

American Trypanosomiasis (Chagas Disease)

Chagas disease is a parasitic infection caused by the protozoan flagellate *Trypanosoma cruzi*, which is spread to animals and people by means of vector-borne transmission. The disease is found only in the Americas (commonly South America, Central America, and Mexico). In countries where Chagas is endemic, the principal method of transmission is through contact with fecal matter from an infected triatomine bug. The triatomine bug, also known as the kissing bug, bites a person or animal host, ingests a blood meal, and then defecates on the host. The host might accidentally scratch or rub the feces into the bite wound, eyes, or mouth, thereby allowing the *T. cruzi* parasite to enter the body through mucous membranes or bloodstream. ^{1, 2, 3}

Infection with Chagas disease can also occur through congenital transmission, transfusion of blood or blood products, organ transplantation, consumption of uncooked food contaminated with feces from infected bugs, and accidental laboratory exposure. Chagas disease is not transmitted from person-to-person. There are two phases of Chagas disease: the acute and chronic phase. Both phases can range from asymptomatic to life threatening. The majority of Chagas disease cases are asymptomatic. The acute phase is characterized by the first 8 weeks of infection, detectable parasitemia, and asymptomatic or symptomatic manifestations of the disease. ^{1, 2, 3}

A. Agent:

Trypanosoma cruzi.

B. Clinical Description:

Most infections are asymptomatic. When they do occur, children are more likely to develop clinical manifestations than adults. In the acute phase there can be unilateral, firm edema of the eyelids (Romaña's sign) in cases where the site of inoculation is the conjunctiva of the eye. In some patients a red nodule or chagoma develops at the site of original inoculation (usually face or arms) with surrounding skin becoming hardened (indurated) and later hyperpigmented (lasting up to 8 weeks). Other symptoms include fever, malaise, lymphadenopathy, and hepatosplenomegaly. More serious, life threatening acute myocarditis and meningoencephalitis can also develop. Nearly all cases of acute Chagas disease resolve after 1-3 months. However, if untreated, infections can be lifelong. In people who have suppressed immune systems, Chagas disease can reactivate with parasites found in the circulating blood. This occurrence can potentially cause severe disease. ^{1, 2, 3, 4}

In the chronic phase, sequelae are serious and irreversible and include cardiac dilation, arrhythmias, and major conduction abnormalities which often lead to heart failure and death. Also important is intestinal tract involvement with dilation of the esophagus (megaesophagus) and colon (megacolon), leading to difficulties with eating or passing stool. ^{1, 2, 3, 4}

▪ Differential Diagnosis:

Mild to severe allergic reactions, including **anaphylaxis**, can be associated with Triatomine bug bites but are a separate health issue unrelated to *T. cruzi* infections. However, as such

reactions can cause a variety of symptoms, some of which might be mistaken for acute phase symptoms, they need to be differentiated from those of acute phase chagasic infections. These include intense itching of the scalp, palms, and soles of the feet, welts, rashes, fever, nausea, vomiting, diarrhea, body aches, and cramps. More serious symptoms involve fainting, and swelling throughout the body, especially of the tongue and throat (if these symptoms develop the individual will require immediate medical attention, call the Arizona Poison and Drug Information Center 1-800-222-1222)¹³. The latter can make speaking, breathing, and swallowing difficult.^{5, 6, 7} The key to a differential diagnosis is the onset of symptoms: allergic reactions arise within hours of bites and dissipate a few hours to a day later whereas acute phase chagasic symptoms develop a few days to two weeks after inoculation and last for upwards of 3 months.^{1, 2}

C. Reservoirs:

Various native rodents and other small mammals serve as the reservoir for *T. cruzi*. In Arizona and much of the America Southwest, native wood rat populations (colloquially referred to as 'pack rats') of the genus *Neotoma* are recognized as the principal reservoir.^{7, 8, 9}

D. Mode of Transmission:

The most common means of transmission is through contact with the feces of infected triatomine bugs (commonly called 'Kissing' or 'Conenose bugs'^{7, 8, 9}). *T. cruzi* contained in the feces enters the bloodstream through a wound or an intact mucosal membrane, such as the conjunctiva (membrane around the eyes). Infections occur less frequently through congenital transfer from mother-to-baby, transfusions with contaminated blood products and organ transplants from chagasic donors, laboratory accidents, or eating infected bugs or contaminated food or drink.^{1, 2, 3}

E. Incubation period:

In the symptomatic acute phase 5-14 days after inoculation with infective feces; 30-40 days in infections acquired through blood transfusion; in some newborn infants with congenital infection, usually one to three days.^{1, 2, 3}

In the chronic phase, symptoms occur in 20-30% of infections following a period of 10-40 years after the acute phase. The asymptomatic period between the acute phase and onset of chronic manifestations is often referred to as the 'indeterminate phase'.^{1, 2, 3}

