251 Leishmaniasis

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DEFINITION

Encompassing a complex group of disorders, leishmaniasis is caused by unicellular eukaryotic obligatory intracellular protozoa of the genus *Leishmania* and primarily affects the host's reticuloendothelial system. *Leishmania* species produce widely varying clinical syndromes ranging from self-healing cutaneous ulcers to fatal visceral disease. These syndromes fall into three broad categories: visceral leishmaniasis (VL), cutaneous leishmaniasis (CL), and mucosal leishmaniasis (ML).

ETIOLOGY AND LIFE CYCLE

Leishmaniasis is caused by ~20 species of the genus *Leishmania* in the order Kinetoplastida and the family Trypanosomatidae (Table 251-1). Several clinically important species are of the subspecies *Viannia*. The organisms are transmitted by phlebotomine sandflies of the genus *Phlebotomus* in the "Old World" (Asia, Africa, and Europe) and the genus *Lutzomyia* in the "New World" (the Americas). Transmission may be anthroponotic (i.e., the vector transmits the infection from infected humans to healthy humans) or zoonotic (i.e., the vector transmits the infection from an animal reservoir to humans). Human-to-human transmission via shared infected needles has been documented in IV drug users in the Mediterranean region. In utero transmission to the fetus occurs rarely.

Leishmania organisms occur in two forms: extracellular, flagellate promastigotes (length, 10–20 μm) in the sandfly vector and intracellular, nonflagellate amastigotes (length, 2–4 μm; Fig. 251-1) in vertebrate hosts, including humans. Promastigotes are introduced through the proboscis of the female sandfly into the skin of the vertebrate host. Neutrophils predominate among the host cells that first encounter and take up promastigotes at the site of parasite delivery. The infected neutrophils may undergo apoptosis and release viable parasites that are taken up by macrophages, or the apoptotic cells may themselves be taken up by macrophages and dendritic cells. The parasites multiply as amastigotes inside macrophages, causing cell rupture with subsequent invasion of other macrophages. While feeding on infected hosts, sandflies pick up amastigotes, which transform into the flagellate form in the flies' posterior midgut and multiply by binary fission; the promastigotes then migrate to the anterior midgut and can infect a new host when flies take another blood meal.

EPIDEMIOLOGY

Leishmaniasis occurs in 98 countries—most of them developing—in tropical and temperate regions (Fig. 251-2). More than 1.5 million cases occur annually, of which 0.7–1.2 million are CL (and its variations) and 200,000–400,000 are VL. More than 350 million people are at risk, with an overall prevalence of 12 million. Although the distribution of *Leishmania* is limited by the distribution of sandfly vectors, human leishmaniasis is on the increase worldwide.

VISCERAL LEISHMANIASIS

VL (also known as *kala-azar*, a Hindi term meaning "black fever") is caused by the *Leishmania donovani* complex, which includes *L. donovani* and *Leishmania infantum* (the latter designated *Leishmania chagasi* in the New World); these species are responsible for anthroponotic and zoonotic transmission, respectively. India and neighboring Bangladesh, Sudan, South Sudan, Ethiopia, and Brazil are the four largest foci of VL and account for 90% of the world's VL burden, with India being the worst affected. Zoonotic VL is reported from all countries in the Middle East, Pakistan, and other countries from western Asia to China. Endemic foci also exist in the independent states of the former Soviet Union, mainly Georgia and Azerbaijan. In the Horn of Africa, Sudan, South Sudan, Ethiopia, Kenya, Uganda, and Somalia report VL. In Sudan and South Sudan, large outbreaks are thought to be anthroponotic, although zoonotic transmission also occurs. VL is rare in West and sub-Saharan Africa.