

# Chagas' disease

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Acute Chagas' disease or reactivation of chronic Chagas' can be diagnosed by:

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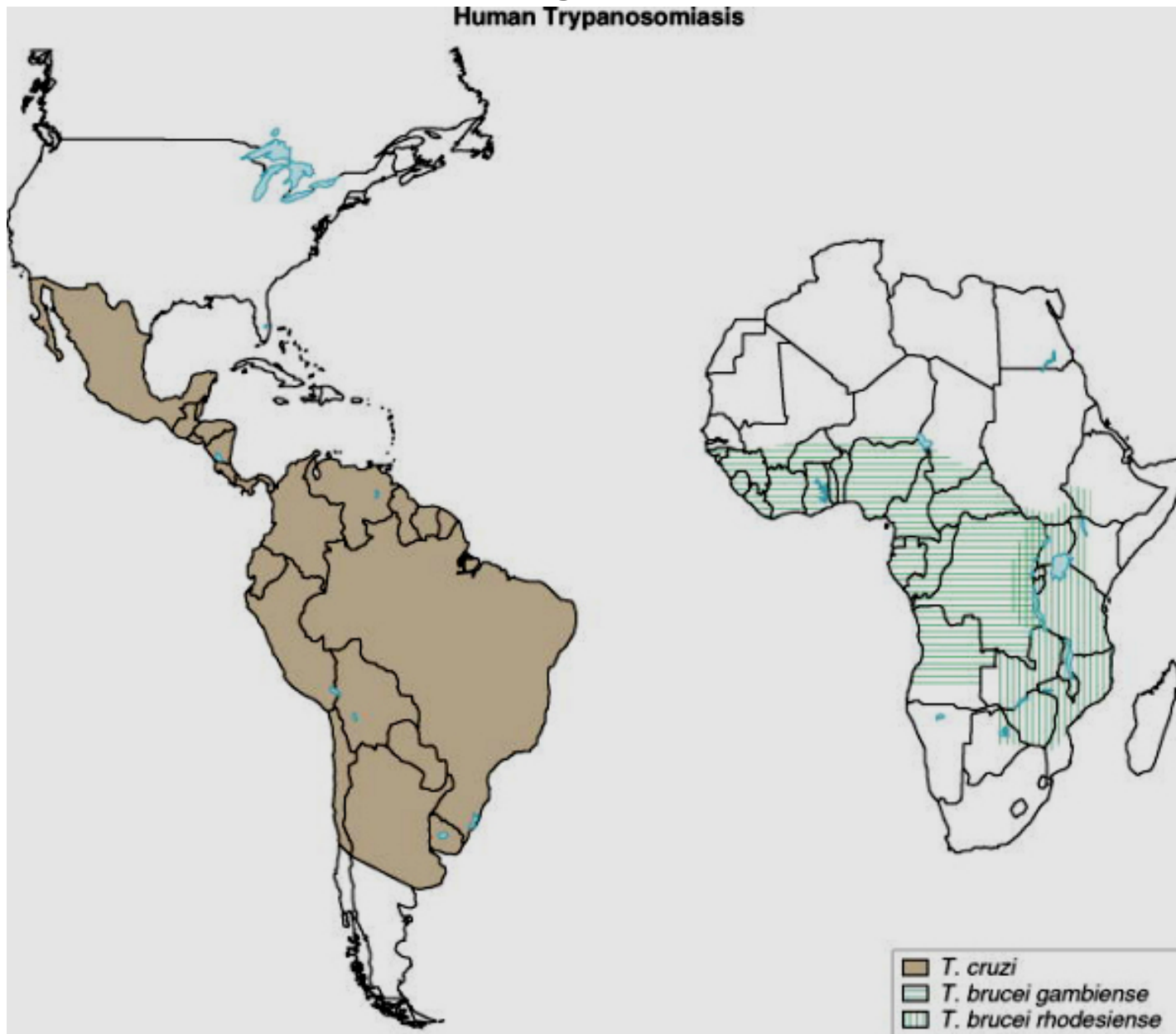
1. Myocardial biopsy
  2. IgG antibody detection
  3. IgM antibody detection
  4. Giemsa stain of any fluid or tissue
  5. IgG and IgM detection
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*Trypanosoma cruzi*, a protozoan hemoflagellate, is the cause of Chagas' disease

