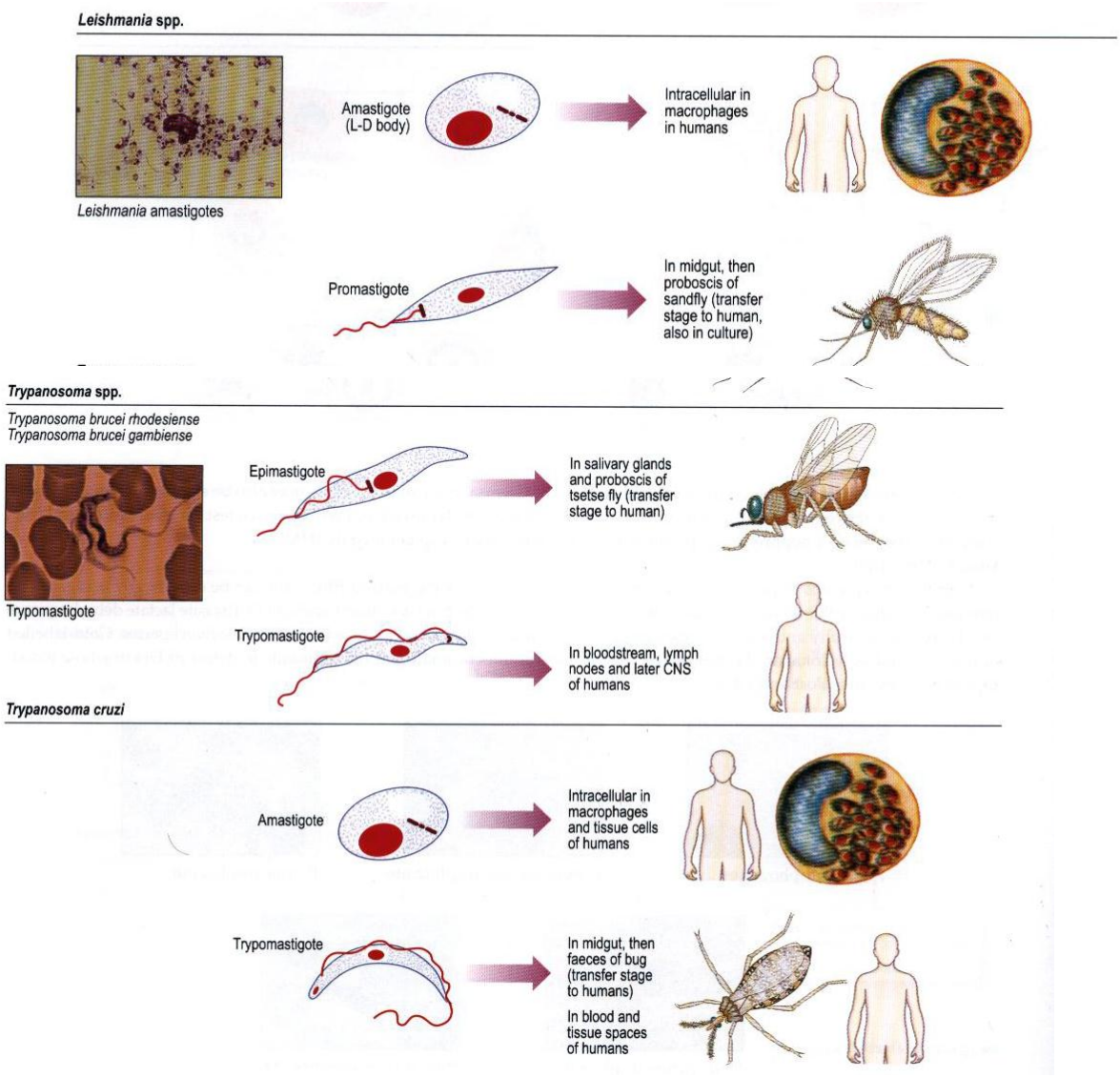
BLOOD AND TISSUE PROTOZOA

Blood protozoa of major clinical significance include members of genera Trypanosoma (T. brucei and T. cruzi); and Leishmania Spp.

