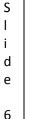
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S I d e 1	American Trypanosomiasis Chagas Disease New World Trypanosomiasis South American Trypanosomiasis Mal de Chagas Chagas-Mazza Disease	
S I d e 2	Overview • Organism • History • Epidemiology • Transmission • Disease in Humans • Disease in Animals • Prevention and Control • Actions to Take	In today's presentation we will cover information regarding the organism that causes Chagas disease and its epidemiology. We will also talk about the history of the disease, how it is transmitted, species that it affects (including humans), and clinical and necropsy signs observed. Finally, we will address prevention and control measures for Chagas disease, as well as actions to take if Chagas disease is suspected.
S I d e 3	ORGANISM	
S I d e 4	 The Organism Protozoan parasite Trypanosoma cruzi Cause of American trypanosomiasis (Chagas disease) Susceptible to: Disinfectants, direct sunlight, other harsh environments 	 American trypanosomiasis (Chagas disease) results from infection with the protozoan parasite <i>Trypanosoma cruzi</i>, a member of the family Trypanosomatidae. Most strains of this parasite can be classified into two major groups, <i>T. cruzi</i> I and <i>T. cruzi</i> II, which can be separated further into various lineages (e.g., <i>T. cruzi</i> IIa). Lineages tend to be associated with certain host species, although this relationship is not absolute. <i>T. cruzi</i> is susceptible to many disinfectants. It is destroyed by several hours of exposure to direct sunlight or other harsh environments. [Photo: <i>Trypanosoma</i> forms in blood smear from patient with African trypanosomiasis. Source: CDC Public Health Image Library]
S I d e 5	HISTORY	



History of Chagas

1907: Dr. Carlos Chagas
first becomes aware
of the *barbiero*I 1909: First publications on newly discovered

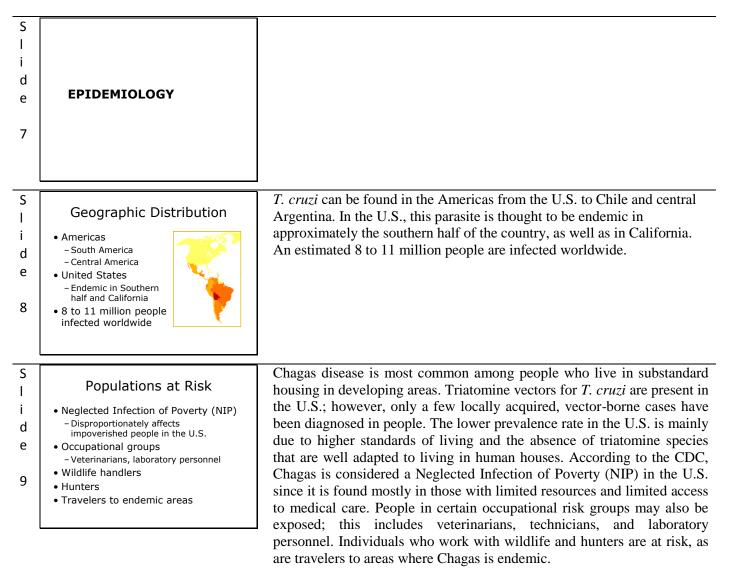
trypanosome • 1930s: Public health importance becomes known

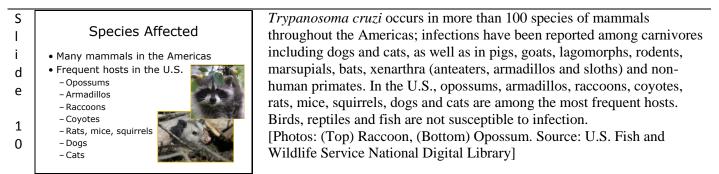


In 1907, while working among railroad workers in Brazil, physician Carlos Chagas first became aware of the *barbiero*, a blood-sucking bug infesting huts of the region. He quickly became interested in the insect and investigated whether it could be a transmitter of any parasites of man. By 1909, a new species of trypanosome was discovered, and the first published reports followed. Until the 1930s, little attention was given to Chagas disease as a public health issue.

Source: R. Lewinsohn. Carlos Chagas and the discovery of Chagas' disease (American trypanosomiasis). J R Soc Med. 1981 June; 74(6): 451–455.

