Trypanosoma

 The hemoflagellates of the genus trypanosoma occur in the blood of mammals as mature elongated

trypomastigote.

The trypomastigote is an Elongated bodies supporting a longitudinal lateral undulating membrane and a flagellum that borders the free edge of the membrane and emerge at the anterior end as a whip like extension. The kinetoplast is a darkly staining body lying in the posterior end of the body immediately adjacent to tiny node (blepharoplast) from which the flagellum arise, this form called trypomastigote (Figure 1).

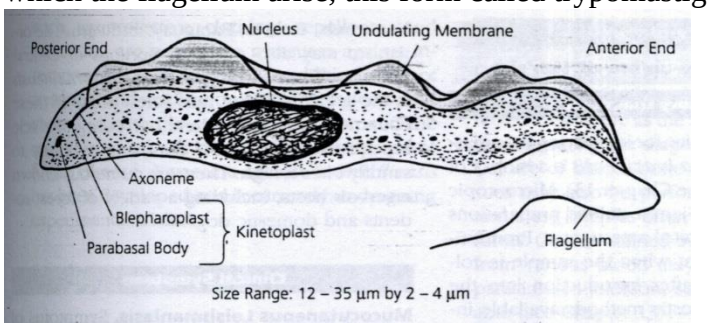
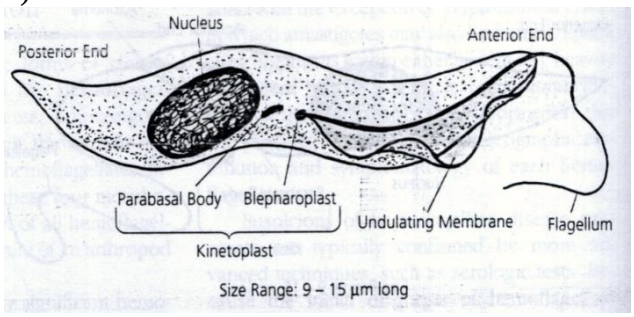


Figure 1: Trypomastigote

 The forms that are seen in the vectors are called **epimastigote (crithidia)**

Elongated extracellular stage with short undulating membrane and a kinetoplast placed posteriorly in the anterior end near the nucleus, this form called epimastigote (Figure 2)



(Figure 2: Epimastigote)

Some species of trypanosomes apparently lives in their natural vertebrate hosts without causing evident disease, other cause variable degree of tissue pathology. Three species of trypanosomes that commonly parasitize man are all pathogenic and not infrequently cause death.

The three species are:

1) Trypanosoma brucei rhodesiense.
2) Trypanosoma brucei gambiense.
3) Trypanosoma cruzi.

Trypanosoma brucei brucie, Trypanosoma brucei rhodesiense, Trypanosoma brucei gambiense and Trypanosoma rangeli are called **salivarian trypanosomes** because the forms of parasite that are infective for the mammalian host develop in the saliva.

Trypanosoma cruzi differ in two aspects:

1) It is leishmania like in having dividing amastigote tissue forms.

2) The infective stage develops in the hindgut of the vector and emerges from the intestine (posterior station) in the feces and this is called stercorian trypanosome.

Trypanosoma cruzi (Schizotrypanum)

Disease: chagas´ disease or American trypanosomiasis.

Life cycle (Figure 3):

 Reservoirs are domestic cats, dogs and wild species such as armadillo, raccoon, and rats.
 Two main stages of *Trypanosoma cruzi* are found in mammalian host, amastigote and trypomastigote, while epimastigote (crithidial) and trypomastigote are found in triatomine bug.
 The reduviid bugs ingest trypomastigotes in the blood of the reservoir hosts. In the insect gut, they multiply and differentiate first into epimastigotes and then into trypomastigote.
 When the bug bites again, the site is contaminated with feces containing metacyclic trypomastigotes, which enter the blood of the host (or reservoir) through the bite wound or intact mucous membrane (conjunctiva, mouth). The parasites are engulfed by macrophages and become amastigotes. After 4 or 5 days of multiplication by binary fission, amastigotes again become trypomastigotes, disrupt the cell, and enter the blood stream and other tissues where the cycle continues as long as the host lives.
 Many cells are affected, but myocardial, glial, and reticuloendothelial cells are the most frequent sites.
 To complete the cycles, amastigotes differentiate into trypomastigotes, which enter the blood and are taken up again by the reduviid bug.
 In tissues the accumulation of multiplying parasites produces pseudocysts; the amastigote are indistinguishable from those of *L.donovani* but *in L.donovani*, it invades only macrophages whereas in T.cruzi, amastigote invades the cells of any tissue.
 Other less frequent modes of human infection are by blood transfusion and by congenital or transmammary transmission, organ transplantation, rarely by eating food contaminated with infective bug feces or by ingestion of infected meat. Accidental laboratory infections have been reported.
 Infective stage = Metacyclic trypomastigote**.**

Pathogenesis:

The amastigote can kill cells and cause inflammation, consisting mainly of mononuclear cells. Cardiac muscle is the most frequently and severely affected tissue. Neuronal damage leads to cardiac arrhythmias and loss of tone in the colon (megacolon) and esophagus (megaesophagous).

