Blood & Tissue Flagellates

(*Leishmania* & *Trypanosoma*)

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protozoa

- The tissue and blood protozoa include the apicomplexan (without flagella, cilia, or pseudopods.
  - ❑Plasmodium spp
  - ❑ Babesia spp
  - ❑Toxoplasma gondii
- The flagellates
  - ❑Leishmania spp
  - ❑Trypanosoma spp.
  - ❑Trichomonas vaginalis
- The free-living amebae
  - ❑Naegleria fowleri
  - ❑Acanthamoeba spp
  - ❑Balamuthia mandrillaris.

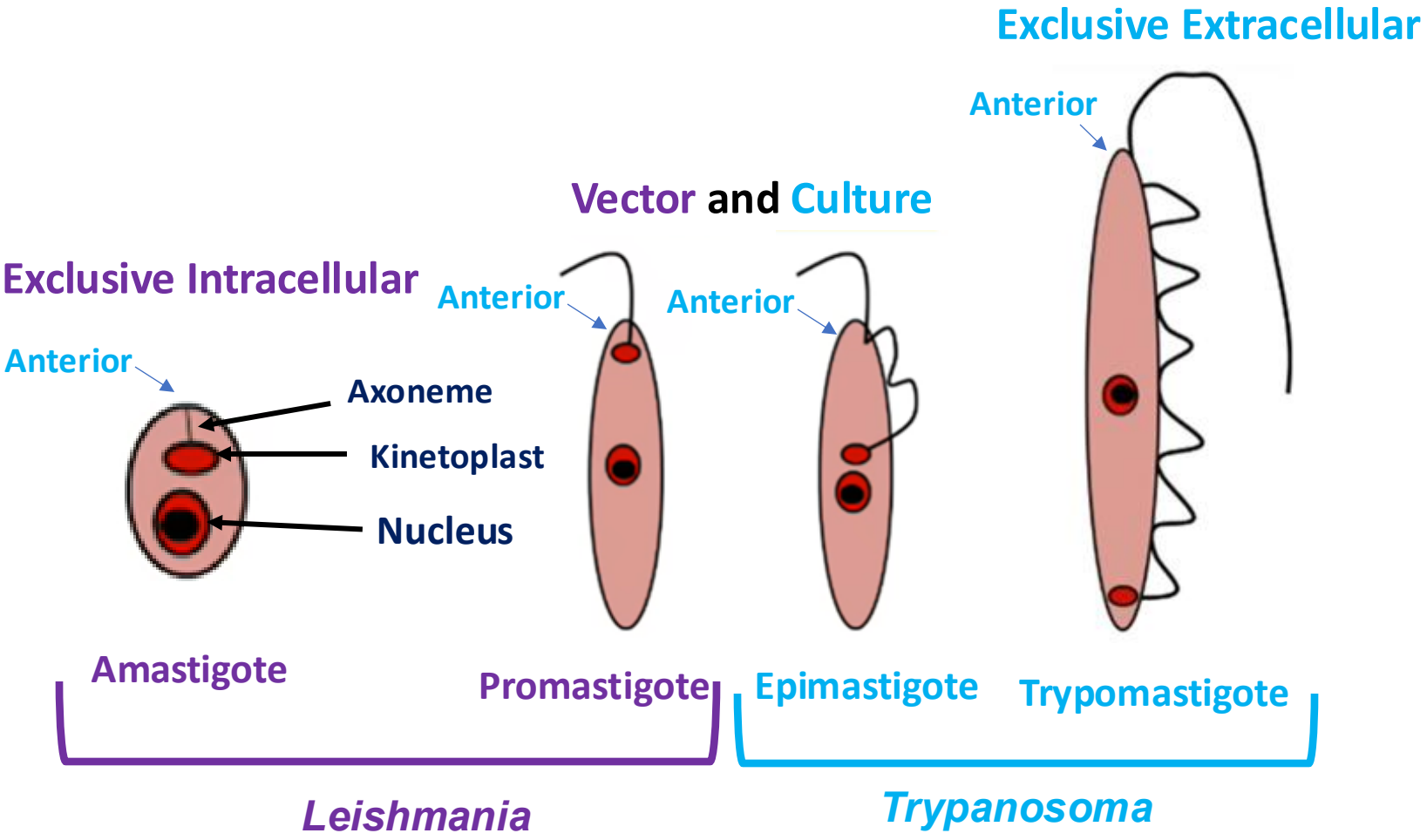
Leishmania & Trypanosoma (Haemoflagellates)

Rule: (the flagellum should originates from kinetoplast and goes out from the anterior end)

Promastigotes: They have a large central nucleus and a kinetoplast located near the anterior end

Epimastigote: the kinetoplast is above the nucleus

Trypomastigote: They have a large posterior kinetoplast



Why do they proceed into chronic infections?

