A conversation with Dr. Koert Ritmeijer, August 15, 2018

Participants

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Note: These notes were compiled by GiveWell and give an overview of the major points made by Dr. Ritmeijer.

Summary

GiveWell spoke with Dr. Ritmeijer of Médecins Sans Frontières and the KalaCORE Consortium as part of its investigation into leishmaniasis control. Conversation topics included the KalaCORE Consortium's work on leishmaniasis control and global room for more funding for leishmaniasis control.

Leishmaniasis landscape

Visceral leishmaniasis

Visceral leishmaniasis (VL) is a neglected tropical disease (NTD) caused by *Leishmania* parasites that are transmitted by sandfly bites. It has an almost 100 percent mortality rate.

Cutaneous leishmaniasis

Cutaneous leishmaniasis (CL) is another NTD, which Dr. Ritmeijer believes is more neglected than VL because it is not fatal. However, it remains a significant public health problem because of its high incidence and the disfiguring ulcers it causes, which can subject patients to stigma. In most CL-endemic countries, treatment is unavailable from the public sector and available only at high cost and often low quality from the private sector.

Non-governmental organizations (NGOs)

Médecins Sans Frontières (MSF) is the primary NGO working on VL control, and it also works on CL control in Pakistan, Afghanistan, and Syria. Other organizations working on leishmaniasis control include SOS Children's Villages International, which provides VL services in two hospitals in Somalia, and the MENTOR Initiative, which runs a large CL control program in Syria.

KalaCORE Consortium's work on leishmaniasis control

The KalaCORE Consortium is implementing a UK government-funded program for control and elimination in VL in South Asia and East Africa. The consortium partners are MSF, the Drugs for Neglected Diseases initiative (DNDi), London School of Hygiene and Tropical Medicine (LSHTM), and Mott MacDonald. The program supports national VL control programs in six countries where VL is highly endemic: India, Bangladesh, Nepal, Sudan, South Sudan, and Ethiopia. Its goals in these

countries are to increase access to diagnostic and treatment services and to improve surveillance and outbreak response. In East Africa, it also aims to identify cost-effective vector control strategies.

South Asia

Elimination goal and strategies

In South Asia, elimination of VL is possible, and the governments of India, Bangladesh, and Nepal aim to achieve elimination by 2020. Elimination is defined as 1 case per 10,000 people, or fewer, at the sub-district level.

In recent years, incidence of VL has declined naturally, and elimination efforts can accelerate this progress. Control programs in South Asia perform active case finding of patients in endemic areas. They diagnose patients with high-performing rapid diagnostic tests (RDTs) and treat patients with an intravenous, single-dose treatment called AmBisome, which has over a 95% cure rate. When combined, these two highly effective methods allow diagnosis and treatment to occur quickly, easily, and on the spot, without requiring laboratory work or hospitalization. In addition, because VL is transmitted in South Asia by sandflies that live in or near human homes, indoor residual spraying is an effective means of vector control.

Progress to elimination

In the countries where it works in South Asia, the KalaCORE Consortium has supported active case finding and introduced AmBisome to dozens of rural hospitals and clinics. It has also worked to improve surveillance conducted by national programs so that they can monitor progress to elimination and identify areas that require further support. Nepal and Bangladesh have now achieved the elimination target, which the World Health Organization (WHO) is in the process of validating. Dr. Ritmeijer estimates that 95% of India's endemic sub-districts have achieved the elimination target.

Sustained elimination

In contrast with eradication, elimination does not completely interrupt disease transmission. After a successful treatment, most patients develop lifelong immunity to the disease. However, immunocompromised patients (e.g. those who are co-infected with HIV) cannot be permanently cured, and will remain a source of transmission. In addition, some successfully treated patients will later develop post-kala-azar dermal leishmaniasis (PKDL), which causes dermatitis and skin lesions that transmit *Leishmania* parasites.

Thus, countries must work to sustain elimination after it is achieved. This will require a vigilant surveillance system that can detect new cases or outbreaks and respond quickly with treatment and vector control. Dr. Ritmeijer believes that sustained elimination will also require identifying and treating PKDL patients, which is currently not systematically done. A major concern is that political commitment to VL control will decline post-elimination. This has occurred in several countries that successfully eliminated leprosy but now see its incidence increasing again.

East Africa

Elimination of VL is not an objective in the East African countries of Sudan, South Sudan, and Ethiopia because the appropriate tools to achieve elimination — simple, effective diagnostics; short, safe, and effective treatment; and effective vector control methods — are lacking. Therefore, disease control is the main aim.

Lack of political commitment

Unlike in India, Bangladesh, and Nepal, the commitment to VL control of the governments of Sudan, South Sudan, and Ethiopia is more ambiguous. These governments have limited resources with which to address significant health needs and have chosen to allocate those resources to leading causes of death, including maternal health issues, malaria, diarrheal diseases, and pneumonia. Consequently, national VL control programs are under-resourced, and VL-endemic areas go unserved. These areas are typically home to poor and marginalized communities. They are generally isolated, possess poor health infrastructure, and are often affected by active conflict. For example, South Sudan is affected by significant political turmoil, conflict, and insecurity. In Ethiopia, VL mainly affects geographically isolated migrant workers. For these reasons, the VL programs in these countries rely upon external funding and aid from NGOs.

