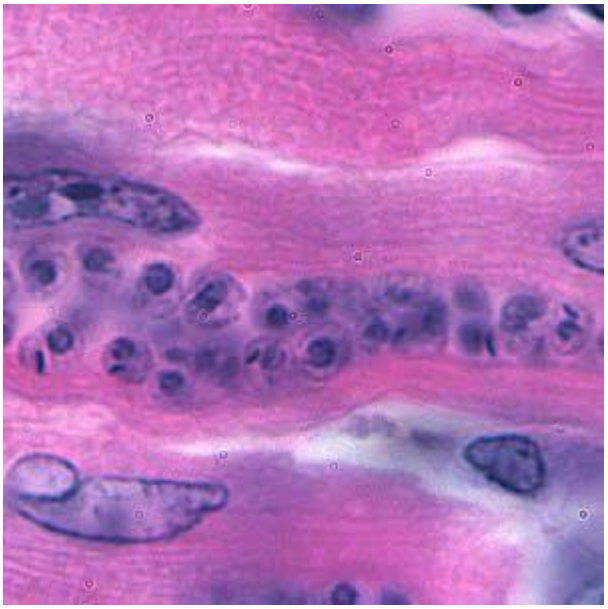
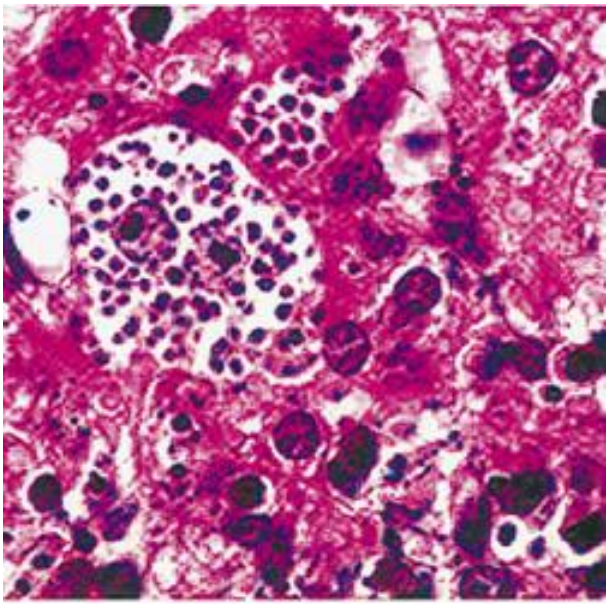
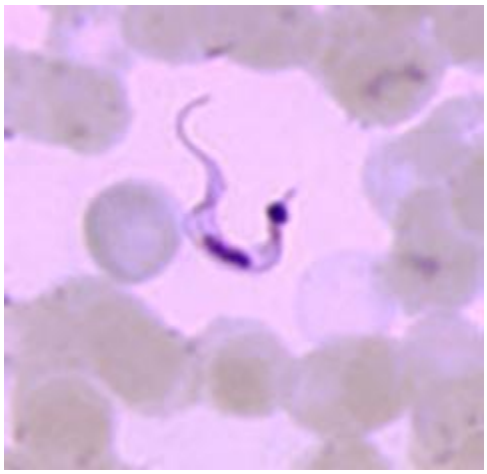
## PARASITOLOGY CASE HISTORY #15 (BLOOD PARASITES)
## (Lynne S. Garcia)

The patient was a 31-year-old white male from Brazil. He had renal failure secondary to diabetes. At a later date he received a donor cadaveric kidney. The patient was undergoing immunosuppression therapy with azathioprine, cyclosporine A, and prednisone. After the transplant, he developed acute cardiac symptoms and complications from diabetes and died 2 months later. The following image was seen from the autopsy (cardiac muscle/left, liver/right)







This image was photographed from a stained thin blood film using the oil immersion objective (100X). Please identify the organism.

