opening, causing intermittent obstruction that may be position-dependent. Sometimes mobile tumors exert a "wrecking-ball" effect, causing damage to the valve leaflets.

Histologically, myxomas are composed of stellate or globular myxoma cells embedded within an abundant acid mucopolysaccharide ground substance (Fig. 12-38*B*). Peculiar vessel-like or gland-like structures are characteristic. Hemorrhage and mononuclear inflammation are usually present.

The major clinical manifestations are due to valvular "ball-valve" obstruction, embolization, or a syndrome of constitutional symptoms, such as fever and malaise. Sometimes fragmentation and systemic embolization calls attention to these lesions. Constitutional symptoms are probably due to the elaboration by some myxomas of the cytokine interleukin-6, a major mediator of the acute-phase response. Echocardiography provides the opportunity to identify these masses noninvasively. Surgical removal is usually curative; rarely, presumably with incomplete excision, the neoplasm can recurs months to years later.

Lipoma. Lipomas are localized, well-circumscribed, benign tumors composed of mature fat cells that can occur in the subendocardium, subepicardium, or myocardium. They may be asymptomatic, or produce ball-valve obstructions or arrhythmias. Lipomas are most often located in the left ventricle, right atrium, or atrial septum. In the atrial septum, nonneoplastic depositions of fat sometimes occur that are called "lipomatous hypertrophy." These lesions include white and brown adipose tissue, as well as small interspersed areas of myocardium.

Papillary Fibroelastoma. *Papillary fibroelastomas* are curious, usually incidental, sea-anemone-like lesions, most often identified at autopsy. They may embolize and thereby become clinically important. Clonal cytogenetic abnormalities have been reported, suggesting that fibroelastomas are unusual benign neoplasms. They resemble the much smaller, usually trivial, *Lambl excrescences* that may represent remotely organized thrombus on the aortic valves of older individuals.

MORPHOLOGY

Papillary fibroelastomas are usually (>80%) located on valves, particularly the ventricular surfaces of semilunar valves and the atrial surfaces of atrioventricular valves. Each lesion, typically 1 to 2 cm in diameter, consists of a distinctive cluster of hairlike projections up to 1 cm in length. Histologically, the projections are covered by a surface endothelium surrounding a core of myxoid connective tissue with abundant mucopolysaccharide matrix and elastic fibers.

Rhabdomyoma. *Rhabdomyomas* are the most frequent primary tumor of the pediatric heart, and are commonly discovered in the first years of life because of obstruction of a valvular orifice or cardiac chamber. Approximately half of cardiac rhabdomyomas are due to sporadic mutations; the other 50% of cases are associated with tuberous sclerosis (Chapter 28), with mutations in the *TSC1* or *TSC2* tumor suppressor gene. The *TSC1* and *TSC2* proteins (hamartin and tuberin, respectively) function in a complex that inhibits the activity of the mammalian target of rapamycin (mTOR), a kinase that stimulates cell growth and regulates cell size. *TSC1* or *TSC2* expression is often absent in tuberous sclerosis-associated rhabdomyomas, providing a mechanism for myocyte overgrowth. Because rhabdomyomas often regress spontaneously, they may be considered as hamartomas rather than true neoplasms.

MORPHOLOGY

Rhabdomyomas are gray-white myocardial masses that can be small or up to several centimeters in diameter. They are usually multiple and involve the ventricles preferentially, protruding into the lumen. Microscopically, they are composed of bizarre, markedly enlarged myocytes. Routine histologic processing often artifactually reduces the abundant cytoplasm to thin strands that stretch from the nucleus to the surface membrane, an appearance referred to as "spider" cells.

Sarcoma. Cardiac *angiosarcomas* and other sarcomas are not clinically or morphologically distinctive from their counterparts in other locations, and so require no further comment here.

Cardiac Effects of Noncardiac Neoplasms

With enhanced patient survival due to diagnostic and therapeutic advances, significant cardiovascular effects of noncardiac neoplasms and their therapy are increasingly encountered (Table 12-15). The pathologic consequences include direct tumor infiltration, effects of circulating mediators, and therapeutic complications.

The most frequent metastatic tumors involving the heart are carcinomas of the lung and breast, melanomas, leukemias, and lymphomas. Metastases can reach the heart and pericardium by retrograde lymphatic extension (most carcinomas), by hematogenous seeding (many tumors), by direct contiguous extension (primary carcinoma of the lung, breast, or esophagus), or by venous extension (tumors of the kidney or liver). Clinical symptoms are most often associated with pericardial spread, which can cause

Table 12-15 Cardiovascular Effects of Noncardiac Neoplasms

Direct Consequences of Tumor
Pericardial and myocardial metastases
Large vessel obstruction
Pulmonary tumor emboli
Indirect Consequences of Tumor (Complications of Circulating Mediators)
Nonbacterial thrombotic endocarditis
Carcinoid heart disease
Pheochromocytoma-associated heart disease
Myeloma-associated amyloidosis
Effects of Tumor Therapy
Chemotherapy
Radiation therapy

Modified from Schoen FJ, et al: Cardiac effects of non-cardiac neoplasms. Cardiol Clin 2:657, 1984.