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# Chagas Disease

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## Epidemiology

Chagas disease is an infection caused by the protozoan parasite, *Trypanosoma cruzi* (*T. cruzi*). Chagas disease is an emerging health concern in the United States [1]. It is estimated that 300,000 persons living in the United States have chronic Chagas disease, including approximately 40,000 women of childbearing age [2]. An estimated 63–315 infants are born each year with congenital Chagas disease [2, 3].

Identifying women who have lived in regions where Chagas disease is endemic is important for determining those for whom diagnostic testing during pregnancy should be considered. Most women in the childbearing years who have Chagas disease acquired the infection while living in Mexico, Central America, or South America. The country of origin for approximately 85% of *T. cruzi*-infected women living in the United States is Mexico, El Salvador, Guatemala, Honduras, or Nicaragua. Among the remainder, many acquired infection in endemic regions in Argentina, Ecuador, Colombia, Brazil, or Bolivia [2].

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## Pathogenesis

Chagas disease is a vector-borne infection. The usual mode of transmission is through exposure to bloodsucking triatomine insects, known as kissing bugs, which carry *T. cruzi* in their intestinal tracts. Triatomines defecate when they bite, and feces of infected insects containing *T. cruzi* trypomastigotes enter the human body through a bite wound, intact mucous membranes, or conjunctivae. Risk of infection among persons living in Chagas disease-endemic regions is greater for those with repeated and prolonged exposure to triatomine bugs, for example, through residence in a rural setting or living in adobe or thatched-roofed dwellings.

The vector of *T. cruzi* or a mammalian reservoir, or both, has been documented in at least 28 states in the southern half of the United States. Vector-borne Chagas disease acquired in the United States can occur but has been documented, to date, in fewer than 50 persons. These individuals have lived in locales in which the vector or an infected mammalian reservoir was identified, and they have had potential for exposure through working outdoors or participating in outdoor leisure activities [4]. Blood transfusion and organ transplantation are potential modes of transmission, but donor screening for *T. cruzi* has rendered these modes of transmission rare in the United States [5]. Breast milk-associated transmission has not been reported.

Newborn infants are at risk for congenital infection if their mothers have acute or chronic *T. cruzi* infection. Acute Chagas disease in children or adults usually manifests as a mild and self-limited influenza-like illness that lasts 4–8 weeks; parasitemia is present during acute phase infection. Infection then enters a chronic phase that, without treatment, persists for life. In chronic phase infection, the parasite is found in tissues of the body and is undetectable in peripheral blood. After years or decades, 20–40% of people with untreated infection develop Chagas cardiomyopathy or gastrointestinal disease. Features of cardiomyopathy can include arrhythmias, left ventricular dysfunction, congestive heart failure, apical rupture, and death. Gastrointestinal disease, including megaesophagus or megacolon, occurs less commonly but can cause substantial morbidity. Most women in the childbearing years who are living in the United States have chronic Chagas disease without symptoms and are unaware that they are infected.

Congenital transmission of *T. cruzi* occurs during the second or third trimesters of pregnancy [6]. Congenital infection is not thought to lead to congenital malformation, presumably because transmission occurs only after organogenesis is complete. The risk of transmission from a mother with chronic Chagas disease to her infant is 1–5% [2]. Factors thought to influence the likelihood of transmission include parasite strain, as there may be differences in strain virulence and invasiveness, level of parasites in the blood, and advancing maternal age, as this can impact integrity of the placental barrier. The risk is further increased for mothers with untreated human immunodeficiency virus coinfection.

