Infectious Disease Epidemiology Section
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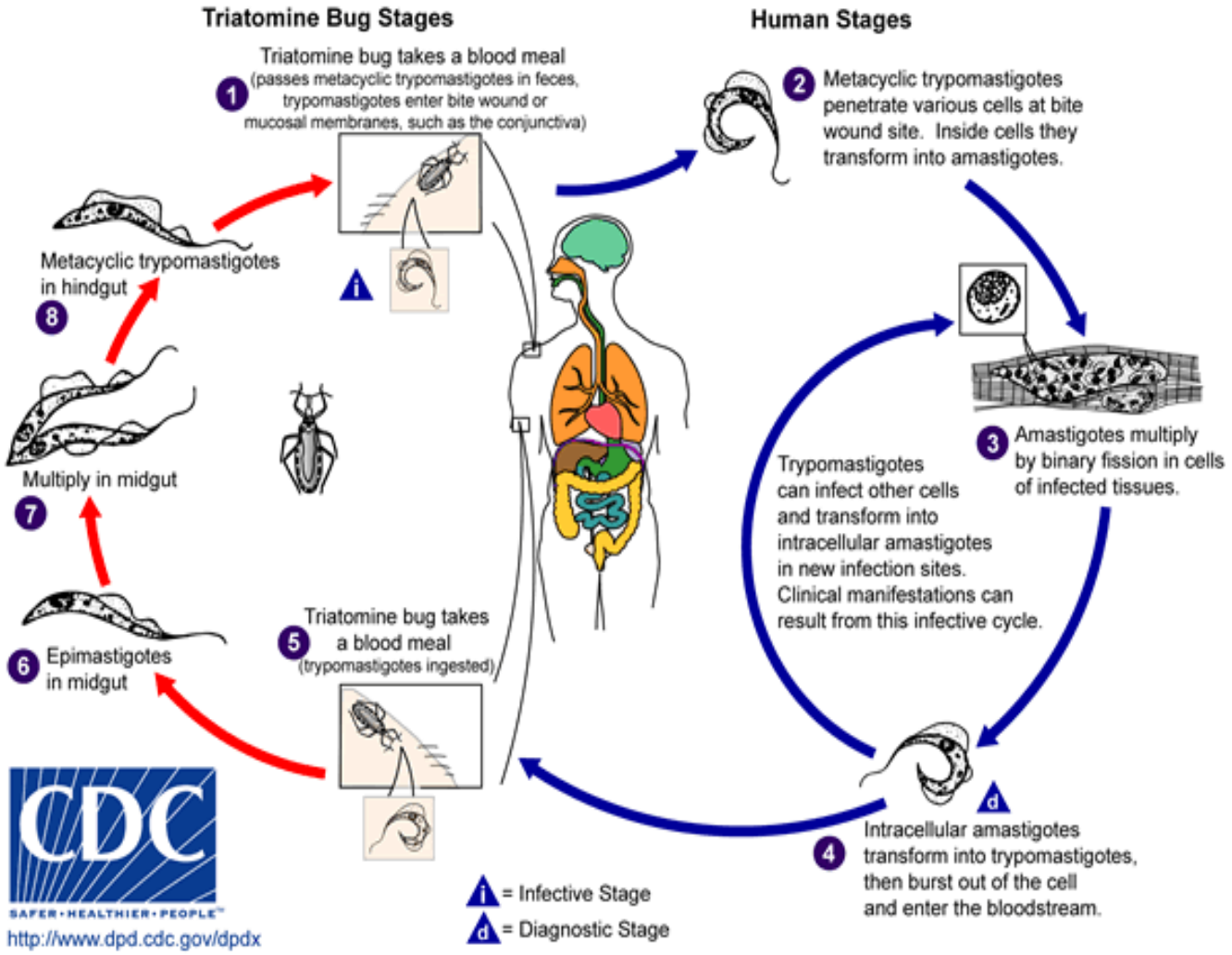
Chagas Disease or American Trypanosomiasis

Chagas disease is named after the Brazilian physician Carlos Chagas, who discovered the disease in 1909. It is caused by the parasite *Trypanosoma cruzi*, which is transmitted to animals and people by insect vectors and is found only in the Americas (mainly, in rural areas of Latin America where poverty is widespread). Chagas disease (*T. cruzi* infection) is also referred to as American trypanosomiasis.

