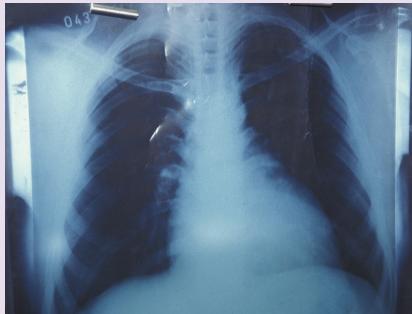


# 38

## Trypanosoma spp.



**Figure 38.1** A chest X-ray showing enlargement of the heart due to Chagas disease. From the World Health Organization, Special Programme for Research and Training in Tropical Diseases, <http://www.who.int/tdr/index.html>. Image #9905349. Additional photographic credit is given to Andy Crump who took the photograph in 1999 in Argentina.

A 32-year-old female from Brazil presented to her local hospital with a sudden onset of left leg, arm, and facial weakness. She was able to speak and reported being in good health in the past except that she became short of breath running after her 4-year-old son. She grew up as a child in Brazil but came to the UK in her early twenties. A CT scan of her brain showed an acute **stroke**. The ECG tracing of her heart was abnormal with broadened QRS complexes. A chest X-ray showed enlargement of the heart (**Figure 38.1**). An **ECHO scan** of the heart showed a dilated left ventricle with an apical **aneurysm**, in which there was a small thrombus. An **ELISA** test for *Trypanosoma cruzi* antibodies was performed because of her Brazilian origin and proved positive. She was diagnosed with Chagas disease with cardiomyopathy and an embolic stroke. She was treated with intensive rehabilitation, anticoagulated, and commenced on ACE inhibitors. For her infection, she was treated with benznidazole.

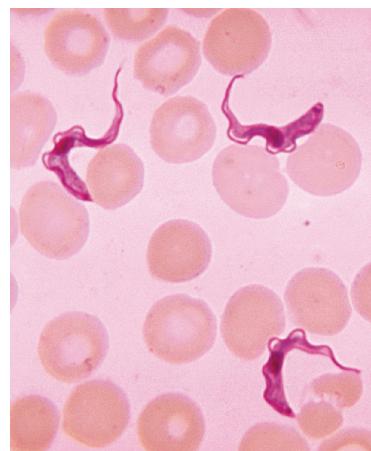
### 1. WHAT IS THE CAUSATIVE AGENT, HOW DOES IT ENTER THE BODY AND HOW DOES IT SPREAD A) WITHIN THE BODY AND B) FROM PERSON TO PERSON?

#### CAUSATIVE AGENT

Trypanosomes are flagellated protozoan parasites. In Africa, the species of *Trypanosoma brucei* has two subspecies that infect humans (**Figure 38.2**). In Central and West Africa, this is *T. brucei gambiense* and in East and Southern Africa it is *T. brucei rhodesiense*. The species in South America is *Trypanosoma cruzi* (**Figure 38.3**). It is estimated that in the course of evolution *T. brucei* and *T. cruzi* diverged from each other about 100 million years ago. The life cycle and clinical features arising from these two species differ.

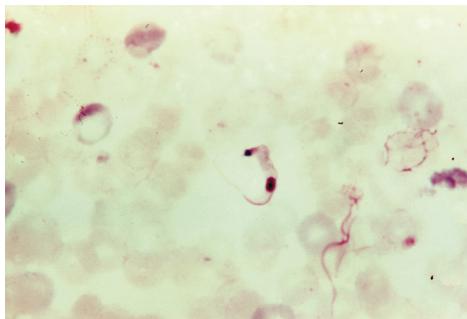
#### ENTRY AND SPREAD WITHIN THE BODY

When *T. brucei* is inoculated into a new human host by tsetse flies local multiplication occurs under the skin. There is spread to lymph nodes and then entry into the bloodstream. Multiplication occurs in blood. Within a few weeks, *T. brucei rhodesiense* passes from the bloodstream, probably through the choroid plexus, into the central nervous system (CNS). This CNS invasion takes several months with *T. brucei gambiense*.



**Figure 38.2** *Trypanosoma brucei* spp. in a blood film. The trypanosomes are slender with an undulating membrane leading to the flagellum. From the Centers for Disease Control & Prevention, Atlanta, Georgia. Image is found in the Public Health Image Library #613. Additional photographic credit is given to Dr Myron G Schultz who took the photo in 1970.

