VISCERAL LEISHMANIASIS & AFRICAN TRYPANOSOMIASIS

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General Characters of Blood & Tissue Flagellates (*Leishmania* & *Trypanosoma*)

1)Live in blood and tissues.

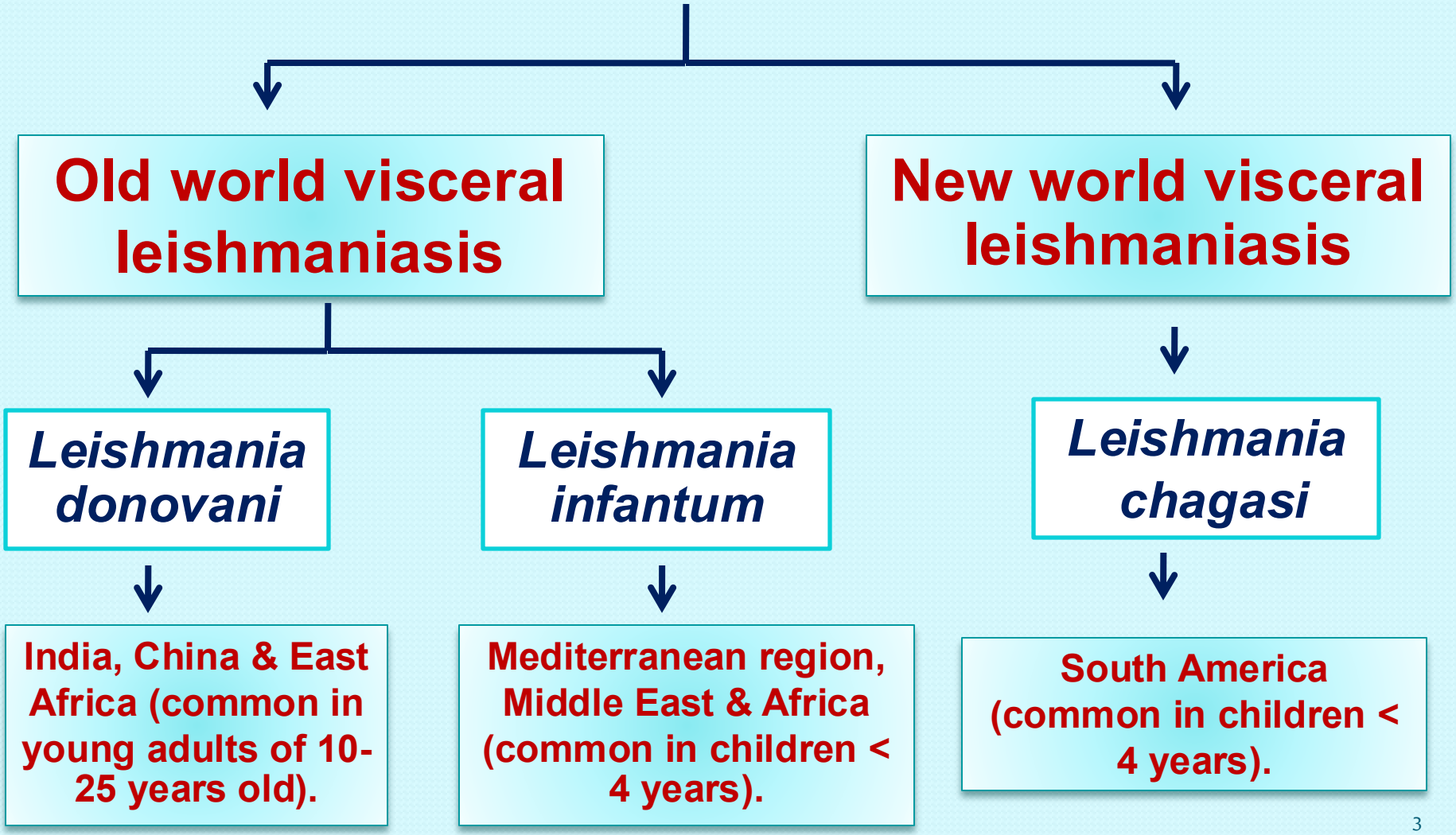
2) Move by one flagellum.

3) Need vector for transmission.

4) Require 2 hosts (vertebrate and invertebrate).

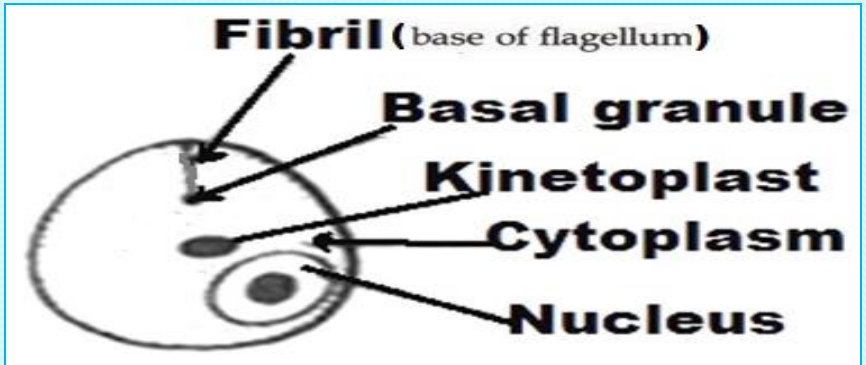
Visceral Leishmaniasis

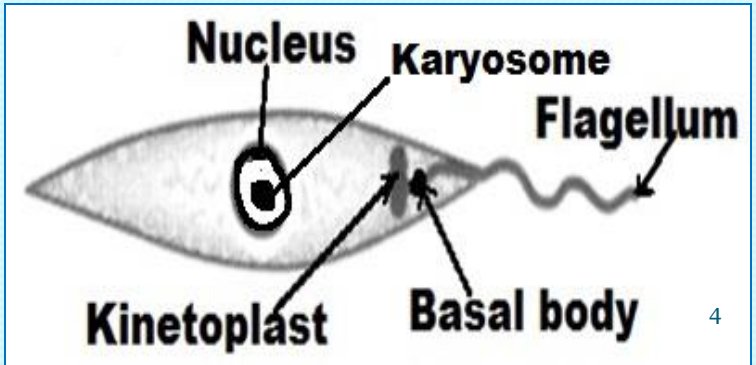
(Kala azar, Dum dum fever, Black sickness)



Morphological characters

	1- Amastigote	2- Promastigote
Shape:	Oval	Fusiform or spindle
Kinetoplast:	Beside the nucleus	At the anterior end
Flagellum:	Absent	Present
Nucleus:	-Eccentric with central Karyosome	-Central with central Karyosome
Habitat:	-Intracellular (macrophage) -Tissue culture	-Midgut of the insect -Culture media(NNN)





❖ **Definitive host:** Man.

