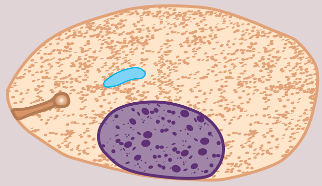
CASE STUDY 5-1 UNDER THE MICROSCOPE

Nine-year-old Charles, an African boy, recently emigrated to the United States from Kenya with his family. He began complaining of chills and diarrhea 2 weeks prior to the office visit. After taking his temperature, which revealed a fever, his mother took him into his pediatrician's office. During the examination, the doctor found a skin lesion on his right arm and marked hepatosplenomegaly. A complete blood count (CBC) was ordered, which revealed that Charles was anemic. The doctor, afraid that the child was experiencing dum dum fever (kala-azar), ordered a biopsy of the infected skin lesion and blood for parasite study.

When the specimens were received in the laboratory, the laboratory technician on duty made slides of the skin lesion material and blood, stained them with Giemsa stain, and carefully examined the slides. No parasites were found in the blood slide. The biopsy slide revealed an oval organism (see diagram); it contained one nucleus, a parabasal body, and an axoneme-like structure.



Questions for Consideration

1. What parasite do you suspect? (Objective 5-10B)
2. Which morphologic form of the parasite was described in the biopsy slide? (Objective 5-10B)
3. Indicate where Charles might have come into contact with parasites and identify the factors that most likely contributed to this contact. (Objectives 5-10D)
4. Name two other geographic populations at risk of contracting parasitic infections. (Objectives 5-10D)
5. Name two other symptoms associated with parasitic infections that individuals such as the patient in this case study may experience. (Objective 5-10C)
6. Why did the physician additionally order blood to be examined for parasites? (Objectives 5-10F)

FOCUSING IN

Members of the clinically significant group of parasites located in blood and tissue that move by means of flagella, known as the hemoflagellates, belong to the genera *Leishmania* and *Trypanosoma*. There are four morphologic forms of clinical significance associated with these **hemoflagellates:** amastigote, promastigote, epimastigote, and trypomastigote, all of which are defined and described in detail in this chapter. Although the specific life cycle may vary, all the organisms in these two genera involve some combination of the four morphologic forms. The transmission of all hemoflagellates is via the bite of an arthropod vector. The major difference between the two genera is the primary diagnostic form found in each; for *Leishmania* it is the amastigote and for *Trypanosoma* it is the trypomastigote, with the exception of *Trypanosoma cruzi,* in which amastigotes may also be found. Speciation within the genera usually depends heavily on the patient history and clinical symptoms. Because of the importance of this information, this text provides a discussion of the geographic distribution and symptomatology of each hemoflagellate.

Suspicions of hemoflagellate disease processes are typically confirmed by more advanced diagnostic techniques, such as serologic tests. Because the initial diagnosis of hemoflagellate infections relies primarily on the detection of the morphologic forms, this text will begin with a detailed discussion of the morphologic forms.

MORPHOLOGY AND LIFE CYCLE NOTES

Morphology

Amastigotes. The average roundish to oval **amastigote** measures 5 by 3 µm in size (Figs. 5-1 and 5-2; Table 5-1). The amastigote contains a nucleus, a basal body structure (called a **blepharoplast**), and a small parabasal body. The large single nucleus is typically located off-center, sometimes present more toward the edge of the

organism. The dotlike blepharoplast gives rise to and is attached to an axoneme. The axoneme extends to the edge of the organism. The single parabasal body is located adjacent to the blepharoplast. **Kinetoplast** is an umbrella term often used to refer to the blepharoplast and small parabasal body.

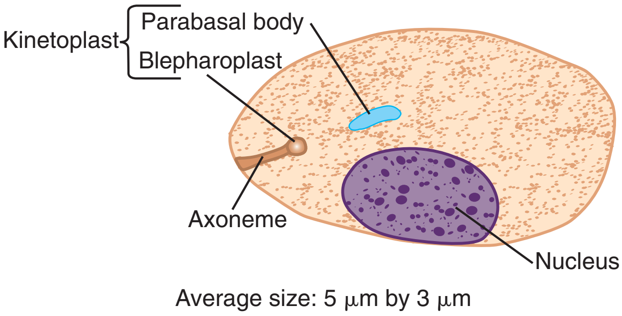


FIGURE 5-1 Amastigote.

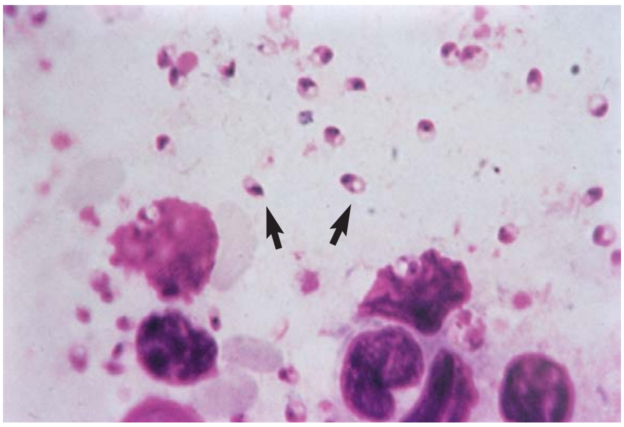


FIGURE 5-2 Amastigotes of *Leishmania* spp. *(From Mahon CR, Lehman DC, Manuselis G: Textbook of diagnostic microbiology, ed 4, St Louis, 2011, Saunders.)*

Promastigotes. The typical **promastigote** measures 9 to 15 µm in length (Figs. 5-3; Table 5-2). The large single nucleus is located in or near the center of the long slender body. The kinetoplast is located in the anterior end of the organism. A single free flagellum extends anteriorly from the axoneme.

Epimastigotes. The average **epimastigote** measures approximately 9 to 15 µm in length (Fig. 5-4; Table 5-3). The body is slightly wider than

TABLE 5-1 Amastigote: Typical Characteristics at a Glance

Parameter	Description
Size	5 by 3 µm
Shape	Round to oval
Nucleus	One, usually off center
Other features	Kinetoplast present, consisting of dotlike blepharoplast from which emerges a small axoneme Parabasal body located adjacent to the blepharoplast

TABLE 5-2 Promastigote: Typical Characteristics at a Glance

Parameter	Description
Size	9-15 µm long
Appearance	Long and slender
Nucleus	One, located in or near center
Other features	Kinetoplast, located in anterior end Single free flagellum, extending from anterior end

