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Control of visceral leishmaniasis in East Africa: fragile progress, new threats

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Significant progress has been made in reducing the global burden of visceral leishmaniasis (also known as 'kala azar'), a vectorborne disease that is 100% fatal if left untreated, but new threats are on the horizon. So far, the success has been particularly striking in India, Bangladesh and Nepal, where reported cases have declined from more than 77 000 in 1992 to under 3200 in 2019.[1 2] In contrast, in East Africa, existing diagnostics and treatments are not as effective and progress has been more fragile. Around 11 000 cases were reported in 2019[3] and the true burden is likely to be far higher due to under-reporting. In addition to the probable disruptive effects of the COVID-19 pandemic on visceral leishmaniasis programmes,[4] three major threats have emerged to the control of this disease.

First, the UK, the leading donor of the global leishmaniasis response, has announced cuts in their overseas aid budget. This will lead to the premature termination of their flagship ASCEND (Accelerating Sustainable Control and Elimination of Neglected Tropical Diseases) programme to control and eliminate five neglected tropical diseases, including visceral leishmaniasis.[5 6] Funding for this programme included the purchasing of life-saving drugs. No other funder has yet stepped in, which will inevitably lead to shortages and increased mortality later this year. The anticipated reduction in detection and treatment will also enhance the risk of outbreaks during the upcoming peak season.

Second, Bio-Rad Laboratories has announced that it will discontinue the production of IT-Leish next year, the only rapid diagnostic test with a high enough sensitivity for visceral leishmaniasis in East Africa.[7] If no longer available, thousands of cases may go undetected due to the decreased sensitivity of other tests. Bio-Rad argues that it is not cost-effective for them to invest to comply with the new European In Vitro Diagnostic Regulation requirements for rapid diagnostic tests[8] like IT-Leish, which will be applied in May 2022 after a 5-year transition period. No concrete plan for transfer of the know-how on IT-Leish production to another potential manufacturer has been developed.

Finally, a global shortage of liposomal amphotericin B (L-AmB), the first-line treatment for many patients with visceral leishmaniasis, is looming (figure 1). AmBisome, the originator of L-AmB product, is donated by Gilead Sciences for patients with visceral leishmaniasis in high-burden countries. A preferential price of US$16.25 per vial is also accessible for other not-for-profit visceral leishmaniasis treatment providers in the developing world, while the commercial price

Summary box

- Significant progress has been made in reducing the global burden of visceral leishmaniasis, but new threats are on the horizon.
- Funding for elimination of visceral leishmaniasis programmes will be reduced through cuts in the UK's overseas aid budget.
- Thousands of cases may go undetected in East Africa as a result of Bio-Rad Laboratories' planned discontinuation of production of the only effective rapid test.
- A global shortage of AmBisome, a first-line treatment produced by Gilead, is looming due to COVID-19-related demand for the drug.
- The achievement of both the WHO neglected tropical diseases road map for visceral leishmaniasis by 2030 and Sustainable Development Goal 3.3 could be jeopardised.
- The UK government, Bio-Rad and Gilead must honour their commitments in order to avoid undermining decades of progress.

Figure 1 Nurse preparing liposomal amphotericin B. Photo credit: Matthew Smeal/MSF. Date taken: 11July 2015. Location: Bihar, India.

of AmBisome for other usages and markets often exceeds US$200 per vial. The recent outbreak of COVID-19-related mucormycosis in India has significantly increased global demand for L-AmB. Half of the doses of AmBisome donated to India for visceral leishmaniasis have already been diverted to respond to the urgent needs for mucormycosis.[9] The few generic manufacturers of L-AmB in India and Taiwan have struggled to provide L-AmB in sufficient quantities.[10] Additionally, since these generic sources are not prequalified by the WHO, this represents a barrier to the procurement and use by international organisations including Médecins Sans Frontières. Meanwhile, Gilead's new manufacturing plant for AmBisome has been repurposed to produce remdesivir for COVID-19, which has debatable clinical effectiveness. The supply capacity of AmBisome is now clearly insufficient to meet all needs for the drug.

Without immediate action, these multiple threats will impede efforts to achieve both the WHO neglected tropical diseases road map for visceral leishmaniasis by 2030 and Sustainable Development Goal 3.3.

In view of these concerns, we recommend a contingency plan to coordinate global activities against visceral leishmaniasis. Five actions are urgently needed: (1) Funding of life-saving tools for visceral leishmaniasis (ie, diagnostic tests, drugs) should be continued and ring fenced by the UK government. More broadly, we encourage an independent analysis to evaluate the impact of UK's funding cuts, including on visceral leishmaniasis control. (2) Other donors and endemic countries should now prioritise visceral leishmaniasis funding. (3) Bio-Rad must reconsider or delay its decision to cease production of IT-Leish and alternative solutions must be sought to maintain access to this product. (4) Gilead must prioritise manufacturing of AmBisome. (5) Generic manufacturers of quality-assured L-AmB must also prioritise production to better secure the global supply.

This deadly confluence of threats occurs in a disastrous moment of health system fragility, drought and food insecurity across endemic countries. We have two alternatives: finally eliminate this devastating disease by prioritising diagnostics, treatments and putting patients first, or to put thousands of lives from the most vulnerable and neglected populations at stake, undermining decades of progress. The UK government, Bio-Rad and Gilead must honour their commitments: the alternatives are rarely so stark.

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