❖**Reservoir host:** Dogs & rodents.

❖**Vector:** Female sand fly (*Phlebotomus* for OWVL & *Lutzomyia* in NWVL)

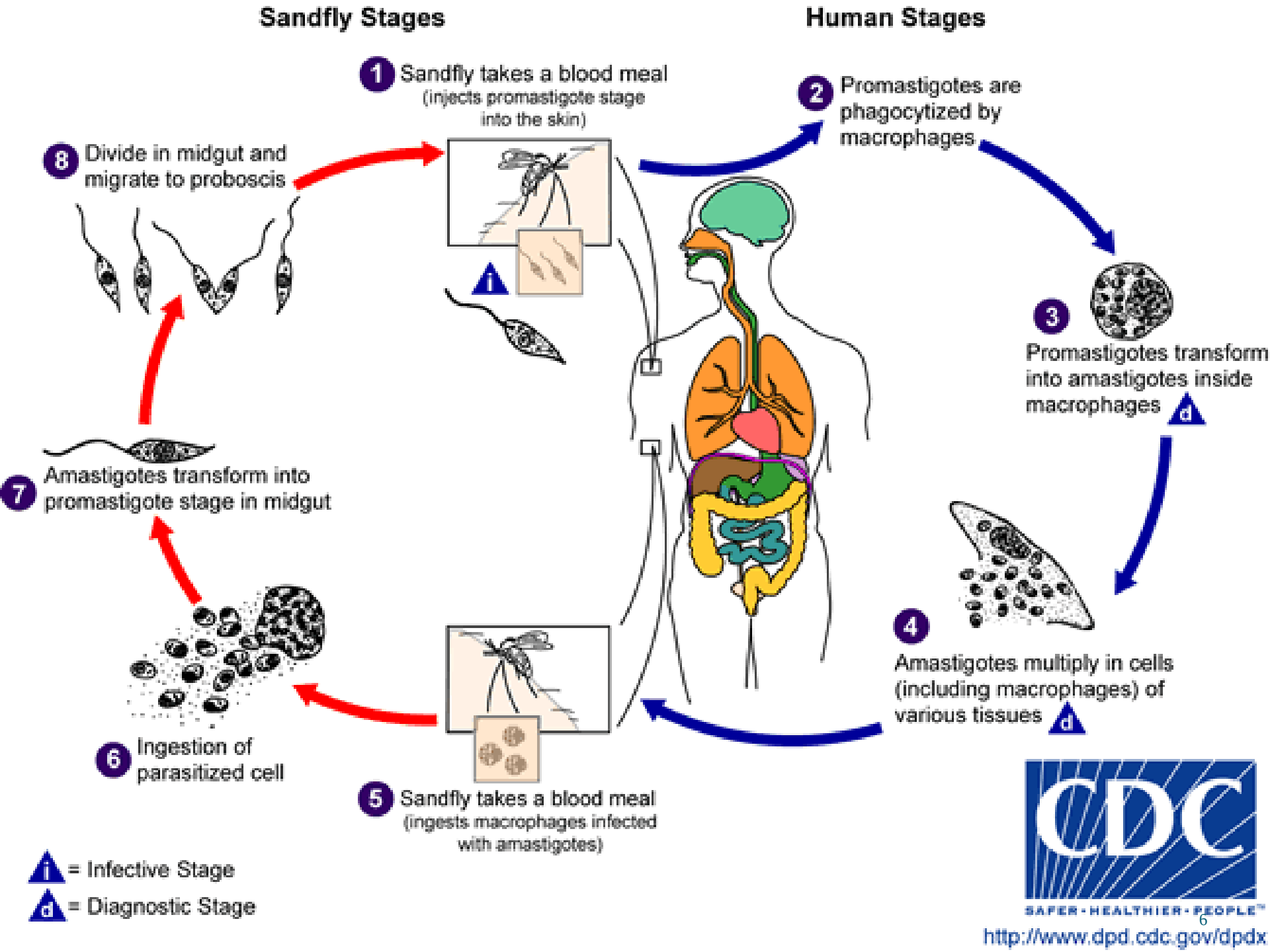
❖ **Infective stage:** Metacyclic promastigotes in the mouth parts of female sand fly.

Mode of transmission

1-Bite of infected sand fly.

2- Blood transfusion.

3- Congenital transmission.



http://www.dpd.cdc.gov/dpdx

Pathogenesis

Amastigotes multiply inside the macrophages ➲ the cells rupture ➲ the organisms pass to the blood and reach viscera ➲ invade and multiply in different organs (ex. Spleen, liver, lymph nodes, bone marrow, skin & intestine) ➲ hyperplasia and enlargement of the affected organs.

❖N.B: Visceral leishmaniasis is one of the opportunistic infections noted in AIDS patients.

Clinical pictures

1)Local lesion (leishmanioma):
A small papule at the site of insect bite.

2)Systemic manifestations

1-Fever

↓

Intermitted with double or triple daily rise

2- Hepatomegaly, splenomegaly and lymph node enlargement

3- Diarrhoea or dysentery with ulceration of the intestine ➲ malabsorption

4- Oedema & ascites due to liver and kidney affection (decrease albumin).

