

A conversation with the World Health Organization, June 7, 2018

Participants

- Adebowale Akin-Akintunde – Technical Officer, Department of Control of Neglected Tropical Diseases, World Health Organization
- Dr. Saurabh Jain – Scientist, Department of Control of Neglected Tropical Diseases, World Health Organization
- Stephan Guyenet – Senior Fellow, GiveWell
- Dan Brown – Senior Fellow, GiveWell

Note: These notes were compiled by GiveWell and give an overview of the major points made by World Health Organization.

Summary

GiveWell spoke with Mr. Akin-Akintunde and Dr. Jain of the World Health Organization (WHO) as part of its early investigation into leishmaniasis. Conversation topics included an overview of leishmaniasis, WHO's work on leishmaniasis control, its room for more funding, and other organizations working on leishmaniasis control.

Overview of leishmaniasis

Leishmaniasis is an epidemic-prone infectious disease endemic in 97 countries or territories. Cases of leishmaniasis are reported in all six World Health Organization (WHO) regions: African Region (AFR), Region of the Americas (AMR), South-East Asia Region (SEAR), European Region (EUR), Eastern Mediterranean Region (EMR), and Western Pacific Region (WPR).

Leishmaniasis appears in two main forms, the most common of which is cutaneous leishmaniasis (CL), a skin infection that primarily affects children; over 170,000 cases are reported every year to WHO, but underreporting is believed to be substantial. Visceral leishmaniasis (VL, also known as kala-azar) has the most severe presentation and primarily affects the internal organs. An estimated 50,000-90,000 new cases of VL occur worldwide each year. It is responsible for approximately 20,000-30,000 deaths annually, possibly the second highest number of deaths caused by a parasitic disease after malaria. The case fatality rate for untreated VL is approximately 95% within two years of the disease's development.

Coinfection with HIV

Leishmania-HIV coinfection has been reported in 35 countries. The case fatality rate of VL is higher in individuals with HIV.

Control options

The two main options for leishmaniasis control are a) early detection and treatment of the disease and b) disease prevention, by reducing the vector population or the animal reservoir population.

Vector and reservoir control

The most common vector control methods include indoor residual insecticide spraying and insecticide-treated bed nets. Animals can be hosts of *Leishmania* parasites, and as such can be targeted by some interventions, for example mechanical ploughing to destroy their burrows.

In certain settings, vector control methods can be used to protect domestic animals from infection through insecticide-treated animal collars or animal shampoos.

Treatment

In settings that are targeting elimination of VL, such as the South-East Asia Region, the first-line treatment recommendation is single-dose AmBisome (liposomal amphotericin B). Clinical trials have demonstrated that a single dose of AmBisome is effective and produces results comparable with a multiple-dose regimen.

Single-dose AmBisome, which requires a patient to be admitted to a health facility for only a few hours prior to discharge, has significantly altered the treatment paradigm for VL. An earlier treatment option was Miltefosine, an oral medication requiring administration over a four-week period. Prior to AmBisome, typical VL treatment involved a two-month treatment with antimonial drugs that caused pain, significant side effects, and often death.

Treatment recommendations for VL may vary depending on a setting's particular conditions, such as the type of *Leishmania* parasite found in the area, transmission of disease, availability of drugs such as AmBisome, and others. For example, first-line treatment for VL in East Africa involves a combination of an antimonial and paromomycin rather than a single dose of AmBisome.

Treatment of cutaneous leishmaniasis still largely relies on injections of pentavalent antimonials, either directly in the skin lesion or intramuscularly.

Cost-effectiveness of different control options

The cost-effectiveness of different leishmaniasis control options depends significantly on the setting, with important factors including:

- The prevalence of the disease
- The local species of *Leishmania* and sandflies
- The population at risk
- The percentage of the population that requires coverage
- Existing infrastructure and human resources
- Other disease control priorities for the area

WHO's work on leishmaniasis control

- Supporting national leishmaniasis control programs technically and financially to produce updated guidelines and develop and implement

disease control plans, including sustainable, effective surveillance systems and epidemic preparedness and response systems.

- Monitoring disease trends and assessing the impact of control activities that support awareness and advocacy of the global burden of leishmaniasis, and promoting equitable access to health services.
- Developing evidence-based policy guidelines, strategies, and standards for leishmaniasis prevention and control, and monitoring their implementation.
- Strengthening collaboration and coordination among partners, stakeholders, and other bodies.
- Promoting research and use of effective leishmaniasis control including safe, effective, and affordable medicines, as well as diagnostic tools and vaccines.

Organizational structure

The WHO Global Leishmaniasis Program is located within the Department of Control of Neglected Tropical Diseases at WHO Headquarters in Geneva. It is one of WHO's innovative and intensified disease control programs and relies on WHO regional and country offices for the implementation of its mandate. WHO staff work directly with national governments, implementation partners, researchers, academia, and other institutions at the global, regional and country level.