Leishmania

Intracellular pathogen

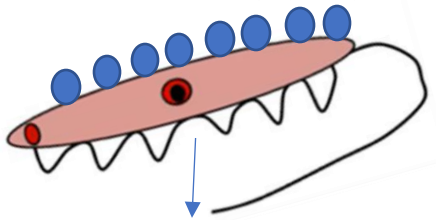
Use macrophages as a vehicle

Travel into different lymphoid organs
Causing generalized LAP

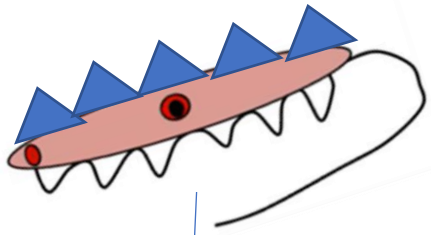
Trypanosoma

Immune evasion

Variant surface glycoprotein (VSG)



Continuous change in the structure of the VSG



Continuous production of antibodies

Continuous production of immune complexes

Tissue and blood vessel precipitation and damage

Breach the blood brain barrier

CNS abnormalities

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

1)Live in blood and /or tissues.

2) Move by one flagellum.

3) Need vector for transmission.

4) Require 2 hosts (vertebrate and invertebrate).

Visceral Leishmaniasis

(Kala- azar, Dumdum fever, Black sickness)

Why called……

- From the Hindi word for black (kala) and the Persian word for disease (azar).
- The agent of the disease was also first isolated in India by Scottish doctor William Leishman (who observed the parasite in spleen smears of a soldier who died of the disease in Dumdum, Calcutta, India - hence the name dumdum fever)
- Irish physician Charles Donovan, who was working on the other cases.

Visceral Leishmaniasis

(Kala- azar, Dumdum fever, Black sickness)

Old world visceral leishmaniasis (OWVL)

New world visceral leishmaniasis (NWVL)

Leishmania donovani
Classic Kala-azar

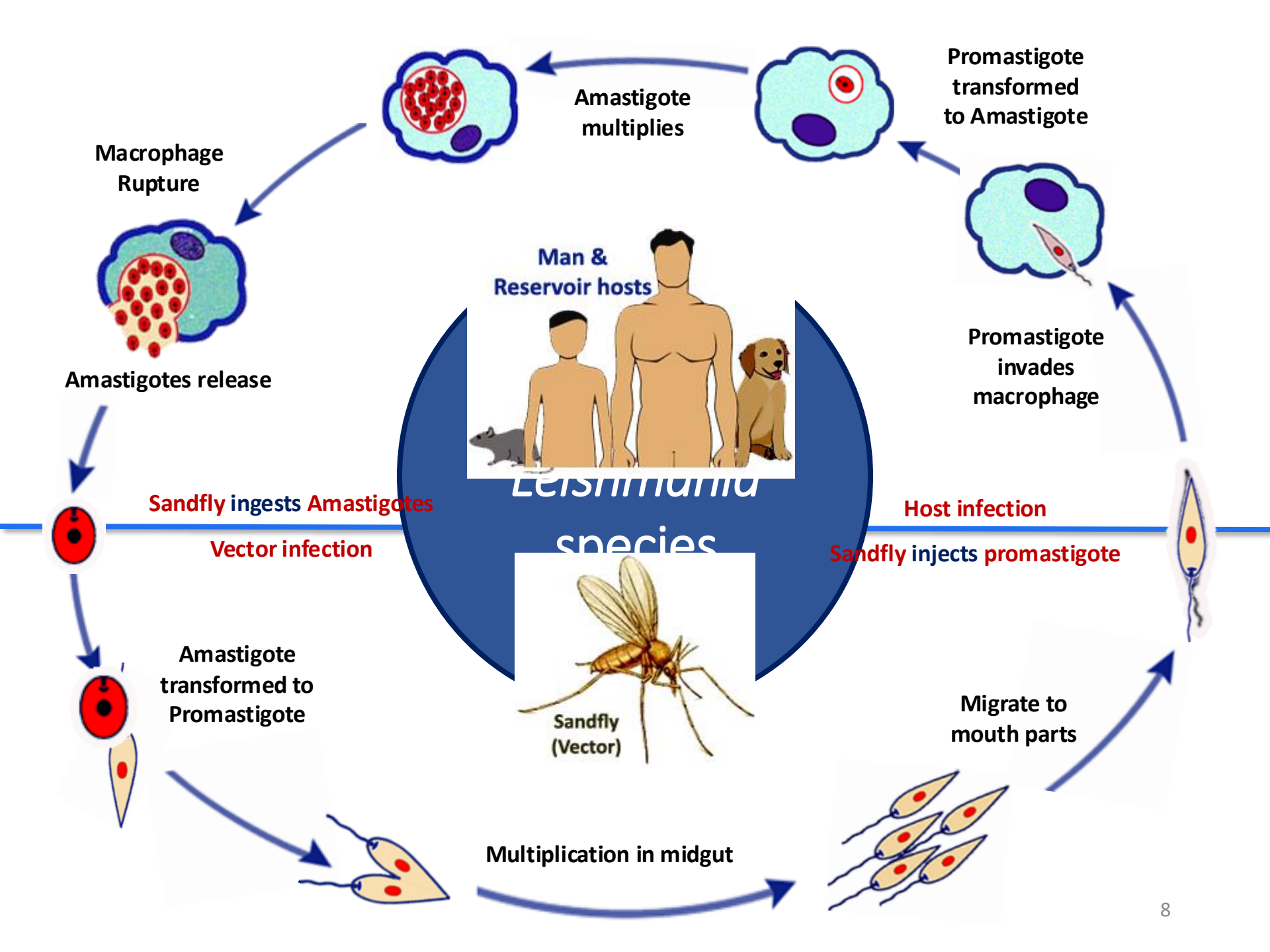
India, China & East Africa (common in young adults of 10-25 years old).