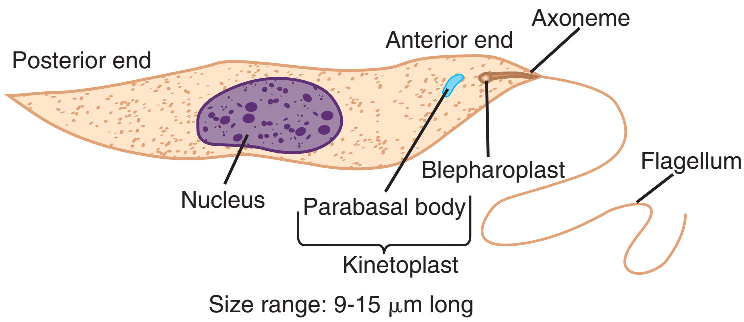
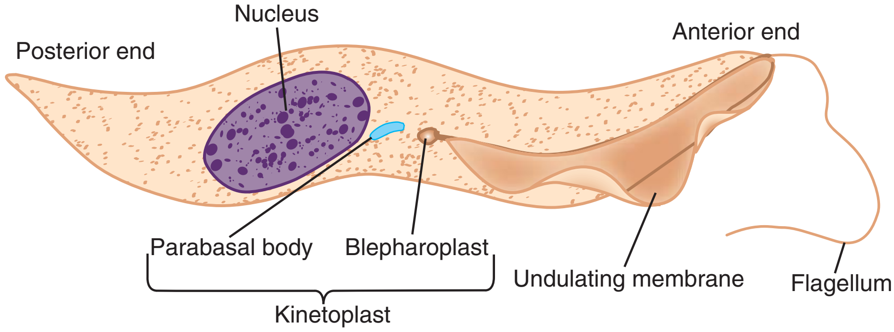
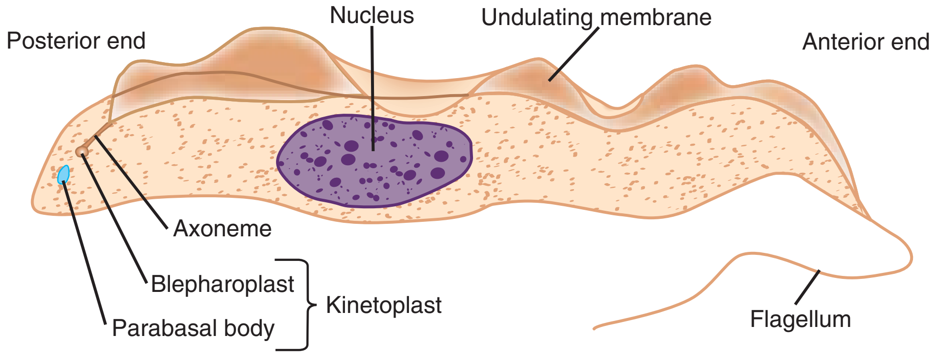


FIGURE 5-3 Promastigote.



Size range: 9-15 μm long

FIGURE 5-4 Epimastigote.



Size range: 12-35 μm by 2-4 μm

FIGURE 5-5 Trypomastigote.

TABLE 5-3	Epimastigote: Typical Characteristics at a Glance
Parameter	**Description**
Size	9-15 μm long
Appearance	Long and slightly wider than promastigote form
Nucleus	One, located in posterior end
Other features	Kinetoplast located anterior to the nucleus Undulating membrane, extending half of body length Free flagellum, extending from anterior end

that of the promastigote. The large single nucleus is located in the posterior end of the organism. The kinetoplast is located anterior to the nucleus. An undulating membrane, measuring half the body length, forms into a free flagellum at the anterior end of the epimastigote.

Trypomastigotes. The typical **trypomastigote** measures 12 to 35 μm long by 2 to 4 μm wide, and may often assume the shape of the letters C, S or U in stained blood films (Figs. 5-5 to 5-7; Table 5-4). The trypomastigote in Figure 5-5 is represented in its straight form for comparison purposes because it clearly denotes the individual structures. The long slender organism is characterized by a posteriorly located kinetoplast from which emerges a full body length undulating membrane. The single large nucleus is located anterior to the kinetoplast. An anterior free flagellum may or may not be present.

General Morphology and Life Cycle Notes

The amastigote and trypomastigote are the two forms routinely found in human specimens. Amastigotes are found primarily in tissue and

FIGURE 5-6 *Trypanosoma cruzi* trypomastigote exhibiting a characteristic full body length undulating membrane *(arrow).* Note the S shape of the organism (Giemsa stain, ×1000). *(Courtesy of WARD'S Natural Science Establishment, Rochester, NY; http://wardsci.com.)*

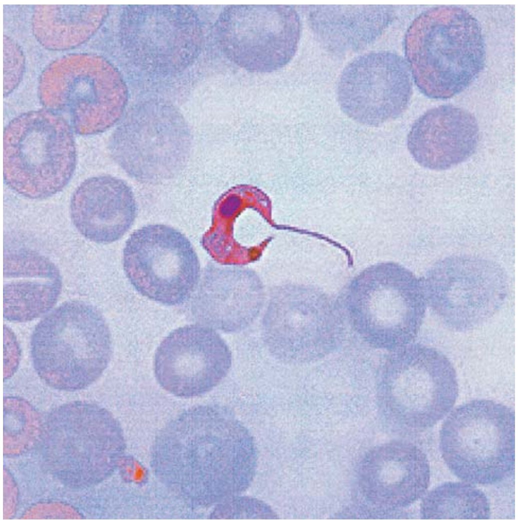


FIGURE 5-7 *Trypanosoma cruzi* C-shaped trypomastigote in a blood smear. *(From Mahon CR, Lehman DC, Manuselis G: Textbook of diagnostic microbiology, ed 4, St Louis, 2011, Saunders.)*

muscle, as well as the central nervous system (CNS) within macrophages, where they multiply. Trypomastigotes reproduce and are visible in the peripheral blood. The promastigote stage may be seen only if a blood sample is collected immediately after transmission into a healthy individual or when the appropriate sample is cultured. Although they may be seen in human blood samples, epimastigotes are found primarily in the arthropod vector. Specific life cycle information is found under the discussion of each individual hemoflagellate.

TABLE 5-4 Trypomastigote: Typical Characteristics at a Glance

Parameter	Description
Size	12-35 µm long by 2-4 µm wide
Shape	C, S or U shape often seen in stained blood films
Appearance	Long and slender
Nucleus	One, located anterior to the kinetoplast
Other features	Kinetoplast located in the posterior end Undulating membrane, extending entire body length Free flagellum, extending from anterior end when present

Quick Quiz! 5-1

This is the only hemoflagellate morphologic form that does not have an external flagellum. (Objective 5-11A)

A. Trypomastigote
B. Amastigote
C. Promastigote
D. Epimastigote

Laboratory Diagnosis

Blood, lymph node and ulcer aspirations, tissue biopsies, bone marrow, and cerebrospinal fluid (CSF) are the specimens of choice for diagnosing the hemoflagellate morphologic forms. In addition, serologic and molecular tests are also available for confirming the presence of these organisms. Representative laboratory diagnosis methodologies are presented in Chapter 2, as well as in each individual parasite discussion, as appropriate.

Subphylum	Class	Blood Tissue Species
Mastigophora	Zoomastigophora	*Leishmania braziliensis* complex
		Leishmania donovani complex
		Leishmania mexicana complex
		Leishmania tropica complex
		Trypanosoma brucei gambiense
		Trypanosoma brucei rhodesiense
		Trypanosoma cruzi
		Trypanosoma rangeli

FIGURE 5-8 Parasite classification—the hemoflagellates.

Quick Quiz! 5-2

Hemoflagellates are typically found in stool samples. (Objective 5-8)

A. True

B. False

Pathogenesis and Clinical Symptoms

The symptoms associated with hemoflagellate infections range from a small red papule at the infection site, with intense itching, secondary bacterial infections, fever, and diarrhea, to kidney involvement, mental retardation, a comatose state, and death. In some cases, the initial skin lesions spontaneously heal, whereas in others they may remain dormant for months or even years.

Quick Quiz! 5-3

The symptoms of hemoflagellate infections range from minor, such as irritation at the infection site, to serious (comatose state and death). (Objective 5-6)

A. True

B. False

HEMOFLAGELLATE CLASSIFICATION

There are a number of hemoflagellate species known to cause human infections, some of which have only been known to occur on rare occasions. A discussion of each of these organisms is beyond the scope of this chapter. For the purpose of discussing the *Leishmania* species, this chapter will address them within the classification complexes of more popular texts and literature, as opposed to the individual species. Only those hemoflagellates known to cause more frequent human disease are covered. The individual species are identified and classified in Figure 5-8.

