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80 Million People Now Treated to Prevent Elephantiasis

One of World's Most Disfiguring Diseases Could Be Eliminated in 20 Years

Simple Treatment Costs Only Pennies Per Person

David Molyneux, PhD, of the Liverpool School of Tropical Medicine, Eric A. Ottesen, M.D., a professor at Emory University and Director of the Emory LF Support Center and J.P. Garnier, GlaxoSmithKline CEO, are available for media interviews. B-rolls are available for television producers, photo images and a map of LF endemic countries and regions are available for all at http://209.123.255.51/hhwpress

In only four years, a massive World Health Organization-led global program to eliminate one of the world's most disfiguring and disabling tropical diseases, lymphatic filariasis (LF), has already provided remarkable benefits for the populations of at least 37 endemic countries.

A simple 2-drug, once-yearly treatment of all 'at risk' individuals using very safe and effective medicines (albendazole *plus* either ivermectin or DEC) has been responsible for the fastest ramp up of a global public health program in history. The World Health Organization (WHO) reports that today nearly 80 million people -- 30 million of whom are children -- have begun to be protected from LF by stopping transmission of the disease, which can lead to the huge enlargement and disfigurement of the arms, legs and genital organs known as elephantiasis. Two of these drugs are being donated by their manufacturers – albendazole by GlaxoSmithKline and Mectizan™ (ivermectin) by Merck & Co., Inc.

"Our company has already donated 250 million treatments of albendazole to this program, and we will continue to donate as much of the drug as is needed," says J.P. Garnier, CEO of GlaxoSmithKline. "We estimate that it will take about 20 years to break the cycle of the disease globally. But we have the proof now that it is practical to eliminate this ghastly disease completely, within our lifetimes."

Some one billion people in 80 tropical countries are at risk from LF, and 120 million people actually carry the infection, which is spread by a microscopic, parasitic worm that invade the human lymphatic system. The disease is spread by parasite-carrying mosquitoes, which act as vectors for the disease when they bite multiple people.

In many endemic regions, the infection is found in as much as 25 percent of children 4-6 years old. However, early damage is hidden and no immediate signs of LF are visible. LF generally begins to be recognized only in the victim's teen years. The disease often leads to profound psychological disability as a very understandable consequence of the severe physical disfigurements.

Efforts to eliminate the carrier of the parasite, the mosquito, are rarely sufficient to stop the spread of infection. Medical studies of the 1990s showed that the best opportunity for eliminating lymphatic filariasis is through medicines—combinations of the inexpensively purchased diethylcarbamazine (DEC) and the donated albendazole and Mectizan™ (ivermectin). The principal goal of treating affected communities is to eliminate the microfilariae from the blood of infected individuals so that transmission of infection by the mosquito can be interrupted.

The crucial research of the 1990s demonstrated that a single dose of two drugs administered concurrently (albendazole with either DEC or ivermectin) could be 99 percent effective in killing microfilariae from the blood for a full year after treatment. It is this level of treatment effectiveness that has made feasible the new global efforts to eliminate lymphatic filariasis. But everyone living in areas at risk for the disease must be targeted for drug treatment. In Yemen and Sub-Saharan African countries where river blindness (treated with Mectizan) and LF co-exist, the two donated drugs – albendazole and Mectizan (ivermectin) – are used against the disease**.** Elsewhere in the world the combination of DEC and albendazole is used.

The cost-benefit ratio of LF treatment is also astounding, according to The Global Alliance for the Elimination of Lymphatic Filariasis (GAELF), a global partnership of 80 health ministries, GlaxoSmithKline, Merck, WHO, UNICEF, World Bank and others.

Administration of LF treatment costs between US$0.10 and US$2.00 per person for the full five-year course. GlaxoSmithKline and Merck provide all necessary quantities of albendazole and Mectizan – at no cost – to assist the Global Programme in achieving its goals.

Data gathered by the WHO have revealed that LF is endemic in 32 of the 38 least developed countries (referred to in the Report of the WHO-established Commission on Macroeconomics and Health) and

more than 80 percent of the LF endemic population live in these countries. Considering the close link between poverty and LF, elimination of the disease will also provide an opportunity to reduce poverty and inequality.

The strong community participation and capacity-building components of the Global Programme that have been developed, are highly-effective means of producing skilled personnel, reliable information systems and ultimately strengthening the health system.

The elimination of LF is expected to provide tremendous economic advantages in affected areas. Economists estimate that people protected from the effects of LF could be expected to contribute billions more dollars to the economies of endemic regions throughout their lifetimes than they would have had they been stricken by the disease. In India alone, the economic losses resulting from decreased productivity and lost work days are estimated to be in the order of US$1 billion annually.

“The fight against LF is absolutely winnable,” says Dr. Garnier. “What’s required is the continuous commitment of the major players involved in the effort - governments, non-governmental organizations, international institutions, pharmaceutical companies and the communities themselves.”

GlaxoSmithKline expects to donate more than US$1 billion worth of medicine and cash donations over the projected 20 -year program.