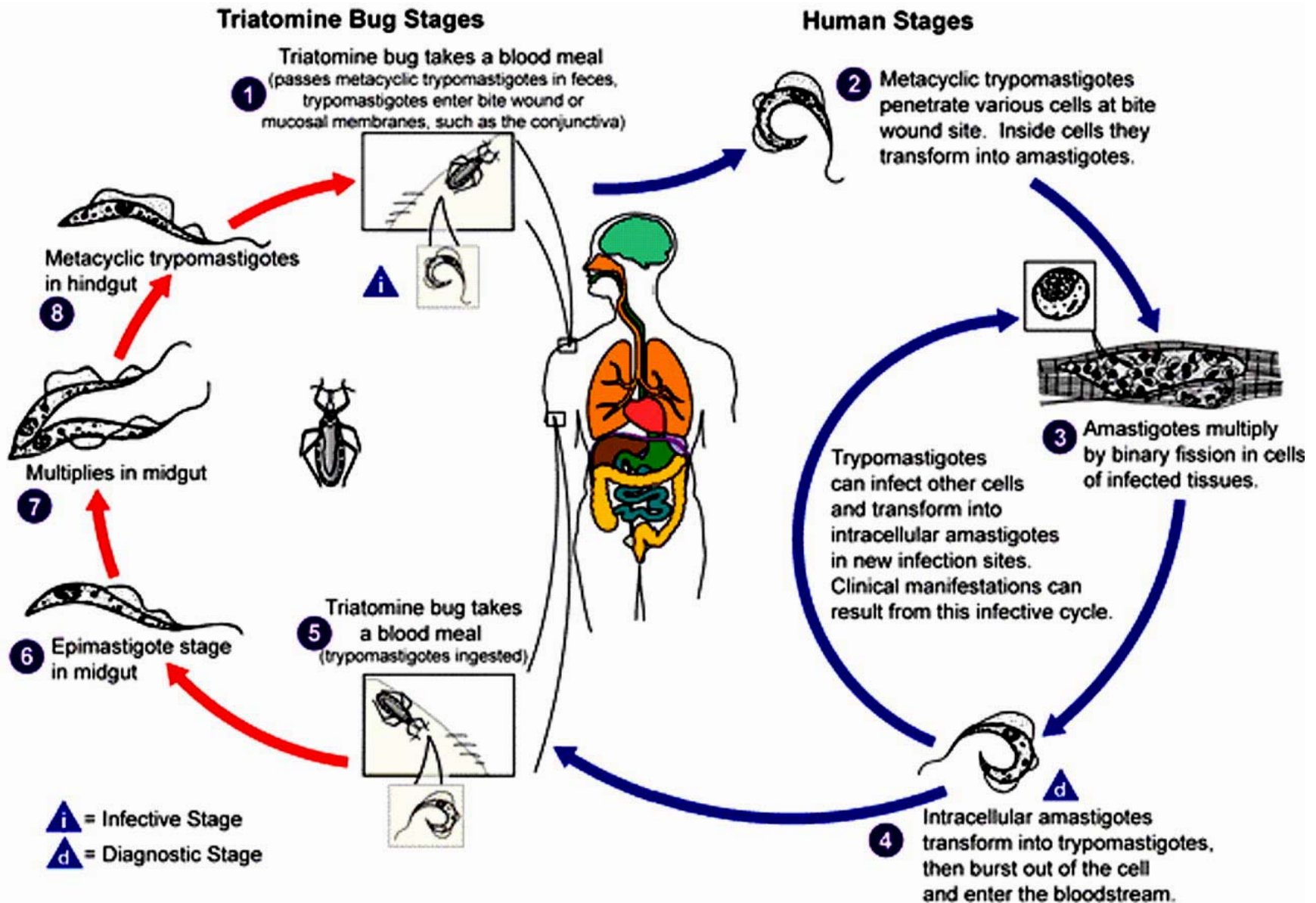
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- disease is limited to the Western hemisphere
  - vectorborne transmission to humans is rare in the United States
  - infection is common in immigrants from Central and South America
  - 80,000 to 100,000 *T. cruzi*-infected persons now living in the United States
  - several transfusion- and transplantation-associated cases have been documented in the United States
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In Latin America, between 8 and 11 million people are infected, mostly affecting those living in rural areas and poor housing conditions (e.g. mud walls, thatched roofs)



*T. cruzi* has been isolated from more than 150 species of wild and domestic mammals





***Triatoma infestans* (“kissing bug”), a vector for Chagas’ disease,  
is primarily found in Central and South America and Mexico**