Leishmania infantum
Infantile Kala-azar

Mediterranean region, Middle East & Africa (common in children < 4 years).

Leishmania infantum
American infantile Kala-azar

South America (common in children < 4 years).


Amastigote multiplies
Promastigote transformed to Amastigote
Macrophage Rupture
Man & Reservoir hosts
Promastigote invades macrophage
Amastigotes release
Leishmania species
Sandfly ingests Amastigotes
Vector infection
Host infection
Sandfly injects promastigote
Amastigote transformed to Promastigote
Sandfly (Vector)
Migrate to mouth parts
Multiplication in midgut

❖ **Definitive host:** Man.

❖**Reservoir host:** Dogs & rodents.

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

❖ **Infective stage: -** Promastigote (when transmitted by sand fly)

- Amastigote by other modes

❖ **Habitat:** Reticuloendothelial cells

Mode of transmission

1-Bite of infected sand fly (biological transmission)

2- Blood transfusion.

3- Congenital transmission.

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) ➲ hyperplasia and enlargement of the affected organs.


leishmanioma

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 affection (decrease albumin).**
- **5- Loss of weight & cachexia especially in thorax & shoulder girdle**

2)Systemic manifestations

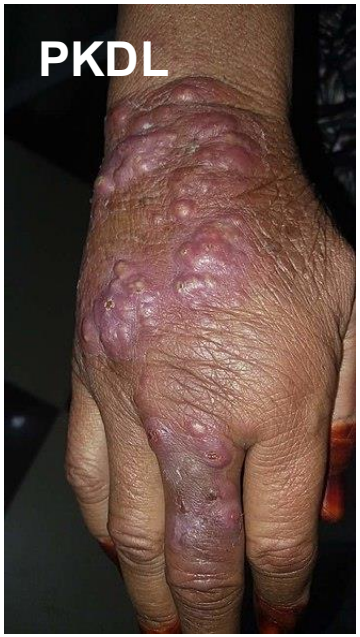
6-Skin lesions

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

Macular, papular or nodular skin lesions on the face, trunk & extremities (Post-kala azar dermal leishmanoid, PKDL) It appears after incomplete therapy & without other systemic signs. Its nodules may be mistaken for lepromatous leprosy.

7-Congenital transmission ➲ abortion

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



(PKDL) is a complication of visceral leishmaniasis (VL); it is characterised by a macular, maculopapular, and nodular rash

❖**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.

