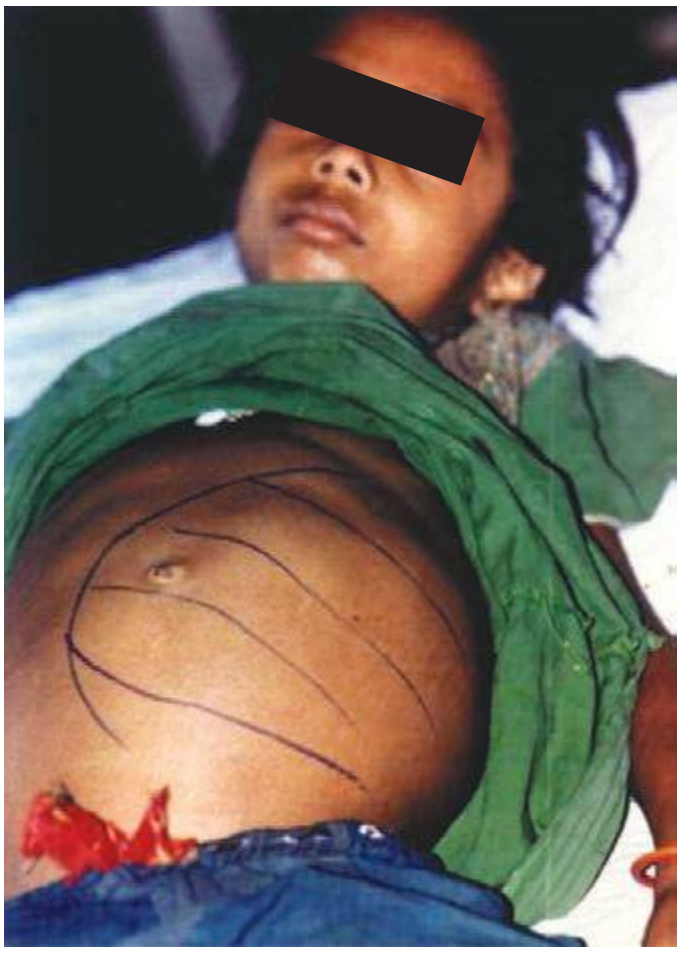

FIGURE 251-3 A patient with visceral leishmaniasis has a hugely enlarged spleen visible through the surface of the abdomen. Splenomegaly is the most important feature of visceral leishmaniasis.

sensitivity of splenic smears is >95%, whereas smears of bone marrow (60–85%) and lymph node aspirates (50%) are less sensitive. Culture of tissue aspirates increases sensitivity. Splenic aspiration is invasive and may be dangerous in untrained hands. Several serologic techniques are currently used to detect antibodies to *Leishmania*. An enzyme-linked immunosorbent assay (ELISA) and the indirect immunofluorescent antibody test (IFAT) are used in sophisticated laboratories.

In the field, however, a rapid immunochromatographic test based on the detection of antibodies to a recombinant antigen (rK39) consisting of 39 amino acids conserved in the kinesin region of *L. infantum* is used worldwide. The test requires only a drop of fingerprick blood or serum, and the result can be read within 15 min. Except in East Africa (where both its sensitivity and its specificity are lower), the sensitivity of the rK39 rapid diagnostic test (RDT) in immunocompetent individuals is ~98% and its specificity is 90%. In Sudan, an RDT based on a new synthetic polyprotein, rK28, was more sensitive (96.8%) and specific (96.2%) than rK39-based RDTs. Qualitative detection of leishmanial nucleic acid by polymerase chain reaction (PCR) and quantitative detection by real-time PCR are confined to specialized laboratories and have yet to be used for routine diagnosis of VL in endemic areas. PCR can distinguish among the major species of *Leishmania* infecting humans.