5- Loss of weight & cachexia especially in thorax & shoulder girdle

2)Systemic manifestations

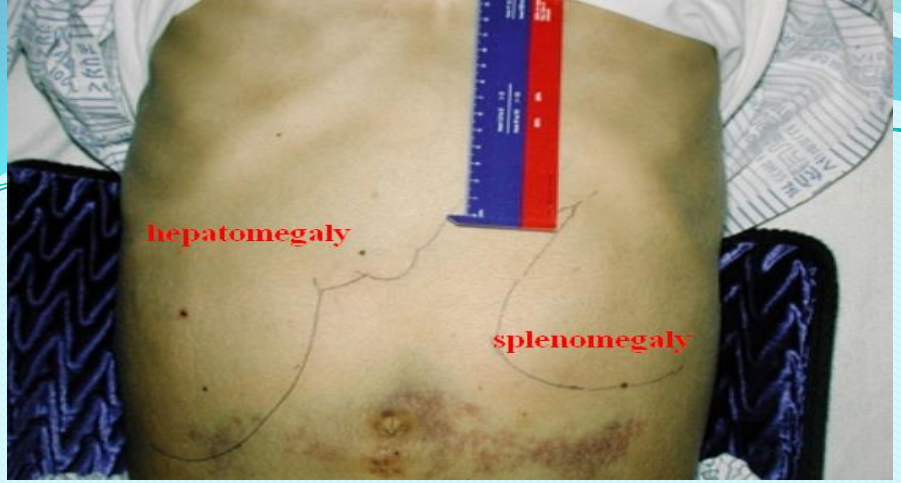
6-Skin lesions

Pigmented skin patches early in the disease ➲ the skin turns dark (so the disease is called **Kala azar or black sickness**).

Depigmented macular, papular or nodular skin lesions on the face, trunk & extremities **(Post-kala azar dermal leishmanoid)** It appears later (few months in Africa and several years in India) after successful treatment & recovery from the disease **without other systemic signs.** Its nodules may be mistaken for **lepromatous leprosy**.

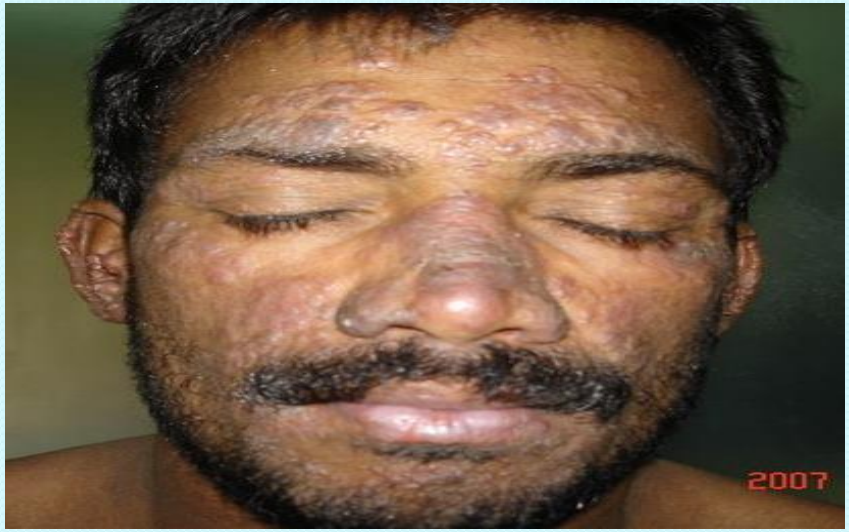
7-Congenital transmission
➲ abortion

8-Pancytopenia:
Anaemia (hypoplastic), **leucopenia** & **thrombocytopenia** due to invasion and depression of bone marrow.

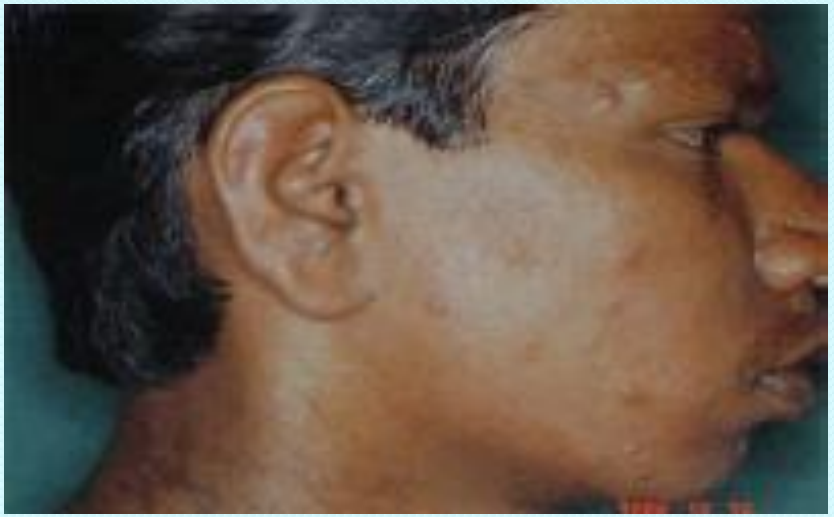


Hepatosplenomegaly

Lymph nodes enlargement



Post kala azar



Pigmented skin

❖**Death occurs in untreated severe cases due to:**

➢**Organ failure and wasting.**

➢**Secondary bacterial infection as pneumonia, tuberculosis due to suppression of the cellular immunity by the parasite.**

➢**Septicemia, severe anaemia and haemorrhage.**

✍**N.B. Visceral leishmaniasis is followed by lifelong immunity.**

Laboratory diagnosis

Direct methods

Examination of blood, biopsy from (liver, spleen, LNs) or bone marrow puncture for detection of the parasite by:

1- Smear to detect amastigotes

2- Culture on N.N.N medium➲ for 2-3 weeks ➲ motile promastigotes.

3- Animal inoculation: Intraperitoneal inoculation of the specimen into hamster. Amastigotes are detected in smears from a splenic aspiration.