F. Period of Communicability:

In the acute phase *T. cruzi* organisms are commonly present in the blood and may persist in small numbers throughout life in symptomatic and asymptomatic individuals.^{1, 2, 3}

G. Susceptibility and Resistance:

All ages are susceptible, but the acute phase is usually more severe in younger people. Immunosuppressed people, especially those with AIDS, are at risk of serious infections and complications. Resistance is not documented.^{1, 2, 3}

H. Treatment:

Treatment for Chagas disease is recommended for all people diagnosed with an acute infection, congenital infection, for those with suppressed immune systems, and for all children with chronic infection. Adults with chronic infection may also benefit from treatment, but for adults

older than 50 years with chronic *T. cruzi* infection, the decision to treat with antiparasitic drugs should be individualized, weighing the potential benefits and risks for the patient. Physicians should consider factors such as the patient’s age, clinical status, preference, and overall health. . For cardiac or gastrointestinal problems resulting from Chagas disease, symptomatic treatment may be helpful. Patients should consult with their primary health care provider. Some patients may be referred to a specialist, such as a cardiologist, gastroenterologist, or infectious disease specialist.^{1, 2, 10}

In the U.S., medication for Chagas is available only through CDC. Health care providers can talk with CDC staff about whether and how patients should be treated.¹⁰

Contraindications for treatment include severe hepatic and/or renal disease. As safety for infants exposed through breastfeeding has not been documented, withholding treatment while breastfeeding is also recommended.¹⁰ The following table outlines recommended dosage regimens by age group:

DRUG	AGE GROUP	DOSAGE & DURATION ¹⁰
Benznidazole	2-12 years of age	5-8 mg/kg per day orally in 2 divided doses for 60 days
Nifurtimox	Birth to younger than 18 years of age, weighing at least 2.5kg	Body weight \geq 40 kg: 8-10 mg/kg day orally in 3 divided doses for 60 days. Body weight $<$ 40 kg: 10-20 mg/kg per day orally in 3 divided doses for 60 days.

*Questions regarding treatment should be directed to Parasitic Diseases Public Inquiries (404-718-4745; chagas@cdc.gov).

a. Kissing Bugs Control

To control Kissing bugs infestations it is helpful to¹³:

- Seal cracks and crevices so bugs cannot enter your home
- Install screens on windows and doors
- Change outside lights to yellow bulbs
- Removing wood, brush, and rock piles near your house
- Prevent pack-rats from nesting
- Keeping your house and any outdoor pet resting areas clean, in addition to periodically checking both areas for the presence of bugs
- Use insecticide around the home.

b. Kissing bugs testing

CDC is offering *Trypanosoma cruzi* testing of kissing bugs that come in contact with humans. They offer identification via submission of a picture and testing for bugs identified as triatomine (agent of Chagas disease). Please email vbzd@azdhs.gov for approval with the following information:

- The location of where the bug was found
- Information about the exposure

If approved, the triatomine bug can be sent to the Arizona State Public Health Lab (using [the Environmental Submission Form](#)) which will forward it to CDC. Approximate turnaround time for testing is at least 3 weeks.

I. Clinical Case Definition¹⁴:

There are two phases of Chagas disease: the acute and chronic phase. Both phases can be asymptomatic to life threatening. The majority of Chagas disease cases are asymptomatic.

The **acute phase** is characterized by the first 8 weeks of infection, detectable parasitemia, and asymptomatic or symptomatic manifestations of the disease. Symptoms can include:

- Fever
- Malaise
- Rash
- Body aches
- Headache
- Loss of appetite
- Vomiting
- Diarrhea
- Hepatomegaly
- Splenomegaly
- Lymphadenopathy
- Chagoma (nodular swelling at site where the parasite entered the body)
- Romaña's sign (swelling of the eyelid on the side of the face near the bite wound or where the bug feces were deposited or accidentally rubbed into the eye)
- Acute myocarditis (rare) and/or
- Meningoencephalitis (rare)

Even if symptoms develop during the acute phase, they usually fade away on their own, within a few weeks or months. However, the acute phase may be severe in people with weakened immune systems.

The **chronic intermediate phase** occurs after the acute phase when infected individuals enter into a prolonged asymptomatic form of the disease. The infection remains silent during this phase and few or no parasites are found in the bloodstream. During this time, most people are unaware of their infection. Many people remain asymptomatic for their entire life and never develop chronic Chagas-related symptoms.

It is estimated that 20-30% of infected people will develop the **chronic symptomatic phase** of Chagas disease. This phase is characterized by undetectable parasitemia and severe life-threatening cardiac or intestinal medical complications. These include:

- Cardiomyopathy, heart failure, altered heart rate or rhythm, and cardiac arrest; and/or
- Intestinal complications, such as megaesophagus or megacolon, which can lead to difficulties with eating or with passing stool.

