

Current Perspectives on Leishmaniasis

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Sir William Boog **Leishman** first demonstrated *Leishmania donovani* parasite in spleen smear of English soldier from London, who died of **Dum Dum fever** or **kala azar** contracted at Dum-Dum in Kolkata, India, in 1903. In the same year, **Sir Donovan** also reported the same parasite in spleen smear of a patient from Madras (Chennai), India. The name *Leishmania donovani* was therefore given to this parasite.

Their simultaneous discovery of *Leishmania donovani* first alerted the scientific community to the life threatening disease of visceral leishmaniasis. Now a century later, millions are still afflicted by *Leishmania*. It is a disease known for its complexity and diversity. It is endemic in regions ranging from the rainforests of South America to the deserts of Asia, and afflicts both rural and urban communities. A host of about 21 different species of *Leishmania* are classified under its primary syndromes; cutaneous, mucocutaneous and visceral, which result from parasite multiplication in macrophages in the skin, nasal-oral mucosa and internal organs, respectively. These protozoan species are transmitted by over 30 species of **phlebotomine sand flies**. Charles Nicolle, a 1928 Nobel laureate, at the Pasteur Institute of Tunis, characterized the new World visceral leishmaniasis and cultivated the etiologic agent.

While most modes of transmission are vector borne, some are congenital and parenteral (i.e. by blood transfusion, needle sharing, and laboratory accident). Also increases in travel and international migration have brought this disease to the attention of developed nations. Available treatments for leishmaniasis are expensive or have serious associated toxicities and may lead to the development of drug-resistant parasites. Prevention and control regimens focusing on vector reservoir control had not changed in decades. However international attention has now shifted towards the development of effective and cost-efficient treatment. Exciting recent advances in diagnosis, treatment, prevention makes most interesting to learn about Leishmaniasis.

Genus *Leishmania* is a **protozoan parasite** belongs to Phylum *Sarcomastigophora*, subphylum *Mastigophora*, family *Trypanosomatidae*, class *Kinetoplastidea*, and order *Trypanosomatida*. Genus *Leishmania* has two subgenera **L. Leishmania** and **L. Viannia**. The main difference between the two subgenera is that promastigotes of the subgenus *Viannia* develop in the midgut and hindgut of sandfly where as that of subgenus *Leishmania* develop in the anterior portion of the alimentary tract of sandfly. Both the subgenera comprise of nearly 20 species that are nearly identical in morphology. Differentiation is, therefore, based on a number of biochemical and epidemiological criteria, use of monoclonal antibodies to detect specific antigens, promastigote growth patterns *in vitro* in the presence of antisera, vectors and reservoir hosts.

Leishmania parasite exists in two stages: 1. **Amastigote** or aflagellar stage or **LD bodies** or leishmanial form is an obligate intracellular parasite of reticuloendothelial system (macrophages, monocytes, neutrophils, endothelial cells) predominantly of liver, spleen, bone marrow, lymph nodes etc of humans, and other vertebrate hosts (dogs, hamsters and other rodents), and 2. **Promastigote** or flagellar stage or **leptomonad** form is an extracellular form, lives in the digestive tract of insect vector, sand fly (genus *Phlebotomus* and *Lutzomyia*) and in cultures in the laboratory, which is an infective stage to the humans.

Fig 1: a) A macrophage filled with intracellular amastigotes of *Leishmania donovani* (Source: cdc.gov) b) Promastigotes (Leptomonad forms) (Source: pinterest.com)



Leishmaniasis is a disease caused by obligate intracellular protozoan parasites of the genus *Leishmania*, primarily affecting the reticuloendothelial system transmitted by the bite infected female phlebotomine sandflies. *Leishmania* species produce widely varying group of clinical syndromes ranging from self-healing cutaneous ulcers to fatal visceral disease, each with its own clinical manifestations and epidemiology. The parasite is transmitted by bite of the **female sandfly vector**.

