



Review on Leishmaniasis

Gaurav Verma ^{a#}, Subham R. Nayak ^{a*}, Nikhar Gupta ^b, Ratindra Bisht ^{c‡}
and Snigdha Tripathy ^d

^a Department of Microbiology, Kalinga Institute of Medical Sciences, Bhubaneswar, Odisha, India.

^b Department of Microbiology, Maharishi Markandeshwar University, Mullana, Ambala, Haryana, India.

^c All India Institute of Medical Sciences, Rishikash, Uttarakhand, India.

^d Department of Microbiology, Vikash Multispecialty Hospital, Bargarh, Odisha, India.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Leishmaniasis disease is caused by parasites and its spread by the bite of different types of sand flies. The genus *Leishmania* is named after the death Sir William Leishman, who discovered the flagellate protozoa which is the causative agent of Kala-azar, the *Indian visceral leishmaniasis* (VL). On clinical symptoms they have three species: *Cutaneous leishmaniasis*, *visceral leishmaniasis* and *mucocutaneous leishmaniasis*. This infection diagnosis is based on the severity of the condition. In comparison to two other types of leishmaniasis, cutaneous leishmaniasis is not more dangerous. The treatment's effectiveness varies depending on the type of resistance pattern and the infecting species. The lack of a vaccination for human leishmaniasis may be due to a lack of funding in this neglected parasitic disease.

Keywords: *Leishmania*; leishmaniasis; donovani; visceral leishmaniasis; vector-born disease; kala-azar; old world leishmaniasis; dum dum fever; sand fly; black fever.

[#]PhD Scholar;

[‡]Junior Resident;

^{*}Corresponding author: E-mail: subham.ravinayak@gmail.com, 2181025@gmail.com;

1. INTRODUCTION

Leishmaniasis is caused by the parasitic protozoan which belongs to the genus *Leishmania* of the family Trypanosomatidae. It is generally a zoonotic vector-borne disease which is generally caused by the intracellular parasitic protozoan which belongs to the genus *Leishmania*. It is generally a disease of concern in the subtropical and tropical regions. Humans get affected by the disease when the same environment is shared by human, flies and the reservoir host [1-3]. When an infected fly bites human or any other mammals *Leishmania* infection get transmitted [4]. *Leishmania* infections can be transmitted by other means such as blood transfusions, sharing of used needles [5] or placental transfer [6], but these cases are too rare [7]. "World health organisation (WHO) has listed Leishmaniasis among the seven most vital tropical diseases. It signifies a significant world health illness problem which represents a broad spectrum of clinical manifestations with a potentially fatal outcome" [8,9].

Leishmaniasis is endemic in several Mediterranean countries making this parasitic disease for locals and also for travelers. Leishmaniasis is mostly spread in poor countries like East Africa, South East Asia and Latin America. Among all the diseases caused by parasites, mortality from leishmaniasis is among the second most mortality rate after malaria infections, and in terms of disability adjusted life years (DALYs), the 3rd common origin of morbidity after schistosomiasis and malaria with children <15 years suffering from all of the disease burden.

2. HABITAT

The amastigote form of the *Leishmania donovani* is found in the reticuloendothelial system of the body and they are mostly found within the macrophages in the liver, bone marrow, spleen and less often in other locations such as mesenteric lymph nodes, skin and intestinal mucosa.

3. CLASSIFICATION

Leishmania genus includes a number of altered subspecies and varieties, which is dissimilar in several aspects such as the isoenzymes, structure of antigen and other biochemical properties, datumicity of host, properties of growth.

4. EPIDEMIOLOGY

Leishmaniasis is geographically distributed in the tropics and subtropics all over the world, in more than 60 countries worldwide leishmaniasis becomes endemic [10], ranging from most of the Central and South America, part of the North America, Central and South-East Asia, India, China, and Mediterranean region and Africa. "This disease affects the low socioeconomic group of people. Poor ventilation, overcrowding and collection of organic material inside house enhances the transmission of the disease. The burden distribution of the disease, the 90% of cases belongs to Afghanistan, Syria, Pakistan, Saudi Arabia, Algeria, Iran, Peru and Brazil which generally involves cutaneous leishmaniasis disease, and by India, Nepal, Bangladesh, Sudan and Brazil involves visceral leishmaniasis" [11]. According to a study recently the number of cases reported and "the distribution of geographical areas have increased" [12] and "this has raised concern related to the global warming is the reason of high spread of this disease" [13,14].