Blood and tissue flagellate cyclo morphsium



TRYPANOSOMIASIS

1-African trypanosomiasis (Sleeping sickness)

Etiology: There are two clinical forms: 1) a slow developing disease caused by Trypanosoma brucei gambiense and a rapidly progressing disease caused by T. b. rhodesiense.

Epidemiology: **T. b. gambiense is predominant in the western and central regions of Africa, whereas T. b. rhodesiense is restricted to the eastern third of the continent. 6,000 to 10,000 human cases are documented annually. 35 million people and 25 million cattle are at risk. Regional epidemics of the disease are cause of major health and economic disasters.**

Morphology: **T. b. gambiense and T. b. rhodesiense are both similar: 10-30µ x 1-3µ, single central nucleus and a single flagellum originating at the kinetoplast and joined to the body by an undulating membrane (Figure 2). The outer surface of the organism is densely coated with a layer of glycoprotein, the variable surface glycoprotein (VSG).**

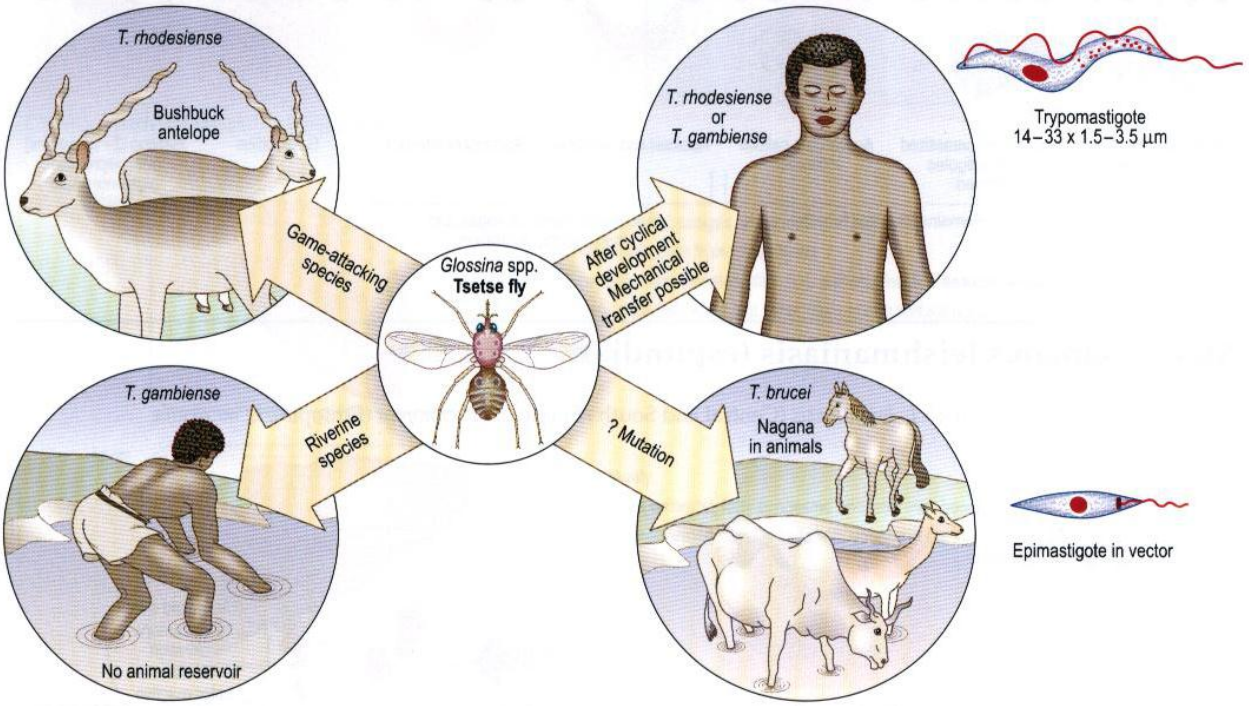
Life cycle: ***Trypansoma brucei. T. brucei is transmitted by tsetse flies of the genus Glossina. Parasites are ingested by the fly when it takes a blood meal on an infected mammal. The parasites multiply in the fly, going through several developmental stages in the insect gut and salivary glands (procyclic trypanosomes, epimastigotes, metacyclic trypanosomes). The cycle in the fly takes approximately 3 weeks. When the fly bites another mammal, metacyclic trypanosomes are inoculated, and multiply in the host's blood and*** **extracellular fluids such as spinal fluid.**

Trypomastigotes can traverse the walls of blood and lymph capillaries into the connective tissues and, at a later stage, cross the choroid plexus into the brain and cerebrospinal fluid. The organism can be transmitted through blood transfusion.