## Clinical Findings

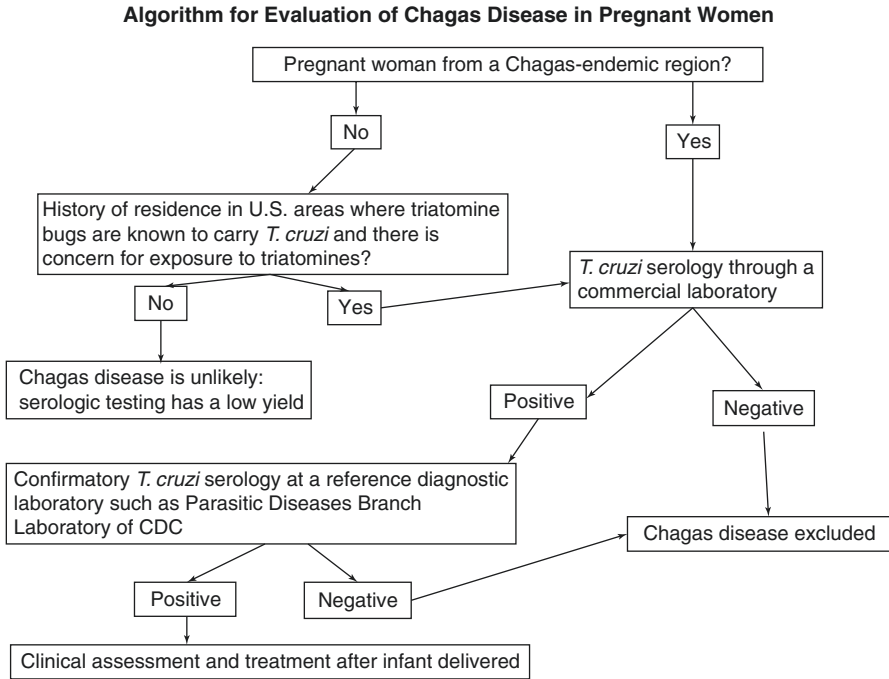
Approximately 10–40% of *T. cruzi* congenitally infected infants have clinical findings at birth [7, 8]. Congenital Chagas disease can be associated with premature rupture of the membranes and preterm delivery [9]. Congenitally infected infants can present with low birth weight for gestational age, low Apgar scores, and findings such as hepatosplenomegaly, jaundice, anemia, or thrombocytopenia. Less common manifestations of congenital Chagas disease include hydrops fetalis, hepatitis, pneumonitis, cardiac failure, and meningoencephalitis. There are no pathognomonic clinical features of congenital Chagas disease. The diagnosis should also be considered when the maternal history is consistent with exposure to triatomines. There have been two confirmed cases reported in the United States, both to mothers who had immigrated from a country endemic for Chagas disease. Each infant presented with hydrops fetalis. There are no reports of congenital Chagas disease in the US birth cohort [10, 11].

Healthy-appearing, congenitally infected infants generally do well in infancy. However, 20–30% of children with untreated congenital Chagas disease, with or without signs of infection at birth, will develop irreversible life-threatening and often fatal heart disease after years or decades of silent infection [12]. Conduction system abnormalities are an early manifestation of Chagas heart involvement. Cardiac arrhythmias, apical or ventricular aneurysms, and progressive dilated cardiomyopathy with congestive heart failure carry a high risk of sudden death [13]. Gastrointestinal tract manifestations, which include megaesophagus and megacolon, are a debilitating but usually nonfatal late manifestation of untreated infection. Reactivation of infection, potentially causing severe disease, can occur in people who have suppressed immune systems in association with chemotherapy, organ transplantation, or human immunodeficiency virus infection.

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## Diagnosis

The diagnosis of Chagas disease in chronically infected pregnant women is established by serologic testing (Fig. 1) [14]. Pregnant women who have lived in a Chagas disease-endemic region should undergo screening for *T. cruzi* IgG antibodies through a commercial laboratory. Most commercial laboratories employ enzyme-linked immunoassay (ELISA)-based tests. Because no single serologic test is sufficiently sensitive and specific to establish the diagnosis, women who screen positive for *T. cruzi* antibody require confirmatory testing at a reference laboratory, such as the Parasitic Diseases Branch Laboratory at the Centers for Disease Control and Prevention (CDC). The standard approach for confirmation of the diagnosis is to perform at least two tests that use different techniques and different antigen preparations to detect antibodies to *T. cruzi* antigens. Testing at CDC is performed at no charge to the patient. The state health department should be contacted regarding



**Fig. 1** Algorithm for the evaluation of Chagas disease in pregnant women

requests for testing at CDC; in many states, including those in which Chagas disease is a reportable infection, routing of specimens to CDC through the state public health laboratory is required. As of 2018, Chagas disease is a reportable infection in Arizona, Arkansas, Louisiana, Mississippi, Tennessee, and Texas. Women identified as having Chagas disease should be referred for clinical evaluation and, after the infant is delivered, treatment.