J. Laboratory Criteria for Diagnosis¹⁴:

The diagnosis of Chagas disease can be made by observation of the parasite in a blood smear by microscopic examination. A thick and thin blood smears are made and stained for visualization of parasites. However, a blood smear works well only in the acute phase of infection when parasites are seen circulating in blood.^{1, 2, 11}

Diagnosis of chronic Chagas disease is made after consideration of the patient's clinical findings, as well as by the likelihood of being infected, such as having lived in an endemic country. Diagnosis is generally made by testing with at least two different serologic tests.¹¹

Confirmatory Testing

- Isolation of *T. cruzi* by microscopy (microscopic examination, wet mount, thick and thin smears-Giemsa stain), OR
- Isolation of *T. cruzi* by culture, OR
- Detection of *T. cruzi* DNA by polymerase chain reaction (PCR), OR
- Detection of antibody specific to *T. cruzi* by two distinct diagnostic assays (can only be performed at CDC)

Presumptive Testing

- Evidence of *T. cruzi* antibodies on a single serologic diagnostic assay (IgG positive) (not blood screening); OR
- Reactive blood donor screen AND a secondary positive diagnostic assay (IgG positive). (Note that 'additional' or 'confirmatory' antibody tests performed by a blood screening agency do not count as diagnostic tests. See Comments.)

Case Classification¹⁴

Confirmed	A case that meets the confirmatory laboratory criteria.
Probable	A case that meets the presumptive laboratory criteria.

Type Classification

Acute phase

- Asymptomatic or symptomatic within 8 weeks of documented exposure* or symptom onset/diagnosis

Chronic, intermediate phase

- Asymptomatic case >9 months of age and >8 weeks since documented exposure*

Chronic, symptomatic phase

- Symptomatic case >9 months of age and >8 weeks since documented exposure*

Comments

*Documented exposure may include contact with triatomine bug, recipient of contaminated blood products, congenital exposure, or travel to an endemic country.

Note that the testing performed by a blood screening/blood donation agency (even those tests listed as "additional" or "confirmatory") should not be considered diagnostic. Blood donor

testing is very sensitive by design, for the purposes of protecting the safety of the blood supply. Evidence of antibodies against *T. cruzi* on blood screening may prompt a patient to have further diagnostic testing performed, but only the results of the diagnostic testing should be considered in either the confirmatory or presumptive laboratory criteria.

Additionally, only the **IgG** results need to be considered when using presumptive testing criterion of a single serological diagnostic assay. Per communications with CDC (2019), the IgM assays are nonspecific; in general, positive IgM tests have been confirmed as infections only when the patients also tested positive for IgG.

K. Classification of Import Status:

An 'Internationally Imported Case' is defined as a case in which *T. cruzi* infection results from exposure triatome bugs outside the U.S. 1-3 weeks prior to onset of acute symptoms. A 'U.S. Acquired Case' is defined as a case in which the patient had not been outside the U.S. prior to onset. If infection was thought to occur in Mexico or Canada, mark as *bi-national* in MEDSIS.

L. Laboratory Testing:

Parasitological methods are most effective during acute infections. Circulating parasite levels decrease rapidly within a few months and are undetectable by most methods during the chronic phase. Diagnosis of chronic Chagas disease is made by serologic tests for antibody to the parasite. A single test is not sufficiently sensitive and specific to make the diagnosis. The standard approach is to apply two or more tests that use different techniques and/or that detect antibodies to different antigens. Two commonly used techniques are enzyme-linked immunosorbent assay (ELISA) and indirect fluorescent antibody test (IFA).¹²

M. Assessing Laboratory Results:

Some blood centers test blood donations that are reactive (positive) by the blood screening test with an investigational assay, radioimmunoassay (RIA). Donors who are positive on the screening test can no longer donate blood, regardless of their supplemental test or RIA result. Donors are contacted by the blood center and are requested to contact their physician.¹²

N. Outbreak Definition:

An unexpected increase in cases of Chagas disease that is clustered by time, place, or person (ex. people that might be part of the same cohort).

Investigation Guidelines

O. Time Frame:

Within five working days of a positive result by laboratories (*Trypanosoma cruzi*).

P. Form:

- ADHS Chagas Case Investigation Form:
<https://www.azdhs.gov/documents/preparedness/epidemiology-disease-control/disease-investigation-resources/chagas-investigation-form.pdf>

Q. Investigation Steps:

Epidemiological investigation report should be submitted in MEDSIS by filling out the Travel Table and the DSO morbidity 'type' .

Specific procedures for investigating Chagas disease cases will be case-dependent. Factors that may affect the investigation include: symptomatology, exposure to kissing bugs, travel history, and differentiation between actual chagasic symptoms and bite-related allergic reactions. Upon identification of a case under investigation, ADHS and the local health department should work together, in coordination with ASPHL and CDC, to develop a plan for the investigation.

