

The pathogenesis diagnosis and treatment of leishmaniasis health essay



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Leishmaniasis is a tropical, protozoan disease caused exclusively by intracellular parasites belonging to the genus *Leishmania*. Leishmaniasis is a worldwide problem and due to the various species of *Leishmania*, can manifest in humans as 3 main clinical forms: Cutaneous Leishmaniasis, Mucocutaneous Leishmaniasis, or Visceral Leishmaniasis. Consequently, the severity of the infection and symptoms differ from self healing infections that produce significant scars to the fatal infections.

Pathogenesis

Leishmaniasis is transmitted by the bite of female insect vector sand flies of the species *Phlebotomus* in the Old World and *Luzomyia* in the New World (Figure 1). The life cycle for all *Leishmania* species is relatively simple and similar (Figure 2).

When the sand fly takes a blood meal, it inoculates the source with the 2-3 mm long parasite. At this stage, the *Leishmania* parasite is known as a promastigote as it contains a singular flagellum. Promastigotes are injected into the host skin, after which they attach themselves to the hosts' macrophages, and are induced by phagocytosis. These white blood cells are present at the inoculation site because of the hosts' natural immune response to the sand fly bite. Once inside the macrophages, the promastigotes transform into their non-flagellate form, known as amastigotes. From here the amastigotes reproduce by binary fission and continue to proliferate within the white blood cells until the cell bursts. The parasites are then free to infect and invade other reticulo-endothelial cells, which share the same fate and are destroyed due to the reproduction of

amastigotes within. The amastigotes and infected macrophages enter the blood circulation.

The life cycle of Leishmania is continued when a female sand fly feeds on the infected hosts' blood and the amastigotes are taken up by the sand flies.

Amastigotes transform into promastigotes, which proliferate by binary fission in the midgut of the sand fly over a period of 4-25 days (WHO, 2010).

Hereafter, the promastigotes migrate to the fly proboscis or 'mouthparts', where the parasite can infect a new host during feeding (Murray et al, 2009) and thus the Leishmania lifecycle is continued.

Mammals are more often reservoirs for infection. As well as humans; dogs, rodents, wolves and foxes are examples of common reservoirs (Neuber, 2008) and thus, can suffer from leishmaniasis diseases too.

Figure 2: The life cycle of Leishmania. Adapted from Chappuis et al (2007).

Figure 1: A Sand fly vector of Leishmania parasites. Extracted from Neuber (2008).

Epidemiology

Leishmaniasis is endemic in 88 countries, 72 of which are developing countries. An estimated 12 million people are infected with leishmaniasis and 70, 000 people die each year (Reithinger et al, 2007). There are currently about 350 million people worldwide that are at risk and threatened by leishmaniasis because they live within 40° north and south of the equator (Jones et al., 2005; Neuber, 2008) and according to the World Health Organisation (2010), there are an estimated 1-2 million new cases each year.

There are approximately 20 species of *Leishmania* which are pathogenic for humans (Chappuis et al., 2007). These species vary in their geographical location and have an effect on the leishmaniasis which manifests (Table 1).

Cutaneous leishmaniasis is the most common form of leishmaniasis and is endemic in over 70 countries worldwide (Figure 3). It is found throughout Africa and the Middle East in Afghanistan, Algeria, Iran, Iraq, Kabul, Pakistan, Saudi Arabia, Syria; however, more particularly in South America, in Brazil and Peru (Reithinger et al, 2007; Murray et al, 2009).

Over 90% mucocutaneous leishmaniasis often occurs in Bolivia, Brazil and Peru and the majority (over 90%) of visceral leishmaniasis cases, the most dangerous form, is localised to 6 countries; Bangladesh, Brazil, Ethiopia, India, Nepal and Sudan. There are an estimated 500, 000 new cases of visceral leishmaniasis each year (WHO, 2010; Chappuis et al., 2007).

Figure 3: Geographical distribution of Cutaneous Leishmaniasis. Extracted from Reithinger et al (2007).

Main Clinical Presentation

Leishmania Parasite

Main Geographical Distribution

Cutaneous Leishmaniasis

*L. tropica**

Africa, Asia, Middle East, Mediterranean area

Cutaneous Leishmaniasis

L. major*

Middle East, Africa

Cutaneous Leishmaniasis

L. aethiopia*

Ethiopia, Kenya

Cutaneous Leishmaniasis

L. amazonensis ^

South America (Brazil, Venezuela)

Cutaneous Leishmaniasis

L. columbiensis ^

Northern South America (Columbia, Panama)

Cutaneous Leishmaniasis

L. garnhami ^

South America (Venezuela)

Cutaneous Leishmaniasis

L. peruviana ^

Peru, Panama, Costa Rica, Columbia

Cutaneous Leishmaniasis

L. venezuelensis ^

Northern South America (Venezuela)

Mucocutaneous Leishmaniasis

L. braziliensis ^

Central and South America

Visceral Leishmaniasis

L. donovani*

Africa, Asia

Visceral Leishmaniasis

L. infantum (L. chagasi)

Europe, north Africa, Central and South America, Mediterranean area

Table 1: Overview of clinical presentation and geographical distribution of species of Leishmaniasis that cause human disease. L. = Leishmania. *

Leishmania species of the Old World. ^ Leishmania species of the New world.

Data adapted from Reithinger et al (2007), Neuber (2008) and Murray et al (2009).

Clinical Presentation

Cutaneous Leishmaniasis

Cutaneous leishmaniasis is a localised reaction at the inoculation site, which tends to be uncovered areas such as the face, hands and lower legs.

Between 2 weeks and 2 months after the sand fly's bite, a red papule forms. The area begins to swell and become irritated and after 3-4 weeks, flat ulcers form which eventually harden and form crusted margins. The volcano-like lesions that form can heal without treatment; however, sufferers are commonly left with significant, disfiguring scars.

