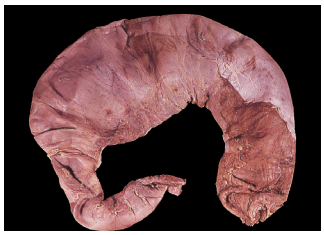

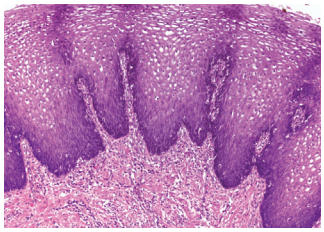

2

American Trypanosomiasis

Ellen M. Andersen,
Mary K. Klassen-Fischer, and Ronald C. Neafie

Introduction

Definition

American trypanosomiasis is a zoonosis caused by the flagellate protozoon *Trypanosoma cruzi* (previously *Schizotrypanum cruzi*). In humans, *T. cruzi* can infect parenchymal cells of many different organs, most commonly the heart, brain, esophagus, and colon.

Synonyms

American trypanosomiasis is commonly known as Chagas' disease or South American trypanosomiasis.

General Considerations

Carlos Chagas (Fig 2.1) first identified *T. cruzi* in the intestines of reduviid bugs (order Hemiptera, suborder Heteroptera, family Reduviidae, subfamily Triatominae), the arthropod vector, in Brazil in 1909.[1,2] Chagas used infected reduviid bugs to experimentally infect a monkey, from which he subsequently isolated blood-stage parasites. Chagas later identified the same parasites in the blood of a child with an unspecified illness, the only time a human parasite and its arthropod vector have been identified before the disease itself.

Epidemiology

Trypanosoma cruzi is enzootic throughout Latin America. Chagas' disease causes significant morbidity and mortality in Argentina, Bolivia, Brazil, Ecuador, Honduras, Paraguay, Peru, and Venezuela. It occurs less frequently in Colombia, Costa Rica, El Salvador, Mexico and Panama. Some indigenous infections have been reported from the southwestern United States, Belize, Guyana, and Trinidad and Tobago.[3]

Figure 2.1
Carlos Chagas, Brazilian scientist who identified the cause and described the clinical features of Chagas' disease.

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In South America, trypanosomiasis is the most significant endemic disease, particularly among children under 2 years of age. From 1980 to 1985, 16 to 18 million cases of Chagas' disease were reported in Latin America, with at least 120 million people at risk of infection.[4] Two-thirds of reported cases occur in the Southern Cone countries (Argentina, Bolivia, Brazil, Chile, Paraguay, southern Peru and Uruguay) a fact which prompted the development of the Southern Cone Initiative, one of the largest disease control programs ever established.[5] Several other programs concentrating on various geographical areas within Latin America have also been developed. Through the combined efforts of such programs, Chagas' disease transmission has been markedly reduced in endemic areas.[6,7]

Trypanosoma rangeli, a related and similarly distributed protozoan, is nonpathogenic. It does not invade and destroy cells and usually causes only a mild parasitemia.

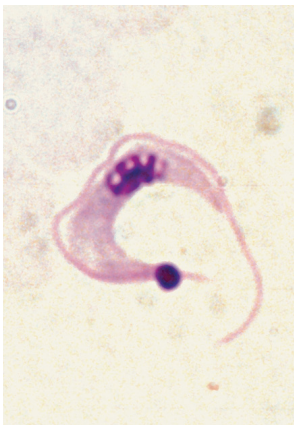


Figure 2.2
Trypomastigote of *Trypanosoma cruzi* in peripheral blood of experimentally infected mouse. Note C-shaped configuration, free anterior flagellum, central nucleus, and large spherical kinetoplast at sharply pointed posterior end. Giemsa x1320

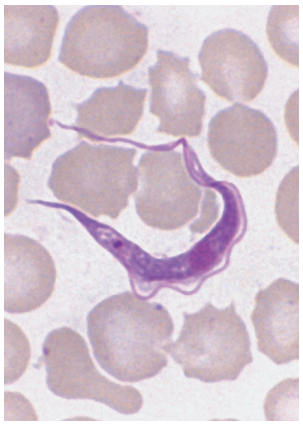


Figure 2.3
Trypanosoma rangeli trypomastigote in peripheral blood film. Note free anterior flagellum, central nucleus, and small spherical kinetoplast distal to posterior end. Giemsa x1320

Infectious Agent

Morphologic Description

Two morphologically distinct forms of *T. cruzi*, the trypomastigote and the amastigote, are found in infected humans and other mammalian hosts.

Trypomastigotes

Trypomastigotes of *T. cruzi* circulate as free organisms in peripheral blood. They are slender, elongate, and 16 to 22 µm long, with a large central nucleus and a prominent round kinetoplast at the sharply pointed posterior end. An undulating membrane arises from the kinetoplast and runs along the cell membrane, terminating in a single free flagellum at the anterior end. On stained blood films, *T. cruzi* trypomastigotes are often C-shaped (Fig 2.2).

There are significant morphologic differences among the trypomastigotes of *Trypanosoma* sp. Trypomastigotes of *T. rangeli* are much longer (25 to 50 µm) than those of *T. cruzi*, have a broader, more prominent undulating membrane, and a much smaller round subterminal kinetoplast (Fig 2.3). *Trypanosoma rangeli* is transmitted to humans directly through the bite, and not through the feces, of a reduviid bug. Trypomastigotes of *T. cruzi* do not divide in peripheral blood in contrast to those of *T. rangeli* and the similar African trypanosomes that do.

Amastigotes.

Amastigotes of *T. cruzi* are intracellular and primarily infect mesenchymal cells. In histologic sections, amastigotes are readily visible with hematoxylin and eosin stain (Fig 2.4). They are usually spherical and 2 to 4 µm in diameter, with a thin cell membrane, cytoplasm, a large round nucleus, and a rod-shaped kinetoplast (Fig 2.5). The kinetoplast is sometimes more prominent when stained with Brown-Hopps tissue gram stain (Fig 2.5a), Giemsa (Fig 2.5b), or Wilder's reticulum (Fig 2.5c). Amastigotes multiply by binary fission. Amastigotes of *T. cruzi* are slightly larger, but otherwise are morphologically indistinguishable from those of *Leishmania* sp. An amastigote stage has not been described for *T. rangeli*.

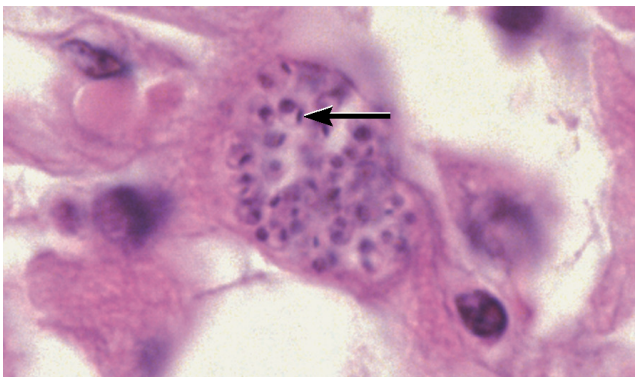


Figure 2.4
Cluster of readily observable *Trypanosoma cruzi* amastigotes in myocardial fiber. Note cell membrane, spherical nucleus, and rod-shaped kinetoplast (arrow). x1000

Life Cycle and Transmission

The life cycle of *T. cruzi* includes a mammalian phase and an arthropod phase (Fig 2.6). Numerous domestic and wild mammals serve as reservoir hosts, including opossums (Fig 2.7), raccoons (Fig 2.8), armadillos, rats, canines, and livestock. Trypomastigotes circulating in the peripheral blood of infected mammals are ingested by a reduviid bug as it takes a blood meal. The now infected bug can remain infective for life serving as a reservoir of infection.

