Malaria and filaria – synergies in tropical disease control

Prof William R Brieger urges health workers to think outside the box. Co-endemicity means a broader approach to disease control and can reap much greater rewards than the traditional vertical programmes

Many endemic tropical diseases are co-endemic in a given country and environment. Therefore, it only makes sense to learn whether there can be common strategies and synergies in disease control and elimination efforts. In this case we examine malaria in comparison with efforts to control and eliminate two filarial infections, lymphatic filariasis (LF) and onchocerciasis, commonly known as elephantiasis and river blindness respectively.

Lymphatic filariasis

Throughout Africa one of the main vectors that carry LF is the Anopheles mosquito, which also carries the malaria parasite. The Carter Centre has been promoting use of insecticide-treated nets (ITNs) for many years as part of its LF control efforts,[1] but others may not have gotten the message.

The global community is targeting LF for elimination in 2020. The primary strategy is mass drug administration (MDA) annually with ivermectin and albendazole. The plan is that up to seven annual rounds of drug distribution in endemic communities where 90% of population coverage is achieved is necessary to stop LF transmission. The Carter Centre explains that distribution of long-lasting insecticidal bed nets (LLINs) protects pregnant women and children who cannot take drug treatment.

The LF strategy often builds on and integrates with onchocerciasis control efforts where these diseases overlap.[2] The community directed treatment with ivermectin model pioneered by the African Programme for Onchocerciasis Control, wherein communities or villages plan together the distribution process, including selecting their own community directed distributors.

A second component of the LF strategy is morbidity management which focuses on enhanced personal hygiene or cleaning of the parts of the body that experience lymphedema. Another aspect uses surgery to address some of the worst effects, hydrocele. While this component does not 'control' LF, it is a necessary effort to reduce suffering and the negative stigma from the disease.

To judge whether transmission has stopped and elimination has been achieved, Transmission Assessment Surveys (TAS) are conducted with rapid diagnostic tests on young children after at least five years of MDA in a community.[3] Specifically, the World Health Organization (WHO) recommends an implementation unit must have completed five effective rounds of annual MDA defined as achieving rates of drug coverage exceeding 65% in the total population.

For example, the Carter Centre in support of the Nigerian Federal Ministry of Health worked in Plateau and Nasarawa States through community health education, delivery of LLINs and 33 million drug treatments for LF and river blindness between 2000 and 2011. 'In 2012, it was confirmed (through TAS) that lymphatic filariasis transmission had stopped. Post-treatment surveillance is currently underway to assure that the parasite is not reintroduced into the area.'

Another component of the assessment process is yet to be fully realised. That is the testing of mosquitoes for the presence of microfilariae. This indirectly implies an important role in preventing human-vector contact as would be achieved through the use of ITNs, as well as indoor residual spray (IRS).

Vector control can benefit more than one disease.[4] Integrated vector management is seen as a key tool to prevent reintroduction of LF[5] in areas where anopheles mosquitoes carry the disease and where ITN campaigns are successful.

Ivermectin or Mectizan® supplies are provided free for onchocerciasis and lymphatic filariasis control by Merck. Countries order and ensure that these drugs reach each district and health facility for onward provision to community distributors

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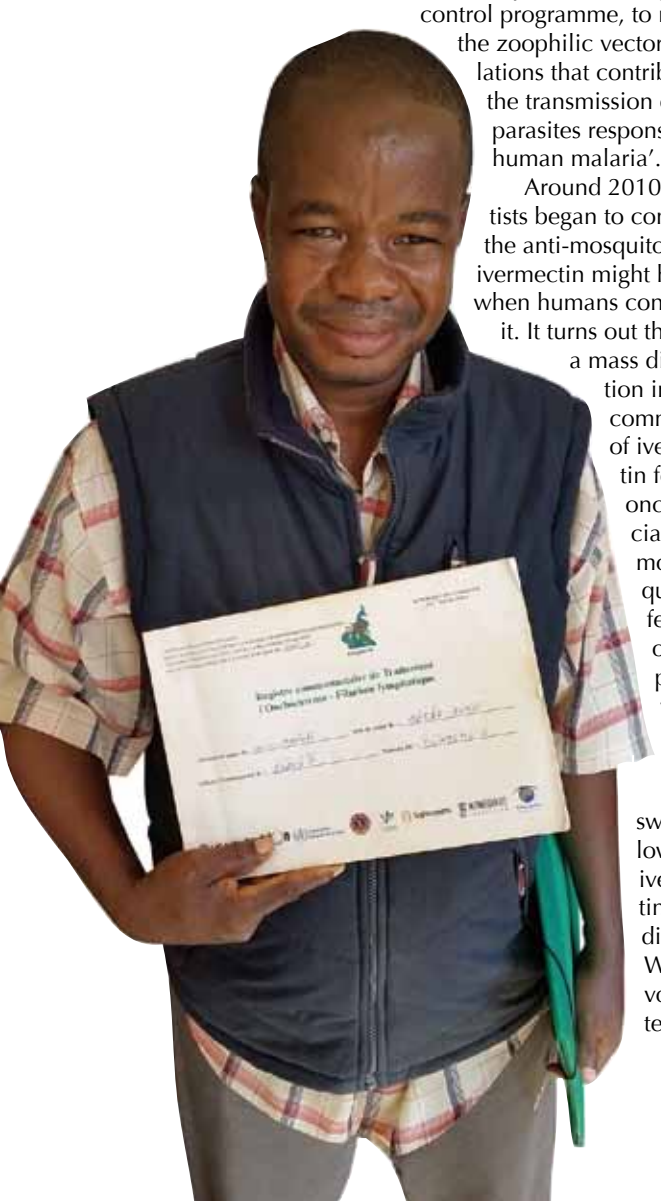
Onchocerciasis

While LF and malaria may share a common vector in many African settings, onchocerciasis is carried by the black fly (*simulium damnosum*) that breeds along the banks of fast-flowing rivers. Onchocerciasis was eliminated in many settings in the Sahel through the process of aerial spraying of these riverbanks to kill the black fly larvae. Though the insecticide used was often the same as used on malaria larviciding, the habitats differed and no synergies were achieved.

