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Editorial: **The Global Programme to Eliminate Lymphatic Filariasis**

Eric A. Ottesen
Department for Communicable Diseases Eradication and Elimination, WHO, Geneva

Summary Ten years ago, no one foresaw that in the year 2000 there would be a Global Programme to Eliminate Lymphatic Filariasis (GPELF) that is already 2 years old, active in 18 of the 80 endemic countries, and operating under a wholly new paradigm in public health – a paradigm affirming that public/private sector partnerships are essential in sharing both responsibilities and responses to global health problems. What has driven the LF Elimination Programme to this point? Where it is now headed? What will be required to sustain its momentum? What will its impact be? These are the issues addressed below.

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correspondence Dr E. Ottesen, World Health Organization, CEE/FIL, 1211 Geneva 27, Switzerland. Tel.: 41–22–791–3225. Fax: 41–22–791–4777. E-mail: ottesene@who.int.

Breaking down the barriers to LF elimination

A decade ago, the three greatest barriers to lymphatic filariasis (LF) elimination were: lack of tools necessary to interrupt transmission and halt disease progression; lack of understanding of disease dynamics and pathogenesis; and lack of both public awareness of LF's impact and public commitment to overcome it. Indeed, few dared to consider it a target for elimination.

Lymphatic filariasis has a number of biological features that favour the possibility of its elimination: the fact that it is almost exclusively a parasite of humans, its inability to amplify its numbers in vector mosquitoes and its relatively inefficient mechanism of transmission. LF elimination was seriously considered once two essential sets of tools (Ottesen *et al*. 1997; Ottesen 2000) had been developed. The first were safe, single-dose, two-drug treatment regimens capable of reducing microfilaraemia to zero or near-zero levels for long periods of time (1 year or more); the second were diagnostic techniques both for field diagnosis of infection by simple, finger-prick, anytime-of-day antigen-detection tests and for clinical diagnosis by ultrasound identification of living adult parasites. With these tools, infections in endemic communities are detected simply and efficiently, adulticidal effects of antifilarial drugs can be assessed directly, and the pathogenesis of lymphatic disease and the importance of this infection even in children has become much more well understood (Dreyer *et al*. 1999).

The strategy underlying the Programme to Eliminate Lymphatic Filariasis

The Programme has two principal goals: to interrupt transmission of infection, and to alleviate and prevent both the suffering and the disability caused by the disease. Almost as important, however, is the necessity to achieve these goals in a cost-effective, socially responsible manner ensuring appropriate health and economic benefits.

To interrupt transmission of the infection, the entire 'at risk' population must be treated for a period long enough to ensure that levels of microfilariae in the blood remain below those necessary to sustain transmission. For the yearly, single-dose, two-drug regimens being advocated (albendazole 400 mg plus diethylcarbamazine (DEC) 6 mg/kg; or albendazole 400 mg plus ivermectin 200 μg/kg), this period has been estimated to be 4–6 years, corresponding to the reproductive lifespan of the parasite; for the treatment regimen based on the use of DEC-fortified salt, the period has been empirically determined to be 6–12 months of daily fortified salt intake.

To alleviate suffering and decrease the disability caused by LF disease, the principal strategy focuses on decreasing secondary bacterial and fungal infection of limbs or genitals whose lymphatic function has already been compromised by filarial infection, since secondary infection is the primary pathogenetic determinant of worsening lymphoedema and elephantiasis. Meticulous hygiene in treating affected areas and the creation of hope and understanding among the pa-

tients, their communities and their care-givers are the principal approaches (Addiss & Dreyer 2000).

To ensure appropriate cost-effectiveness and cost-benefit ratios, national programme design involves close links with compatible public health programmes using similar intervention strategies (e.g. onchocerciasis control, intestinal helminth control, malaria control, leprosy elimination, micronutrient supplementation). The impact of the Programme both in terms of health and economics requires close monitoring to permit immediate feedback of information to affected countries and donor agencies.

Building the Programme

Even with the extraordinary advances in diagnosis and treatment of LF and with the development of strategies for its elimination, it was clear that all of these 'right answers' alone could not change the status quo; something was needed to translate these advances into action – to raise awareness of available possibilities and to enlist the support necessary to implement them. Three events became critical building blocks of the Programme's foundation.

First, in 1993 the International Task Force for Disease Eradication completed its review of almost 100 medical conditions (mostly infectious diseases) and categorized six as eradicable or potentially eradicable with the tools then available (CDC 1993). One of these was lymphatic filariasis. This assessment by independent experts raised awareness and interest in the goal of LF elimination and enhanced its plausibility among the scientific and public health communities.

