Trypanosoma: A group of unicellular parasitic flagellate protozoa. Most trypanosomes are heteroxenous (requiring more than one obligatory host to complete life cycle) and most are transmitted via a vector.

Two distinct types of human Trypanosomes are present:
• **African**, which causes Sleeping sickness, and is transmitted by tsetse flies. The disease caused by two species:
  • *Trypanosoma brucei rhodesiense*
  • *Trypanosoma brucei gambiense*
• **American**, which causes Chagas disease, is transmitted by kissing bugs, and caused by
  • *Trypanosoma cruzi.*

**African Trypanosoma**: The genus Trypanosoma appears in the blood as:

• **Trypomastigotes** with elongated bodies supporting an undulating membrane and a flagellum emerges at the anterior end as a whiplike extension. The kinetoplast (circular DNA inside the single mitochondrion) is a darkly staining body lying immediately adjacent to the basal body from which the flagellum arises.
it is a non-dividing form that is infectious spread to lymph nodes, Bloodstream, and, in terminal stages, to the CNS where they produce:
- the typical sleeping sickness syndrome.
- inability to eat
- unconsciousness, and death.
- CNS involvement is most characteristic of African Trypanosomiasis.
- The Trypanosomes are transmissible through the placenta, and congenital infections occur in hyperendemic areas.

B- **Amastigote** is the intracellular dividing form in the cytoplasm of vertebrate cells.
C- **Epimastigote** is found in the intestinal tract of the insect vector.

**Pathology and pathogenesis**
Infective Trypanosomes of *T. bruci gambiense* and *T. bruci rhodesiense* are introduced through the bite of the tsetse fly and multiply at the site of inoculation to cause swelling (the primary lesion), which may progress to form a trypanosomal chancre.

- The African trypanosomes of the *T brucei* complex are remarkable in that they undergo antigenic variation through a series of genetically controlled surface glycoproteins that coat the surface of the organism (variant surface glycoproteins, or VSGs).
- By producing VSGs, the parasite is able to evade the host’s antibody response.
- Each trypanosome is thought to possess about 1000 VSG genes, an example of mosaic gene formations.

**American trypanosoma**

*Trypanosoma cruzi* has three developmental stages:

1. Epimastigotes in the vector.

2. **Trypomastigotes (in the bloodstream):** The blood forms of *T. cruzi* are present during the early acute stage and at intervals thereafter in smaller numbers. They contain a large, rounded terminal kinetoplast, but they are difficult to morphologically distinguish from African trypanosomes.

3. **Amastigote (rounded intracellular stage).** The tissue forms, which are most common in heart muscle, liver, and brain.

Pathology and pathogenesis
• Infective forms of *T. cruzi* are introduced when infected bug feces are rubbed into the conjunctiva, the bite site, or a break in the skin.
• At the site of *T. cruzi* entry, there may be a subcutaneous inflammatory nodule or Chagoma. Swelling of the eyelids, especially in children.
• The primary lesion is accompanied by
  • Fever
  • acute regional lymphadenitis
  • dissemination to blood and tissues.
  • Interstitial myocarditis is the most common serious condition in chagas disease
  • other organs affected are the liver, spleen, and bone marrow

The genus Leishmania
Leishmania species are unicellular eukaryotes having a well-defined nucleus and other cell organelles including kinetoplast and flagella. Divided into a number of species infecting humans and causes
1. **Cutaneous** (Oriental sore, Baghdad boil, wet cutaneous sore, dry cutaneous sore, Delhi boil, and other names). Cased by: *Leishmania tropica, L major, L mexicana, L braziliensis*, and other cutaneous forms and induce a dermal lesion at the site of inoculation by the Sandflyis.
2. **Mucocutaneous** (*Leishmania braziliensis* causes mucocutaneous or nasopharyngeal leishmaniasis in South America. The lesions are slow growing but extensive.)
3. **Visceral (kala-azar) leishmaniasis.** *Leishmania donovani,* which causes visceral leishmaniasis, spreads from the site of inoculation to multiply in reticuloendothelial cells, especially macrophages in spleen, liver, lymph nodes, and bone marrow.

**All of these infections are transmitted by sandflies**

**Morphology & Identification**
- The sandfly transmits the infective **Promastigotes** by bite. The promastigotes rapidly change to **Amastigotes** after phagocytosis by macrophages, and then multiply, filling the cytoplasm of the macrophages. The infected cells burst, the released parasites are again phagocytosed, and the process is repeated, producing a cutaneous lesion or visceral infection depending upon the species of parasite and the host response.

The **Amastigotes** are oval, 2–6 × 1–3 μm, with a laterally placed oval vesicular nucleus and a dark staining, rod-like kinetoplast.

![Morphology Diagram]

- The parasite exists in 2 forms:
  1. **Amastigotes** — aflagellar stage
  2. **Promastigotes** — flagellar stage

- Only the intracellular Amastigote occurs in mammals

**Pathogenesis, Pathology, & Clinical Findings**
*L donovani,* which causes kala-azar, spreads from the site of inoculation to multiply in reticuloendothelial cells, especially macrophages in spleen, liver, lymph nodes, and bone marrow. This is accompanied by
• hyperplasia of the spleen.
• weakness.
• Irregular fever
• Untreated cases with symptoms of kala-azar usually are fatal.

**Diagnostic Laboratory Tests**

**A. SPECIMENS**

- Lymph node aspirates, blood, and spleen, liver, or bone marrow puncture are important in kala-azar.
- An (ELISA) technique using a 70-kDa antigen has been studied as a rapid and accurate field-applied tool to detect visceral leishmaniasis.

