is supported by evidence of increased tissue edema and gadolinium enhancement (Fig. 287-6), particularly in the mid-wall (as distinct from usual coronary artery territories).

Endomyocardial biopsy is not often indicated for the initial evaluation of suspected viral myocarditis unless ventricular tachyarrhythmias suggest possible etiologies of sarcoidosis or giant cell myocarditis. The indications and benefit of endomyocardial biopsy for evaluation of myocarditis or new-onset cardiomyopathy remain controversial.