The dog has been found to be naturally infected with *Leishmania donovani* in the Mediterranean region. A small rodent of North China, called a **hamster** (*Cricetulus griseus*) has been found to be very susceptible to *Leishmania donovani* infection. **Leishmaniasis** is mainly a **zoonotic** disease affecting dogs, foxes, jackals, and rodents. Animal reservoir hosts play major role in transmission of the disease. In Mediterranean region, China, and Brazil the dog is considered to be reservoir of infection. But in Indian subcontinent it is **anthroponotic** and non-zoonotic affecting only in humans and canine leishmaniasis does not exist. In Sudan and East Africa, rodents are reservoir hosts, and in Russia, the jackals are the reservoirs of infection. The hamster is the laboratory animal of choice for the isolation of *Leishmania* spp.

Fig 2: Phlebotomine sandfly



Leishmaniasis occurs in 98 countries; most of them developing countries of tropical and temperate regions. More than 350 million people are at risk, with an overall prevalence of 12 million. Two million cases occur annually, of which 1 – 1.5 million are cutaneous leishmaniasis and its variations and 500,000 cases are visceral leishmaniasis. **Four largest foci of visceral leishmaniasis (90%) are India, Nepal, Bangladesh, Sudan, Brazil.** In Indian subcontinent, visceral leishmaniasis is anthroponotic, while zoonotic visceral leishmaniasis is reported from Middle East, Pakistan, and other countries from Western Asia to China.

India is the worst affected country. Bihar is affected the most followed by Jharkhand, West Bengal and Uttar Pradesh. Forty eight districts with more than 165 millions of people are at risk. In 2012, more than 20,000 cases are reported from India with 23 deaths. Sporadic cases have been reported from Tamil Nadu, Pondicherry, Assam, Orissa, and Gujarat. Visceral leishmaniasis is an important opportunistic infection in AIDS patients.

In **Nepal**, the disease affects Eastern Terai region which lies adjacent to the Bihar state of India. Data collected from eight zonal hospitals in the Terai region suggests that the first confirmed case of visceral leishmaniasis was recorded in 1980. By 2003, the disease has spread to 14 districts of Central and Eastern regions of Nepal, and nearly six million people residing in these districts were at the risk of acquiring the disease. A total of 25,890 cases with 599 deaths were reported during the year 1980-2006 (up to July). District-wise analysis showed that, during 2003, highest incidence (per 100,000) was in Mahottari district (184), followed by Sarlahi (100) and Sunsari (96). The highest case fatality rate was in Dhanusha (2.9%) followed by Bara (2.4%) and Saptari (2.0%). The incidence of visceral leishmaniasis in Nepal seems to be increasing at a faster rate.

Leishmaniasis can be categorized by **geographic occurrence** into old world leishmaniasis and new world leishmaniasis. The term '**New world**' refers to the Americas and the '**Old world**' is used for the rest of the World.

i) **Old world leishmaniasis** caused by *Leishmania* species found in Africa, Asia, the Middle East, the Mediterranean, and India, which produces cutaneous or visceral leishmaniasis. The parasites of the old world leishmaniasis (*Leishmania donovani*, *L.L. infantum*, *L.L. tropica*, *L.L. major*, *L.L. aethiopica*) are transmitted to humans by the bite of female sandflies of the genus *Phlebotomus*.

ii) **New world leishmaniasis** caused by *Leishmania* species found in Central and South America, which produces cutaneous, mucocutaneous or visceral leishmaniasis. The parasites of the new world leishmaniasis (*L. Viannia peruviana*, *L.L. chagasi*, *L.L. mexicana complex*, and *L.Viannia braziliensis complex*) are carried by sandflies of the genera *Lutzomyia* and *Psychodopygus*.

Table 1: Clinical syndromes of leishmaniasis

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

OLD WORLD LEISHMANIASIS

I) VISCERAL LEISHMANIASIS

Visceral leishmaniasis, also known as **kala azar** (A Hindi term meaning **black fever**), **Dumdum fever** is fatal if left untreated in over 95% of cases. It is caused by *Leishmania donovani* complex that consists mainly of *L. infantum*, *L. donovani*, and *L. chagasi*.