HISTORICAL PERSPECTIVE OF LEISHMANIASIS

Leishmaniasis is a general term used to describe diseases caused by the hemoflagellate genus *Leishmania*. Although its origins remain unclear, what is obvious is that the organisms in this genus and their respective vectors have made successful migrations and adaptations to many environments worldwide. Leishmaniasis has a long history, as evidenced by the depictions on pottery from Ecuador and Peru around the first century AD. The different groups of people exposed to the organism have provided us with a number of common names for the diseases caused by *Leishmania* spp. (e.g., **Baghdad boils, bay sore, chiclero ulcer, dum dum fever, espundia, forest yaws, kala-azar, oriental sore, pian bois,** and **uta**). Table 5-5 describes each of these conditions. Increased travel and exposure to different environments has resulted in the transmission of the various **parasitemias,** a general term

TABLE 5-5 Diseases and Conditions Associated with Leishmaniasis

Disease or Condition	Description
Baghdad boils	A common name for an infection with *Leishmania tropica*; it is a cutaneous form of leishmaniasis presenting with pus-containing ulcers
Bay sore	A common name for a cutaneous form of infection caused by *Leishmania mexicana*
Chiclero ulcer	A form of cutaneous leishmaniasis cased by *L. mexicana*; it is commonly found in Belize, Guatemala, and the Yucatan peninsula in areas where chicle sap is harvested for making chewing gum
Dum dum fever	A common name for the visceral leishmaniasis caused by *Leishmania donovani*
Espundia	Another name for an infection resulting from *Leishmania braziliensis*, the principle cause of mucocutaneous disease in Central and South America, particularly in Brazil
Forest yaws	Another name for an infection with *Leishmania guyanensis*, the principle cause of mucocutaneous leishmaniasis in the Guianas, parts of Brazil and Venezuela; also known as pian bois
Kala-azar	Another name for the most severe form of visceral leishmaniasis caused by members of the *Leishmania donovani* complex
Oriental sore	A common reference for the cutaneous leishmaniasis caused by the infecting agents comprising the *Leishmania tropic* complex
Pian bois	Another name for infection with *L. guyanensis*; also known as forest yaws
Uta	A reference to mucocutaneous leishmaniasis in the Peruvian Andes

describing parasitic infection of the blood, into new environments, finding new host organisms and new vectors.

Leishmania spp. are generally grouped for discussion in one of several ways—in complexes of organisms or taxonomic groupings, their vectors, or the clinical nature of the disease caused. The four main complexes considered and described herein are the *Leishmania braziliensis*, *Leishmania donovani*, *Leishmania mexicana*, and *Leishmania tropica* complexes.

Leishmania braziliensis complex
(leesh-may′ nee-uh/bra-zil″ i-en′sis)

Common associated disease and condition names: Mucocutaneous leishmaniasis, chiclero ulcer, espundia, forest yaws, pian bois, uta.

The *Leishmania braziliensis* complex of organisms is found in Mexico, Argentina, Panama, Colombia, the Peruvian Andes, Guiana, Brazil, Bolivia, Paraguay, Ecuador, and Venezuela. This group of parasites is comprised of *Leishmania braziliensis*, *Leishmania panamensis*, *Leishmania peruviana*, and *Leishmania guyanensis*. This leishmanial complex and the diseases for which its organisms are the causative agent may also be referred to as New World because of their geographic location in what is commonly considered the New World.

Laboratory Diagnosis

The specimen of choice for identifying the amastigotes of *L. braziliensis* complex is a biopsy of the infected ulcer. Microscopic examination of the Giemsa-stained preparations should reveal the typical amastigotes. Promastigotes may be present when the sample is collected immediately after introduction into the patient. Other more commonly used diagnostic methods include culturing the infected material, which often demonstrates the promastigote stage, and serologic testing. As enzyme analysis and molecular techniques have become more widely available, diagnostic criteria have begun to change as well. However, restriction analysis of kinetoplast DNA, a technique referred to as **schizodeme analysis**, nuclear DNA hybridization, and isoenzyme patterns, known as **zymodeme analysis**, still tend to remain research procedures and are

TABLE 5-6 *Leishmania braziliensis* Complex: Epidemiology

Subspecies	Geographic Distribution	Vector	Reservoir Hosts
L. braziliensis	Mexico to Argentina	*Lutzomyia* and *Psychodopygus* sandflies for all species comprising this complex	Dogs and forest rodents for all species comprising this complex
L. panamensis	Panama and Colombia		
L. peruviana	Peruvian Andes		
L. guyanensis	Guiana, Brazil, Venezuela		

not currently performed in mainstream clinical diagnostic testing environments.

Life Cycle Notes

Sandflies of the genera *Lutzomyia* and *Psychodopygus* are responsible for transmitting the promastigotes of the species of the *L. braziliensis* complex into unsuspecting humans via a blood meal, resulting in a skin bite. The promastigotes quickly invade the reticuloendothelial cells and transform into amastigotes, which actively reproduce, causing tissue destruction. Reproduction and invasion of additional cells then occur. The skin and mucous membrane areas of the body are primarily affected. The diagnostic stage for the species of the *L. braziliensis* complex is the amastigote. In addition, the amastigote serves as the infective stage for the sandfly. On ingestion, during a blood meal of an infected human, the amastigotes transform back into promastigotes in the fly midgut. These promastigotes multiply and the resulting developed forms eventually migrate into the salivary gland of the fly, where they are ready to be transferred to a new human during a blood meal. Thus, the cycle repeats itself.

Epidemiology

The *L. braziliensis* complex is composed of *L. braziliensis* (found from Mexico to Argentina), *L. panamensis* (found in Panama and Colombia), *L. peruviana* (found in the Peruvian Andes), and *L. guyanensis* (found in Guiana, parts of Brazil, and Venezuela). The organisms in this complex may also be found in Ecuador, Bolivia, Paraguay, and other Central and South American countries, particularly in the rain forest regions, where chicle sap for chewing gum is harvested (known under these circumstances as chiclero ulcer). Transmission is generally through the bite of the *Lutzomyia* or *Psychodopygus* sandfly and there are numerous reservoir hosts, including a variety of forest rodents and domestic dogs. Table 5-6 illustrates the relationships among the members of this complex, the geographic region in which they tend to thrive, vectors, and host reservoirs.

Clinical Symptoms

Mucocutaneous Leishmaniasis. Symptoms of an infection with a member of the *L. braziliensis* complex typically occur within a few weeks to months after transmission into a previously uninfected human. Large ulcers in the oral or nasal mucosa areas (**mucocutaneous**) develop in a number of these patients after the initial invasion of the reticuloendothelial cells. There may be large cutaneous lesions, mucosal lesions, or a combination of both. A **cutaneous** (**meaning affecting or relating to the skin**) lesion may heal on its own. However, untreated cases of mucosal lesions result in the eventual destruction of the nasal septum. The lips, nose, and other surrounding soft parts may also be affected in these infections. Edema and secondary bacterial infections, combined with numerous mucosal lesions,

may cause disfigurement of the patient's face. Death is usually attributed to a secondary bacterial infection.

Treatment

The most widely used antileishmanial agent for the treatment of mucocutaneous leismaniasis is with antimony compounds. However, *L. braziliensis* has shown an increased resistance to pentavalent antimonials such as sodium stibogluconate (Pentosam). Even with drug resistance and the adverse side effects, these classes of drugs are still considered the most effective treatment for *L. braziliensis* complex infections. Alternative treatments for *L. braziliensis* complex infections include liposomal amphotericin B (Ambisome) and oral antifungal drugs such as fluconazole (Diflucan), ketoconazole (Nizoral) and itraconazole (Sporonox).

Prevention and Control

Public awareness through education programs in endemic areas and exercising personal protection against contact with sandflies (e.g., protective clothing, repellents, screening) are preventive measures against infections with *L. braziliensis* complex members. In addition, prompt treatment and eradication of infected ulcers, and control of the sandfly population and reservoir hosts, help prevent the spread of future disease. Work to produce a vaccine against members of the *L. braziliensis* complex and other *Leishmania* spp. is ongoing, with some vaccines for animals (dogs) presently in experimental trials.

