Protozoa

Subkingdom: Protozoa

Phylum: Sarcomastigophora

Class: Zoomastigophora(Flagellates)

Family: Trypanosomatidae / Blood and Tissue Flagellates

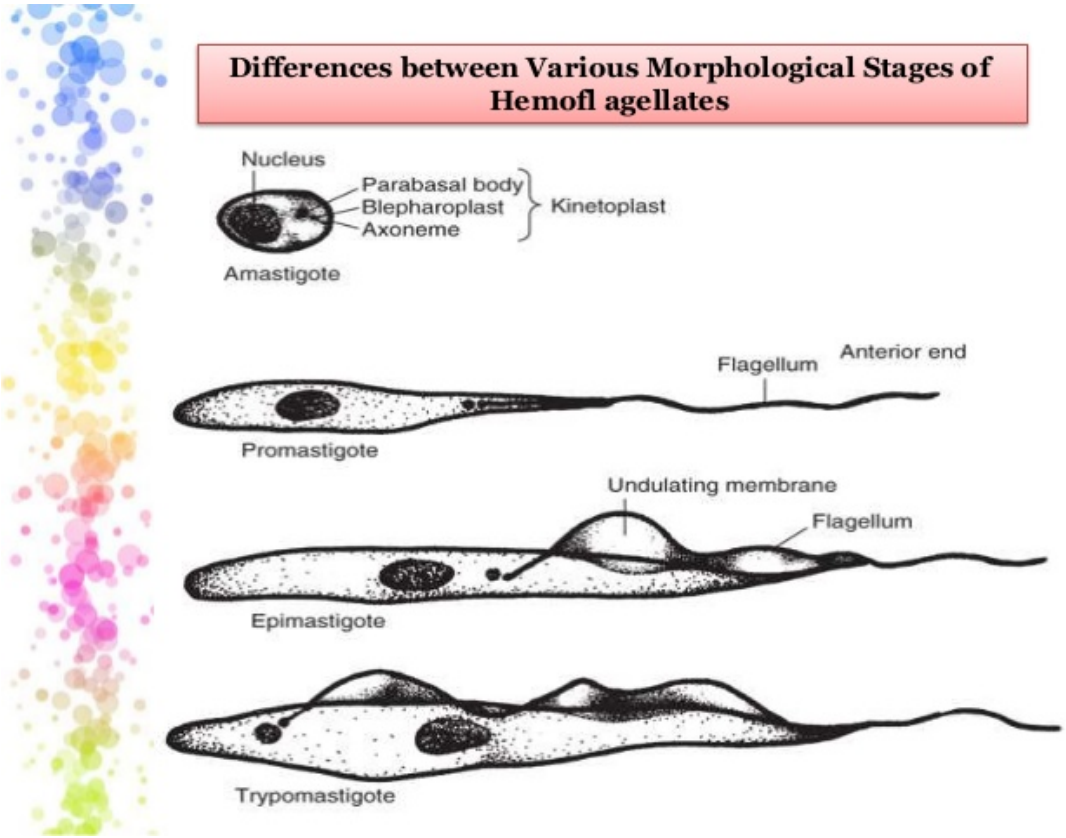
Members of this family which parasitize man belong to 2 genera: ***Leishmania*** **and** ***Trypanosoma*****,** they acquire 2 or more of the following morphological forms:

1- Amastigote: small oval intracellular stage and contains a one nucleus and a rod- shaped kinetoplast (formed of parabasal body, blepharoplasty and an axoneme which is a short intracellular flagellum).

2- Promastigote: elongated, motile, nucleus is situated centrally. Kinetoplast lies near the anterior end arises from which anterior flagellum.

3- Epimastigote: spindle shaped, the kinetoplast located in anterior of nucleus. It has a free flagellum with a short undulating membrane.

4- Trypomastigote: spindle shaped, kinetoplast at the posterior end from which arises a flagellum that passes along the edge of a long undulating membrane and project anteriorly as a free flagellum.



Leishmania spp.

Morphology

The parasite exists in 2 forms.