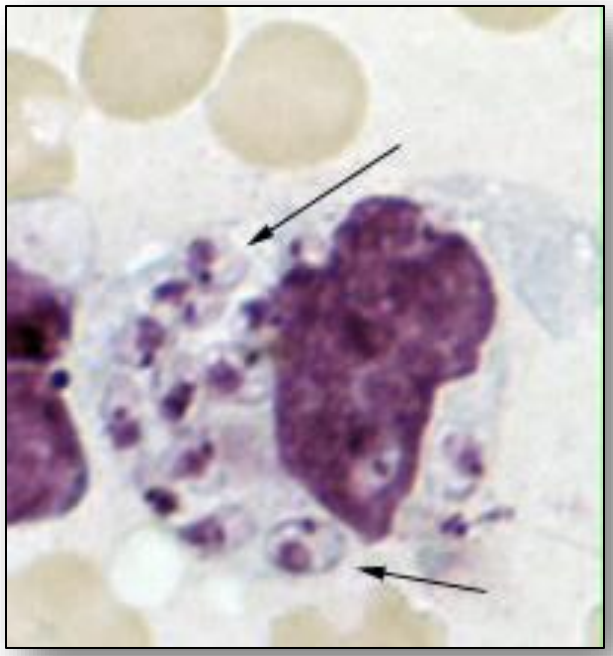
Indirect methods

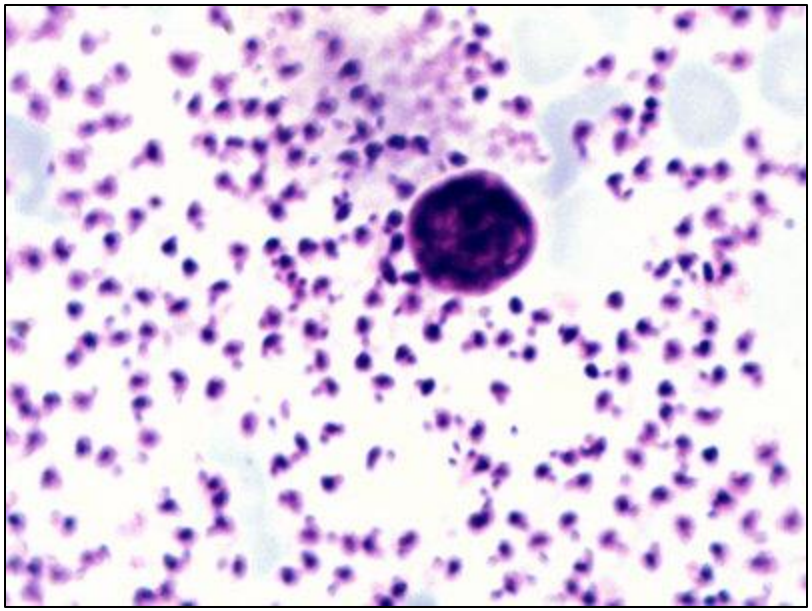
Specific tests (immunodiagnosis)

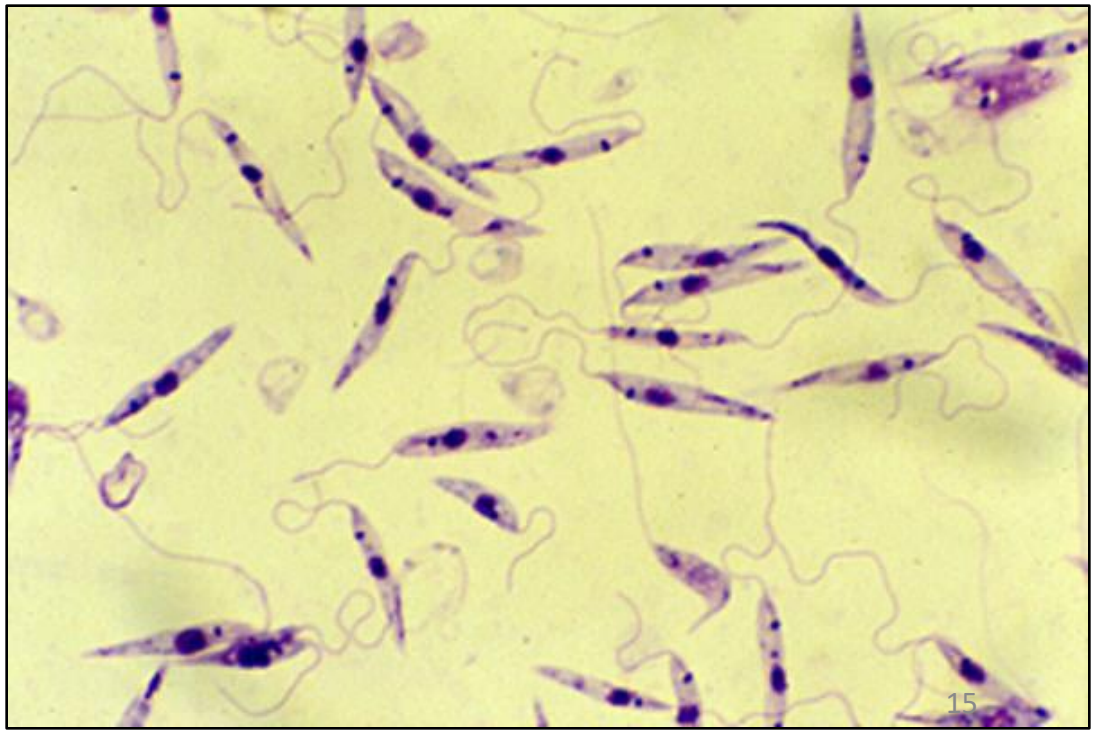
- leishmanin or Montenegro test (IDT): -ve due to supression of T. cells & +ve after recovery .
- Serological tests: CFT, IHAT, ELISA, IFAT➲ to detect anti-leishmania antibodies.
- PCR

