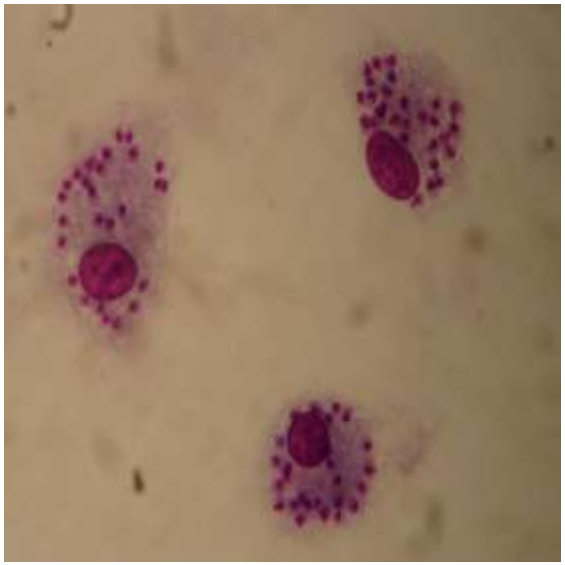
Hematoflagellates



By Dr.Raghed M.Jassem

Hemoflagellates :- protozoa parasites located in blood and tissue (moves through flagella)

1. The family Trypanosomatidae, (includes hemoflagellates) contain only two geniuses' that parasitize humans.

a. **Genus *Leishmania* are always intracellular, principally in cells of the reticuloendothelial system.**

b. **Genus *Trypanosoma* contains members that may be found both in the circulating blood (intercellular)ex :- African *trypanosomiasis*; and intracellularly in cardiac muscle. American *trypanosomiasis***

2. Hemoflagellates were originally parasites of insects. They are transmitted by insects, and in them undergo a developmental cycle (the arthropod serves as intermediate host).

a. "Old World" leishmaniasis - transmitted by the bite of various species of sandflies of the genus *Phlebotomus*.

b. South American leishmaniasis - carried by *Lutzomyia* spp.

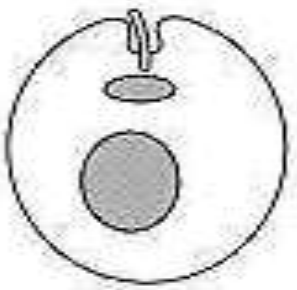
sandflies.

c. American trypanosomiasis - transmitted by Triatomid bug (Kissing bug): *Triatoma spp.* ; Transmission occurs when infective feces of the bug contaminates the wound made by the insect's bite or by scraping of the skin.

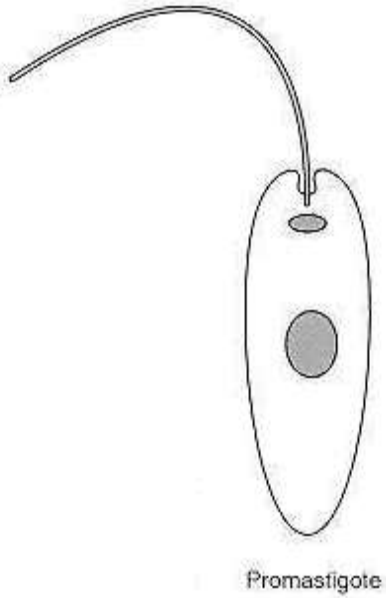
d. African trypanosomiasis - transmitted by *Glossina spp.* tsetse flies.

3. No cyst stage

Morphological forms of hemoflagellates :-

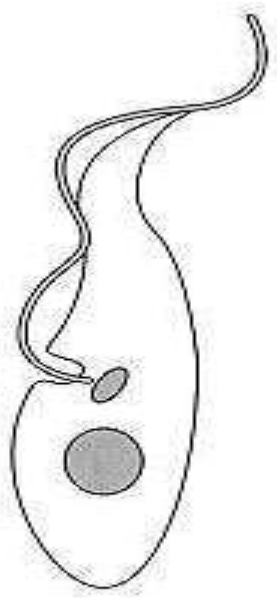


1-Amastigote (Leishmania) form:- Round or oval in shape, 2-5 microns in diameter, have single nucleus with large central karyosome, the kinetoplast lies at right angle to the nucleus. This form (amastigote) has no flagellum.