In the triatome midgut, trypomastigotes transform

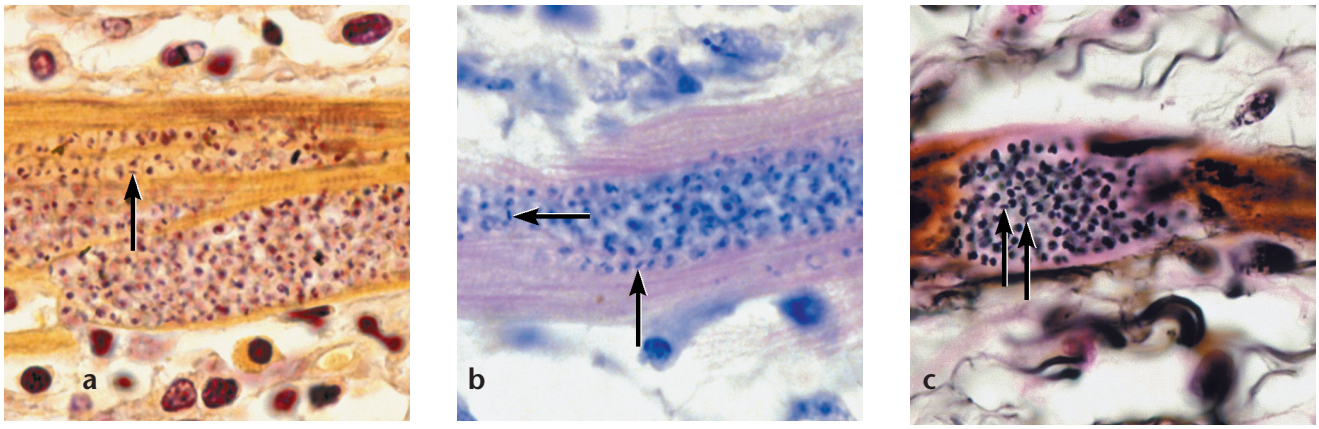


Figure 2.5 a,b,c
Amastigotes of *Trypanosoma cruzi* in myocardium in acute Chagas' disease. a. Note dark-staining rod-shaped kinetoplasts (arrows). B-H x375 b. Note dark-staining rod-shaped kinetoplasts (arrows). Giemsa x460 c. Note spherical nucleus and black-staining rod-shaped kinetoplasts (arrows). Wilder's reticulum x450

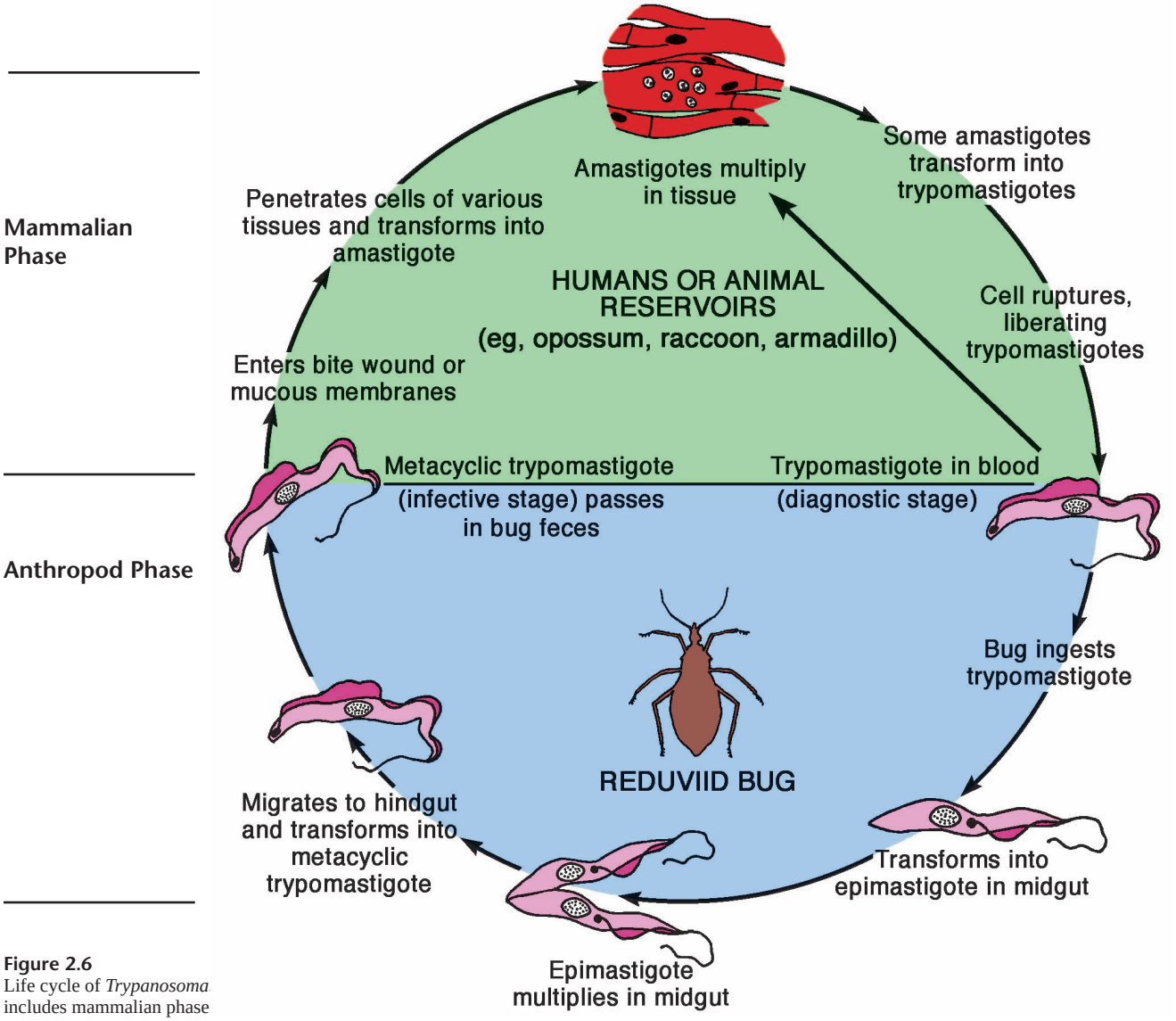


Figure 2.6
Life cycle of *Trypanosoma* includes mammalian phase arthropod phase.

Figure 2.7
Opossums naturally infected with *Trypanosoma cruzi* are reservoir hosts in southwestern United States and Central and South America.

Figure 2.8
Raccoons naturally infected with *Trypanosoma cruzi* are reservoir hosts in southwestern United States.

Figure 2.9
Triatoma infestans, probably the most important vector of *Trypanosoma cruzi*, is widely distributed in South America.