[Photo: Carlos Chagas. Source: J. Pinto/Biblioteca Virtual Carlos Chagas via wikipedia.org]





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е	TRANSMISSION
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S	Turn and in sign

Transmission Vector-borne - Triatomine insects d Reduviid insects, kissing beetle/bug, е assassin bug - Multiple species capable of transmission 1 Triatoma Rhodnius 2 Panstrongylus

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Transmission

i	Three transmission cycles
d	 Sylvatic (wild) Wildlife-insect transmission
е	Human infections rare
1 3	 Domestic Human-insect transmission Peridomestic Transmitted via: Blood, organs, ingestion, <i>in utero</i>, milk

Chagas disease is a vector-borne disease transmitted primarily by triatomine insects, which are also called reduviid insects, "kissing beetles/ bugs" or "assassin bugs." More than 130 species of these insects appear to be capable of transmitting T. cruzi, with the most important species in the genera Triatoma, Rhodnius and Panstrongylus. The parasite usually completes its life cycle by cycling between an insect species and a mammalian species with which the insect lives in close association. [Photo: Dorsal view of the "kissing bug", Triatoma infestans, a vector for Chagas disease. Source: CDC Public Health Image Library]

There are three basic cycles of transmission for *T. cruzi*. In the sylvatic (wild) cycle, this organism cycles between wildlife and triatomine insects that live in sylvatic environments. Humans and domesticated animals are infected occasionally when they contact these bugs in the wild. The sylvatic cycle is responsible for relatively few cases of Chagas disease. It is the only cycle in the U.S. A domestic transmission cycle also exists in Mexico and parts of Central and South America. In this cycle, some insect vectors have colonized primitive adobe, grass and thatched houses, resulting in transmission between humans and insects. Transmission cycles between insects and domesticated animals (peridomestic cycles) can also provide opportunities for the parasite to infect humans. T. cruzi is not spread between mammals by casual contact; however, it can be transmitted directly via blood (e.g., in a blood transfusion) and in donated organs. Carnivores can acquire this organism when they eat infected prey. Vertical transmission has been reported in dogs and other animals, both in *utero* and in the milk. Transmission in milk is very rare in humans, but transplacental transmission can occur at each pregnancy, and during all stages of infection. Laboratory infections usually occur when the parasites contact mucous membranes or broken skin, or are accidentally injected via needlestick injuries, but aerosol transmission might be possible in this setting. [Photo: House with Chagas disease vectors. Source: Pan American Health Organization]

S I d e 1 4		This figure, from the CDC [http://www.cdc.gov/parasites/chagas/biology.html], shows how Chagas is transmitted. An infected triatomine insect vector (or "kissing" bug) takes a blood meal and releases trypomastigotes in its feces near the site of the bite wound. Inside the host, they differentiate into other forms, and are released into the bloodstream. Cells from a variety of tissues can be infected. 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.
S I d e 1 5	DISEASE IN HUMANS	
S I d e 1 6	Chagas Disease • Incubation period - 5 to 14 days after exposure to triatomine insect feces - 20 to 40 days after blood transfusion - 5 to 40 years after infection • Chronic stage	In humans, the incubation period is usually at least 5 to 14 days after exposure to triatomine insect feces, and 20 to 40 days after infection by blood transfusion. Many people do not become symptomatic until the chronic stage, which can occur 5 to 40 years after infection.
S I d e 1 7	Chagas Disease • Acute phase • Parasites found in blood • Most adults asymptomatic • Chagoma • Localized painless induration • Romaña's sign • Edema of eyes, conjunctivitis • Usually resolves in weeks to months	The acute phase is defined as the period during which the parasites can be found easily in the blood. Many people, particularly adults, are asymptomatic during this stage. The symptoms of the acute phase are highly variable and may include fever, headache, anorexia, malaise, myalgia, joint pain, weakness, nausea, vomiting, diarrhea, hepatomegaly, splenomegaly, and generalized or localized lymphadenopathy. Edema, either generalized or localized to the face and/or lower extremities, occurs in some cases. Sometimes, a chagoma (a localized painless induration) is seen where the parasite has entered through the skin. If entry occurs via the ocular mucous membranes, there may be painless edema of one or occasionally both eyes, often accompanied by conjunctivitis and enlargement of the local lymph nodes. This syndrome, which is called Romaña's sign, usually persists for 1 to 2 months. Patients occasionally develop a rash, but this usually disappears within several days. In most cases, the clinical signs resolve within weeks to months without treatment; however, some acute cases can be fatal. [Photo: This child from Panama is suffering from Chagas disease manifested as an acute infection with swelling of the right eye. Source: CDC Public Health Image Library]