During the acute phase, there are both trypomastigote in the blood and amastigote intracellularly in the tissue .In the chronic phase, the organism persist in the amastigote form.

Clinical features:

 Incubation period = 5-12 days
 The disease is seen most commonly, and in its severe form, in children younger than 5 years, in whom CNS symptoms predominate, while in older children and adults, the disease may be mild, subacute or chronic.
 The first signs of acute Chagas´ disease develop at least 1 week after invasion by the parasites. When the organisms enter through a break in the skin, an indurated area of erythema and swelling (the chagoma), accompanied by local lymphadenopathy, may appear.
 Romana's sign—the classic finding in acute Chagas´ disease, which consists of unilateral painless edema of the palpebrae and periocular tissues—can result when the conjunctiva is the portal of entry.

 These initial local signs may be followed by malaise, fever, anorexia, and edema of the face and lower extremities. A morbilliform rash may also appear. Generalized lymphadenopathy and hepatosplenomegalymay develop. Severe myocarditis develops rarely; most deaths in acute Chagas disease are due to heart failure.
 Neurologic signs are not common, but meningoencephalitis occurs occasionally. The acute symptoms resolve spontaneously in virtually all patients, who then enter the asymptomatic or indeterminate phase of chronic *T.cruzi* infection
 Symptomatic chronic Chagas´ disease becomes apparent years or even decades after the initial infection. The most commonly involved is the heart, also dilatation of hollow viscera (megaesophagus, megacolon and
megaureter).
Death from chronic chagas´ disease is usually due to cardiac arrhythmias and failure.

Laboratory diagnosis:
1) Acute disease
a. Wet blood preparation for motile organisms
b. Thick and thin blood film for demonstration of Cshaped trypomastigote.
c. Culture in NNN medium
d. Muscle biopsy for amastigote
e. Polymerase chain reaction (PCR) when repeated attempts to visualize the organisms are unsuccessful
2) Chronic Chagas´ disease It is difficult because few trypomastigote in the blood It is diagnosed by the detection of specific antibodies that bind to T. cruzi antigens (serology) and by xenodiagnosis.
a) Serological test.
a) ELISA
b) Indirect fluorescent – antibody test
c) Indirect haemagglutination and
d) Complement fixation test.
b) **Xenodiagnosis** for chronics disease which consists of allowing an uninfected, laboratory – raised reduviid bug to feed on the patient and, after several weeks, examining the intestinal contents of the bug for the organism.

Trypanosoma gambiense and Trypanosoma rhodesiense.

Disease:
They cause sleeping sickness (African trypanosomiasis).
 Trypanosoma gambiense (Gambian or West African sleeping sickness).
 Trypanosoma rhodesiense (Rhodesian or East African sleeping sickness).

Trypanosoma rhodesiense (Rhodesian or East African sleeping sickness)

Life cycle (Figure 1)
 The vector for both is the tsetse fly, but different species of fly are involved.
 Humans are the reservoir for **Trypanosoma gambiense,** whereas **Trypanosoma rhodesiense** has reservoirs in both domestic animals (especially cattle) and wild animals (e.g., antelopes). Tsetse fly ingests trypomastigote in blood meal from a reservoir host.
They multiply in the insect gut and then migrate to the salivary glands, where they transform into epimastigotes, multiply further, and then form metacyclic trypomastigotes, which are transmitted by the tsetse fly.

The development within the fly requires 3 weeks.
 In man: Metacyclic trypanosomes injected in the skin by tsetse fly, multiply at the site of injection. Inside human, multiplication in blood, lymph nodes, and spleen is by binary fission as trypanosomal form.