Parasitology

Infection is most commonly acquired through contact with the feces of an infected triatomine bug (or "kissing bug"), a blood-sucking insect that feeds on humans and animals.



An infected triatomine insect vector takes a blood meal and releases metacyclic trypomastigotes in its feces near the site of the bite wound. Trypomastigotes enter the host through the wound or through intact mucosal membranes, such as the conjunctiva.

Inside the host, the trypomastigotes invade reticulo-endothelial cells near the site of inoculation, causing a localized swelling with adenopathy.

In the cells they differentiate into intracellular amastigotes. The amastigotes multiply by binary fission and differentiate into trypomastigotes, and then are released into the circulation as bloodstream trypomastigotes. Trypomastigotes infect cells from a variety of tissues (cardiac muscle, gastro-intestinal smooth muscle and create pseudocysts of trypomastigotes. Pseudocysts may later release infective trypomastigotes in the circulatory system. These may be ingested by a biting reduviid bug to continue the infection cycle.

Clinical manifestations can result from this infective cycle. The bloodstream trypomastigotes do not replicate (different from the African trypanosomes). Replication resumes only when the parasites enter another cell or are ingested by another vector. The "kissing" bug becomes infected by feeding on human or animal blood that contains circulating parasites. The ingested trypomastigotes transform into epimastigotes in the vector's midgut. The parasites multiply and differentiate in the midgut and differentiate into infective metacyclic trypomastigotes in the hindgut.

Transmission

The transmission of Chagas disease from a bug to a human is not easy. The parasite that causes the disease is in the bug feces. The bug generally defecates on or near a person while it is feeding on his or her blood, generally when the person is sleeping. Transmission occurs when fecal material gets rubbed into the bite wound or into a mucous membrane (for example, the eye or mouth), and the parasite enters the body.

It is important to note that not all triatomine bugs are infected with the parasite that causes Chagas disease. The likelihood of getting Chagas disease from a triatomine bug in the United States is low, even if the bug is infected.

The saliva of certain types of triatomines can cause an allergic reaction in some people. An allergic reaction may be characterized by severe redness, itching, swelling, welts, hives, or, rarely, anaphylactic shock (severe allergic reaction). Persons at risk of anaphylactic shock should consult a physician to obtain medication to use in case of a bite. It is important to note that not all triatomines are infected with the parasite even though they may cause an allergic reaction.

Transmission can also occur from:

- mother-to-baby (congenital)
- contaminated blood products (transfusions)
- an organ transplanted from an infected donor
- laboratory accident, or
- contaminated food or drink (rare)

Triatomine Bugs

Some triatomine bugs, if infected, can transmit *T. cruzi*. The triatomine bug thrives under poor housing conditions (for example, mud walls, thatched roofs), therfore in endemic countries, people living in rural areas are at greatest risk for acquiring infection.

Triatoma sanguisuga

Triatomines are primarily nocturnal and feed on the blood of mammals (including humans), birds and reptiles. Triatomine bugs live in a wide range of environmental settings, generally within close proximity to a blood host. In areas of Latin America where human Chagas disease is an important public health problem, the bugs nest in cracks and holes of substandard housing.

Triatoma aerstaeckeri

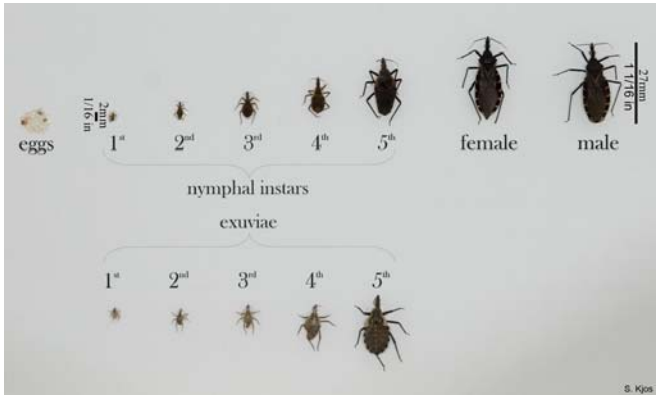
Resting places

Because most indoor structures in the United States are built with plastered walls and sealed entryways to prevent insect invasion, triatomine bugs rarely infest indoor areas of houses. Discovery of immature stages of the bug (wingless, smaller nymphs) inside may be an indication of infestation. When the bugs are found inside, they are likely to be in one of the following settings:

- Near pet resting areas
- In areas of rodent infestation
- In and around beds and bedrooms, especially under or near mattresses or night stands

Identifying a bug

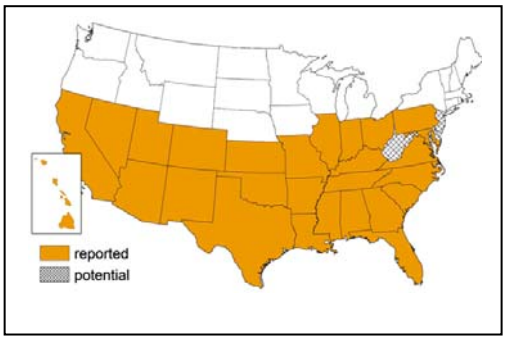
- Do not touch or squash the bug. Place a container on top of the bug, slide the bug inside, and fill it with rubbing alcohol or, if not available, freeze the bug in the container. Then, take it to the local extension service or health unit, for species identification or *T. cruzi* testing.



- Any material containing bug parts or feces should also be submitted for testing, preferably in a plastic bag or clean sealable container. Surfaces that have come into contact with the bug should be cleaned with a solution made of one part bleach to nine parts water (or seven parts ethanol to three parts water).

- There are many beetles and non-triatomine reduviid bugs that resemble the triatomine bug. Two examples of non-triatomine reduviid bugs that do not feed on human blood are the wheel bug and the assassin bug. Some plant-feeding bugs, such as Coreidae, also resemble the triatomine.

Geographic Distribution



By applying published seroprevalence figures to immigrant populations, the Centers for Disease Control and Prevention (CDC) estimates that more than 300,000 persons with *Trypanosoma cruzi* infection live in the United States. Most people with Chagas disease in the United States acquired their infections in endemic countries.

Chagas disease is endemic throughout much of Mexico, Central America, and South America where an estimated eight to 11 million people are infected.

T,cruzi in Wildlife

Although rare in humans and domestic animals in the United States, *T. cruzi* is commonly detected in some wildlife species, most commonly raccoons (*Procyon lotor*) and Virginia opossums (*Didelphis virginiana*). Among 11 species of mammals from the southern states, testing by immuno-fluorescence and culture, evidence of *T. cruzi* was found in every state. In general, the highest seroprevalence rates were found in raccoons (0% to 68%) and opossums (17% to52%), but antibodies to *T. cruzi* were also detected in small numbers of striped skunks (*Mephitis mephitis*) from Arizona and Georgia, bobcats (*Lynx rufus*) from Georgia, coyotes (*Canis latrans*) from Georgia and Virginia, and ringtail (*Bassariscus astutus*) from Arizona. For both raccoons and opossums, seroprevalence is significantly higher in females than in males. No difference is detected in seroprevalence between adults and juveniles and between animals caught in urban and rural locations. *T. cruzi* prevalence varies by host species, host characteristics and geographic region.

Other wildlife species in the United States that are naturally infected with the parasite based on either serology or culture include the armadillo (*Dasypus novemcinctus*) badger (*Taxidea taxus*), coyote, gray fox (*Urocyon cinereoargenteus*), striped skunk and various rodent species.

The majority of previous studies of *T. cruzi* in wildlife have focused on blood culture as the primary method for determining infection status, but this method has been shown to have a lower sensitivity than serologic testing.

