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Leishmaniasis: An Emerging and Re-emerging Disease of Global Public Health Concern

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Abstract Emerging and re-emerging diseases are causing health and economic concerns in developing as well as developed nations of the world. Leishmaniasis is an emerging and re-emerging parasitic disease caused by a protozoa belonging to the *Trypanosomatidae* family, *Kinetoplastida* order, and *Leishmania* genus. The female infected sand fly transmits the disease to the vertebrate host. The following are the several kinds of leishmaniasis: The most deadly form of leishmaniasis is visceral leishmaniasis, which can be fatal if left untreated. Cutaneous leishmaniasis is the most prevalent type of leishmaniasis, which causes a sore at the bite site. Mucocutaneous leishmaniasis begins with skin ulcers that extend to the nose, mouth, and throat, causing tissue damage. Rodents, edentates, canids, procyonids, marsupials, primitive ungulates, and primates are possible disease's reservoir. Direct visualization of the amastigotes in the haematology laboratory is used to diagnose leishmaniasis (Leishman-Donovan bodies). If leishmaniasis in dogs is to be suspected and diagnosed, it is critical to recognize the clinicopathologic features associated with the disease. Finally, demonstrating *Leishmania* sp. amastigotes, either cytologically or histopathologically, is the most reliable diagnostic test. Controlling sand flies and taking precautions to avoid exposure to them can help to prevent and control canine and human leishmaniasis.

Keywords: *control, diagnosis, etiology, Leishmaniasis, prevention, public health, sand flies*

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1. Introduction

Leishmaniasis is a serious vector-borne protozoan disease caused by an obligatory intra-macrophage protozoon of the genus *Leishmania* that affects a variety of mammalian species, including humans [1]. Leishmaniasis spreads through the bite of *Phlebotomine* sand flies, which may be found on all continents except Antarctica [2]. *Phlebotomine* sand flies are dipteran insects belonging to the *Psychodidae* family, with over 700 species documented to date. With varied degrees of certainty, 10% of these have been implicated as leishmaniasis vectors; persuasive evidence of vectorial capacity has been proven for roughly 30 species [3].

Leishmaniasis has emerged or re-emerged in a variety of geographical places, causing global health and economic concerns about human, domestic animal, and wildlife infection [4,5]. In the tropics, subtropics, and southern Europe, leishmaniasis is endemic [6]. On a global scale, roughly 350 million people live in locations where *Leishmania* is actively transmitted, with 14 million people directly impacted by the disease in Africa, Asia, Europe, and the Americas [7]. It is a slowly progressive disease that can take up to seven years to manifest clinically [8]. Even then, the symptoms are typically nonspecific, and diagnosis of *Leishmania* is rarely investigated [9]. The purpose of this communication is to review the growing importance of leishmaniasis as a global public health concern.

2. Etiology

A protozoa in the family *Trypanosomatidae*, order *Kinetoplastida*, genus *Leishmania* causes leishmaniasis. The amastigote and promastigote are the two stages of development, with the former infecting phagocytic cells' lysosomal vacuoles. The promastigote is an extracellular type of bacteria that clings to the microvilli of insects (sand fly). The sand fly (Figure 1), the insect vector, has several species but different subgroups [10]. The disease is classified as cutaneous, mucocutaneous, or visceral leishmaniasis depending on the clinical manifestation. In the Old World, members of the *L. aethiopica, L. major,* and *L. tropica* complexes are linked to human cutaneous leishmaniasis, while in the New World, members of the

L. mexicana and *L. braziliensis* complexes are linked to human cutaneous leishmaniasis. In the Old World, *L. donovani* and *L. infantum* produce visceral leishmaniasis, whereas in the New World, *L. chagasi* is the primary source of visceral disease. *L. infantum* is the most common cause of canine leishmaniasis; infections in dogs are frequently classified as visceral, despite the fact that they frequently produce both visceral and cutaneous disease [11].

Figure 1. Sand fly (Phlebotomus) (Source, a public domain image provided by the US Centers for Disease Control and Prevention, and originally donated from the World Health Organization)

3. Epidemiology

Leishmaniasis has a high rate of morbidity and mortality. The disease is passed from a female infected sand fly to its vertebrate host. Blood is required only by the female sand fly for the maturation of her eggs. The protozoa's life cycle is quite complex. These parasites have two fundamental life cycle stages: an extracellular stage in the invertebrate host (*Phlebotomine* sand fly) and an intracellular stage in the vertebrate host. *Leishmania* parasites are spread by bites from infected female *Phlebotomine* sand flies, which feed on blood to lay eggs [12]. Non-sand fly transmission has been attributed to the transmission of contaminated body fluids (e.g., by biting, blood transfusion, needles, or sexual contact) or congenital transmission [13]. Infection by blood transfusion from infected to uninfected hosts, both in foxhounds [14] and humans [15], human organ transplantation [16], and sexual transmission in dogs are other methods of transmission [17]. Another option is transmission via shared syringes, which has been reported among IV-drug users in Southwest Europe [18].

