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Lymphatic filariasis elimination: progress in global programme development

D. H. MOLYNEUX* and N. ZAGARIA†

**Lymphatic Filariasis Support Centre, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool L3 5QA, U.K.*

†*Strategy Development and Monitoring for Eradication and Elimination, World Health Organization, 1211 Geneva 27, Switzerland*

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The Global Programme to Eliminate Lymphatic Filariasis (GPELF) is an innovative, public–private partnership for health improvement. The progress made since the programme was initiated, in 1998, is here reviewed. The programme is largely based on the regular mass administration of albendazole with either ivermectin (Mectizan®) or diethylcarbamazine. Both albendazole and ivermectin have been donated by their manufacturers, for as long as necessary. The first national campaigns based on these drugs commenced in late 1999. Since then, rapid progress has been made in confirming the safety of the drug combinations, establishing a regional approach, and recognizing that experiences, epidemiological settings, health systems, the best drug combinations and disease burdens all vary with the country involved.

There is a continuing trend towards decentralization, and this should lead to greater regional and national ownership and more inter-country activities. The progress made in mapping the geographical distribution of lymphatic filariasis (LF), by designated implementation units and, ultimately, by country, is also summarized. Country-specific methods of social mobilization and drug distribution, that are compatible with health planning at central and district level, need to be developed. However, the assessment of coverage by mass drug administration (MDA) needs to be strengthened, to allow reliable national monitoring and inter-country or inter-region comparisons.

Valuable contributions made by non-governmental development organizations (NGDO) and civil society organizations (CSO) are acknowledged, such organizations (and particularly local NGDO) should be encouraged to help more in implementing the various activities at district level.

The GPELF has developed during an era of considerable change in international health policy. The programme can contribute to the relief of poverty, as LF is closely associated with low-income communities in the least developed countries and MDA is a pro-poor intervention. There are clear opportunities for linking the activities of the GPELF (which uses cheap or free drugs that bring considerable incidental health benefits, in addition to arresting the transmission of the parasites causing LF) with other health interventions. New evidence indicates that annual treatments with antifilarial drugs greatly reduce the clinical abnormalities of the disease.

The programme has expanded rapidly, with the annual number of people treated rising from 2.9 million (in 12 countries) in the year 2000 to 25.89 million (in 22 countries) in 2001 and an estimated 80 million (in 34 countries) in 2002. At the recent meeting of the Global Alliance, held in New Delhi in May 2002, a significant but realistic challenge — of scaling-up the programme to cover up to 350 million of those at risk, by the end of 2005 — was set. The rate of growth necessary to meet this target presents considerable strategic and managerial challenges to all of the partners involved in the programme, from the development of synergies with other, large-scale, public-health interventions to the logistics of drug manufacture, shipping and local transportation and resolving the problems of social mobilization, reporting, evaluation and monitoring on such a scale. Such challenges are, however, easily outweighed by the potential benefits of success. If the international health community cannot provide the necessary support to complement the investments being made by the endemic countries (as they scale-up their LF-elimination campaigns and ensure yearly access to two free and efficacious drugs that bring major benefits to those treated), significant progress in the control of other infectious diseases becomes a very distant goal.

Reprint requests to: D. H. Molyneux.
E-mail: fahy@liv.ac.uk; fax: +44 (0)151 709 0354.

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Lymphatic filariasis (LF), also known as elephantiasis, is one of the major tropical diseases. Approximately 40 million people, almost all in the 80 or so countries where the disease is endemic, have clinical LF, and another 80 million are also infected with the nematodes that cause the disease. More than 1000 million people live in the endemic areas and are at risk of becoming infected, via the mosquitoes that transmit the parasites from person-to-person.

Human infection with the parasites leads to damage in the lymphatic vessels and then to a large range of temporary and permanent disabilities. LF is particularly associated with the disfigurement of grossly swollen limbs and genitals. It is now regarded as one of the few infectious diseases of the world that, thanks to the availability of good diagnostics and effective methods of control or prevention, are potentially eliminable.