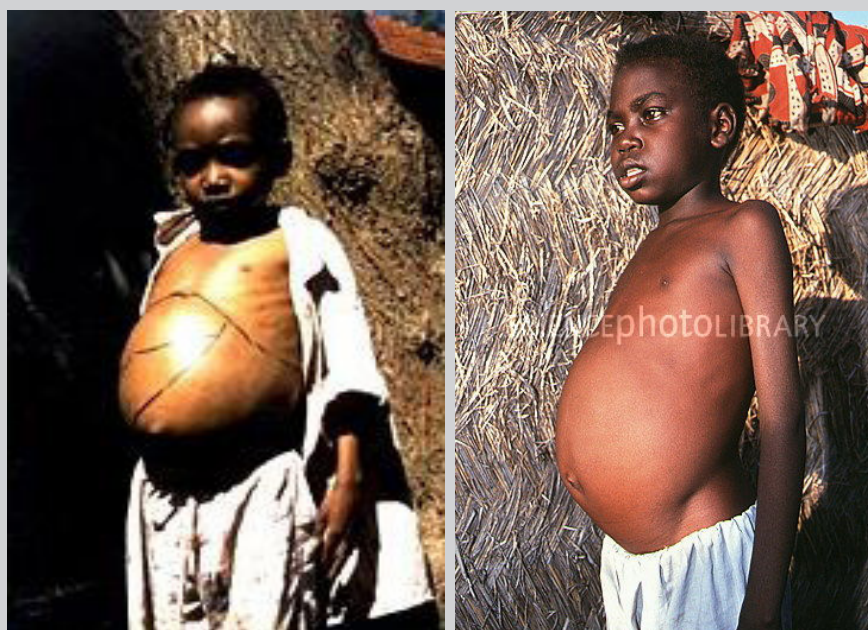
Visceral leishmaniasis is a systemic disease characterized by a triad of fever, hepatosplenomegaly, and pancytopenia.

- Pyrexia is often an early symptom with irregular bouts of fever and rigor and chills, typically described as classical double rise of fever in 24 hours. Waves of pyrexia may be followed by apyrexial period
- Weight loss (Cachexia)
- Splenic enlargement is one of the most striking features and the organ progressively enlarges. With the progress of the disease, it extends several inches below the costal margin, often filling up the entire abdomen and palpable below the umbilicus.
- Hepatomegaly, usually moderate soon follows splenomegaly
- Lymphadenopathy is rare in Indian subcontinent but common in Africa and China.
- The skin over the entire body is dry, rough and harsh and is often pigmented (Darkened skin). The hair tends to be brittle and falls out.
- Pedal edema and ascites occur due to hypoalbuminemia in advanced stages of illness.
- In African kala azar watery eruption on the skin and mucosal lesions in mouth and nasopharynx are commonly seen, rare in India.
- Anemia (Normocytic and normochromic) appears early and may become severe enough to cause congestive heart failure
- Leucopenia
- Thrombocytopenia can lead to epistaxis, retinal hemorrhages, and gastrointestinal bleeding
- Hypergammaglobulinemia due to polyclonal B cell activation
- Nodular skin lesions (Leishmanioma) seen in African cases only
- If left untreated, 75 – 95% of the patients die within a period of two years. Death in kala azar is always due to some secondary complications, such as bacillary or amoebic dysentery, gastroenteritis, pneumonia, pulmonary tuberculosis, measles, and other septic infections. Cancrum oris seen in cases of severe neutropenia. It is to be noted that a profound immunosuppressive effect has been observed in kala azar and this may lead to bacterial invasion, which the patient will not be able to resist.

Table 2: Various forms of visceral leishmaniasis

	Old World visceral leishmaniasis			New World visceral leishmaniasis
	Indian visceral leishmaniasis (Kala azar)	Infantile visceral leishmaniasis	African visceral leishmaniasis	Mediterranean visceral leishmaniasis
Causative agent	<i>Leishmania donovani</i>	<i>Leishmania infantum</i>	<i>Leishmania donovani</i>	<i>Leishmania chagasi</i>
Vector	<i>Phlebotomus argentipes</i>	<i>Phlebotomus perniciosus</i>	<i>Phlebotomus orientalis</i> , <i>P. martini</i>	<i>Lutzomyia longipalpis</i>
Epidemiology	Indian subcontinent, East Africa	Middle East, Central Asia, China and Mediterranean basin	Sudan, Ethiopia, Kenya, Uganda	Central and South America
Age group affected	Young adults	Infants and children <5 years of age	Adults	Children
Reservoir	Anthroponotic (Human)	Zoonotic (Canine)	Anthroponotic, rarely zoonotic (Rodents)	Zoonotic (Canine)
PKDL	Common	Less common	Common	Less common
Lymph node involvement	Less common	More common, aggravated by poor response	Less common	Less common