In 1900, Sir William Leishman observed the parasite inside the spleen smears of a soldier who died of "dumdum fever" or kala-azar at Dum Dum, Calcutta. In 1903, Leishman reported "these findings from London and in the same year Donovan also reported the same parasite in spleen smears of the patients from Madras. Due to this the name *Leishmania donovani* was given to the parasite. Kala-azar or visceral leishmaniasis is a major public health problem in many parts of the world. According to the World Health Organization (WHO), a complete of 500,000 cases of VL occurs per annum in the world. Of these new cases, the 90% are found in the Indian subcontinent, Brazil and Sudan".

The reactivation of Kala-azar in India, beginning in the mid 1970, imposed a property like epidemic in 1977 and involved over 110,000 cases in humans. At first, the disease was confined to some district of Bihar like Muzaffarpur, Samastipur, Vaishali and Sitamarhi. The epidemic increases to West Bengal and first outbreak occurred in 1980 in Malda district.

5. SYMPTOMS/PATHOLOGY

Depending on the species, host immune response and geographical region *Leishmania* can cause 3 types of disease:-

1. *Leishmania donovani* produces visceral leishmaniasis (kala-azar): Symptoms include fever (often 2 fever raises per day) expansion of the liver and spleen, weakness and recurrent emaciation. The disease is usually fatal without treatment, but survivors often develop immunity.
2. "*Leishmania tropica* and *L. mexicana* produces cutaneous leishmaniasis: which can be differentiated by skin lesions (oriental sore). Infected macrophages having amastigote are found predominantly at the site of infection around the sores. The sores are characterized by an increase rim encircling the lesion. The sores generally heal by themselves within a year, but secondary bacterial infections are a cause of concern in open sores" [15-19].
3. *Leishmania braziliensis* causes mucocutaneous leishmaniasis: characterized by lesions near mucosal membranes. The starting site of infection is a small red papule that ulcerates in a few days to few weeks. The lesions are flat (no increased rim) and sometimes oozing. Infections of the nose, ear and mouth area cause degeneration of the cartilage and soft tissues, leading to disfigurement.
2. Macrophages phagocytize the promastigotes.
3. Promastigote converts into amastigote.
4. Amastigotes multiply in cells and macrophages by binary division until cell lysis; and also throughout this time, the signs and symptoms of the disease become extremely prevalent.
5. The sand fly takes a blood and ingests macrophages having amastigote.
6. Amastigote reaches the infective stage when they convert into promastigote in the sand fly's midgut.
7. Promastigotes transfer to the proboscis, ready to be released during the next blood sucking.

7. CULTURE MEDIA USED FOR CULTIVATION OF LEISHMANIA

There are two main culture media used i.e.

1. NNN medium: This medium was first discovered by Novy and McNeal and was later modified by Nicolle. This medium contains two part of the salt and one part of removed fibrin from rabbit blood. In this the specimens are inoculated into water of condensation of the medium and incubated at 22° C to 24° C. In this the amastigote form is present in specimen will change into promastigote forms which then multiply in the water of condensation of the medium.
2. Hockmeyer's medium: This liquid medium contains Schneider's insect culture medium with added fetal calf serum and antibiotics like Penicillin and Streptomycin. The specimen is inoculated into the medium and incubated at 22° C to 24° C. After incubation the medium is examined microscopically daily for the presence of promastigotes.

8. DIAGNOSE

8.1 Cutaneous Leishmaniasis

By sweeping one of the body's ulcers, a little bit of skin is retrieved for a biopsy. To identify the parasite, the samples are examined under a microscope or in a culture. A culture is a technique for determining whether or not a material contains parasites. A tiny number of parasites can develop to a detectable level in culture. Visceral Leishmaniasis.

6. LIFE CYCLE

Leishmania completes its life cycle in two hosts i.e. Definitive host and Vector.

Definitive Host: Dog, Man and other mammals.

Vector: Female sand fly (*Phlebotomus* species).

Infective form: metacyclic promastigote.

Mode of Transmission:

- Humans get the parasite infection by the bite of an infected female sand fly that inoculates the promastigote form in skin.
- It can also be transmitted direct from mother to fetus, by the blood transfusion and accidental inoculation in the diagnostic laboratory and experimental studies (in vivo and in vitro).

Incubation Period: Usually it takes 2-8 months, occasionally; it may be as short as 10 days or as long as 2 years.

