underappreciated. The severity of intestinal schistosomiasis is often related to the intensity of the worm burden. The disease runs a chronic course and may result in colonic polyposis, which has been reported from some endemic areas, such as Egypt and Uganda.

The hepatosplenic phase of disease manifests early (during the first year of infection, particularly in children) with liver enlargement due to parasite-induced granulomatous lesions. Hepatomegaly is seen in ~15–20% of infected individuals; it correlates roughly with intensity of infection, occurs more often in children, and may be related to specific HLA haplotypes. In subsequent phases of infection, presinusoidal blockage of blood flow leads to portal hypertension and splenomegaly (Fig. 259-3). Moreover, portal hypertension may lead to varices at the lower end of the esophagus and at other sites. Patients with schistosomal liver disease may have right-upper-quadrant "dragging" pain during the hepatomegaly phase, and this pain may move to the left upper quadrant as splenomegaly progresses. Bleeding from esophageal varices may, however, be the first clinical manifestation of this phase. Patients may experience repeated bleeding but seem to tolerate its impact, because an adequate total hepatic blood flow permits normal liver function for a considerable period. In late-stage disease, typical fibrotic changes occur along with liver function deterioration and the onset of ascites, hypoalbuminemia, and defects in coagulation. Intercurrent viral infections of the liver (especially hepatitis B and C), toxic insults (excessive ethanol ingestion or exposure to organic poisons or aflatoxin), or nutritional deficiencies may well accelerate or exacerbate the deterioration of hepatic function.

The extent and severity of intestinal and hepatic disease in schistosomiasis mansoni and japonica have been well described. Although it was originally thought that *S. japonicum* might induce more severe disease manifestations because the adult worms can produce 10 times more eggs than *S. mansoni*, subsequent field studies have not supported this claim. Clinical observations of individuals infected with *S. mekongi* or *S. intercalatum* have been less detailed, partly because of the limited geographic distribution of these organisms.

The clinical manifestations of *S. haematobium* infection occur relatively early and involve a high percentage of infected individuals. Up to 80% of children infected with *S. haematobium* have dysuria, frequency, and hematuria. Hematuria may sometimes occur only at the end of voiding. Urine examination reveals blood and albumin as well as an unusually high frequency of bacterial urinary tract infections and urinary sediment cellular metaplasia. These manifestations correlate with the intensity of infection, the presence of urinary bladder granulomas, and subsequent ulceration. Along with local effects of granuloma formation in the urinary bladder, obstruction of the lower end of the ureters results in hydroureter and hydronephrosis, which may be seen in 25–50% of infected children. As infection progresses, bladder granulomas undergo fibrosis, which results in typical sandy patches visible on cystoscopy. In many endemic areas, an association between squamous cell carcinoma of the bladder and *S. haematobium* infection has been observed. Such malignancy is detected in a younger age group than is transitional cell carcinoma. In fact, *S. haematobium* has now been classified as a human carcinogen. Genital schistosomiasis (described in the previous section) is a common presenting symptom among adults of both sexes.

Significant disease may occur in other organs during chronic schistosomiasis. Lung and CNS disease have been documented; other sites, such as the skin and the genital organs, are less frequently affected. In pulmonary schistosomiasis, embolized eggs lodge in small arterioles, producing acute necrotizing arteriolitis and granuloma formation. During *S. mansoni* and *S. japonicum* infection, schistosome eggs reach the lungs after the development of portosystemic collateral circulation; in *S. haematobium* infection, ova may reach the lungs directly via connections between the vesical and systemic circulation. Subsequent fibrous tissue deposition leads to endarteritis obliterans, pulmonary hypertension, and cor pulmonale. The most common symptoms are cough, fever, and dyspnea. Cor pulmonale may be diagnosed radiologically on the basis of prominence of the right side of the heart and dilation of the pulmonary artery. Frank evidence of right-sided heart failure may be seen in late cases.

