

جامعة الانبار

كلية : الصيدلة

قسم : الصيدلة

اسم المادة باللغة العربية: الطفيليات الطبية

اسم المدة باللغة الإنكليزية: **Medical Parasitology**

المرحلة: الثانية

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عنوان المحاضرة باللغة العربية: السوطيات الدموية (تريبانوسوما)

عنوان المحاضرة باللغة الإنكليزية: **Haemoflagelates (Trypanosomiasis)**

محتوى المحاضرة:

(HAEMOFLAGELATES)

Trypanosomiasis:-

Introduction:

Trypanosomes are hemoflagellates and three species of the genus *Trypanosoma* are responsible for disease in humans such as sleeping sickness. Trypanosomes occur in the blood of the majority of vertebrate animals. The life cycle involves intermediate host, which usually is an insect. Many species of trypanosomes can live in harmony with their hosts producing no pathogenic effect, but the best known species are those that are pathogenic to their definitive hosts. The disease is caused by the pathogenic types is called trypanosomiasis.

Salivarian Trypanosomes:

Trypanosoma brucei rhodesiense and *Trypanosoma brucei gambiense* - The metacyclic trypanosomes are found in the proboscis of the insect vector - infection is therefore inoculative. The above are the causative agents of African trypanosomiasis. It is a zoonotic species in that it multiplies in the blood of a range of many mammals including

man. *Trypanosoma brucei rhodesiense* causes acute sleeping sickness in East Africa, while *T. b. gambiense* causes chronic sleeping sickness in West Africa.

These are known as salivarian trypanosomes as they complete their development in the salivary system (anterior portion of the vector). Transmission takes place by inoculation of the metacyclic stage.

Stercorarian Trypanosomes:

Trypanosoma cruzi - The metacyclic trypanosomes occupy a posterior position in the gut of the insect vector and are passed out in the feces - infection is therefore contaminative. This is the causative agent of American Trypanosomiasis.

These trypanosomes are known as stercocarian as they complete their development in the posterior region of the vector, so that the infective forms appear in the insect's feces. Hosts are infected by the contaminative route.

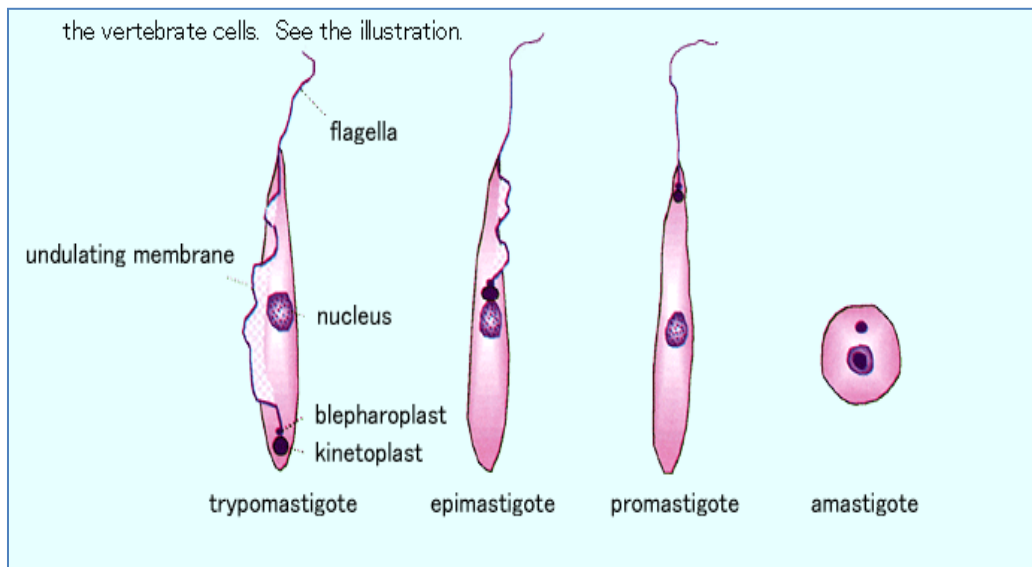
Etiologic agents:

Trypanosoma brucei complex – African trypanosomiasis (sleeping sickness)

Trypanosoma cruzi – American trypanosomiasis (Chagas' disease)

Important features:

These species may have **amastigote**, **promastigote**, **epimastigote**, and **trypomastigote** stages in their life cycle. In human trypanosomes of the African form, however, the amastigote and promastigote stages of development are absent. Typical trypanosome structure is an elongated spindle-shaped body that more or less tapers at both ends, a centrally situated nucleus, a kinetoplast posterior to nucleus, an undulating membrane arising from the kinetoplast and proceeding forward along the margin of the cell membrane and a single free flagellum at the anterior end.



African Trypanosomiasis:

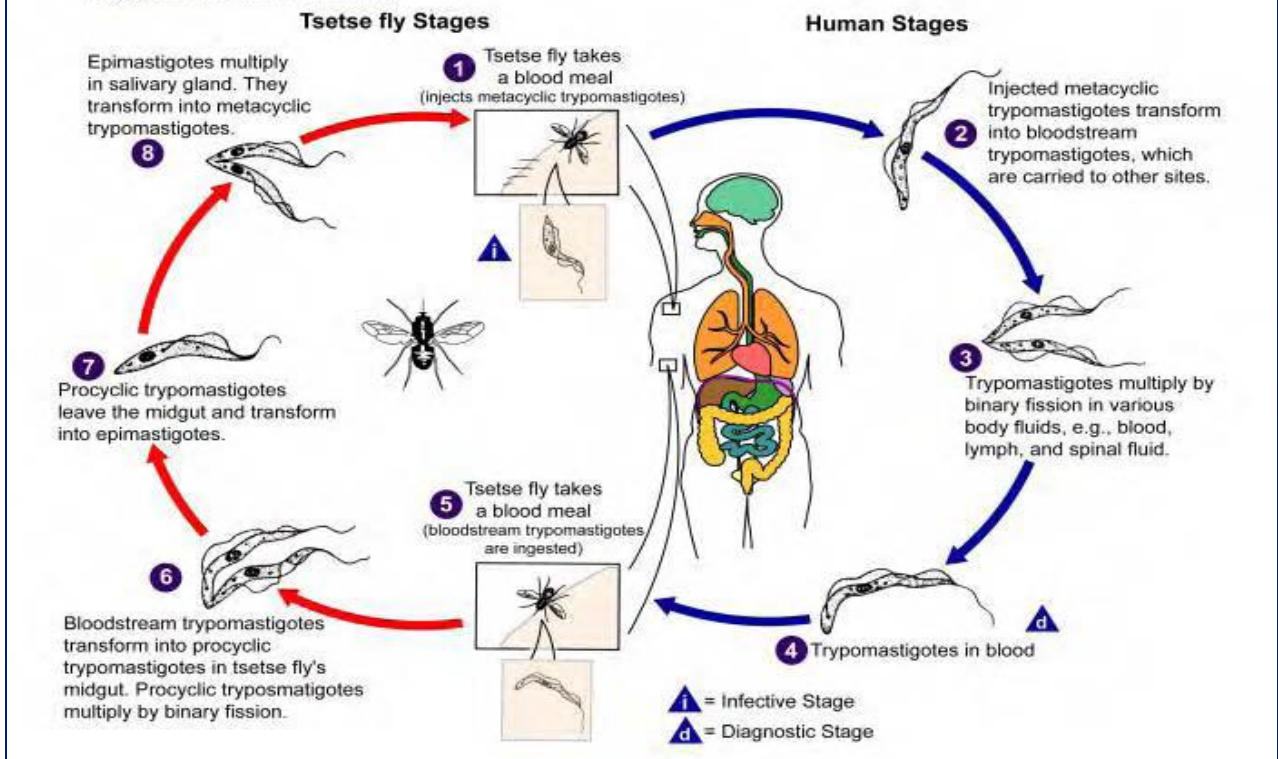
Life Cycle

Transmission from one vertebrate to another is carried out by blood-sucking invertebrates, usually an insect. The vector for African Trypanosomiasis is the Tsetse fly, *Glossina* spp. which cause the diseases *Trypanosoma brucei gambiense* and *Trypanosoma brucei rhodesiense*. Metacyclic (infective) trypomastigotes are inoculated through the skin when a tsetse fly takes a blood meal. The parasites develop into long slender trypomastigotes which multiply at the site of inoculation where ulceration occurs. The trypanosomes continue to develop and then may invade the lymphatic tissues, the heart, various organs and in later stages, the central nervous system. Trypomastigotes are taken up by the tsetse fly (male and female) during a blood meal. The parasites develop in the midgut of the fly where they multiply. 2-3 weeks later the trypomastigotes move to the salivary glands transforming from epimastigotes into metacyclic (infective) trypomastigotes. The tsetse fly remains infective for life i.e. about three months.

Sleeping Sickness, African (African trypanosomiasis)

(*Trypanosoma brucei gambiense*)

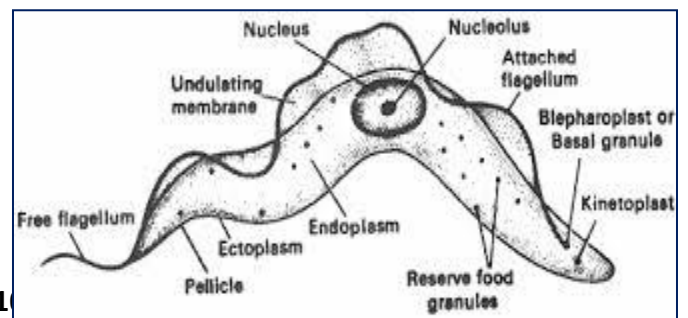
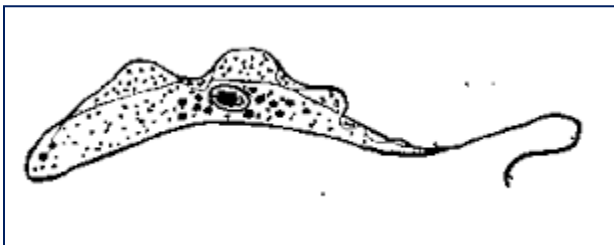
(*Trypanosoma brucei rhodesiense*)



Morphology