Indirect methods

Specific tests (immunodiagnosis)

- leishmanin or Montenegro test (IDT): -ve due to supression of T.cells & +ve after recovery .
- Serological tests: CFT, IHAT, ELISA,➲ to detect anti-leishmania antibodies.
- PCR

Blood picture

Anaemia, leucopenia & thromocytopenia

Treatment

General (supported treatment)

- Proper diet rich in proteins, vitamins and iron.
- Blood transfusion for severe anaemia.
- Splenectomy.
- Antibiotics for secondary infection.

Specific treatment

Parenteral therapy

- Sodium stibogluconate (Pentostam).
- Pentamidine, Amphotericin B, Paromomycin

Oral therapy

Miltefosine

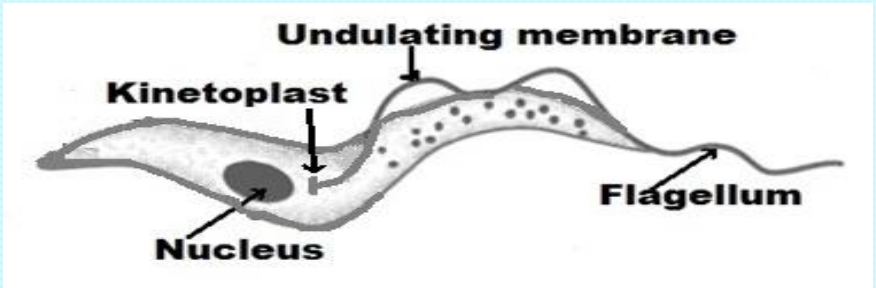
African Trypanosomiasis

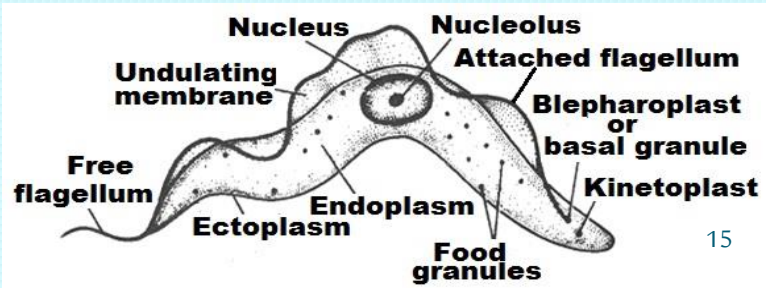
(polymorphic trypanosomes)

Trypanosoma gambiense	*Trypanosoma rhodesiense*
Chronic West African sleeping sickness (Gambian trypansomiasis)	Acute East African sleeping sickness (Rodesian trypanosomiasis
Transmitted by *Glossina palpalis* (both male and female)	Transmitted by *Glossina morsitans* (both male and female)

Morphological characters

	1- Epimastigote	2- Trypomastigote
Shape:	Fusiform or spindle	Fusiform or spindle
Kinetoplast:	Anterior to the nucleus	At the posterior end
Flagellum:	Present	Present
Nucleus:	- Slightly moved posterior	-Central with central Karyosome
Undulent membrane	-Short	- Long
Habitat:	- In the salivary glands of vector - Culture media	- Blood and lymphatics - In vector



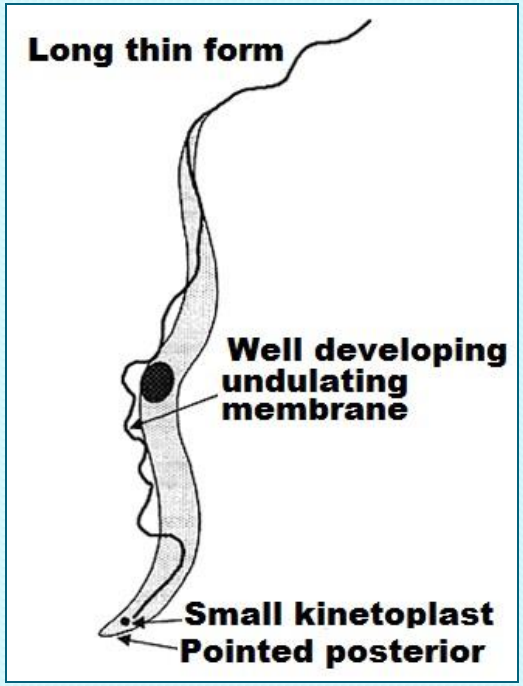


In the blood,trypomastigote (*Trypanosoma*) has different shapes:

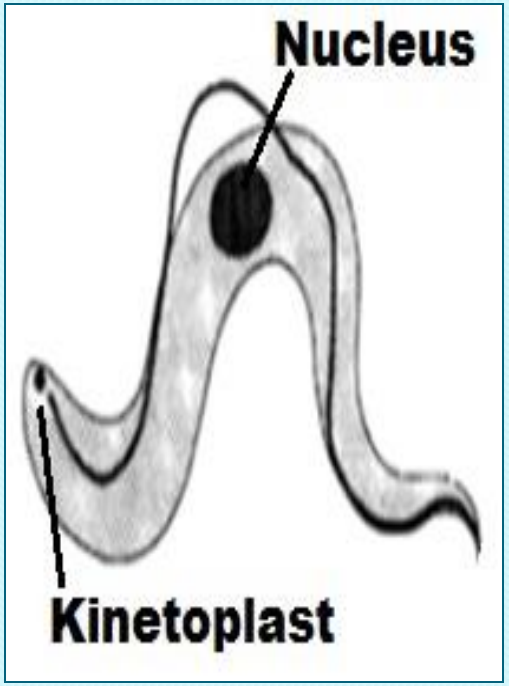
1- Long slender form (30 µm), active and with long free flagellum.

2- Short stumpy form (15µm), sluggish in motility and without free flagellum.