Figure 2.10
Panstrongylus megistus, an efficient and important vector of *Trypanosoma cruzi* in southern Brazil. Adults are approximately 2.5 cm long.

into shorter epimastigotes that multiply by binary fission. Daughter epimastigotes migrate to the hind-gut, where they transform into metacyclic trypomastigotes, the infective form for humans. Infective trypomastigotes appear in the feces of reduviid bugs within 20 days after contaminated blood is ingested from an infected mammal. Metacyclic trypomastigotes are excreted in the bug's feces at the bite site during or immidiately after the bug takes a blood meal. Infective metacyclic trypomastigotes deposited on the skin surface during or after a bite are introduced at the bite site or reach neighboring conjuctival or oral mucosae. The trypomastigotes then invade, or are engulfed by, primarily histiocytes within which they transform into amastigotes and multiply by binary fission. Within a few days amastigotes fill and distend the parasitized histiocytes which then rupture releasing the amastigotes to invade other cells. Thus the mammalian phase of the life cycle becomes established. Amastigotes spread throughout the body as parasitized histiocytes disseminate through the blood. Some amastigotes transform into trypomastigotes that also enter the blood and pass through virtually every organ.

It is only during the acute febrile stage of disease, that large numbers of trypomastigotes are present, and that free trypomastigotes are found in peripheral blood smears. Circulating trypomastigotes can invade cells in many different tissues and where they transform into amastigotes. Although cells of any organ may potentially be invaded, amastigotes are most commonly found in the heart, brain, smooth muscle, and striated muscle.

Humans most commonly acquire Chagas' disease from infected reduviid bugs, including *Triatoma* sp, *Panstrongylus* sp, and *Rhodnius* sp (Figs 2.9 & 2.10). These large bugs (sometimes called kissing or assassin bugs) have well-developed wings, cone-shaped heads, and large eyes.

During the day, these large bugs seek shelter and hide in

Figure 2.11
Thatched roof of hut in Costa Rica is typical daytime habitat of reduviid bugs. At night, bugs emerge to feed on sleeping humans.

the cracks of trees and houses (Fig 2.11). At night, male and female nymphal and adult stages emerge from their hiding places to feed on sleeping humans. During or immediately after their bite and blood meal, they defecate infective parasites that the host self-inoculates by inadvertently scratching or rubbing the parasite-laden fecal material into the bite wound or a neighboring mucosae, e.g. of the eyes or mouth.

The life cycle of a reduviid bug comprises egg, 5 instars, and adult (Fig 2.12). Molting to the next stage requires a full blood meal, and development from egg to adult may take a year or longer.

Trypanosoma cruzi can also be transmitted congenitally, through blood and blood-product transfusions, needle-sharing, organ transplantation, laboratory accident, and through food and drink contaminated by infected triatomes.[8,9,10]

Clinical Features and Pathogenesis

Primary lesion

The initial lesion develops at the bite site within several days in approximately 50% of patients after a typically painless bite of an infected reduviid bug. The fecal trypomastigotes of the reduviid bug penetrate the skin or neighboring mucosa where they proliferate and induce an inflammatory response characterized by erythema, urticaria, and interstitial edema leading to the formation of the characteristic cutaneous lesion, a chagoma. The chagoma evolves and grows as inflammatory cells proliferate at the bite site and spread to proximal lymph nodes where they cause lymphostasis and regional edema. In young children bites near the eye result in a combination of palpebral and periorbital edema and swelling of the preauricular lymph node known as Romaña's sign (Fig 2.13).

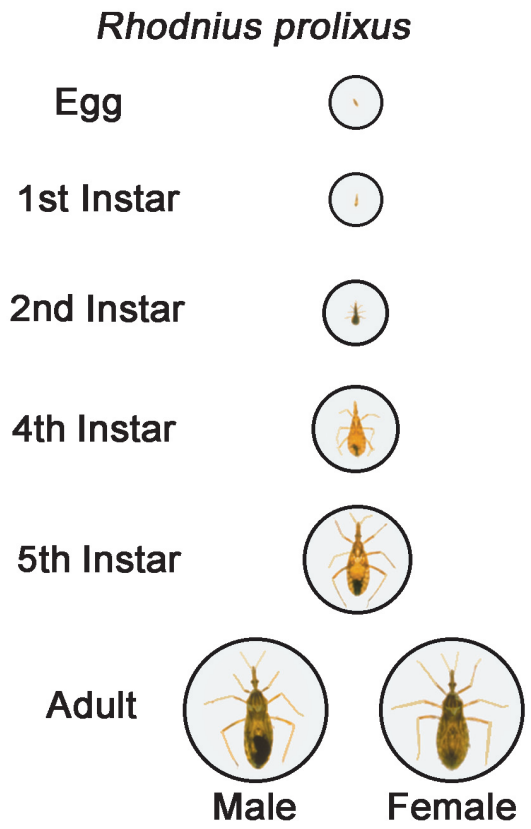


Figure 2.12
Rhodnius prolixus, a principal vector of *Trypanosoma cruzi* in Central America and northern South America, and principal vector of *Trypanosoma rangeli*.

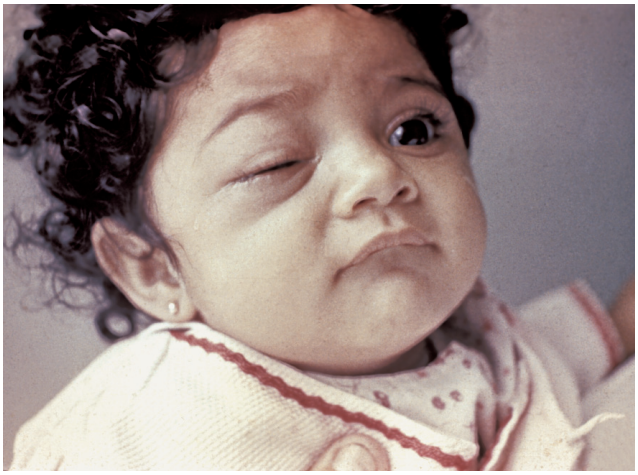


Figure 2.13
Child with classic Romaña's sign: unilateral conjunctivitis, palpebral and periorbital edema, and preauricular lymphadenopathy.

Acute Chagas' Disease

Only 3% of patients develop acute clinical manifestations of Chagas' disease which is usually mild with fever, malaise, edema of the face and lower extremities, generalized

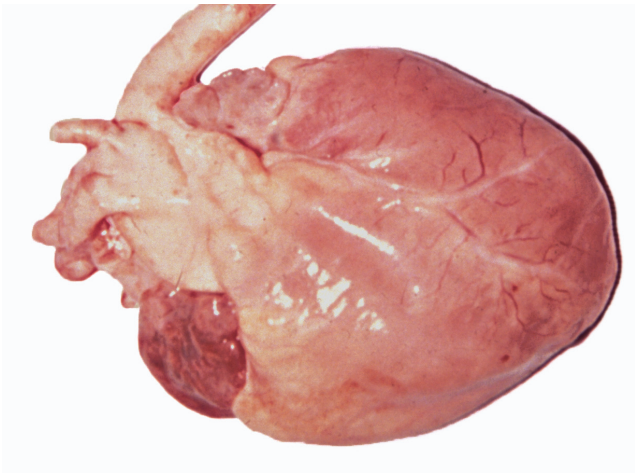


Figure 2.14
Anterior aspect of heart of 14-month-old patient who died of acute chagasic myocarditis. Note dilated ventricles and pale myocardium.

