Chagas Disease

Aaron W. Tustin, MD, MPH,* Natalie M. Bowman, MD, MPH[†]

*Department of Environmental Health Sciences, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD.

[†]Department of Medicine, Division of Infectious Diseases, University of North Carolina at Chapel Hill, Chapel Hill, NC.

AUTHOR DISCLOSURE Dr Tustin has disclosed no financial relationships relevant to this article. Dr Bowman has disclosed that she receives grant support from NIH (NIAID) and BWF/ASTMH to research Chagas disease (Grants K23 AI113197-02, P30 AI50410, and others). This commentary does contain a discussion of an unapproved/investigative use of a commercial product/device.

Approximately 8 million people worldwide are infected by the protozoan parasite *Trypanosoma cruzi*, the causative agent of Chagas disease. After a latent period that can last years or decades, 10% to 30% of infected people develop serious complications, such as cardiomyopathy or gastrointestinal dysfunction. Contrary to popular belief, Chagas disease is not solely a vector-borne infection of Latin America. Clinicians in nonendemic regions must be aware of the potential for childhood *T cruzi* infections.

Humans typically acquire the parasite through contact with the infected feces of blood-feeding triatomine insects. Vector-mediated transmission occurs in endemic regions that extend from the southern United States to the southern cone of South America. *T cruzi* can also be transmitted in food and beverages contaminated with triatomine feces, via infected organ transplants and blood transfusions, and vertically from mother to child. In the United States, human contact with triatomines is minimal, and blood donations are screened for *T cruzi*. However, more than 300,000 US residents, mostly immigrants from Latin America, may harbor chronic *T cruzi* infections. Many of those infected are children and reproductive-age women.

Vertical transmission is an underrecognized problem. Children born to infected mothers have an approximately 5% chance of acquiring the parasite. Although there has been only one reported case of congenital *T cruzi* infection in the United States (in an infant born in 2010 to a Bolivian mother), several hundred undetected congenital *T cruzi* infections are estimated to occur in the United States each year. Diagnosis is difficult because most infected newborns are asymptomatic. A minority of infected infants demonstrate nonspecific signs and symptoms, including low Apgar scores, low birthweight, respiratory distress, hepatosplenomegaly, anasarca, pericardial and pleural effusions, and meningo-encephalitis. The presentation can easily be confused with neonatal sepsis or TORCH infections (which include toxoplasmosis, rubella, cytomegalovirus, and herpes viruses). Clinicians may overlook *T cruzi* in the differential diagnosis, especially in nonendemic areas.

To improve detection of congenital infections, the World Health Organization recommends antenatal *T cruzi* screening in all pregnant women who have ever lived or received a blood transfusion in an endemic region. Infected women are not treated prenatally to prevent vertical transmission because antitrypanosomal medications are contraindicated during pregnancy and breastfeeding. Instead, children born to *T cruzi*-infected mothers should be tested during infancy and treated if necessary. Unfortunately, prenatal screening recommendations are not widely followed, even in endemic countries. Many at-risk infants are born to mothers with unknown *T cruzi* status. Pediatricians should consider testing these newborns for *T cruzi*, especially if they are symptomatic. Diagnostic testing should

Congenital Chagas Disease: Recommendations for Diagnosis, Treatment and Control of Newborns, Siblings and Pregnant Women. Carlier Y, Torrico F, Sosa-Estani S, et al. *PLoS Negl Trop Dis*. 2011;5(10):e1250

***Trypanosoma cruzi* and Chagas Disease in the United States.** Bern C, Kjos S, Yabsley MJ, Montgomery SP. *Clin Microbiol Rev*. 2011;24(4):655-681

Congenital Transmission of Chagas disease - Virginia, 2010. Centers for Disease Control and Prevention (CDC). *MMWR Morb Mortal Wkly Rep*. 2012;61(26):477-479

Congenital Chagas Disease: An Update. Carlier Y, Sosa-Estani S, Luquetti AO, Buekens P. *Mem Inst Oswaldo Cruz*. 2015;110(3):363-368

be offered to siblings of any child diagnosed with Chagas disease, and the mother should also be referred for treatment evaluation.

Newborns at risk for *T cruzi* infection should be tested with polymerase chain reaction (PCR), the preferred diagnostic technique in children younger than age 9 months. PCR is more sensitive than microscopy-based techniques to detect *T cruzi* in blood, although it may not be available in resource-limited areas. If the initial test result is negative, PCR should be repeated at 4 to 6 weeks of age because parasitemia may increase over the first postnatal month. Infants who lack detectable parasitemia should undergo serologic testing after age 9 months to confirm the absence of infection. Serologic methods such as enzyme-linked immunosorbent assay (ELISA) and immunofluorescent antibody test (IFA) should not be used in children younger than 9 months, in whom circulating maternal antibodies can cause false-positive results. After 9 months of age, serology becomes the diagnostic method of choice because parasitic DNA is often undetectable by PCR during the chronic stage of infection. Positive serology should be confirmed with a second assay because these tests have imperfect sensitivity and specificity.

All children diagnosed with *T cruzi* infection should receive antitrypanosomal therapy with either benznidazole or nifurtimox. Although these medications are not approved by the US Food and Drug Administration (FDA) in the United States, they can be obtained from the Centers for Disease Control and Prevention under investigational permits. Standard therapy is a 60- to 90-day course of benznidazole 5 to 7 mg/kg per day or nifurtimox 10 to 15 mg/kg per day divided in 2 to 3 daily doses. Both drugs have a high rate of adverse effects but are tolerated better in children than

adults. Cure rates of nearly 100% are observed in congenitally infected infants who receive treatment within the first postnatal year. The cure rate decreases to approximately 60% in older children with chronic infections. Prompt detection and treatment of congenital *T cruzi* infection is, therefore, essential to avoid future complications.

COMMENT: I found this In Brief fascinating because I have not been familiar with the presentation of Chagas disease nor considered it in the differential diagnosis of patients. Yet, the World Health Organization estimates that Chagas disease is the most prevalent parasitic disease in the American continents, including North, Central, and South America.

As the authors noted, the presentation in newborns is diverse, making diagnosis challenging for those who are not familiar with the wide range of possibilities. Congenital Chagas disease must be considered in infants born to mothers who are from endemic areas, such as the southern portion of South America: Brazil, Paraguay, Argentina, and Bolivia. Early identification and treatment can prevent progression to more serious manifestations associated with chronic infection. Chronic Chagas disease can affect the heart, leading to cardiomyopathy, associated arrhythmias, and cardiac dysfunction. Although less common, gastrointestinal involvement can affect the esophagus or colon and lead to motility disorders. Because treatment is available and effective, diagnosis in both congenital and chronic states is important to patient quality of life and prevention of resultant morbidity.

– Janet Serwint, MD
Associate Editor, *In Brief*