**B. MICROSCOPIC EXAMINATION**

Giemsa-stained smears and sections may show Amastigotes, especially in material from kala-azar.

![Image of Amastigotes](Prof. George Lubas)

**Culture and growth characteristics**

NNN medium is the medium most generally used. A diphasic rabbit blood agar culture, Tobie’s medium, at about 26–28 °C, is especially suitable. Only the promastigotes are found. *L donovani* usually grows slowly.

- Lymph node aspirates are suitable.
- Tissue aspirates.
- Biopsy material.
• scrapings

Only Promastigotes can be cultivated in the absence of living cells. In tissue cultures, intracellular Amastigotes may occur in addition to the extracellular Promastigotes.

D. SEROLOGY

• IHA (indirect hemagglutination antibody)
• IFA (indirect fluorescent antibody) test may be useful, but they lack sufficient sensitivity.
• ELISA test
• polymerase chain reaction (PCR)
• A skin test (Montenegro test is a DTH test) is epidemiologically important in indicating past exposure to any of the leishmanias. (0.2 ml of killed Promastigotes injected and the erythema of $\geq 5$ mm means positive results)

Epidemiology, Prevention, & Control

• Kala-azar, caused by $L$ donovani, is found in most tropical and subtropical countries. Its local distribution is related to the prevalence of specific sand fly vectors.

• In the Mediterranean and in middle Asia and South America, domestic and wild canis are reservoirs, and in the Sudan, various wild carnivores and rodents are reservoirs of endemic kala-azar.
• Control is aimed at destroying breeding places and dogs, where appropriate, and protecting people from sand fly bites.

**Filariasis (helminthiases)**

Filariasis is a **parasitic disease** caused by an infection with **roundworms**. These are spread by blood-feeding **black flies** and **mosquitoes**.

Eight known filarial nematodes use humans as their definitive hosts. These are divided into three groups according to the niche they occupy in the body:

**A. Lymphatic**

[Hyperlink](https://en.wikipedia.org/wiki/Lymphatic_filariasis) is caused by the worms *Wuchereria bancrofti, Brugia malayi,* and *Brugia timori*. These worms occupy the **lymphatic system**, including the lymph nodes; in chronic cases, these worms lead to the syndrome of **elephantiasis**.
B. **Subcutaneous filariasis** is caused by *Loa* HYPERLINK "https://en.wikipedia.org/wiki/Loa_loa"loa (the eye worm), *Mansonella streptocerca*, and *Onchocerca volvulus*.

- These worms occupy the subcutaneous layer of the skin, in the fat layer.
- *L. loa* causes *Loa* filariasis, while *O. volvulus* causes river blindness.

C. **Serous Cavity Filariasis** is caused by the worms

- **Mansonella perstans**
- **Mansonella ozzardi**, which occupy the serous cavity of the abdomen.

**Life cycle**

- Life cycle consists of five stages. After the male and female worms mate, the female gives birth to live Microfilariae. The Microfilariae are taken up by the vector insect (intermediate host) during a blood meal. In the intermediate host, the microfilariae molt and develop into third-stage (infective) larvae. Upon taking another blood meal, the vector insect injects the infectious larvae into the dermis layer of the skin. After about one year, the larvae molt through two more stages, maturing into the adult worms.
- Individuals infected by filarial worms may be described as either "Microfilaraemic" or "Amicrofilaraemic", depending on whether microfilariae can be found in their peripheral blood.
• Filariasis is diagnosed in microfilaraemic cases primarily through direct observation of microfilariae in the peripheral blood. Occult filariasis is diagnosed in amicrofilaraemic cases based on clinical observations and, in some cases, by finding a circulating antigen in the blood.

Signs and symptoms

• The most important symptom of lymphatic filariasis is elephantiasis—edema with thickening of the skin and underlying tissues

• Elephantiasis results when the parasites lodge in the lymphatic system.

• Elephantiasis affects mainly the lower extremities. However, different species of filarial worms tend to affect different parts of the body

• *Wuchereria*  
  "https://en.wikipedia.org/wiki/Wuchereria_bancrofti"  
  "https://en.wikipedia.org/wiki/Wuchereria_bancrofti"
affect the legs, arms, vulva, breasts, and scrotum (causing hydrocele formation),


• Those who develop the chronic stages of elephantiasis are usually free from microfilariae (Amicrofilaraemic)

• The subcutaneous worms present with rashes, urticarial papules, and arthritis, as well as hyper- and hypopigmentation macules.

**Lymphatic filariasis**

**PATHOLOGY AND PATHOGENESIS**

• Pathologic changes, which are confined primarily to the lymphatic system, can be divided into acute and chronic lesions.

• In acute disease, the presence of molting adolescent worms and dead or dying adults stimulates dilatation of the lymphatics, hyperplastic changes in the vessel endothelium, infiltration by lymphocytes, plasma cells, and eosinophils, and thrombus formation (ie, acute lymphangitis).

• These developments are followed by granuloma formation, fibrosis, and permanent lymphatic obstruction.

• Repeated infections eventually result in massive lymphatic blockade. The skin and subcutaneous tissues become edematous, thickened, and fibrotic. Dilated vessels may rupture, spilling lymph into the tissues or body cavities. Bacterial and fungal superinfections of the skin often supervene and contribute to tissue damage.

**DIAGNOSIS**

• Eosinophilia is usually present during the acute inflammatory episodes

• The presence of microfilaria in the blood or lymphatic, ascitic, or pleural fluid sought in Giemsa- or Wright-stained thick and thin smears is evidense.
• Because the appearance of the microfilariae is usually periodic, specimen collection must be properly timed (usually at night).
• Circulating filarial antigens can be found in most microfilaremic patients.