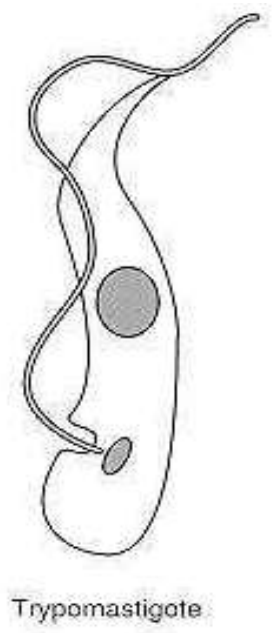
2-Promastigote (leptomonad) form :-Elongated (spindle in shape) measuring 15-20 microns X 1-2 microns, have centrally located nucleus and the kinetoplast situated at the anterior end. Single free flagellum project from the anterior end, equal or longer than the body length . This form has no undulating membrane.

3-Epimastigote form Elongated form:- 15-20 microns long and slightly wider than promastigote, nucleus near middle, kinetoplast is anterior to the nucleus. Flagellum arise forming the undulating membrane extending half of the body length, and project from the anterior end as a free flagellum.



4-Trypomastigote (Trypanosome) form :- Elongated form with highly polymorphism from rather short (15micron X 2-4micron) to a long slender from (35micron X 2-4micron). In stained blood film, *Trypanosoma cruzi* appears as C or U shape.

The nucleus near middle, kinetoplast is at the posterior end, the flagellum and undulating membrane pass anteriorly along entire body length and free flagellum extends from anterior end when present.



Leishmania spp.

- It is single-cell flagellated prtozoa parasite .
- Obligate intracellular
- Multiply by binary fission.
- Cause disease called Leishmaniasis
- It spread by the bite of female sand flies.

There are several different forms of leishmaniasis in people:-

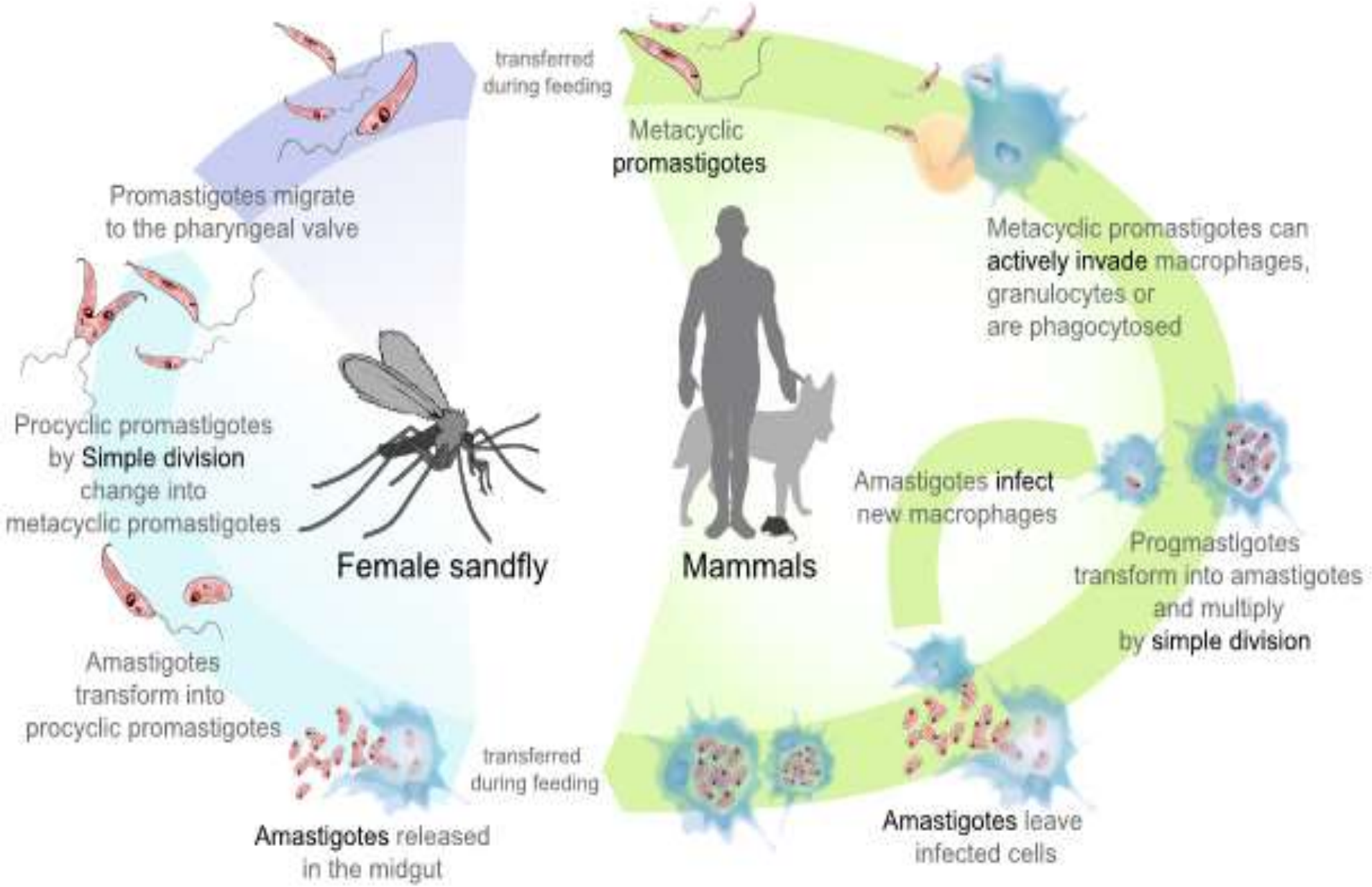
1- **Cutaneous leishmaniasis** :- is the most common forms, which causes skin sores ((oriental sore, Baghdad boil).