And while early support for the Global Alliance has also come from the Ministries of Health of the endemic countries and a number of international organizations, including the Arab Fund for Economic and Social Development, the US Centers for Disease Control and Prevention, the US Agency for International Development, the UK Department for International Development and the Bill & Melinda Gates Foundation, there is a need for additional donors to join the campaign.

“The main problem is that LF disease (elephantiasis and genital damage) is mostly unknown in the West, because travelers and tourists rarely become infected, since multiple mosquito bites over a long period are usually necessary before a victim begins to show symptoms. So LF has been ignored by policymakers in many developed countries,” says David Molyneux, PhD, a tropical disease expert from the Liverpool School of Tropical Medicine. “This is a disease that affects the poorest of the poor.”

“In diseases like tuberculosis, HIV and malaria where parasites, bacteria and viruses develop resistance, part of the medical challenge is to stay ahead of the mutations,” says Professor Molyneux.

The LF worms, on the other hand, are slow growing and for a number of reasons are less likely to develop drug resistance. It makes the goal of ending the disease realistic."

The disease elimination program involves very close collaboration with Ministries of Health of participating nations. WHO Headquarters, Regional Offices and Country Offices support mapping the extent of the diseases in endemic regions with a new test that can determine almost instantly whether a person, including a child, is infected.

In tropical and subtropical areas of Africa, Asia and the Americas where lymphatic filariasis is highly endemic, the prevalence of infection is continuing to increase. A primary cause of this increase is the rapid and unplanned growth of cities, which creates numerous breeding sites for the mosquitoes that transmit the disease.

Approximately one-third of people infected with the disease live in India; one third are in Africa and most of the remainder are in Southeast Asia, the Pacific and the Americas.

Background on disease

The thread-like, parasitic filarial worms *Wuchereria bancrofti, Brugia malayi,* and *Brugia timori* that cause lymphatic filariasis live almost exclusively in humans. These worms lodge in the lymphatic system, the network of nodes and vessels that maintain the delicate fluid balance between the tissues and blood and that are an essential component for the body's immune defense system. They live for 4-6 years, producing millions of immature microfilariae, minute larvae that circulate in the blood.

The disease is transmitted by mosquitoes that bite infected humans, ingesting the microfilariae. In 7-14 days, the microfilariae mature and migrate to the mosquito's biting mouthparts, ready for inoculation into the bloodstream of the next unsuspecting individual, thus completing the infection cycle.

The appearance of the disease itself in humans is still something of an enigma to scientists. Though the infection is generally acquired early in childhood, the disease may take years to express itself. Indeed, many people never acquire the outward clinical manifestations of their infections.

An asymptomatic form of infection, characterized by the presence of millions of microfilariae in the blood and adult worms in the lymphatic system, may have no recognizable clinical manifestations at all. However, recent studies now show clearly that such victims, outwardly healthy, actually have hidden lymphatic pathology, kidney damage and defects in their immune responsiveness.

The worst symptoms of the chronic disease generally appear in adults, and in men more often than women. In endemic communities, some 10-50 percent of men suffer from genital damage, especially hydrocoele (fluid-filled balloon-like enlargement of the sacs around the testes) and elephantiasis of the penis and scrotum. Elephantiasis of the entire leg, the entire arm, or the breast -- swelling up to three times normal size -- can affect up to 10 percent of men and women in these communities. The psychological and social stigmata associated with the disease are immense, including sexual dysfunction and social ostracism of men and women. Young women and men often can never marry or are subsequently rejected.

Acute episodes of local inflammation involving skin, lymph nodes and lymphatic vessels often accompany the chronic lymphedema or elephantiasis. Some of these are caused by the body's immune response to the parasite, but most are the result of the bacterial infection of skin where normal defenses have been partially lost due to underlying lymphatic damage. Careful cleansing can be extremely helpful in healing the infected surface areas and in both slowing and, even more remarkably, reversing much of the overt damage that has occurred already.

In endemic areas, chronic and acute manifestations of filariasis tend to develop more often and sooner in refugees or newcomers than in local populations continually exposed to infection. Lymphedema may develop within six months and elephantiasis as quickly as a year after arrival. Once damaged, the lymphatic system never recovers.

The previous treatment regimen thought necessary for LF was a long, 2-week course of DEC. It is now recognized, however that when a *single dose* of either DEC or ivermectin is administered with albendazole, the results are even more effective than the old treatment regimen.

Unexpected Benefits of LF Campaign

The campaign to eliminate LF has also been found to have important ancillary benefits. "Albendazole is highly effective not only against the LF parasites but also against the most serious intestinal parasites of children and childbearing women that inhibit mental development and stunt physical growth of hundreds of millions of newborns and young children yearly," says Eric A. Ottesen, M.D., a professor at Emory University's Rollins School of Public Health and Director of the Emory LF Support Center.

The three most serious parasites are roundworms, which infect nearly a half billion children; whipworms, which infect 350 million children; and hookworms, which infect nearly 300 million

children. In some regions, more than 90 percent of children are infected with one or more of these parasites.

Intestinal parasites take a severe toll on the nutritional status of infected children, resulting in poor physical growth, anemia and an inability to absorb vital nutrients.

