Flagellates—II

(Hemoflagellates)

- Hemoflagellates are the flagellated protozoa that are found in peripheral blood circulation.
- They complete their life cycle in two hosts, i.e. vertebrate host and insect vector; therefore, called as **digenetic** or **heteroxenous parasites.**
- Hemoflagellates of medical importance belongs to:

Phylum: protozoa

Class: Kinetoplastea

Order: Trypanosomatida

Family: Trypanosomatidae

Genera: *Leishmania* and *Trypanosoma*

MORPHOLOGY of Hemoflagellates

1. Hemoflagellates have an oval to elongated body, nucleus, and a single flagellum arising from kinetoplast.

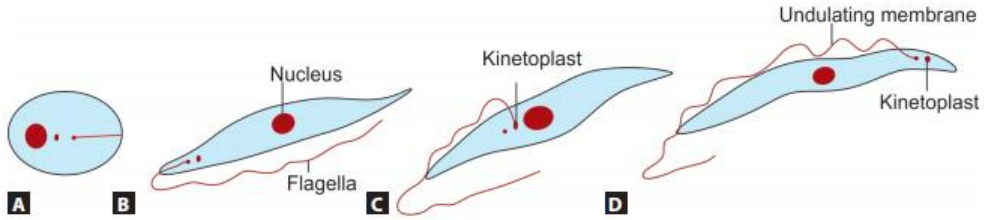
2. **Kinetoplast:** It consists of blepharoplast and parabasal body connected by a delicate fibril (cytoskeleton).
3. **Axoneme (or axostyle):** It extends from blepharoplast to the cell wall.
4. they exist in four morphological stages—(1) amastigote, (2) promastigote, (3) epimastigote and (4) trypomastigote. (Fig. 5.1)

1. Amastigote form: Round to oval, lacks flagellum, found in reticuloendothelial cells of man infected with *Leishmania* and *Trypanohsoma cruzi*

2. Promastigote form: Lanceolate shaped; It is found in the mid gut of insect vector. This is the infective stage of *Leishmania* to man

3. Epimastigote form: Elongated, This form is seen for *Trypanosoma* in insect vector.

4.Trypomastigote form: Elongated and spindle shaped with central nucleus. Kinetoplast lies near the posterior end. It is the infective stage of *Trypanosoma* found in insect vector and peripheral blood of humans.



Figs 5.1A to D: Various morphological forms of flagellates (schematic diagrams) (A) amastigote; (B) promastigote; (C) epimastigote; (D) trypomastigote

LEISHMANIA

- Leishmaniasis is caused by the obligatory intracellular protozoa of the genus *Leishmania*.
- Primarily it affects the reticuloendothelial system of the host.
- *Leishmania* species produce widely varying group of clinical syndromes ranging from self-healing cutaneous ulcers to fatal visceral disease
- Leishmaniasis is mainly a zoonotic disease affecting dogs, foxes, and rodents.
- Animal reservoir plays a major role for transmission
- The parasite is transmitted by bite of the female sand fly vector.

- **Old world leishmaniasis:** Affects Asia, Africa and Europe and transmitted by sandfly (Genus *Phlebotomus*)
- **New World Leishmaniasis:** Affects Central and South America and transmitted by sandfly (Genus *Lutzomyia*)
- Clinical syndromes of leishmaniasis include:

✓ Visceral leishmaniasis (VL)
✓ Post–kala-azar dermal leishmaniasis (PKDL)
✓ Cutaneous leishmaniasis (CL)
✓ Diffuse cutaneous leishmaniasis (DCL)
✓ Leishmaniasis recidivans (LR)
✓ Mucocutaneous leishmaniasis (MCL)

- **OLD WORLD LEISHMANIASIS**
- ***Leishmania donovani***
- *Leishmania donovani* causes VL or kala azar
- Sir Donovan who found the amastigotes in the splenic smear from a patient.

