Mature male-female worm pairs then migrate once again and settle in the venous system (commonly the portal or pelvic veins). Females produce hundreds to thousands of eggs per day which secrete proteases and elicit localized inflammatory reactions. This inflammatory response to egg migration is necessary for passive transfer across the intestine and, in the case of *S. haemtobium*, bladder walls, allowing the eggs to be shed in stool or urine, respectively. Infection of freshwater snails completes the life cycle.

Eggs that are carried by the portal circulation into the hepatic parenchyma can cause severe chronic inflammation in the liver. This immune response to *S. mansoni* and *S. japonicum* eggs is responsible for the most serious complication of schistosomiasis , liver fibrosis. The helper T-cell response in the early stage is dominated by T_H1 cells that produce IFN-γ, which stimulates macrophages to secrete high levels of the cytokines TNF, IL-1, and IL-6 that cause fever. Chronic schistosomiasis is associated with a dominant T_H2 response, associated with the presence of alternatively activated macrophages. Both types of helper T cells contribute to the formation of granulomas surrounding eggs in the liver. Hepatic fibrosis is a serious manifestation of chronic schistosomiasis in which T_H2 cells and alternatively activated macrophages may play the major role.

MORPHOLOGY

In early *S. mansoni* or *S. japonicum* infections, white, pinhead-sized granulomas are scattered throughout the gut and liver. At the center of the granuloma is the schistosome egg, which contains a miracidium; this degenerates over time and calcifies. The granulomas are composed of macrophages, lymphocytes, neutrophils, and eosinophils, which are distinctive for helminth infections (Fig. 8-54). The liver is darkened by regurgitated heme-derived pigments from the schistosome gut, which, like malaria pigments, are iron-free and accumulate in Kupffer cells and splenic macrophages.

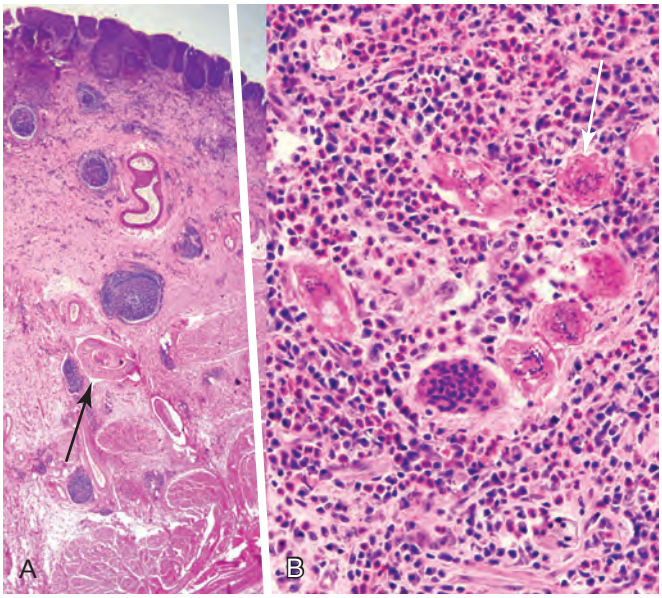

Figure 8-54 *Schistosoma hematobium* infection of the bladder (left) showing dense fibrosis, scattered granulomas, and a cross section of adult worms in a vessel *(arrow)*. High magnification (right) demonstrates miracidium-containing eggs *(arrow)*, prominent eosinophils, histiocytes, and giant cells.

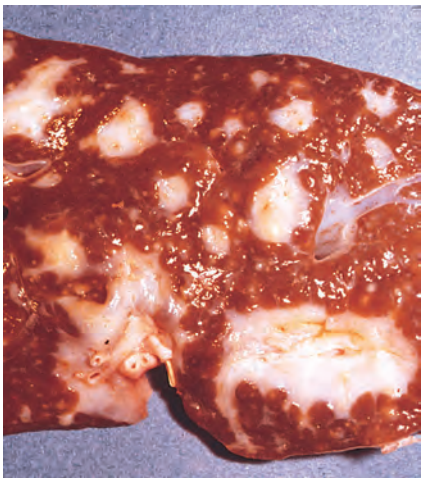

Figure 8-55 Pipe-stem fibrosis of the liver due to chronic *Schistosoma japonicum* infection.

In late *S. mansoni* or *S. japonicum* infections, inflammatory patches or pseudopolyps may form in the colon. The surface of the liver is bumpy, and cut surfaces reveal granulomas and widespread fibrosis and portal enlargement without intervening regenerative nodules. Because these fibrous triads resemble the stem of a clay pipe, the lesion is named **pipe-stem fibrosis** (Fig. 8-55). The fibrosis often obliterates the portal veins, leading to portal hypertension, severe congestive splenomegaly, esophageal varices, and ascites. Schistosome eggs, diverted to the lung through portal collaterals, may produce granulomatous pulmonary arteritis with intimal hyperplasia, progressive arterial obstruction, and ultimately heart failure (cor pulmonale). On histologic examination, arteries in the lungs show disruption of the elastic layer by granulomas and scars, luminal organizing thrombi, and angiomatoid lesions similar to those of idiopathic pulmonary hypertension (Chapter 15). Patients with hepatosplenic schistosomiasis also have an increased frequency of mesangioproliferative or membranous glomerulopathy (Chapter 20), in which glomeruli contain deposits of immunoglobulin and complement but rarely schistosome antigen.

In *S. haematobium* infection, inflammatory cystitis due to massive egg deposition and granulomas appears early, leading to mucosal erosions and hematuria. Later, the granulomas calcify and develop a sandy appearance, which, if severe, may line the wall of the bladder and cause a dense concentric rim (calcified bladder) on radiographic films. The most frequent complication of *S. haematobium* infection is inflammation and fibrosis of the ureteral walls, leading to obstruction, hydronephrosis, and chronic pyelonephritis. There is also an association between urinary schistosomiasis and squamous cell carcinoma of the bladder (Chapter 21).

Lymphatic Filariasis

Lymphatic filariasis is transmitted by mosquitoes and is caused by closely related nematodes, *Wuchereria bancrofti* and *Brugia* species (*B. malayi* or *B. timori*), which are responsible for 90% and 10%, respectively, of the 90 million infections worldwide. In endemic areas, which include parts of Latin America, sub-Saharan Africa, and Southeast Asia, filariasis causes a spectrum of diseases.