Second, in 1997 the World Health Assembly called for countries 'to strengthen activities toward eliminating lymphatic filariasis as a public health problem' and requested the Director General of WHO 'to mobilize support for global and national elimination activities'. The importance of this resolution has been principally in its collective recognition of both the achievements to date and the potential benefits to be gained from local and global programmes to eliminate LF. It has also raised awareness among national health ministries and international organizations (initially the Arab Fund for Economic and Social Development, the World Bank and the United Kingdom's Department for International Development) that this severely handicapping disease, the second leading cause of permanent and long-term disability (WHO 1995), could be eliminated in a relatively short period of time.

Third, in 1998, the global health care company SmithKline Beecham (SB) and the WHO initiated a Memorandum of Understanding to establish a formal collaboration in support of the elimination of lymphatic filariasis globally. This followed the discovery of the added anti-filarial therapeutic benefits of albendazole when co-administered with DEC or ivermectin (Ottesen *et al*. 1999) and the broad ancillary benefits of albendazole, particularly against hookworm and other intestinal parasites. Though there are numerous facets to the SB contribution, the centrepiece is the extremely generous donation of all the albendazole required to see the LF Elimination Programme through to its conclusion. With this unprecedentedly large gesture the company provided an extraordinary example of being both an outstanding corporate citizen and a responsible partner willing to work hard to bridge the differences between the corporate world and international agencies for the benefit of the developing world. Indeed, Merck & Co., Inc. then offered to expand its 11 year-old, very successful Mectizan® (ivermectin) Donation Program for onchocerciasis (Dull & Meredith 1998) to include lymphatic filariasis in all of those countries where the two infections coexist. This extremely generous donation is particularly important since the alternative drug, DEC, cannot be safely used in these countries because of the side-effects it induces in patients with onchocerciasis.

This twin foundation of technical advances and political commitment has supported the building during the past two years of a now very functional Global Programme to Eliminate Lymphatic Filariasis (GPELF). Some of this building activity has been technical and programmatic, focused on mapping the prevalence/distribution of LF, defining the economics of LF, two-drug regimen efficacy and safety, disease management and disability prevention, programme management, and publication of practical guidelines (documents available at http://www.filariasis.org). Other activity has focused on developing the partnerships necessary to support these global and country efforts to eliminate LF, partnerships which include the ministries of health of the 80 endemic nations, academic and research organizations, NGOs, international development agencies, private sector concerns and international organizations (Ottesen 2000).

To bridge the technical and political 'halves' of the Programme most effectively, a strategic plan document entitled 'Building partnerships for Lymphatic Filariasis' was jointly developed by all partners. This plan not only charts the future in targets and milestones, but also states clearly what each of the partners in the Programme will endeavour to accomplish. More recently, the structure of this partnership has been defined in terms of a 'Global Alliance' recognized as 'a free, nonrestrictive partnership forum for the exchange of ideas and coordination of activities', with WHO serving as the secretariat reinforced by an expert Technical Advisory Group. The first meetings of this Global Alliance and Technical Advisory Group took place in May 2000 (documents available at http://www.filariasis.org).

Current Programme activities

While the Programme's overall policies and procedures are de-

fined in concert with the Global Alliance and the Technical Advisory Group, individual countries start with a national plan of action (developed independently or with WHO, its Collaborating Centres or independent LF support centres, as needed). Along with a request for donated drugs the plans are reviewed by an independent Programme Review Group (PRG, for which WHO serves as the secretariat), particularly in terms of the feasiblity of reaching the goal of LF elimination from the country. After PRG approval of applications from countries outside Africa, WHO requests shipment of the donated albendazole from SmithKline Beecham to the countries. For African countries where ivermectin is used instead of DEC, the PRG commends an approved proposal to a Joint Albendazole Mectizan® Expert Committee (associated with the Mectizan® Donation Program). Both drug companies (SB and Merck & Co., Inc.) follow these activities closely and dispatch the drugs after application approval by the respective committee.

To date, 29 of the 80 defined endemic countries have entered this process, 10 with active programmes underway, eight more with approved applications for donated drugs, and 11 with national plans of action and applications under development. By the end of 2000 another seven countries will have programmes underway, with the total number of at-risk individuals treated under national Programmes to Eliminate LF being more than 25 million. Since first-year programme activities usually comprise a pilot-phase, the number of at risk individuals to be treated will rise sharply in subsequent years. The long-term goal is to achieve LF elimination by 2020; specific targets and milestones leading to 2020 are detailed in the Strategic Plan (documents available at http://www.filariasis.org).