The parasite is an elongated cell with single nucleus which usually lies near the centre of the cell. Each cell bears a single flagellum which appears to arise from a small granule - the kinetoplast. The kinetoplast is a specialized part of the mitochondria and contains DNA. The length and position of the trypanosome's flagellum is variable. In trypanosomes from the blood of a host the flagellum originates near the posterior end of the cell and passes forward over the cell surface, its sheath is expanded and forms a wavy flange called an undulating membrane. Development is characterized by the occurrence of three types of blood forms (polymorphic), **these are:**

- 1) Slender forms:** long and thin, about 29µm long, free flagellum.
- 2) Stumpy forms:** thick and short, average length 18µm, typically no free flagellum, but a short one may be present.
- 3) Intermediate forms:** about 23µm long with a moderately thick body and a free flagellum of medium length.



Pathogenesis

The trypomastigotes spread from the skin through the blood to the lymph node and the brain. The typical somnolence (sleeping sickness) usually progresses to coma as a result of demyelinating encephalitis. In acute form, cyclical fever spike (approximately every 2 weeks) occurs that is related to antigenic variation. As antibody mediated agglutination and lysis of the trypomastigotes occurs, the fever subsides. With a few remains of antigenic variants new fever spike occurs and the cycle repeats itself over a long period.

Clinical features

Although both species cause sleeping sickness, the progress of the disease is different. *T.gambiense* induced disease runs a low-grade chronic course over a few years. One of the earliest signs of disease is an occasional ulcer at the site of the fly bite. As reproduction of organisms continues, the lymph nodes are invaded, and fever, myalgia, arthralgia, and lymph node enlargement results. Swelling of 56 the posterior cervical lymph nodes is characteristic of Gambian sleeping sickness and is called winterbottom's sign.

