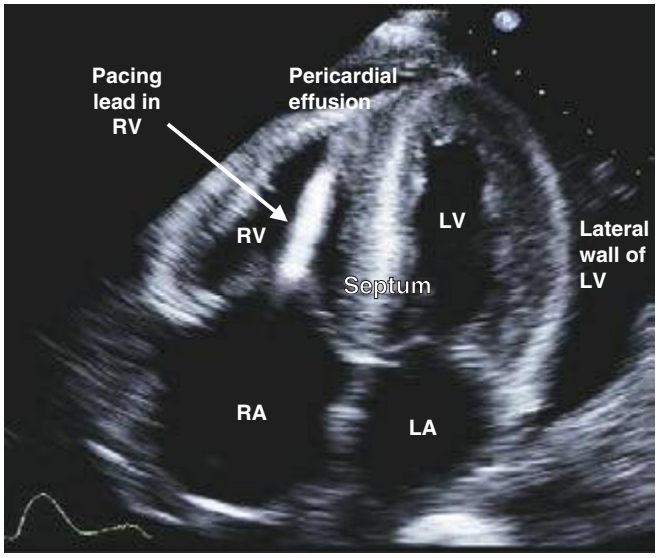

FIGURE 287-13 Restrictive cardiomyopathy—amyloidosis. Echocardiogram showing thickened walls of both ventricles without major chamber dilation. The atria are markedly dilated, consistent with chronically elevated ventricular filling pressures. In this example, there is a characteristic hyperrefractile "glittering" of the myocardium typical of amyloid infiltration, which is often absent (especially with more recent echocardiographic systems of better resolution). The mitral and tricuspid valves are thickened. A pacing lead is visible in the right ventricle (RV), and a pericardial effusion is evident. Note that the echocardiographic and pathologic images are vertically opposite, such that the left ventricle (LV) is by convention on the top right in the echocardiographic image and bottom right in the pathologic images. LA, left atrium; RA, right atrium. *(Image courtesy of Justina Wu, MD, Brigham and Women's Hospital, Boston.)*

The diagnosis of primary or familial amyloidosis can sometimes be made from biopsies of an abdominal fat pad or the rectum, but cardiac amyloidosis is most reliably identified from a biopsy of the heart, in which amyloid fibrils infiltrate the myocardium diffusely, particularly around the conduction system and coronary vessels (Fig. 287-14). Diagnosis of the type of amyloid protein requires immunohistochemistry of biopsied tissue rather than serum or urine electrophoresis, which can lead to incorrect classification.

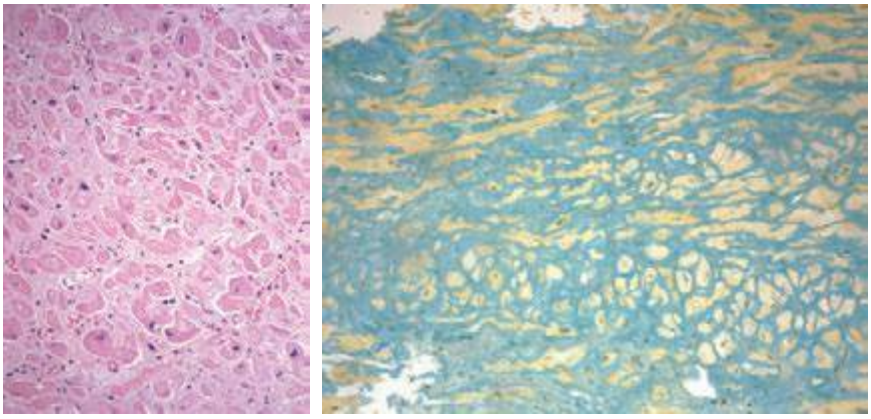

FIGURE 287-14 Amyloidosis—microscopic images of amyloid involving the myocardium. The left panel (hematoxylin and eosin stain) shows glassy, grey-pink amorphous material infiltrating between cardiomyocytes, which stain a darker pink. The right panel shows a sulfated blue stain that highlights the amyloid green and stains the cardiac myocytes yellow. (The Congo red stain can also be used to highlight amyloid; under polarized light, amyloid will have an apple-green birefringence when stained with Congo red.) Images at 100× original magnification. *(Image courtesy of Robert Padera, MD, PhD, Department of Pathology, Brigham and Women's Hospital, Boston.)*

