

factor that can also cause migratory thrombophlebitis (Trousseau syndrome, Chapter 4). Endocardial trauma, as from an indwelling catheter, is another well-recognized predisposing condition, and right-sided valvular and endocardial thrombotic lesions frequently track along the course of pulmonary artery catheters.

### Endocarditis of Systemic Lupus Erythematosus (Libman-Sacks Disease)

Mitral and tricuspid valvulitis with small, sterile vegetations, called *Libman-Sacks endocarditis*, is occasionally encountered in systemic lupus erythematosus. Due to the use of steroids, the incidence of this complication has been greatly reduced. The lesions are small (1 to 4 mm in diameter), single or multiple, sterile, pink vegetations with a warty (verrucous) appearance. They may be located on the undersurfaces of the atrioventricular valves, on the valvular endocardium, on the chords, or on the mural endocardium of atria or ventricles. Histologically the vegetations consist of a finely granular, fibrinous eosinophilic material containing cellular debris including nuclear remnants. Vegetations are often associated with an intense valvulitis, characterized by fibrinoid necrosis of the valve substance and reflecting the activation of complement and recruitment of Fc-receptor-bearing cells.

Thrombotic heart valve lesions with sterile vegetations or rarely fibrous thickening can occur in the setting of the antiphospholipid syndrome, which can also induce a hypercoagulable state (Chapter 4). The mitral valve is more frequently involved than the aortic valve, and regurgitation is the usual functional abnormality.

### Carcinoid Heart Disease

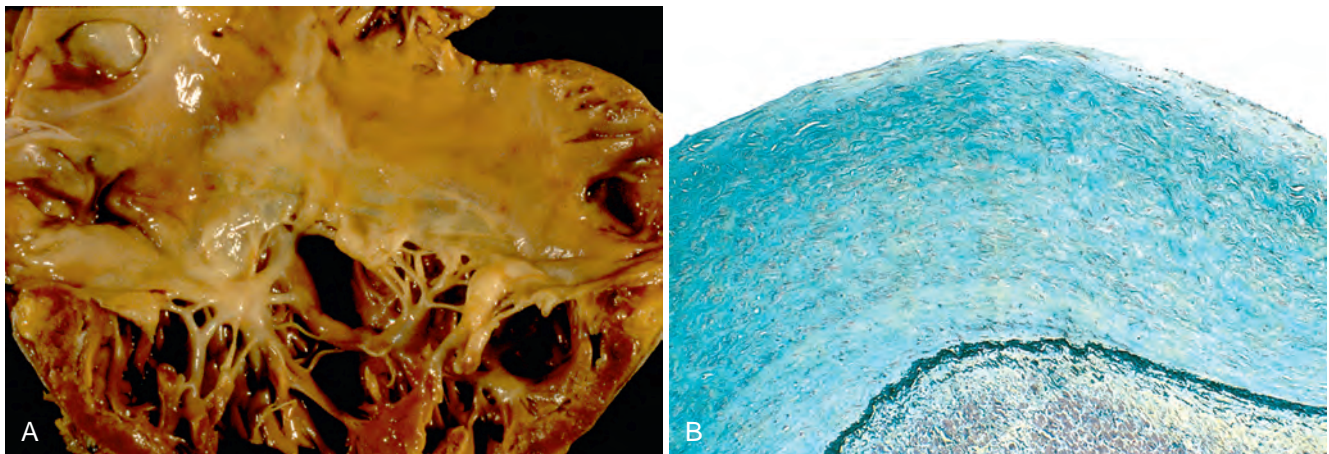
The *carcinoid syndrome* refers to a systemic disorder marked by flushing, diarrhea, dermatitis, and bronchoconstriction that is caused by bioactive compounds such as serotonin released by *carcinoid tumors* (Chapter 17). *Carcinoid heart disease* refers to the cardiac manifestations caused by the bioactive compounds and occurs in roughly half of the patients in whom the systemic syndrome develops. Cardiac lesions do not typically occur until there is a

massive hepatic metastatic burden, since the liver normally catabolizes circulating mediators before they can affect the heart. Classically, endocardium and valves of the right heart are primarily affected since they are the first cardiac tissues bathed by the mediators released by gastrointestinal carcinoid tumors. The left side of the heart is afforded some measure of protection because the pulmonary vascular bed degrades the mediators. However, left heart carcinoid lesions can occur in the setting of atrial or septal defects and right-to-left flow, or can be elicited by primary pulmonary carcinoid tumors.

**Pathogenesis.** The mediators elaborated by carcinoid tumors include serotonin (5-hydroxytryptamine), kallikrein, bradykinin, histamine, prostaglandins, and tachykinins. Although it is not clear which of these is causal, plasma levels of serotonin and urinary excretion of the serotonin metabolite 5-hydroxyindoleacetic acid correlate with the severity of the cardiac lesions. The valvular plaques in carcinoid syndrome are also similar to lesions that occur in patients taking fenfluramine (an appetite suppressant) or ergot alkaloids (for migraine headaches); interestingly, these agents affect systemic serotonin metabolism. Similarly, left-sided plaques have been reported following methysergide or ergotamine therapy for migraines; notably, these drugs are metabolized to serotonin as they pass through the pulmonary vasculature. Despite this tantalizing evidence, however, it is not known how serotonin might induce the observed cardiac changes, nor has it been proven that treatment with serotonin inhibitors has any effect on the development or progression of heart lesions.

### MORPHOLOGY

The cardiovascular lesions associated with the carcinoid syndrome are distinctive, glistening white intimal plaque-like thickenings of the endocardial surfaces of the cardiac chambers and valve leaflets (Fig. 12-27). The lesions are composed of smooth muscle cells and sparse collagen fibers embedded in an acid mucopolysaccharide-rich matrix material. Underlying structures are intact. With right-sided involvement, typical findings are tricuspid insufficiency and pulmonary stenosis.



**Figure 12-27** Carcinoid heart disease. **A**, Characteristic endocardial fibrotic lesion involving the right ventricle and tricuspid valve. **B**, Microscopic appearance of carcinoid heart disease with intimal thickening. Movat stain shows myocardial elastic tissue (black) underlying the acid mucopolysaccharide-rich lesion (blue-green). The underlying myocardium is unaffected.