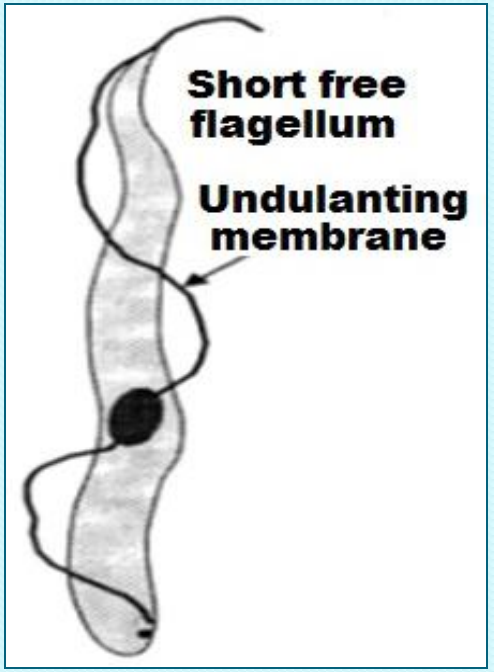
3-Intermediate form (20µm), with a short free flagellum.



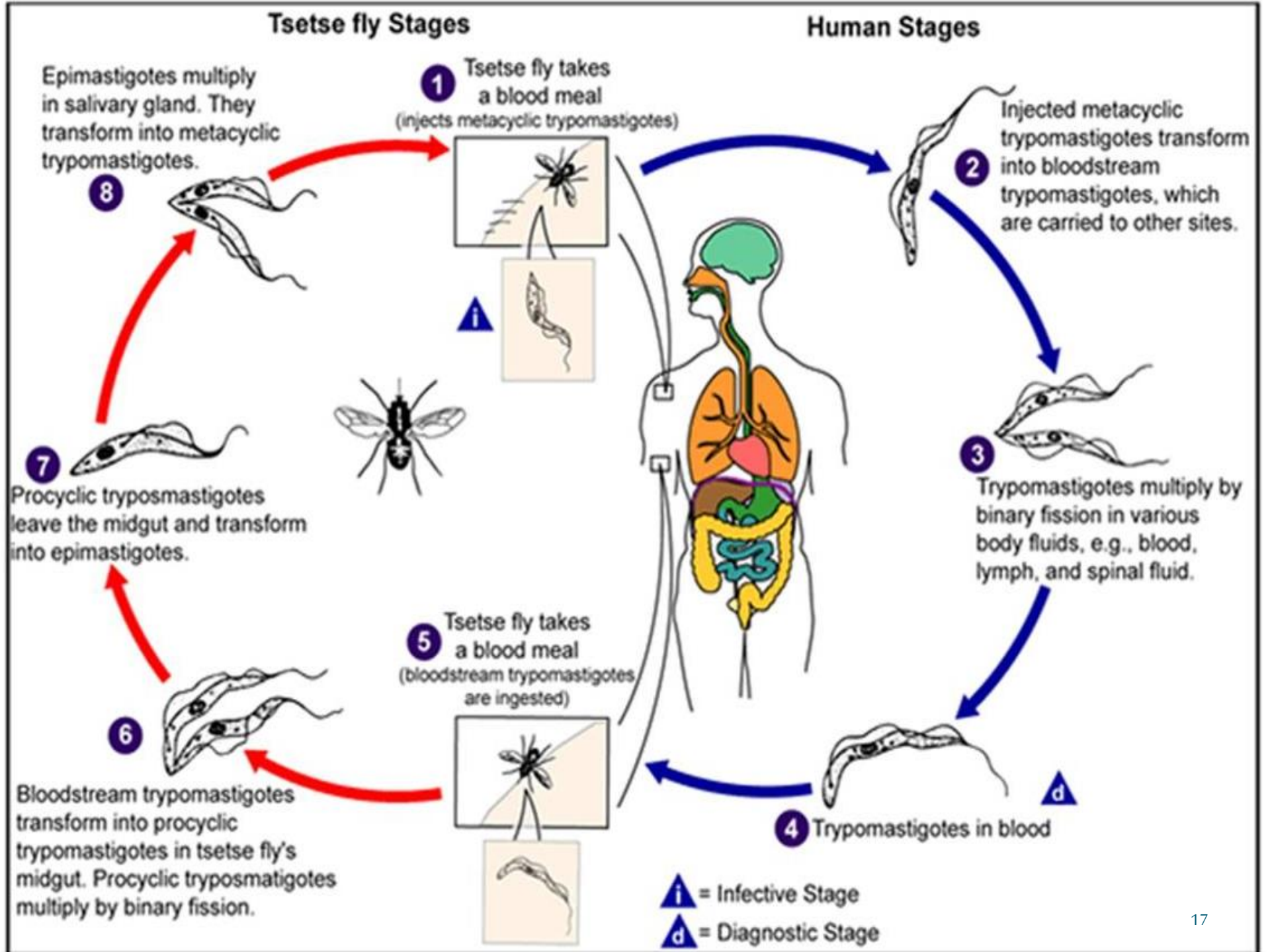
Long form



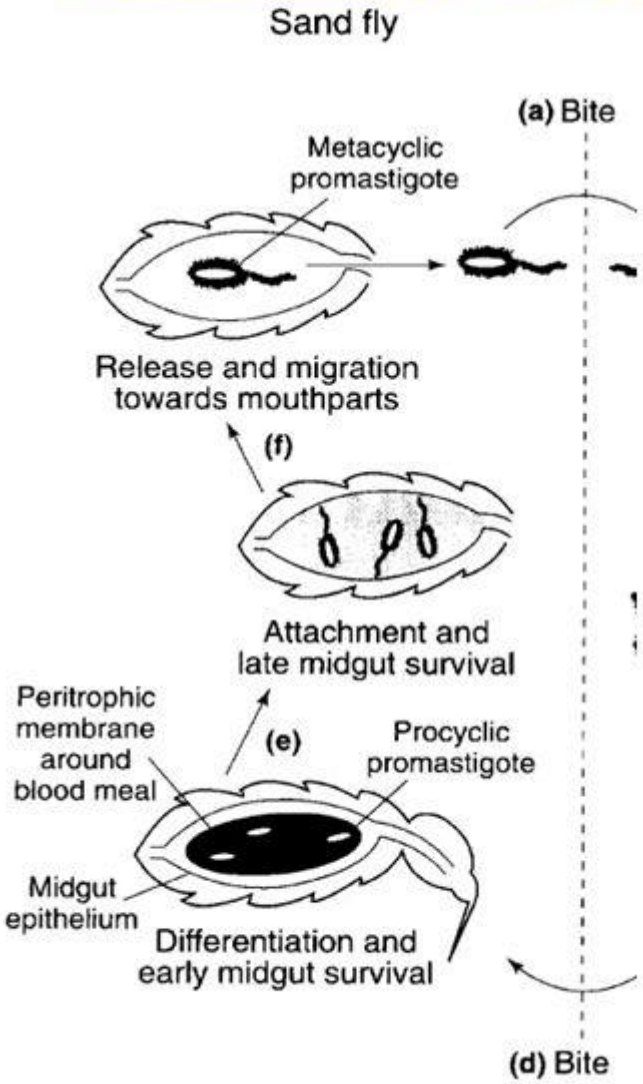
Short form



Intermediate form


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
2 Injected metacyclic trypomastigotes transform into bloodstream trypomastigotes, which are carried to other sites.
3 Trypomastigotes multiply by binary fission in various body fluids, e.g., blood, lymph, and spinal fluid.
d
4 Trypomastigotes in blood
5 Tsetse fly takes a blood meal
(bloodstream trypomastigotes are ingested)
6 Bloodstream trypomastigotes transform into procyclic trypomastigotes in tsetse fly's midgut. Procyclic tryposmatigotes multiply by binary fission.
7 Procyclic tryposmastigotes leave the midgut and transform into epimastigotes.
i = Infective Stage
d = Diagnostic Stage

procyclics and metacyclics



- Infected macrophages are taken up with the blood meal and amastigotes released by digestion transform into procyclic promastigotes which attach to the midgut epithelium
- Attached promastigotes divide rapidly
- Metacylcic promastigote detach and pass forward into the pharynx from where they are regurgitated into the bite site

Mode of transmission

- Bite of infected *Glossina* (Tsetse fly).
- Blood transfusion.
- Congenital transmission.
- Sexual transmission may be possible.
- Accidental infections in laboratories due to pricks from infected needle.

N.B. Infective stage: **Metacyclic trypomastigotes** in salivary glands of the vector.

	Trypanosoma gambiense	*Trypanosoma rhodesiense*
G.D:	West and Central Africa	Eastern parts of Africa