Infants born to women identified as positive for acute or chronic *T. cruzi* infection should undergo testing as soon as possible after birth (Fig. 2) [14]. Serologic testing is appropriate to determine infant risk if the mother was not tested during pregnancy. The only method to establish the diagnosis of congenital Chagas disease conclusively in a neonate is by detection of trypomastigotes, either by microscopic examination of fresh anticoagulated blood specimens or by PCR testing of whole blood through the Parasitic Diseases Branch Laboratory at CDC. The CDC reference laboratory employs a multi-targeted PCR testing algorithm using *T. cruzi* minicircle TaqMan real-time PCR and nuclear *T. cruzi* minisatellite TaqMan real-time PCR assays to detect circulating parasite DNA [10, 15]. Results of testing are usually available within 1 week.

A positive initial PCR result requires confirmation by testing a second blood specimen, because low levels of maternal DNA can, on occasion, be detected in uninfected infants born to infected mothers (Fig. 2). Detection of maternal DNA is

### Algorithm for Evaluation of Congenital Chagas Disease: Infant <3 Months of Age\*

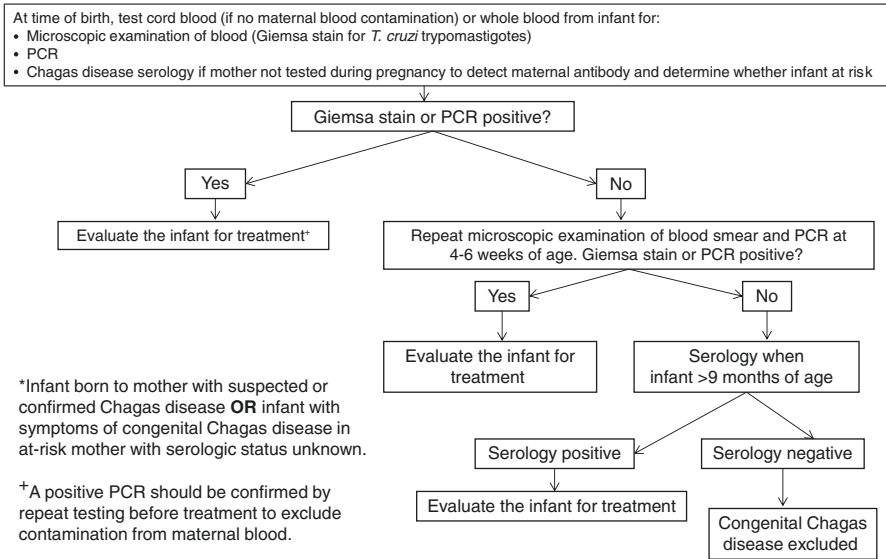


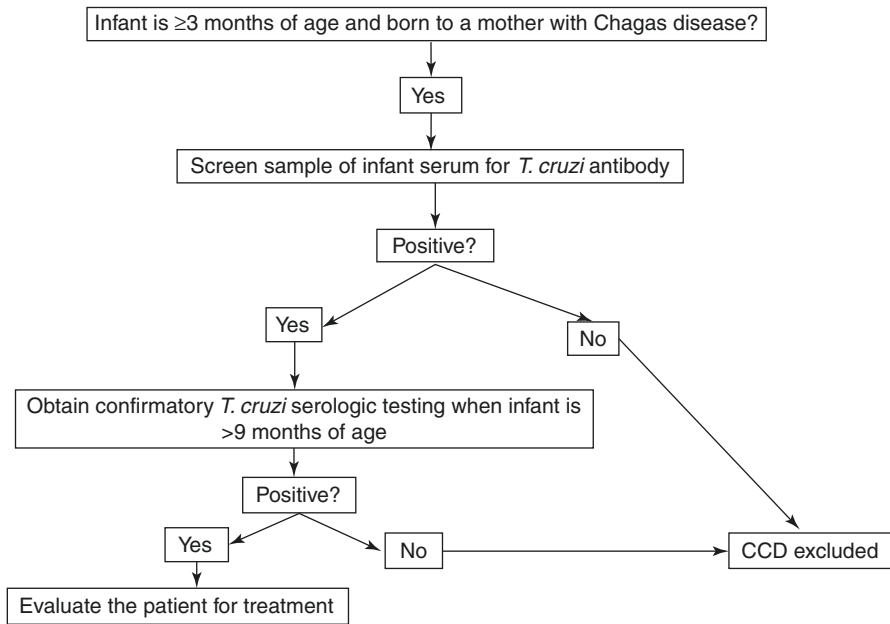
Fig. 2 Algorithm for evaluation of congenital Chagas disease in infants age <3 months