Fig 3: Splenomegaly seen in visceral leishmaniasis (Sources: web.stan and slideshare.net)



II) POST-KALA AZAR DERMAL LEISHMANIASIS (PKDL)

It develops months to years after the patient’s recovery from visceral leishmaniasis (A sequel of visceral leishmaniasis), with cutaneous lesions ranging from hypopigmented macules to erythematous papules and from nodules to plaques usually on face, upper arms, trunks and other parts of the body. The lesions may be numerous and persist for decades. It occurs mainly in East Africa and on the Indian subcontinent, where 5-10% of

patients with kala-azar develop the condition. It usually appears six months to one or more years after kala azar has apparently been cured, but can occur earlier. People with PKDL are considered to be a potential source of kala azar infection.

PKDL develops as hypopigmented macule (Most common feature) near mouth which later on spreads to face and then to arms and trunks and finally becomes nodules resembling leprosy. Erythematous patches may occur as early lesions which appear on the nose, cheeks and chin, often having butterfly distribution (butterfly erythema). They are very photosensitive, becoming prominent towards the middle of the day. The nodules are soft, painless granulomatous growths of varying sizes generally found on the skin (Usually on face but can occur in any part of the body) and rarely on the mucus membrane of the tongue and eyes. Ocular lesions like conjunctivitis and uveitis are associated in some patients. Sometimes, PKDL occurs in patients with subclinical infection without a history of visceral leishmaniasis.

The diagnosis is based on detection of amastigote in the skin in more than 80% cases in the Sudan. Amastigote is more easily detected from nodular lesions than other lesions. Direct agglutination test to demonstrate antibodies to rK39 antigen are positive in most of the cases.

The treatment of PKDL is by giving extended course of antimonial for a period of two to four months. PKDL cases often serve as reservoir of infection.

Fig 4: Post kala azar dermal leishmanoid (PKDL) a) Hypopigmented skin in early PKDL; b, c) Extensive facial nodular lesions in late PKDL (Source: El Hassan "Manual on visceral leishmaniasis control" WHO)



***Leishmania*-HIV coinfection**

HIV and *Leishmania* co-infection has become a significant concern for developing nations with high numbers of HIV immunocompromised individuals. *Leishmania*-HIV coinfecting people have high chance of developing full blown clinical disease, and high relapse and mortality rates.

Both HIV and *Leishmania* affect each other's pathogenesis. *Leishmania* appears to cause activation of latent HIV by expressing high level of chemokine receptors (CCR5) on macrophages. HIV causes activation of TH₂ (T helper cells) cell response leading to disease progression and more relapses. *Leishmania* uptake is enhanced by the uptake HIV infected macrophages.

HIV co-infected patients do not show the classic signs of kala azar like hepatosplenomegaly but present with atypical features due to loss of immunity with presence of more gastrointestinal and pulmonary symptoms. The CD4 T cell count, often fall below 50/ μL (Almost always $<200/\mu\text{L}$). There is a consideration to include leishmaniasis in Center for Disease Control and Prevention (CDC) clinical category C for the definition of AIDS as an opportunistic pathogen. Serodiagnostic tests for leishmaniasis are usually negative. Amastigotes are demonstrated in unusual sites such as bronchoalveolar lavage fluid and buffy coat region of blood.

Liposomal amphotericin B is the drug choice for HIV-visceral leishmaniasis co-infection, but response is poor with frequent relapses. Antiretroviral treatment reduces the development of the disease, delays relapses and increases the survival of the co-infected patients.