D.H:	Man	Man
R.H:	Cattle, pigs and goats	Wild animals

Pathogenesis and symptomatology of gambian trypanosomiasis

The disease has 3 stages

↓

1-Chancer
(primary lesion at the site of bite)

- Firm painful nodule➲ulcerate with oedema and erythema after few days of biting.
- After 3 weeks the parasite invades the lymphatic system and blood.

2-Haemolymphatic stage

Invasion of the blood

- Fever, headache, joint pains, muscle pain, malaise and itching (skin rash).
- Toxic depression of bone marrow ➲ anaemia (hypoplastic), leukopenia & thrombocytopenia.

Invasion of lymphatic system

- LNs enlargement especially cervical lymph nodes in the posterior triangle of the neck (Winterbottom's sign).
- Hyperplasia ➲hepatomegaly & splenomegaly.
- Hypersplenism ➲ anaemia and thrompocytopenia

3-Neurological stage
(Sleeping sickness syndrome)

The parasite invades the CNS after one year or more by passing through the blood brain barrier ➲ multiply there ➲ petechial haemorrhage ➲ atrophy of nerve cells ➲ chronic meningoencephalitis

Manifested by

Fever, severe headache, nausea, vomiting, neck rigidity, mental dullness, apathy, reduced coordination, convulsion, paralysis and all day and night sleeping.

Without treatment, the disease is fatal with progressive mental deterioration leading to **coma and death** either from the disease or from intercurrent secondary infections as malaria & pneumonia

✍**N.B.** Damage caused in the neurological stage is irreversible.

Rodesian trypanosomiasis

It differs from gambian trypanosomiasis in :

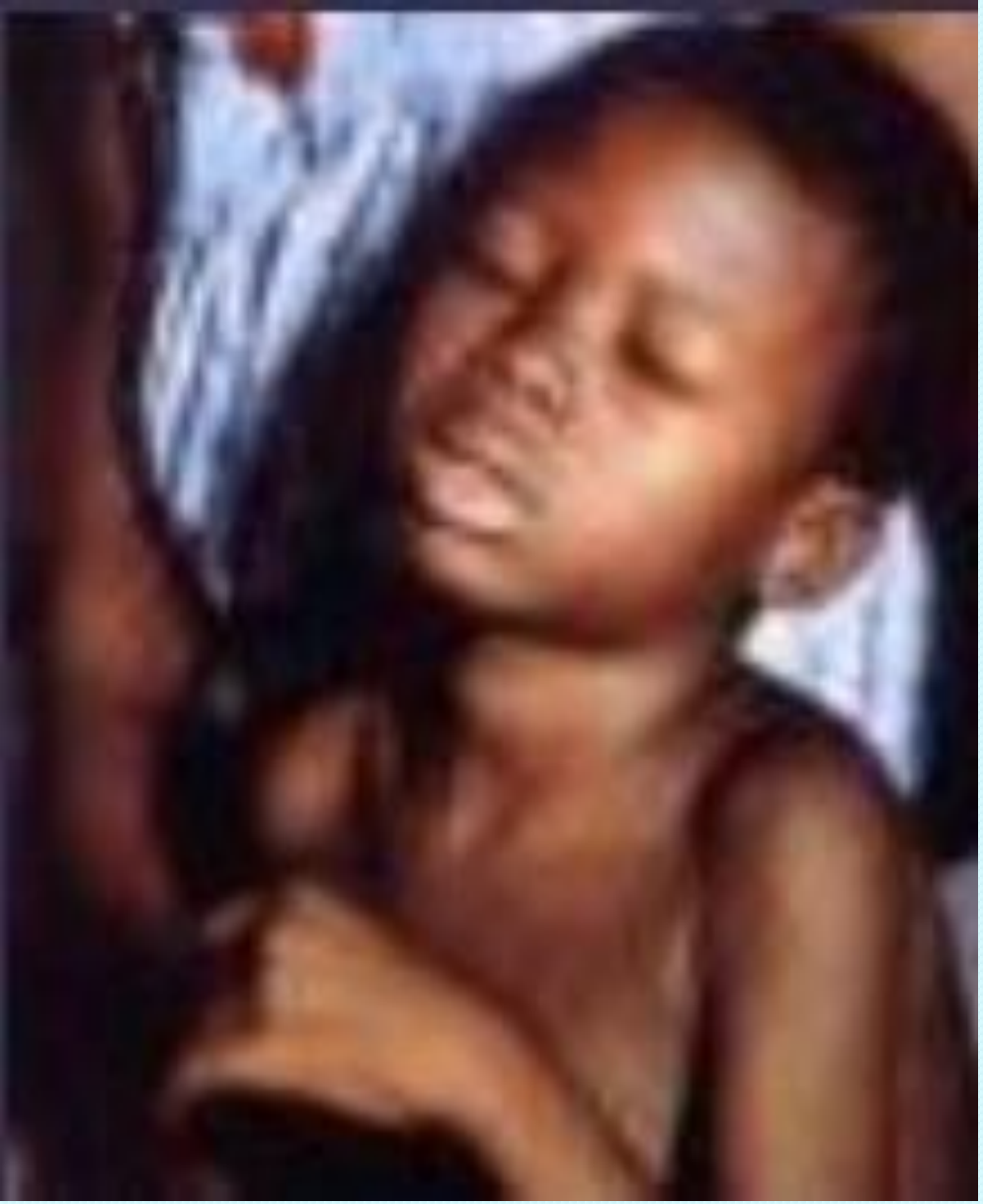
-Short incubation period (in gambian, 2 ws to several months) .