1. Amastigote form: is intracellular found inside macrophages in the reticuloendothelial system. in humans and other mammals.

2. Promastigote form: is found in the sandfly and in culture.

Leishmania donovani

Leishmania donovani is the causative agent for visceral leishmaniasis, also known as kala-azar, In the mammalian host, amastigote infected cells are found at numerous sites (e.g., spleen, liver, bone marrow, lymph glands).

*** *Leishmania tropica* Complex**

It includes 3 species:

1. *Leishmania tropica*
2. *Leishmania major*
3. *Leishmania aethiopica*

These species cause **old world cutaneous leishmaniasis** (oriental sore or Baghdad boil).

*** *Leishmania braziliensis* Complex and *L. mexicana* Complex**
Leishmania braziliensis complex and *L. mexicana* complex **cause new world leishmaniasis** in Central and South America, present in human, amastigote are found in the naso-oral mucosa.

Life Cycle of *Leishmania*

Modes of transmission is via bite of sandfly vectors of genus ***Phlebotomus*** in Leishmania donovani and Leishmania tropica, while transmission is via bite of sandfly vectors of genus ***Lutzomyia*** in *Leishmania braziliensis* .

1. People are infected when they are bitten by an infected female sand fly. Sand flies inject a form of the protozoa (called Promastigote) that can cause infection.

2. Promastigote are ingested by certain immune cells called macrophages.

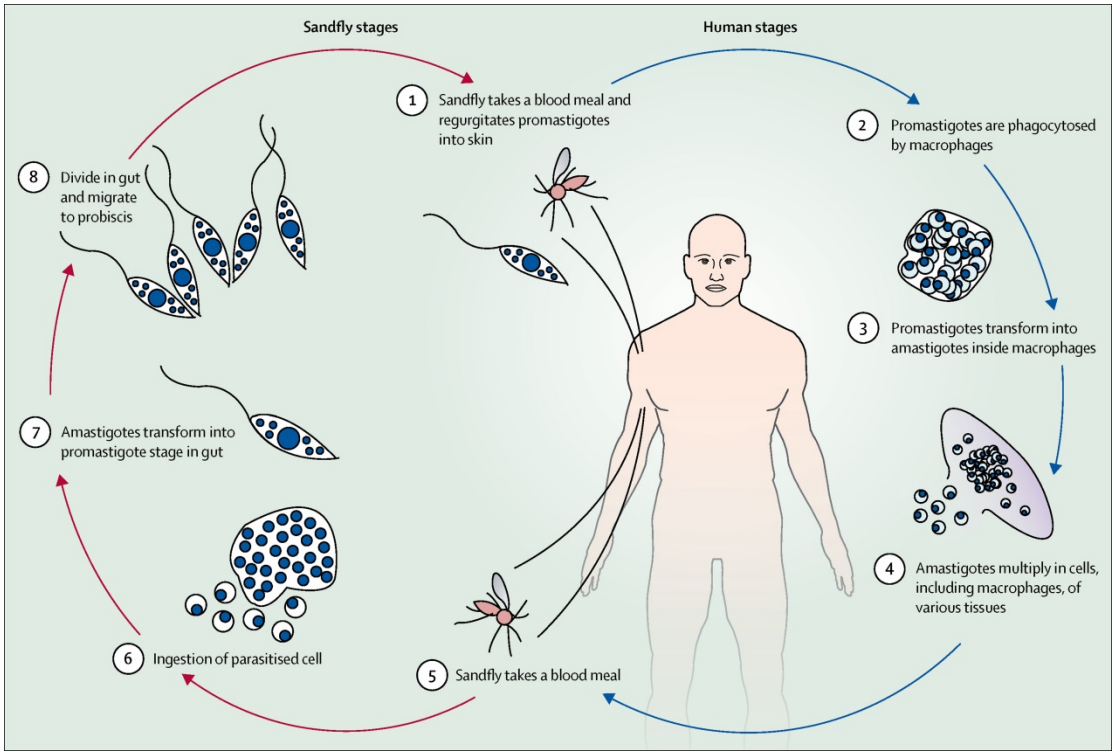
3. In these cells, Promastigote develop into another form (called amastigote).