unlikely after the first week or two of life. If a second PCR is positive, the diagnosis of congenital Chagas disease is confirmed, and the infant should be evaluated clinically for signs of infection and treated. A negative initial PCR result should be followed by repeat testing when the infant is age 4–6 weeks to confirm absence of infection because the level of parasitemia increases after birth and is not always detectable in the first weeks of life [16]. If PCR testing at age 4–6 weeks is positive in an infant born to a mother with *T. cruzi* infection, the diagnosis of congenital Chagas disease is confirmed, and the infant should be evaluated clinically and treated.

If an infant born to a mother with chronic Chagas disease has no detectable parasitemia by molecular testing, the infant’s serologic status should be monitored. Passively acquired maternal antibody wanes to undetectable levels by 9 months after birth. Infants who are uninfected should be antibody negative when tested at age 9–12 months. Similarly, if an infant born to a mother with chronic Chagas disease is first evaluated at age >3 months, serologic testing at age 9–12 months is the appropriate approach to document or exclude congenital infection (Fig. 3) [14].

Serologic testing through a commercial laboratory is indicated for all siblings of an infant exposed to maternal Chagas disease. Maternal relatives, including the grandmother, should also undergo screening serologic testing. Other family or household members who share the same risk history should also be screened for infection.

**Algorithm for Evaluation of Congenital Chagas Disease (CCD) for Infants  
≥3 Months of Age**



**Fig. 3** Algorithm for evaluation of congenital Chagas disease for infants age ≥3 months

## Treatment

The American Academy of Pediatrics recommends treatment for all cases of acute or congenital Chagas disease as well as chronic *T. cruzi* infection in children age <18 years [17]. The two medications employed for treatment of Chagas disease, including congenital infection, are benznidazole and nifurtimox. The dosing for both medications is age-specific. Benznidazole is administered at a dose of 10 mg/kg/day orally in two divided doses for 60 days in infants and children age <12 years. Nifurtimox is administered at a dose of 15–20 mg/kg/day orally in three or four divided doses for 90 days in infants and children age <10 years. Benznidazole is considered first-line treatment based upon the accumulated clinical experience and a more favorable side effect profile. The medications are generally well tolerated in neonates and infants [18]. In 2017, the US Food and Drug Administration granted accelerated approval to benznidazole for use in children ages 2–12 years with Chagas disease [19]. Information regarding treatment of *T. cruzi* infection for neonates or young infants with confirmed congenital Chagas disease can be obtained by contacting CDC’s Parasitic Diseases Inquiries Service at (404) 718–4745 or [parasites@cdc.gov](mailto:parasites@cdc.gov), including assistance with release of nifurtimox under an investigational protocol.

Mothers identified as having chronic Chagas disease should receive treatment after delivery for their own well-being and because untreated infection can be transmitted during subsequent pregnancies. Treatment is contraindicated during pregnancy. Safety for infants exposed to antitrypanosomal medications through breastfeeding has not been evaluated; withholding maternal treatment until cessation of breastfeeding is recommended. Breastfeeding by mothers with chronic Chagas disease should be withheld only if there is bleeding around the nipples and then only until bleeding has resolved.

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## Prevention

There are important challenges to providing optimal care for infants with congenital Chagas disease. Enhanced awareness of Chagas disease as a health concern for women and infants born in the United States is needed to prompt diagnostic evaluation of at-risk infants and improve long-term outcomes from congenital Chagas disease. Substantial knowledge gaps regarding Chagas disease awareness and knowledge have been identified among healthcare providers, including obstetrician-gynecologists [20, 21]. In particular, education to promote targeted screening of at-risk pregnant women is needed.

Data are needed to better understand the extent and distribution of Chagas disease in the United States in the ~40,000 women of childbearing age with chronic *T. cruzi* infection so that efforts to identify and treat infants with congenital infection can be expanded. Diagnostic tests with improved specificity and sensitivity as well as validated rapid screening tests are needed to simplify the process of identification of *T. cruzi*-infected adults and infants. Safe, effective, and easily accessible drugs for treatment are needed. As these advances are underway, caregivers of neonates have an unparalleled opportunity to initiate evaluation of infants at risk for congenital Chagas disease so that those with confirmed *T. cruzi* infection can receive curative treatment early in life.