**Triatomine bug defecating on the wound after taking a  
blood meal**



***Rhodnius prolixus***

# Transmission of *T. cruzi* to humans

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- insect bite
  - transplacentally
  - blood transfusion
  - organ transplantation
  - laboratory accident
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# Clinical Manifestations

Incubation Period: 1 to 2 weeks or longer

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- acute disease (x 4 to 8 weeks)
    - asymptomatic
    - chagoma
    - myocarditis
    - CNS disease
  - indeterminate disease
  - chronic disease (decades after acute infection)
    - cardiomyopathy
    - heart conduction defects
    - gastrointestinal disease
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## Acute disease as a result of insect bite mostly occur in children

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- local signs: chagoma; Romana sign
  - systemic manifestations:
    - fever, malaise, anorexia, and edema of the face and lower extremities. Generalized lymphadenopathy and mild hepatosplenomegaly also may appear
    - meningoencephalitis
    - myocarditis: may lead to CHF, significant rhythm disturbances are rare in the acute phase
  - acute phase is followed by the indeterminate phase
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**Chronic disease become clinically apparent years to decades after the initial infection in 10 to 30% of infected people**

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- cardiac disease: gradual progression, sudden death
    - congestive heart failure: cardiomegaly, right side more common
    - arrhythmias: right branch and the left anterior branch of the bundle of His more common
    - thromboembolism to the brain and other areas: mural thrombi, apical aneurysms
  - pathology: thin, dilated ventricular walls with diffuse lymphocytic infiltration, interstitial fibrosis and atrophy of myocardial cells. Conduction system with fibrosis and chronic inflammation
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## Gastrointestinal disease may be manifested by mega -esophagus or -colon

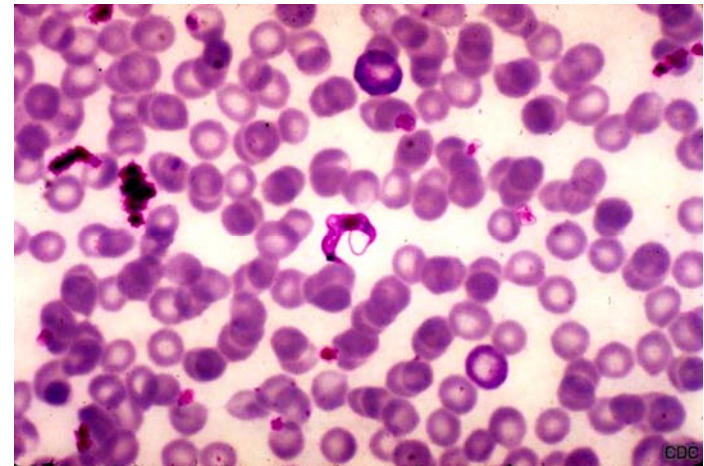
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- megaesophagus: dysphagia, odynophagia, chest pain, cough, and regurgitation; weight loss and aspiration pneumonia; increase incidence of esophageal cancer hypersalivation and salivary gland hypertrophy
  - megacolon: chronic constipation and abdominal pain; acute obstruction, volvulus, perforation, septicemia, and death may occur
  - pathology: dilation of the organ with hypertrophy of the muscle layer but marked decrease in the number of cells in the myenteric plexus, and peri- and intraganglion fibrosis in the presence of Schwann cell proliferation and lymphocytosis (similar lesions in other viscera)
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# Acute Chagas' disease is diagnosed by detecting *T. cruzi*. IgM is not helpful