Differential Diagnosis VL is easily mistaken for malaria. Other febrile illnesses that may mimic VL include typhoid fever, tuberculosis, brucellosis, schistosomiasis, and histoplasmosis. Splenomegaly due to portal hypertension, chronic myeloid leukemia, tropical splenomegaly syndrome, and (in Africa) schistosomiasis may also be confused with VL. Fever with neutropenia or pancytopenia in patients from an endemic region strongly suggests a diagnosis of VL; hypergammaglobulinemia in patients with long-standing illness strengthens the diagnosis. In nonendemic countries, a careful travel history is essential when any patient presents with fever.

TREATMENT VISCERAL LEISHMANIASIS

GENERAL CONSIDERATIONS

Severe anemia should be corrected by blood transfusion, and other comorbid conditions should be managed promptly. Treatment of VL is complex because the optimal drug, dosage, and duration vary with the endemic region. Despite completing recommended treatment, some patients experience relapse (most often within 6 months), and prolonged follow-up is recommended. A pentavalent antimonial is the drug of choice in most endemic regions of the world, but there is widespread resistance to antimony in the Indian state of Bihar, where either amphotericin B (AmB) deoxycholate or miltefosine is preferred. Dose requirements for AmB are lower in India than in the Americas, Africa, or the Mediterranean region. In Mediterranean countries, where cost is seldom an issue, liposomal AmB is the drug of choice. In immunocompetent patients, relapses are uncommon with AmB in its deoxycholate and lipid formulations. Antileishmanial therapy has recently evolved as new drugs and delivery systems have become available and resistance to antimonial compounds has emerged.

Except for AmB (deoxycholate and lipid formulations), antileishmanial drugs are available in the United States only from the Centers for Disease Control and Prevention.

PENTAVALENT ANTIMONIAL COMPOUNDS

Two pentavalent antimonial (Sb^V) preparations are available: sodium stibogluconate (100 mg of Sb^V/mL) and meglumine antimoniate (85 mg of Sb^V/mL). The daily dose is 20 mg/kg by IV infusion or IM injection, and therapy continues for 28–30 days. Cure rates exceed 90% in Africa, the Americas, and most of the Old World but are <50% in Bihar, India, as a result of resistance. Adverse reactions to Sb^V treatment are common and include arthralgia, myalgia, and elevated serum levels of aminotransferases. Electrocardiographic changes are common. Concave ST-segment elevation is not significant, but prolongation of QT_c to >0.5 s may herald ventricular arrhythmia and sudden death. Chemical pancreatitis is common but usually does not require discontinuation of treatment; severe clinical pancreatitis occurs in immunosuppressed patients.

AMPHOTERICIN B

AmB is currently used as a first-line drug in Bihar, India. In other parts of the world, it is used when initial antimonial treatment fails. Conventional AmB deoxycholate is administered in doses of 0.75–1.0 mg/kg on alternate days for a total of 15 infusions. Fever with chills is an almost universal adverse reaction to AmB infusions. Nausea and vomiting are also common, as is thrombophlebitis in the infused veins. Acute toxicities can be minimized by administration of antihistamines like chlorpheniramine and antipyretic agents like acetaminophen before each infusion. AmB can cause renal dysfunction and hypokalemia and, in rare instances, elicits hypersensitivity reactions, bone marrow suppression, and myocarditis, all of which can be fatal.

The several lipid formulations of AmB developed to replace the deoxycholate formulation are preferentially taken up by reticuloendothelial tissues. Because very little free drug is available to cause toxicity, a large amount of drug can be delivered over a short period. Liposomal AmB has been used extensively to treat VL in all parts of the world. With a terminal half-life of ~150 h, liposomal AmB can be detected in the liver and spleen of animals for several weeks after a single dose. This is the only drug approved by the U.S. Food and Drug Administration (FDA) for the treatment of VL; the regimen is 3 mg/kg daily on days 1–5, 14, and 21 (total dose, 21 mg/kg). However, the total-dose requirement for different regions of the world varies widely. In Asia, it is 10–15 mg/kg; in Africa, ~18 mg/kg;