

Study triggers change in WHO treatment guidelines for lymphatic filariasis

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Researchers from Case Western Reserve University School of Medicine have shown that a single "cocktail" of three pill-based anti-parasite medications is significantly more effective at killing microscopic larval worms in people diagnosed with lymphatic filariasis, commonly known as elephantiasis, than other standard two-drug combinations previously used in the global effort to eliminate this infectious disease. A combination of all three drugs given simultaneously had never been tested until now. An estimated 120 million people in over 50 tropical and subtropical countries are infected with lymphatic filariasis and another 856 million people are at risk.

As a result of these findings, published in today's issue of the *New England Journal of Medicine*, the World Health Organization has revised its treatment guidelines for preventive chemotherapy of [lymphatic filariasis](#) in numerous countries worldwide where current mass treatment regimens have been unsuccessful in achieving elimination or have not yet been started. Countries that plan mass [drug](#) treatment with this new regimen include Papua New Guinea (where the study was conducted), Haiti, Indonesia, Fiji, India, Samoa, Madagascar, Kenya, São Tomé and Príncipe, Zimbabwe, and Guyana.

The disease is characterized by grossly enlarged limbs and breast (elephantiasis) and massive swelling of the scrotum (hydrocele). Of those infected, an estimated 25 million men suffer from hydrocele and 15 million, mostly women, exhibit elephantiasis of the limbs and breast.

"Lymphatic filariasis has been targeted for global elimination by the WHO in arguably the largest mass drug administration program ever attempted for an infectious disease," said the study's lead author, Christopher L. King, MD, Ph.D., professor of international health, medicine, and pathology at Case Western Reserve University School of Medicine. "Our findings offer the promise of effectively banishing this disease from a long list of health threats facing people in many developing countries." In 2000 the World Health Organization targeted lymphatic filariasis for global elimination by 2020.

Although strides have been made with the existing two drug regimens—a 32 percent reduction in the number people at risk for lymphatic filariasis globally has been achieved to date—countries with weaker health infrastructures have struggled with the requirement to deliver at least five annual rounds of mass drug treatment at a population coverage of 65 percent in order to achieve elimination. This new drug regimen promises to require fewer rounds of annual treatment because of its greater efficacy and, therefore, increases the potential of achieving global elimination. However, even with better drug regimens, elimination cannot be achieved if people living in areas where lymphatic filariasis is endemic fail to take the drugs. An important aspect of the elimination program going forward will be to assure better coverage at the population level.

Ivermectin (IVM), diethylcarbamazine (DEC), and albendazole (ALB) are all established anti-parasite medications. In the study of 182 participants conducted in Papua New Guinea, the researchers found that a single dose of a three-drug regimen of IVM, DEC and ALB resulted in a far greater sustained clearance of microscopic worms than a single dose of a two-drug regimen of DEC and ALB. The three-drug, single dose was as effective as the two-drug regimen administered once a year for three years. This finding is especially noteworthy because public health programs find it challenging to ensure people living in filariasis

endemic areas take anti-parasitic drugs annually over five or more years.

"Lymphatic filariasis is a leading cause of permanent disability worldwide," said the study's senior author, James W. Kazura, MD, Distinguished University Professor and director of the Center for Global Health and Diseases at Case Western Reserve University School of Medicine. "In addition to its devastating physical ramifications, which often make it challenging to work and conduct normal daily activities, the gross disfigurement can have psychosocial consequences, such as being shunned by their communities."

Lymphatic filariasis is a round worm infection related to the dog heart worm where adult male and female worms localize in the human body's lymphatic system. The female worms release microscopic larvae (microfilaria) that circulate in the blood and which can be ingested by mosquitoes. Mosquitoes can then allow the development of infective larvae that can be transmitted to new hosts during the blood feeding. The larvae grow into adult threadlike worms that obstruct the human lymph system, causing major fluid retention and swelling in the arms, legs, breasts, and scrotum.

To date, 6.7 billion two-drug treatments have been administered to more than 850 million people in 66 countries at least once. For more than three decades, the pharmaceutical companies Merck Inc. and GlaxoSmithKline have donated the medications used to eradicate lymphatic filariasis. More recently Eisai Co. Ltd. in Japan has donated DEC.

More information: Christopher L. King et al, A Trial of a Triple-Drug Treatment for Lymphatic Filariasis, *New England Journal of Medicine* (2018). [DOI: 10.1056/NEJMoa1706854](https://doi.org/10.1056/NEJMoa1706854)

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