Different steps:-

1. While sucking blood, the sandfly press promastigote through the proboscis into the skin.

Table 1. The main species of *Leishmania* that cause human disease

Species	Disease	Vector	Reservoir	Transmission	Geographical distribution
<i>Leishmania donovani</i>	Visceral leishmaniasis (kala-azar or dumdum fever)	Phlebotomus argentipes, Phlebotomus orientalis	Humans	Arthroponotic, Occasionally zoonotic.	Middle East, Africa & India subcontinent
<i>Leishmania infantum</i>	Visceral leishmaniasis, cutaneous leishmaniasis	Phlebotomus perniciosus, Phlebotomus ariasi, Phlebotomus papatasi	Dog, fox, wolf and jackal.	Zoonotic	Mediterranean coast, Middle East and China
<i>Leishmania major</i>	Cutaneous leishmaniasis	Phlebotomus papatasi, Phlebotomus duboscqi.	Gerbil	Zoonotic	Africa, Indian subcontinent and central Asia
<i>Leishmania infantum chagasi</i>	Visceral leishmaniasis	Lutzomyia longipalpis.	Fox and wild canines	Zoonotic	Tropical South America
<i>Leishmania tropica</i>	Cutaneous leishmaniasis (oriental sore, Baghdad boil)	Phlebotomus sergenti	Humans	Anthroponotic	Middle East and Central Asia
<i>Leishmania aethiopica</i>	Cutaneous and diffuse cutaneous leishmaniasis	Phlebotomus longipes, Phlebotomus pedifer	Hydraxes	Zoonotic	Ethiopia and Kenya
<i>Leishmania braziliensis complex</i>	Mucocutaneous leishmaniasis (Espundia)	Lutzomyia umbratilis	Forest rodents and peridomestic animals	Zoonotic	Tropical South America
<i>Leishmania mexicana complex</i>	Mucocutaneous leishmaniasis (Chiclero's ulcer)	Lutzomyia olmeca, Lutzomyia flaviscutellata	Forest rodents and marsupials	Zoonotic	Central America and Amazon basin

The majority of people do not recall a sand fly bite or a skin irritation. In those circumstances, diagnosing the problem is challenging. In some circumstances, a doctor may do a physical examination to rule out the possibility of a liver or spleen problem. A bone marrow biopsy or a blood sample for testing may be performed. They'll look for the parasite in these samples. If a culture is required, the diagnosis may take 2 to 4 weeks. Leishmanin or Montenegro test.

It was first introduced in the South America by Montenegro. It is a delayed hypersensitivity reaction to intradermal *Leishmania* antigen. This is a skin test; Leishmanin skin test is negative in Kala-azar.

In Leishmanin test, 0.2 mL of killed suspension of promastigotes of *L. donovani* is injected intradermally. This test is read after 72 hours. A positive reaction is indicated by an area of erythema and in duration of 5 mm or more in diameter. This test is also positive in dermal leishmaniasis and in persons who have recovered from kala-azar. The test becomes positive 6-8 weeks after cure from kala-azar.

9. PROPHYLAXIS

The annihilation of the vector through insecticides, discarding of stagnant water, use of insect impervious, and prophylaxis are often achieved through the utilization of thick clothes with long sleeves that can be inseminate with insecticides [20] and long pants and by avoiding going to jungles at night [21]. The WHO is putting an effort to develop a vaccine that would protect against all types of the leishmaniasis [22].

10. TREATMENT

In addition to be Anti parasitic drugs, like amphotericin B, treat this condition.

10.1 Cutaneous Leishmaniasis

Cutaneous ulcers will healed without treatment. However, there are some treatments that can help to speed up the healing process and reduce scarring. It has the ability to prevent the spread of disease. Damaged facial ulcers will necessitate plastic surgery.

10.2 Visceral Leishmaniasis

Visceral illness necessitates medical attention. There are some drugs available. Antimony-containing chemicals are the most commonly

used medicines. Meglumine antimoniate and sodium stibogluconate are two of them. Mucocutaneous Leishmaniasis.

These lesions don't heal naturally. They need to be treated. Mucocutaneous leishmaniasis is treated with liposomal amphotericin B and paromomycin. The World Health Organization (WHO) has initiated an advocacy campaign to help cut the cost of these drugs. Liposomal amphotericin B's value was reduced by 90%, and meglumine antimoniate's value was reduced by 60%. The goal is to make it easier for patients to access these therapies by lowering the cost.

11. CONCLUSION

"Although leishmaniasis becomes a serious public health problem in several countries, its epidemiological status is unevenly situated in several parts of the world" [23]. "Leishmaniasis remains a devastating infection need either potentially toxic treatments or less toxic, but expensive drugs. However, the supply of newer oral agents may change the way this disease is treated. Relapse may occur, especially in situations where immunosuppression is present; secondary prophylaxis must tend during this setting. The difficulty of *Leishmania* transmission lays on its involvement of various mammalian hosts, ranging from small rodents to big domestic animals, as reservoir hosts" [24]. "Human foist environmental changes result in the modification of the micro-ecology of the parasite, the vector and the reservoir host favoring the higher transmission of leishmaniasis in areas" [25].

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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