Quick Quiz! 5-4

Of the following laboratory diagnostic methods, which is the most commonly used for the recovery of members of the *L. braziliensis* complex? (Objective 5-8)

A. Schizodeme analysis
B. Culture of infected material
C. Identifying amastigotes in infected material
D. Zymodeme analysis

Quick Quiz! 5-5

The organism causing chiclero ulcer is most likely found in: (Objectives 5-1 and 5-2)

A. Texas
B. South American rainforest region
C. Nova Scotia
D. Egypt

Quick Quiz! 5-6

Which of the following is not an acceptable treatment for mucocutaneous leishmaniasis caused by *L. braziliensis?* (Objective 5-7A)

A. Amoxicillin
B. Pentosam
C. Ambisome
D. Fungizone

Leishmania donovani complex
(leesh-may' nee-uh/don" o-vay' nigh)

Common associated disease and condition names: Visceral leishmaniasis, kala-azar, dum dum fever.

The *Leishmania donovani* complex of organisms is found in India, Pakistan, Thailand, Africa, the Peoples Republic of China, the Mediterranean, Europe, Africa, the Near East, parts of the former Soviet Union, the Middle East, Yemen, Oman, Iraq, Kuwait, Saudi Arabia, United Arab Emirates, Bahrain, and Central and South America. This group is comprised of *L. donovani*, *Leishmania infantum*, and *Leishmania chagasi*. This leishmanial complex and the diseases for which its organisms are the causative agent may also be referred to as Old or New World, depending on the geographic location of the species of *Leishmania* involved.

Laboratory Diagnosis

The **Montenegro skin test** is a screening test similar to that of the tuberculin skin test; it is

TABLE 5-7 ***Leishmania donovani*** **Complex: Epidemiology**

Subspecies	Geographic Distribution	Vector	Reservoir Hosts
L. donovani chagasi	Central America, especially Mexico, West Indies, South America	*Lutzomyia* sandfly	Dogs, cats, foxes
L. donovani donovani	Parts of Africa, India, Thailand, Peoples Republic of China, Burma, East Pakistan	*Phlebotomus* sandfly	India, none; China, dogs
L. donovani infantum	Mediterranean Europe, Near East, Africa; also in Hungary; Romania, southern region of former Soviet Union, northern China, southern Siberia	*Phlebotomus* sandfly	Dogs, foxes, jackals, porcupines

used for screening large populations at risk for infections caused by *Leishmania* spp. Its reliability in detecting exposure to the organisms causing leishmaniasis is related to the patient's disease status. It is not a good method for diagnosing active disease. Giemsa-stained slides of blood, bone marrow, lymph node aspirates, and biopsies of the infected areas are better choices for demonstrating the diagnostic amastigote forms. Some consider the sternal marrow aspirate to be the specimen of choice, but the organism can be seen in Giemsa-stained buffy coat films prepared from venous blood, a safer, less invasive procedure. Blood, bone marrow, and other tissues may also be cultured; these samples often show the promastigote forms. Serologic testing is available using IFA (indirect fluorescent antibody), ELISA (enzyme-linked immunosorbent assay), and DAT (direct agglutination test). In addition, schizodeme analysis, zymodeme analysis, and nuclear DNA hybridization are primarily available on a research basis; these may become a more popular diagnostic method in the future.

Life Cycle Notes

The life cycle of the members of the *L. donovani* complex is identical to that of *L. braziliensis*, with only two exceptions. First, the specific sandfly species responsible for *L. donovani* transmission vary with each of the three subspecies (Table 5-7). Second, *L. donovani* primarily affects the visceral tissue of the infected human.

Epidemiology

The *L. donovani* complex is composed of *L. donovani* (found in India, Pakistan, Thailand, parts of Africa, and the Peoples Republic of China), *L. infantum* (found in the Mediterranean area, Europe, Africa, the Near East, and parts of the former Soviet Union), and *L. chagasi* (found in Central and South America). *L. donovani* and *L. infantum* are known to be endemic in areas of the Middle East, including Yemen, Oman, Kuwait, Iraq, Saudi Arabia, the United Arab Emirates, and Bahrain. The vector species and reservoir hosts vary among the three subspecies of the *L. donovani* complex and are listed in Table 5-7.

Clinical Symptoms

Visceral Leishmaniasis. Patients suffering from **visceral** (pertaining to the internal organs of the body) leishmaniasis, also known as kala-azar or dum dum fever, often present with a nondescript abdominal illness and **hepatosplenomegaly** (enlargement of the spleen and liver). Early stages of disease may resemble malaria (see Chapter 6) or typhoid fever with the development of fever and chills. The onset of these symptoms is gradual and follows an incubation period ranging from

2 weeks to 18 months. Diarrhea, as well as anemia, may often be present. Additional symptoms, including weight loss and emaciation, tend to occur following parasitic invasion of the liver and spleen. Other than a rare papule, which most likely occurs at the bite site, skin lesions are absent. Advanced stages of disease result in kidney damage (e.g., **glomerulonephritis**, inflammation of the glomeruli of the kidney) and granulomatous areas of skin. A characteristic darkening of the skin may be noted. This symptom is referred to by the common disease name, kala-azar, which means black fever. Chronic cases usually lead to death in 1 or 2 years, whereas acute disease debilitates the patient and becomes lethal in a matter of weeks.

Treatment

Liposomal amphotericin B (Ambisome) is the drug of choice for treating visceral leishmaniasis. Sodium stibogluconate (Pentosam) is also an effective treatment for infections with *L. donovani* complex, but resistance has been demonstrated by organisms in India and the Mediterranean. Successful treatment has been accomplished with the use of gamma interferon combined with pentavalent antimony. Infected patients suffering from AIDS appear to respond well to allopurinol. It is further recommended that HIV-infected persons receive secondary prophylaxis as part of their treatment plan.

In the past decade two new drugs have been added to the treatment regimen for visceral leishmaniasis which include a combination of paramomycin and miltefosine. Neither of these drugs is available in the United States at this time.

Prevention and Control

Protection against sandflies by repellents, protective clothing, and screening are essential measures to reduce future *L. donovani* complex infections. Prompt treatment of human infections, as well as control of the sandfly population and reservoir hosts, will also help halt the spread of disease.

Notes of Interest and New Trends

It is important to note that *L. donovani* is capable of being transmitted person to person via blood transfusions. Particular concern over this mode of leishmaniasis transmission arose during and following the Gulf War. It is still of concern today because of the number of armed forces personnel stationed in the Persian Gulf region. Persons who are in and around this region may have been or are presently at risk of contracting the disease. The potential for those presently in the area to contract and bring home these organisms has resulted in the deferment of persons having spent time there for a minimal period of 12 months following their departure.

Research has been done to investigate the persistent levels of galactosyl-alpha(1-3)galactose antibodies in patients successfully treated for visceral leishmaniasis. There is some suspicion that these high levels may indicate parasite remnants, which remain even after the disease is cured. Further studies into this mystery may provide scientists with additional valuable information in the understanding and treatment of *L. donovani*.

Quick Quiz! 5-7

A common name for disease caused by *L. donovani* is: (Objective 5-3)

A. Visceral leishmaniasis
B. Kala-azar
C. Dum dum fever
D. All of the above

Quick Quiz! 5-8

The vector responsible for the transmission of *L. donovani* is: (Objective 5-5)

A. *Lutzomyia* sandfly
B. *Phlebotomus* sandfly
C. *Psychodopygus* sandfly
D. None of the above

TABLE 5-8 *Leishmania mexicana* Complex: Epidemiology

Subspecies	Geographic Distribution	Vector	Reservoir Hosts
L. mexicana	Belize, Guatemala, Yucatan Peninsula	*Lutzomyia* sandfly for all species comprising this complex	Forest rodents for all species comprising this complex
L. pifanoi	Amazon River Basin, Brazil, Venezuela		
L. amazonensis	Amazon River Basin, Brazil		
L. garnhami	Venezuelan Andes		
L. venezuelensis	Venezuela		

Quick Quiz! 5-9

Which of the following items does not describe kala-azar? (Objectives 5-2, 5-5, and 5-12)

A. Commonly found in Iraq
B. Transmitted by the *Phlebotomus* and *Lutzomyia* sandfly species
C. Is not transmitted by blood transfusion
D. Can be serologically determined by ELISA, IFA, and DAT methods

Leishmania mexicana complex
(leesh-may' nee-uh/mek-si-kah-nuh)

Common associated disease and condition names: New World cutaneous leishmaniasis, chiclero ulcer, bay sore.