Chronic disease progresses to CNS involvement with lethargy, tremors, meningoencephalitis, mental retardation, and general deterioration. In the final stages, convulsions, hemiplegia, and incontinence occur. The patient becomes difficult to arouse or obtain a response from, eventually progressing to a comatose state. Death is the result of CNS damage and other infections, such as pneumonia.

In *T.rhodesiense*, the disease caused is a more acute, rapidly progressive disease that is usually fatal. This more virulent organism also develops in greater numbers in the blood. Lymphadenopathy is uncommon, and early in the infection, CNS invasion occurs, resulting in lethargy, anorexia, and mental disturbance. The chronic stages described for *T.gambiense* are not often seen, because in addition to rapid CNS disease, the organism produces kidney damage & myocarditis, leading to death.

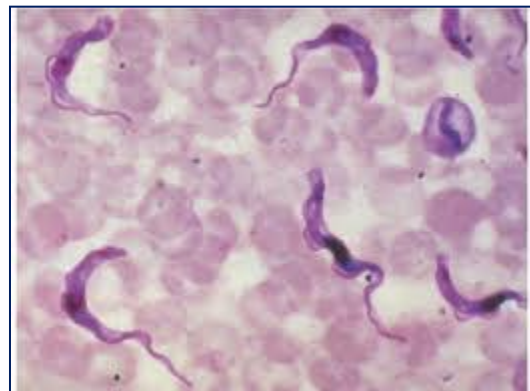
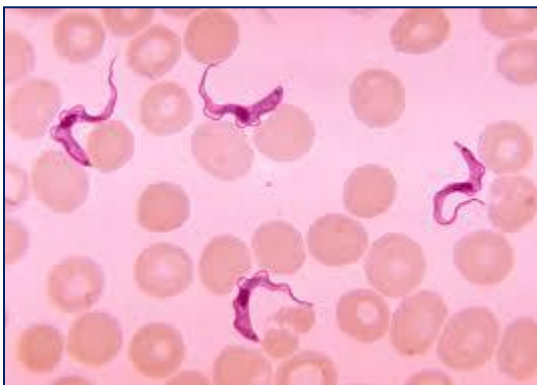


Immunity

Both the humoral and cellular immunity involve in these infections. The immune responses of the host to the presence of these parasites, however, is faced with antigenic variation, in which organisms that have changed their antigenic identity can escape the host immune response and initiate another disease process with increased level of parasitemia.

Laboratory Diagnosis of African trypanosomiasis

Examination of thin and thick films, in concentrated anticoagulated blood preparations, in aspiration from lymph nodes and concentrated spinal fluid. Methods for concentrating parasites in blood may be helpful approaches including centrifugation of heparinized samples and an ion-exchange chromatography. Levels of parasitosis vary widely, and several attempts to visualize the organism over a number of days may be necessary.



Treatment:

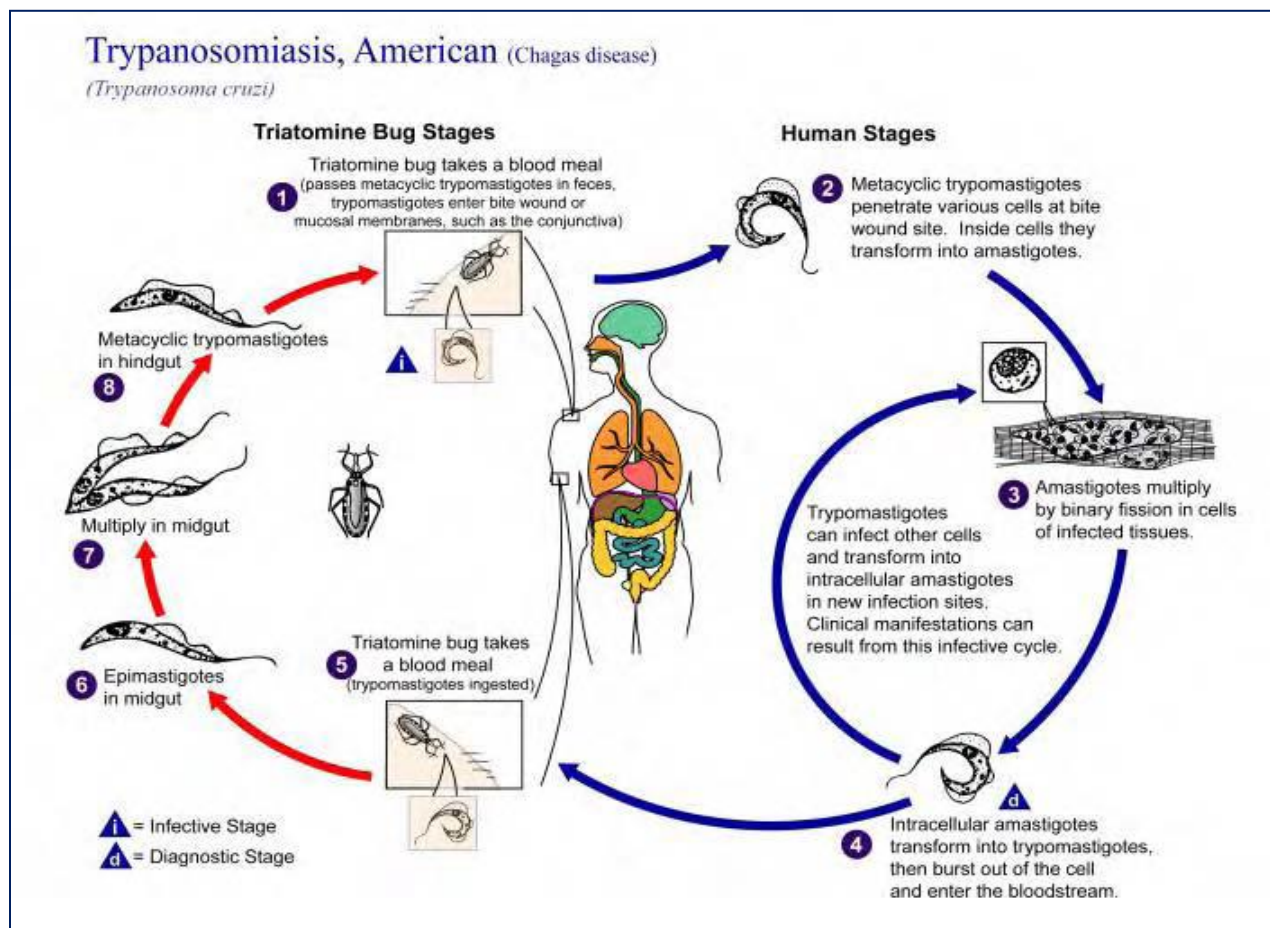
The same treatment protocol is applied for these parasites. For the acute stages of the disease the drug of choice is **suramin with pentamidine** as an alternative. In chronic disease with CNS involvement, the drug of choice is **melarsoprol**. Alternatives include trypars amide combined with suramin.

Prevention:

- Control of breeding sites of tsetse flies and use of insecticides.
- Treatment of human cases to reduce transmission to flies.
- Avoiding insect bite by wearing protective clothing & use of screen, bed netting and insect repellants.

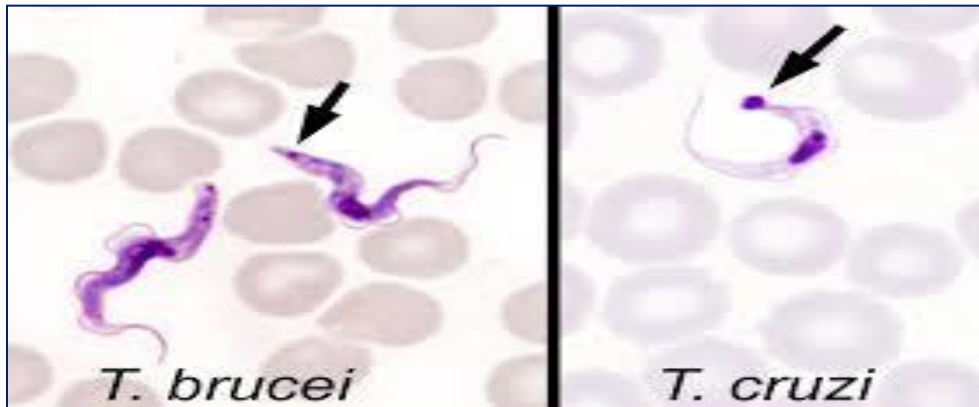
American trypanosomiasis

Trypanosoma cruzi is a pleomorphic trypanosome that includes an additional form of amastigote in its life cycle. The vector for transmission is reduviid bugs.