Mucocutaneous Leishmaniasis

Mucocutaneous leishmaniasis, also known as espundia, is most often caused by *Leishmania viannia braziliensis* and has a similar incubation time as cutaneous leishmaniasis. However, this form causes more devastating disfigurement to disease sufferers as the parasites metastasise towards to the mucosal membranes and destroy them and nearby unrelated tissue structures also (Murray et al, 2009). This form is more commonly seen after a primary infection of cutaneous leishmaniasis, where the lesions have eventually healed. Untreated lesions can transform into mucocutaneous forms and year later the oral and nasal mucosas become infected.

Inflammation of the nose, mouth, oropharynx and trachea cause severe mutilation and facial disfigurement. Death can sometimes arise as mucosal lesions do not self-heal and prolonged infection compromises both immune and respiratory systems.

Visceral Leishmaniasis

Visceral leishmaniasis, also known as, kala-azar, dum dum fever or black fever, is the most severe form of leishmaniasis, and if left untreated, those <https://assignbuster.com/the-pathogenesis-diagnosis-and-treatment-of-leishmaniasis-health-essay/>

infected will die. It is the most dangerous because parasites leave the skin and colonise the entire reticulo-endothelial system (Neuber, 2008) and spread to internal organs. Incubation period may be from several weeks to a year and can present as a rapidly fatal disease or as an asymptomatic, self-limiting infection (Murray et al, 2009). As the parasites proliferate and destroy the host's cells, sufferers present with a marked enlargement of the liver, spleen lymph nodes as well as fatigue, weight loss, fever chills, severe anaemia and kidney damage. Death is caused by haemorrhage, complications relating to anaemia or a weakened immune system which cannot deal with bacterial co-infections (Chappuis et al, 2007).

As is the case with all forms of leishmaniasis, the chances of the sufferer developing a secondary infection, such as a bacterial infection, are very high and doing so, can complicate the disease further and may lead to death.

To add: one photo for each CL, ML and VL.

Canine Leishmaniasis

Leishmania infantum not only cause severe disease in humans, but in dogs also. Millions of dogs in Europe, Asia, North Africa, and South America are affected by the parasite. There are some clinical manifestations of the disease in dogs which re similar to that of humans including cutaneous alterations, enlargement of lymph nodes, liver and spleen, weight loss and glomerulopathy. As well as this, ocular lesions, epistaxis (nose bleeds), onychogryphosis (abnormal curving of claws) and lameness (disability in walking) are classic symptoms found in infected dogs (Maia and Campino,

2008). As with visceral leishmaniasis, canine leishmaniasis may also present as an asymptomatic infection, thus delaying necessary treatment.

Diagnosis

Due to the clinical presentations of the disease, a diagnosis can be made; however, for a definitive diagnosis the *Leishmania* parasite must be detected to confirm the diagnosis. Parasitological techniques are routinely used and involve demonstrating promastigotes in a direct examination of tissue aspirates, or detecting amastigotes in biopsy specimens, which are then, examined using a microscope.

Serological techniques to diagnose leishmaniasis are based upon indirectly identifying specific host humoral and cell-mediated responses after inoculation of the parasite. Diagnostic methods include direct agglutination test (DAT), the immunofluorescence antibody test (IFAT), the enzyme-linked immunosorbent assay (ELISA), immunoblotting and antigen detection.

Molecular techniques involve detecting leishmanial DNA or RNA have been beneficial in not only diagnosis, but species identification also. The molecular techniques include using various versions of polymerase chain reactions (PCR) to amplify species specific parasite sequences, DNA probes, monoclonal antibodies (MAbs) and isoenzyme electrophoresis.

Treatment

All forms of leishmaniasis should be treated due to their mortality and morbidity consequences. Drugs are available to treat the disease and choice

for all forms is the pentavalent antimonial compound sodium stibogluconate (Pentostam).

Cutaneous leishmaniasis is also treated with injections of other antimonial compounds, such as fluconazole and litemfosine, directly into the infected lesions (* Figure). Miltefosine has also proven to be an effective treatment for visceral leishmaniasis (Murray et al, 2009).

However, as with all drug treatments, the development of drug resistance is a huge issue and over use of this drug in previous years could lead to Leishmania species becoming resistant. As well as this, there are considerable side effects associated with most drugs (Neuber, 2008). A safe and effective vaccine against the various species is urgently required particularly in endemic areas; however, there is currently no vaccine available although work to develop one is still ongoing.

(To add: * Figure of such treatment)

Social and Economical Implications

Leishmaniasis is found in developing countries or the poorer regions of a country and thus commonly affects the poorest of the poor. Having such a disease can cause many problems in the lives of those infected and their families as they become poorer due to the direct and high costs of diagnosis and treatment of the disease, and the indirect costs such as loss of income (Chappuis et al, 2007).

Another impact of the disease is the social and psychological stigma associated with leishmaniasis, because of the disfigurement and significant

scarring caused. Thus, even after the disease has been treated or self-healed, patients must deal with a constant reminder of what they had to endure.

Cheap, rapid and accurate diagnostic methods are needed to allow all those infected, especially the poor, to get the medical attention they need, and to also allow treatment to start as soon as possible thus ensuring symptoms may not be as detrimental.

Project Aims

The aim of this project is to compare the different methods for diagnosis of leishmaniasis in humans and dogs. These methods will be critically analysed in order to test the following hypothesis: ' A Leishmania infection can be detected unequivocally'. In doing so, the necessary requirements for a correct diagnosis for those who live in endemic areas and for those whom leishmaniasis is a threat, will also be discussed.