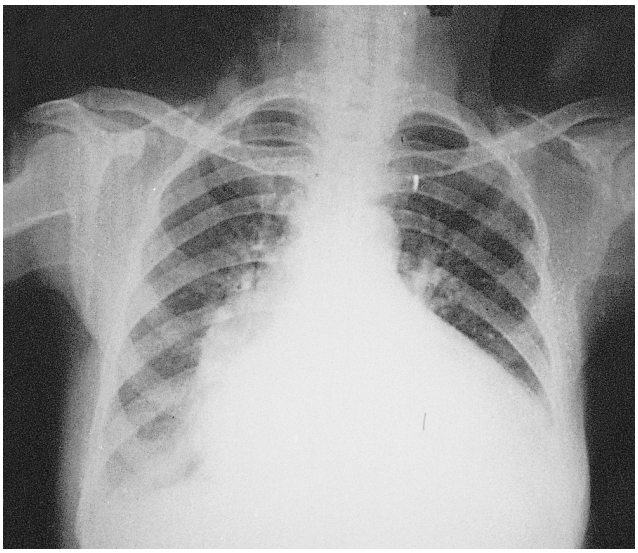


Figure 2.15
Chest x-ray of patient with severe cardiomegaly caused by chagasic myocarditis.

lymphadenopathy, hepatosplenomegaly, and leukocytosis.[11] Symptoms usually follow an incubation period which varies according to the mode of infection. For vector-transmitted infection, incubation takes 7 to 14 days; in transfusion-related transmission incubation takes up to 3 to 5 weeks. Severe myocarditis (Fig 2.14) develops in a small proportion of patients and results in electrocardiographic alterations, arrhythmia, hypotension, and cardiomegaly (Fig 2.15). Meningoencephalitis is rare in acute Chagas' disease and may present with nuchal rigidity, paralysis, and coma.

Most patients who develop acute Chagas' disease recover spontaneously in 2 to 4 months, less than 5% die during the acute disease. In some patients the acute phase is followed by an indeterminate, usually asymptomatic, phase of low-grade parasitemia that may last years or decades. In these patients immunosuppression may lead to reactivation of acute Chagas' disease years after infection, which may present as meningoencephalitis or myocarditis. Immunosuppressed patients, such as those with AIDS, hematologic malignancies, organ transplants, or receiving corticosteroids are at highest risk of reactivation disease.[12]

Chronic Chagas' Disease

Symptomatic chronic infection occurs in only 10 to 30% of infected patients, most are 20 to 50 years old, in which circulating trypomastigotes are rare. The heart is the most commonly affected organ and may take the form of chronic chagasic cardiopathy as a result of severe myocarditis (Fig 2.14). The chronic myocardial damage is probably due, at least in part, to autoimmune mechanisms and continual antigenic stimulation by parasite antigens. Down-regulation of the immune response prevents massive chronic pathological changes in most patients.[13,14] The progressive and cumulative effects of cellular necrosis, inflammatory infiltrates, fibrosis, myocytic hypertrophy, and changes in the microcirculation, together with autoimmune factors, are believed to contribute to the cardiopathy. In patients with symptomatic chronic Chagasic cardiac disease the clinical manifestations vary and may include arrhythmia, cardiac failure, or thromboembolism. Electrocardiographic alterations are evident, especially right bundle branch block, first-degree or total atrioventricular block, and ventricular repolarization.[11]

Two important clinical forms of chronic Chagas' disease involve dilation of the esophagus or the colon either separately or together. These mega syndromes occur in about 10% of patients and vary in prevalence and predominant form by geographic region. Megaesophagus and megacolon have been related to denervation of the ganglia of the myenteric plexus of the intestinal tract, with accompanying disruption of the neural coordination that is necessary for peristalsis. It has been suggested that the degree of neuronal loss beyond a certain threshold causes dilatation of the segment above the affected area and result in the progressive dilation of the viscus, which can be massive. The most common clinical manifestation of megaesophagus is dysphagia and it can be associated with regurgitation, aspiration, pneumonia and death. Up to 25% of patients with megaesophagus also exhibit hypertrophy of the parotid glands. The most common symptom of megacolon is chronic constipation, with some patients reporting complete absence of bowel movements for as long as several weeks. Fecal impaction

or volvulus are common complications in these patients and can lead to infarction or perforation of the intestinal wall and precipitate a surgical crisis.[11] Rarely, patients with either megaesophagus or megacolon also show some form of stomach involvement. Enlargement of other hollow viscera have also been reported in some patients with chronic Chagas' disease.

Congenital Chagas' Disease

Intrauterine infection by trypanosomes may cause abortion of the fetus or its premature delivery by the infected mother. Congenitally acquired infection may be asymptomatic or it may exhibit clinical features of hepatosplenomegaly, jaundice, cutaneous hemorrhage, and neurologic signs. The mortality rate from congenitally acquired infection is approximately 50%.

Pathologic Features

The initial dermal chagoma is seldom biopsied. Typically, polymorphonuclear cells, monocytes, and lymphocytes infiltrate the dermis and subcutaneous tissue. Infection of myocardial, neuroglial, and smooth muscle cells causes the most serious histopathologic changes in acute systemic Chagas' disease.

Acute Chagas' Disease

Grossly, the most conspicuous changes are in the heart, which is enlarged and dilated, particularly the right chambers (Fig 2.14). There may be pericarditis and excess serous fluid in the pericardial cavity. The myocardium is soft and pale, with focal hemorrhages and a yellowish tinge in some areas (Fig 2.14). Cardiac failure leads to congestion of the liver, lungs, spleen, and intestine to various degrees, depending on the severity of the cardiac dysfunction. The brain and meninges are also congested, often accompanied by petechiae.

Microscopically, there are trypomastigotes in peripheral blood (Fig 2.2) and amastigotes in the heart (Fig 2.5), smooth muscles, striated muscles, and sometimes the central nervous system.

There is severe myocarditis with degeneration of muscle fibers, and an interstitial inflammatory infiltrate consisting mostly of lymphocytes, monocytes, plasma cells, and sometimes neutrophils (Figs 2.16 & 2.17). Fragmentation, vacuolization, hyalinization, destruction of myofibers, and interstitial edema are other manifestations of acute chagasic cardiopathy (Fig 2.16). Transitional forms (Fig 2.18) and amastigotes (Fig 2.19) are found within myocardial fibers. There is usually some degree of pericarditis and endocarditis (Figs 2.20 & 2.21).

In the central nervous system the leptomeninges are infiltrated by mixed inflammatory cells extending into the perivascular space and penetrating the cortex (Fig 2.22). Inflam-

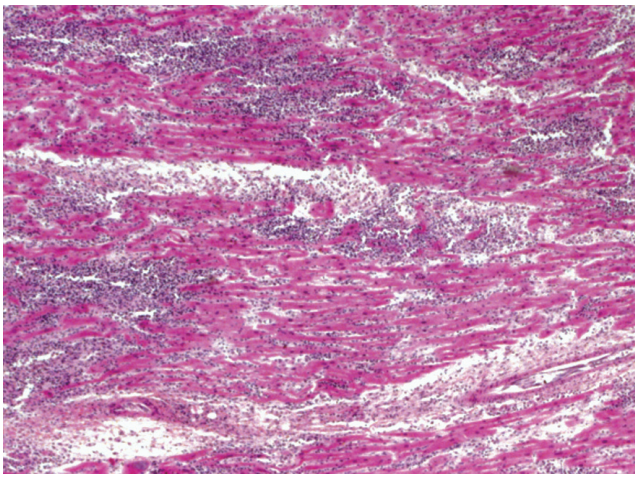


Figure 2.16
Fatal acute chagasic myocarditis with inflammatory cell infiltrates, interstitial edema, and ruptured muscle fibers. x30