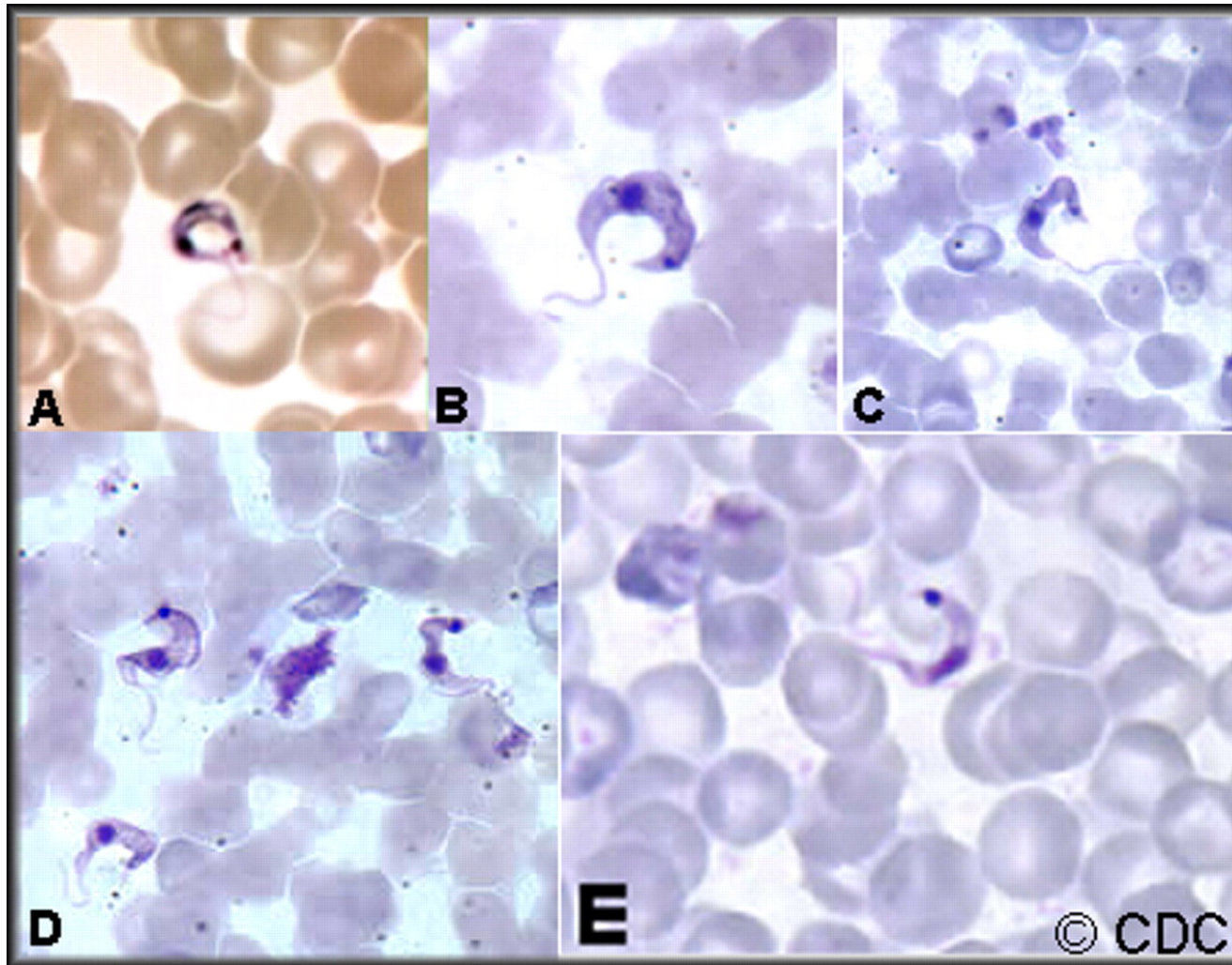
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- Peripheral blood, bone marrow aspirates, cerebrospinal fluid, lymph node, pericardial fluid
  - visualization of the motile parasite in wet mounts (anticoagulated blood or buffy coat )
  - Wright-Giemsa stain



- PCR (nuclear and kinetoplast DNA)
  - isolation of the parasite
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Trypanosomes measure from 12 to 30  $\mu\text{m}$  in length  
(erythrocyte  $\approx 7\mu\text{m}$ )

