UG CBCS Semester-I

Leishmania donovani

Leishmania is an important pathogenic zooflagellate genus closely related to *Trypanosoma*. Various species of *Leishmania* (Table I) infect man, cattle, dog, sheep, horse, etc. and cause serious diseases collectively known as Leishmaniasis. All types are carried by the blood-sucking sandflies of the genus Phlebotomus, and all are intracellular parasites in leucocytes of blood or in cells of liver and spleen. *Leishmania donovani* causes a malaria-like oriental disease in man called Kala-azar, Dumdum fever or Black fever.

1. Ecology Discovery. Genus *Leishmania* was created by Ross in 1903. The species *L. donovani* was reported simultaneously by Leishman from London (1903) and Donovan from Madras (1903), hence the name *Leishmania donovani*.

2. Distribution. *L. donovani* infects man in India, China, Russia, Mediterranean countries, and in parts of Africa and South America. In India, it is endemic in Assam, Bengal, Bihar, Orissa, Tamilnadu and eastern parts of Uttar Pradesh.

3. Habits and habitat. In man, *L. donovani* lives as an intracellular parasite in leucocytes or cells of liver, spleen, bone marrow, lymphatic glands, etc. It is the causative agent of the disease known as Kala-azar resulting in fever, enlargement of spleen and a reduction in the number of white corpuscles in blood. It is transmitted through the bite of sandflies.

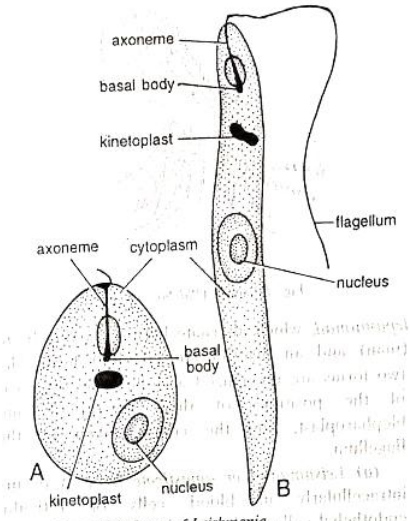

Fig. 1. Two forms of *Leishmania*.
A- Amastigote or leishmanial form in man.
B- Promastigote or leptomonad form in sandfly.

Morphology

1. Shape and size. The genus *Leishmania* occurs only in two forms or stages; leishmanial and leptomonad, which alternate between a vertebrate (man) and an invertebrate (sandfly) host. The two forms are recognized as follows on the basis of the positions of their kinetoplast and blepharoplast, and the course taken by the flagellum.

(a) Leishmanial or amastigote form. It occurs intracellularly in blood cells or reticuloendothelial cells of the vertebrate host or man. It is microscopic, rounded or oval, with a central or eccentric nucleus, blepharoplast and kinetoplast, but no free flagellum. It measures 2μ to 4μ in diameter.

(b) Leptomonad or promastigote form. It is found in the midgut of the invertebrate host or sandfly. It is elongated, slender and spindle-shaped with a large centrally placed nucleus, blepharoplast, kinetoplast and a long free flagellum. A fully formed promastigote stage measures 15-20μ in length and 1-2μ in width.

2. Cell membrane. The whole body is covered externally by a very thin, delicate, elastic and firm covering or pellicle. It gives definite shape to the body and does not form an undulating membrane.

3. Flagellum. *Leishmania* is uniflagellate, bearing a single flagellum. In the leptomonad form of parasite in sanctity, the flagellum is long and free. It arises from a minute basal body or blepharoplast situated near the anterior end. Closely associated with the blepharoplast lies a disc-shaped parabasal body or kinetoplast. There is, however, no cytostome. In the leishmanial form of parasite in man, there is no free flagellum, as it is greatly reduced, fibril-like and lies

embedded in cytoplasm. A transverse section of flagellum under electron-microscope shows the typical 9+2 internal fibril arrangement, as in case of Euglena.

4. Cytoplasm. Underneath pellicle, the body cytoplasm is colourless, homogeneous and not differentiated into ectoplasm and endoplasm Electron microscopic studies show that cytoplasm is marked by longitudinal striations of microtubules which may be contractile. Other structures present in cytoplasm are the blepharoplast, kinetosome, rhizoplast, Golgi body, mitochondrion, vacuole and nucleus.

5. Nucleus. A single large spherical nucleus lies eccentrically or in the middle, of the body. It is vesicular and with a distinct central karyosome or nucleolus. It is covered by a double unit membrane with pores and measures about 1μ diameter.