1. **Morphology**

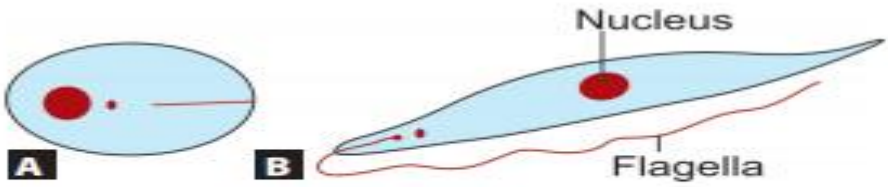
Leishmania occurs in two forms:

a) Amastigote form

- It is an obligate intracellular form and the infective stage to vector, sand fly.
- Found in reticuloendothelial cells like macrophages, neutrophils, endothelial cells of liver, spleen, bone marrow, of the vertebrate hosts like humans, dogs and rodents
- Round to oval, 3-5 µm in size
- **Nucleus***:* It measures less than 1 µm, oval to round, located in center or side of the cell
- **Kinetoplast:** Consists of copies of mitochondrial DNA. It is made up blepharoplast and parabasal body connected by a delicate fibril (cytoskeleton).

b) Promastigote form

- This is an extracellular form, infective stage to humans.
- It is mainly found in sandfly and in culture
- It is motile and contains single anterior flagellum
- Pear shaped, 8–15 µm length



Figs 5.2A and B: *Leishmania* species (schematic diagram) (A) amastigote form; (B) promastigote form

2) Life cycle (Fig. 5.3)

1 **Host:** *Leishmania* completes its life cycle in two hosts:

- **Vertebrate host** (man, dog, rodents, etc.)
- **Insect vector (female sandfly):** *Phlebotomus argentipes*

2 **Infective form:** Promastigote forms present in the midgut or foregut of female sandfly.

3 **Mode of transmission:** By bite of an infected sandfly mainly during the late evening or the night time. Minimum 10–1,000 promastigotes per infective bite are required to initiate the infection.

4 **In vertebrate hosts, including humans:**

- Promastigotes are regurgitated from the midgut rarely or directly discharged from foregut (proboscis) of the female sandfly into the skin of the vertebrate host
- Promastigotes are phagocytosed by the skin macrophages and transform into amastigote forms within 12–24 hours
- The amastigote forms inside the macrophages multiply further causing cell rupture and release into the circulation
- Amastigotes are carried out in the circulation to various organs like liver, spleen and bone marrow and invade the reticuloendothelial cells like macrophages, endothelial cells, etc.

5 In sand fly:

- During the blood meal taken up by the sandfly, the amastigotes are ingested and transformed into promastigote forms in the insect midgut
- Promastigotes multiply by longitudinal fission and pass through various stages such as:

Amastigote → procyclic promastigote → nectomonad promastigote → haptomonad promastigote → leptomonad promastigote → metacyclic promastigote

- The metacyclic promastigotes multiply in the midgut of vector by binary fission and a small proportion migrates to the foregut (proboscis). They infect a new host during another blood meal
- The duration of the life cycle in sandfly varies from 4 to 18 days depending on the species.