Results from treating these infections have been dramatic in the developing countries where evaluations have been carried out. Examples include:

• **Growth and development** – *five months* after being treated with albendazole and ivermectin, children gained over 0.5 kg more than children treated with placebo [Haiti];
• **Physical fitness** – *seven weeks* after being treated with albendazole for intestinal worms, school children had improved resting heart rates and increased physical fitness [Kenya];
• **Physical activity –** *nine weeks* after treatment with albendazole, school children showed demonstrable increases in spontaneous play and other measurable activities [Kenya];
• **School attendance** – *six months* after treatment with albendazole, stunted children with whipworm infection showed improved school attendance [Jamaica].

“These results demonstrate convincingly that such drugs as albendazole can dramatically improve the health development of the poorest of the poor children throughout the world,” says Dr. Ottesen. “What is more, this can be done with essentially no additional cost to them or to the healthcare systems responsible for them, since everyone living in areas where the Global Programme to Eliminate Lymphatic Filariasis is active – including the particularly vulnerable populations of children and women of childbearing age – will already be receiving these drugs.”

The Global Alliance to Eliminate Lymphatic Filariasis: (http:// www.filariasis.org)

Partners

National Ministries of Health
- Ministries of Health of the 80 endemic countries

International Organizations
- The World Bank Group
- United Nations Children's Fund (UNICEF)
- World Health Organization (WHO)

Private Sector
- Binax, Inc., USA
- GlaxoSmithKline, UK
- Merck & Co., Inc., USA

International Development Agencies and Foundations
- Arab Fund for Economic and Social Development (AFESD), Kuwait
- Bill and Melinda Gates Foundation, USA
- Centers for Disease Control and Prevention (CDC), Atlanta, USA
- Department for International Development (DFID), UK
- Directorate General for Development Cooperation (DGCS), Italy
- Japan International Cooperation Agency (JICA), Japan
- Ministry of Health and Welfare, Japan
- Ministère fédéral des Affaires sociales, de la Santé publique et de l'Environnment, Belgium
- Ministerio de Sanidad y Consumo, Spain
- Ministry of Health Welfare and Sport, The Netherlands

Non-Governmental Organizations
- Amaury Couthino, Brazil
- Handicap International
- Health and Development International (HDI), Norway
- Interchurch Medical Assistance (IMA), USA
- International Foundation for Dermatology, UK
- International Skin Care Nursing Group, UK
- International Volunteers in Urology, USA
- The Carter Center, Atlanta, USA
- The Centres for Partnerships in Health, Australia
- The Mectizan® Donation Program, USA
- World Alliance for Community Health, Canada

Academia and Research Institutions
- Ain Shams University, Egypt
- Bernhard Nocht Institute for Tropical Medicine, Germany
- Chinese Academy of Preventive Medicine, China
- Danish Bilharziasis Laboratory (DBL), Denmark
- Institute for Medical Research (IMR), Malaysia
- James Cook University, Australia
- Lymphatic Filariasis Support Center, Emory University, USA
- Lymphatic Filariasis Support Centre, Liverpool School of Tropical Medicine, UK
- Michigan State University, USA
- Notre Dame University, USA
- Smith College, USA
- Universidade Federal de Pernambuco, Brazil
- Vector Control Research Centre (VCRC), Indian Council of Medical Research, India
- Washington University in St. Louis - Barnes-Jewish Hospital, USA

The Global Alliance to Eliminate Lymphatic Filariasis

List of LF Endemic Countries by Regional Program Review Groups

Africa (39)
Angola
Benin
Burkina Faso
Burundi
Cameroon
Cape Verde
Central African Rep.
Chad
Comoros
Congo, Dem. Rep.
Congo, Rep.
Cote d'Ivoire
Equatorial Guinea
Ethiopia
Gabon
Gambia, The
Ghana
Guinea
Guinea –Bissau
Kenya
Liberia
Madagascar
Malawi
Mali
Mauritius
Mozambique
Niger
Nigeria
Reunion
Rwanda
Sao Tome and Principe
Senegal
Seychelles
Sierra Leone
Tanzania
Togo
Uganda
Zambia
Zimbabwe

Americas (7)
Brazil
Costa Rica
Dominican Republic
Guyana
Haiti
Suriname
Trinidad and Tobago

Eastern Mediterranean (3)
Egypt, Arab Rep.
Sudan
Yemen, Rep.

Indian Subcontinent (5)
Bangladesh
India
Maldives
Nepal
Sri Lanka

Mekong Plus (12)
Brunei Darussalam
Cambodia
China
Indonesia
Lao, PDR
Malaysia
Myanmar
Philippines
South Korea
Thailand
Timor-Leste
Vietnam

Pac-ELF (17)
American Samoa
Cook Islands
Fiji
French Polynesia
Kiribati
Marshall Islands
Micronesia, Fed Sts
New Caledonia
Niue
Palau
Papua New Guinea
Samoa
Solomon Islands
Tonga
Tuvalu
Vanuatu
Wallis & Futuna

* countries in *italics* are formerly endemic countries working to establish absence of transmission

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