Table 1. **Species of *Leishmania* infecting man**

Species	Geographical distribution	Primary hosts	Position	Disease produced & symptoms	Transmission in host
1. *Leishmania donovani*	India, China, North Africa, South Europe, Russia, South America	Man, dogs, cats, etc.	Intracellular in leucocytes and cells of spleen, liver, bone marrow and lymph glands.	*Kala-azar* or Dumdum fever with fever, anaemia, enlargement of spleen and liver and darkening of skin. Also *Dermal leishmanoid.*	Cyclic, through bite of blood-sucking sandfly *Phlebotomus argentipes* in India.
2. *L.infantum*	Mediterranean areas. Considered identical to *L.donovani*	Children	Intracellular	Infantile Kala-azar with enlargement of spleen.	Bite of sandfly.
3. *L.chagasi*	South America. Identical to *L.donovani*	Man	Intracellular	S.American *Kala-azar*	Bite of sandfly
4. *L.canis*	Mediterranean areas. Identical to *L.donovani*	Dogs	Intracellular	similar to visceral leishmaniasis or kala-azar	Bite of sandfly
5. *Leishmania tropica*	Syria, Arabia, Iraq, Iran, Central Asia, Central and Western India	Man, dogs, cats, etc.	Intracellular in skin	Skin lesions called Oriental sores spps.	Bite of Sandfly *Phlebotomus*
6. *Leishmania brasiliensis*	Mexico, Central and South America	Man, dogs	Intracellular in mucous membrane of nose & throat	Naso-pharyngeal leishmaniasis called Espundia in Brazil, Uta in Peru, etc.	Bite of *Phlebotomus intermedius*

Metabolism

As in *Trypanosoma*, a mouth or cytostome also lacking in *Leishmania*, so that nourishment is obtained saprozoically through body surface from host cells. Gaseous exchange in respiration and elimination of excretory products also occur by diffusion through body surface. Sexual reproduction is unknown and asexual reproduction always takes place by longitudinal binary fission in the same manner as in *Trypanosoma*.

Life Cycle Hosts.

Leishmania is a digenetic parasite and requires two hosts for completion of its life cycle. Primary or principal host is a vertebrate or man, in which the parasite feeds and multiplies asexually. The secondary or intermediate host or vector is an invertebrate or blood-sucking insect or sandfly, belonging to, the genus Phlebotomus. Some mammals like dogs, jackals (Russia) and gerbils and ground squirrels (Kenya) also serve as reservoir hosts in which the parasite does not undergo any change but simply waits for its introduction into the human host. In India, canine leishmaniasis does not exist so that man is the main and sole host. Under laboratory conditions small burrowing rodents or hamsters (*Cricetulus griseus*) are also susceptible to infection and utilized for testing the drugs for *Leishmania* infections.

(A) Life cycle in man

1. Infection. In India, *L. donovani* is transmitted to man by the sandfly *Phlebotomus argentipes*. The insect vector, which has fed on some suitable fruit or plant juice after infected human blood meal, shows an enormous number of parasites in its buccal cavity and pharynx. Salivary glands of the vector are not involved as in case of a tsetse fly transmitting the trypanosomes. When such a sandfly bites a man, it liberates the parasites in the skin wound caused by its proboscis. However, the actual mode of transmission is not clear in India. Perhaps the Indian vector (sandfly) does not bite but spreads infection by being crushed possibly by slapping.

Multiplication. The parasites introduced by sandfly into human body are in the promastigote or leptomonad form. Some of them entering the blood circulation directly become destroyed. While those entering the cells of reticuloendotheleal system (liver, spleen, hone marrow and lymph nodes) change into amastigoite or leishmanial forms. These undergo slow multiplicaion by binary fission so that the host cells become greatly enlarged.

Spread of infection. When the number parasite reaches 50 to 200 or even more, the host cell ruptures. The liberated parasites arc taken up by new host cells and the multiplication cycle is repeated so that the reticulo - endothelia, system becomes progressively infected. Some of the free amastigotes become phagocytosed by neutrophils and monocytes (macrophages). These heavily parasitized cells wander through the general blood circulation leading to a general infection.

(B) Life cycle in sandfly

1. Transfer to sandfly. When a sandfly sucks blood of an infected person, it obtains free amastigotes as well as the parasitized neutrophils and monocytes along with the blood-meal.

2. Development in sandfly. In the midgut of sandfly, the amastigote forms become elongated and acquire a free flagellum, thus changing into the promastigote forms. These multiply by longitudinal binary fission. In 6 to 9 days, the number of parasites becomes enormous and they spread into the pharynx and buccal cavity. The salivary glands are not infected. Transmission into a new host occurs when such a heavily infested sandfly bites the host.