Every year, between 700,000 and 1 million new cases of leishmaniasis are reported. The majority of cases of visceral leishmaniasis (VL), often known as kala-azar, occur in Brazil, East Africa, and India. In 2019, ten countries accounted for more than 90% of new cases reported to WHO: Brazil, Ethiopia, Eritrea, India, Iraq, Kenya, Nepal, Somalia, South Sudan, and Sudan. The most common form of leishmaniasis is cutaneous leishmaniasis (CL). The Americas, the Mediterranean basin, the Middle East, and Central Asia account for nearly 95% CL cases. Bolivia, Brazil, Ethiopia, and Peru account for almost 90% of mucocutaneous leishmaniasis cases [12]. Sand flies thrive in the poorer suburbs of Middle Eastern countries, where population density is high and sanitation is poor, making them perfect breeding grounds. As a result, the number of cases of cutaneous leishmaniasis has been steadily increasing [19].

4. Clinical Spectrum

In humans: The following are the several kinds of leishmaniasis: The most serious form of leishmaniasis, visceral leishmaniasis, is potentially lethal if left untreated. It is characterized by fevers that come and go, weight loss, spleen and liver enlargement, and anaemia. The most common form of leishmaniasis is cutaneous leishmaniasis (Figure 2), which causes a sore at the bite site that cures in a few months to a year and leaves an unsightly scar. This type of leishmaniasis can advance to diffuse cutaneous leishmaniasis, which causes widespread skin lesions that look like leprosy and is extremely difficult to treat. Mucocutaneous leishmaniasis begins with skin ulcers that extend to the nose, mouth, and throat (Figure 2) causing tissue damage [12,20].

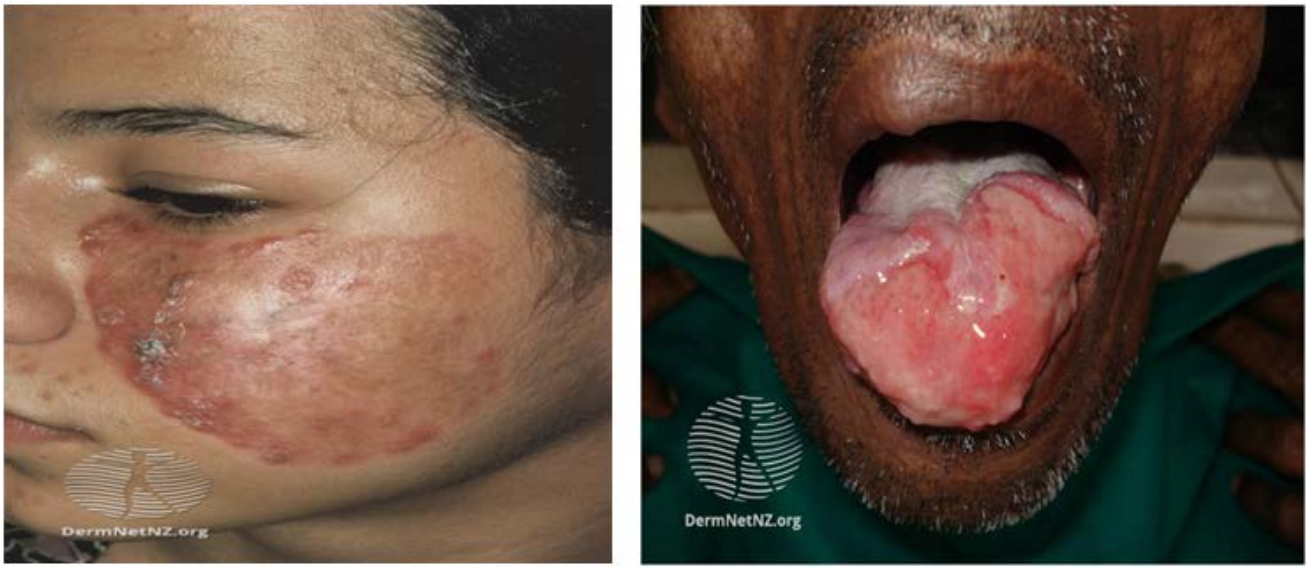

Figure 2. Cutaneous Leishmaniasis in Humans (Source: DermNet New Zealand, 2019)