4. Amastigote multiply inside macrophages in various tissues.

5–6. When a sand fly bites an infected person or animal, it becomes infected by ingesting blood containing macrophages with amastigote inside.

7. In the middle part of the fly's gut (midgut), amastigote develop into Promastigote.

8. In the fly's midgut, Promastigote multiply, develop, and migrate to the fly's mouth parts. They are injected when the fly bites another person, completing the cycle.

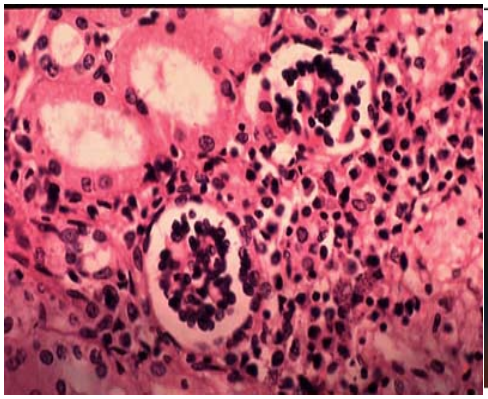


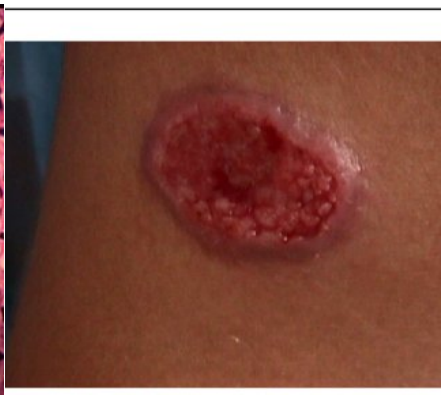
Pathogenesis and Clinical Features

Leishmania donovani causes visceral leishmaniasis or kala-azar. The parasitized macrophages disseminate the infection to all parts of the body. In the reticuloendothelial system, the amastigote multiply in the fixed macrophages. This causes a marked proliferation and destruction of reticuloendothelial tissue in these organs. It causes hepatosplenomegaly and lymphadenopathy. Severe anaemia may occur in kala-azar, as a result of infiltration of the bone marrow as well as by the increased destruction of erythrocytes.

Leishmania tropica cause early lesions are papular, followed by ulceration necrosis. Papule and ulcer are the main pathological lesions. Amastigote are found in skin. There is an inflammatory granulomatous reaction with infiltration of lymphocytes and plasma cells. They heal over months to years, leaving scars.

Leishmania mexicana **complex** causes cutaneous leishmaniasis which closely resembles the old world cutaneous leishmaniasis. However, a specific lesion caused by *L. mexicana* is **chiclero ulcer** which is characterized by ulcerations in pinna. *L.braziliensis* complex causes both cutaneous and mucocutaneous leishmaniasis.





Leishmania donovani *Leishmania tropica*

Leishmania braziliensis

Diagnosis

There are more than one method for diagnosis such as:-

1- Microscopic examination

In ***Leishmania donovani*** demonstration of amastigote in blood smears and tissue aspirates (bone marrow, spleen, lymph nodes), or smear made from the indurated edge of nodule or sore in ***Leishmania tropica*** and from skin lesions and mucous membrane in ***Leishmania braziliensis*** stained with Geimsa to demonstrate amastigote.

2- Culture in Novy, McNeal, and Nicolle ((NNN) medium.

3- Molecular diagnosis by PCR on clinical specimens.

Treatment

Pentavalent antimonials compound given intravenously or intramuscularly, Amphotericin B.Topical treatment consists of a paste of 10% charcoal in sulphuric acid or liquid nitrogen exactly in *Leishmania tropica.*

Trypanosoma spp.

Trypanosomes live in human and other vertebrate hosts. From the blood, they invade regional lymph nodes and finally CNS.