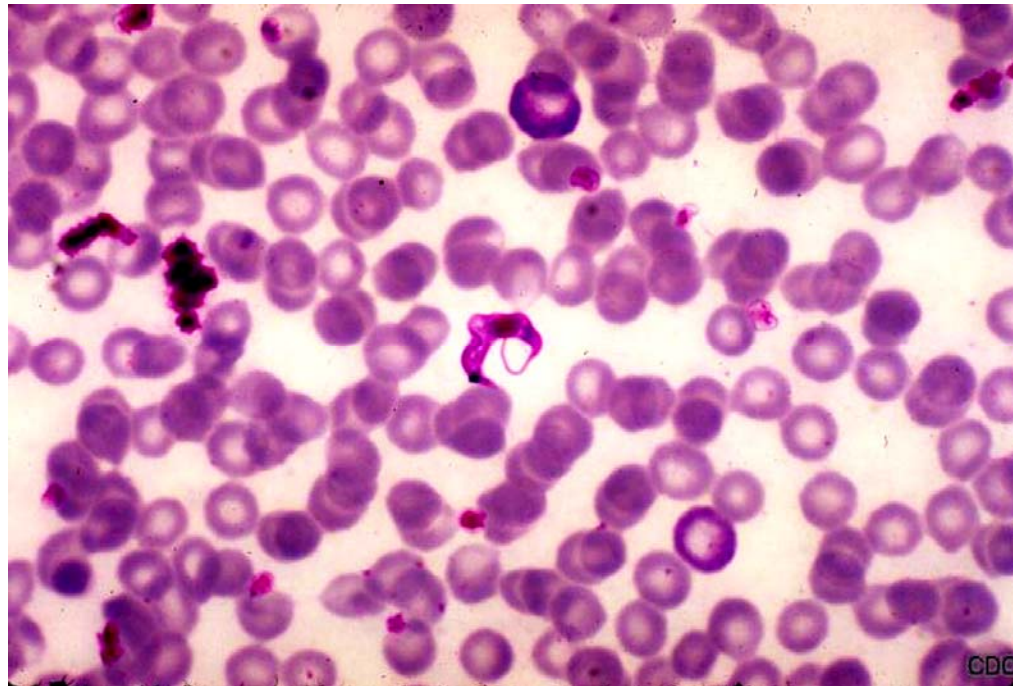




## Chronic Chagas' disease is diagnosed by detecting *T. cruzi*-specific IgG antibodies

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- ELISA, IHA, IFA: positive in at least two serological tests
- false-positive reactions can occur (e.g. leishmaniasis, malaria, syphilis)





## Reactivation of *T. cruzii* infection in immunocompromised patients can occur

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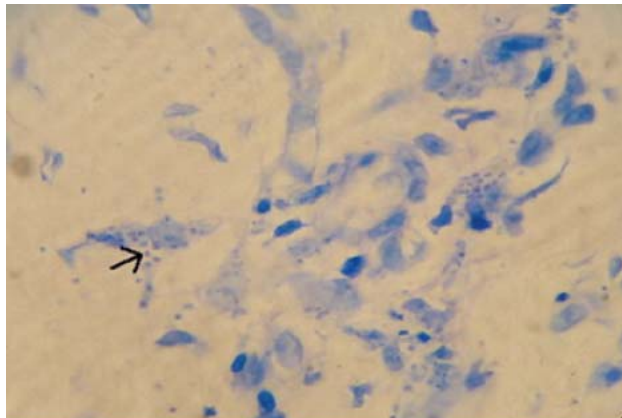
- In AIDS patients (Ferreira M. et al. CID 1997;25:1397-400)
    - CNS disease predominates (75%); brain abscesses can occur; CSF with low level pleocytosis, elevated protein, *T. cruzi* trypomastigotes may be visualized
    - early diagnosis and treatment with benznidazole or nifurtimox may improve survival rate
  - In the setting of organ transplantation
    - immunosuppression for organ transplantation has resulted in Chagas disease in previously infected individuals
    - skin lesions
    - serological screening for recipients is not mandatory in the United States. In donors, it is performed based on individual risk factors
    - previous infection with *T. cruzi* should not preclude organ transplantation but close monitoring and early therapy are mandatory
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**Chagas' disease in a kidney transplant patient with skin symptoms.  
2-week evolution of an erythematous, infiltrated lesion of  $\approx 15$  cm  
on the anterior aspect of the right thigh**

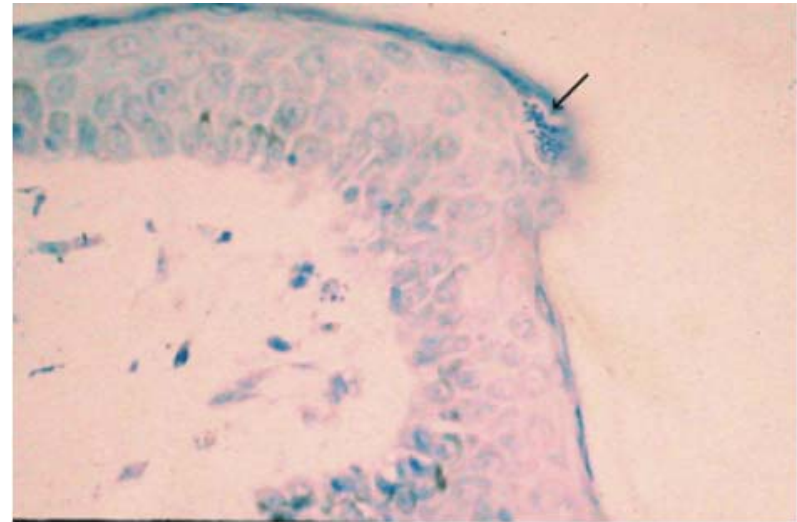
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**Figure 1** Infiltrated erythematous plaque on the trunk