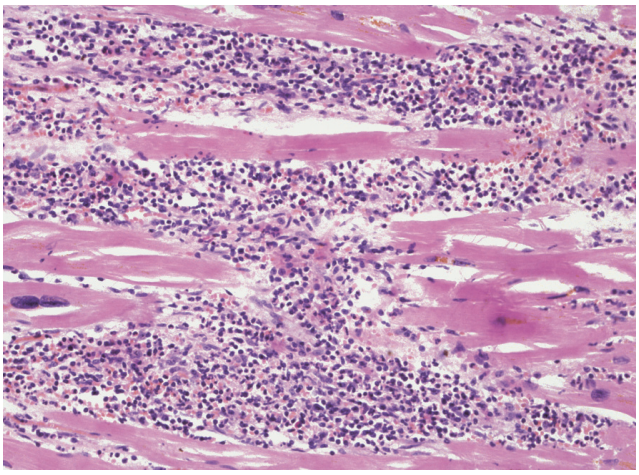


Figure 2.17
Fatal acute chagasic myocarditis. Focal accumulations of polymorphonuclear neutrophils may be present in areas of severe degeneration of muscle. x130

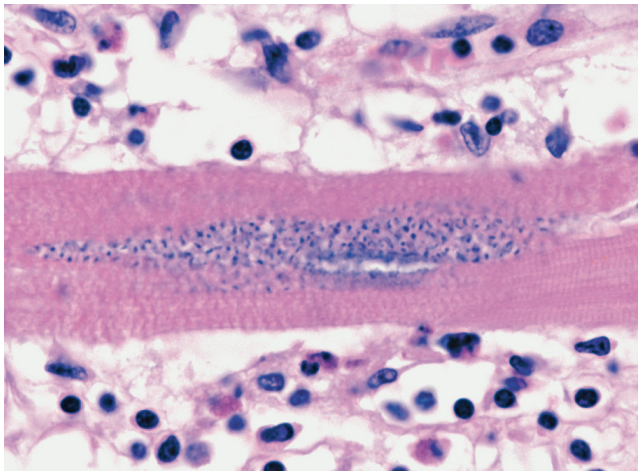


Figure 2.18
Transitional forms of *Trypanosoma cruzi* within muscle fibers in fatal acute chagasic myocarditis. Individual cell boundaries are obscured and kinetoplasts are more rounded than rod-shaped. x640

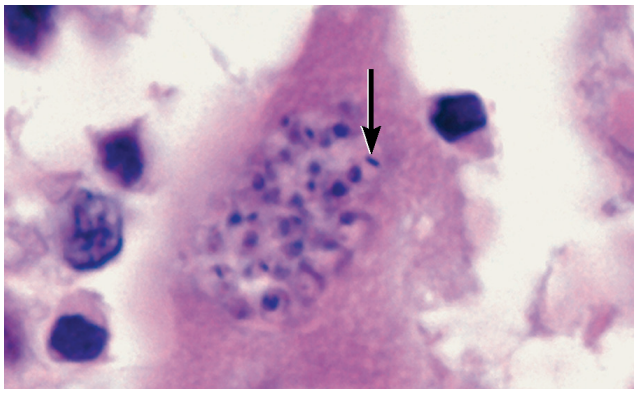


Figure 2.19
Cluster of amastigotes within muscle fibers in fatal acute chagasic myocarditis. Note rod-shaped kinetoplast (arrow). x1540

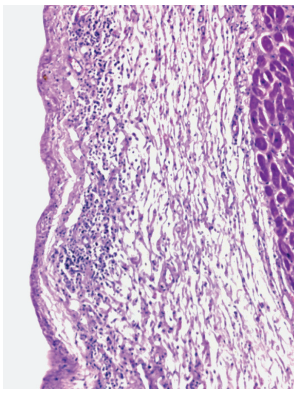


Figure 2.20
Pericarditis in fatal acute Chagas' disease. x46

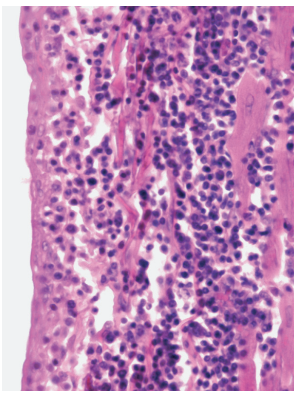


Figure 2.21
Endocarditis in fatal acute Chagas' disease. x170

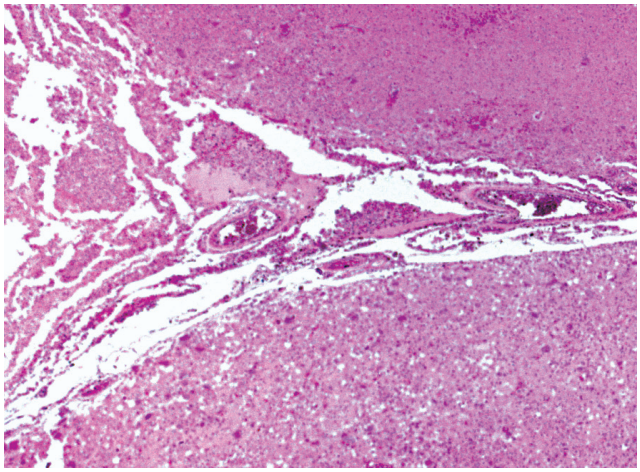


Figure 2.22
Brain of 30-year-old Brazilian with Chagas' disease and AIDS. Patient was treated for toxoplasmosis, but became comatose and died 20 days after hospital admission. Note exudate in meninges. x25

mation of the brain parenchyma produces small nodules of glial cells, lymphocytes, and plasma cells (Fig 2.23), and perivascular cuffing by lymphocytes and plasma cells (Figs 2.24a & 2.24b) Parasites invade neurons and glial cells of the brain and spinal cord. Patients with AIDS usually experience severe acute Chagas' disease. Inflammation, necrosis, and numerous amastigotes are seen in various cells of the brain parenchyma and histiocytes (Figs 2.25 to 2.27).

There may be foci of lymphocytes and plasma cells in almost any organ or tissue.[15]

Chronic Chagas' Disease

The most common findings in chronic Chagas' disease are cardiopathy and megaviscera. Chronic chagasic cardiopathy results from severe myocarditis.

Chronic chagasic myocarditis

The heart is dilated and heavy (400 to 800 g), and the

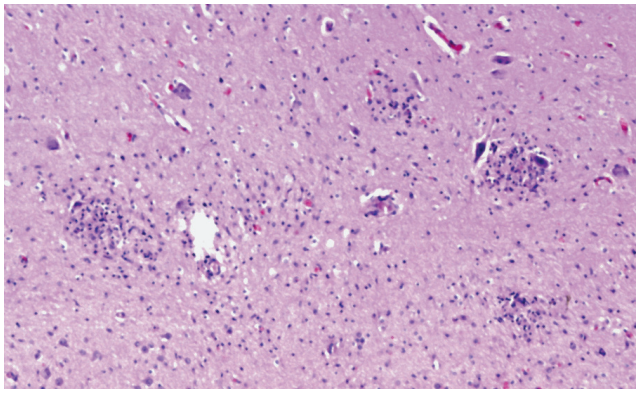
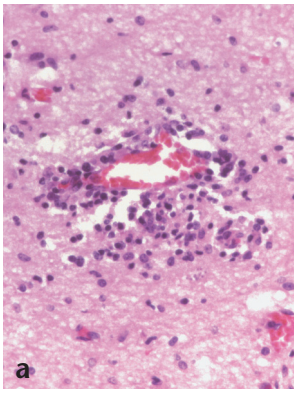


Figure 2.23
Several foci of inflammation in brain from autopsy of 3-month-old Venezuelan infant clinically diagnosed with meningoencephalitis. Foci did not contain amastigotes. x72