In Animals: Many of the organisms that cause leishmaniasis in humans have been discovered in animal clinical cases. *Leishmania macropodum* and *L. enriettii* are two other species that affect animals but have yet to be discovered in humans. The distinction between cutaneous and visceral symptoms is not seen in animals, at least with *L. infantum.* Because dogs are significant reservoir hosts for *L. infantum*, infections with this organism are sometimes referred to as "canine leishmaniasis." Other *Leishmania* species, on the other hand, can infect dogs [21]. The most common clinical indications of leishmaniasis in dogs include listlessness, fatigue, and activity intolerance, as well as anorexia and weight loss, which eventually lead to wasting disease [8]. Fever, local or generalized lymphadenopathy (90%), and/or hepatosplenomegaly may or may not accompany these symptoms [9]. Up to 89% of infected dogs have cutaneous lesions, with or without overt symptoms of visceral involvement [11].

5. Diagnosis

In humans: Direct visualization of the amastigotes (Leishman-Donovan bodies) in the haematology laboratory is used to diagnose leishmaniasis. Buffy-coat peripheral blood or aspirates from marrow, spleen, lymph nodes, or skin lesions should be spread on a slide to produce a thin smear, then stained for 20 minutes with Leishman's or Giemsa's stain (pH 7.2). Amastigotes are most typically seen in monocytes, although they can also be found in neutrophils and macrophages in aspirates. They are small, spherical bodies with indistinct cytoplasm, a nucleus, and a small, rod-shaped kinetoplast, around 2-4m in diameter. Amastigotes can occasionally be seen floating between cells. The enzyme-linked immunosorbent assay (ELISA), antigen coated dipsticks, and the direct agglutination test (DAT) is some more indirect immunological methods of diagnosis. For the detection of *Leishmania* DNA, polymerase chain reaction (PCR) techniques are used [21,22].

In Animals: If leishmaniasis in dogs is to be suspected and diagnosed, it is critical to recognize the clinicopathologic features associated with the disease. Finally, the most reliable diagnostic test is the presence of *Leishmania* sp. amastigotes in stained preparations of bone marrow, lymph node, spleen, skin, or other tissues and organs (skeletal muscle, peripheral nerves, renal interstitial, and synovial membranes), either cytologically or histopathologically [8]. Serologic testing is performed to detect *Leishmania* sp. circulating antibodies in the blood. Other tests have been developed, such as enzyme-linked immunosorbent assays (ELISA), complement fixation, Western blot analysis, and other agglutination assays; however, none of them has a high specificity and sensitivity [23].

6. Treatment

The parasites are sensitive to pentavalent antimonials (e.g., sodium stibogluconate, meglumine antimoniate), which can be used to treat leishmaniasis. Unfortunately, the parasite has developed resistance to antimony when used to treat visceral or mucocutaneous leishmaniasis in many parts of the world; however the extent of resistance varies by species. Allopurinol, liposomal amphotericin B, paromomycin, and miltefosine are some of the other drugs that can be used [21,24]. Visceral leishmaniasis is more difficult to treat in dogs than it is in humans for unknown reasons. Furthermore, oral medicines like as ketoconazole, miconazole, fluconazole, and itraconazole may be useful in containing the condition, but they are expensive and carry the risk of drug resistance when used to treat patients symptomatically [23].

7. Prevention and Control

Controlling sand flies and taking precautions to avoid exposure to them can help prevent and control canine and human leishmaniasis. Dogs should not be let outside at night in endemic areas, and fine mesh nets should be used to cover windows. Dogs can be protected against sand fly bites and *Leishmania* infection by wearing a repellent deltamethrin collar [25]. In endemic areas, however, treating all seropositive dogs (symptomatic and asymptomatic) has considerably reduced the number of new infection cases [26]. The transmission of *L. donovani* and *L. tropica* can be reduced by treating sick patients. In the past, live vaccines were used on occasion, with inoculation into an inconspicuous spot to avoid disfiguring facial sores. In most countries, live vaccinations are no longer available, but research into safer and more effective vaccines continues [21].

8. Conclusion

The protozoon *Leishmania* causes human and animal leishmaniasis, which is spread by *Phletobomous* sand flies. Leishmaniasis is endemic in the tropics, subtropics, and southern Europe. Depending on the clinical manifestation, the disease is characterized as cutaneous, mucocutaneous, or visceral leishmaniasis. Visceral leishmaniasis is the most serious type, while cutaneous leishmaniasis is the most prevalent. The amastigotes (Leishman-Donovan bodies) are directly visualized in the haematology laboratory to detect leishmaniasis. Canine and human leishmaniasis can be prevented and controlled by controlling sand flies and taking steps to avoid exposure. Vaccines that are both safer and more effective are still being researched.

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Contributions of Authors

All the authors contributed equally. They read the final version, and approved it for the publication.

Conflict of Interest

The authors declare that they do not have conflict of interest.

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