Co-infection of HIV with visceral leishmaniasis has been reported from more than 35 countries. Mainly it is reported from Southern Europe (France, Italy, Spain and Portugal) where 5 - 75% of adult cases of visceral leishmaniasis are HIV positive and 7 - 17% of HIV infected people with fever have amastigotes. Also, reported from other places like sub-Saharan African and Indian subcontinent. In India, it is reported from Bihar, sub-Himalayan region and other North Indian States. Various studies reported the co-infection prevalence around 2 - 6%. High *Leishmania*-HIV co-infection rates are reported from Brazil, Ethiopia and the state of Bihar in India.

III) CUTANEOUS LEISHMANIASIS

It is also known as **Oriental sore, Tropical sore, Delhi boil, Aleppo boil, Baghdad button** is the most common form of leishmaniasis and causes skin lesions, mainly ulcers, on exposed parts of the body, leaving life-long scars and serious disability. It is caused by *Leishmania tropica* complex.

Leishmania tropica complex includes three species- *L. tropica*, *L. aethiopica*, and *L. major*. They cause old World cutaneous leishmaniasis. *L. tropica* is reported from Western India (mainly Rajasthan), Middle East and Mediterranean coast. It mainly affects urban area hence known as agent of urban anthroponotic cutaneous leishmaniasis. *L. aethiopica* infections are common in Ethiopia, Uganda, and Kenya. *L. major* is reported from Middle East, India, China, Africa, and Central Western Asia. It mainly affects rural area hence known as agent of rural zoonotic cutaneous leishmaniasis.

It is to be noted that *Leishmania tropica* exists in many countries where *L. donovani* is prevalent; the two parasites are not found in the same locality, and kala azar is very rare from places where oriental sore is endemic. In India, kala azar is confined to moist Eastern parts, whereas oriental sore is limited to dry Western parts. In Central Asia and Eastern Mediterranean region, they may be found side by side in a single family.

Table 3: *Leishmania tropica* complex of cutaneous leishmaniasis

Species	Geographical distribution	Clinical syndrome	Vector (Sandfly)	Reservoir	Transmission
<i>Leishmania tropica</i>	Western India, North Africa, Middle East	Cutaneous leishmaniasis, Leishmaniasis recidivans	<i>Phlebotomus sergenti</i>	Humans	Anthroponotic

<i>L.L. aethiopica</i>	Ethiopia, Uganda, Kenya	Cutaneous leishmaniasis, Diffuse cutaneous leishmaniasis	<i>Phlebotomus longipes</i>	Hyraxes	Zoonotic
<i>L.L. major</i>	Middle East, India, China, Africa, Central and Western Asia	Cutaneous leishmaniasis	<i>Phlebotomus papatasi</i>	Rodents	Zoonotic

The oriental sore usually occurs on face and hands. It begins as papule, becomes nodular and finally it ulcerates. The margins of the ulcers are raised, painless and indurated. 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. There may be satellite lesions, especially in *L. major* and *L. tropica* infections.

Fig 4: Cutaneous leishmaniasis (Source: dermatologyoasis.net)



Fig 5: Multilesional cutaneous leishmaniasis (Source: cmaj.ca)



IV) LEISHMANIASIS RECIDIVANS

It is a granulomatous response or relapse or recurrence of lesions at the site of apparently healed cutaneous leishmaniasis disease years after the original infection, typically on the face and often involving the cheek. It is characterized by new lesions formed on the face, usually scaly, erythematous papules and nodules develop in the center or periphery of a previously healed sore. The relentless expansion at the periphery may cause significant facial destruction similar to the lupus vulgaris variant of cutaneous tuberculosis, may persist for many years with a chronic and relapsing course. Cell mediated immunity (CMI) is intact and skin test (Leishmanin test or Montenegro test) is positive. Very few parasites can be demonstrated in the smears from the lesions.