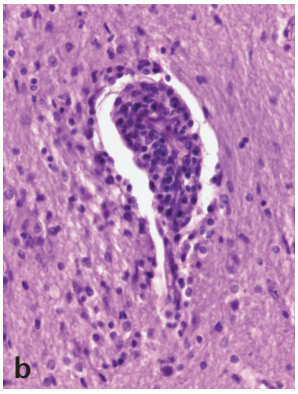


Figure 2.24 a,b
a. Perivascular inflammation in patient described in Figure 2.23. x160;
b. Autopsy specimen of brain of Panamanian patient with acute Chagas' disease showing perivascular cuffing by lymphocytes and plasma cells. x185

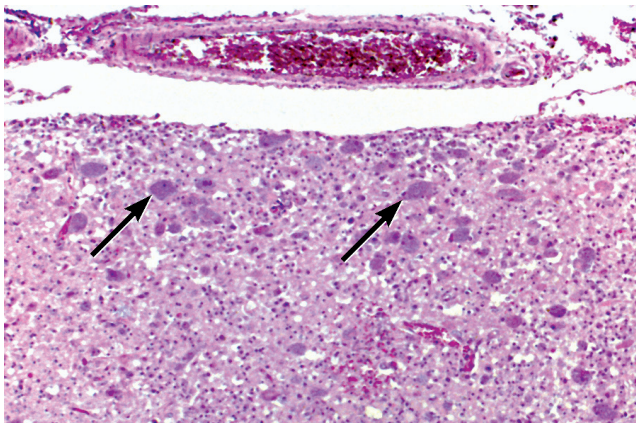


Figure 2.25
Brain of patient described in Figure 2.22, showing numerous clusters of amastigotes (arrows). x65

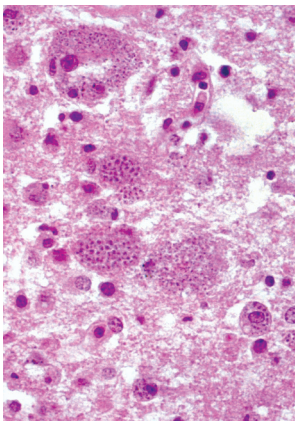


Figure 2.26
Brain of patient described in Figures 2.22. Note massive numbers of amastigotes within histiocytes and throughout parenchyma. x230

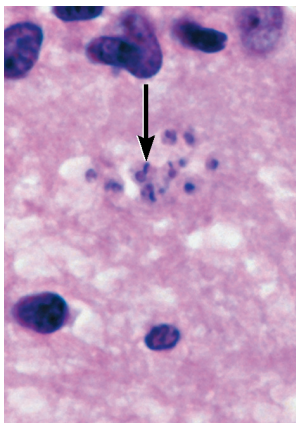


Figure 2.27
Brain of patient described in Figure 2.23 with scattered clusters of amastigotes in brain on autopsy. Note odd-shaped kinetoplast (arrow) of amastigote. x975

right ventricular outflow tract is prominent. Valve rings are dilated and atrial walls are fibrotic. The interventricular septum is deviated to the right, which may immobilize the adjacent tricuspid leaflet (Fig 2.28). Rarely, the defect at the apex of the left ventricle forms an aneurysm (Figs 2.29a to 2.29c). Distortion of the papillary muscles of the left ventricle and an increase in trabeculae carneae in the distal parts of the ventricles are common. Coronary arteries are usually normal, but capillaries and small veins are dilated and irregular.

Microscopically, there is marked interstitial fibrosis of the myocardium and rare amastigotes (Figs 2.30 to 2.32), with focal infiltrates of lymphocytes, monocytes, and plasma cells in which multinucleated giant cells are occasionally present (Fig 2.33). Focal accumulations of neutrophils and an occasional eosinophil may also be found. Apical lesions regularly appear as segments of acellular fibrous tissue associated with epicardial vessels and adipose tissue (Fig 2.29c).

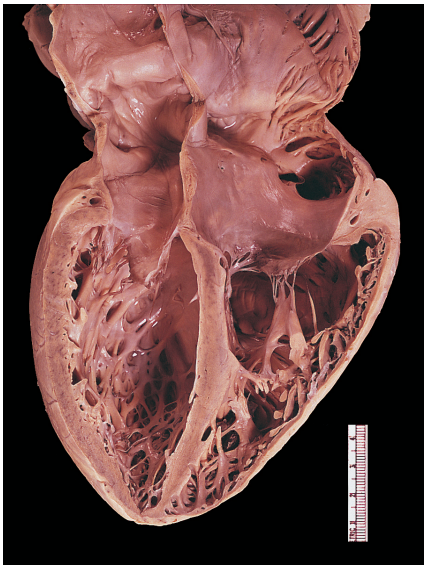


Figure 2.28
Posterior half of heart of 36-year-old Brazilian patient who had chronic Chagas disease and died of congestive heart failure. Note thinning of ventricular walls and interventricular septum, left ventricular dilatation, and increased complexity of trabeculae.

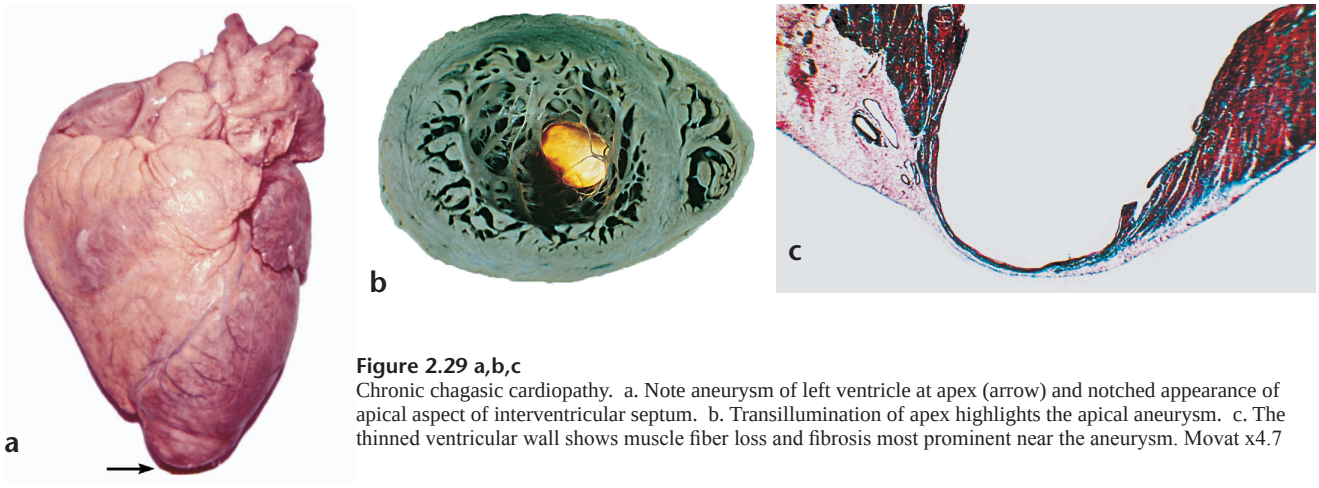


Figure 2.29 a,b,c
Chronic chagasic cardiopathy. a. Note aneurysm of left ventricle at apex (arrow) and notched appearance of apical aspect of interventricular septum. b. Transillumination of apex highlights the apical aneurysm. c. The thinned ventricular wall shows muscle fiber loss and fibrosis most prominent near the aneurysm. Movat x4.7

