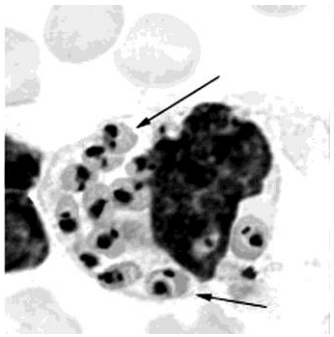
Leishmania spp. (Pathogen – Leishmaniasis)

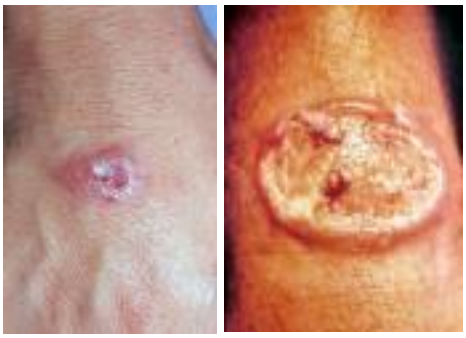
Organism:

Leishmania spp. are protozoa belonging to the family *Trypanosomatidae*. They are obligate intracellular parasites that are transmitted to the mammalian host by the bites of infected sand flies. Leishmaniasis is mainly a zoonosis, although in certain areas of the world there is primarily human-vector-human transmission. The World Health Organization (WHO) estimates that 1.5 million cases of cutaneous leishmaniasis (CL) and 500,000 cases of visceral leishmaniasis (VL) occur every year in 88 countries. Estimates indicate that there are approximately 350 million people at risk for acquiring leishmaniasis, with 12 million currently infected.

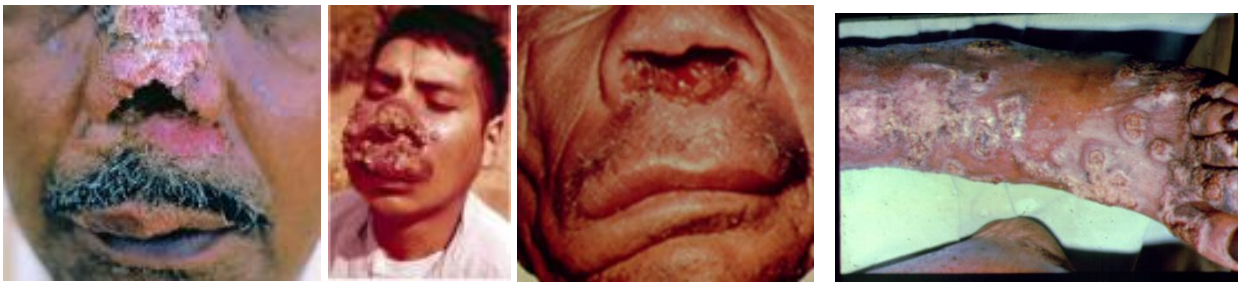
Note: During August, 2002, to February, 2004, over 500 cases of parasitologically confirmed cases of CL were found in military personnel serving in Afghanistan, Iraq, and Kuwait. The majority of these cases were probably acquired in Iraq, with *L. major* being confirmed for most of the cases through isoenzyme electrophoresis of cultured parasites. Based on the data from Fort Campbell, Kentucky, approximately 1% of troops returning from Iraq were diagnosed with CL, most by laboratory confirmation, including PCR.



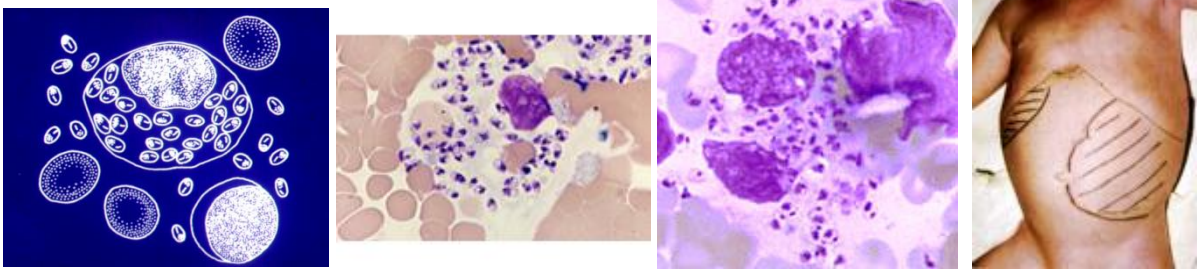
L-D bodies in skin biopsy



Cutaneous leishmaniasis – cutaneous lesions



Mucocutaneous leishmaniasis – skin and mucous membranes



Visceral leishmaniasis – reticuloendothelial system (spleen, liver, bone marrow

Life Cycle:

The parasite has two distinct phases in its life cycle. The organism is engulfed by reticuloendothelial cells (RE cells) of the mammalian host, where it can be found in the amastigote form (Leishman-Donovan body, L-D body) within the phagocytic cell. The amastigote forms are small, round or oval bodies of 3 to 5 μm. The large nucleus and small kinetoplast in the amastigote can be seen when stained with a blood stain. Sometimes the short intracytoplasmic portion of the flagellum can also be seen. The amastigote multiplies by binary fission within the parasitophorous vacuole of the macrophage until the cell is destroyed, and the liberated parasites are phagocytized by other RE cells or ingested by the insect vector.