Therapy for all types of amyloid is predominantly for symptoms of fluid retention, which often requires high doses of loop diuretics. Digoxin bound to the amyloid fibrils can reach toxic levels, and should therefore be used only in very low doses, if at all. There is no evidence regarding use of neurohormonal antagonists in amyloid heart disease, where the possible theoretical benefit has to be balanced against the possibility of aggravating postural hypotension and diminishing the crucial heart rate reserve. The risk of intracardiac thrombi may warrant chronic anticoagulation.

The prognosis is worst for primary amyloid, with a median survival of 6–12 months after symptoms of heart failure. If present, multiple myeloma is treated with chemotherapy, the extent of which is often limited by the potential of worsening cardiac dysfunction. Immunoglobulin-associated amyloid has occasionally been treated with sequential heart transplantation and delayed bone marrow transplant, with frequent recurrence of amyloid in the transplanted heart. Abnormal transthyretin-associated cardiac amyloid has a somewhat better prognosis and can be treated in selected patients with heart and liver transplantation. Senile cardiac amyloid has the slowest progression and best overall prognosis.

FIBROTIC RESTRICTIVE CARDIOMYOPATHY

Progressive fibrosis can cause restrictive myocardial disease without ventricular dilation. Thoracic radiation, common for breast and lung cancer or mediastinal lymphoma, can produce early or late restrictive cardiomyopathy. Patients with *radiation cardiomyopathy* may present with a possible diagnosis of constrictive pericarditis, as the two conditions often coexist. Careful hemodynamic evaluation and, often, endomyocardial biopsy should be performed if considering pericardial stripping surgery, which is unlikely to be successful in the presence of underlying restrictive cardiomyopathy.

Scleroderma causes small vessel spasm and ischemia that can lead to a small, stiff heart with reduced ejection fraction without dilation. The pulmonary hypertension associated with scleroderma may lead to more clinical right heart failure because of concomitant fibrotic disease of the right ventricle. Doxorubicin causes direct myocyte injury usually leading to dilated cardiomyopathy, but the limited degree of dilation may result from increased fibrosis, which restricts remodeling.

ENDOMYOCARDIAL DISEASE

The physiologic picture of elevated filling pressures with atrial enlargement and preserved ventricular contractility with normal or reduced ventricular volumes can result from extensive fibrosis of the endocardium, without transmural myocardial disease. For patients who have not lived in the equatorial regions, this picture is rare, and when seen is often associated with a history of chronic hypereosinophilic syndrome (*Löffler's endocarditis*), which is more common in men than women. In this disease, persistent hypereosinophilia of >1500 eos/mm^3 for at least 6 months can cause an acute phase of eosinophilic injury in the endocardium (see earlier discussion of eosinophilic myocarditis), with systemic illness and injury to other organs. There is usually no obvious cause, but the hypereosinophilia can occasionally be explained by allergic, parasitic, or malignant disease. It is postulated to be followed by a period in which cardiac inflammation is replaced by evidence of fibrosis with superimposed thrombosis. In severe disease, the dense fibrotic layer can obliterate the ventricular apices and extend to thicken and tether the AV valve leaflets. The clinical disease may present with heart failure, embolic events, and atrial arrhythmias. While plausible, the sequence of transition from eosinophilic myocarditis or Löffler's endocarditis to endomyocardial fibrosis has not been clearly demonstrated.

In tropical countries, up to one-quarter of heart failure may be due to *endomyocardial fibrosis*,