Although less common than pulmonary manifestations, CNS schistosomiasis is important, characteristically occurring in association with *S. japonicum* infection. Migratory worms deposit eggs in the brain and induce a granulomatous response. The frequency of this manifestation among infected individuals in some endemic areas (e.g., the Philippines) is calculated at 2–4%. Jacksonian epilepsy due to *S. japonicum* infection is the second most common cause of epilepsy in these areas. *S. mansoni* and *S. haematobium* infections have been associated with transverse myelitis. This syndrome is thought to be due to eggs traveling to the venous plexus around the spinal cord. In schistosomiasis mansoni, transverse myelitis is usually seen in the chronic stage after the development of portal hypertension and portosystemic shunts, which allow ova to travel to the spinal cord veins. This proposed sequence of events has been challenged because of a few reports of transverse myelitis occurring early in the course of *S. mansoni* infection. More information is needed to confirm these observations. During schistosomiasis caused by *Schistosoma haematobium*, ova may travel through communication between vesical and systemic veins, resulting in spinal cord disease that may be detected at any stage of infection. Pathologic study of lesions in schistosomal transverse myelitis may reveal eggs along with necrotic or granulomatous lesions. Patients usually present with acute or rapidly progressing lower-leg weakness accompanied by sphincter dysfunction.

DIAGNOSIS

Physicians in areas not endemic for schistosomiasis face considerable diagnostic challenges. In the most common clinical presentation, a traveler returns with symptoms and signs of acute syndromes of schistosomiasis—namely, cercarial dermatitis or Katayama syndrome. Central to a correct diagnosis is a thorough inquiry into the patient's history of travel and exposure to freshwater bodies—whether slow- or fast-running—in an endemic area. Differential diagnosis of fever in returned travelers includes a spectrum of infections whose etiologies are viral (e.g., dengue fever), bacterial (e.g., enteric fever, leptospirosis), rickettsial, or protozoal (e.g., malaria). In cases of Katayama syndrome, prompt diagnosis is essential and is based on clinical presentation, high-level peripheral-blood eosinophilia, and a positive serologic assay for schistosomal antibodies. Two tests are available at the CDC: the Falcon assay screening test/enzyme-linked immunosorbent assay (FAST-ELISA) and the confirmatory enzyme-linked immunoelectrotransfer blot (EITB). Both tests are highly sensitive and ~96% specific. In some instances, examination of stool or urine for ova may yield positive results.

Individuals with established infection are diagnosed by a combination of geographic history, characteristic clinical presentation, and presence of schistosome ova in excreta. The diagnosis may also be established with the serologic assays mentioned above or with those that detect circulating schistosome antigens. These assays can be applied to blood, urine, or other body fluids (e.g., cerebrospinal fluid). For suspected schistosome infection, stool examination by the Kato thick smear or any other concentration method generally identifies most patients with heavy infection but does not identify all lightly infected individuals. For the latter patients, a point-of-care test to detect parasite circulating cathodic antigen in urine may prove very useful in establishing the presence of active *S. mansoni* infection and in monitoring the clearance of infection after treatment. For *S. haematobium*, urine may be examined by microscopy of sediment or by filtration of a known volume through Nuclepore filters. Sensitivity can be further improved by testing for parasite DNA in urine sediment. The Kato thick smear and Nuclepore filtration provide quantitative data on the intensity of infection, which is of value in assessing the degree of tissue damage and in monitoring the effect of chemotherapy. Schistosome infection may also be diagnosed by examination of tissue specimens, typically rectal biopsy samples; except in rare circumstances, other biopsy procedures (e.g., liver biopsy) are not needed.

The differential diagnosis of schistosomal hepatomegaly must include viral hepatitis of all etiologies, miliary tuberculosis, malaria, visceral leishmaniasis, ethanol abuse, and causes of hepatic and portal vein obstruction. The differential diagnosis of hematuria in *S. haematobium*