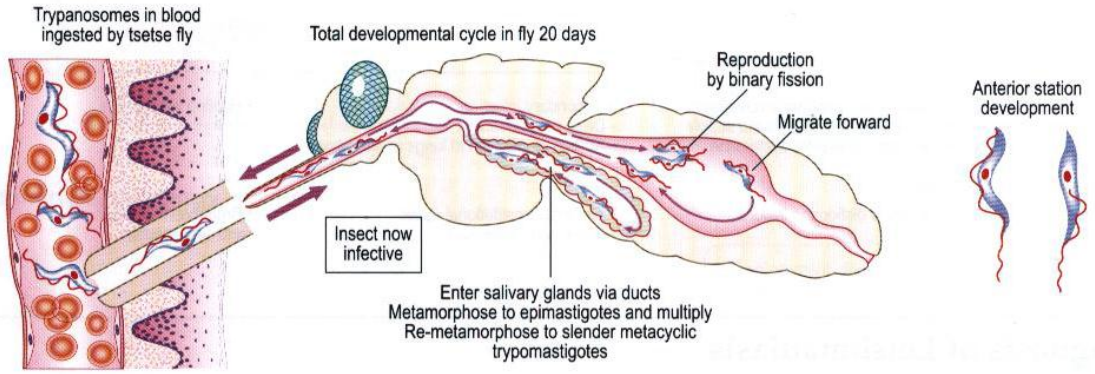
- **Humans are the main reservoir for T. b. gambiense, but this species can also be found in animals. Wild game animals are the main reservoir of T. b. rhodesiense.**

African type: sleeping sickness

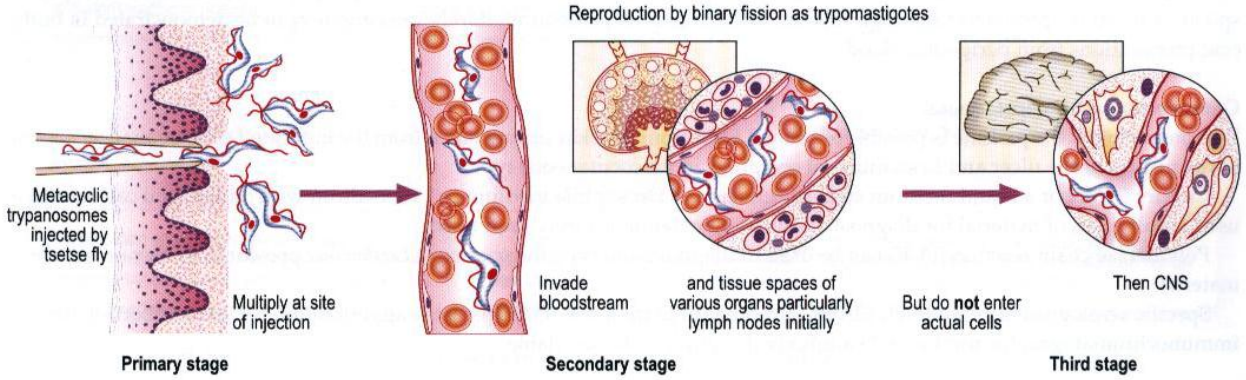
Caused by either *Trypanosoma gambiense* (chronic sleeping sickness, found in West Africa, the Congo, Zaire) or by *T. rhodesiense* (acute sleeping sickness, found in Zimbabwe, Tanzania, Zambia, Angola). Both have similar life cycle and morphology.