Local health department investigators are responsible for:

- Communicating with ADHS investigators to coordinate the investigation based on current information available for Chagas disease.
- Obtaining medical records from the case's health care provider and interviewing the case, as needed, to determine medical information (illness course, severity, complications); travel history and kissing bug bites; blood transfusions or organ transplants; and other relevant information.
- Coordinating submission of additional laboratory specimens, as needed. Most commonly, if an individual is positive for *T. cruzi* IgG by blood screening, additional commercial diagnostic tests are indicated. If this second test is also IgG positive, then confirmatory testing can be done at CDC. Working with ADHS and other partners to conduct contact investigations, conduct additional surveillance, implement control measures following an environmental assessment, or provide educational information, as needed.

ADHS investigators are responsible for:

- Communicating with local health department investigators, ASPHL, and CDC to coordinate the investigation based on current information available for Chagas disease.
- Working with ASPHL to ensure blood and tissue specimens are sent to CDC for confirmatory testing following protocols for testing and submission from the Association of Public Health Laboratories.
- Identifying an appropriate investigation form.
- Assisting the local health department in gathering case information, as needed.
- Working with the local health department, CDC, and other partners to conduct contact investigations, conduct additional surveillance, implement control measures following an environmental assessment, or provide educational information, as needed.

R. Outbreak Guidelines:

While outbreaks involving multiple cases of Chagas disease have not been reported in the U.S., extensive investigations, confirmatory laboratory testing, and control measures may be needed if such events should occur. These will be situation-dependent and determined through consultation among the involved agencies.

S. Special Situations:

Guidance will be provided or determined based on the situation and information known at the time. Some special situations that may require additional investigation or response include: an environmental assessment to determine exposure risks to kissing bugs and/or level of bug infestation, contaminated blood or tissue products, and other risk factors potentially exposing individuals to *T. cruzi* infections. For the rare instances of transfusion or transplant-transmitted *T. cruzi* infections or congenital Chagas cases, PCR should be performed at CDC.

References

1. Heymann, DL, ed., Control of Communicable Diseases. Manual, 19th Edition. Washington, DC, American Public Health Association, 2008: pp. 630-639.
2. American Academy of Pediatrics. 2021 Red Book: Report of the Committee on Infectious Disease, 32nd Edition. Illinois, Academy of Pediatrics, 2021.
3. Centers for Disease Control and Prevention. Chagas Disease: Epidemiology & Risk Factors. <https://www.cdc.gov/parasites/chagas/epi.html>
4. Centers for Disease Control and Prevention. Chagas Disease: Disease. <https://www.cdc.gov/parasites/chagas/disease.html>
5. Centers for Disease Control and Prevention. Chagas Disease: Triatomine Bug FAQs. https://www.cdc.gov/parasites/chagas/gen_info/vectors/index.html
6. Klotz, J.H., Dorn, P.L., Logan, J.L., et al. "Kissing Bug": Potential Disease Vectors and Cause of Anaphylaxis. Clinical Infectious Diseases 50(12): 1629-1634; 2010.
7. Smith, RL, Venomous Animals of Arizona. Tucson: Cooperative Extension, College of Agriculture, University of Arizona, 1982, pp. 38-40.
8. Stoops, ED, Martin, J, Scorpions and Venomous Insects of the Southwest. Phoenix: Golden West Publications, 1995, pp. 80-81.
9. Werner, F, Olson, C. Insects of the Southwest. Tucson: Fisher Books, 1994, pp. 22-23.
10. Centers for Disease Control and Prevention. Chagas Disease: Antiparasitic Treatment. https://www.cdc.gov/parasites/chagas/health_professionals/tx.html
11. Centers for Disease Control and Prevention. Chagas Disease: Diagnosis. <https://www.cdc.gov/parasites/chagas/diagnosis.html>
12. Centers for Disease Control and Prevention. Chagas Disease: American Trypanosomiasis: Laboratory Diagnosis. <https://www.cdc.gov/dpdx/trypanosomiasisAmerican/index.html>
13. Shujuan Li, Dawn H. Gouge, Shakunthala Nair, Alfred J Fournier and W. Eugene Hall: Arizona Kissing Bugs, For pest management and Extension professionals. The University of Arizona Cooperative Extension. March 2019 <https://extension.arizona.edu/sites/extension.arizona.edu/files/pubs/az1787-2019.pdf>
14. Arizona Department of Health Services. In: Case Definitions for Reportable Communicable Morbidities: 2021. 2021 [cited 2022Feb24]; Available from: <https://www.azdhs.gov/documents/preparedness/epidemiology-disease-control/disease-investigation-resources/casedefinitions/case-definitions.pdf>