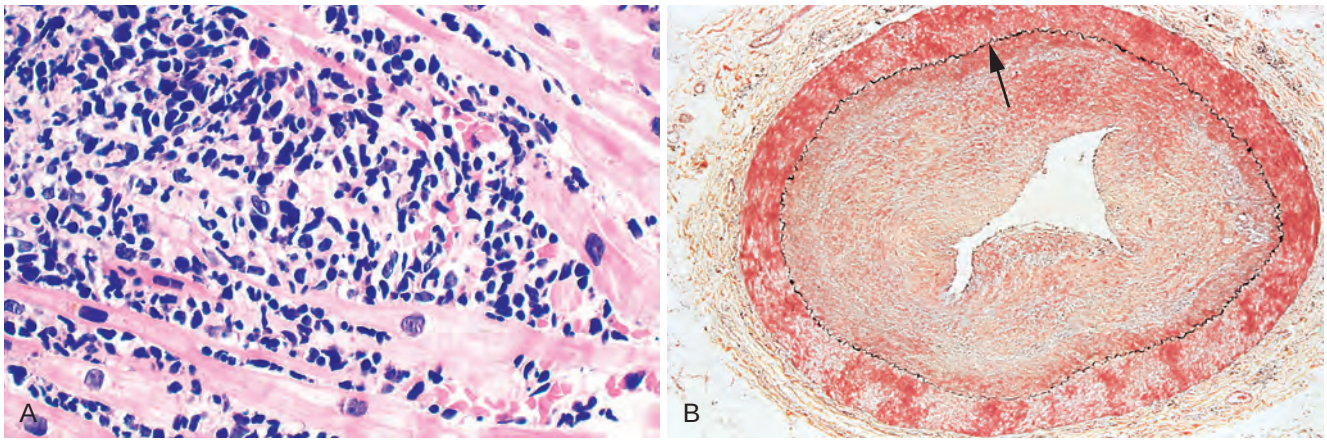

Figure 12-39 Complications of heart transplantation. **A,** Cardiac allograft rejection typified by lymphocytic infiltrate associated with cardiac myocyte damage. **B,** Allograft arteriopathy, with severe diffuse concentric intimal thickening producing critical stenosis. The internal elastic lamina *(arrow)* and media are intact (Movat pentachrome stain, elastin black). (**B,** Reproduced with permission from Salomon RN, et al: Human coronary transplantation-associated arteriosclerosis. Evidence for chronic immune reaction to activated graft endothelial cells. Am J Pathol 138:791, 1991.)

symptomatic pericardial effusions or a mass-effect that is sufficient to restrict cardiac filling. Myocardial metastases are usually clinically silent or have nonspecific features, such as a generalized defect in ventricular contractility or compliance. Bronchogenic carcinoma or malignant lymphoma may infiltrate the mediastinum extensively, causing encasement, compression, or invasion of the superior vena cava with resultant obstruction to blood coming from the head and upper extremities *(superior vena cava syndrome)*. Renal cell carcinoma often invades the renal vein, and may grow as a continuous column of tumor up the inferior vena cava and into the right atrium, blocking venous return to the heart.

Noncardiac tumors may also affect cardiac function indirectly, sometimes via circulating tumor-derived substances. The consequences include nonbacterial thrombotic endocarditis, carcinoid heart disease, pheochromocytoma-associated myocardial damage and myeloma-associated AL-type amyloidosis.

Complications of chemotherapy were discussed earlier in this chapter. Radiation used to treat breast, lung, or mediastinal neoplasms can cause pericarditis, pericardial effusion, myocardial fibrosis, and chronic pericardial disorders. Other cardiac effects of radiation therapy include accelerated coronary artery disease and mural and valvular endocardial fibrosis.

Cardiac Transplantation

Transplantation of cardiac allografts is now frequently performed (approximately 3000 per year worldwide) for severe, intractable heart failure of diverse causes—most commonly DCM and IHD. Three major factors have contributed to the improved outcome of cardiac transplantation since the first human to human transplant in 1967: (1) more effective immunosuppressive therapy (including the use of cyclosporin A, glucocorticoids, and other agents), (2) careful selection of candidates, and (3) early histopathologic diagnosis of acute allograft rejection by endomyocardial biopsy.

Of the major complications, allograft rejection is the primary problem requiring surveillance; routine endomyocardial biopsy is the only reliable means of diagnosing acute cardiac rejection before substantial myocardial damage has occurred and at a stage that is reversible in the majority of instances. Classic *cellular rejection* is characterized by interstitial lymphocytic inflammation with associated myocyte damage; the histology resembles myocarditis (Fig. 12-39*A*). There may also be interstitial edema due to vascular injury, and local cytokine elaboration can impact myocardial contractility without necessarily eliciting myocyte damage. Increasingly, *antibody-mediated rejection* is also recognized as a pathologic mechanism of injury; donor-specific antibodies directed against major histocompatibility complex proteins lead to complement activation and the recruitment of Fc-receptor-bearing cells. Mild rejection may resolve spontaneously, while prompt recognition of more severe episodes allows successful treatment by augmenting baseline levels of immunosuppression; occasionally aggressive anti-T cell or anti-B cell immunotherapy, with or without plasmapheresis may be necessary.

Allograft arteriopathy is the single most important long-term limitation for cardiac transplantation. It is a late, progressive, diffusely stenosing intimal proliferation in the coronary arteries (Fig. 12-39*B*), leading to ischemic injury. Within 5 years of transplantation, 50% of patients develop significant allograft arteriopathy, and virtually all patients have lesions within 10 years. The pathogenesis of allograft arteriopathy involves immunologic responses that induce local production of growth factors that promote intimal smooth muscle cell recruitment and proliferation with ECM synthesis. Allograft arteriopathy is a particularly vexing problem because it can lead to silent MI (transplant patients have denervated hearts and do not experience angina), progressive CHF, or sudden cardiac death.

Other postoperative problems include infection and malignancies, particularly Epstein-Barr virus-associated B-cell lymphomas that arise in the setting of chronic T-cell immunosuppression. Despite these problems, the overall outlook is good; the 1-year survival is 90% and 5-year survival is greater than 60%.