Life cycle in insect



Life cycle in humans



Symptoms: The clinical features of Gambian and Rhodesian disease are the same, however they vary in severity and duration. Rhodesian disease progresses more rapidly. The symptoms of the two diseases are also more pronounced in the Caucasians than in the local African population. Classically,

the progression of African trypanosomiasis can be divided into three stages

1- the bite reaction (chancre)

2- parasitemia (blood and lymphoid tissues

3- CNS stage

- **Bite reaction**: A non-pustular , painful, itchy chancre forms 1-3 weeks after the bite and lasts 1-2 weeks and leaves no scar.
- **Parasitemia**: Parasitemia and lymph node invasion is marked by attacks of fever which starts 2-3 weeks after the bite and is accompanied by malaise, lassitude, insomnia headache and lymphadenopathy and edema . The more characters symptoms

(Kerandel's sign) Painful sensitivity of palms and ulnar region to pressure may develop in some Caucasians.

(Winterbottom's sign) Very characteristic of Gambian disease is visible enlargement the glands of the posterior cervical region .

CNS Stage: The late or CNS stage is marked by changes in character and personality. 1- They include lack of interest

2-disinclination to work,

3-avoidance of acquaintances,

4-morose and melancholic attitude alternating with exaltation,

5- mental retardation and lethargy,

6- low and tremulous speech, and tremors of tongue and limbs,

8- slow and shuffling gait,

9- altered reflexes, etc. .

There is a slow progressive involvement of cardiac tissue. Febrile episodes may last few months as in Rhodesian disease or several years as in Gambian disease.

Parasitemia is more prominent during the acute stage than during the recurrence episodes

The later stages are characterized by •

1- Drowsiness and uncontrollable urge to sleep. •

2-The terminal stage is marked by wasting and emaciati •

3-Death results from coma, intercurrent infection . •

The clinical features of Rhodesian •

1- disease are similar but briefer and more acute. •

2-The acuteness and severity of disease . •

3-Death is due to cardiac failure within 6-9 months

Treatment and Control: The blood stage of African trypanosomiasis can be treated with reasonable success with Pentamidine isethionate or Suramin. These drugs have been reported also to be effective in prophylaxis although they may mask early infection and thus increase the risk of CNS disease. Cases with CNS involvement should be treated with Melarsoprol, an organic arsenic compound.

Most effective prevention is to avoid contact with tsetse flies. Vector eradication is impractical due to the vast area involved. Immunization has not been effective due to antigenic variation.

American trypanosomiasis (Chagas disease)

Epidemiology: American trypanosomiasis, also known as Chagas' disease is scattered irregularly in Central and South America. It is estimated that 10 million people are infected by the parasite and 50 million are at risk.

- More than a 100 mammalian species of wild and domestic animals including cattle, pigs, cats, dogs, rats, are naturally infected and serve as the reservoir.

Morphology: Depending on its host environment, the organism occurs in four different forms. The trypanosomal (trypomastigote) form found in mammalian blood is 15 to 20 micron long and morphologically similar to African trypanosomes. The leishmanial (amastigote) form, found intracellularly or in pseudocysts in mammalian viscera (particularly in myocardium and brain), (epimastigote) form is found in the insect intestine.

Life cycle: The organism is transmitted to mammalian host by many species of kissing (riduvid) bug , most prominently by Triatoma infestans,

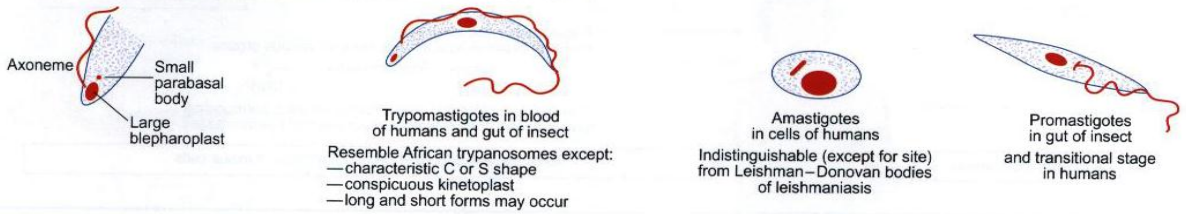
- Transmission takes place during the feeding of the bug which normally bites in the facial area (hence the name, kissing bug) and has the habit of defecating during feeding.
- The metacyclic trypamastigotes contained in the fecal material gain access to the mammalian tissue and subsequently enter macrophages where they multiply.