**** Trypanosoma brucei gambiense***

**** Trypanosoma brucei rhodesiense***

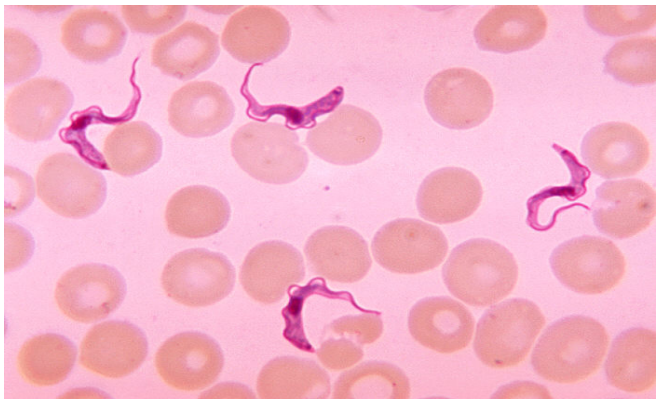
Morphology

1. In vertebrate host (human and domestic animals)/ Trypomastigote form
2. In vector (tsetse fly)

Occurs in 2 forms:

(a) Epimastigote

(b) Metacyclic trypomastigotes



Trypanosoma brucei

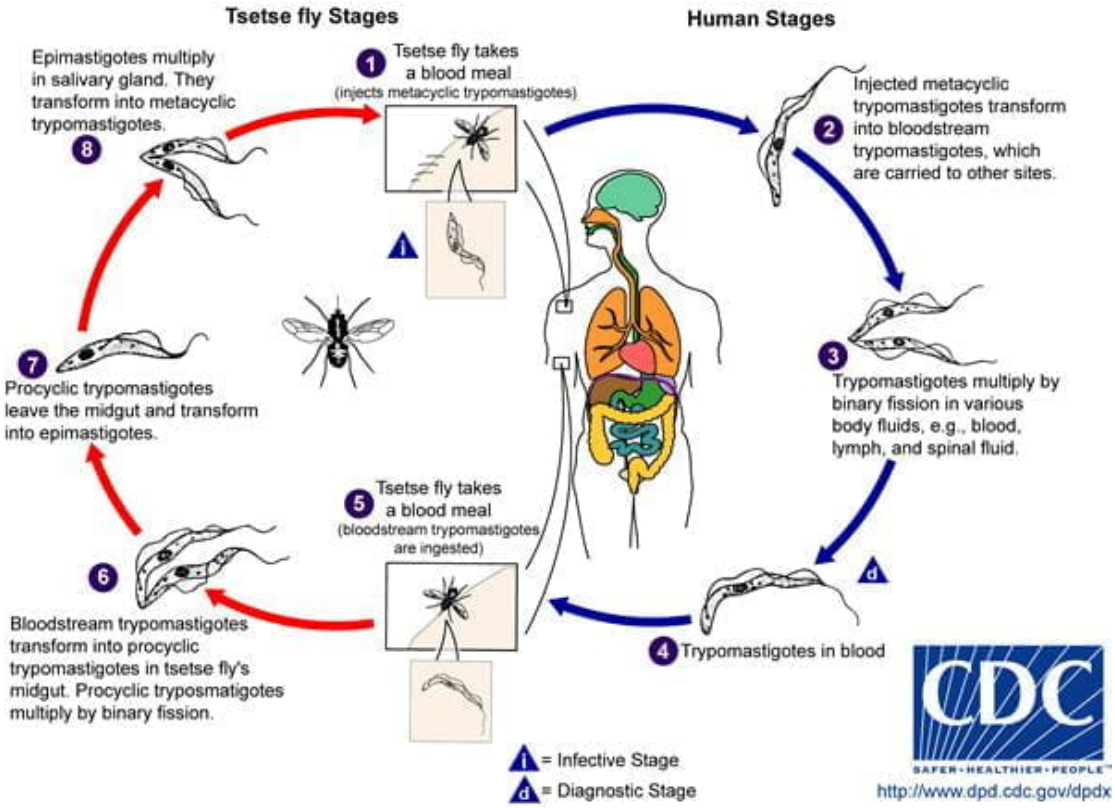
Life Cycle

Modes of transmission is via bite of infected male and female tsetse flies genus ***Glossina palpalis*** and ***Glossina morsitans*** during suck blood.