Pathogenesis:
 In the acute form, a cyclical fever spike occurs that is related to **antigenic variation of the surface glycoprotein**. The antigenic variation of surface
glycoprotein is explained by the fact that trypanosomes may have 1000 or more variant surface glycoprotein (VSG) genes and trypanosomes change their surface antigen glycoprotein by turning off one gene coding for a (VSG) and turning on another. As a result, one antigenic type will coat the surface of the parasites for approximately 10 days, followed by other types. These antigenic variations allow the organism to evade the host immune response .
 A self-limited inflammatory lesion (trypanosomal chancre) may appear a week or so after the bite of an infected tsetse fly. The chancre subsides in a week or two as the trypanosomes gain entry to the circulating blood.
Then they enter the lymph nodes, where a second focus of inflammation occurs, with hyperplasia of the endothelial lining of the blood sinuses and perivascular infiltration of leukocytes. Thos process is rapid, fulminating, and often causes death in a few months. Rarely the patient lives long enough for the trypanosomes to invade the central nervous system and produce the signs of the third stage of the infection (Sleeping Sickness).
Clinical features:
 Incubation periods= 1-2 weeks.
 After the incubation period, the patient suffers from headache, febrile paroxysms that recur frequently, weakness, loss of weight. Lymph node enlargement is not pronounced. Skin rash, odema and myocarditis may be
present. CNS signs are not common.
 Death occurs within 1 year due to intercurrent infections.

Trypanosoma gambiense (Gambian or West African sleeping sickness)

Life cycle: As for *Trypanosoma rhodesiense* (Figure 1)
Pathogenesis:
As for *Trypanosoma rhodesiense*, but the difference is that T. gambiense enter the arachinoid spaces of the CNS and the in brain substance. Thus following the initial lesion in the skin, three progressive stages occur:
Parasitemia, Lymphadenitis, and CNS involvement.
Clinical features:
Incubation period = 6-14 days. The initial lesion is an indurated painful skin ulcer (trypanosomal chancre) at the site of bite. A Blood film reveals trypanosomes. This period of symptom free last for weeks or months, then the infection may be abortive or the parasites invade lymphatic tissues leading to intermittent weekly fever(febrile attack of about a week's duration and then afebrile period) and lymphadenopathydevelop. **Enlargement of the posterior cervical lymph node (Winterbottom´s sign)** is commonly seen. Axillary and groin lymph nodes are also involved with splenomegaly After some months in the absence of treatment, the central nervous system is invaded and is characterized initially by headache, insomnia by night and sleepiness by day, mood changes followed by muscle tremor, slurred speech and apathy progress to somnolence, coma and death.

Diagnosis:

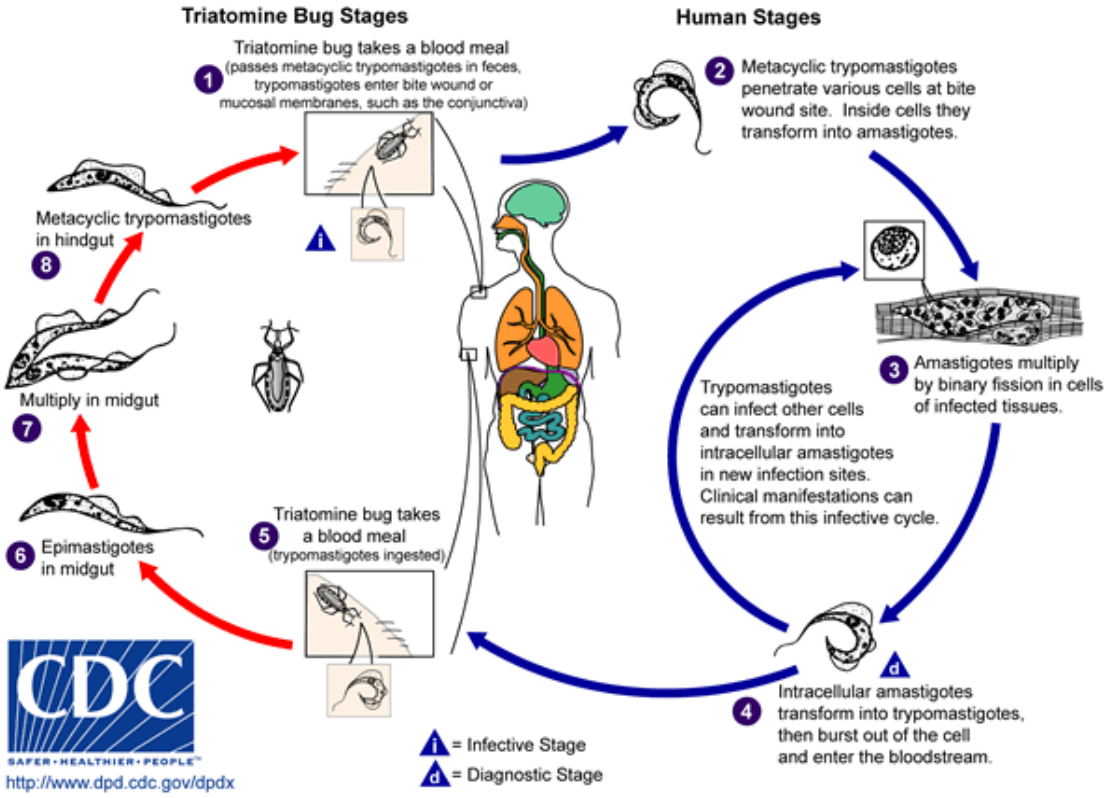
1) Thick or thin blood film, an aspirate of the chancre or enlarged lymph node, bone marrow biopsy to reveals the trypomastigote.