**Figure 2** Intracellular amastigotes in dermal macrophages (arrow) and some scattered in the extracellular matrix (Giemsa stain,  $\times 100$ )



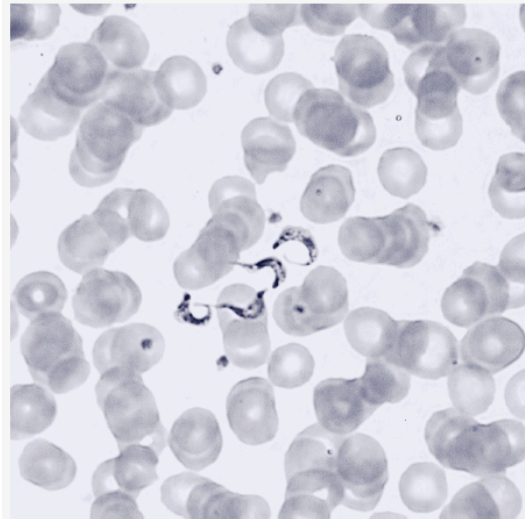
**Figure 3** Amastigotes in the epidermis (arrow) (Giemsa stain,  $\times 100$ )

# Chagas' disease can be transmitted in the United States through organ transplantation

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- Chagas disease has developed in seronegative recipients who receive an organ from a previously infected donor
- organs from a single donor (immigrant from Central America) were transplanted to a 37 yo wm (kidney and pancreas); 32 yo wm (kidney); 69 yo wm (kidney)
- six weeks later the 37 yo wm returns with fever

FIGURE 1. *Trypanosoma cruzi* trypomastigotes on a peripheral blood smear from a patient aged 37 years



Photo/CDC file

## Chagas' disease in seronegative recipients of infected donors (D+/R-)

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- the 32 yo wm (liver) and 69 yo wm (kidney) were also found to be infected
- *T. cruzi* was isolated from the three recipients and each of them received nifurtimox
  - 69 yo (kidney), nifurtimox for 4 months, lived
  - 37 yo (kidney-pancreas), recurrent parasitemia after 4 months of nifurtimox, died of chagasic myocarditis (two weeks into her second course of nifurtimox)
  - 32 yo (liver), nifurtimox for several weeks, died of sepsis and hepatic and renal failure (apparently unrelated to Chagas' disease)

## Transplant recipient who receives a liver from a previously infected donor

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- 45 yo man with history of hepatocellular carcinoma and end-stage liver disease secondary to Hep C
  - 35 yo donor, brain death secondary to subarachnoid hemorrhage, immigrated to the United States at the age of 25. Hx of dilated cardiomyopathy and found to have a 1:128 positive titer for *T. cruzi* (confirmed in ELISA)
  - patient and family member explained of pros and cons
  - PCR baseline obtained in donor and recipient
  - nifurtimox therapy for 3 months
  - PCR every week for 1 month, followed by every month for 6 months
  - serologies every month for 6 months
  - close clinical follow up (cardiac, CNS, systemic disease)
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# Chagas' disease & blood transfusions

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- seven cases have occurred in the US and Canada since 1989 (in 6 the donor emigrated from a *T. cruzi*-endemic region)
  - *T. cruzi* can be transmitted via whole blood or platelet transfusions
  - Screening for infected blood donations was broadly implemented in January 2007, shortly after licensing of the first screening test in the US
  - ELISA for detection of *T. cruzi*-IgG (Ortho *T. cruzi* ELISA Test System, purified *T. cruzi* epimastigote lysate on a solid phase)
  - The prevalence of confirmed positive blood donors after 3 months of routine screening was approx 1:21,000
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*T. Cruzi* can be transmitted to the fetus in 1% to 10% of women with chronic infection