**Discussion of Blood Parasite Quiz #15**

The images presented in Diagnostic Blood Parasite Quiz #15 are the following:

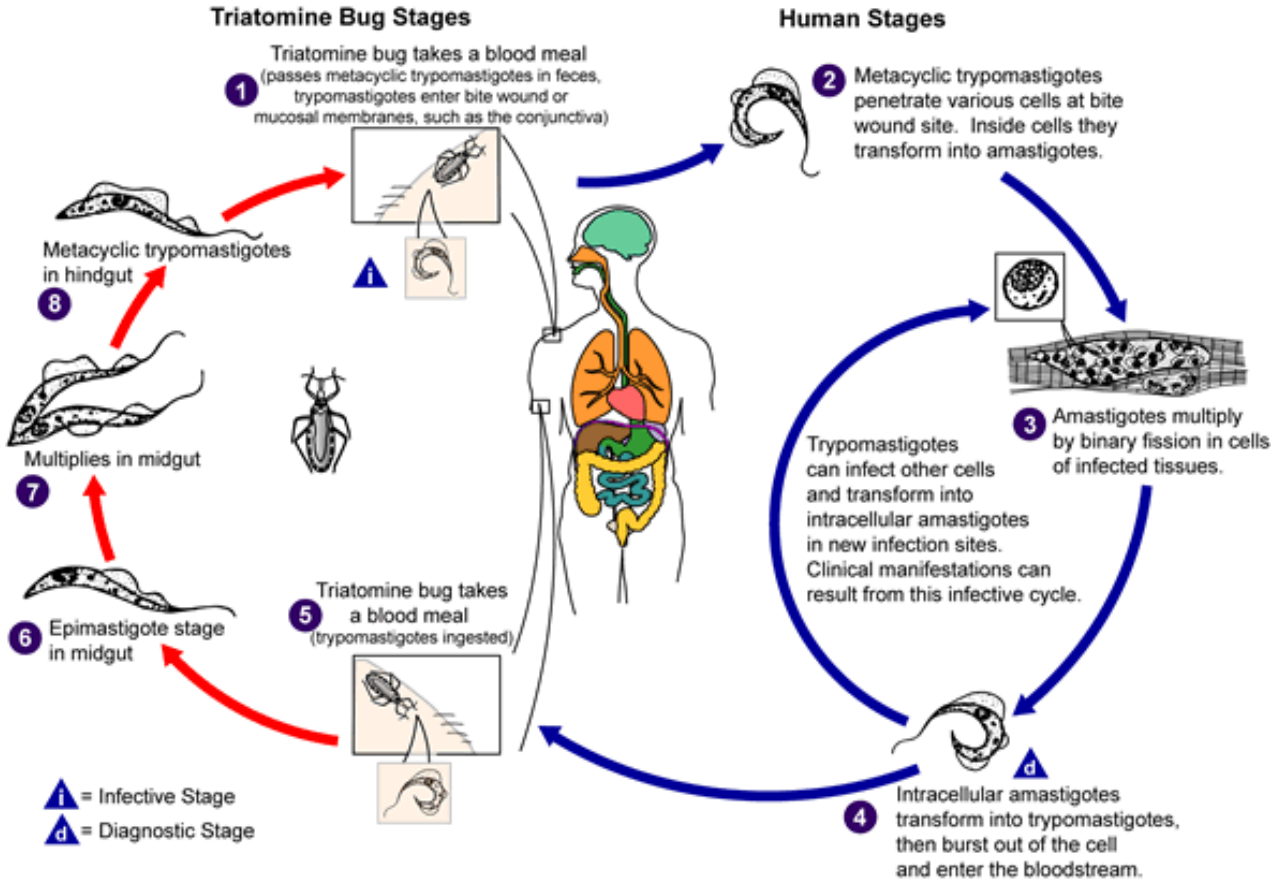
These images are consistent with a case of Chagas' disease caused by *Trypanosoma cruzi*. In the autopsy, *T cruzi* amastigotes were found in the transplanted kidney, heart, bladder, liver, and pancreas. An important reduction in the parasitemia was obtained through the treatment of the infection with benznidazole; however, the patient died due to complications from diabetes associated with tissue lesions caused by *T cruzi.* The assumption was that the source of the infection was the transplanted kidney.