2- **Visceral leishmaniasis**:- which affects several internal organs (usually spleen, liver, and bone marrow)

3- **Mucocutenous leishmaniasis**:-

- The parasite requires Two different hosts to complete life cycle humans as the definitive host and sandflies female (*Phlebotomus sergenti)* as the intermediate
- Reservoir host: canine family & rodents (zoonotic disease)
- Two developmental forms are found, Amastigote and Promastigote. Amastigote in human & Promastigote in the vector (Sand fly).
- Normal habitat: human macrophages

Life cycle


transferred during feeding
Metacyclic promastigotes
Promastigotes migrate to the pharyngeal valve
Metacyclic promastigotes can actively invade macrophages, granulocytes or are phagocytosed
Procyclic promastigotes by Simple division change into metacyclic promastigotes
Female sandfly
Mammals
Amastigotes infect new macrophages
Progmastigotes transform into amastigotes and multiply by simple division
Amastigotes transform into procyclic promastigotes
transferred during feeding
Amastigotes released in the midgut
Amastigotes leave infected cells

Definitive host :-

1- In humans the promastigotes are injected by sandfly biting through the skin during its blood meal.

2- When sandfly bites using its proboscis it ejects the parasites that are stored inside the hollow tube.

3- The parasites engulfed by macrophage and endothelial cells of skin capillaries .

4- Inside the cells they undergo spontaneous transformation into oval-shaped amastigotes (Leishman-Donovan (LD) bodies)

5- The surviving amastigotes undergo cell division using simple binary fission. Multiplication continues until the host cell can no longer hold and ruptures and released into tissue cavities.

6- Free amastigote either infect other cells (macrophages) in skin as in cutaneous leishmaniasis or other cells in skin and the adjacent cells in mucous membrane as in mucocutaneous leishmaniasis or pass to different organ by blood stream (spleen, liver, bone marrow and lymph nodes) as in visceral leishmaniasis

7- A free and phagocytosed amastigotes (inside macrophage) in peripheral blood are then sucked up by blood-feeding sandfly.

Intermediate host

1- Once the amastigotes are ingested, they enter the midgut of the sandfly. Then they undergo structural modification into flagellated promastigotes, becoming larger and elongated.

2- They get attached to the gut epithelial lining where they multiply rapidly by binary fission.

3- Then they migrate towards the anterior part of the digestive system such as pharynx & buccal cavity . This process is known as anterior station development.

4- A heavy infection of pharynx can be observed within 6 to 9 days after initial blood meal & the promastigotes become infective only by this time, and the event is called the metacyclic stage.

5- The metacyclic promastigotes then enter the hollow proboscis where they accumulate , upon biting a human, the parasites are released, which results in infection.