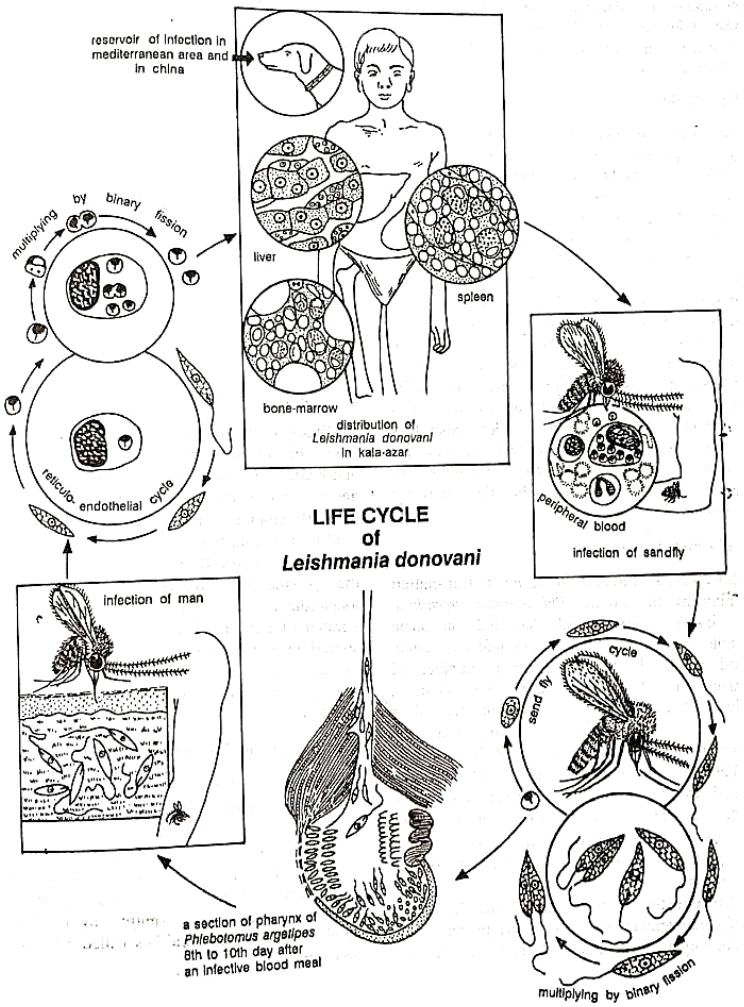

Fig. 4. *Leishmania donovani*. Complete life cycle.

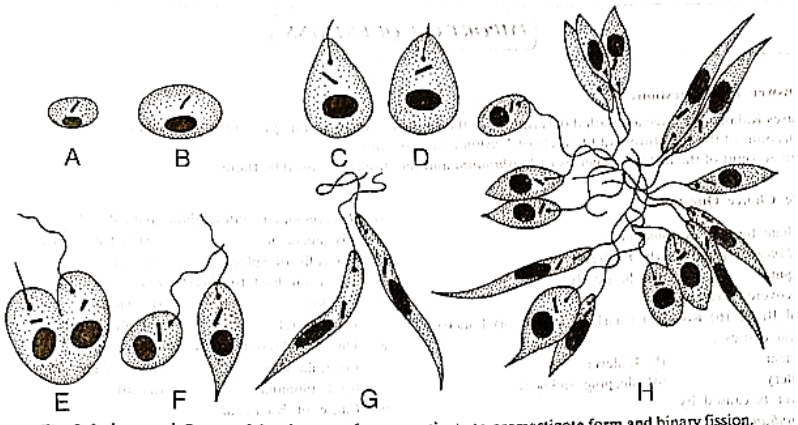

Fig. 5. *L.donovani*. Stages of development from amastigote to promastigote form and binary fission.

Kala-azar or Dumdum Fever

1. Occurrence. Kala-azar, also known as Black fever or Dumdum fever, is a serious oriental disease of man. It occurs in India, China. Mediterranean countries and parts of Africa and South America. Its causative agent is a pathogenic flagellate, called *L. donovani*, which is transmitted By the bite of small blood-sucking sandflies called *Phlebotomus argentipes.*

2. Symptoms and pathogenesis. Incubation period is long, from 3 to 6 months and symptoms may appear even after 2 years. Early symptoms of Kala-azar include swelling, high fever and enlargement of spleen and liver. It is followed by general weakness, emaciation, anaemia due to reduction in number of blood cells, and a peculiar darkening of skin. The word "Kala-azar" has been derived. from two Indian words, kala and azar, meaning "Black sickness". In advanced stage, skin becomes dry, rough and dark or pigmented. Hair becomes brittle and falls out. If not properly treated, the patient dies within 2 years. Death is generally due to secondary infections by bacteria or viruses. The defense mechanism of body becomes so weak that the patient is unable to resist them.

3. Diagnosis. Kala-azar can be diagnosed by microscopical examination of blood film or biopsy material taken from spleen or bone marrow of patient, for the presence of amastigote forms of *L. donovani*. Examination of WBC count shows decrease of neutrophils but increase of lymphocytes and monocytes. Number of erythrocytes (RBC) is also decreased.

4. Treatment (Therapy). For treatment of Kala-azar, two groups of drugs are used. Pentavalent antimony compounds extensively used are sodium-antimony tartrate and gluconate, urea stibamine, aminostiburea, neostibosan, etc. Pentamidine isethionate is also used.

5. Prevention (Prophylaxis). Prevention measures include:

(a) Eradication of the insect vector, i.e., sandfly. In endemic areas, low trees and bushes, etc. should be cleared out. Periodic.fumigation and spray of insecticides of sleeping quarters should be done.

(b) Attack on the parasite. In areas where.dogs act as reservoir hosts, all street dogs should be killed. Control measure in India should be proper treatment campaign.

(c) Personal defense. For avoiding bite of sandflies, use mosquito-nets or screens and avoid sleeping on ground floors.

References:

Kotpal RL (2013). Modern Text Book of Zoology: Invertebrates (10th edition). Rastogi Publications, India.