Chagas Disease Indeterminate phase - Asymptomatic phase of varying length - Parasites disappear from blood
 Most patients enter chronic phase within 5 to 15 years
Chagas Disease Chronic phase - Characterized by organ failure Heart disease - Most common form of chronic Chagas - Many manifestations may occur Digestive system abnormalities - Megaesophagus - Megaecolon

S Chagas Disease T i • Immunocompromised people can be severely affected d Pregnant women е - Congenital infection, premature birth AIDS patients 2 Brain abscesses - Higher likelihood of reactivation 0

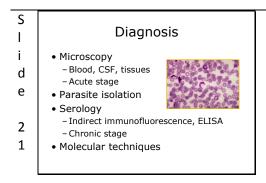
The acute phase is usually followed by an asymptomatic period of varying length; this stage is called the indeterminate phase. During the indeterminate phase, the parasites disappear from the blood. Although estimates vary, approximately 70% to 90% of the patients in the indeterminate phase never become symptomatic. Most of the remaining patients enter the chronic phase after 5 to 15 years, but in a few patients, the indeterminate phase can last as long as 40 years.

The chronic phase is typically represented by organ failure, usually of the heart or digestive system. Heart disease, the most common form of chronic Chagas disease, may be characterized by arrhythmias and conduction abnormalities, cardiac failure, apical aneurisms, embolic disease including stroke or pulmonary embolism, and sudden death. Signs of isolated left heart failure may occur first. Digestive system abnormalities lead to megaesophagus and/or megacolon, which can occur concurrently with heart disease. The symptoms of megaesophagus may include pain during swallowing, excessive salivation, regurgitation and chest pain. In severe cases, there may be weight loss or cachexia, and the esophagus may rupture. The symptoms of megacolon include severe constipation, which can last for a few days to months, and abdominal pain that is often associated with episodes of constipation. Patients with Chagas disease also have an increased chance of developing gastric ulcers or chronic gastritis, due to abnormalities in the stomach.

Women who are infected with *T. cruzi* can give birth to infected children. Congenital infections may occur during any of the woman's pregnancies, whether she is symptomatic or not. In congenitally infected infants, the most common symptoms are premature birth, hepatosplenomegaly, meningoencephalitis, changes in the retina and signs of acute myocarditis/ cardiac insufficiency. Transplacental infections are also associated with abortions. Patients with AIDS suffer a more severe form of the disease with a high percentage of neurological and cardiac signs. Many of these patients develop *T. cruzi* brain abscesses, which are not seen in immunocompetent patients. HIV-infected individuals and others who are immunosuppressed, including those who receive organ transplants, are at risk for reactivation of *T. cruzi* replication.

[Photo: Mother and infant. Sourcee: Pan American Health Organization]

Chagas disease can be diagnosed by microscopy, isolation of the parasite, serology or molecular techniques. Light microscopy can sometimes detect *T. cruzi* in Giemsa or Wright stained samples of blood, cerebrospinal fluid or tissues. *T. cruzi* can be found in the heart, skeletal and smooth muscle cells, and the glial cells of the nervous system. It sometimes occurs in chagomas. In immuno-compromised patients, parasites may also be detected in atypical sites such as the pericardial fluid, bone marrow, brain, skin and lymph nodes. Active parasitemia is much more likely to be found during the acute than the chronic stage. *T. cruzi* can be cultured from heparinized blood samples or tissues. Various specialized media including liver infusion tryptose medium or Novy-MacNeal-Nicolle medium, as well as Vero cell lines can be used. Culture may take



1 to 6 months. Serology is most often used to diagnose chronic infections. Commonly used serological tests in humans include indirect enzyme-linked immunofluorescence (IFA), hemagglutination and immunosorbent Other including assays (ELISAs). tests radioimmunoprecipitation and complement fixation may also be used. Cross-reactions can occur with other parasites, particularly Leishmania species. Polymerase chain reaction (PCR) techniques can be used for diagnosis. Immunoblotting (Western blotting) is another option.