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

- Pentostam
- Pentamidine,
- Amphotericin B
- Paromomycin

Oral therapy

- Miltefosine

LeiShmaniaZis Mnemonic

... major
... infantum
... braziliens

(Trypanosomatida → Leishmania → donovani)
- Family - -Genus- - Species -

vector: ♀ Sandfly < LutZomyia phlebotomuS

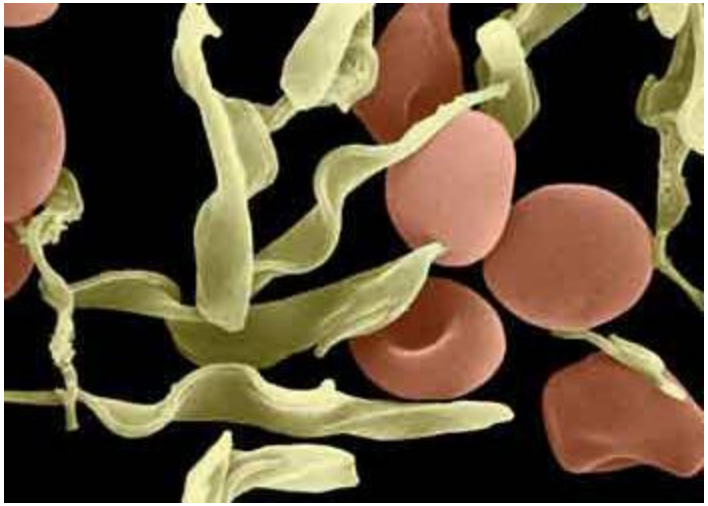
Organism: ProtoZoa (parasite) "Zones"

Symptoms: Spiking fevers, large liver & Spleen, ulcers → Scars

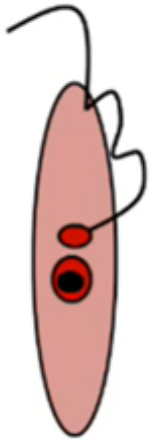
"Kala aZar" (Black Fever) "Baghdad Boil" "Delhi Boil"

Biopsy: AmaStigobes in macrophages, kinetoplaSt

Tx: Sodium Stibogluconate, liposomal Amphotericin B

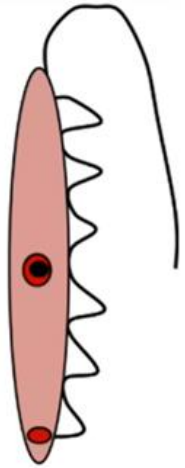


African trypanosomes



African Trypanosomiasis

(Polymorphic trypanosomes)



Trypanosoma brucei gambiense	*Trypanosoma brucei 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)

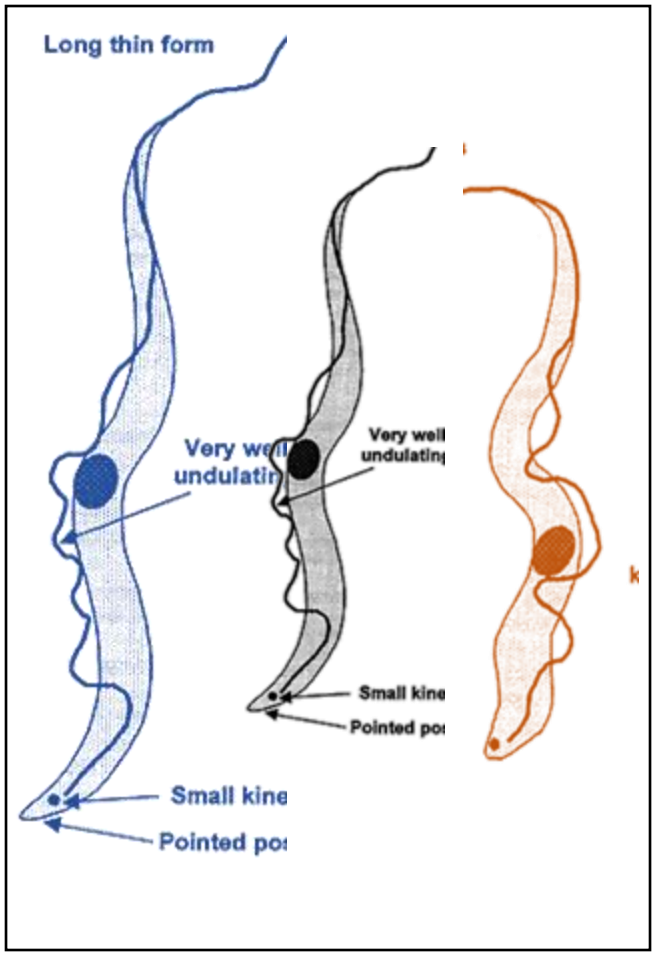
Glossina= Tse-tse fly

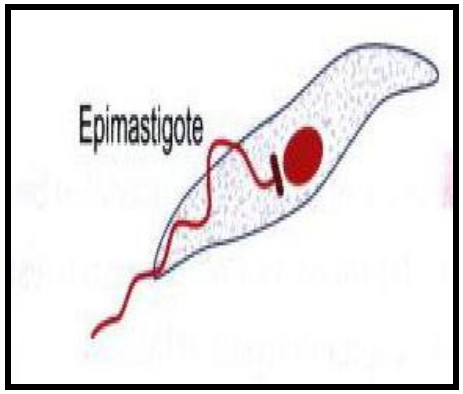
Morphology:

Vertebrate host (man)

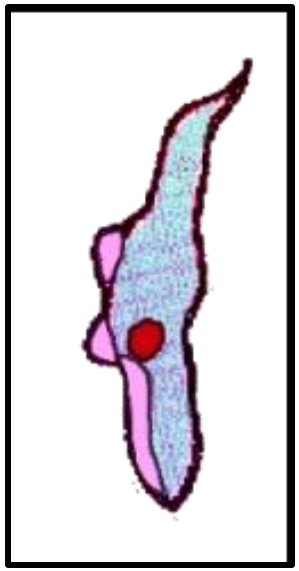
Trypomastigotes

Long: 30 x 1-2µm
Intermediate: 20 µm
Short stumpy: 15 µm





Epimastigotes



Metacyclic

Salivary glands

Midgut **Trypomastigotes**

Invertebrate host Tse-tse fly

Inver. Hosts

HOSTS

Ver. Hosts

Metacyclic trypomastigote
Infective stage

Tsetse inoculates
MT into the bite wound

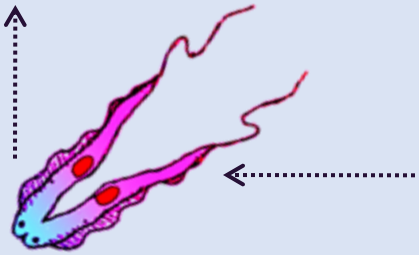
Glossina
Tsetse fly

MT → Trypomastigotes

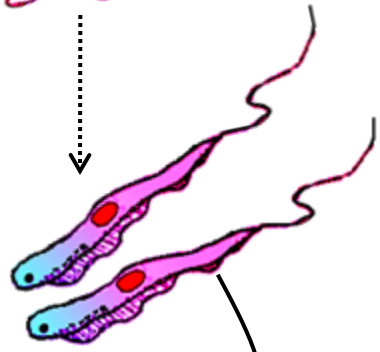
Multiplication

Migrate to salivary glands
→Epimastigotes & multiply

Tsetse ingests TM



Multiplication in midgut



TM invade blood, lymph and CNS & multiply

Mode of transmission

- Bite of infected *Glossina* (Tsetse fly).
- Blood transfusion.
- Congenital transmission.
- Sexual transmission may be possible.

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

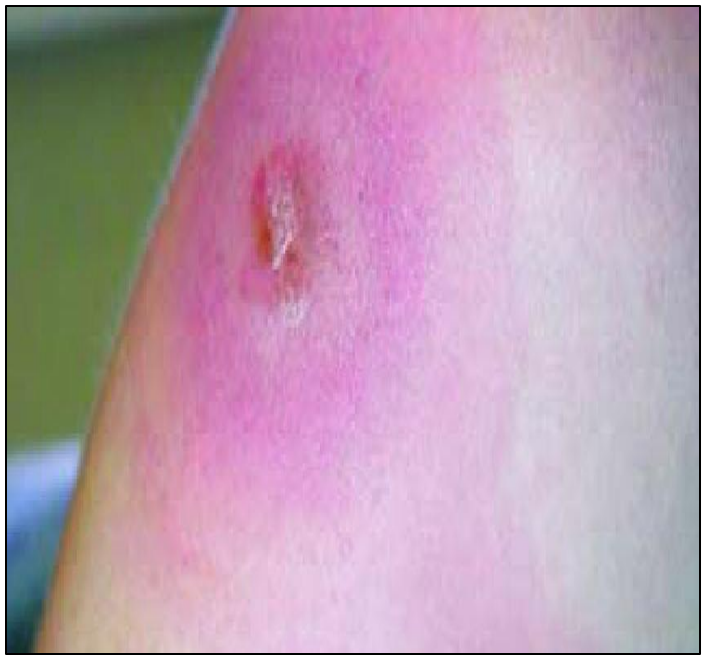
	Trypanosoma gambiense	*Trypanosoma rhodesiense*
G.D:	West and Central Africa	Eastern parts of Africa
D.H:	Man	Man
R.H:	No reservoir host	Wild game animals

Pathogenesis and symptomatology of gambian trypanosomiasis

The disease has 3 stages

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

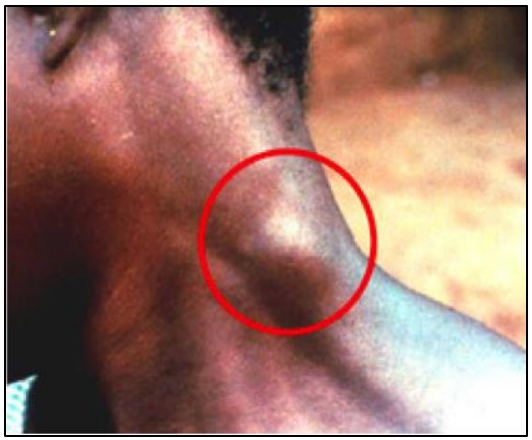
- Firm painful and tender nodule with regional lymphadenitis.
- After 3 weeks the parasite invades the lymphatic system and blood.



