EPIDEMIOLOGY

T. cruzi is found only in the Americas. Wild and domestic mammals harboring *T. cruzi* and infected triatomines are found in spotty distributions from the southern United States to southern Argentina. Humans become involved in the cycle of transmission when infected vectors take up residence in the primitive wood, adobe, and stone houses common in much of Latin America. Thus human *T. cruzi* infection is a health problem primarily among the poor in rural areas of Mexico and Central and South America. Most new *T. cruzi* infections in rural settings occur in children, but the incidence is unknown because most cases go undiagnosed. Historically, transfusion-associated transmission of *T. cruzi* was a serious public health problem in many endemic countries. Transmission by this route has been largely eliminated, however, as effective programs for serologic screening of donated blood have been implemented. Several dozen patients with HIV and chronic *T. cruzi* infections who underwent acute recrudescence of the latter have been described. These patients generally presented with *T. cruzi* brain abscesses, a manifestation of the illness that does not occur in immunocompetent persons. Currently, it is estimated that 8 million people are chronically infected with *T. cruzi* and that 14,000 deaths due to the illness occur each year. The resulting morbidity and mortality make Chagas disease the most important parasitic disease burden in Latin America.

In recent years, the rate of *T. cruzi* transmission has decreased markedly in several endemic countries as a result of successful programs involving vector control, screening of donated blood, and education of at-risk populations. A major program, which began in 1991 in the "southern cone" nations of South America (Uruguay, Paraguay, Bolivia, Brazil, Chile, and Argentina), has provided the framework for much of this progress. Uruguay and Chile were certified free of transmission by the main domiciliary vector species (*Triatoma infestans*) in the late 1990s, and Brazil was declared transmission-free in 2006. Transmission has been reduced markedly in Argentina as well. Similar control programs have been initiated in the countries of northern South America and in the Central American nations.

Acute Chagas disease is rare in the United States, where 22 cases of autochthonous transmission and seven instances of transmission by blood transfusion have been reported. Moreover, *T. cruzi* was transmitted to five recipients of organs from three *T. cruzi*–infected donors, two of whom became infected through cardiac transplants. Acute Chagas disease has been reported in only one tourist returning to the United States from Latin America, although three such instances have been reported in Europe as well as one in Canada. In contrast, the prevalence of chronic *T. cruzi* infections in the United States has increased considerably in recent years. An estimated 23 million immigrants from Chagas-endemic countries currently live in the United States, ~17 million of whom are Mexicans. The total number of *T. cruzi*–infected persons living in the United States is estimated to be 300,000. Screening of the U.S. blood supply for *T. cruzi* infection began in January 2007. The overall prevalence of *T. cruzi* infection among donors is ~1 in 13,300, and to date nearly 3000 infected donors have been identified and deferred permanently (see "Diagnosis," below).

CLINICAL COURSE

The first signs of acute Chagas disease develop at least 1 week after invasion by the parasites. When the organisms enter through a break in the skin, an indurated area of erythema and swelling (the *chagoma*), accompanied by local lymphadenopathy, may appear. *Romaña sign*—the classic finding in acute Chagas disease, which consists of unilateral painless edema of the palpebrae and periocular tissues—can result when the conjunctiva is the portal of entry. These initial local signs may be followed by malaise, fever, anorexia, and edema of the face and lower extremities. Generalized lymphadenopathy and hepatosplenomegaly may develop. Severe myocarditis develops rarely; most deaths in acute Chagas disease are due to heart failure. Neurologic signs are not common, but meningoencephalitis occurs occasionally, especially in children <2 years old. Usually within 4–8 weeks, acute signs and symptoms resolve spontaneously in virtually all patients, with commencement of the asymptomatic or indeterminate form of chronic *T. cruzi* infection.

Symptomatic chronic Chagas disease becomes apparent years or even decades after the initial infection. The heart is commonly involved, and symptoms are caused by rhythm disturbances, segmental or dilated cardiomyopathy, and thromboembolism. Right bundle branch block is a common electrocardiographic abnormality, but other types of intraventricular and atrioventricular blocks, premature ventricular contractions, and tachy- and bradyarrhythmias occur frequently. Cardiomyopathy often results in biventricular heart failure, with a predominance of right-sided failure at advanced stages. Embolization of mural thrombi to the brain or other areas may take place. Sudden death is the main cause of death in Chagas heart disease; congestive heart failure and stroke are next most common. Patients with megaesophagus suffer from dysphagia, odynophagia, chest pain, and regurgitation. Aspiration can occur (especially during sleep) in patients with severe esophageal dysfunction, and repeated episodes of aspiration pneumonitis are common. Weight loss, cachexia, and pulmonary infection can result in death. Patients with megacolon are plagued by abdominal pain and chronic constipation, which predisposes to fecaloma formation. Advanced megacolon can cause obstruction, volvulus, septicemia, and death.

DIAGNOSIS

The diagnosis of acute Chagas disease requires the detection of parasites. Microscopic examination of fresh anticoagulated blood or the buffy coat is the simplest way to see the motile organisms. Parasites also can be seen in Giemsa-stained thin and thick blood smears. Microhematocrit tubes containing acridine orange as a stain can be used for the same purpose. When used repeatedly by experienced personnel, all of these methods yield positive results in a high proportion of cases of acute Chagas disease. Serologic testing does not play a major role in diagnosing acute Chagas disease. PCR assays often give positive results in infected patients in whom traditional parasitologic tests are negative, including infants with congenital Chagas disease.

Chronic Chagas disease is diagnosed by the detection of specific IgG antibodies that bind to *T. cruzi* antigens. Demonstration of the parasite is not of primary importance. In Latin America, ~30 assays are commercially available, including several based on recombinant antigens. Although these tests usually show good sensitivity and reasonable specificity, false-positive reactions may occur—typically with samples from patients who have other infectious and parasitic diseases or autoimmune disorders. In addition, confirmatory testing has presented a persistent challenge. For these reasons, the World Health Organization recommends that specimens be tested in at least two assays and that well-characterized positive and negative comparison samples be included in each run. The Chagas radioimmune precipitation assay (RIPA), a highly sensitive and specific confirmatory method for detecting antibodies to *T. cruzi*, is approved under the Clinical Laboratory Improvement Amendment and available in the laboratory of one of the authors (L.V.K.). In 2006, the U.S. Food and Drug Administration (FDA) approved a test to screen blood and organ donors for *T. cruzi* infection (Ortho *T. cruzi* ELISA Test System; Ortho-Clinical Diagnostics, Raritan, NJ). Since January 2007, the vast majority of U.S. blood donors have been screened, and positive units have undergone confirmatory testing with the Chagas RIPA. A second test for donor screening was approved by the FDA in 2010 (Abbott PRISM® Chagas Assay; Abbott Laboratories, Abbott Park, IL), as was an enzyme strip assay (Abbott ESA Chagas) in 2011. The use of PCR assays to detect *T. cruzi* DNA in chronically infected persons has been studied extensively; unfortunately, the sensitivity of this approach has not been shown to be reliably greater than that of serology.

TREATMENT CHAGAS DISEASE

Therapy for Chagas disease is still unsatisfactory. For many years now, only two drugs—nifurtimox and benznidazole—have been available for this purpose. Regrettably, both drugs lack efficacy and may cause bothersome side effects.

In acute Chagas disease, nifurtimox markedly reduces the duration of symptoms and parasitemia and decreases the mortality rate.