*T. cruzi* is transmitted by triatomine bugs (**Figure 38.4**). Local inflammation occurs at the site of inoculation. Again, there is spread to local lymph nodes and then entry into the bloodstream. Various tissues may be invaded but key targets are the heart and the gastrointestinal (GI) tract.



**Figure 38.3** *Trypanosoma cruzi* in a blood film. It often appears as a "C" shape. From the Centers for Disease Control & Prevention, Atlanta, Georgia. Image is found in the Public Health Image Library #543.



**Figure 38.4** *Triatoma infestans*, which transmits *Trypanosoma cruzi*. From the Centers for Disease Control & Prevention, Atlanta, Georgia. Image is found in the Public Health Image Library #613. Additional photographic credit notes that the images was donated by the World Health Organization, Geneva, Switzerland, in 1976.



**Figure 38.5** Tsetse fly, *Glossina morsitans*, the vector for African trypanosomiasis. From Martin Dohm / Science Photo Library, with permission.

Multiplication occurs in the tissues. The intracellular life form is the amastigote, which lacks a flagellum. Replication of the amastigote produces a pseudocyst within a cell. The extracellular life form is the trypomastigote. *T. cruzi* emerges from infected cells and passes onto other cells.

## PERSON-TO-PERSON SPREAD

Human African trypanosomiasis (HAT) is spread by tsetse flies belonging to the genus *Glossina* (Figure 38.5). The

geographic distribution of HAT is determined by the ecologic requirements of tsetse flies. This is patchy in countries between the sub-Saharan region and the Kalahari and Namib deserts. Infection of humans can be person to person but also a **zoonosis** with tsetse flies transmitting trypanosomes from a reservoir of ungulates (see below). *Glossina morsitans* usually transmits *T. brucei rhodesiense* and *G. palpalis* usually transmits *T. brucei gambiense*. Trypanosomes ingested from an animal host pass through the mid-gut of the tsetse fly, undergo developmental changes, and reach the salivary glands. Here, they are referred to as metacyclic trypomastigotes. When tsetse flies bite humans, their saliva passes into the bites bearing these trypomastigotes. This is called **salivarian transmission**. The lifecycle of HAT is shown in Figure 38.6.

In South America, various animals can serve as a reservoir, examples include the armadillo and the opossum. Triatomine bugs ingest trypanosomes when biting infected animals. The trypanosomes remain within the intestine of the bug. If they next feed on humans, they bite the skin and defecate at the same time. Humans scratching in the vicinity of the bite rub feces bearing metacyclic trypomastigotes into the open wound. This is called **stercorarian transmission**, the Latin root *sterco* referring to feces. The life cycle of South-American trypanosomiasis is shown in Figure 38.7.

Regrettably, another rare form of transmission is through blood transfusion. In resource-poor settings, blood screening may not be feasible. However, transfusion-related transmission has been described in the US from blood donated by South-American immigrants. Understandably, antibody screening of blood is not routine in nonendemic countries.