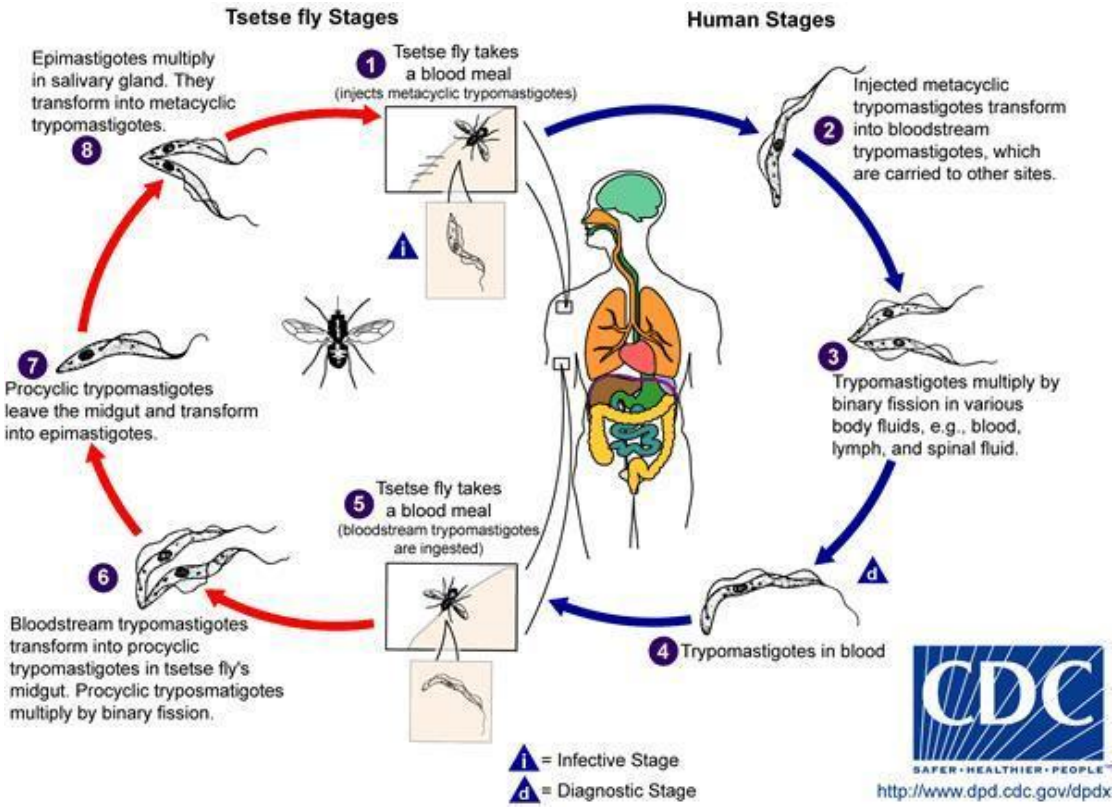
The likelihood of finding parasites in blood is higher in stage I,II than in stage III disease and in patients infected with *T. b. rhodesiense* rather than *T. b. gambiense*.

2) CSF in case of encephalitis reveals trypanosomes with elevated protein level, pleocytosis, high IgM and CSF pressure.

3) Culture in NNN medium.

4) Serological tests: card indirect agglutination test for trypanosomiasis, and ELISA for IgM Ab.




Tsetse fly Stages
Human Stages
Epimastigotes multiply in salivary gland. They transform into metacyclic trypomastigotes.
8
1 Tsetse fly takes a blood meal
(injects metacyclic trypomastigotes)
i
Injected metacyclic trypomastigotes transform into bloodstream trypomastigotes, which are carried to other sites.
2
3
Trypomastigotes multiply by binary fission in various body fluids, e.g., blood, lymph, and spinal fluid.
7
Procyclic trypomastigotes leave the midgut and transform into epimastigotes.
5 Tsetse fly takes a blood meal
(bloodstream trypomastigotes are ingested)
d
6
Bloodstream trypomastigotes transform into procyclic trypomastigotes in tsetse fly's midgut. Procyclic tryposmatigotes multiply by binary fission.
4 Trypomastigotes in blood
i = Infective Stage
d = Diagnostic Stage
CDC
SAFER·HEALTHIER·PEOPLE™
http://www.dpd.cdc.gov/dpdx