Support for control programs in the South-East Asia Region

The WHO NTD roadmap (2012) has set an ambitious target of elimination of VL as a public health problem in the South-East Asia Region by 2020, specifically in Bangladesh, India, and Nepal. WHO's goal for these countries is to achieve annual incidence of less than one case of VL per 10,000 people by 2020. Conditions that make these countries particularly conducive settings for elimination include the following:

- Only one disease vector exists
- Humans are the only hosts for the parasite
- High political commitment is available
- Elimination programs are in place
- Rapid diagnostic tests are effective
- Single-dose AmBisome is effective
- AmBisome is being donated by Gilead Sciences

Success

Through active surveillance of the disease, VL control programs in the South-East Asia Region have achieved significant reductions in the number of cases reported. For example, India once contributed 50% of the global disease burden for VL, but in 2017, the nation reported a historic low of fewer than 6,000 cases.

Control programs have also achieved operational success, including strong maintenance of the cold chain required for AmBisome and zero reports of AmBisome stockouts.

Implementation partners in India

Partners supporting ground-level implementation of visceral leishmaniasis control in India include CARE India, supported by the Bill and Melinda Gates Foundation and the KalaCORE Consortium, which is composed of Médecins Sans Frontières (MSF), the London School of Hygiene & Tropical Medicine (LSHTM), Drugs for Neglected Diseases Initiative (DNDi), and Mott MacDonald. Program activities include expanding the availability of leishmaniasis health services, behavior change communication campaigns, support in implementation and monitoring of indoor residual spray, and management of health information systems.

WHO's work in other regions

Outside the South-East Asia Region, the goal for both visceral and cutaneous leishmaniasis is control. In the other five regions, WHO's efforts focus on strengthening disease control measures as well as surveillance. Both visceral and cutaneous leishmaniasis have more complex epidemiological dynamics and are more difficult to control in these areas.

Monitoring stock

Leishmaniasis control relies heavily on the availability of antileishmanial drugs and, in the case of VL, on rapid diagnostic tests. For most of the drugs and diagnostics there are sole manufacturers, hence it is important to prevent stock outs. WHO has developed a stock dashboard based on the District Health Information System 2 (DHIS2), which enables partners and WHO to monitor the AmBisome stock at regular intervals.

In addition to providing AmBisome to local health facilities, WHO maintains a reserve stock of essential antileishmanial drugs and rapid diagnostic tests for emergency situations.

Building capacity

WHO supports significant donor funding towards capacity-building activities in Ethiopia, Kenya, South Sudan, and Sudan—including sponsoring online courses globally for community health workers and supporting training for technical officers.

Room for more funding

Donors for leishmaniasis control

WHO currently receives support for leishmaniasis control from the following donors:

- **Gilead Sciences** – Gilead Sciences is an American biopharmaceutical company that manufactures AmBisome. It currently donates AmBisome to WHO and also provides funding for implementation.

- **Sanofi** – Sanofi is a multinational pharmaceutical company that provides funding to WHO for work on leishmaniasis control.
- **Probitas Partners** – Probitas Partners is a global investment firm that recently began providing funding to WHO for work on leishmaniasis control.
- **The United Kingdom’s Department for International Development (DFID)** – DFID provides funding support to WHO for work on leishmaniasis control.

Funding gap

By 2019, DFID will cease funding for WHO’s leishmaniasis control efforts, which will result in a large funding gap—particularly for the support of technical work and the procurement of drugs and diagnostic tests. Beyond this period, there is no indication of continued support.

Use of additional funding

Components of its leishmaniasis control work that WHO views as strongly in need of funding include:

- Procurement of drugs for cutaneous leishmaniasis
- Procurement of drugs and rapid diagnostic tests for visceral leishmaniasis
- Disease surveillance, data compilation and management
- Vector control
- Capacity building
- Advocacy – WHO requires further support for its advocacy efforts, which are costly and include providing member states with marketing materials and publishing material online.

Expanding support to other countries

With additional funding, WHO would expand its support to more countries where leishmaniasis is endemic but where governments have difficulty procuring drugs and diagnostic tests, such as Syria, Pakistan, and various countries in Africa. Support would focus on strengthening health systems’ capacity for case management, diagnosis, and vector control.

Areas of opportunity for GiveWell

Aspects of its leishmaniasis control work that WHO believes would fit particularly well with GiveWell’s priorities include:

- **Procurement of drugs and diagnostic tests** – This is a discrete funding opportunity whose cost-effectiveness may be easier to quantify than other leishmaniasis interventions. The number of individuals who receive diagnostic tests and the number of individuals who receive treatment are monitored at regular intervals.

- **Training health workers** – This is another funding opportunity for which costs and benefits may be easier to quantify than other leishmaniasis interventions.

Other organizations working on leishmaniasis control

Organizations working on leishmaniasis control—at international, national, and subnational levels—include:

- **Implementing organizations** – Implementers of leishmaniasis control include KalaCORE Consortium, Médecins Sans Frontières (MSF), and CARE India.
- **Research organizations** – Major organizations include DNDi, which has been developing new diagnostic tests and treatment regimens; International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR); London School of Hygiene and Tropical Medicine; Liverpool School of Tropical Medicine; Rajendra Memorial Research Institute of Medical Sciences, India; B P Koirala Institute of Health Sciences, Nepal; and several universities and organizations globally.

Although many organizations are involved in leishmaniasis control, significantly more organizations work on controlling other diseases, such as HIV.

All GiveWell conversations are available at <http://www.givewell.org/conversations>