**Organism:** American trypanosomiasis (Chagas' disease) is a zoonosis caused by *T. cruzi*, which was discovered in the intestine of a triatomid bug in Brazil in 1909 by Carlos Chagas, who described the entire life cycle in reservoir hosts. After infected bugs were allowed to feed on a monkey, the trypomastigote form was found in the blood of the animal. Chagas then found the organisms in the blood of a child who had fever, anemia, and enlargement of the lymph nodes; he proved that the parasites were the cause of this common illness endemic in areas of Brazil. It is interesting that this represents the first example where an animal parasite causing the disease and the insect vector were discovered prior to the disease itself. *T. cruzi* causes an acute or chronic parasitemia and invades the cells of many organs (e.g., the heart, esophagus, and colon, as well as others). It is one of the major health problems in Latin American countries.

It is estimated that 100 million persons are at risk of infection; between 16 million to 18 million are actually infected. There are approximately 200,000 new cases each year and 50,000 deaths per year due to Chagas' disease. In certain areas of endemic infection, approximately 10% of all adult deaths are due to Chagas' disease. Two-thirds of reported cases occur in the Southern Cone countries (Argentina, Bolivia, Brazil, Chile, Paraguay, southern Peru and Uruguay). The southern United States, particularly Texas, is also now identified as having a number of cases.

**Life cycle:** The disease is transmitted to humans through the bite wound caused by reduviid bugs (triatomids, kissing bugs, or conenose bugs). Humans are infected when metacyclic trypomastigotes are released with the feces while the insect is taking a blood meal and the feces are rubbed or scratched into the bite wound or onto mucosal surfaces such as eyes or mouth, an action stimulated by the allergic reaction to the insect's saliva. The

organisms can also be transmitted as congenital infections, by blood transfusion, or by **organ transplantation**. On entry into the body, the metacyclic forms invade local tissues, transform to the amastigote stage, and begin to multiply within the cells. The local inflammatory process continues, forming the primary lesion, the chagoma, which blocks the lymphatic capillaries and causes edema. The trypomastigote does not divide in the blood but carries the infection to all parts of the body. The amastigote form multiplies within virtually any cell, preferring cells of mesenchymal origin such as reticuloendothelial, myocardial, adipose, and neuroglial cells. The parasites also occur in histiocytes of cutaneous tissue and in cells of the epidermis, as well as in the intestinal mucous membrane.




**Clinical Disease:** The clinical syndromes associated with Chagas' disease can be broken down into acute, indeterminate, and chronic stages. The acute stage is the result of the first encounter of the patient with the parasite, whereas the chronic phase is the result of late sequelae. In children younger than 5 years, the disease is seen in its severest form, whereas in older children and adults, the disease is milder and is commonly diagnosed in the

subacute or chronic form rather than in the acute form. Overall, the incubation period in humans is about 7 to 14 days but is somewhat longer in some patients.

Recrudescence of *T. cruzi* infections in immunosuppressed patients, particularly transplantation patients, is a grave concern. Transplant recipients can also become infected through receipt of infected organs. For patients with end-stage Chagas' cardiomyopathy, heart transplantation is an option which has had variable success. Reactivation of the disease with the -development of cutaneous lesions has been seen. Bone marrow transplant recipients are also at risk of Chagas' disease due to reactivation or transfusion. Prophylactic treatment of these patients has led to favorable outcomes.

**Diagnosis:** Health care personnel working with specimens from patients suspected of having Chagas' disease must use standard precautions. Trypomastigotes are highly infectious, and certain strains of the parasite are more virulent than others. The diagnosis of Chagas' disease should be considered if there is a history of consistent exposure to reduviid bug bites, residence in or travel to areas where the disease is endemic, laboratory accident, or recent blood transfusion in an area where the disease is endemic. Chagomas appear similar to injury caused by trauma, insect bites, or bacterial and mycotic infections. The differential diagnosis of acute Chagas' disease should include brucellosis, endocarditis, salmonellosis, schistosomiasis, toxoplasmosis, tuberculosis, connective tissue diseases, and leukemia. Chronic Chagas' disease with cardiomyopathy may be confused with endocarditis, ischemic heart disease, and changes associated with rheumatic heart disease.