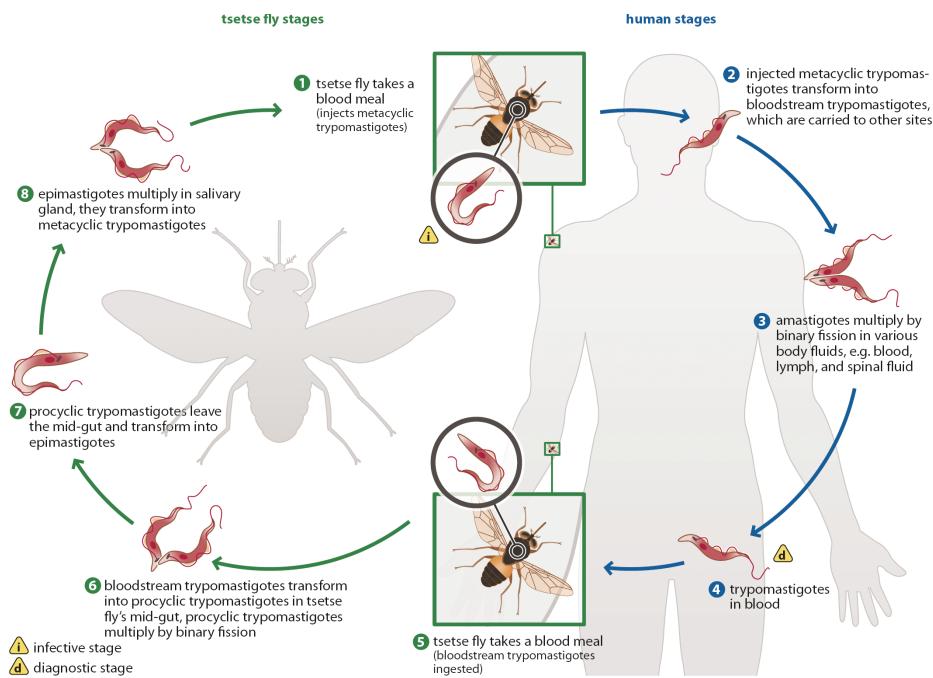
## EPIDEMIOLOGY

The WHO estimates that 6–7 million people are infected with *T. cruzi*, this representing a considerable decline over previous decades. There has been a dramatic decline in HAT. In 2004, the WHO estimated a prevalence of 0.5 million with 4800 deaths per annum. By contrast, in 2019, the WHO reported that fewer than 1000 cases of HAT were detected, and 98% of these were due to *T. brucei gambiense*. *T. brucei gambiense* primarily affects humans, while *T. brucei rhodesiense* is primarily within ungulates, including cattle and wild game, with occasional human cases.

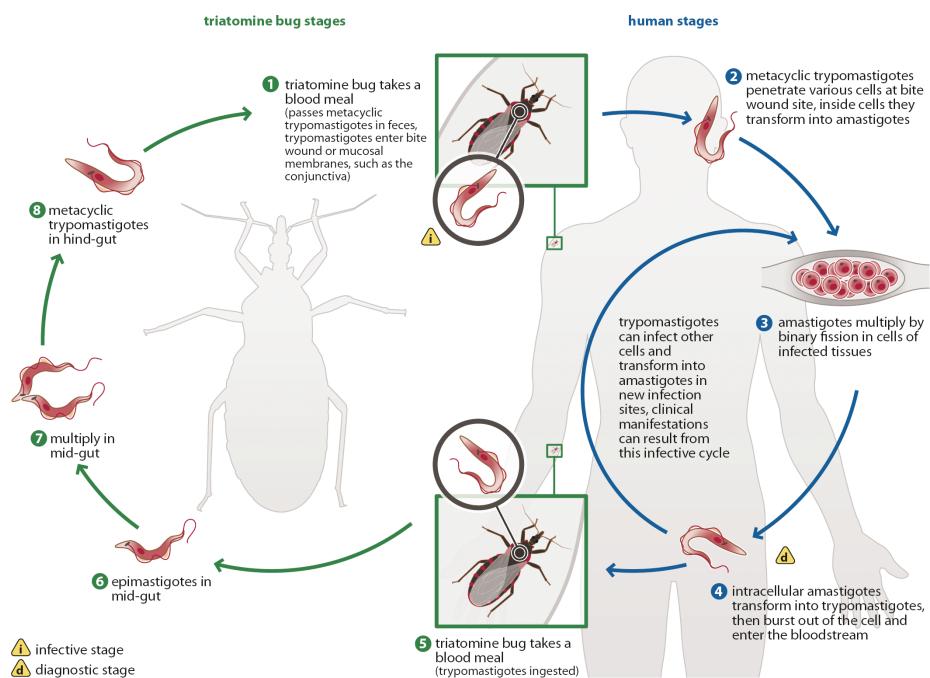
HAT is endemic in 36 countries and South-American trypanosomiasis in 21 countries.

## 2. WHAT IS THE HOST RESPONSE TO THE INFECTION AND WHAT IS THE DISEASE PATHOGENESIS?

There are innate and adaptive host responses to trypanosomal infection. Humans may be exposed to nonpathogenic species of trypanosomes. However, in normal human serum, apolipoprotein L-1 (APOL1) binds to the trypanosome surface and is endocytosed. Within the



**Figure 38.6** Life cycle of African trypanosomiasis. Tsetse flies inoculate humans with metacyclic trypomastigotes when they take a blood meal (1). Trypomastigotes multiply in tissue fluid, then in lymph nodes, and then enter the bloodstream (2). In the bloodstream, they continue multiplying with antigenic variation to avoid the host response. Eventually, they enter the central nervous system (3). Circulating parasite may be engulfed by tsetse flies when they take a blood meal (4). There is then development within the mid-gut of the tsetse fly before migration to the salivary glands (6–8). From the Centers for Disease Control & Prevention, Atlanta, Georgia. Image is found in the Public Health Image Library #613. Additional photographic credit notes that the images was donated by the World Health Organization, Geneva, Switzerland, in 1976.