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- most infected newborns are asymptomatic or have nonspecific findings such as low birth weight, prematurity, or low Apgar scores
  - hepatosplenomegaly, anemia and thrombocytopenia
  - Myocarditis
  - Meningoencephalitis
  - respiratory distress
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# Nifurtimox and Benznidazole are used for the Treatment of Chagas' Disease

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For nifurtimox, contact CDC  
Centers for Disease Control and Prevention  
National Center for Zoonotic, Vector-borne and Enteric  
Diseases (NCZVED)  
1600 Clifton Road  
MS D76  
Atlanta, GA 30333  
Call: 770-488-7775  
FAX: 770-488-7761  
E-mail: [chagas@cdc.gov](mailto:chagas@cdc.gov)  
[24 Hours/Every Day]: 800-CDC-INFO (800-232-4636)

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# Nifurtimox

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- trypanocidal
  - nitrofuran derivative that generates a nitro-anion radical metabolite which reacts with the nucleic acids of the parasite, causing a significant breakage in the deoxyribonucleic acid (DNA)
  - production of superoxide anions, and hence, hydrogen peroxide (both of which are very toxic to the parasite) and inhibition of trypanothione reductase, which is a parasite-specific antioxidant defense enzyme
- indications: acute disease; congenital disease; laboratory accidents; reactivation or acute in immunosuppressed patients
- parasitologic cure in 70% of patients

## Nifurtimox -30 and 120 mg tablets

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- the recommended dose of nifurtimox in adults is 8 to 10 mg/kilogram/day orally in 4 divided doses for 120 days; in adolescents 12.5 to 15 mg/kg/day, and for children 1 to 10 years 15 to 20 mg/kg/day
  - side effects: nausea, vomiting, insomnia, headache, vertigo, tremor, paresthesias, and seizures
  - consider prophylaxis for select immunocompromised patients: nifurtimox at a dosage of 5 mg/kg 3 times a week (Ferreira M. et al. CID 1997;25:1397-400)
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# Benznidazole

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- trypanocidal
  - inhibit protein and ribonucleic acid (RNA) synthesis in the trypanosome parasite
  - able to specifically inhibit macrophage NF- $\kappa$ B activation after LPS plus IFN- stimulation (Piaggio E. et al. The Journal of Immunology, 2001, 167: 3422-3426)
- indications: acute early disease, early chronic phase
- for adults: 5 to 7 mg/kg daily in two divided doses usually for 60 days (30 to 90 days); for children 10 mg/kg daily in two divided doses
- for prophylaxis in IC patients: a single oral dose of 5 mg/kg 3 times a week
- side effects include nausea, vomiting, abdominal pain, peripheral neuropathy, blood dyscrasias, and severe skin reactions

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Lancet 1996; 348: 1407-13; Am Heart J 1994; AJT 127: 151-62; 2007;7(3):680-4

# Prevention

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- international control programs: improved housing and spraying insecticide inside housing to eliminate triatomine bugs has significantly decreased the spread of Chagas disease
  - treatment of infected people
  - blood donors in areas with endemic infection should be screened by serologic tests
  - congenital transmission
  - consider prophylaxis for select immunocompromised patients
  - anti-TNF drugs?
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## 'Silent killer' Tropical disease threatens Canadian blood supply, experts warn

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- "It's a silent killer," says Dr. Keystone, of the tropical disease unit at the Toronto General Hospital. "If somebody comes to you with heart failure, you would say, 'Oh, you probably have coronary artery disease.' He'd send you to a cardiologist. We have no idea how much Chagas disease is out there."
  - Chagas's disease: fever, heart failure, CNS disease; in the setting of contact with Central and South America; visiting rural poor areas, immigrants, blood transfusion, congenital transmission, organ donation, laboratory accidents
-

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# Neglected tropical diseases (NTDs)

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- about 1 billion people are affected by one or more NTDs
  - persist exclusively in the poorest and the most marginalized communities
  - largely eliminated and thus forgotten in wealthier places
  - unsafe water, poor sanitation, and limited access to basic health care
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# Fourteen diseases are currently listed as NTDs

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- Buruli ulcer
  - Chagas' disease
  - Cholera
  - Dengue
  - Dracunculiasis (guinea-worm)
  - Endemic treponematoses (yaws, pinta, endemic syphilis)
  - Human African trypanosomiasis (sleeping sickness)
  - Leishmaniasis
  - Leprosy
  - Lymphatic filariasis
  - Onchocerciasis
  - Schistosomiasis
  - Soil-transmitted helminthiasis
  - Trachoma
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