The *Leishmania mexicana* complex of organisms is found in Belize, Guatemala, the Yucatan Peninsula, the Amazon River Basin, Venezuela, Brazil, and the Venezuelan Andes. *L. mexicana, Leishmania pifanoi, Leishmania amazonensis, Leishmania venezuelensis,* and *Leishmania garnhami* are the members of this group. This leishmania complex and the diseases for which its organisms are the causative agent may also be referred to as New World because of the geographic location of its members.

Laboratory Diagnosis

Definitive diagnosis of disease caused by members of the *L. mexicana* complex is made by demonstrating the amastigote form in Giemsa-stained preparations of lesion biopsy material. Culture on NNN medium demonstrates the promastigote stage of these organisms. Serologic testing using monoclonal antibodies and other techniques are available. Schizodeme analysis, zymodeme analysis, and nuclear DNA hybridization are available on a research basis.

Life Cycle Notes

The life cycle of the members of the *L. mexicana* complex is identical to that of *L. braziliensis*. The primary vectors are sandfly species of the genus *Lutzomyia*. Table 5-8 lists the organisms of this complex, geographic location of each species, vector for each organism, and reservoir host.

Epidemiology

The *L. mexicana* complex is composed of *L. mexicana* (found in Belize, Guatemala, and the Yucatan peninsula), *L. pifanoi* (found in the Amazon River basin and parts of Brazil and Venezuela), *L. amazonensis* (found in the Amazon basin of Brazil), *L. venezuelensis* (found in the forested areas of Venezuela), and *L. garnhami* (found in the Venezuelan Andes). Members of this complex are often transmitted by the bite of a *Lutzomyia* sandfly, with forest rodents serving as the reservoir host.

Clinical Symptoms

New World Cutaneous Leishmaniasis. Also known as bay sore and chiclero ulcer, **cutaneous**

leishmaniasis is usually characterized by a single pus-containing ulcer, which is generally self-healing. Approximately 40% of infections affect the ear and can cause serious damage to the surrounding cartilage. Infected patients initially develop a small red papule, located at the bite site, which is typically 2 cm or larger in diameter and may cause **pruritis** (intense itching). The incubation time and appearance of the papule vary with each subspecies. On occasion, because of **anergic** (the inability of an individual to mount an adequate immune response) and hypersensitivity immunologic responses, spontaneous healing of the ulcers does not occur. Diffuse cutaneous leishmaniasis (DCL) is rare in the New World, but incidents have been reported with all species comprising this complex. In diffuse cutaneous infections with *L. pifanoi,* the initial lesion appears, ulcerates or disappears and, after a period of months to years, appears in local and distant areas from the bite site with lepromatous-appearing lesions. *L. amazonensis* infections have been known to progress to an incurable diffuse cutaneous form of the disease. This latter form of cutaneous leishmaniasis usually occurs when the patient is anergic. A detailed discussion of the associated immunologic details relating to this disease process is beyond the scope of this chapter.

Treatment

Pentavalent antimonials, such as sodium stibogluconate (Pentosam), are considered the drug of choice for treating infections related to the species comprising the *L. mexicana* complex. Antimony combined with pentoxifylline taken orally three times a day for 30 days has been shown to be superior to antimony alone. Amphotericin B and liposomal amphotericin B (Ambisome) have also proven to be effective.

Prevention and Control

Protection against sandflies by repellents, protective clothing, and screening are essential measures to reduce future *L. mexicana* complex infections. Prompt treatment of human infections, as well as control of the sandfly and reservoir host populations, will also help halt the spread of disease.

Quick Quiz! 5-10

The specimen of choice for the recovery of *L. mexicana* complex members is: (Objective 5-8)

A. CSF
B. Stool
C. Lesion biopsy material
D. Duodenal contents

Quick Quiz! 5-11

Which of the following is not a reservoir host for *L. mexicana* complex? (Objective 5-5)

A. Squirrels
B. Chipmunks
C. Rats
D. Snakes

Quick Quiz! 5-12

Which of the following best describe disease caused by the *L. mexicana* complex? (Objective 5-6)

A. Can disseminate into a diffuse cutaneous form
B. Appears around the ears in approximately 40% of patients
C. Both A and B are correct.
D. None of the above

Leishmania tropica complex
(leesh-may′ née-uh/trop′i-kuh)

Common associated disease and condition names: Old World cutaneous leishmaniasis, oriental sores, Delhi boils, Baghdad boils, dry or urban cutaneous leishmaniasis.

The *Leishmania tropica* complex of organisms is found in the Mediterranean, Middle East, Armenia, Caspian region, Afghanistan, India, Kenya, Ethiopian highlands, southern Yemen, Turkmenistan deserts, Uzbekistan, Kazakhstan,

TABLE 5-9 *Leishmania tropica* Complex: Epidemiology

Subspecies	Geographic Distribution	Vector	Reservoir Hosts
L. aethiopica	Highlands of Ethiopia, Kenya, perhaps Southern Yemen	*Phlebotomus* sandfly for all species comprising this complex	Rock hyrax
L. major	Former Soviet Union, Iran, Israel, Jordan, parts of Africa, Syria (esp. in rural areas)		Gerbils, other rodents
L. tropica	Mediterranean, parts of the former Soviet Union, Afghanistan, India, Kenya, Middle East (especially in urban areas)		Possibly dogs

northern Africa, the Sahara, Iran, Syria, Israel, and Jordan. It is comprised of *L. tropica, Leishmania aethiopica,* and *Leishmania major*. This leishmania complex and the diseases for which its organisms are the causative agent may also be referred to as Old World.

Laboratory Diagnosis

The laboratory diagnosis of *L. tropica* consists of microscopic examination of Giemsa-stained slides of aspiration of fluid underneath the ulcer bed for the typical amastigotes. Culture of the ulcer tissue may also reveal the promastigote forms. Serologic tests, such as IFA testing, are available. Schizodeme analysis, zymodeme analysis, and nuclear DNA hybridization are also available on a research basis.

Life Cycle Notes

With the exception of the specific sandfly species and the area of the body most affected, the life cycle of *L. tropica* complex is basically identical to that of *L. braziliensis*. All three of the *L. tropica* subspecies are transmitted by the *Phlebotomus* sandfly. *L. tropica* complex primarily attacks the human lymphoid tissue of the skin.

Epidemiology

The Leishmania tropica complex is composed of *L. tropica* (found in the Mediterranean region, Middle East, Armenia, Caspian region, Afghanistan, India, and Kenya), *L. aethiopica* (found in the highlands of Ethiopia, Kenya, and Southern Yemen), and *L. major* (found in the desert regions of Turkmenistan, Uzbekistan, and Kazakhstan, Northern Africa, the Sahara, Iran, Syria, Israel, and Jordan). Members of this complex are often transmitted by the bite of the *Phlebotomus* sandfly, but the reservoir hosts for each of the three members of this complex differ (Table 5-9).

