Review Article

REVIEW ON LEISHMANIASIS

ABSTRACT

Leishmani~~a~~~~s~~is 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 *mucocutanious leishmaniasis*. This infection diagnosis is depending on the disease severity. The cutaneous leishmaniasis isn't more dangerous in compare two other kind of leishmaniasis. ~~There is a different techniques are available for diagnosis purpose of leishmaniasis.~~ The efficacy of the treatment varies with the kind of resistance pattern and infecting species. The persistent lack of vaccine against human leishmaniasis may be a result of the poor investment in this neglected parasitosis.

Keywords: Leishmania, Leishmaniasis, Donovani, Visceral leishmaniasis, vector-born disease, Kala-azar, old world leishmaniasis, Dumdum fever, Sand fly, black fever.

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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 [6] or placental transfer [7] , but these cases are too rare [5].World health organisation (WHO) has listed Leishmaniasis among the seven most vital tropical diseases. It signifies a significant world health illness

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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 travellers. 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 (*REFERENCE UNCLEAR).

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.

CLASSIFICATION

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

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

Species	Disease	Vector	Reservoir	Transmission	Geographical distribution
Leishmania donovani	Visceral leishmaniasis (kala-azar or dumdum fever)	Phlebotomus argentipes, Phlebotomus orientalis	Humans	Arthroponotic, Occasionally zoonotic.	Middle East, Afric & India subcontinent.
Leishmania infantum	Visceral leishmaniasis, cutaneous leishmaniasis	Phlebotomus perniciosus, Phlebotomus ariasi, Phlebotomus papatasi.	Dog, fox, wolf and jackal.	Zoonotic	Mediterranean coast, Middle East and China.
Leishmania major	Cutaneous	Phlebotomus	Gerbil	Zoonotic	Africa, Indian

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	leishmaniasis	papatasi, Phlebotomus duboscqi.			subcontinent and central Asia
Leishmania infantum chagasi	Visceral leishmaniasis	Lutzomyia longipalpis.	Fox and wild canines	Zoonotic	Tropical South America
Leishmania tropica	~~c~~Cutaneous leishmaniasis (oriental sore, Baghdad boil)	Phlebotomus sergenti	Humans	Anthroponotic	Middle East and Central Asia~~.~~
Leishmania aethiopica	C~~c~~utaneous and diffuse cutaneous leishmaniasis	Phlebotomus longipes, Phlebotomus pedifer	Hydraxes	Zoonotic	Ethiopia and Kenya~~.~~
Leishmania braziliensis complex	Mucocutaneous leishmaniasis (Espundia)	Lutzomyia umbratilis	Forest rodents and peridomestic animals	Zoonotic	Tropical South America~~.~~
Leishmania mexicana complex	Mucocutaneous leishmaniasis (Chiclero's ulcer)	Lutzomyia olmeca, Lutzomyia flaviscutellata	Forest rodents and marsupials	Zoonotic	Central America and Amazon basin

EPIDEMIOLOGY

Leishmaniasis is geographically distributed in the tropics and subtropics all over the world, in more than 60 countries worldwide ~~l~~L~~l~~eismaniasis 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 (*REFERENCE UNCLEAR).

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 (REFERENCE UNCLEAR).

SYMPTOMS/PATHOLOGY

The Infection with Leishmania species can result in 3 types of disease depending on the species, host immune response and geographical region.

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 (REFERENCE).
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. ~~The~~ *Leishmania braziliensis* causes mucocutaneous leishmaniasis: characterized by lesions near mucosal membranes (usually on the oral and nasal mucosa). 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 (REFERENCE).

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: ~~The midgut of female sand fly contains the~~ metacyclic p~~P~~romastigote.

Comment [A10]: Also *L. chagasi*

Comment [A11]: Also *L. braziliensis* and *L. amazonensis*

Comment [A12]: mucosal lesions usually appear two years after the skin lesion (cutaneous leishmaniasis untreated)

Comment [A13]: Kidney?

Comment [A14]: Human – accidental host. For dogs, its until unclear.

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Mode of transmission:

- Humans get the parasite infection ~~infected~~ 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 sand-fly press promastigote through the proboscis into the skin.
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.

CULTURE MEDIA USED FOR CULTIVATION OF LEISHMANIA:

There are two main culture media used i.e.

I. NNN medium: This medium was first discovered by Novy and McNeal and was later modified by Nicolle (year?). 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 ~~condensatrion~~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 (REFERENCE UNCLEAR).

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Comment [A18]: The authors could cite or show a figure of *leishmanial* life cycle.

Comment [A19]: the signs and symptoms are consequence of immune response of host and depending of parasite specie.

Comment [A20]: For culture of Promastigote forms of Leishmania

II. 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 (REFERENCE UNCLEAR).

DIAGNOSE

~~Diagnosing~~ Cutaneous Leishmaniasis

Small amount of skin is taken for a biopsy by sweeping one of the ulcers present in the body. The samples are observed under a microscope or in a culture to distinguish the parasite. A culture is a method to identify whether there are parasites present in a sample. Culture provides a small amount of parasites to grow to a detectable level.

~~Diagnosing~~ Visceral Leishmaniasis

More often~~,~~ people does not remember a bite from a sand fly or a skin sore. In those cases there is a difficulty in diagnosis. I those cases a doctor may first perform a physical exam to look for an explanation liver or spleen. They may carry out a bone marrow biopsy or take a blood sample for examination. They will study these samples for the parasite. Diagnosis may take 2 to 4 weeks if a culture is necessary.

Leishmanin or Montenegro test

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

In Leishmanin test, 0.2 mL~~l~~ 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.

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Comment [A22]: Or scarification

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Comment [A25]: The authors could explain this item by clinical form of leishmaniasis. Because also L. braziliensis is used for this diagnosis. And people infected by L. amazonensis is usually negative in this test.

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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 ~~develope~~develop –a vaccine that would protect against all types of the leishmaniasis [22].

TREATMENT (explore more this item and give references)

The first choice recommended by WHO? Meglumine antimoniate.

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

Cutaneous Leishmaniasis

Cutaneous ulcers will -healed without treatment. However; some specific treatment can speed up -healing and decrease scarring. It can stop the development of further disease. Facial Ulcers causing damage -will require plastic surgery.

Visceral Leishmaniasis

Visceral disease needs treatment. Some medications are available (which?). The main sets of medicine used are compounds that contain antimony. These include meglumine antimoniate and sodium stibogluconate.

Mucocutaneous Leishmaniasis

These lesions don't heal naturally. They require some treatment. Liposomal amphotericin B and paromomycin is used for the treatment of mucocutaneous leishmaniasis. WHO launched an advocacy campaign to assist reduce the worth of those drugs. The program reduced the worth of liposomal amphotericin B by 90 percent and meglumine antimoniate by 60 percent. The motive is that lowering the value will make it easier for people to get these treatments.

CONCLUSION

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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].

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