Upon ingestion during a blood meal by the insect vector, a species of phlebotomine sand fly, the amastigote transforms into the promastigote stage, a motile, slender organism (10 to 15 μm) with a single anterior flagellum. Promastigotes multiply by longitudinal fission in the gut of the insect, where they attach to the gut wall by their flagella. Stages found in the sand fly vary from rounded or stumpy forms to elongated highly motile metacyclic promastigotes. The metacyclic promastigotes migrate to the hypostome of the sand fly where they are inoculated into humans when the infected sand fly attempts to take its next blood meal.

Acquired:

Bite: sandflies, blood, shared needles, congenital infections

Epidemiology:

Old and New world; sandflies to humans, human to human transmission

Clinical Features:

Disease syndromes range from self-healing cutaneous lesions to debilitating mucocutaneous infections, subclinical viscerotropic dissemination, and fatal visceral involvement. Since disease presentations vary considerably, a well-defined classification system based on clinical findings is difficult, and sometimes confusing. With recent outbreaks in many areas of the world, including Brazil, India, Italy, Spain, Sudan, and Kenya, leishmaniasis has become more widely recognized as an important emerging infectious disease in many developed as well as underdeveloped countries.

Cases of leishmaniasis are diagnosed each year in the United States and can be attributed to immigrants from countries with endemic infection, military personnel, and American travelers. Another concern is the potential for more infections occurring in areas of endemic infection in Texas and Arizona. Organisms can remain latent for years, and even when the potential exposure history is in the past, leishmaniasis should be considered, particularly in immunocompromised patients such as those infected with human immunodeficiency virus HIV.

Complications: The onset of visceral leishmaniasis in naïve patients (migrants, soldiers, travelers to areas of endemic infection) may be acute, with high fever, chills, anorexia, malaise, weight loss, and, frequently, diarrhea. This syndrome can easily be confused with typhoid fever, malaria, or other febrile illnesses caused by bacteria or viruses. Death may occur after a few weeks or several years. Generally, untreated visceral leishmaniasis will lead to death; secondary bacterial and viral infections are also common in these patients.

Clinical Specimen:

Cutaneous, Mucocutaneous Lesions: microscopic examination of Giemsa-stained touch preparations and cultures are recommended. Aspirates or biopsy specimens should be taken from the margin or base of the most active lesion (papule or ulcer). The lesion should be cleaned prior to taking the sample, to reduce the chances of contamination with fungi or bacteria. Tissue imprints or smears should be stained with Giemsa stain or another of the blood stains. Amastigote stages should be found within macrophages or close to disrupted cells.

Visceral: A clinical diagnosis of Old World VL is often made based on clinical findings and local epidemiologic factors. However, confirmation of the diagnosis requires demonstration of the amastigotes in tissues or clinical specimens or the promastigotes in culture.

Examination of buffy coat smears shows that there is a significance difference in recovery between samples collected during the day (46%) and those collected during the night (66%) (69). Prior to an invasive

procedure (spleen/liver/bone marrow biopsy), blood specimens should be collected, keeping in mind the amastigote diurnal periodicity.

Immunocompromised patients: The majority of AIDS patients present with the classical picture of VL, but asymptomatic CL, mucocutaneous leishmaniasis, DCL, and post-kala-azar dermal leishmaniasis can be seen. VL can manifest atypical aspects in HIV-positive patients depending on the degree of immunosuppression and should therefore be listed among AIDS-defining conditions. The most common symptoms are fever, splenomegaly, hepatomegaly, and pancytopenia.

Laboratory Diagnosis:

There are a number of testing options, including the following: cutaneous/mucocutaneous lesion scrapings, biopsies; liver/spleen/bone marrow biopsies; blood for buffy coat cells; culture for promastigotes; antigen detection methods; molecular methods; formol-gel test for hypergammaglobulinemia seen in visceral leishmaniasis; and serologic tests (some better than others).

Note: Leishmaniasis should be suspected in individuals who resided in or traveled to areas where the disease is endemic. The diagnosis of visceral leishmaniasis would be supported by findings of remittent fevers, hypergammaglobulinemia with anemia, circulating immune complexes, rheumatoid factors, weight loss, leukemia, and hypersplenism. Differential diagnosis should include African trypanosomiasis, brucellosis, endocarditis, malaria, schistosomiasis, tuberculosis, typhoid, cirrhosis, leukemia, and lymphoma. Lesions caused by post-kala azar dermal leishmaniasis are confused with those of leprosy.

Organism Description:

Amastigotes: The amastigotes are small (3 to 5 µm in diameter), ovoid, nonmotile intracellular forms that are found in various tissues in the reticuloendothelial system. The large nucleus and small kinetoplast in the amastigotes can be seen in tissue after staining with one of the blood stains.

Promastigotes: The promastigotes are elongated, motile, extracellular stages (1.5 to 3.5 by 15 to 20 µm with a single free flagellum 15 to 28 µm long). The form introduced into the skin of the mammalian host by the sand fly is the promastigote.

Laboratory Report:

A number of reports can be relevant – remember to add the appropriate report comments.

Report 1: No Parasites Seen:

Report 2: *Leishmania* spp. Amastigotes Seen: Unable to identify to the species level; however, source of the specimen may provide guidance for therapy.

Report 3: *Leishmania* spp. promastigotes isolated from culture: Unable to identify to the species level; however, source of the specimen may provide guidance for therapy.

Treatment:

Garcia, L.S. 2007. Diagnostic Medical Parasitology, 5th ed., ASM Press, Washington, D.C.

Control:

Vector control, no use of shared needles, checking blood supply