**Figure 38.7** Life cycle of South-American trypanosomiasis. Humans are infected by stercorarian transmission from triatomine bugs (1). At the site of infection, metacyclic trypomastigotes enter cells (2), transform into amastigotes and multiply (3). Trypomastigotes arise from infected cells, enter the bloodstream and infect other cells in the body (4). Any circulating parasite may be engulfed by triatomine bugs when they take a blood meal (5). Further development occurs in the mid-gut of the bugs (6–8). Adapted with kind permission from the Centers for Disease Control & Prevention, Atlanta, Georgia. Image is found in the Public Health Image Library #3384. Additional photographic credit is given to Alexander J da Silva, PhD, and Melanie Moser who created the image in 2002.

trypanosomal cytoplasm, APOL1 forms pores in **lysosomes**. Release of lysosomal contents causes trypanosomal killing. Species of trypanosomes that are usually nonpathogenic may only cause infection in humans with APOL1 deficiency. The pathogenic species *T. brucei rhodesiense* possesses a serum resistance-associated protein (SRA), which strongly binds to APOL1, inhibiting its toxic action. The other pathogenic species, *T. brucei gambiense*, does not possess SRA, but has reduced uptake of APOL1, increased degradation in the cytoplasm, and increased membrane stiffening.

*T. brucei* remains extracellular in the bloodstream and is exposed to the host immune response. Specific antibodies appear against the surface glycoprotein and lyse the trypanosomes through activation of complement. However, in *T. brucei rhodesiense*, there are an estimated 1000 different variants of the surface glycoprotein. *T. brucei* switches the gene from one variant to another (**antigenic variation**). Each new antibody response is met with a gene switch and the escaping, new variants of trypanosomes multiply in successive waves (**Figure 38.8**).

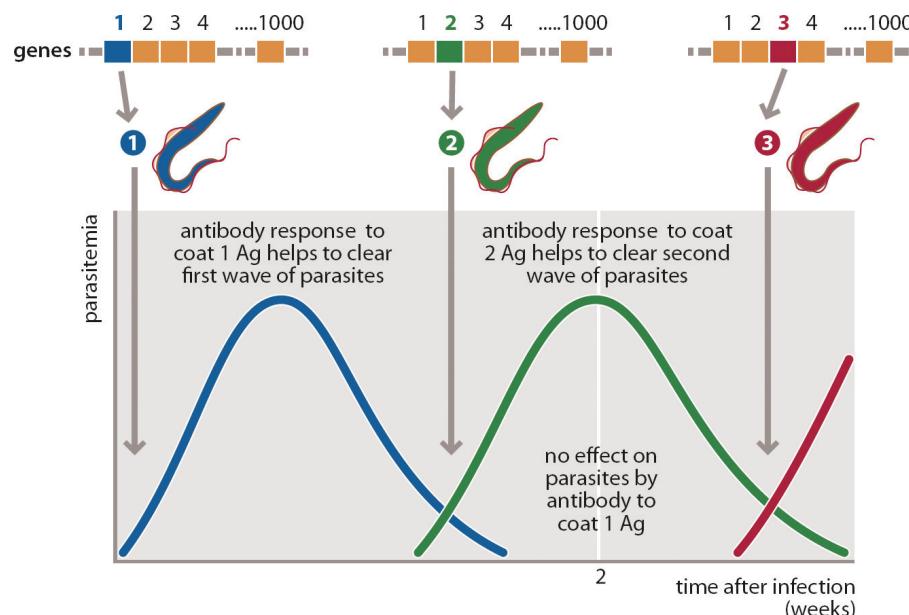
The variant specific glycoproteins (VSG) stimulate B lymphocytes to produce IgM in a T-cell independent manner. Eventually, host serum has an excess of polyclonal IgM antibodies. The polyclonal activation of B cells compromises their ability to respond to other pathogens (another escape mechanism, like the antigenic variation to fool the host immune system). Other trypanosomal antigens pass through antigen-presenting cells and stimulate CD4+ lymphocytes to mount a T-cell-dependent antibody response. Trypanosomes directly release factors, such as Trypanosome-derived

lymphocyte triggering factor (TLTF) and trypanosomal macrophage activating factor (TMAF), that stimulate CD8+ T lymphocytes and macrophages. Through this cellular activation, various **cytokines** and mediators appear. **Tumor necrosis factor- $\alpha$**  (TNF- $\alpha$ ) contributes to the weight loss of chronic infection. It seems to inhibit trypanosomal growth, but conversely **interferon- $\gamma$**  (IFN- $\gamma$ ) seems to help trypanosomal proliferation.

