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Editorial

Rapid Diagnostics for the Endgame in Lymphatic Filariasis Elimination

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Lymphatic filariasis (LF) is a mosquito-borne parasitic infection of neglected people in Africa, Asia, the Pacific, and the Americas. It is caused by three parasites (*Wuchereria bancrofti*, *Brugia malayi*, and *B. timori*) that are transmitted by different mosquitoes, including *Anopheles*, *Aedes*, *Culex*, and *Mansonia* species.[1] It is a major cause of acute and chronic morbidity and a hindrance to economic development in resource-limited countries. Effective and simple diagnostic tools are central to estimating the burden of the disease and monitoring the impact of the Global Program to Eliminate Lymphatic Filariasis (GPELF).

GPELF is a rapidly expanding public health initiative that coordinated the administration of treatments to over 539 million people in 53 of 73 endemic countries in 2011.[2] Preventive chemotherapy, through mass drug administration (MDA), is the strategy used for delivering treatment to eliminate LF by 2020. The steps recommended by the World Health Organization (WHO) to implement and monitor MDA depend on effective and reliable diagnostics for mapping, baseline data collection, impact assessment at sentinel sites, and transmission assessment surveys (TASs) to verify transmission interruption. It is also important to initiate surveillance activities after MDA has been stopped to ensure that transmission interruption is maintained.[3] By 2011, 59 LF-endemic countries had completed mapping, 13 LF-endemic countries had mapping in progress, and only 1 LF-endemic country, Eritrea, had not started mapping.[2] Among the countries implementing MDA, 12 countries have moved to a post-MDA surveillance phase. Enhanced rapid diagnostic tools are now required to complete mapping in 14 endemic countries and scale up MDA and access progress to interruption of transmission in those countries implementing MDA.

The introduction of the immunochromatographic (ICT) card test for field application in the late 1990s was a major breakthrough for mapping LF in resource-limited settings.[4] Before that time, LF endemicity was estimated from historical data obtained from night blood surveys to detect microfilaria-positive individuals. This process was a labor-intensive exercise that required highly trained technicians to detect patent infection.

The new diagnostic test described by Weil and others[5] in this issue represents a major breakthrough for rapid diagnosis of LF in human blood. The standard BinaxNOW filariasis card test that has been used to determine the presence of infection for over 10 years was compared with a new filarial antigen test (the Alere Filariasis test strip). The specificity and sensitivity, determined by laboratory tests, observed for the strip test were as high as for the standard ICT card test, but the strip test was more sensitive in the field surveys, detecting 26.5% more people with LF infection than the standard ICT card test. Moreover, the new strip test is more stable, with sharper positive test lines that are easier to read. The ICT card has a short shelf life of about 3 months (at ambient temperature in the tropics) and a narrow time window to read the results. The development of this new strip test, which has significant advantages over the current ICT card test, was supported by the Bill and Melinda Gates Foundation through a generous grant to Alere Scarborough (formally Binex Inc). It will be marketed in 2013 at a much lower cost compared with the standard ICT card that is currently in use.

This new test could not have come at a better time, because GPELF is preparing for the endgame phase and ensuring that robust monitoring and evaluation processes are in place to complete mapping and conduct transmission assessment and post-MDA surveillance surveys. The target to complete mapping in all LF-endemic countries was 2012, but mapping has not been completed in 14 countries in Africa. A more reliable and user-friendly mapping tool will be welcome to facilitate the mapping process in the more challenging post-conflict countries like the Demographic Republic of Congo, where nearly 50 million people are estimated to be at risk.

According to the WHO forecast in the GPELF strategic plan for 2010–2020, all 73 LF-endemic countries will achieve 100% geographic coverage by 2016, and 55 countries will stop MDA and be in the post-MDA surveillance phase.[6] By 2018, 33 countries will have interrupted transmission and received certification from the WHO. Meeting these targets will require a significant strengthening of the monitoring and evaluation systems that hinge on highly sensitive, reliable, and user-friendly diagnostic tools.

In 2011, the WHO published a program manager's manual for monitoring and epidemiological assessment of MDA with a standard methodology called TAS to assess if MDA can be stopped after repeated annual treatments in children below a pre-determined critical cutoff threshold for the various vector–parasite relationships that influence transmission efficiency.[3] The more sensitive strip test described here will be invaluable in accurately determining when to stop MDA to ensure that newly infected children are detected and the true LF prevalence is estimated. ICT cards are currently used for the TAS surveys, which could benefit from a more sensitive tool for detecting antigenemia in newly infected children.

Very sensitive diagnostic tools are also required for routine surveillance after MDA has been stopped to detect if recrudescence of transmission has occurred. Ramaiah and Vanamail[7] working in India concluded that, in some epidemiological settings, up to 6 years of post-MDA surveillance may

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be required to verify the status of transmission interruption and inform appropriate decision-making. The WHO recommends that TAS surveys should be repeated at least two times, with an interval of 2–3 years, after MDA has been stopped after the first TAS with a pass result. After stopping MDA in 2009, Togo initiated post-MDA surveillance activities, including passive surveillance in health facilities and laboratories.[8] Active surveillance, based on repeated cross-sectional surveys, will also provide information on existing infections. Also, data from sentinel groups, such as military personnel and university students' blood banks, will provide information.

The higher sensitivity of the new test may also influence the threshold for TAS and could significantly raise the bar for LF elimination programs that will use it to guide decisions on when to stop MDA and post-MDA surveillance activities. Weil and others[5] suggest that TAS cutoffs should not be modified in response to improved sensitivity of the test strip, because antigenemia in young children (6–7 year olds) detected by TAS indicates true infection and reflects recent transmission events. Nevertheless, additional studies may be required to validate the cutoff for TAS based on the new strip test.

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