

Visceral Leishmaniasis Fact Sheet

Visceral Leishmaniasis (VL, or kala-azar) is a fatal systemic infection caused by various species of *Leishmania* parasites; transmission occurs through the bite of a sandfly, causing chronic fever, weight loss, splenomegaly, hepatomegaly, and anemia. VL is endemic in 65 countries, primarily in the developing world, and the population at risk is estimated at 200 million. The disease often strikes people living in rural villages, who are frequently the poorest and may not be able to afford the treatments currently available. If left untreated VL is nearly always fatal. Available therapies cost from US\$30 to US\$300 and can be toxic or ineffective.

OneWorld Health's Response

The Institute for OneWorld Health is developing Paromomycin IM Injection, a safe, affordable and effective therapy that can cure VL throughout the world. In June 2003, OneWorld Health initiated the largest Phase 3 clinical trial performed for VL; enrolling 667 VL patients in India in collaboration with the Special Programme for Research and Training in Tropical Diseases of the World Health Organization (WHO/TDR). The clinical trial concluded in November 2004 and results showed Paromomycin IM Injection to be safe with initial cure rates comparable to current hospital-based therapies.

In the Phase 3 clinical trial, nearly all patients (94.6%) treated with Paromomycin IM Injection were cured of VL. Efficacy endpoints were defined as cure after 21 days of treatment, improved clinical signs and symptoms, and no relapse of VL after 6 months of follow-up. Paromomycin IM Injection has a well-established safety profile. The most common adverse reaction among patients treated with Paromomycin IM Injection was pain at the injection site. Serious adverse events occurred in 4/500 Paromomycin IM Injection treated patients (0.8%).

In June 2006, OneWorld Health's partner Gland Pharma Limited submitted an application for Paromomycin IM Injection to the Indian regulatory agency DCGI (Drug Controller General of India) for review, and this application was approved on August 31st, 2006. The Institute for OneWorld Health will be conducting a Phase 4 Program aimed at expanding access to Paromomycin IM Injection treatment for patients in resource-constrained settings, through appropriate referral and outpatient treatment.

With the approval of Paromomycin IM Injection, India has a safe, new and effective therapy for kala-azar. OneWorld Health, Gland Pharma Limited, IDA Solutions and WHO/TDR partnered to develop Paromomycin IM Injection as a public health tool to be sold on a not-for-profit basis at a very low price. The Phase 3 clinical trials and Phase 4 program are funded by the Bill and Melinda Gates Foundation.

Disease Transmission

When taking a blood meal from a reservoir host, about 30 species of sandflies can become infected with a species of flagellate protozoa belonging to the genus *Leishmania*

and then transmit the leishmania parasite to a person through a bite. Hosts include infected humans, wild animals such as rodents, and domestic animals such as dogs. Most leishmaniases are zoonotic (transmitted to humans from animals), and humans become infected only when accidentally exposed to the natural transmission cycle. However, in the anthroponotic forms (those transmitted from human to human through the sandfly) humans are the sole reservoir host.

Disease Characteristics

Visceral leishmaniasis is the severest form among leishmaniases. Without treatment VL has a mortality rate of almost 100 percent. It is characterized by irregular bouts of fever, substantial weight loss, anemia and swelling of the spleen and liver. The parasites invade bone marrow causing the immune system to weaken and increasing a person's vulnerability to infection and disease. The risk for co-infection with AIDS is also rising.

Geographic Distribution and Prevalence

VL typically strikes people in rural villages, often in the poorest regions and among the people least able to afford treatment. Of the estimated 500,000 new cases of VL occurring annually, 90 percent occur in five countries: Bangladesh, India, Nepal, Brazil and the Sudan.

India Situational Profile: In Bihar, Jharkhand and West Bengal VL is a serious public health problem; since resurging in Bihar in the early seventies, the disease has spread from four districts to roughly 36 districts of Bihar and 10 districts of West Bengal. While the disease is present predominantly in the districts adjoining the Ganges an ever-increasing trend is evident. In 2006, in India 38,656 cases of VL were officially reported: in Bihar (29,711), Jharkhand (7,211), West Bengal (1,628), Uttar Pradesh (80) and few imported cases in Delhi. Precise morbidity and mortality rates for VL are difficult to obtain in many regions because official counts provided in endemic areas include only passive case detection from patients who obtain treatment in government facilities. VL is frequently unrecognized and undiagnosed, especially when access to drugs is very poor. Most patients seek treatment in the private sector and are not tracked for treatment efficacy and compliance.

Current Therapies

- Antimonials (pentavalent): 28-day intramuscular- or intravenous-injection regimen. Resistance reported in as many as 60 percent of cases in parts of India. Expensive (if name brand product), otherwise the generic SSG is relatively cheap (US\$ 30). Infusion side effects include nausea, pain, anorexia, myalgia, arthralgia, headache, malaise, reversible cardiotoxicity and chemical and clinical pancreatitis.
- Amphotericin B: 4-8 week intravenous regimen. Expensive. Side effects include fever, chills, hypokalemia, renal toxicity, anemia and cardiotoxicity.
- AmBisome: 5-day intravenous regimen. Liposomal Amphotericin B (encapsulated in liposomes) is well tolerated, but is expensive (US\$ 300).
- Miltefosine: 28-day oral regimen. Expensive. Risk of teratogenicity.

Sources

Desjeux, P. (2004) *Leishmaniasis: current situation and new perspectives*, Comparative Immunology, Microbiology and Infectious Diseases. 27:5, pp 305-318.

World Health Organization, <http://www.who.int/topics/leishmaniasis/en/>

World Health Organization, Regional Office for South-East Asia