Clinical Symptoms

Old World Cutaneous Leishmaniasis. Also known as Old World leishmaniasis, oriental sore, and Baghdad or Delhi boil, cutaneous leishmaniasis is characterized by one or more ulcers containing pus that generally self-heal. Infected patients initially develop a small red papule, located at the bite site, which is typically 2 cm or larger in diameter and may cause intense itching. The incubation time and appearance of the papule vary with each subspecies (Table 5-10). On occasion, because of anergic and hypersensitivity immunologic responses, spontaneous healing of the ulcers does not occur. DCL occurs especially on the limbs and face when an immune response fails to take place. Thick plaques of skin, along with multiple lesions or nodules, usually result. A detailed discussion of the associated immunologic details relating to this disease process is beyond the scope of this chapter.

TABLE 5-10 ***Leishmania tropica* Complex: Clinical Symptoms**

Subspecies	Clinical Symptoms
L. aethiopica	Incubation: 2 mo-3 yr; small dry, red papule with possible intense itching; ulceration of papule occurs after several months
L. major	Incubation: as little as 2 wk; small red papule covered with serous exudate; possible intense itching; ulceration of papule occurs early
L. tropica	Incubation: 2 mo-3 yr; small dry, red papule with possible intense itching; papule ulcerates after several months

Treatment

As with the other leishmaniases, an effective treatment of *L. tropica* complex is sodium stibogluconate (Pentosam). The use of steroids, application of heat to the infected lesions, meglumine antimonate (Glucantime), pentamidine, and oral ketoconazole may be indicated for treating *L. tropica* complex infections. Paromomycin ointment may also be given to aid in healing.

Prevention and Control

In addition to controlling the sandfly and reservoir host populations, protection by the use of protective clothing, repellents, and screening are essential to prevent future *L. tropica* complex infections. In addition, the prompt treatment and eradication of infected ulcers are crucial to halt disease transmission. A vaccine has been developed and the preliminary results are promising; however, the clinical trials for this vaccine are still ongoing.

Notes of Interest and New Trends

A number of troops who participated in the Gulf War were stationed in Saudi Arabia and neighboring areas known to be endemic for *L. tropica*. It is estimated that there are approximately 16,000 cases of leishmaniasis reported in Saudi Arabia every year. Following the war, a number of veterans, as well as members of their families, began to experience vague symptoms, including joint and muscle pains (**arthralgias** and **myalgias**, respectively), headaches, bleeding gums, hair loss, and intestinal disorders. Although a skin test (the Montenegro skin test) for leishmaniasis has been developed, patients in active disease will test negative. There is still a great deal of concern that undiagnosed patients may actually have leishmaniasis and are unknowingly spreading the disease.

Quick Quiz! 5-13

All the following are geographic regions in which the members of the *L. tropica* complex can be found except: (Objective 5-2)

A. Brazil
B. Uzbekistan
C. Iran
D. Syria

Quick Quiz! 5-14

The specimen of choice for the recovery of *L. tropica* complex members is: (Objective 5-8)

A. CSF
B. Fluid underneath the ulcer bed
C. Blood
D. Tissue biopsy

Quick Quiz! 5-15

The most common morphologic form seen in samples positive for *L. tropica* complex members is: (Objective 5-5)

A. Trypomastigote
B. Promastigote
C. Epimastigote
D. Amastigote

HISTORICAL PERSPECTIVE OF TRYPANOSOMIASIS

Trypanosomiasis is a general term used to refer to human diseases caused by hemoflagellates of the genus *Trypanosoma*. These diseases have been well documented through the ages. Ancient papyri discussed the disease from veterinary and human perspectives. In 1895, David Bruce, a Scottish pathologist, identified *Trypanosoma brucei* as the causative agent of the trypanosomal diseases known as **nagana** (a form of the disease often found in cattle) and sleeping sickness. The *T. brucei* first described has become known as *Trypanosoma brucei gambiense* (often abbreviated as *T.b. gambiense)*. *Trypanosoma brucei rhodesiense* (*T.b. rhodesiense)* was not described until 1910 by Stephens and Fantham. *Trypanosoma cruzi*, the causative agent of **Chagas' disease,** was later described in 1909 by a young medical student in Brazil named Carlos Chagas.

Trypanosoma brucei gambiense

(trip-an″ o-so′ muh/broo′sye/ gam-bee-en′see)

Common associated disease and condition names: West African sleeping sickness, Gambian trypanosomiasis.

T. brucei gambiense is found in the tropical areas of western and central Africa. Commonly called West African sleeping sickness or Gambian trypanosomiasis, the disease course for the illness caused by this organism is less aggressive than that of its East African counterpart.

Laboratory Diagnosis

Blood, lymph node aspirations, and CSF are the specimens of choice for diagnosing *T.b. gambiense*. Giemsa-stained slides of blood and lymph node aspirations from infected patients reveal the typical trypomastigote morphologic forms. Several tests may be performed on CSF—microscopic examination of the sediment for trypomastigotes, detection of the presence of immunoglobulin M (IgM), and detection of the presence of proteins. Infected patients typically have high levels of both IgM and proteins in their CSF. In addition, serum IgM testing may be indicated. The presence of IgM in serum and/or CSF is generally considered diagnostic. A number of serologic tests are also available.

Life Cycle Notes

Humans become infected with *T.b. gambiense* following the injection of trypomastigotes by the tsetse fly during its blood meal. The entering trypomastigotes migrate through the bloodstream and into the lymphatic system, multiplying by binary fission. Although the healthy host's immune system is activated and some of the circulating trypomastigotes are destroyed, mutations of the parasite manage to escape and continue to reproduce. Eventually, invasion of the CNS may occur. The trypomastigotes are transmitted back to the tsetse fly vector when it feeds on an infected human. Once ingested by the tsetse fly, the trypomastigotes continue to multiply and eventually migrate back to the salivary gland, converting into epimastigotes along the way. Once in the salivary gland, the epimastigotes transform back into trypomastigotes, thus completing the cycle.

Epidemiology

T.b. gambiense is found in tropical West Africa and Central Africa, especially in shaded areas along stream banks where the tsetse fly vector breeds. The two species of tsetse flies responsible for the transmission of *T.b. gambiense* are *Glossina palpalis* and *Glossina tachinoides*. There are no known animal reservoir hosts.

Clinical Symptoms

West African (Gambian) Sleeping Sickness. Symptoms associated with West African sleeping sickness begin to occur after an asymptomatic incubation period of a few days to several weeks. The first notable symptom that may appear is the

development of a painful **chancre** (ulcer), surrounded by a white halo at the bite site. Fever, malaise, headache, generalized weakness, and anorexia are often experienced when the trypomastigotes settle into the lymphatic system. In addition, lymph node enlargement (**lymphadenopathy**) may be apparent during this time. A condition known as **Winterbottom's sign** refers to the enlargement of the cervical lymph nodes in reference to this trypanosomal disease. Other symptoms that may be seen during the glandular phase of the disease include **erythematous** (red) rash, pruritis, localized **edema** (swelling), and **Kerandel's sign** (a delayed sensation to pain). In patients in whom the central nervous system (CNS) becomes involved, mental retardation, tremors, meningoencephalitis, **somnolence** (excessive sleepiness), and character changes may develop. In the final stage of disease, the patient slips into a coma and death occurs, resulting from damage to the CNS, which is often coupled with other conditions, such as pneumonia or malaria. The course of the disease can last as long as several years.

Treatment

There are several medications available for the treatment of *T.b. gambiense* infections. These include melarsoprol, suramin, pentamidine, and eflornithine. The treatment of choice is situation-dependent and is dictated by a number of factors, including patient age (adult, child), stage of disease, and whether the patient is pregnant at the time. In addition, the toxicity levels of these medications are high; caution must be used when selecting the specific treatment and appropriate dosage.

Prevention and Control

The control of tsetse flies may be accomplished by destroying their breeding areas via chemical treatment and clearing of brush. Proper protective clothing, repellents, and screening, as well as prompt treatment of infected persons, will reduce the risk of future *T.b. gambiense* infections.