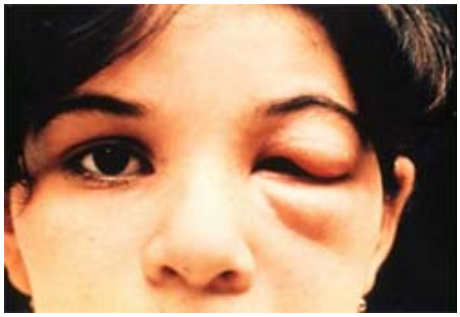
Disease Burden

In South and Central America, there about 20 million people who have been infected (serology positive). Chronic Chagas disease occurs in about 30% of all infected individuals, i.e. six million people. The chronic phase occurs after a long latent period of 20 to 30 years. In the U.S. there are an estimated 100,000 seropositive people who could transmit the parasite through a blood transfusion.

In the U.S., autochthonous cases in humans are rare, with only six cases previously reported for the years from 2000 to 2007. However, serologic studies indicate that many autochthonous cases may be undiagnosed: A survey of more than 11,000 post-operative cardiac surgery patients in Houston showed a prevalence of 0.05% of seropositive patients (six out of 11,000).

Although the reported incidence of human Chagas disease due to vector exposure in the United States is low, U.S. strains of *T. cruzi* have proven to be virulent as confirmed by clinical disease and death in a wide range of mammalian species including domestic dogs, primates and humans.

Clinical Picture



The mild swelling that may develop at the site of parasite inoculation (where the parasite entered the body through the skin or mucous membranes) is called a chagoma.

When the parasite enters the body through the conjunctiva of the eye, the swelling around the eye is called Romaña's sign. Chagomas, including Romaña's sign, usually last longer than an allergic reaction and are less likely to be severely itchy. Romaña's sign, the swelling of the child's eyelid, is a marker of acute Chagas disease. The swelling is due to bug feces being accidentally rubbed into the eye, or because the bite wound was on the same side of the child's face as the swelling.

Infection may be mild or asymptomatic. There may be fever or swelling around the site of inoculation (where the parasite entered into the skin or mucous membrane). Some of the asymptomatic patients may show some minor electro-cardiographic and radiographic abnormalities typical of myocarditis with conduction disturbances.

Acute Chagas disease occurs immediately after infection and may last up to a few weeks or months; parasites may be found in the circulating blood. The symptoms are non-specific: influenza-like illness, fever, malaise, nausea, vomiting and diarrhea. Neonates and Adults with AIDS may develop a fulminant illness with generalized adenopathies, myocarditis, hepato-splenomegaly and meningo-encephalitis. Rarely, acute infection may result in severe inflammation of the heart muscle or the brain and lining around the brain.

The initial high parasitemia peaks at ten days and may last one or two months and then resolve.

Following the acute phase, most infected people enter into a prolonged asymptomatic form of disease (called "chronic indeterminate") during which few or no parasites are found in the blood. During this time, most people are unaware of their infection. Many people may remain asymptomatic for life and never develop Chagas-related symptoms. However, an estimated 20% to 30% of infected people will develop debilitating and sometimes life-threatening medical problems over the course of their lives.

Cardiac disease usually begins with conduction abnormalities such as right bundle branch block and/or left anterior fascicular block, which may be followed years later by dilated cardiomyopathy. Later cardiac disease is sometimes accompanied by apical aneurysm and thrombus formation.

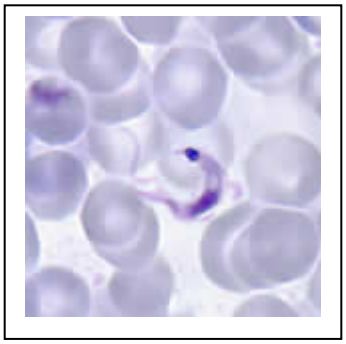
Less frequently, patients with Chagas disease experience gastrointestinal disease (megasyndromes). Once the characteristic pathology is established (e.g., dilated cardiomyopathy, megaesophagus), antiparasitic treatment will not reverse it.

In people who have suppressed immune systems (for example, due to AIDS or chemotherapy), Chagas disease can reactivate with parasites found in the circulating blood. This occurrence can potentially cause severe disease.

Diagnosis

Parasitologic methods, including identification of trypomastigotes in blood by microscopy, 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.