[Photo: Micrograph of Trypanosoma cruzi in a blood smear using Giemsa staining technique. CDC Public Health Image Library]

Acute Chagas disease can be treated with antiparasitic drugs. In the U.S., drugs may be available only under an Investigational New Drug protocol from the CDC Drug Service. Treatment of acute or congenital cases is recommended to prevent the development of chronic disease. Antiparasitic drugs are less effective in the indeterminate and chronic stages, and treatment recommendations may vary with the age of the patient and other factors. There are significant side effects with these drugs, which must be given long term. In the chronic stage, treatment of cardiomyopathy is mainly symptomatic and similar to the treatment of other causes of heart disease. A pacemaker may be necessary, and a heart transplant can be considered. Surgery, balloon dilation of the gastroesophageal junction and/or symptomatic relief may be used for chagasic megaesophagus or megacolon.

The morbidity and mortality rates vary with the stage of the disease. Approximately 5% of people infected with T. cruzi develop acute symptoms. Estimates of the case fatality rate for acute Chagas disease range from less than 5% to approximately 8%; among immunologically competent individuals; deaths occur mainly in young children with acute myocarditis or meningoencephalitis. The CDC estimates that 20 to 30% of humans infected with T. cruzi eventually develop chronic disease; estimates from other sources vary from 10% to 50%. The reason for the progression of disease in some patients but not others is unknown. It may be related to host genetic factors, the dose of the parasites, the number of inoculations, the strain of the parasite, and immunological or nutritional factors. Cardiac disease is often fatal. Occasionally, deaths are also caused by volvulus of a dilated sigmoid megacolon.

 Antiparasitic drugs
 Treat acute or congenital cases
to prevent chronic disease
– Administer long term
 Significant side effects

Treatment

Chronic stage

- Symptomatic treatment of cardiac
- and digestion disease

Morbidity and Mortality

- Acute myocarditis, meningoencephalitis

• Acute symptoms: 5%

 Case fatality rate: 5 to 8% - Deaths mostly in children

Chronic disease: 20 to 30%

- Exact causes for disease progression unknown

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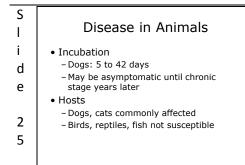
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The incubation period for acute disease in dogs appears to be 5 to 42 days; in experimental infections, symptoms of acute heart disease are usually reported after 2 to 4 weeks. Like humans, some dogs may not develop clinical signs until the chronic stage, which occurs after a few years; the exact length of this period is not known. Trypanosoma cruzi occurs in more than 100 species of mammals throughout the Americas; dogs and cats are commonly affected. Birds, reptiles, and fish are not susceptible.

Clinical Signs: Dogs

• Acute phase - Lymphadenopathy, ataxia, diarrhea, weakness - Acute myocarditis develops 2 to 3 weeks post-infection Chronic phase Congestive heart failure, cardiac dilatation, sudden death

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S I	Disease in Other Species
i d	Cats - Usually asymptomatic
e	 Rarely fever, edema, weight loss, neurological signs
2 7	 Other species Mostly unknown Myocarditis reported in wildlife Cardiac, reproductive disease in rats and mice
S I	Post Mortem Lesions