Fig 6: Leishmaniasis recidivans (Source: slideplayer.com)



V) DIFFUSE (DISSEMINATED) CUTANEOUS LEISHMANIASIS

It is a rare form of leishmaniasis, caused by *L. amazonensis* and *L. mexicana* in South and Central America (New World) and by *L. aethiopica* in Ethiopia and Kenya (Old world). It is characterized by the absence of a Cell mediated immune response (CMI) to the parasite. Low CMI leads to widespread cutaneous disease, symmetric or asymmetric distribution of various lesions like papules, nodules, plaques, and areas of diffuse infiltration, non-ulcerative lesions (Analogous to lepromatous leprosy lesions) with heavy load of parasites. The delayed type hypersensitivity (DTH) response is negative therefore skin test (Montenegro test) is negative.

Fig 7: Diffuse cutaneous leishmaniasis (Sources: f1000Research and scholarship.org)

TREATMENT OF OLD WORLD LEISHMANIASIS

Supportive therapy: Correction of pancytopenia by blood transfusion, prompt management of other associated conditions.

Specific antileishmanial drugs: Pentavalent antimonial compound is the drug of choice in most endemic regions of the world, except in Bihar, India (due to emergence of drug resistance). Two pentavalent antimonial (SbV) preparations are available, **sodium stibogluconate** (100 mg of SbV/mL) and **meglumine antimoniate** (85 mg of SbV/mL).

WHO recommendations, 1995: For visceral leishmaniasis, the daily dose is 20 mg/kg by rapid intravenous infusion or intramuscular injection, and therapy continues for 28 – 30 days till smear microscopy is negative. For cutaneous leishmaniasis, 1 – 3 mL of antimonial preparation should be infiltrated at the base of the lesions for two to three times at interval of 1 – 2 days.

Resistance to antimonials: Increased resistance has been reported to *L. tropica*, *L. major*, and *L. mexicana* in comparison to *L. donovani*. Resistance to *L. donovani* is only reported from North Bihar, India. Mishandling of antileishmanial drugs is the single most important contributor to the development of drug resistance. The mechanism of emergence of this drug resistance is due to failure of reduction of SbV (prodrug) to its active form SbIII inside the resistant *L. donovani* amastigotes.

Amphotericin B is currently used as a first-line drug in Bihar, India for the treatment of visceral leishmaniasis. In other parts of the world, it is used when initial antimonial treatment fails. It is also the drug of choice for the new World mucocutaneous leishmaniasis. Conventional amphotericin B deoxycholate is administered in doses of 0.75 - 1.0 mg/kg on alternate days for a total of 15 infusions. Alternatively, the lipid formulations of amphotericin B are used which have lower side effects.

Paromomycin: It is an aminoglycoside antibiotic with antileishmanial activity. It is given intramuscularly at a dose of 11 mg of base/kg daily for 21 days.

Miltefosine: It is the first oral compound approved for the treatment of leishmaniasis. It is given as daily dose of 50 mg once or twice for 28 days.

PREVENTION OF OLD WORLD LEISHMANIASIS

Control measures to eradicate vector sandfly and personal prophylaxis by using insect repellents or bed nets. *Phlebotomus* doesn't fly high above the ground level and it is nocturnal in habitat. So, sleeping at top floors also can prevent transmission. Control of canine or rodent reservoir hosts is another preventive measure. Early treatment of all cases (Mainly anthroponotic visceral leishmaniasis and PKDL cases).

Currently no vaccine is available for the prevention of leishmaniasis. However, several trials are going on. Both killed and live-attenuated vaccine trials are ongoing targeting antigens derived from killed promastigotes. Trials for recombinant and synthetic vaccines are also ongoing using gp-63 antigen.

NEW WORLD LEISHMANIASIS

It is mainly caused by *Leishmania Viannia (L.V.) braziliensis complex*, *Leishmania Leishmania (L.L.) mexicana complex*, *L. L. chagasi (new World variant of L.L. infantum)*.

The main difference between the two subgenera is promastigotes of the subgenus *Viannia* develop in the midgut and hindgut of sand fly where as that of subgenus *Leishmania* develop in the anterior portion of the alimentary tract of sand fly.

The morphology and life cycle of new world *Leishmania* species are identical to that of *L. donovani* except: Geographical distribution restricted to central and South America, vector *Lutzomyia* species, reservoir hosts include dogs and foxes (Zoonotic), and the amastigote forms in humans reside in reticuloendothelial cells of skin and mucus membranes, and do not invade viscera.

