The lips, cheeks, and soft palate may also be affected. Secondary bacterial infection is common, and aspiration pneumonia may be fatal. Despite the high degree of T_H1 immunity and the strong DTH response, ML does not heal spontaneously.

Laboratory Diagnosis Tissue biopsy is essential for identification of parasites, but the rate of detection is poor unless PCR techniques are used. The strongly positive DTH response fails to distinguish between past and present infection.

TREATMENT MUCOSAL LEISHMANIASIS

The regimen of choice is a pentavalent antimonial agent administered at a dose of 20 mg of Sb^V/kg for 30 days. Patients with ML require long-term follow-up with repeated oropharyngeal and nasal examination. With failure of therapy or relapse, patients may receive another course of an antimonial but then become unresponsive, presumably because of resistance in the parasite. In this situation, AmB should be used. An AmB deoxycholate dose totaling 25–45 mg/kg is appropriate. There are no controlled trials of liposomal AmB, but administration of 2–3 mg/kg for 20 days is considered adequate. Miltefosine (2.5 mg/kg for 28 days) cured 71% of ML patients in Bolivia. The more extensive the disease, the worse the prognosis; thus prompt, effective treatment and regular follow-up are essential.

PREVENTION OF LEISHMANIASIS

No vaccine is available for any form of leishmaniasis. Inoculation with live *L. major* ("leishmanization") is practiced in Iran. Anthroponotic leishmaniasis is controlled by case finding, treatment, and vector control with insecticide-impregnated bed nets and curtains and residual insecticide spraying. Control of zoonotic leishmaniasis is more difficult. Use of insecticide-impregnated collars for dogs, treatment of infected domestic dogs, and culling of street dogs are measures that have been used with uncertain efficacy to prevent transmission of *L. infantum*. In Brazil, a canine vaccine has been found to promote a decrease in the human and canine incidence of zoonotic VL. Two vaccines, Leishmune® and Leish-Tec®, are licensed in Brazil; Leishmune provides significant protection to vaccinated dogs. CaniLeish® is the first licensed canine vaccine developed in Europe. Personal prophylaxis with bed nets and repellants may reduce the risk of CL infections in the New World.

252 Chagas Disease and African Trypanosomiasis

Louis V. Kirchhoff, Anis Rassi Jr.

Although the genus *Trypanosoma* contains many species of protozoans, only *T. cruzi*, *T. brucei gambiense*, and *T. brucei rhodesiense* cause disease in humans. *T. cruzi* is the etiologic agent of Chagas disease in the Americas; *T. b. gambiense* and *T. b. rhodesiense* cause African trypanosomiasis.

CHAGAS DISEASE (AMERICAN TRYPANOSOMIASIS)

DEFINITION

Chagas disease, or American trypanosomiasis, is a zoonosis caused by the protozoan parasite *T. cruzi*. Acute Chagas disease is usually a mild febrile illness that results from initial infection with the organism. After spontaneous resolution of the acute illness, most infected persons remain for life in the indeterminate phase of chronic Chagas disease, which is characterized by subpatent parasitemia, easily detectable IgG antibodies to *T. cruzi*, and an absence of associated signs and symptoms. In 10–30% of chronically infected patients, cardiac and/or gastrointestinal symptoms develop that can lead to serious morbidity and even death.

LIFE CYCLE AND TRANSMISSION

T. cruzi is transmitted among its mammalian hosts by hematophagous triatomine insects, often called reduviid bugs. The insects become infected by sucking blood from animals or humans with circulating parasites. Ingested organisms multiply in the gut of the triatomines, and infective forms are discharged with the feces at the time of subsequent blood meals. Transmission to a second vertebrate host occurs when breaks in the skin, mucous membranes, or conjunctivae become contaminated with bug feces that contain infective parasites. *T. cruzi* can also be transmitted by transfusion of blood donated by infected persons, by organ transplantation, from mother to unborn child, by ingestion of contaminated food or drink, and in laboratory accidents.

PATHOLOGY

Initial infection at the site of parasite entry is characterized by local histologic changes that include the presence of parasites within leukocytes and cells of subcutaneous tissues and the development of interstitial edema, lymphocytic infiltration, and reactive hyperplasia of adjacent lymph nodes. After dissemination of the organisms through the lymphatics and the bloodstream, primarily muscles (including the myocardium) **(Fig. 252-1)** and ganglion cells may become heavily parasitized. The characteristic pseudocysts present in sections of infected tissues are intracellular aggregates of multiplying parasites.

In persons with chronic *T. cruzi* infections who develop related clinical manifestations, the heart is the organ most commonly affected. Changes include thinning of the ventricular walls, biventricular enlargement, apical aneurysms, and mural thrombi. Widespread lymphocytic infiltration, diffuse interstitial fibrosis, and atrophy of myocardial cells are often apparent. Although parasites are difficult to find in myocardial tissue by conventional histologic methods, more sensitive techniques of parasite detection, such as immunohistochemistry and polymerase chain reaction (PCR), have more frequently demonstrated *T. cruzi* antigens and parasite DNA in chronic lesions. Conduction-system abnormalities often affect the right branch and the left anterior branch of the bundle of His. In chronic Chagas disease of the gastrointestinal tract (*megadisease*), the esophagus and colon may exhibit varying degrees of dilation. On microscopic examination, focal inflammatory lesions with lymphocytic infiltration are seen, and the number of neurons in the myenteric plexus may be markedly reduced. Accumulating evidence implicates the persistence of parasites and the accompanying chronic inflammation—rather than autoimmune mechanisms—as the basis for the pathology in patients with chronic *T. cruzi* infection.

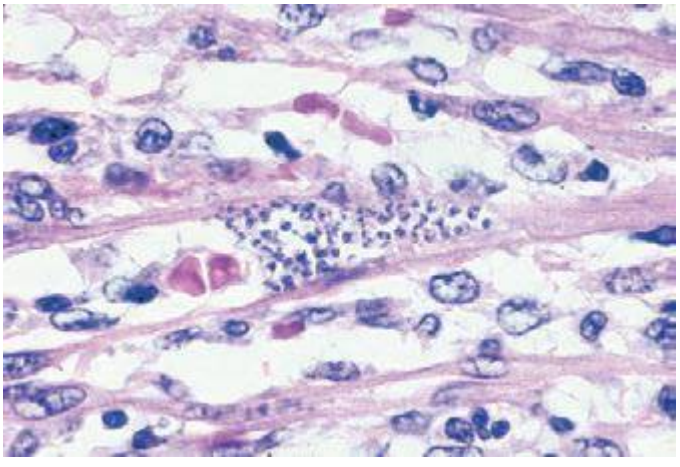

FIGURE 252-1 ***Trypanosoma cruzi*** **in the heart muscle of a child** who died of acute Chagas myocarditis. An infected myocyte containing several dozen *T. cruzi* amastigotes is in the center of the field (hematoxylin and eosin, 900 ×).