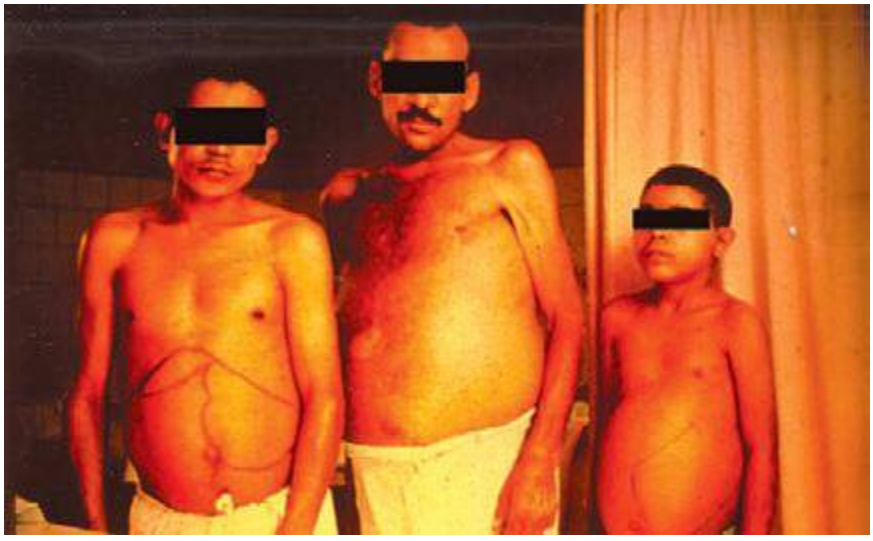

FIGURE 259-3 Chronic hepatosplenomegaly caused by schistosomiasis mansoni. Liver and spleen enlargement, ascites, and wasting are characteristically seen in patients with chronic *Schistosoma mansoni* infection.

chronic infection, the accumulation of antigen–antibody complexes results in deposits in renal glomeruli and may cause significant kidney disease.

The better-studied pathologic sequelae in schistosomiasis are those observed in liver disease. Ova that are carried by portal blood embolize to the liver. Because of their size (~150 × 60 μm in the case of *S. mansoni*), they lodge at presinusoidal sites, where granulomas are formed. These granulomas contribute to the hepatomegaly observed in infected individuals (Fig. 259-3). Schistosomal liver enlargement is also associated with certain class I and class II human leukocyte antigen (HLA) haplotypes and markers; its genetic basis appears to be polygenic. Presinusoidal portal blockage causes several hemodynamic changes, including portal hypertension and associated development of portosystemic collaterals at the esophagogastric junction and other sites. Esophageal varices are most likely to break and cause repeated episodes of hematemesis. Because changes in hepatic portal blood flow occur slowly, compensatory arterialization of the blood flow through the liver is established. Although this compensatory mechanism may be associated with certain metabolic side effects, retention of hepatocyte perfusion permits maintenance of normal liver function for several years.

The second most significant pathologic change in the liver relates to fibrosis. It is characteristically periportal (Symmers' clay pipe–stem fibrosis) but may be diffuse. Fibrosis, when diffuse, may be seen in areas of egg deposition and granuloma formation but is also seen in distant locations such as portal tracts. Schistosomiasis results in pure fibrotic lesions in the liver; cirrhosis occurs only when other toxic factors or infectious agents (e.g., hepatitis B or C virus) are involved. Deposition of fibrotic tissue in the extracellular matrix results from the interaction of T lymphocytes with cells of the fibroblast series; several cytokines, such as interleukin (IL) 2, IL-4, IL-1, and transforming growth factor β, are known to stimulate fibrogenesis. The process may be dependent on the genetic constitution of the host. Furthermore, regulatory cytokines that can suppress T cell responses and fibrogenesis, such as IL-10, interferon γ, or IL-12, may play a role in modulating the response.

Although the above description focuses on granuloma formation and fibrosis of the liver, similar processes occur in urogenital schistosomiasis. Granuloma formation at the lower end of the ureters obstructs urinary flow, with subsequent development of hydroureter and hydronephrosis. Similar lesions in the urinary bladder cause the protrusion of papillomatous structures into its cavity; these may ulcerate and/or bleed. The chronic stage of infection is associated with scarring and deposition of calcium in the bladder wall. Among women, involvement of the birth canal can cause cervical or vaginal wall polyps and friability leading to contact bleeding, with an apparently increased risk of HIV transmission. Secondary infertility or subfecundity can also result from female genital schistosomiasis involving the uterus, fallopian tubes, or ovaries. Among men, *S. haematobium* infection can result in prostatic and testicular lesions with hematospermia. Superficial cutaneous lesions of the perineum can occur in both sexes.

Studies on immunity to schistosomiasis, whether innate or adaptive, have expanded our knowledge of the components of these responses and target antigens. The critical question, however, is whether humans acquire immunity to schistosomes. Epidemiologic data suggest the onset of acquired immunity during the course of infection in young adults. Curative treatment of infected populations in endemic areas is followed by differentiation in the pattern of reinfection. Some (susceptible) individuals acquire reinfection rapidly, whereas other (resistant) individuals are reinfected slowly. This difference may be explained by differences in transmission, immunologic response, or genetic susceptibility. The mechanism of acquired immunity involves antibodies, complement, and several effector cells, particularly eosinophils. Furthermore, the intensity of schistosome infection has been correlated with a region in chromosome 5. In several studies, a few protective schistosome antigens have been identified as vaccine candidates, but none has been fully evaluated in human populations to date.

CLINICAL FEATURES

In general, disease manifestations of schistosomiasis occur in three stages, which vary not only by species but also by intensity of infection and other host factors, such as age and genetics of the human host. During the phase of cercarial invasion, a form of dermatitis may be observed. This so-called swimmers' itch occurs most often with *S. mansoni* and *S. japonicum* infections, manifesting 2 or 3 days after invasion as an itchy maculopapular rash on the affected areas of the skin. The condition is particularly severe when humans are exposed to avian schistosomes. This form of cercarial dermatitis is also seen around freshwater lakes in the northern United States, particularly in the spring and summer months. Cercarial dermatitis is a self-limiting clinical entity. During worm maturation and at the beginning of oviposition (i.e., 4–8 weeks after skin invasion), acute schistosomiasis or Katayama syndrome—a serum sickness–like illness with fever, generalized lymphadenopathy, and hepatosplenomegaly—may develop. Individuals with acute schistosomiasis have a high degree of peripheral-blood eosinophilia. Parasite-specific antibodies may be detected before schistosome eggs are identified in excreta.

Acute schistosomiasis has become an important clinical entity worldwide because of increased travel to endemic areas. Travelers are exposed to parasites while swimming or wading in freshwater bodies and upon their return present with acute manifestations. The course of acute schistosomiasis is generally benign, but central nervous system (CNS) schistosomiasis and even deaths are occasionally reported in association with heavy exposure to schistosomes among travelers and migrants.

The main clinical manifestations of chronic schistosomiasis are species-dependent. Intestinal species (*S. mansoni*, *S. japonicum*, *S. mekongi*, and *S. intercalatum*) cause intestinal and hepatosplenic disease as well as several manifestations associated with portal hypertension. During the intestinal phase, which may begin a few months after infection and may last for years, symptomatic patients characteristically have colicky abdominal pain, bloody diarrhea, and anemia. Patients may also report fatigue and an inability to perform daily routine functions and may show evidence of growth retardation and anemia. This more subtle form of schistosomiasis morbidity is generally