Through subsequent programmes using community directed treatment with ivermectin interventions, sponsored by APOC, as well as through the community MDA efforts for LF control (both of which used ivermectin ivermectin was found to have beneficial effects on malaria transmission.

Ivermectin had been used in agriculture, and not only for internal parasites of animals. The agricultural community have known since at least the late 1990s that Ivermectin, used 'to control worms and other internal infestations in cattle, and is also effective against some external parasites, such as lice' and ticks. In addition, ivermectin remained in cowpats and is toxic to the insects which would normally feed on them.[6] Additional research led to the proposal that 'treatment of cattle with ivermectin could be used, as part of an integrated control programme, to reduce the zoophilic vector populations that contribute to the transmission of the parasites responsible for human malaria'.[7]



Around 2010 scientists began to consider the anti-mosquito effects ivermectin might have when humans consumed it. It turns out that after a mass distribution in a community of ivermectin for onchocerciasis that mosquitoes feeding on people who had recently swallowed ivermectin would die. When volunteers took ivermectin, being bitten led to mosquito mortality of 73%, 84%, and 89% on days two, three, and four, while there was not effect in the group not taking the drug.[8] Of particular interest was the fact that people who had consumed ivermectin would contribute to mosquito mortality even when they were outdoors, especially if malaria vector behaviour changed to more outdoor biting.[9] A concern of course is that the anti-mosquito effect of ivermectin does not last beyond a few days, but onchocerciasis control programmes in the Americas has shown that it is safe to administer two[10] or four[11] times a year.

Looking at regular ivermectin distribution for filariasis between 2008–2013 in Senegal, Liberia and Burkina Faso, a study team found that a week post MDA both mosquito survival and parity was reduced. In addition, 'Sporozoite rates were significantly reduced by >77% for two weeks following the MDAs'.[12] The effect both on mosquitoes and Sporozoite production as seen in a review of studies, led to the conclusion that…

'The use of ivermectin solves many challenges identified for future vector control strategies. It is an effective and safe endectocide that was approved for human use more than 25 years ago. Recent studies suggest it might become an effective and complementary strategy in malaria elimination and eradication efforts; however, intensive research will be needed to make this a reality.'[13]

The delivery mechanism for ivermectin of course would include annual or biannual community distributions in onchocerciasis- and LF-endemic areas up until the time that the diseases are eliminated from an area. Other community mass distribution programmes would continue, such as school-based distribution of deworming medicines to which ivermectin could be added.[14]

Research that looks at the malaria parasite concluded that, 'it is likely that ivermectin treatment is arresting parasite growth'. The researchers note that, 'given the prior use of ivermectin and its safety record in humans and animals, it can be considered in combination therapy with other antimalarials'. The issue of dosage would need to be tested further.[15]

Because of the need to find new and complementary tools the Malaria Policy Advisory Committee (MPAC) of the WHO's Global Malaria Programme considered at its recent meeting the role of ivermectin in the future of malaria control and elimination. In a discussion paper presented to the MPAC the following general considerations were put forward:[16]

- Ivermectin MDA could reduce vectorial capacity primarily by reducing vector survival and fitness, and, to a lesser extent, by partially inhibiting sporogony and negatively affecting vector fertility.
- This potential new application of ivermectin warrants full understanding, particularly in terms of its role in: (a) reducing the residual transmission of malaria, (b) curbing insecticide resistance, and (c) accelerating progress towards elimination.
- Research should be guided by the target product profile (TPP) developed on the basis of ivermectin's expected public health role in malaria control. The critical components of the TPP will be efficacy, safety and regulatory/policy requirements.

Even when Lymphatic Filariasis Transmission Assessment Surveys suggest that mass drug administration can stop, surveillance and use of insecticide-treated nets should continue

Conclusion

The example of malaria and two filarial diseases demonstrate the potential for synergies in disease control efforts. Malaria benefits LF in providing a vector control strategy to complement the main MDA intervention and help guard against recrudescence or reintroduction of disease from surrounding areas. The ITN intervention for malaria will last long past the official elimination of LF in an area.

While malaria interventions can aid LF control, onchocerciasis interventions can help eliminate malaria vectors and maybe the parasites. From the economic and logistical approach, MDAs for either onchocerciasis or LF provide an effective and well established current platform to test and standardise ivermectin consumption in the control of malaria. When these two diseases are eliminated in the near future, there other MDA activities for infectious diseases like soil transmitted helminths for school-aged children could include ivermectin.

The future of malaria elimination requires finding new tools to integrate with and the strengthening of existing tools. If these efforts also benefit the control and elimination of other diseases, the public's health will benefit.

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