Trypanosoma brucei completes its life cycle in 2 hosts. Vertebrate hosts are humans. (1) Tsetse fly (the invertebrate host) takes a blood meal and injects the infective metacyclic trypomastigotes.(2) Injected metacyclic trypomastigotes transform into trypomastigotes and are carried to other sites via blood stream. (3) Trypomastigotes multiply by binary fission.

(4) Trypomastigotes are found in blood extracellular. (5) Trypomastigotes in the blood are ingested by tsetse fly and transform into procyclic trypomastigotes in the midgut of the fly (6). (7–8) Procyclic

trypomastigotes transform into epimastigotes before transforming into metacyclic trypomastigotes in the fly's salivary gland.



Pathogenesis and Clinical Features

Trypanosoma brucei gambiense causes African trypanosomiasis (West African sleeping sickness). The illness is chronic and can persist for many years. There is an initial period of parasitaemia, followed by localization of parasites in the lymph nodes. A painless chancre appears on the skin at the site of bite by tsetse fly, followed by fever, chills, rash, anaemia and weight loss. Invasion of CNS occurs after several months later and is marked by increasing headache, mental dullness and daytime There is cellular infiltration of the brain and spinal cord , neuronal degeneration and sleepiness. *Trypanosoma brucei rhodesiense* causes East African sleeping sickness. It is more acute than the Gambian form and appears

after an incubation period of 4 weeks. It may end fatally within a year of onset.

Diagnosis

The diagnosis of both types of human African trypanosomiasis (HAT) is similar.

1. Microscopic examination

Wet mount preparation of lymph node aspirates, CSF, and chancre fluid are used for demonstration of trypomastigotes. These specimens stained with Geimsa.

2. Molecular diagnosis

PCR on clinical specimens.

Treatment

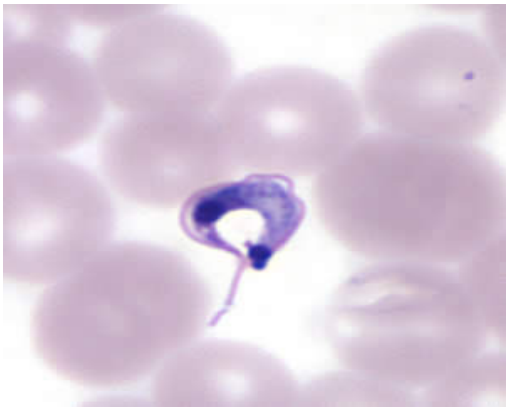
Pentamidine is the drug of choice for gambiense human African trypanosomiasis . Suramin is the drug of choice for rhodesiense.

**** Trypanosoma cruzi***

In human, trypomastigotes are in the blood and amastigote are in tissue. it causes Chagas' disease, which is a zoonotic disease.