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, early sign).
- Hyperplasia of REC➲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 ➲ vasculitis and petechial haemorrhage ➲ ischemia and pressure atrophy of nerve cells ➲ chronic meningoencephalitis

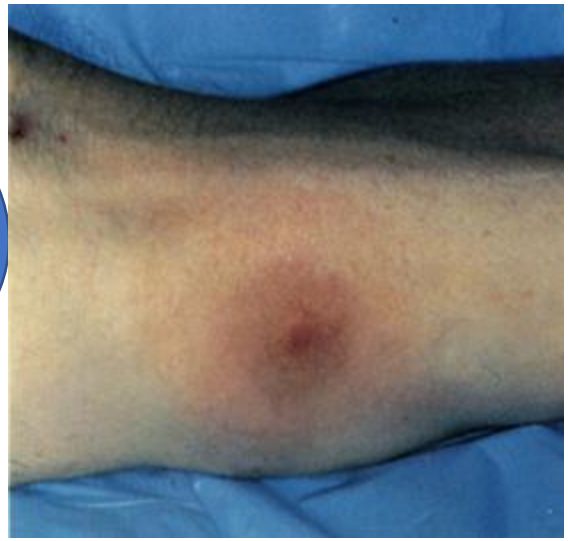
Manifested by

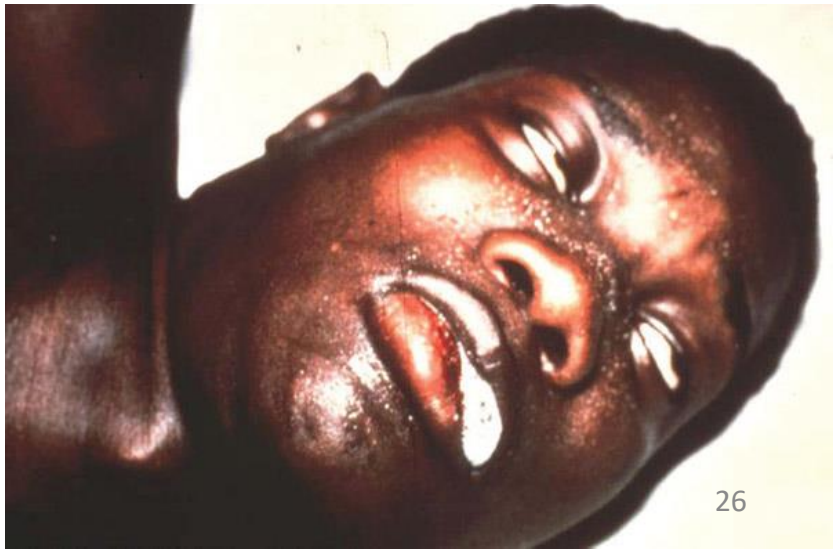
Fever, severe headache, nausea, vomiting, neck rigidity, mental dullness, apathy, reduced coordination, convulsion, paralysis and all day and night sleeping (sleep regulating center affection).

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.

African trypanosomiasis





Laboratory diagnosis

Direct methods

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

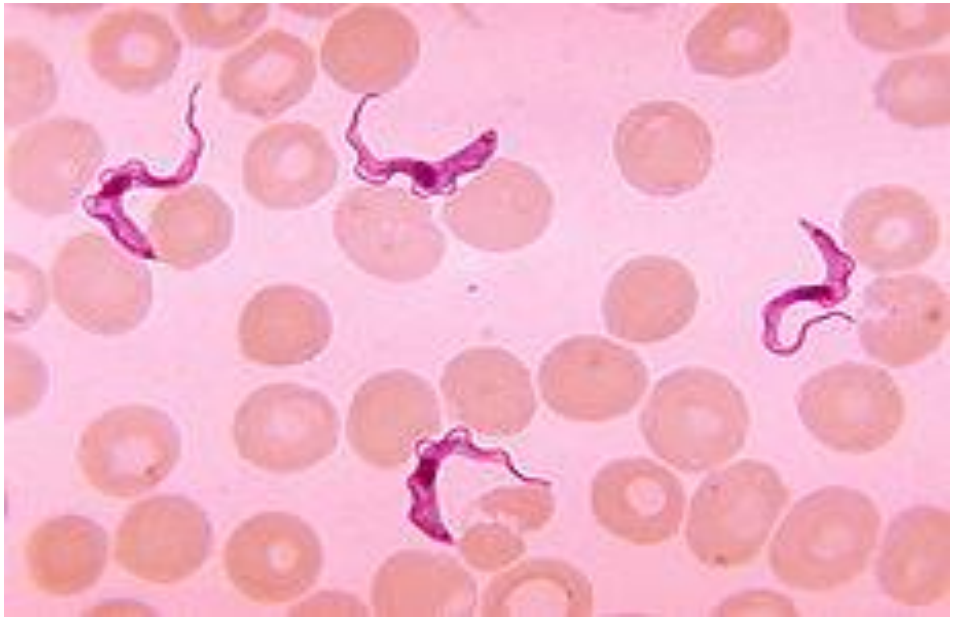
1- Microscopic examination of stained and unstained films.