Future needs that must be met for Programme success

Reflecting the Programme structure itself, the future needs for the Global Programme fall into three broad categories – financial, technical and managerial. Financially, the most urgent challenge is to identify private, national or international (bilateral or multilateral) funding mechanisms to support the relatively low-cost country programmes underway or envisaged for the future. Major commitments above and beyond general Programme development have come from the Arab Fund for Economic and Social Development and from the governments of the United Kingdom, Australia, Belgium, Italy, Japan and the Netherlands. Other generous contributions have come from SB, CDC, Merck & Co., Inc., Liverpool University LF Support Centre, Health and Development International, the Carter Center and the Government of Spain. This funding base must now be further expanded.

On the technical side, the greatest initial challenge is to implement the programme activities themselves. In practical terms this means the development by Ministries of Health, WHO and other on-the-ground partners of training, logistics and management support sufficient to sustain the intervention. Obtaining the widest possible drug coverage in at risk communities is required for successful interruption of transmission; hence the most important operational research challenge is to develop mechanisms to ensure broad drug coverage, whether by yearly doses of drugs or daily consumption of DEC-fortified salt. Operational research will be necessary both to determine the effectiveness of current treatment, monitoring and assessment techniques (including predictive models for programme operations) and to optimize these and other new techniques as they are developed.

Finally, repeated, regular and rigorous impact assessment is necessary to celebrate programme successes and to identify arizing problems and technical solutions. Such review is critical not only for the success of individual programmes but also for providing programme supporters with the kind of information needed to justify and further extend their commitments.

Potential benefits of the Global Programme to Eliminate Lymphatic Filariasis

Three distinct types of benefits will accrue from this Programme. First, there are the direct benefits of eliminating the disease. LF elimination programmes based on mass-drug treatment have already been successful in Japan, Taiwan, and, most notably, mainland China. The LF elimination programme in China was initially motivated by the drain the disease caused on agricultural productivity, and the Chinese now estimate that a 15:1 return has been achieved on their investment in filariasis elimination (Sun 1995). While the health and economic impact of LF has not been well quantified in most endemic countries, a recent study suggests that in India alone economic losses approach US$1 billion yearly (Ramaiah *et al*. 2000). To these must be added the personal anguish, suffering, disability and stigmatization of the estimated 50 million clinically affected individuals worldwide (Dreyer *et al*. 1997). Reversal of all quantifiable and nonquantifiable consequences of LF infection and protection of the next generation's children from the threat of LF disease can be expected as a direct consequence of successful elimination programmes.

Secondly, the ancillary benefits of the GPELF are so profound that they ensure very broad public health impact and support. Albendazole, used in the LF elimination programme worldwide, is unsurpassed for the treatment of hookworm and other intestinal parasite infections (Horton 2000). Repeated treatment of entire communities with this drug will dramatically reduce the intensity of intestinal helminth infections, major causes of anaemia in women and children and of stunting and inhibited cognitive development in children (Stephenson *et al*. 2000). Hence SB's donation of albendazole will also have an extraordinary impact on one of the most fundamental drains on health and productivity in countries throughout the

developing world. Ivermectin is also the most effective drug to treat most ectoparasite infestations (lice and scabies) (Brown *et al*. 1995). Such ancillary benefits make these drugs extremely popular, with the result that while they are improving the overall health of the community, they will also foster the extensive community support necessary for the LF elimination programme to be successful.

The third, and perhaps most broadly important, consequence of the GPELF is its reinforcement of a new approach to the health problems of the developing world. Good health is directly beneficial to all sectors of society. While responsibility for health problems has generally fallen to the public sector, resources and skills to address these problems are increasingly found in the private sector. Hence shared responsibility by the public and private sectors for the health problems of the world is extraordinarily important, and the network of partners that form the Global Alliance for the Elimination of Lymphatic Filariasis can become a model for approaching the health concerns of under-served populations worldwide. Such partnerships, however, do not form spontaneously, naturally nor easily. The work cultures of businesses, nongovernmental organizations, religious organizations, local governments, national governments and international agencies are often extremely different, and sometimes even seemingly incompatible. Learning to overcome these differences is a critical prerequisite for the success of public health initiatives in the 21st century. Clearly, the Global Programme to Eliminate Lymphatic Filariasis will be a pioneer in fashioning the approaches needed to overcome the public health problems of today's developing world.

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