-More acute and fatal course than Gambian sleeping sickness. The patient dies before the cerebral stage develops.

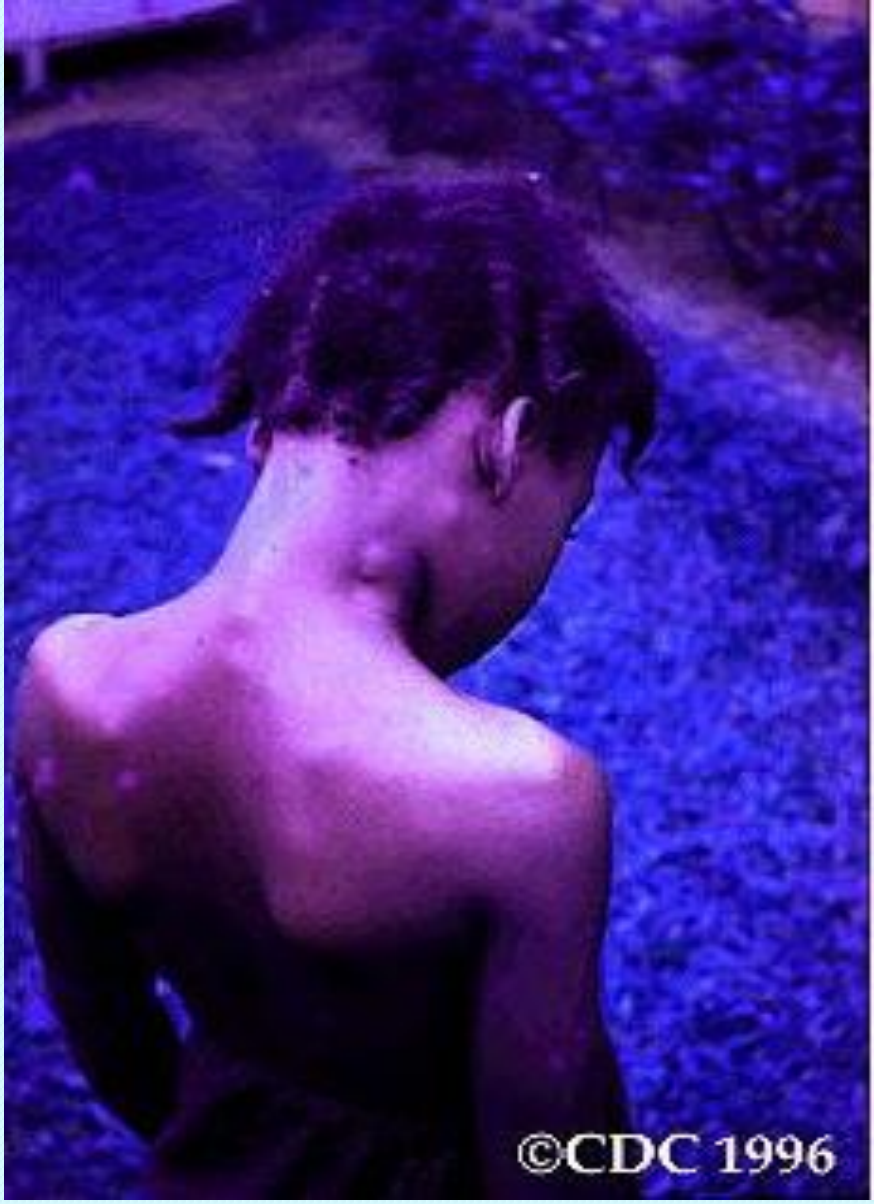
-Fever is more frequent, severe anaemia, myocarditis and jaundice.

-Lymph nodes involvement is less and Winterbottom's sign may be absent.

-Death occurs due to arrythmia and heart failure.



Sleeping sickness



Winterbottom's sign.