• Right side cardiac lesions - Dilation, hemorrhages,

> effusion Pulmonary edema

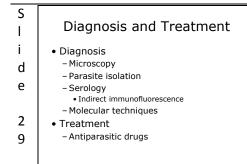


 Peritoneal transudate - Liver, spleen, kidney condestion

Acute, latent and chronic stages of infection occur in experimentally infected dogs. Clinical signs reported in the acute stage include fever, anorexia, lethargy, an unkempt hair coat, lymphadenopathy, hepatomegalv and splenomegalv. Anorexia, diarrhea, ascites and/or weight loss may also be seen. Cardiac dysfunction can occur during the acute phase; acute myocarditis may cause arrhythmias or sudden collapse and death. After the acute phase, infected dogs enter the indeterminate (latent) stage, during which the parasites are difficult to find and the animal is asymptomatic. The indeterminate stage can be as short as 27 days in some experimentally infected animals, but it seems to last for years in some natural infections. Congestive heart failure is the most common sign during the chronic stage. Right-sided heart failure usually occurs first. Eventually, dogs with heart disease develop chronic myocarditis with cardiac dilatation and arrhythmias. Sudden death can occur. [Photo: Dog. Source: AVMA Press Room Photo Gallery] Symptomatic Chagas disease has been rarely described in cats. Reported clinical signs include fever, edema, weight loss and neurological signs such as convulsions and paresis. There is little information about Chagas disease in other species, including wild animals. Mild, histologically evident myocarditis (without clinical signs of heart disease) has been reported at necropsy in infected wild raccoons and opossums. Naturally infected rats can develop arrhythmias and more severe cardiac lesions. Infertility, fetal losses, reduced birth weights, and early postnatal deaths have been reported in pregnant mice.

In dogs, acute disease is characterized mainly by cardiac lesions, which are particularly prominent on the right side. The myocardium may be pale, and subendocardial and subepicardial hemorrhages are often present. Multiple yellowish-white spots and streaks, mainly involving the coronary groove, may be found in the heart. In addition, there may be secondary pulmonary edema, congestion in the liver, spleen and kidneys, and a modified transudate in the peritoneal cavity. Pericardial effusion has been reported in some naturally infected dogs. Gross lesions may be absent in some infected animals. In chronic Chagas disease, the heart is bilaterally enlarged and flaccid, with thinning of areas in the ventricular walls. Atypical cases without cardiac lesions have also been reported.

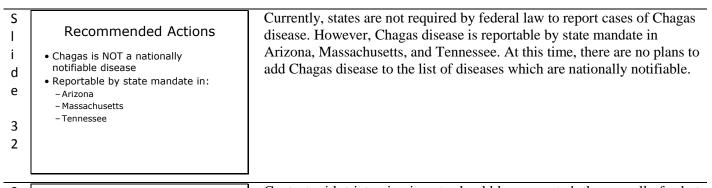
[Photo: Dog, heart. There are multiple white linear streaks on the surface of the right and left ventricles corresponding to myocardial necrosis and myocarditis. Source: Dr. S. Barr, Cornell University, College of Veterinary Medicine, Department of Clinical Sciences/CFSPH]



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3 	Morbidity and Mortality
i	Prevalence in wildlife
d	- 2 to 62% in raccoons and opossums
е	Prevalence in dogs
C	– 1.1 to 8.8% (U.S.) – 10 to 17% (Mexico)
3	Mortality
З	 High in experimentally infected animals
0	

Chagas disease can be diagnosed by microscopy, isolation of the parasite, serology and molecular techniques. A presumptive diagnosis can be made if T. cruzi is observed by light microscopy in a stained blood smear or buffy coat sample, or in tissues such as the heart. T. cruzi can be cultured from blood samples or tissues; culture is usually more successful in the acute stage. This organism often occurs in the myocardium, but it can also be isolated from other organs such as the lymph nodes, liver, gastrointestinal tract, brain, cerebrospinal fluid and adrenal gland. Various specialized media including liver infusion tryptose medium or Novy-MacNeal-Nicolle medium, as well as Vero cell lines may be used. Indirect immunofluorescence is the most commonly used serological test. Other assays include radio-immuno-precipitation, direct and indirect hemagglutination, complement fixation and ELISAs. Cross-reactions can occur with other parasites, particularly Leishmania species. Molecular detection methods including PCR and western blot (immunoblot) analysis techniques can detect T. cruzi DNA in tissues and blood. Occasionally, dogs have been treated with anti-parasitic drugs. These drugs appear to be more effective in the early stages; by the time of diagnosis, treatment may be too late to prevent the progression of the disease.