Dysregulated antibody production leads to the appearance of autoantibodies. **Immune complexes** damage vascular endothelium and on binding to the surface of red blood cells cause **hemolysis**. Chronic infection suppresses bone marrow function, probably through cytokine effects. This, added to hemolysis, causes **anemia**. Equally, platelet numbers may fall and disturbance of clotting may lead to hemorrhage or conversely **thrombosis**.

Inflammation occurs in tissues containing *T. brucei*. This ranges from the skin at the site of local inoculation, to lymph nodes, to organs seeded from the bloodstream such as the heart, the kidneys, and eventually the CNS. Within the CNS, there is progressive inflammation of the **leptomeninges**. The inflammatory response, immune complexes, local cytokines, and **prostaglandins** all contribute to CNS pathology, which eventually involves disruption of the **choroid plexus** and the blood-brain barrier.

While *T. brucei* is extracellular, *T. cruzi* is principally intracellular. The pseudocysts within tissues do not excite an inflammatory response. This only occurs once they rupture from cells and release antigens. *T. cruzi* is coated with a mucin-type glycoprotein that is anchored to the surface



**Figure 38.8** Antigenic variation of *T. brucei*. An antigen-specific response is made against the surface coat antigen, which gradually removes the parasites from the bloodstream (coat 1). During this time, some of the parasites escape by switching their surface coat gene and the antibody response has to start from scratch. Antibodies to the second coat antigen (coat 2) are made, which remove these new parasites from the circulation. Some of the parasite will then escape again by switching their gene usage to coat 3 and so on. In *T. brucei rhodesiense*, it is estimated that there are 1000 different variants of the glycoprotein that make up the surface coat. (For simplicity, individual genes are depicted in a linear sequence whereas they are actually scattered about in the genome of the organism.)



by a glycosylphosphatidylinositol (GPI). There are several hundred surface mucin genes, but antigenic variation in *T. cruzi* has not been established. GPI is well recognized as a potent macrophage activator and is thereby pro-inflammatory. Cell-mediated immune responses occur in infected tissue. In mice, CD8+ lymphocytes are essential for survival during the early stages of experimental infection. There is a polyclonal activation of B cells and it is conceivable that autoantibodies arise through dysregulation. Various *T. cruzi* antigens are also cross-reactive with host antigens found in vascular endothelium, muscle interstitium, and cardiac and nervous tissue. Autoimmune pathology is possible as passive transfer of serum or lymphocytes can cause pathology in recipients. However, it is not clear whether chronic pathology is caused by long-term infection-stimulated tissue inflammation or an autoimmune process or both.

### 3. WHAT IS THE TYPICAL CLINICAL PRESENTATION AND WHAT COMPLICATIONS CAN OCCUR?

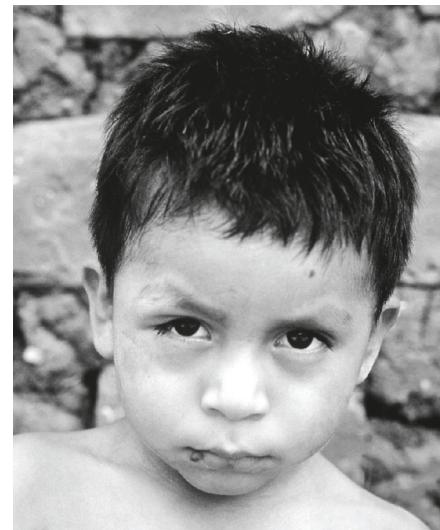
In HAT, local inflammation at the site of tsetse fly inoculation is sometimes apparent and referred to as a trypanosomal **chancre**. This may occur in half of *T. brucei rhodesiense* infections but is rare with *T. brucei gambiense*. It appears after 1–2 weeks, may last for 2–3 weeks, and may reach a diameter of 3–5 cm. There may be regional **lymphadenopathy**.