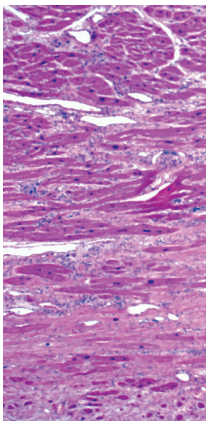


Figure 2.30
Chronic chagasic myocarditis in 27-year-old Brazilian farmer who died of congestive heart failure. There is chronic inflammation, edema, and fibrosis. x16

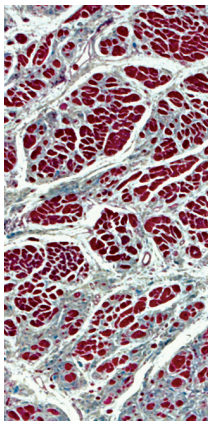


Figure 2.31
Chronic chagasic myocarditis in 56-year-old Brazilian patient. Note marked interstitial fibrosis. Movat x20

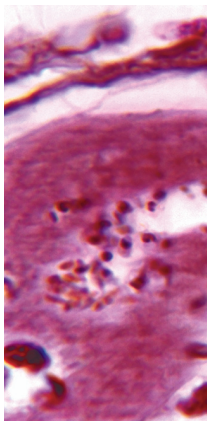


Figure 2.32
Chronic chagasic myocarditis with cluster of amastigotes in muscle fiber. Amastigotes are difficult to find in chronic lesions. x1650

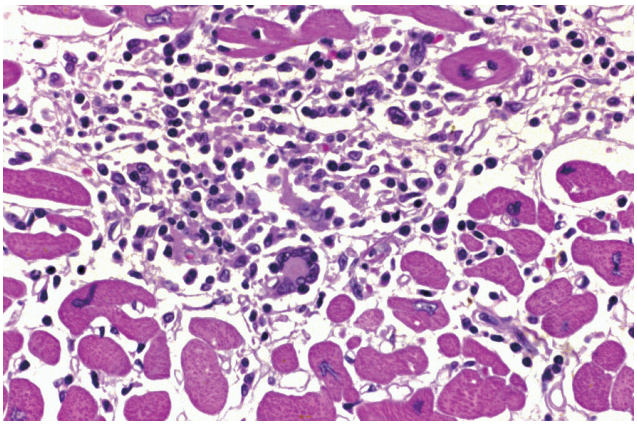


Figure 2.33
Rare giant cell in chronic chagasic myocarditis of patient described in Figure 2.30. x240

Chagasic Megaviscera

In megaviscera of chronic Chagas' disease, the esophagus and colon are most frequently affected (Figs 2.34 and 2.35). In the esophagus, focal round cell infiltrates may be found in the lamina propria (Fig 2.36) and between the muscle layers (Figs 2.37 & 2.38). As megadisease progresses the initially thinned out walls of the esophagus and colon thicken and the smooth muscle fibers become hyperplastic. Along with the hyperplasia of the smooth muscle fibers there is a marked decrease in the number of ganglion cells of the myenteric plexus. Amastigotes are very difficult to find in either the esophagus or colon.

It is possible, though not common, to find amastigotes outside the usual organs. In our experience, a rare finding was chagasic orchitis in a patient from Venezuela. Massive numbers of amastigotes were seen within histiocytes of the testis (Figs 2.39 to 2.41). Unfortunately, the specimen was not accompanied by a clinical history.

Congenital Chagas' Disease

In pregnant patients, *T. cruzi* infection causes chronic villositis (Figs 2.42a to 2.42c). Babies born with *T. cruzi* infection usually die of chagasic encephalitis within a few days or weeks.

Figure 2.34
Megaesophagus in 34-year-old Brazilian patient with chronic Chagas' disease.

Figure 2.35
Megacolon in 50-year-old Brazilian patient with chronic Chagas' disease. Colon is saccular and thin-walled.

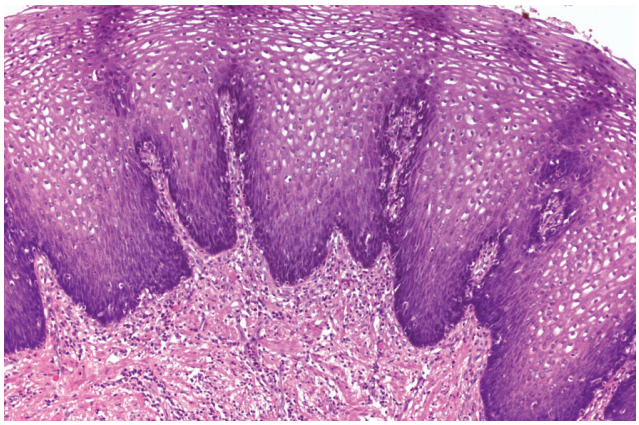


Figure 2.36
Megaesophagus in chronic Chagas' disease, with chronic inflammation of lamina propria. x64

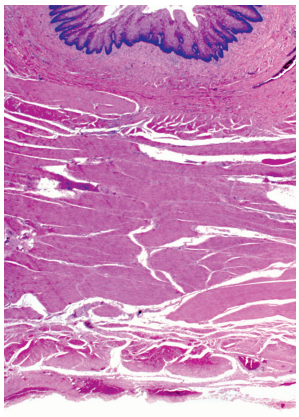


Figure 2.37
Megaesophagus in chronic Chagas' disease. Note thickening of smooth muscles. x8

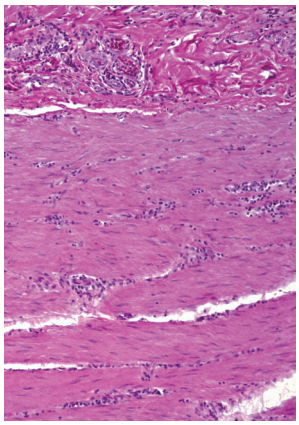


Figure 2.38
Megaesophagus in chronic Chagas' disease with chronic inflammatory infiltrate of smooth muscle. x60

Diagnosis

Diagnosis of Chagas' disease during the acute phase, whether primary or due to reactivation associated with immunosuppression, is established by identifying trypomastigotes of *T. cruzi* in peripheral blood films (Fig 2.2). Highly motile trypomastigotes may be observed in wet preparations of blood or buffy coat, and in specimens of cerebrospinal fluid (CSF), bone marrow, mass lesions, and pericardial fluid. With few exceptions, detecting amastigotes in biopsy specimens also confirms a diagnosis of acute Chagas' disease. Autopsy specimens from immunosuppressed patients with Chagas' disease, and patients who die of acute disease usually reveal large numbers of amastigotes.