Leishmania Leishmania mexicana complex infected people develop cutaneous leishmaniasis similar to those seen with old World cutaneous disease. *L. mexicana* causes a specific form of cutaneous leishmaniasis called as chiclero ulcer or bay sore characterized by persistent ulcerations in pinna seen in Central America among workers living in forests harvesting chicle plants to collect chewing gum latex. Thirty percent of people are infected during the first year of exposure. *L. mexicana* and *L.amazonensis* produce diffuse cutaneous leishmaniasis similar to that of caused by *L. aethiopica*.

Fig 8: Chiclero ulcer (Source: dermatologyadvisor.com)



Table 6: *Leishmania Leishmania mexicana* complex

Species	Clinical syndrome	Geographical distribution	Vector	Reservoir	Transmission
<i>Leishmania Leishmania mexicana</i>	Chiclero ulcer, diffuse cutaneous leishmaniasis, mucocutaneous leishmaniasis				
<i>L.L. amazonensis</i>	Cutaneous leishmaniasis, diffuse cutaneous leishmaniasis, mucocutaneous leishmaniasis	Central America and Northern parts of South America	Lutzomyia spp	Forest rodents, Marsupial and humans	Zoonotic
<i>L.L. venezuelensis</i>	Cutaneous leishmaniasis				
<i>L.L. pifanoi</i>	Cutaneous leishmaniasis, diffuse cutaneous leishmaniasis				
<i>L.L. garnhami</i>	Cutaneous leishmaniasis				

***Leishmania Viannia braziliensis* complex** cause mucocutaneous leishmaniasis and also cutaneous leishmaniasis similar to oriental sore but they are more severe. **Mucocutaneous leishmaniasis** or **espundia** leads to partial or total destruction of mucus membranes of the nose, mouth, oral cavity, throat, and pharynx or larynx months to years after the cutaneous leishmaniasis. It is seen in 1 – 3% of patients infected with *L. braziliensis*, more commonly 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 and nose leading to development of **tapir nose**.

Fig 9: Mucocutaneous leishmaniasis or espundia (Sources: openi.nlm.nih.gov and ResearchGate)



The cutaneous lesions of *L.V. guyanensis* and *L.V. peruviana* are known as **forest yaws** (pain bois) and **uta** respectively.

Leishmania Leishmania chagasi is the new World variant of *L.L. infantum*. It causes Mediterranean visceral leishmaniasis and cutaneous leishmaniasis, occurs in Central and South America. It is zoonotic with a canine reservoir host . Childrens are affected more commonly , the vector is *Lutzomyia* spp.

Table 7: *Leishmania Viannia braziliensis* complex

Species	Clinical syndrome	Geographical distribution	Vector	Reservoir	Transmission
<i>Leishmania Viannia braziliensis</i>	Cutaneous leishmaniasis, mucocutaneous leishmaniasis (Espundia)	Brazil			
<i>L.V. panamensis</i>	Cutaneous leishmaniasis, mucocutaneous leishmaniasis (Espundia)	Panama and Colombia			
<i>L.V. guyanensis</i>	Cutaneous leishmaniasis (Forest yaws), mucocutaneous leishmaniasis (Espundia)	Guyana	<i>Lutzomyia</i> spp	Dogs, foxes, forest rodents and humans	Zoonotic
<i>L.V. peruviana</i>	Cutaneous leishmaniasis (Uta), diffuse cutaneous leishmaniasis	Western Peru			
<i>L.L. garnhami</i>	Cutaneous leishmaniasis				

TREATMENT OF NEW WORLD LEISHMANIASIS

In contrast to old world cutaneous leishmaniasis, systemic therapy is recommended for new world cutaneous leishmaniasis as the lesions are more chronic, multiple and shows tendency for mucosal involvement.

Pentavalent antimonial is the drug of choice, administered as a dose of 20 mg/kg for 30 days. In case of relapse, **liposomal amphotericin B** (2 – 3 mg/kg for 20 days) or **miltefosine** (2.5 mg/kg for 28 days) are given.