Symptoms occur once trypanosomes multiply and circulate in the bloodstream. These commence about 1–3 weeks after infection with *T. brucei rhodesiense*, but weeks to months with *T. brucei gambiense*. There are fevers, headache, malaise, and loss of appetite. The fevers follow a cyclical pattern as the VSGs change. More generalized lymphadenopathy, **hepatomegaly**, and **splenomegaly** appear. There may be skin **rashes**.

Invasion of the CNS represents the second stage of infection, but there is overlap of first- and second-stage features. There is progressive mental deterioration culminating in coma and death, with a variety of intervening CNS manifestations. There is disturbance of motor function, co-ordination, behavior, and sleep. HAT is called sleeping sickness. Patients may sleep in the daytime and be awake at night. *T. brucei rhodesiense* infection progresses more rapidly, with death within 9 months, while *T. brucei gambiense* may take a few years.

In South-American trypanosomiasis, inflammation at the site of inoculation is called a **chagoma**. The disease was originally described by Carlos Chagas in Brazil in 1907 and the disease is also called Chagas disease. Sometimes, the inflammation occurs around the eyelid and the local swelling is called **Romana's sign** (Figure 38.9). Regional lymphadenopathy is followed by fever, headache, malaise, hepatomegaly, splenomegaly, and rash. In the acute phase, inflammation in seeded organs results in **myocarditis**, diarrhea and vomiting or **meningoencephalitis**.

The clinical features of the acute phase last 1–2 months and features may not return despite continued infection. Up to one



**Figure 38.9** Romana's sign in a boy. There is swelling by the right eyebrow. The boy will have been infected in that region by a triatomine bug. From the Centers for Disease Control & Prevention, Atlanta, Georgia. Image is found in the Public Health Image Library #2617. Additional photographic credit notes that the photo was taken by Dr Mae Melvin in 1962.

third of patients suffer chronic complications after one or two decades. These principally affect the heart and the GI tract.

Cardiac muscle weakens and thins. Impaired cardiac function results in heart failure. Aneurysms can develop, typically at the apex of the left ventricle. Clots formed within the aneurysm can embolize. Cardiac conduction is altered with ECG abnormalities. **Dysrhythmias** or complete heart block may cause sudden death.

In Brazil, more than elsewhere, GI involvement results in dilatation and loss of peristalsis. This results in **megaesophagus** and **megacolon**, with accompanying **dysphagia** and constipation (Figure 38.10). The inability to eat causes **cachexia** and death.

### 4. HOW IS THE DISEASE DIAGNOSED, AND WHAT IS THE DIFFERENTIAL DIAGNOSIS?

Unfortunately, many individuals suffer from trypanosomiasis distant from diagnostic facilities. Clinical features are nonspecific. In Chagas disease, Romana's sign and local lymphadenopathy are suggestive.

For *T. brucei gambiense* the simplest test is the Card Agglutination Test for Trypanosomiasis (**CATT**). A drop of heparinized whole blood is placed on a card containing freeze-dried trypanosomes and the presence of agglutination by serum antibodies is observed over 5 minutes. This test has high sensitivity but false positive results can occur. Direct visualization of *T. brucei rhodesiense* and *T. brucei gambiense* may be observed in lymph node aspirates, blood films, and cerebrospinal fluid (CSF). If present in reasonable numbers,



**Figure 38.10** A plain abdominal X-ray. There is marked dilatation of the colon, megacolon, which is easily apparent on the X-ray. From the World Health Organization, Special Programme for Research and Training in Tropical Diseases, <http://www.who.int/tdr/index.html>. Image #9105027. Additional photographic notes indicate the image was taken in Brazil in 1990.

the motile trypanosomes are easily observed. However, the level of parasitemia may be low in later stages of infection making parasitologic diagnosis difficult. Examination of the CSF is essential for staging infection and includes microscopy for both parasites and white cell counts.

In Chagas disease, trypanosomes may be seen in a blood film only during the acute phase. The main diagnostic test is **serology**, which may employ an ELISA. Once there are organ complications, ECGs or ECHOs of the heart reveal structural abnormalities and imaging of the esophagus and colon reveal dilatation.