2- Culture on NNN medium ➲ epimastigotes.

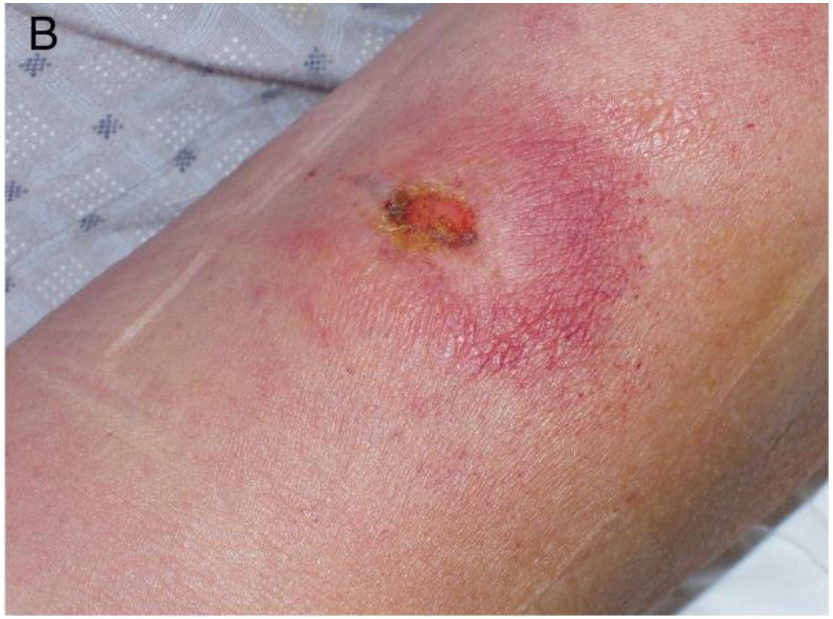
3- Animal inoculation

Indirect methods

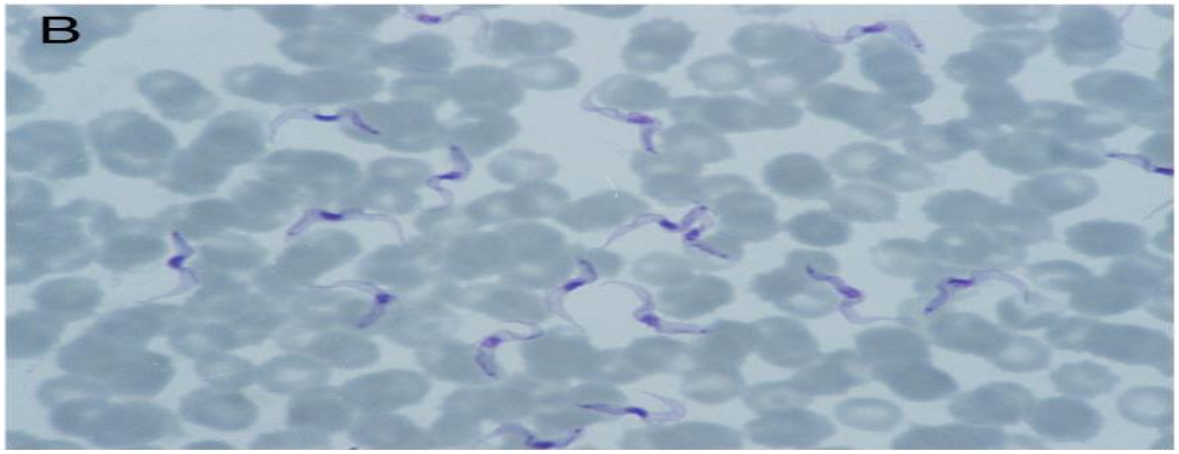
- **Serological tests:** IFAT & ELISA.
- **Serum IgM:** Always elevated in the blood and CSF due to antigenic variation of the trypanosome (changing its antigenic coat) to escape from host immune response (evasion).
- **Blood examination:** Anaemia, leucopenia and thrombocytopenia



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).

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


?
Quiz
Time

Case 1

- **A 24-year-old- male from Pakistan, presented to the emergency hospital suffering from fever, abdominal pain, and diarrhea. He complained of sudden loss of weight and physical examination revealed hepatosplenomegaly, lymphadenopathy and dark pigmented areas of the skin on the forehead and around the mouth.**

Case 2

- **A 20-year-old male from West Africa who presented to the hospital suffering from severe myalgia, abdominal pain, vomiting and diarrhea. Physical examination revealed tender, indurated erythematous lesion on his left forearm with enlargement of the posterior cervical lymph nodes**