Leishmania tropica

Leishmania major

skin

- **Old World cutaneous leishmaniasis**
- **Cutaneous Oriental sores**
- **Delhi boils**
- **Baghdad boils**
- **Dry or urban cutaneous leishmaniasis**

Leishmania donovani

Leishmania infantum

Spleen, liver, bone marrow

- **Visceral leishmaniasis**
- **Kala-azar**
- **Dum-dum fever (Black Fever)**

L. braziliensis

Mucous membrane

mucocutaneous leishmaniasis

Note:

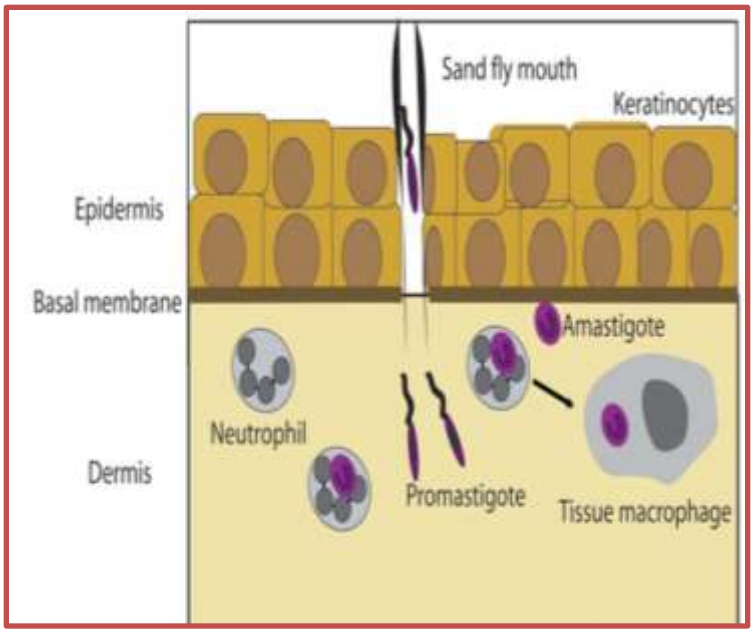
1. *L. tropica* & *L. donovani* are anthroponotic.

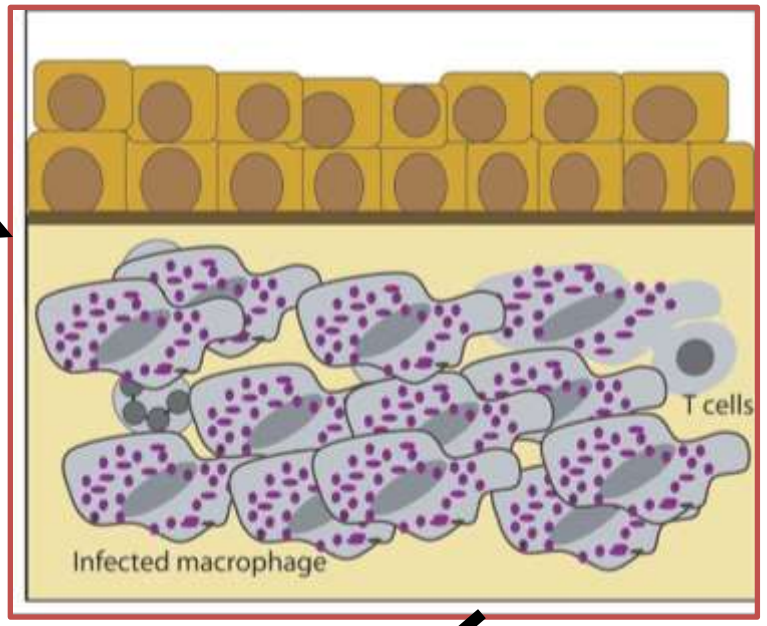
2. No Reservoir hosts in the life cycle.