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## References

1. Centers for Disease Control and Prevention. Parasites-Neglected parasitic infections. Available from: <http://www.cdc.gov/parasites/mpi.index.html>. Accessed 27 Jul 2017.
2. Bern C, Montgomery SP. An estimate of the burden of Chagas disease in the United States. *Clin Infect Dis*. 2009;49:e52–4.
3. Montgomery SP, Starr MC, Cantey PT, Edwards MS, Meymandi SK. Neglected parasitic diseases in the United States: Chagas disease. *Am J Trop Med Hyg*. 2014;90:814–8.

4. Cantey PT, Stramer SL, Townsend RL, et al. The United States *Trypanosoma cruzi* infection study: evidence for vector-borne transmission of the parasite that causes Chagas disease among United States blood donors. *Transfusion*. 2012;52:1922–30.
5. AABB. Chagas Biovigilance Network. Available from: <http://www.aabb.org/research/hemovigilance/Pages/chagas.aspx>. Accessed 2 Sep 2018.
6. Carlier Y, Truyens C. Maternal-fetal transmission of *Trypanosoma cruzi*. In: Telleria J, Tibayrenc M, editors. *American trypanosomiasis-Chagas disease: One hundred years of research*. New York: Elsevier; 2010. p. 539–81.
7. Oliveira I, Torrico F, Muñoz J, Gascon J. Congenital transmission of Chagas disease: a clinical approach. *Expert Rev Anti Infect Ther*. 2010;8:945–56.
8. Freilij H, Altchek J. Congenital Chagas' disease: Diagnostic and clinical aspects. *Clin Infect Dis*. 1995;21:551–5.
9. Gebrekristos HT, Buekens P. Mother-to-child transmission of *Trypanosoma cruzi*. *J Pediatr Infect Dis Soc*. 2014;3:S36–40.
10. Centers for Disease Control and Prevention. Congenital transmission of Chagas disease—Virginia, 2010. *MMWR Morb Mortal Wkly Rep*. 2012;61:477–9.
11. Alarcón A, Morgan M, Montgomery SP, et al. Diagnosis and treatment of congenital Chagas disease in a premature infant. *J Pediatr Infect Dis Soc*. 2016;5:e28–31.
12. Bern C, Martin DL, Gilman RH. Acute and congenital Chagas disease. *Adv Parasitol*. 2011;75:19–47.
13. Rassi A Jr, Rassi A, Martin-Neto JA. Chagas disease. *Lancet*. 2010;375:1388–402.
14. Congenital Chagas disease. Available from: [https://www.cdc.gov/parasites/chagas/health\\_professionals/congenital\\_chagas.html](https://www.cdc.gov/parasites/chagas/health_professionals/congenital_chagas.html). Accessed 8 Aug 2017.
15. Qvarnstrom Y, Schijman AG, Veron V, Aznar C, Steurer F, da Silva AJ. Sensitive and specific detection of *Trypanosoma cruzi* DNA in clinical specimens using a multi-target real-time PCR approach. *PLoS Negl Trop Dis*. 2012;6:e1689.
16. Bern C, Verastegui M, Gilman RH, et al. Congenital *Trypanosoma cruzi* transmission in Santa Cruz, Bolivia. *Clin Infect Dis*. 2009;49:1667–74.
17. American Academy of Pediatrics. American trypanosomiasis (Chagas disease). In: Kimberlin DW, Brady MT, Jackson MA, Long SS, editors. *Red Book: 2015 Report of the Committee on Infectious Diseases*. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015. p. 803–5.
18. Altchek J, Moscatelli G, Moroni S, Garcie-Bourmisen F, Freilij H. Adverse events after the use of benznidazole in infants and children with Chagas disease. *Pediatrics*. 2011;127:e212–8.
19. FDA News Release. FDA approves first U.S. treatment for Chagas disease. Available from: <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm573942.htm>. Accessed 4 Sep 2017.
20. Stimpert KK, Montgomery SP. Physician awareness of Chagas disease, USA. *Emerg Infect Dis*. 2010;16:871–2.
21. Verani JR, Montgomery SP, Schulkin J, Anderson B, Jones JL. Survey of obstetrician-gynecologists in the United States about Chagas disease. *Am J Trop Med Hyg*. 2010;83:891–5.