Uninfected bugs acquire the organism when they feed on infected animals. The trypomastigote divides longitudinally in the mid and hindgut of the insect where they develop into infective metacyclic trypomastigotes, Transmission may also occur from man to man by blood transfusion and by transplacental route.

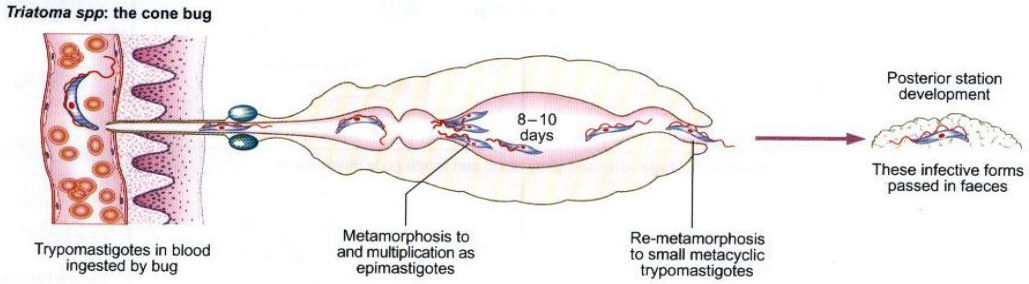
South American type: Chagas' disease

Caused by *Trypanosoma cruzi*. The parasite is harboured in humans, domestic animals such as cats and dogs, and some wild animals, notably armadillos and opossums.

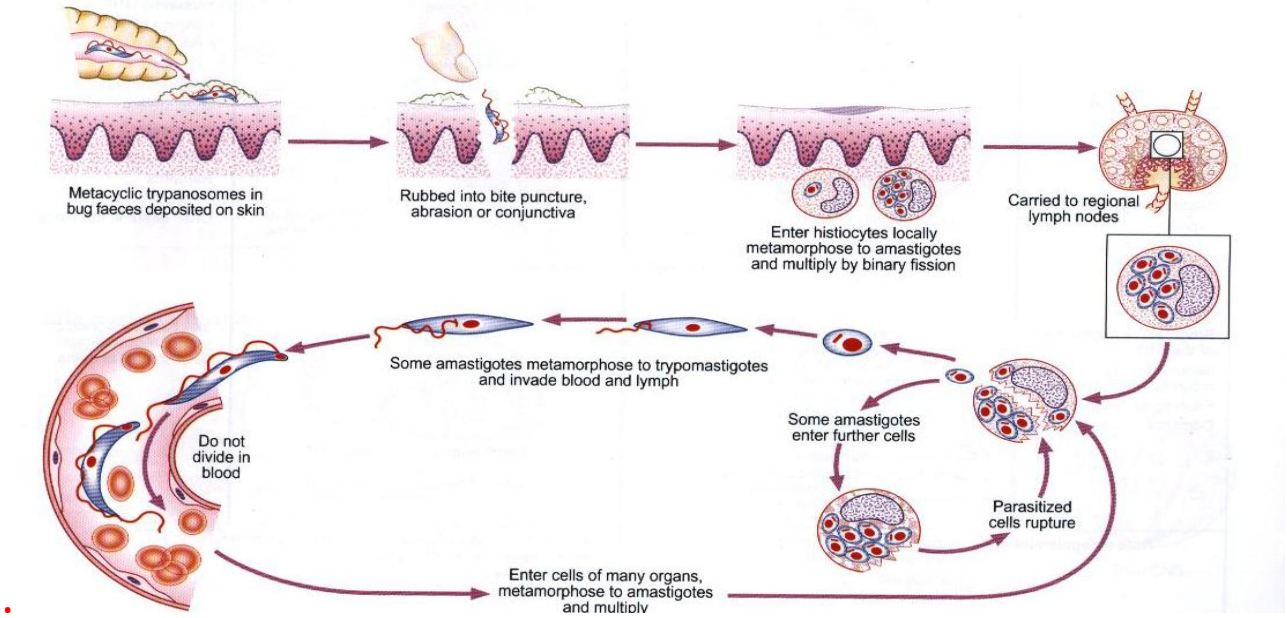
Morphology



Life cycle in insect



Life cycle in humans



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Symptoms: Chagas' disease can be divided into three stages: •