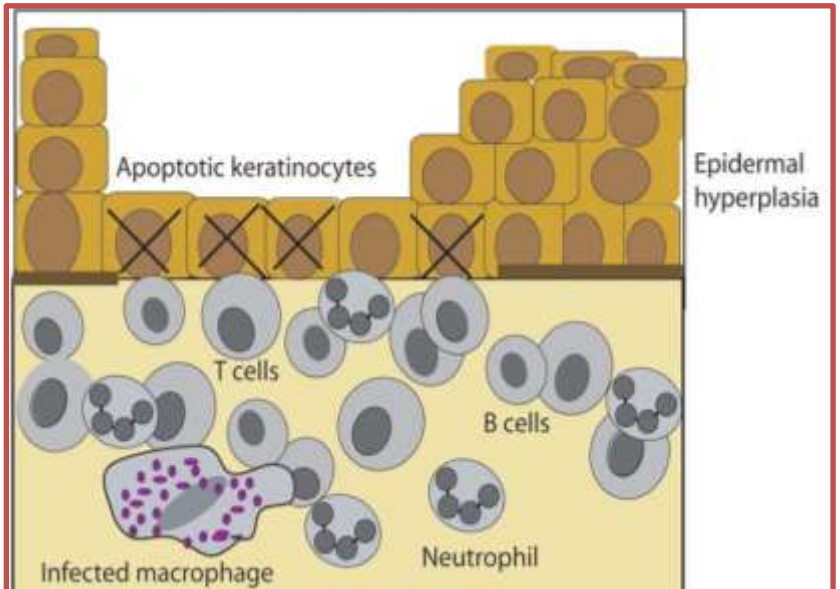
3. *L. infantum*: man is a dead end in the life cycle. The sandfly transmit the parasites from animal to man but cannot transmit the parasites from man to other man or animal.

4. Other spp. are zoonotic (man to man & man to animal & animal to animal)

Pathogenesis (Leishmania tropica)







1. When an individual is bitten by the sandfly, promastigotes are introduced into the skin (epidermis) and enter small blood vessels and macrophages around the affected area.

2. Then the parasites loss the flagella and proliferate as amastigotes inside the macrophages intracellularly.

3. Other white blood cells, called lymphocytes, immediately attack the area and the amastigotes are liberated from the macrophages and spread extracellularly, until the infection penetrates the epidermis to the dermis and induce a dermal lesion (causes ulceration) at the site of inoculation by the sandfly.

4. A mass is form and then breaks causes an open sore at the bite sites

5. The lesion usually heals as the body builds immunity against the parasite, in a few months to a year, leaving an unpleasant-looking scar

6. Mucous membranes are rarely involved

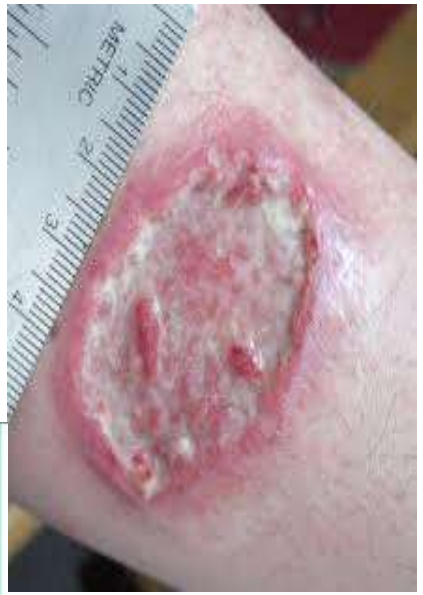
Clinical signs

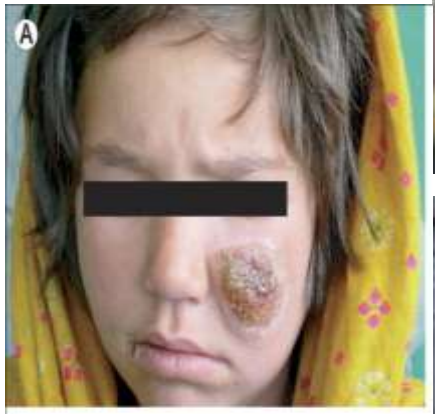
- Begins as a red papule that later becomes itchy
- Develops to one or more skin ulcers on exposed parts of the body, mostly the face, arms and legs.
- Lesion characterized by:

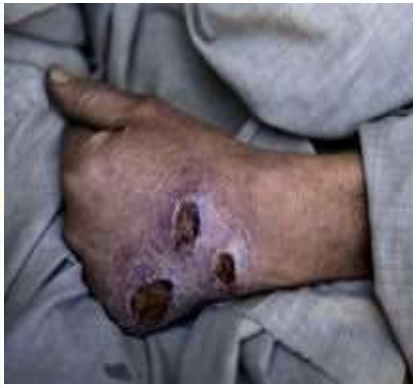
  1. Either large scaly, ulcerated plaques, or shallow ulcerated nodules.