For chronic Chagas' disease, where parasitemia is much lower, polymerase chain reaction[16], hemoculture, and se-

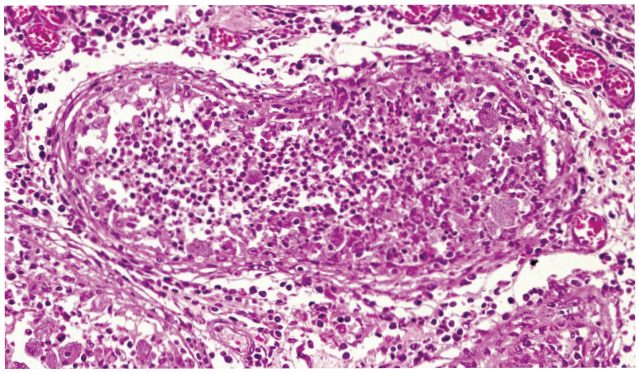


Figure 2.39
Rare chagasic orchitis in Venezuelan patient. Note chronic inflammation. x140

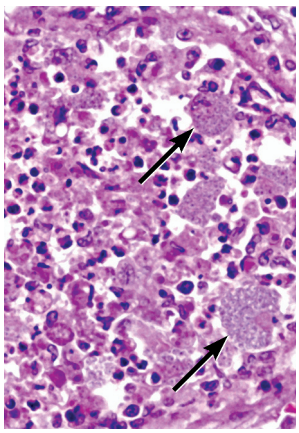


Figure 2.40
Higher magnification of testis illustrated in Figure 2.39, showing clusters of amastigotes within histiocytes (arrows). x295

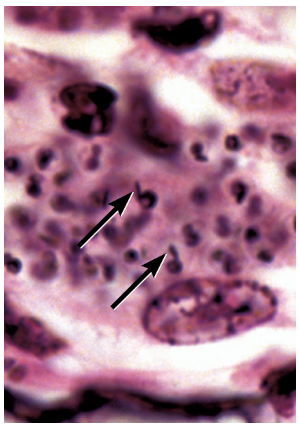


Figure 2.41
Cluster of amastigotes in testis of patient described in Figures 2.39 and 2.40. Note black rod-shaped kinetoplasts (arrows) and large spherical nuclei. Wilder's reticulum x1480

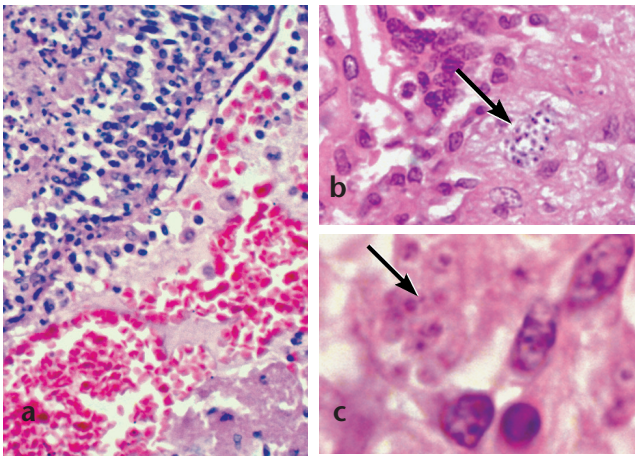


Figure 2.42 a,b,c
a. Placenta with chronic villositis in Chagas' disease. x100
b. Placenta with cluster of amastigotes (arrow) in histiocyte in Chagas' disease. x150
c. Higher magnification of amastigotes in placenta in Figure 2.42a and 2.42b. Note rod-shaped kinetoplasts (arrow). x700

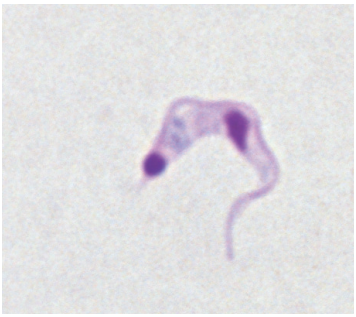


Figure 2.43
Trypomastigote of *Trypanosoma cruzi* in CSF, depicting C-shaped configuration and large spherical kinetoplast at posterior tip. Patient was 38-year-old HIV-positive Salvadoran living in Virginia. Patient had not been to El Salvador for more than a year, indicating reactivation of Chagas' disease. Giemsa x2000

rological testing are required to establish a diagnosis. Trypomastigotes do not usually appear in peripheral blood films, and amastigotes are rarely found in biopsy or autopsy specimens. Immunosuppression by HIV can reactivate chronic Chagas' disease and trypomastigotes may appear in CSF (Fig 2.43) and sometimes in peripheral blood samples. The CSF of these co-infected patients may show a mild pleocytosis (predominantly lymphocytes) and increased protein levels.

Hemoculture and xenodiagnosis are highly specific but not very sensitive. Blood cultures with liver infusion tryptose, Warren, or other suitable media must be examined for up to 120 days postinoculation.[16,17] In xenodiagnosis, sterile, laboratory-reared reduviid bugs are allowed to feed on a patient (Fig 2.44). If the patient is infected, the bugs ingest trypomastigotes and a diagnosis is confirmed for the patient 10 to 30 days later when the bugs' feces and hindgut contents are examined for metacyclic trypomastigotes. This very specific procedure is valuable in diagnosing chronic infections where parasites cannot be found in the patient's blood.[18]

PCR techniques for diagnosis of Chagas' disease are under investigation, but none is yet available for routine use.

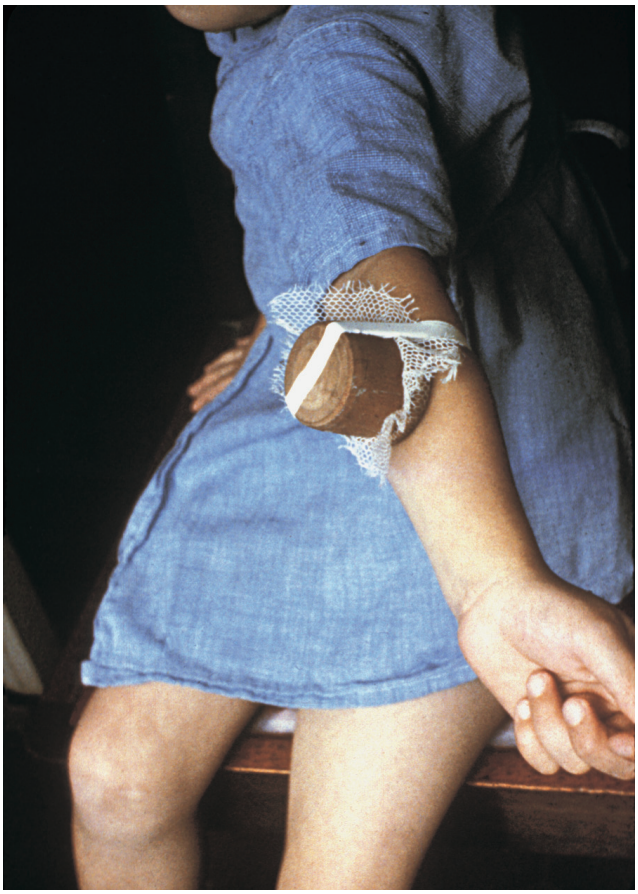


Figure 2.44
Xenodiagnosis technique applied to arm of Costa Rican patient. Procedure is useful in diagnosing chronic Chagas' disease.

Treatment and Prevention

Chemotherapy, which has little apparent effect on chronic Chagas' disease, is reserved for patients diagnosed in the acute phase, accidentally infected laboratory workers, immunocompromised patients, and children with congenital infection. Benznidazole and nifurtimox, both of which are toxic, reduce the duration and severity of acute Chagas' disease, but are curative only for approximately 50% of patients.[19,20] Chronic chagasic cardiopathy is treated with drugs, pacemaker, or transplantation. "Mega" syndromes may require surgery.

With the increasing numbers of serologically positive individuals in the United States, identifying infected blood, tissue and organ donors by exposure questionnaires and screening tests can prevent transmission of Chagas' disease.[21] A few antibody detection screening tests have been approved by the FDA for use in the United States. [22,23] Vector transmission of Chagas' disease can be interrupted through improved housing, community education, and the use of specific insecticides.

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Figure 2.14
Contributed by Gorgas Memorial Laboratory, Panama

Figure 2.29a&b
Contributed by Gorgas Memorial Laboratory, Panama

Figure 2.44
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