## DIFFERENTIAL DIAGNOSIS

Mega syndromes do not have alternative explanations of note. The differential diagnosis for the cardiac complications includes other cardiomyopathies. Otherwise, the systemic **febrile** phase of early Chagas disease and HAT has a long differential diagnosis. In Africa, the CNS phase may have to be distinguished from meningitis, **encephalitis**, cerebral malaria, CNS tuberculosis, HIV-related neurologic disease, and cerebral tumors.

## 5. HOW IS THE DISEASE MANAGED AND PREVENTED?

### MANAGEMENT

The treatments available for HAT are shown in **Table 38.1**. Treatment choices can depend on species, patient age, weight,

stage of disease, CSF white cell count, and the balance between toxicity and efficacy. Melarsoprol is an arsenical drug and causes a reactive encephalopathy in 20% on treatment and mortality in 2–12%. For *T. brucei gambiense*, it has been superseded by an oral agent, fexinidazole, and the combination of nifurtimox plus eflornithine.

Drugs for Chagas disease include benznidazole (first line) or nifurtimox. Again, they are both toxic and it is debated whether they should be used in the asymptomatic phase of infection before complications arise. Potentially older individuals will die with, rather than from, *T. cruzi* infection. Toxicity seems to be less in children than in adults. There are now studies of benznidazole in children showing that a 60-day course is reasonably well tolerated with disappearance of *T. cruzi* antibodies in almost 60%.

### PREVENTION

The control of trypanosomiasis is hampered by its rural occurrence. When possible, it is important to actively diagnose cases and offer treatment for or before complications. Otherwise, vector control is the key strategy employed. Insecticide sprays are used to kill tsetse flies. Insecticide-impregnated traps are positioned in key locations (**Figure 38.11**). The traps are made of blue or black cloth as these colors attract the tsetse flies. Tsetse populations have been reduced in some localities by the release of sterilized male flies. While tsetse flies are principally outdoors, the triatomine bugs of South America live within cracks in walls or in thatched roofs. Improved housing is important in reducing bug populations. Insecticide spraying has also been very successful in eliminating transmission in many areas. In South America, universal blood screening is also important.



**Figure 38.11** Tsetse fly traps in rural Africa. From the World Health Organization, Special Programme for Research and Training in Tropical Diseases, <http://www.who.int/tdr/index.html>. Image #9604658. Additional photographic credit is given to Andy Crump who took the photograph in 1996 in Uganda.

**Table 38.1** Drugs used to treat trypanosomiasis

Pathogen	Drugs and comments
<i>T. brucei gambiense</i>	<p><b>Fexinidazole</b></p> <p>Not approved if &lt; 6 years of age or &lt; 20kg</p> <p>Any stage, but</p> <p>Not for severe second-stage disease with CSF white cell count &gt;100 cells mL<sup>-1</sup></p> <p>Oral agent</p> <p><b>Pentamidine</b></p> <p>Early stage</p> <p>Intravenous or intramuscular</p> <p>Can cause drop in blood pressure, and changes in renal and hepatic function and blood glucose levels</p> <p>Nifurtimox plus Eflornithine</p> <p>Late stage</p> <p>Oral (nifurtimox) and intravenous (eflornithine)</p> <p>Can cause gastrointestinal upset, headache, joint and muscle pains, bone marrow suppression</p> <p><b>Melarsoprol</b></p> <p>Intravenous</p> <p>Can cause encephalopathy, with convulsions and coma, headache, thrombophlebitis, rash</p>
<i>T. brucei rhodesiense</i>	<p><b>Suramin</b></p> <p>Early stage</p> <p>Can cause reversible nephrotoxicity, bone marrow suppression, and rash</p> <p><b>Melarsoprol (see above)</b></p> <p><b>Late</b></p>
<i>T. cruzi</i>	<p>Benznidazole</p> <p>Oral</p> <p>Can cause gastrointestinal upset, headache, joint pains, itch, and rash</p> <p>Nifurtimox</p> <p>Oral</p> <p>Can cause gastrointestinal upset, headache, joint and muscle pains</p>

## SUMMARY

### 1. WHAT IS THE CAUSATIVE AGENT, HOW DOES IT ENTER THE BODY, AND HOW DOES IT SPREAD A) WITHIN THE BODY AND B) FROM PERSON TO PERSON?

- Trypanosomes are flagellated protozoan parasites.
- African trypanosomiasis (HAT) is caused by *Trypanosoma brucei rhodesiense* or *T. brucei gambiense*.
- South American trypanosomiasis is caused by *Trypanosoma cruzi*.
- Tsetse flies transmit infection in Africa from other humans or an animal, ungulate reservoir.