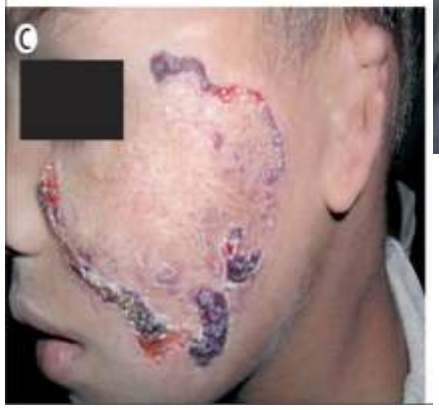
  2. Dry or watery ulcer

- Sores can be covered by a scab.
- Painful associated some time with adenopathy (swollen lymph nodes near the sores).







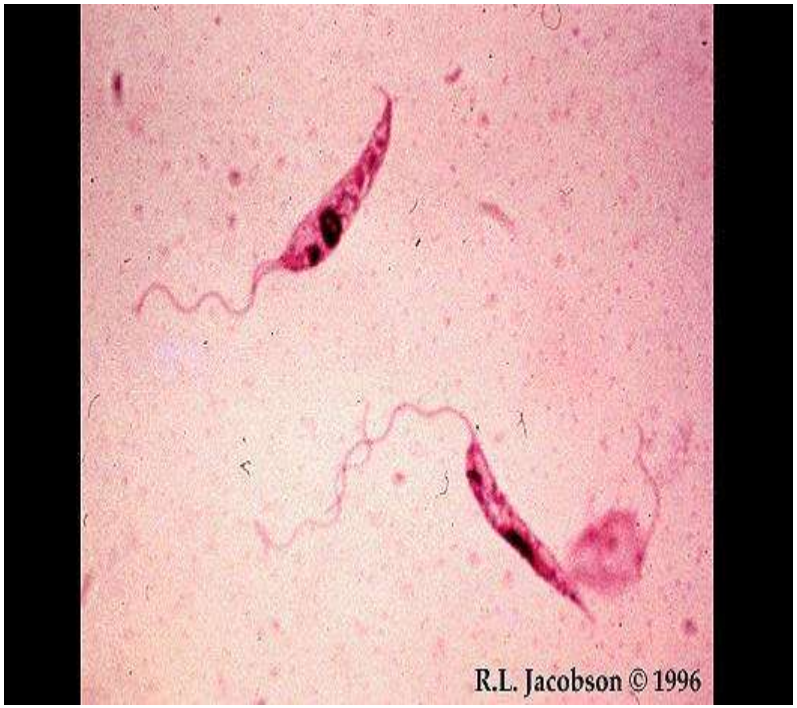


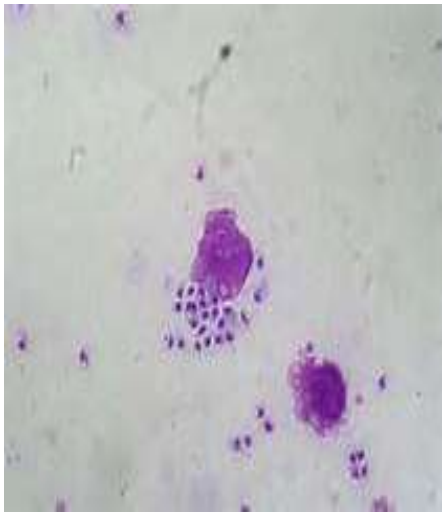
Leishmania donovani

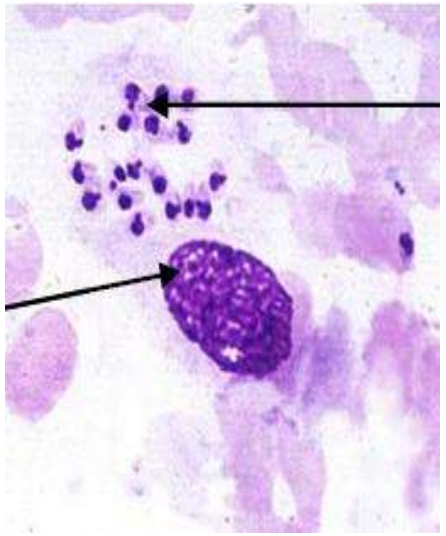
- **It cause visceral leishmaniasis** (**VL**),which is the most severe form of leishmaniasis and, without proper diagnosis and treatment, is associated with high fatality rate This disease is the second-largest parasitic killer in the world (after malaria), responsible for an estimated 200,000 to 400,000 infections each year worldwide.