Morphology

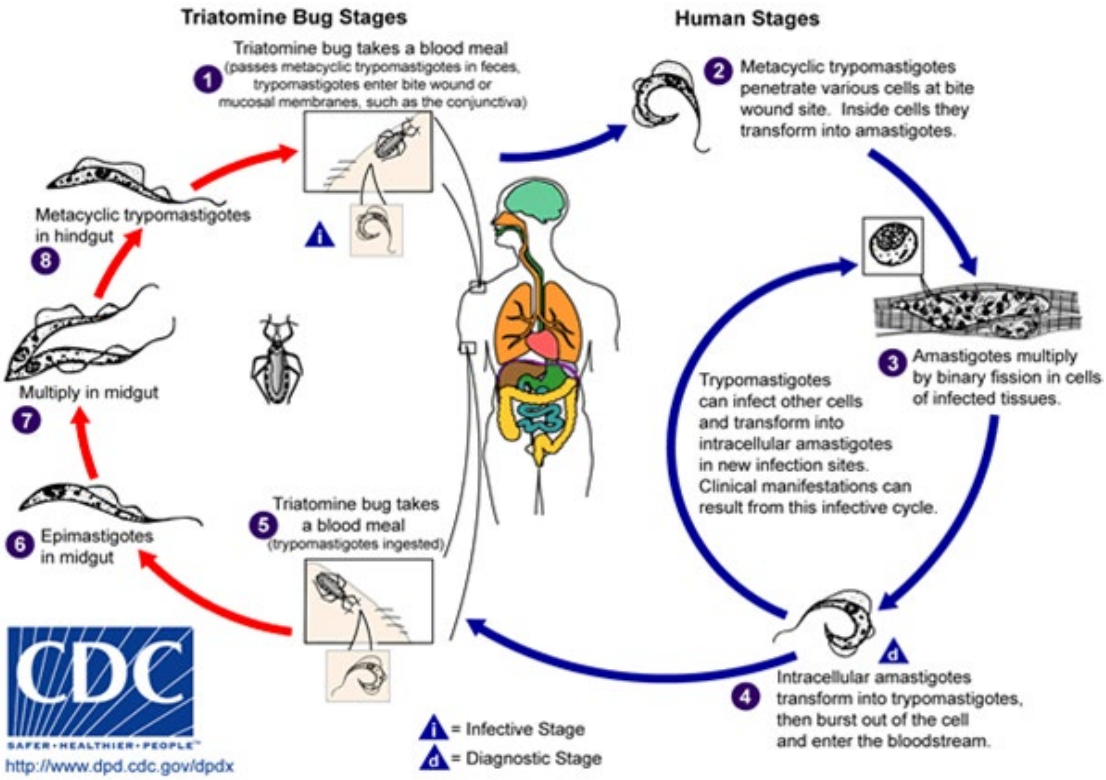
In humans, *Trypanosoma cruzi* exists in 2 forms, amastigote and trypomastigote. Amastigotes are intracellular, Multiplication of the parasite occurs in this stage. This form is found in muscles, nerve cells and reticuloendothelial systems. **In reduviid bugs (vector), amastigotes are found in the midgut.** Trypomastigote is a non-multiplying form found in the peripheral blood of human and other mammalian hosts. In stained blood smears, they are C or U-shaped, and a big kinetoplast . In reduviid bugs, metacyclic trypomastigotes are present in hindgut and faeces.



Trypanosoma cruzi

Life Cycle

Trypanosoma cruzi completes its life cycle in 2 hosts. **Human** is the vertebrate host. Its invertebrate host (vector) is **reduviid bug or triatomine bug** . The infective stage to human is **metacyclic trypomastigotes** which are found in faeces of reduviid bugs. This bug defecates while feeding. The parasite enters human at the biting site. Transmission of infection to human and other reservoir hosts takes place when mucus membranes, conjunctiva, or wound on the surface of the skin is contaminated by faeces of the bug containing Metacyclic trypomastigotes.



Pathogenesis and Clinical Features

Trypanosoma cruzi causes American trypanosomiasis or Chagas' disease This disease manifests in acute and chronic forms.

1. Acute Chagas' disease

Acute phase occurs soon after infection and may last for 1–4 months. It is seen often in children under 2 years of age. First sign appears within a week after invasion of parasite. 'Chagoma' is the subcutaneous lesion occurring at the site of inoculation. Inoculation of the parasite in conjunctiva causes unilateral, painless oedema of periorbital tissues known as Romana's sign. There may be generalized infection with fever, lymphadenopathy and hepatosplenomegaly. The patient may die of acute myocarditis and meningoencephalitis.

2. Chronic Chagas' disease

The chronic form is found in adults and older children and becomes apparent years or even decades after the initial infection. In chronic phase, *T. cruzi* produces inflammatory response, cellular destruction and fibrosis of muscles and nerves which can present with cardiac myopathy.

Diagnosis

1. Microscopic examination

Demonstration of trypomastigotes in thick and thin Giemsa-stained peripheral blood smears in acute infection.

2. Culture

(NNN) medium is used for growing T. cruzi.

7. Molecular diagnosis

PCR on clinical samples.

Treatment

Nifurtimox and benznidazole have been used with limited disease in both acute and chronic Chagas' disease.