Notes of Interest and New Trends

T.b. gambiense has also been shown to be acquired through blood transfusion, organ transplantation, and **congenital transmission** (from pregnant mother to fetus).

Quick Quiz! 5-16

Of the following, which tests are considered diagnostic for trypanosomiasis? (Objectives 5-8 and 5-12)

A. Giemsa-stained blood slides revealing the trypomastigote
B. Giemsa-stained blood slides revealing the amastigote
C. Increased serum and CSF IgM levels
D. Both A and C are correct.
E. All of the above

Quick Quiz! 5-17

There are no known animal reservoir hosts for *T.b. gambiense*. (Objective 5-5)

A. True
B. False

Quick Quiz! 5-18

The enlargement of cervical lymph nodes in reference to trypanosomal disease caused by *T.b. gambiense* is referred to as: (Objective 5-1)

A. Chancre
B. Kerandel's sign
C. Winterbottom's sign
D. Somnolence

Trypanosoma brucei rhodesiense

(trip-an″ o-so′muh/broo′sye/ ro-dee″zee-en′see)

Common associated disease and condition names: East African sleeping sickness, Rhodesian trypanosomiasis.

Trypanosoma brucei rhodesiense is found in eastern and central Africa. Commonly called

East African sleeping sickness or Rhodesian trypanosomiasis, the disease course for the illness caused by this organism is much more aggressive than that of its West African counterpart.

Laboratory Diagnosis

The specimens of choice for the detection of the typical *T.b. rhodesiense* trypomastigotes are blood slides stained with Giemsa and microscopic examination of CSF sediment. Protein and IgM studies on CSF may also be performed. As with *T.b. gambiense*, the presence of IgM in the CSF is diagnostic for *T.b. rhodesiense*. In addition, serologic tests are available.

Life Cycle Notes

The only difference in the life cycles of *T.b. rhodesiense* and *T.b. gambiense* are the species of tsetse fly vector. The two primary species of tsetse fly vectors responsible for transmitting *T.b. rhodesiense* are *Glossina morsitans* and *Glossina pallidipes*. Additional species noted for attacking game animals may also transmit this organism.

Epidemiology

T.b. rhodesiense is found in East and Central Africa, especially in brush areas. Cattle and sheep, as well as wild game animals, are known reservoir hosts of this organism.

Clinical Symptoms

East African (Rhodesian) Sleeping Sickness. *T.b. rhodesiense* is a much more virulent organism than *T.b. gambiense*. Following a short incubation period, patients suffering from acute East African sleeping sickness experience fever, myalgia, and rigors. Winterbottom's sign may or may not be present. Lymphadenopathy is absent. Rapid weight loss is common and the CNS becomes involved early in the disease course. In addition, mental disturbance, lethargy, and anorexia may also be present. A rapid and fulminating disease results, with large numbers of trypanosomes circulating in the blood. Death, in part caused by subsequent kidney damage (glomerulonephritis) and **myocarditis** (inflammation of the heart), usually occurs within 9 to 12 months in untreated patients.

Treatment

The treatment of *T.b. rhodesiense* is identical to that for *T.b. gambiense*.

Prevention and Control

Because infections with *T.b. rhodesiense* tend to be more rapid in their course and often involve the neurologic system, extremely early treatment is crucial to halt further transmission of the disease. Additional measures include prompt medical treatment of infected domestic animals, as well as protective clothing, screening, and repellents. The vast species of potential reservoir hosts, coupled with the fact that breeding may occur wherever brush is abundant, primarily away from water sources, complicates prevention and control efforts. The clearing of brush areas and control of the tsetse fly population may reduce the risk of future disease transmission.

Quick Quiz! 5-19

The diagnostic stage of *T.b. rhodesiense* is the: (Objective 5-5)

A. Trypomastigote
B. Epimastigote
C. Promastigote
D. Amastigote

Quick Quiz! 5-20

Which of the following trypanosomal parasites that causes sleeping sicknesses is the more aggressive form? (Objective 5-11)

A. *Trypanosoma brucei gambiense*
B. *Trypanosoma brucei rhodesiense*
C. *Trypanosoma cruzi*
D. *Trypanosoma rangeli*

Quick Quiz! 5-21

What complicates the prevention and control efforts for *T.b. rhodesiense*? (Objective 5-7B)

A. Vast species of reservoir hosts
B. Breeding occurs wherever brush is abundant
C. Both A and B
D. None of the above

Trypanosoma cruzi
(trip-an″o-so′muh/kroo′zye)

Common associated disease and condition names: Chagas' disease, American trypanosomiasis.

Trypanosoma cruzi is found in southern portions of the United States, Mexico, and Central and South America. Commonly referred to as Chagas' disease or American trypanosomiasis, the disease course for this illness often presents itself with cardiac and gastrointestinal distress.

Laboratory Diagnosis

Giemsa-stained blood slides are the specimen of choice for detection of the typical *T. cruzi* trypomastigotes. Epimastigotes may rarely be seen in the circulating blood; however, this form is primarily found only in the arthropod vector. Lymph node biopsy Giemsa-stained slides, as well as blood culture, may reveal the typical amastigotes. A number of serologic tests, including complement fixation (CF), DAT, and indirect immunofluorescence (IIF), are also available for diagnostic purposes. The polymerase chain reaction (PCR) and ELISA testing methods are also available for diagnosing infections with *T. cruzi*; ELISA is presently used in blood donor screening to help ensure the safety of transfusable blood and transplantable organs.

Life Cycle Notes

T. cruzi is most frequently transferred to a human host when a reduviid bug vector defecates infective trypomastigotes near the site of its blood meal. The presence of the bite produces an itching sensation in the host. As the host scratches the bite area, the trypomastigotes conveniently gain entry into the host by literally being rubbed into the bite wound. Additional routes of transferring *T. cruzi* include blood transfusions, sexual intercourse, transplacental transmission, and entry through the mucous membranes when the bug bite is near the eye or mouth.

Following entry into the host, the trypomastigotes invade surrounding cells, where they transform into amastigotes. The amastigotes proceed to multiply, destroy the host cells, and then convert back into trypomastigotes. The resulting trypomastigotes migrate through the blood, penetrate additional cells in the body, and transform back into amastigotes, and the replication and destruction cycle repeats. A number of areas in the body may become infected, including the heart muscle, liver, and brain.

The *T. cruzi* trypomastigotes are transmitted back to the reduviid bug when it feeds, via a blood meal, on an infected human. On ingestion, the trypomastigotes transform into epimastigotes in the midgut. Multiplication of the epimastigotes produces thousands of additional parasites that convert back into trypomastigotes when they reach the hindgut. These trypomastigotes are then passed with the feces when the bug defecates near the site of its next blood meal, and thus the cycle begins again.

Epidemiology

T. cruzi is found primarily in South and Central America and only rarely in North America. The highest known prevalence of disease is in Brazil. Although first isolated in a *Panstrongylus megistus*, there are additional reduviid bug species that may serve as vectors. Also known as the kissing bug, conenose bug, and triatomid bug, the reduviid bug nests in human homes that are open in design. Although there are a number of known mammalian hosts, dogs and cats are of particular importance as reservoir hosts in Brazil.

