Advancing toward the Elimination of Lymphatic Filariasis

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The Global Program to Eliminate Lymphatic Filariasis (GPELF) was established in 2000 after the adoption of a World Health Assembly resolution in 1997 that called for member states of the World Health Organization (WHO) to eliminate lymphatic filariasis as a public health problem. The condition is caused by one of three filarial parasites. *Wuchereria bancrofti*, the most common of the three, causes 90% of lymphatic filariasis infections worldwide and is transmitted by several genera of mosquitoes — anopheles, aedes, mansonia, and culex. The strategy, known as preventive chemotherapy, is annual treatment by means of mass drug administration of a two-drug combination of diethylcarbamazine and albendazole to all those eligible (with the exclusion of children younger than 2 years of age, pregnant women, and the very sick) in all countries except where onchocerciasis is coendemic (most of Africa and Yemen), in which case a combination of ivermectin and albendazole is used (with the exclusion of children shorter than 90 cm, pregnant women, and the very sick) because of the potential side effects of diethylcarbamazine in patients with onchocerciasis. The strategy is based on the premise that treatments reduce the number of microfilarial parasites circulating in the blood to a level at which transmission by mosquitoes is not sustainable.

Mass drug administration is recommended by the WHO to be undertaken for a period of at least 5 years with an epidemiologic coverage of at least 65% of the total population. Mosquito vector control is an important supplemental intervention aimed at breaking transmission. However, although mass drug administration has been successful in reducing the rate of transmission, a considerable number of people remain clinically impaired and have not, to date, benefited from the program. The effect of lymphatic filariasis on patients and the social and economic effect on caregivers represents the face of what was described by the WHO as the world's second most disabling condition; however, this does not take into consideration the previously ignored burden the condition has on the mental health of the patients.[1] A package of care that is recommended by the WHO for patients with lymphatic filariasis includes surgery for hydrocele, treatment for episodes of adenolymphangitis, and management of lymphedema to prevent episodes of adenolymphangitis and progression of disease. The goal is full geographic coverage of this care package to known patients.

To date, the GPELF has made significant progress using the above strategies to reduce the burden of the disease; 6.7 billion treatments have been given in 66 countries to more than 850 million people at least once. In 2016, the WHO reported a mass drug-administration coverage of 57.9% of the total population that required treatment, with 495.6 million persons treated in 40 reporting countries, and national programs that targeted 669.4 million people for treatment reported a mass drug-administration coverage of 74% in 1996. On the basis of reported results of transmission assessment surveys, almost 500 million persons no longer require treatment. In total, 20 countries have stopped mass drug administration, including 9 countries that were validated as having attained the objectives of the program.[2] However, despite success, 852 million people in 52 countries where infection has not been reduced below target thresholds remain in need of treatment.

In this issue of the *Journal*, King and colleagues[3] report the results of a randomized, controlled trial conducted in Papua New Guinea, in which a single dose of a triple combination of ivermectin plus diethylcarbamazine plus albendazole was shown to be significantly more effective in eliminating microfilariae from the blood for 3 years than a single dose of the standard regimen that has been recommended by the WHO to date (which in Papua New Guinea is a two-drug regimen of diethylcarbamazine and albendazole) and was shown to be similar to the two-drug regimen administered once a year for 3 years. The WHO has recommended that annual triple-drug treatment with ivermectin plus diethylcarbamazine plus albendazole can be used for mass drug administration rather than annual treatment with the two-drug regimen of diethylcarbamazine plus albendazole in areas where

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implementation has not started, in areas where fewer than four effective rounds of treatment with the two-drug regimen have been performed, and in areas where epidemiologic targets in surveys have not been met and hence local transmission might be ongoing.[4] The new triple-drug treatment, however, is not recommended in areas where onchocerciasis is endemic because of the potential adverse effects that result from the action of diethylcarbamazine against the onchocerca parasite or in areas where loiasis is coendemic, also because of the potential serious adverse events that are caused by the anthelmintic effect of ivermectin in persons with high parasitemia levels of *Loa loa*.[5] This precludes the use of the triple-drug treatment in many African countries where all three filarial parasites are endemic and present a public health challenge.[6]

However, elsewhere, the triple-drug treatment provides significant promise for the elimination of transmission within a much shorter time scale and at less cost. The manufacturers of ivermectin have agreed to increase the donation of the product, and in August, Samoa became the first country to implement the triple-drug treatment with the intent of eliminating the infection that has persisted for more than 100 years.[7] The 6.7 billion treatments over the past 18 years has provided public health benefits beyond what was originally envisioned with the filariasis program. In addition, the program has delivered more broad-spectrum anthelmintic drugs than any other deworming program and has contributed to wider health benefits that are as yet unquantified. Ramaiah and Ottesen[8] estimated that 97 million infections, 18 million cases of hydrocele, and at least 5.5 million cases of lymphedema have been prevented or cured during this period. The widespread use of the triple-drug treatment will further facilitate the public health success of the global filariasis elimination efforts, accelerating the reduction of transmission, particularly in what have previously been residual hotspots. It will bring additional health benefits with the incorporation of ivermectin into national programs,[9] thus reducing the transmission of scabies as well as intestinal helminths.

Disclosure forms provided by the author are available with the full text of this editorial at NEJM.org.

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