1-The primary lesion, •

2-The acute stage, and •

3Tthe chronic stage. •

The primary lesion, chagoma, appearing at the site of infection, within a few hours •
of bite, consists of a slightly raised, flat non purulent erythematous plaque

surrounded by a variable area of hard edema.

primary chagoma is usually found on the face, eyelids, cheek, lips or the conjunctiva

When the primary chagoma is on the face, there is an enlargement of the pre- and post-auricular and the sub maxillary glands on the side of the bite. Infection in the eyelid, resulting in a unilateral conjunctivitis and orbital edema (Ramana's sign) ,is the .commonest finding

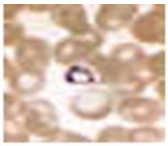
Acute Stage: The acute stage appears 7-14 days after infection. It is characterized byrestlessness, sleeplessness, malaise, increasing exhaustion, chills, fever and bone and muscle pains. Other manifestations of the acute phase are cervical, axillary and iliac adenitis; hepatomegaly; erythematous rash; and acute myocarditis.In children, it may cause meningo-encephalitis and coma.

Death occurs in 5-10 percent of infants.

Chronic Stage: The chronic disease results in an abnormal function of the hollow organs, particularly the heart, esophagus and colon. The cardiac changes include myocardial insufficiency, cardiomegaly, disturbances of atrio-ventricular conduction. Disturbances of peristalsis lead to megaesophagus and megacolon.

Treatment and Control: There is no curative therapy available. Most drugs are either ineffective or highly toxic. Recently two experimental drugs, Benznidazol and Nifurtimox have been used with promising results in the acute stage of the disease, however their side effects limit their prolonged use in chronic cases.

Control are limited to those that reduce contact between the vectors and man. Attempts to develop a vaccine have not been very successful, although they may be feasible



Trypanosoma cruzi,, trypomastigote form in a blood smear (Giemsa stain)

Riduvid bug, the vector of American trypanosomiasis

Ramana's sign: unilateral conjunctivitis and orbital edema

Megacolon in Chaga's disease

Body-fluid and tissue flagellates

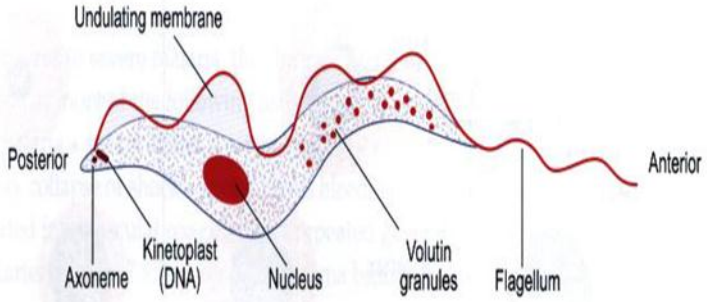
Classification

Phylum Euglenozoa

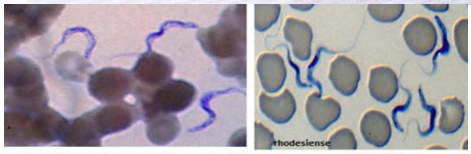
Class Kinetoplastidea

Live in bloodstream and tissues
Vector (blood-sucking invertebrates) required

Trypanosomatidae
Single flagellum



Morphological stages of the Trypanosomatidae affecting humans



blood smear from a patient with African trypanosomiasis. Thin blood smear stained with Giemsa. Typical trypomastigote stages (the only stages found in patients), with a posterior kinetoplast, a centrally located nucleus, an undulating membrane, and an anterior flagellum. The two Trypanosoma brucei species that cause human trypanosomiasis, T. b. gambiense and T. b. rhodesiense, are undistinguishable morphologically. The trypanosomes length range is 14-33 µm CDC