Diagnostic methods

The RDTs that are used in South Asia with around 98-99% sensitivity have only around 85% sensitivity in East Africa. This could be due to differences in either the parasites or the hosts. Higher antibody levels have been measured in South Asian patients than in East African patients, which lead to easier detection by RDTs.

This lower diagnostic sensitivity makes it necessary to use additional methods to ensure accurate diagnoses, particularly when patients receive a negative RDT but present with clinical symptoms. The 15% of VL cases that receive negative RDTs are identified through more advanced methods that cannot be used in the field and instead must be performed in hospitals and laboratories, making the overall diagnostic process slower, more resource-intensive, and more expertise-intensive in East Africa. These backup methods also identify relapsed patients.

Treatment methods

East African VL is not effectively treated with single-dose AmBisome. Patients using AmBisome would need to take higher doses and longer treatment courses, which would prove prohibitively costly because the drug is expensive.

For this reason, the East African standard of care is a 17-day course of a combination of an antimonial and an antibiotic/antiparasitic drug, paromomycin. Antimonials are highly toxic to the liver, kidneys, pancreas, and heart and can be fatal. They are also correlated with high spontaneous abortion rates in pregnant women. Finally, antimonial injections are very painful. Paromomycin is less toxic than antimonials but can cause permanent hearing loss. Patients' hearing must be tested before and monitored during treatment. Due to these risks, vulnerable

patient groups are instead prescribed AmBisome despite the higher cost. Before AmBisome was prescribed to these groups, the standard of care had an overall mortality rate of 10%, which has now fallen to under 3%.

Vector control methods

In East Africa, indoor residual spraying is ineffective because sandflies do not live in the homes. Instead, patients are infected while working or traveling in outdoor spaces, such as fields or forests. As people usually sleep outside, insecticide-treated bed nets offer a partial solution, but their usage is not optimized. This is because the main VL transmission season—when sandfly density is highest—occurs during the second half of the dry season, before the rainy season begins. At this time, high temperatures discourage people from sleeping under bed nets. Further, people are primarily incentivized to use bed nets to prevent mosquito bites, which occur infrequently during the dry season.

KalaCORE Consortium's work

In East Africa, the KalaCORE Consortium helps national VL control programs establish diagnostic and treatment services in endemic areas. This involves training health staff, providing drugs and diagnostic tests, and supporting surveillance and reporting. As a result, the number of health facilities that provide VL services has increased dramatically, from around 11 to 35 in Sudan, 5 to 38 in South Sudan, and 11 to 22 in Ethiopia. This means that VL-affected populations now have increased access to treatment. The KalaCORE Consortium also supports surveillance officers within Ministries of Health who work to improve VL surveillance and integrate it into national health information systems.

Organization-wide monitoring and evaluation (M&E)

The KalaCORE Consortium works by subcontracting partner organizations, primarily NGOs, to implement defined packages of program activities. These activities include ongoing monthly M&E to collect comprehensive data on the program's health impact, spending, capacity building, and more. LSHTM performed both baseline and end line surveys to assess how the program affected specific variables, including the time between disease onset and effective treatment, the financial burden on VL-affected households, and disease incidence.

Global room for more funding for leishmaniasis control

Current funding

The KalaCORE Consortium is funded by the United Kingdom's (UK) Department for International Development (DFID). This funding, which was the first large investment in VL control, will last 5 years and will end in March 2019.

Other large funders of leishmaniasis control include WHO and the Bill & Melinda Gates Foundation, which has provided significant funding for VL vector control in India. MSF also contributes funding, as do smaller stakeholders. Dr. Ritmeijer does not know the total global funding level for leishmaniasis control.

Future funding

In the future, VL control will require continued funding to support both post-elimination work in South Asia and ongoing disease control work in East Africa. In September 2018, DFID will issue an open call for new NTD programs. This funding will be part of the UK government's commitment of around £300 million for NTD programs. The funding will run from 2019 to 2021. The amount of funding targeted for VL will not become known until 2019.

Cost-effectiveness and targets of additional funding

Three factors contribute to the cost-effectiveness of leishmaniasis control. First, every successful VL treatment saves a life. Second, patients who receive successful VL or CL treatment develop lifelong immunity to the disease. Third, because humans are the primary disease reservoir, early detection and prompt treatment can reduce disease transmission. Dr. Ritmeijer believes that there are funding opportunities in CL control that are very cost-effective.

Future funding should support both VL and CL control in Africa. Sudan and Ethiopia should be priority countries for both VL and CL control because they have a high incidence of both diseases and poor access to treatment.

Drugs and tests are a potentially cost-effective intervention for VL. WHO will fund the supply of VL drugs and tests for East Africa until the end of 2019. Afterwards, this will be taken over by the DFID NTD program, which runs until 2021.

Bed nets are another potentially cost-effective invention. While malaria programs currently distribute bed nets, there are no VL-specific bed net distribution programs. However, because the impact of bed nets on VL control is relatively less certain and significant, Dr. Ritmeijer believes that the most cost-effective funding interventions in East Africa are the distribution of drugs and tests in targeted health facilities in the endemic areas, decentralized diagnosis, and regular training, taking into account the high turnover of health workers in health facilities.

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