Blood Smear



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 smear 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.

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.

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. For this reason, 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 immunofluorescent antibody test (IFA). To increase accuracy of diagnosis, careful consideration of the patient's history to identify possible risks for infection may be helpful.

In December 2006, the U.S. Food and Drug Administration approved a screening test for blood donations. Blood donations that are reactive (positive) by the blood screening test are then tested using an investigational assay, radioimmunoprecipitation assay (RIPA). Donors who are positive on the screening test can no longer donate blood, regardless of their RIPA result. Donors are contacted by the blood center and notified about the results of the blood donation testing. In addition, positive donors are requested to contact their physician. Blood donor screening tests are not approved for diagnostic purposes and additional testing may be indicated.

Treatment

Antiparasitic treatment is indicated for all cases of:

- Acute or reactivated Chagas disease; congenital infections are considered acute disease.
- Chronic *Trypanosoma cruzi* infection in children up to age 18.
- Adults up to 50 years old with chronic infection who do not already have advanced Chagas cardiomyopathy.
- 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.

The two drugs used to treat infection with *Trypanosoma cruzi* are **nifurtimox and benznidazole**. In the United States, these drugs are not FDA approved and are available only from CDC under investigational protocols. For both drugs, side effects are fairly common, and tend to be more frequent and more severe with increasing age.

Common side effects of benznidazole treatment include:

- allergic dermatitis
- peripheral neuropathy
- anorexia and weight loss
- insomnia

The most common side effects of nifurtimox are:

- anorexia and weight loss
- polyneuropathy
- nausea
- vomiting
- headache
- dizziness or vertigo

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. The following table outlines recommended dosage regimens by age group:

Drug	Age group	Dosage and duration
Benznidazole	< 12 years	10 mg/kg per day orally in 2 divided doses for 60 days
	12 years or older	5-7 mg/kg per day orally in 2 divided doses for 60 days
Nifurtimox	≤ 10 years	15-20 mg/kg per day orally in 3 or 4 divided doses for 90 days
	11-16 years	12.5-15 mg/kg per day orally in 3 or 4 divided doses for 90 days
	17 years or older	8-10 mg/kg per day orally in 3 or 4 divided doses for 90 days

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.

In the U.S., medication for Chagas is available only through CDC. Your health care provider can talk with CDC staff about whether, and how, you should be treated.

Prevention & Control

Public health efforts aimed at preventing transmission have decreased the number of newly infected people and completely halted vector-borne transmission in some areas. Infection acquired from blood products, organ transplantation, or congenital transmission continues to pose a threat.

In endemic areas of Mexico, Central America, and South America improved housing and spraying insecticide inside housing to eliminate triatomine bugs has significantly decreased the spread of Chagas disease. Further, screening of blood donations for Chagas is another important public health tool in helping to prevent transfusion-acquired disease. Early detection and treatment of new cases, including mother-to-baby (congenital) cases, will also help reduce the burden of disease.

<u>Keeping triatomine bugs away from homes</u>
Synthetic pyrethroid sprays have been used successfully in Latin America to eliminate house infestations. Although similar chemicals are available in the United States, none have been specifically approved for use against triatomine bugs. A licensed pest control operator should be consulted if considering the use of insecticides. Please note that roach hotels or other "bait" formulations do not work against triatomine bugs. Long lasting insecticide treated bednets and curtains have been shown to kill these bugs.
Other precautions to prevent house infestation include:

- Sealing cracks and gaps around windows, walls, roofs, and doors
- Removing wood, brush, and rock piles near your house
- Using screens on doors and windows, and repairing any holes or tears

- If possible, making sure yard lights are not close to your house (lights can attract the bugs)
- Sealing holes and cracks leading to the attic, crawl spaces below the house, and to the outside
- Having pets sleep indoors, especially at night
- Keeping your house and any outdoor pet resting areas clean, in addition to periodically checking both areas for the presence of bugs

In the United States and in other regions where Chagas disease is now found but is not endemic, control strategies are focused on preventing transmission from blood transfusion, organ transplantation and mother-to-baby.