Clinical Symptoms

Chagas' Disease. Named after its discoverer, Carlos Chagas, a Brazilian researcher who was a medical student at the time, Chagas' disease may be asymptomatic, chronic, or acute in nature. The most common initial symptom is the development of an erythematous nodule, known as a **chagoma**, at the site of infection produced by the proliferation of the *T. cruzi* organisms. This lesion may be present anywhere on the body, but it is most frequently located on the face. Edema as well as a rash around the eyes and face may subsequently occur. The painful chagoma may last 2 to 3 months before subsiding. Patients who contract *T. cruzi* through the ocular mucosa develop a characteristic conjunctivitis and unilateral edema of the eyelids, a condition known as **Romaña's sign.**

Chronic Chagas' disease may occur after the initial diagnosis of an acute disease or years to decades after being initially asymptomatic. The destruction of multiple tissues in this phase of infection results in patients who present with myocarditis, enlargement of the colon (sometimes referred to as **megacolon**) and esophagus (sometimes referred to as **megaesophagus**), and hepatosplenomegaly. In addition, CNS involvement, **cardiomegaly** (enlargement of the heart), and electrocardiographic changes may be seen. Complete blockage of the heart, as well as brain damage, may result, causing sudden death. The invasion and destruction of various other organs, including those already mentioned, may also contribute to death in chronic patients.

Patients suffering from acute Chagas' disease typically experience fever, chills, fatigue, myalgia, and malaise. An attack of acute infection may result in one of the following scenarios: (1) recovery; (2) transition to the chronic stage of disease; or (3) death, which usually occurs a few weeks after the attack.

The frequency and form of Chagas' disease seen in small children versus older children and adults vary. In general, Chagas' disease is most commonly seen in children younger than 5 years. These patients characteristically present with symptoms of CNS involvement and experience the most severe form of the disease. After experiencing an initial acute attack, adults and children older than 5 years usually develop a milder chronic or subacute form of the disease.

Treatment

The treatment of choice for infections with *T. cruzi* is nifurtimox (Lampit). Other medications include benznidazole, allopurinol, and the antifungal agent ketoconazole.

Prevention and Control

The eradication of reduviid bug nests and the construction of homes without open design are crucial measures necessary to help alleviate the future spread of the disease. DDT has proved to be useful, not only to control the reduviid population but also to decrease the incidence of malaria (see Chapter 6) when used in bug-infested homes. Educational programs designed to inform people, especially in endemic areas, of the disease, its transmission, and possible reservoir hosts may also prove to be helpful in the fight against *T. cruzi* transmission. In addition, the prospects for developing a vaccine appear to be promising.

Notes of Interest and New Trends

Because of the recent increase of *T. cruzi* infections among persons from the known endemic continent of South America, concern over the safety of donated blood from these individuals has emerged. In 1992, efforts were implemented to minimize the risk of transfusion transmission. All natives of and persons traveling to South America were prohibited from donating blood for transfusion purposes. Travel deferrals are generally 12 months after the departure date.

The traditional method of diagnosing *T. cruzi* trypomastigotes in endemic areas of South America is known as **xenodiagnosis.** In this procedure, a noninfected reduviid bug is allowed to feed on a person suspected of having Chagas'

disease. Several weeks later, the feces of the bug is examined for the presence of trypomastigotes.

The PCR method has successfully detected *T. cruzi* in a number of studies conducted in recent years. One study has suggested that this assay may replace xenodiagnosis in patients with chronic disease and that it can be used in the screening of blood bank donors.

Quick Quiz! 5-22

The specimen of choice for the detection of *T. cruzi* is: (Objective 5-8)

A. Stool
B. Blood
C. Tissue
D. Ulcer

Quick Quiz! 5-23

Which of the following is the vector first identified as responsible for transmitting *T. cruzi*? (Objective 5-5)

A. *Phlebotomus* spp.
B. *Lutzomyia* spp.
C. *Panstrongylus megistus*
D. *Glossina* spp.

Quick Quiz! 5-24

Which of the following is not a characteristic finding in Chagas' disease? (Objective 5-6)

A. Romaña's sign
B. Megacolon
C. Cardiomegaly
D. Somnolence

Trypanosoma rangeli
(trip-an″o-so′muh/ran-jel-ee)

Common associated disease and condition names: None known.

Trypanosoma rangeli is found in many of the same geographic regions as *T. cruzi*. There are presently no common names known for disease caused by this organism. Infections are generally asymptomatic and tend to show no pathologic changes or signs of disease.

Laboratory Diagnosis

Giemsa-stained blood slides are the specimen of choice for the detection of the typical *T. rangeli* trypomastigotes. *T. rangeli* trypomastigotes can be seen in the peripheral blood throughout the course of the illness. It can also be diagnosed by xenodiagnosis and serologic testing methods. PCR-based methods are also available.

Life Cycle Notes

The life cycle for *T. rangeli* is similar to that of *T. cruzi*. The vector responsible for transmitting *T. rangeli* is the reduviid bug, *Rhodius prolixus*. This vector actually transmits the parasitic infection via its saliva. *T. rangeli* can be viewed in the blood throughout the course of the infection.

Epidemiology

T. rangeli is commonly found in the same geographic areas as *T. cruzi*—regions of South and Central America, particularly in the areas surrounding Brazil, Venezuela, Colombia, Panama, El Salvador, Costa Rica, Honduras, and Guatemala. Its vector, *Rhodius prolixus*, is attracted to the same open house design as other reduviid bug species. It has numerous reservoir hosts such as monkeys, raccoons, dogs, cats, armadillos, and rodents.

Clinical Symptoms

Patients infected by *T. rangeli* are generally asymptomatic and demonstrate no evidence of illness. It is generally thought to be a benign infection.

Treatment

The treatment of *T. rangeli* infection is similar to that of *T. cruzi*. Nifurtimox and benzimidazole

are the drugs of choice for treating *T. rangeli* infections.

Prevention and Control

Prevention and control measures for *T. rangeli* are the same as those for *T. cruzi*.

Quick Quiz! 5-25

The diagnostic testing methods for *T. rangeli* are the same as those for identifying and confirming and infection with *T. cruzi*. (Objectives 5-8, 5-11)

A. True
B. False

Quick Quiz! 5-26

The phrase that best describes the infection associated with *T. rangeli* is that it: (Objective 5-6)

A. Mimics that of individuals infected with *T. cruzi*
B. Causes South American sleeping sickness
C. Is considered a benign infection
D. Produces Winterbottom's sign

Quick Quiz! 5-27

Which of the following is not a prevention and control measure for *T. rangeli*? (Objective 5-7)

A. Use of DDT to control reduviid bug populations
B. Better housing construction
C. Removing overgrown vegetation
D. Educational programs in endemic areas

LOOKING BACK

The hemoflagellates have long been known to cause disease in humans and animals, with both *Leishmania* and *Trypanosoma* spp. dating back to prehistoric times. Increased travel and immigration are resulting in these organisms adjusting to and finding new environments in which to thrive, which they have been doing for many years. Diagnostic methods are rapidly changing how laboratory technicians identify these disease-causing parasites. While the new testing methods are evolving and becoming more clinically mainstream, good microscopy and staining techniques are still necessary diagnostic skills. It is also important to remember that these parasites are starting to show resistance to some common treatment modalities, many of which have adverse side effects. Education, prevention and control measures, and rapid treatment of infected persons are key to the health and well-being of those living in areas endemic for these parasites. The development of vaccines and better treatment methods is paramount.

TEST YOUR KNOWLEDGE!

5-1. Match each of the key terms (column A) with its corresponding definition (column B): (Objective 5-1)

Column A	Column B
A. Somnolence	**1.** The inability to mount an adequate immune response
B. Uta	**2.** Delayed sensation to pain
C. Kerandel's sign	**3.** Inflammation and painful ulceration at the insect bite site
D. Anergic	**4.** Excessive sleepiness
E. Chancre	**5.** Mucocutaneous leishmaniasis in the Peruvian Andes

5-2. The diagnostic stage for *Trypanosoma* spp. is the: (Objective 5-5)

A. Amastigote
B. Epimastigote
C. Trypomastigote
D. Promastigote

5-3. American trypanosomiasis is commonly referred to as: (Objective 5-3)

A. Cruzon's syndrome
B. Chiclero ulcer
C. Bay sore
D. Chagas' disease