**Routine Laboratory Methods.** Acute Chagas' disease should be suspected in any individual from an area where the disease is endemic who develops an acute febrile illness with lymphadenopathy and myocarditis. The presence of a chagoma or Romaña's sign may be diagnostic; however, allergic reactions to insect bites may produce similar lesions. The definitive diagnosis depends on demonstration of trypomastigotes in the blood, amastigote stages in tissues, or positive serologic reactions.

**Key Points - Laboratory Diagnosis:**

***Trypanosoma cruzi***

1. Laboratory workers should use blood-borne-pathogen precautions when examining blood from Chagas' disease patients, because the trypomastigotes are infective.

2. Trypomastigotes are prevalent in the blood of patients with acute Chagas' disease; however, organism numbers are much smaller in the indeterminate and chronic stages of the infection.

3. *T. rangeli* cannot be differentiated from *T. cruzi* on the basis of parasite morphology; patient information regarding geographic exposure is required for more appropriate interpretation of laboratory results.

4. In addition to thin and thick blood smears, concentration methods should be used to concentrate the trypomastigotes in the blood.

5. Immunoassays for antigen detection are now available and are highly sensitive and specific. Alternative methods such as culture and serologic testing can be used; however, these approaches may not be feasible without the use of a reference laboratory. Molecular methods are also being more widely used.

**Epidemiology.** Chagas' disease is a zoonosis occurring throughout American continents and involves reduviid bugs living in close association with human reservoirs (dogs, cats, armadillos, opossums, raccoons, and rodents). The most ubiquitous sylvatic reservoir host is the opossum, Didelphus, which is found throughout much of the range of *T. cruzi* in the Americas. Multiple nesting or resting sites of the opossum encompass many types of triatomine habitat. High *T. cruzi* prevalence rates are partly due to the fact that opossums eat triatomines and may also transmit infection via anal gland secretions. Sylvatic cycles of *T. cruzi* transmission extend from southern Argentina and Chile to northern California.

Transmission to humans is highly dependent on the defecation habits of the insect vector. In areas where the local species of reduviid bug does not ordinarily defecate while feeding, there are no human infections. This may explain why there are few human infections originating in the United States, even though sylvatic infections are known to occur in southern states. A number of autochthonous cases have been reported in the United States, in Texas, California, and the Southwest United States.

**Prevention and Control**. Until recently, control of Chagas' disease has been mainly through the use of insecticides to eliminate the reduviid vector. In

certain areas, insecticide resistance in triatomids has been noted. In addition to residual insecticide-spraying programs, construction of reduviid-proof dwellings and education are essential for effective control programs. Improvements in unsanitary living conditions, plastering of walls to obtain a smooth, crack-free surface, and replacement of palm-thatched roofs with metal roofing have been shown to considerably reduce the number of reduviids in houses. Although control of Chagas' disease is feasible, few countries have initiated control programs because of both political and economic constraints.

Transmission can occur through organ transplants and blood transfusion. Some of the countries in areas where the disease is endemic have laws mandating serologic testing of blood donors. Financial constraints may hinder the implementation of these laws, and there is a lack of standardization of currently available serologic tests. An alternative approach to serologic screening in the United States is the use of a questionnaire to identify prospective donors who may have resided in high-risk areas. This approach may not be practical, since even in vector-free areas in countries with endemic infection a significant portion of the donor blood units were positive for antibodies to Chagas' disease. In areas where seroprevalence is high, rather than discarding all positive blood units, laboratorians add gentian violet to the units and store them at 4°C for 24 h before use to kill the organism.

**Treatment:** Although numerous drugs have been tried, including those used to treat African trypanosomiasis and leishmaniasis, few have proven to be effective for therapy of Chagas' disease. In acute and congenital Chagas' disease and infections caused by laboratory accidents, treatment should be administered as soon as possible, even though in some cases symptoms are self-limited. Drug therapy has little effect on reducing the progression of chronic Chagas' disease.

Benznidazole (RO-7-1051, Rochagan, Radanil), an imidazole derivative, is effective in reducing or suppressing parasites in the acute stages of disease but has limited capacity to produce a parasitic cure. It appears to be slightly more active and better tolerated than nifurtimox and is currently the drug of choice

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