The parasite migrates to the internal organs such as the liver ,spleen so it called visceral , and bone marrow and if it left untreated, will almost always result in the death of the host.

- The incubation period generally ranges from 10 days to 3 months.
- Clinical symptoms include pyrexia(recurring high fever which may be continuous or intermittent), enlargement of spleen and liver, and heavy skin pigmentation which darkens the physical appearance (the reason for naming "black fever").
- Low blood counts—a low red blood cell count (anemia), a low white blood cell count (leukopenia), and a low platelet count (thrombocytopenia).

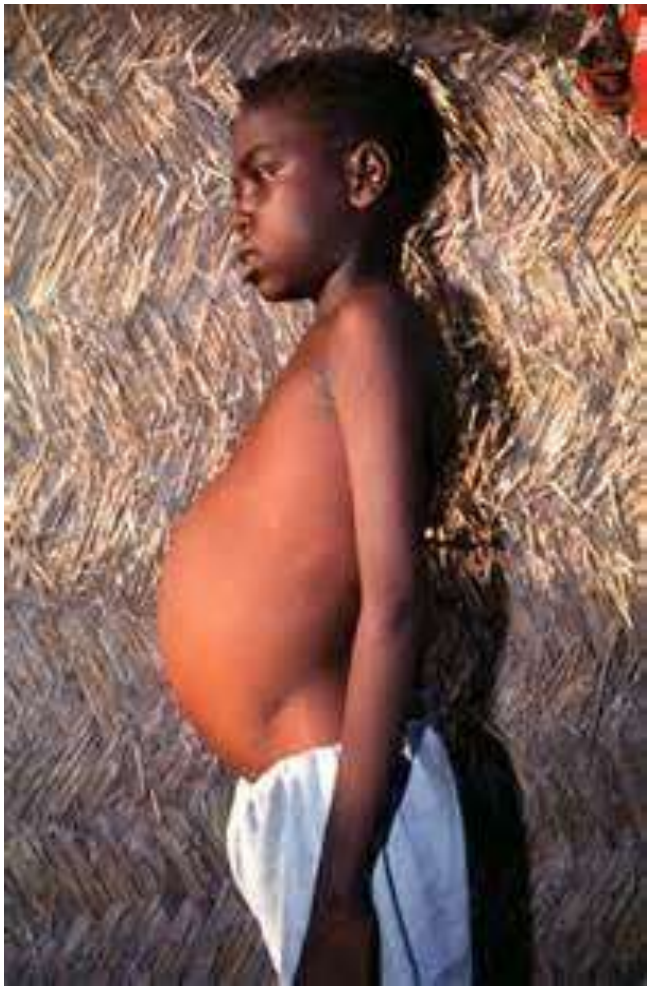






Leishmania donovani promastigote stage

Leishmania donovani amastigote stage



Diagnosis:

- Depend on symptoms & signs
- Specimen: Lymph node aspirates, scrapings, and biopsies from the margin of the lesion, not the center, are important in the cutaneous forms &from bone marrow (usually), spleen, liver, lymph nodes in VL.
- Microscopic Examination: Giemsa-stained or Leishman stain smears. Observed amastigotes.
- Culture with NNN medium
- Leishmanin skin test
- PCR technique, IFA, ELISA.

Treatment:

- For visceral leishmaniasis the treatment is determined by where the disease is acquired
- For single lesions (cutaneous one) may be cleaned and treated with antibiotics if secondarily infected, and then covered and left to heal.
- For larger or non healing forms, pentavalent antimony is the drug of choice

Prevention and control:

1. Treatment of infected cases
2. Insect (sandfly) control:
    a. Insecticides
    b. Fine-mesh netting.
3. Reservoir host control:
    a. Killing of street dogs.
    b. Killing of rodents
4. Protect the lesion from insect bite

Trypanosoma

African Trypanosomes:
1. *Trypanosoma gambiense*
2. *T. rhodesiense*

Cause African sleeping sickness (in Africa only).

3.*Trypanosoma cruzi*

Cause American trypanosomiasis or Chagas disease