The prevalence rate can be high among wildlife in endemic areas. Surveys of wildlife in the U.S., conducted mainly in raccoons and opossums, have reported prevalence rates from 2% to 62%. In the U.S., the reported seroprevalence rates in dogs from Texas, Oklahoma, Louisiana, Georgia and other southern states vary from 1.1% to 8.8%. Over a 15-year period, more than 500 clinical cases of Chagas disease were reported among dogs in Texas, suggesting that this disease occurs regularly in some areas. In the Yucatan region of Mexico, one study reported that 10-14% of dogs were seropositive, but when both serology and PCR were used, the prevalence as high as 17%. The infection rate is highest among dogs that are regularly exposed to wildlife and insect vectors. Cats are frequently infected with T. cruzi in South America. There is little information on the morbidity and mortality rates in dogs, except in experimentally infected animals, where these rates are high. Based on human data, some sources suggest that approximately 5% of naturally infected animals would be expected to develop symptoms during the acute stage. In naturally infected dogs with chronic cardiac disease, the survival time after diagnosis ranged from 0 months to 5 years.





S I	Prevention in Humans
i d e	 Screen blood and organ donors Occupational risk groups Wear gloves, other PPE Dispose of sharps properly
3 4	 Travelers Wear thick clothing Avoid substandard housing Vaccine not available

Contact with triatomine insects should be prevented; they usually feed at night and withdraw to their hiding places in daylight. In endemic areas, houses can be improved by plastering walls, improving flooring and taking other measures to remove the cracks where these insects hide. Triatomine insects are often found in basements, which should be avoided. Sleeping inside a screened area, under a permethrin-impregnated bed net, or in an air-conditioned room is safest. Bed nets should be tucked tightly under the mattress before dusk. Animal pens and storage areas should be kept away from homes. Regular spraying of insecticides in and around houses can reduce the number of insects, and in some cases, eliminate them. Foods that might be contaminated should be cooked. Since 1991, the Pan American Health Organization and the World Health Organization have run a joint program to eliminate T. infestans, the most important vector for Chagas disease in humans. This program has decreased the distribution of this insect by more than 80%, although foci can still be found in some regions. [Photo: Personnel applying insecticides in infested household. Source: Pan American Health **Organization**]

Blood and organ donors should be screened to prevent transmission by these routes. In the U.S., transfused blood has been screened for Chagas disease since 2007. Pregnant women can be tested to identify cases where congenital transmission may occur, and the infant should be monitored and treated if necessary. People in occupational risk groups should take additional precautions. Veterinarians and technicians should protect their skin and mucous membranes from contamination with parasites in blood or tissues. This includes using gloves and/or other barriers while drawing blood samples from T. cruzi-infected animals, taking care of IV catheters or performing other invasive procedures. Needles and other "sharps" must be handled and disposed of properly to prevent needlestick injuries. Individuals who work with wildlife and hunters should also take precautions, especially when handling blood and tissues. Laboratory personnel should use appropriate personal protective equipment, including gloves and eye protection, while processing blood samples, cultures or infected insects. If an accidental exposure occurs, the site should be disinfected immediately if possible, and antiparasitic drugs may be given prophylactically. Travelers to areas where Chagas disease is common should wear thick clothing that covers as much of the body as possible; heavy long-sleeved shirts, long pants, socks and shoes are recommended. Sleeping in sub-standard housing should, if possible, be avoided. Vaccines are not available for humans; however, precautions can be taken to reduce the risk of infection, particularly in countries where the prevalence of Chagas disease is high.



Dogs and cats should not be allowed to eat tissues from potentially infected wild animals. Strict indoor housing in well-constructed homes or other facilities reduces the risk of infection. Housing animals indoors at night, when triatomine insects are active, may also be helpful. Residual insecticides sprayed regularly in kennels and surrounding structures may decrease the number of insect vectors. In breeding kennels, testing bitches for *T. cruzi*-might also decrease the incidence of Chagas disease by reducing vertical transmission. No vaccines are available.

[Photo: Indoor dog kennel. Source: USDA APHIS Image Gallery]

S I d e 3 6	Additional Resources • Center for Food Security and Public Health - www.cfsph.iastate.edu • CDC: American Trypanosomiasis/ Chagas Disease - http://www.cdc.gov/parasites/chagas/ • World Health Organization: Chagas Disease - http://www.who.int/topics/chagas_disease/en/ • Pan American Health Organization - http://www.paho.org/english/ad/dpc/cd/chagas.htm	
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