Laboratory diagnosis

Direct methods

Detection of trypomastigotes in blood, lymph nodes aspiration, fluid aspirated from chancre, bone marrow puncture (sternum) and CSF by:

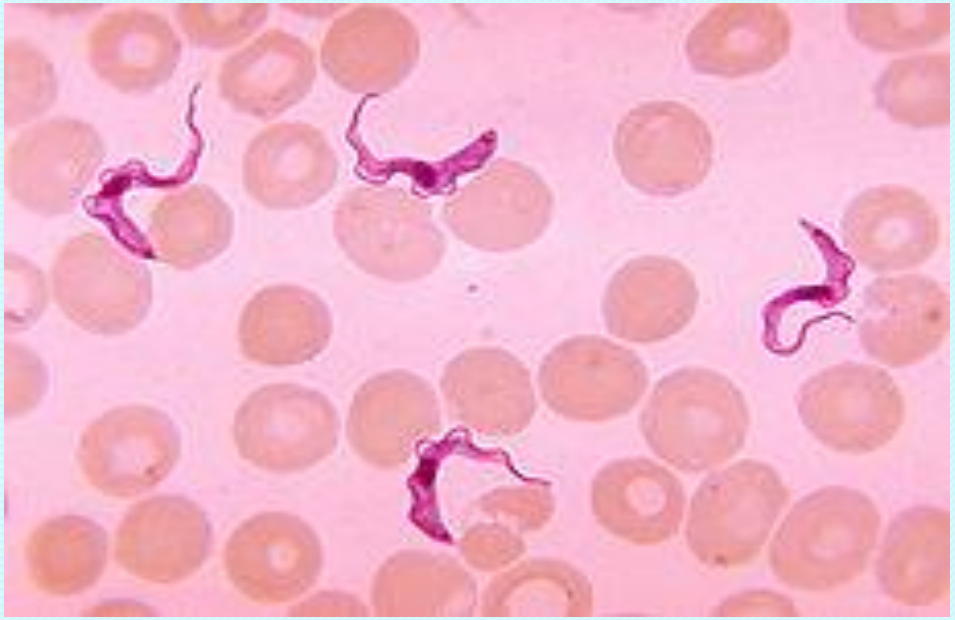
1- Microscopic examination of stained and unstained films.

2- Culture on NNN medium ➲ epimastigotes.

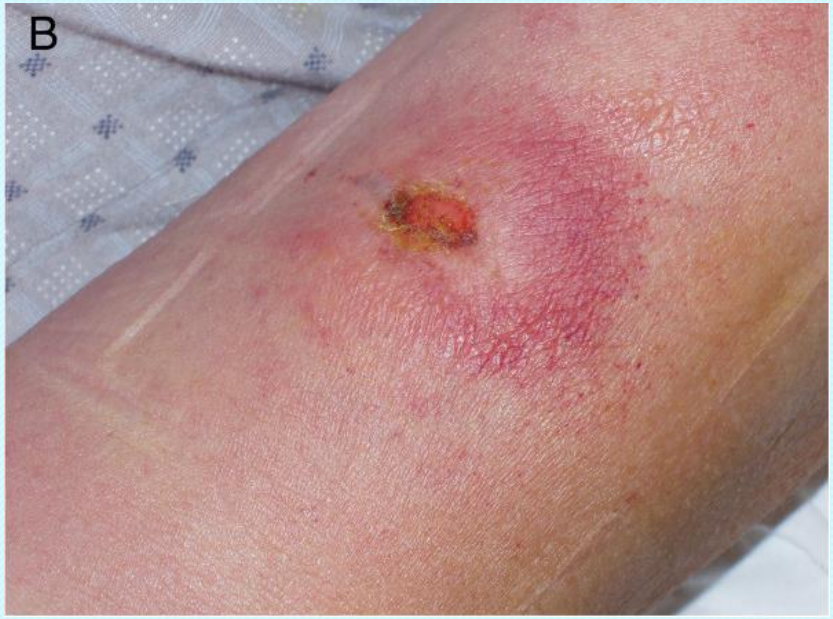
3- Animal inoculation: susceptible to *T. rhodesiense*

Indirect methods

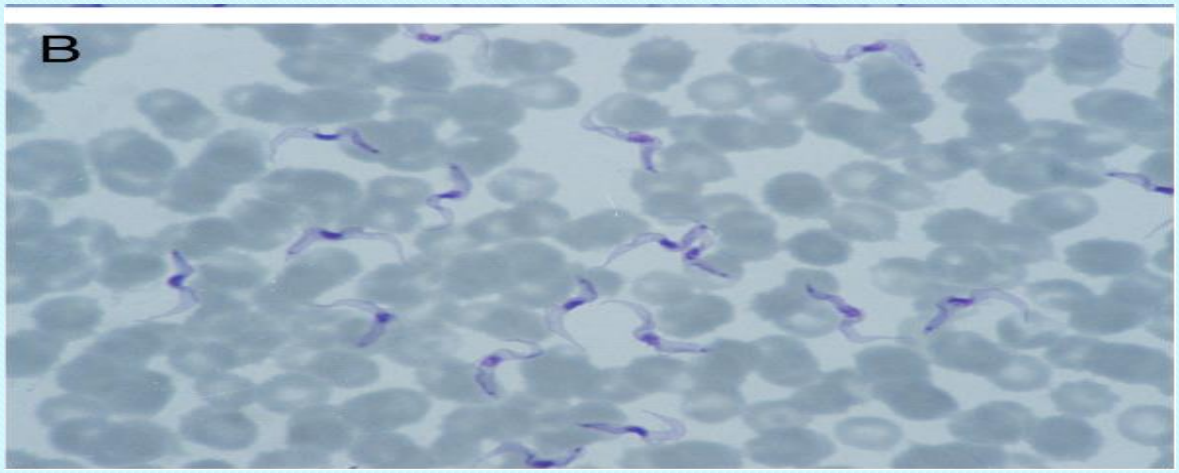
- **Serological tests:** ELISA.
- **Serum IgM:** Always elevated in the blood and CSF due to antigenic variation of the trypanosome (changing its antigenic coat) to escape from host immune response (evasion).
- **Blood examination:** Anaemia, leucopenia and thrombocytopenia



Polymorphic trypanosomes



Chancer



T. rhodesinse

Treatment

1- Early stage treatment (haemolymphatic stage)

Suramin.

Pentamidine.

2- Late stage treatment (Cerebral stage)

- **Melarsoprol.**
- **Tryparsamide.**
- **Eflornithine (New drug): It is effective in the treatment of *T. gambiense* only.**

✍**N.B. *T. rhodesiense* is more resistant to treatment**


ThankYou