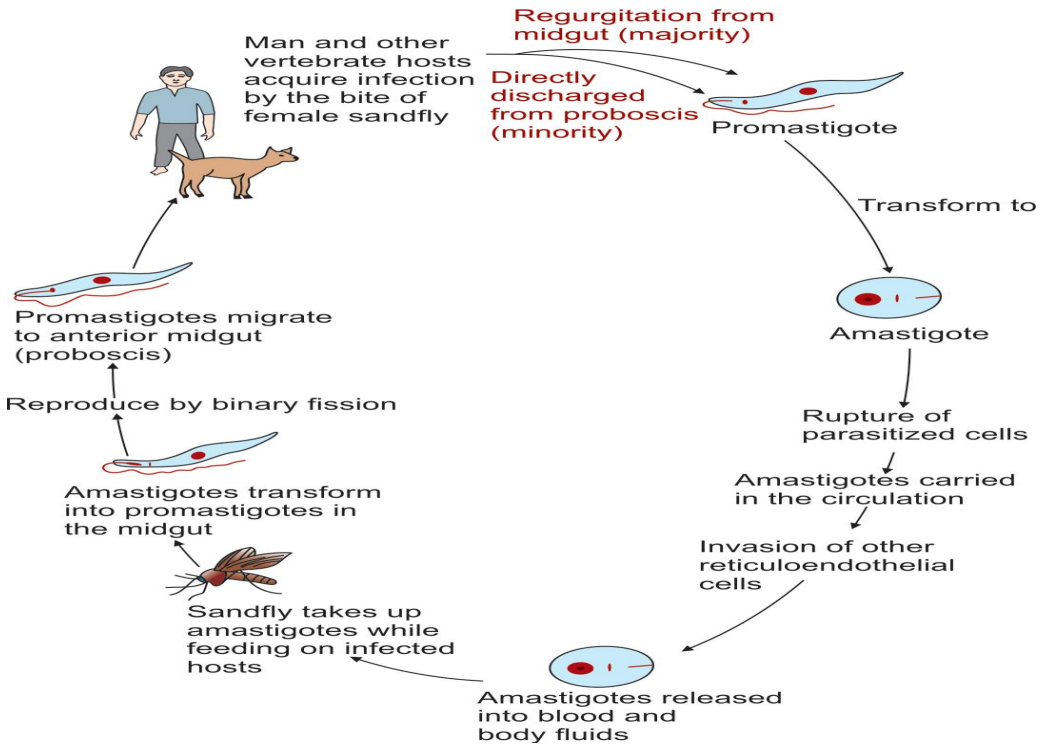


Fig. 5.3: Life cycle of *Leishmania donovani*

3.clinical Features

- Incubation period ranges from 2–6 months.
- **Fever:** The most common symptom of VL
- **Splenomegaly**
- Hepatomegaly (usually moderate in degree)
- Lymphadenopathy: Common in most of the African endemic regions
- Hyperpigmentation: Mostly seen in brown skinned individuals.

- Hematological abnormalities (bone marrow dysfunction):
  1. Anemia (normocytic and normochromic): Appears early and may become severe enough to cause congestive heart failure
  2. Leucopenia
  3. Thrombocytopenia: Can lead to epistaxis, retinal hemorrhages, and gastrointestinal bleeding
  4. Hypergammaglobulinemia (due to polyclonal B cell activation).

Figs 5.4A to D: Real images showing clinical features (A) splenomegaly seen in visceral leishmaniasis; (B) hypopigmented skin changes in early PKDL; (C and D) extensive facial nodular lesions in late PKDL

2. Leishmania tropica Complex

- It includes three species—*L. tropica, L. aethiopica* and *L. major*. They cause old world Cutaneous Leishmaniasis
- *L. tropica* is reported from Western India ,Middle East and Mediterranean coast. It mainly affects urban area hence known as agent of urban anthroponotic CL
- *L. aethiopica* infects people from Ethiopia, Uganda and Kenya
- *L. major* is reported from Middle East, India, China, Africa, and central and western Asia. It mainly affects rural area hence known as agent of rural zoonotic CL.

1. Life cycle

- The life cycle of the *L. tropica* complex is same as *L. donovani* except: The species of vector sand fly are different

✓ *L. tropica*—vector is *P. sergenti*

✓ *L. aethiopica*—vector is *P. longipes*

✓ *L. major*—vector is *P. papatasi*

- Reservoir of infection:

✓ *L. tropica*—is man (anthroponotic)

- ✓ *L. aethiopica*—is *Hyraxes* (Zoonotic)
- ✓ *L. major*—is rodents (zoonotic)
- In humans, the amastigote forms reside in reticuloendothelial cells of skin (they do not migrate to viscera).

clinical Features

Cutaneous leishmaniasis

- It is caused by *L. tropica* complex. This condition is also known as **"Oriental sore"**, Delhi Boil, Aleppo Boil and Baghdad, etc (Fig. 5.8A).
- Oriental sore usually occurs on face and hands
- It begins as papule, becomes nodular and finally it ulcerates
- Lesions may be single or multiple and vary in size from 0.5 cm to more than 3 cm
- Mostly, it heals spontaneously leaving behind a scar

Figs 5.8A and B: Real images showing clinical features of (A) cutaneous leishmaniasis; (B) leishmaniasis recidivans

Leishmania braziliensis

They cause MCL ***Espundia* (*mucocutaneous leishmaniasis*)**

- *L. braziliensis* infects mucous membrane of the nose, oral cavity, pharynx or larynx months to years after the CL.
- It is seen in 1–3% of patients infected with *L. braziliensis*, more in males of age 10–30 years
- The initial symptoms are often nasal stuffiness, erythema and mucopurulent discharge.
- It may eventually involve the upper lip, buccal, pharyngeal, or laryngeal mucosa

- Ulcerative lesions are formed with erosion of the soft tissue and the cartilages leading to loss of lips, soft part of nose and soft palate

- Gradually, the nasal septum may be destroyed, resulting in nasal collapse with hypertrophy of upper lip