- Triatomine bugs transmit infection in South America from an animal reservoir.
- After an insect bite, trypanosomes spread from local tissue to lymph nodes, then enter the bloodstream, and finally invade tissues.
- In HAT, invasion of the central nervous system occurs after weeks to several months.
- In South-American trypanosomiasis, an aflagellate, intracellular life form, the amastigote, forms a pseudocyst within cells.

*Continued...*

*...continued*

## 2. WHAT IS THE HOST RESPONSE TO THE INFECTION AND WHAT IS THE DISEASE PATHOGENESIS?

- Nonpathogenic trypanosomes are killed by normal human serum through the action of apolipoprotein L-1. Pathogenic trypanosomes neutralize this through a serum resistance-associated protein (SRA) and other mechanisms.
- In the bloodstream, *T. brucei* species are killed by the action of antibody and complement.
- *T. brucei* species undergo antigenic variation and evade the antibody response.
- Antigenic stimulation by *T. brucei* causes polyclonal antibody production by B cells.
- Trypanosome-derived lymphocyte triggering factor (TLTF) and trypanosomal macrophage activating factor (TMAF) stimulate CD8+ T cells and macrophages, respectively.
- In HAT, various cytokines are produced, and among these TNF- $\alpha$  can cause weight loss.
- Invasion of the central nervous system and leptomeningeal inflammation cause a "sleeping sickness".
- *T. cruzi* sheds glycosylphosphatidylinositol (GPI), which is a potent macrophage activator.
- Inflammation occurs in *T. cruzi*-infected tissue and this may lead to long-term pathology, particularly of cardiac muscle and gastrointestinal smooth muscle.
- Autoantibodies also appear in *T. cruzi* infection but their relative contribution to pathology is unclear.

## 3. WHAT IS THE TYPICAL CLINICAL PRESENTATION AND WHAT COMPLICATIONS CAN OCCUR?

- Swelling may occur at the site of the insect bite.
- As trypanosomes enter the bloodstream, there are fevers, headache, malaise, and loss of appetite.

- Once the central nervous system is invaded in HAT, there is progression to coma and death with a variety of intervening neurologic problems.
- After clinical features from acute *T. cruzi* infection up to one third of patients suffer complications in the heart or gastrointestinal tract.
- Cardiac muscle can become weak and aneurysmal.
- Weakening of intestinal smooth muscle leads to dilatation and megaeosophagus or megacolon.

## 4. HOW IS THE DISEASE DIAGNOSED, AND WHAT IS THE DIFFERENTIAL DIAGNOSIS?

- The simplest test for HAT due to *T. brucei gambiense* is a card agglutination test for antibody.
- Trypanosomes may be seen on a blood film or in a tissue sample.
- South-American trypanosomiasis may be diagnosed by a serologic test.

## 5. HOW IS THE DISEASE MANAGED AND PREVENTED?

- Drugs for trypanosomes can be toxic.
- For *T. brucei gambiense*, treatment has advanced with the use of oral fexinidazole or the combination of nifurtimox plus eflornithine.
- For chronic South-American trypanosomiasis, treatment with benznidazole is probably beneficial in children but of debated value in adults.
- Tsetse fly numbers can be reduced by outdoor insecticide-impregnated traps.
- Improving housing conditions reduces the population of triatomine bugs, which would otherwise live in cracks in walls or thatched roofs.

## FURTHER READING

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Pays E, Vanhollebeke B, Uzureau P, et al. The Molecular Arms Race Between African trypanosomes and Humans. *Nat Rev Microbiol*, 12: 575–584, 2014.

## WEBSITES

Centers for Disease Control, Parasites – African Trypanosomiasis (also known as Sleeping Sickness), 2022: <https://www.cdc.gov/parasites/sleepingsickness/index.html>

Centers for Disease Control, Parasites – American Trypanosomiasis (also known as Chagas Disease): <https://www.cdc.gov/parasites/chagas/>

World Health Organization, Chagas disease (American trypanosomiasis): <https://www.who.int/health-topics/chagas-disease>

World Health Organization, Human African trypanosomiasis (sleeping sickness): <https://www.who.int/health-topics/human-african-trypanosomiasis>

Students can test their knowledge of this case study by visiting the Instructor and Student Resources: [www.routledge.com/cw/lydyard] where several multiple choice questions can be found.