Morphology

Trypanosoma cruzi has a single form (monomorphic), about 20µm in length, and characteristically curved. The kinetoplast is large, considerably larger than the *Trypanosoma brucei* species already discussed. They sometimes appear as a bulge at the posterior end. The flagellum is medium in length.



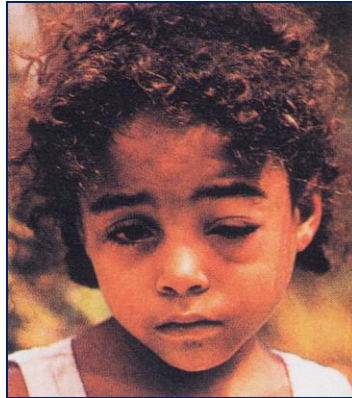
Pathogenesis

During the acute phase, the organism occurs in blood as a typical trypomastigote and in the reticuloendothelial cells as a typical amastigote. The amastigotes can kill cells and cause inflammation, consisting mainly of mononuclear cells. Cardiac muscle is the most frequently and severely affected tissue. In addition, neuronal damage leads to cardiac arrhythmias and loss of tone in the colon (megacolon) and esophagus (megaesophagus). In the chronic phase, the organism persists in the amastigote form.

Clinical features

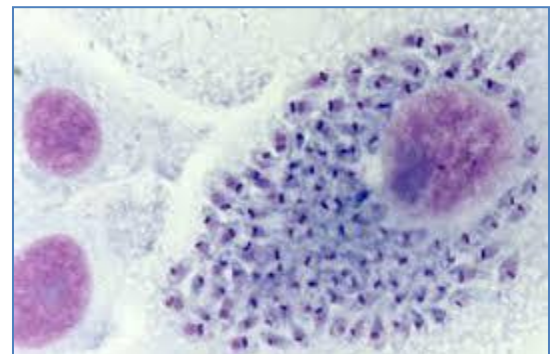
Chagas' disease may be asymptomatic acute or chronic disease. One of the earliest signs is development at the site of the bug bite of an erythematous and indurated area called a chagoma. This is often followed by a rash and edema around the eyes and face; in young children frequently an acute process with CNS involvement may occur. Acute infection is also characterized by fever, chills, malaise, myalgia, and fatigue. The chronic Chagas' disease is characterized by hepatosplenomegaly, myocarditis, and enlargement of the esophagus and colon as a result of the destruction of nerve cells (E.g. Auerbach's plexus) and other tissues that control the growth of these organs. Involvement of the CNS may

produce granulomas in the brain with cyst formation and a meningoencephalitis. Death from chronic Chagas' disease results from tissue destruction in the many areas invaded by the organisms, and sudden death results from complete heart block and brain damage.



Laboratory Diagnosis of American Trypanosomiasis

Examine thin or thick stained preparations for trypomastigotes. Wet preparations should also be examined to look for motile organisms that leave the blood stream and become difficult to find. Biopsy of lymph nodes, liver, spleen, or bone marrow may demonstrate organisms in amastigote stage. Xenodiagnosis - This 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.



Immunity

Unlike African trypanosomiasis, the antigenic variation is less common in *T.cruzi* infection. Therefore, the humoral and cellular immune responses function in the immune system.

Treatment

The drug of choice is **nifurtimox**. Alternative agents include **allopurinol** & **benzimidazole**.

Prevention

- Bug control, eradication of nests
- Treating infected person & exclusion of donors by screening blood.
- Development of vaccine.