Research priorities for elimination of visceral leishmaniasis

Now is a good time to reconsider research priorities as 2015 approaches, the target date originally set for elimination of visceral leishmaniasis. Visceral leishmaniasis is one of the most deadly parasitic diseases and disproportionately affects the poorest and most vulnerable populations. An estimated 200 000–400 000 people contract visceral leishmaniasis every year in developing countries. Spread by sandflies, visceral leishmaniasis can be fought with existing interventions, including treatment and vector control, but, similarly to every other human parasitic disease, no effective vaccine exists.

The elimination target established in 2005 at the World Health Assembly is 1 case in 10 000 in all endemic areas of the Indian subcontinent. Nepal and Bangladesh most notably have reached or are close to reaching the elimination target, and India continues to make impressive progress. Probably the most important achievement in these countries during the past 5 years has been the effective introduction of point-of-care diagnostics and treatment for visceral leishmaniasis at the government primary health-care level. Previously, treatment was most often sought from unqualified medical personnel or distant district tertiary and private hospitals. Reaching the elimination of visceral leishmaniasis in the Indian subcontinent is clearly now a potential reality; however, additional interventions are needed to reduce transmission sustainably, and an improved understanding of the changing epidemiology is needed as the number of cases reduces.

It is now necessary for experts and policy makers to define research priorities, establish who is doing what, and identify technology gaps. WHO-TDR (Special programme for Research and Training in Tropical Diseases) has been supporting visceral leishmaniasis elimination related programmes on the ground for more than 15 years through development and implementation of treatments and diagnostics that are widely used today and developing case detection and novel vector control strategies that have been used by the national programmes. WHO-NTD (Neglected Tropical Diseases) has also shown strong leadership in developing guidelines to control leishmaniasis worldwide[1] and also supporting the implementation of visceral leishmaniasis interventions. WHO is therefore uniquely positioned to continue playing a lead stewardship part to reach and sustain elimination of visceral leishmaniasis.

Several priorities will need both basic and implementation research approaches. With respect to treatment, several effective treatment options now exist, but a short-course, affordable oral drug that could be used in combination with existing drugs would represent a welcome addition. Implementation research is, however, necessary to establish how best to use existing treatments under field conditions and at a scale that will have a high rate of compliance. Implementation research is also needed to establish how best to carry out vector control and case detection in endemic villages without placing an additional load on local health systems and using existing human resources and government infrastructure.

Research is needed to improve understanding of the human reservoir and what part asymptomatic infections play in transmission. Longitudinal studies of patients with visceral leishmaniasis, asymptomatic cases, and their household contacts are needed to identify biomarkers for disease progression and transmission. An improved understanding of the role of post-kala-azar dermal leishmaniasis in disease transmission is also needed because this is a difficult condition to treat and in some cases treatment might not be justified. A simple test to quantify parasite load from small quantities of blood is needed to identify those people who are infected and at risk of developing and transmitting visceral leishmaniasis, and also to provide a test of cure and relapse. Xenodiagnosis studies to establish whether post-kala-azar dermal leishmaniasis and asymptomatic infections transmit parasites to sandflies are necessary to understand disease transmission and to develop public health policy. Understanding *Leishmania* biochemical pathways crucial for its survival in visceral organs will help researchers to understand pathogenesis and might provide insights leading to improved treatment interventions.

A prophylactic vaccine would be the best way to consolidate elimination and possibly eradication of visceral leishmaniasis. There is good reason to believe that a vaccine is feasible because people who recover from visceral leishmaniasis after treatment develop protective immunity against subsequent

visceral leishmaniasis. Studies that focus on the human immune response are needed to understand why people who are cured have protective immunity and why most people who become infected do not develop disease. This will help to establish whether candidate vaccines induce the correct type of protective immunity. With respect to therapeutic vaccines, we could argue that treatment of visceral leishmaniasis with one dose of liposomal amphotericin B can be thought to be a therapeutic vaccine in the Indian subcontinent because this results in a cure and protective immunity to reinfection. The greatest immediate need for a therapeutic vaccine is to treat post-kala-azar dermal leishmaniasis because this is much more difficult to treat than visceral leishmaniasis. Such a vaccine might also represent a good first step in the development of a prophylactic visceral leishmaniasis vaccine and its efficacy would be easier to monitor through the resolution of the skin lesions.

These research activities will need multidisciplinary collaborative efforts from clinicians, public health specialists, and basic science researchers working with patients, experts, and policy makers from the endemic countries. Coordination of these multidisciplinary efforts will need as much consideration as the science itself. Now is the time to do this because elimination of visceral leishmaniasis is within reach.

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1 WHO. Control of the leishmaniases. Geneva: World Health Organization, 2010.