RECOMMENDATIONS OF THE WORLD HEALTH ORGANIZATION

In 1997, the World Health Assembly (WHA) passed a resolution (50.29) that called for the member states of the World Health Organization (WHO) to support the global elimination of lymphatic filariasis as a public-health problem. In consequence, the WHO started a global programme (GPELF), recommending that all of those who live in at-risk communities be treated orally, once a year, with an appropriate, two-drug combination. The drugs used in combination have limited effect on the adult parasites but can clear microfilariae from infected subjects and so deprive mosquitoes of the opportunity to continue transmission. Three antiparasitic drugs are recommended for the global effort: albendazole, ivermectin and diethylcarbamazine (DEC). For countries where onchocerciasis and LF co-exist, DEC cannot be used safely and therefore albendazole and ivermectin are the drugs of choice. For the rest of the world, albendazole and DEC are recommended by the WHO. Use of two drugs together has been shown to provide a more long-lasting suppression of blood microfilariae than can be achieved using one drug alone (Ottesen *et al.*, 1997, 1999; Ismail *et al.*, 1998). For the mass drug administrations (MDA) to be effective in the long-term, a high percentage of those at-risk must be treated every year for four, five or six consecutive years (i.e. the estimated duration of the reproductive life of the adult female parasites). Such an approach has been successful in several countries, such as China, Suriname, and Trinidad and Tobago. In the GPELF, as in disease-prevention campaigns based on vaccinations, there is a need for a high level of community compliance (allowing high coverage) and for continuing support for those who already have symptomatic disease (who will not directly benefit from the intervention).

BUILDING A COALITION OF COMMITTED PARTNERS

Over the past 4 years, since the GPELF was established by the WHO, significant developments have occurred in health policy, scientific knowledge and donor commitment (Molyneux *et al.*, 2000; Ottesen, 2000; Molyneux and Taylor, 2001). In December 1997, the WHO and SmithKline Beecham — now GlaxoSmithKline (GSK) — announced that they would be collaborating in the global initiative to eliminate LF. To forge this public–private partnership, they signed an innovative and unique 'Memorandum of Understanding', as a legal framework. GSK promised not only to donate albendazole (sufficient for all LF-endemic countries that needed it for as long as necessary) but also to support the WHO in building the necessary coalition, and to provide the expertise of its staff and additional grant funding. In October 1998, Merck & Co. Inc. announced their intention to expand their Mectizan (ivermectin) Donation Program (MDP) — initiated for the control of river blindness

(onchocerciasis) — to include LF control in the sub-Saharan countries of Africa where onchocerciasis and LF co-exist and in Yemen.

An LF Partners Forum, convened in Geneva in October 1998, brought together a variety of potential partner organizations from the governments of endemic countries, the WHO and other international organizations, donors, academic and research institutions and international non-governmental development organizations (NGDO). A common vision was agreed and key issues and priorities were addressed, using an original, consensus-building process. The Liverpool School of Tropical Medicine (Liverpool, U.K.) and The Rollins School of Public Health (Emory University, Atlanta, GA) both established dedicated LF-support centres. Initial funding for the Liverpool centre came from the U.K. government's Department for International Development (DFID) and GSK who continue to provide some funding for both centres. DFID also channel operational funds for country programmes through the Liverpool centre. These two support centres have now become important partners in the Global Alliance for the Elimination of Lymphatic Filariasis, contributing expertise and institutional research capabilities together with a wide network of graduates spread around the world in public-health positions.

The NGDO in many aspects of health improvement has been expanding in recent years. A plethora of different, local or international NGDO and civil society organizations (CSO) has become involved in the GPELF. Although such organizations may differ, in terms of governance, mandate, mission, geographical focus, and technical, administrative and managerial capacities and resources, their involvement in disease control can be (and has been) very beneficial. The GPELF must seek to increase involvement of NGDO, particularly those that are locally based and those currently involved in similar and potentially synergistic initiatives (such as bed-net distribution, onchocerciasis control and the delivery of basic healthcare services — particularly community-based rehabilitation), as it expands from the base provided by the national programmes. Several NGDO have already made major contributions to the control of onchocerciasis in Africa, by assisting in various aspects of the ivermectin distribution and supporting national onchocerciasis-control programmes (NOCP), funded by the African Programme for Onchocerciasis Control (APOC) and the Onchocerciasis Control Programme in West Africa (OCP), in 21 countries (Drameh *et al.*, 2002). However, linking some of these NGDO to LF elimination, in areas where onchocerciasis and LF are co-endemic, becomes difficult if those NGDO have mandates specifically directed to blindness prevention and not a wider commitment to basic healthcare delivery.

It is anticipated that NGDO may play a significant role at country level, as national programmes for the elimination of LF expand and the opportunities and relevance of incorporating a two-drug regimen into on-going health programmes become evident (Cross, 2000). The GPELF requires such links, provided they are nested within national programmes and bring additional and complementary skills and resources to the programme. The particular skills required from NGDO will vary with the region or country involved, with the drug-distribution system(s) adopted, with the strength of the national health system, and with the local level of civil unrest/political stability. To date, no formal mechanism, comparable with that described by Drameh *et al.* (2002) for onchocerciasis, exists to involve NGDO in LF control. The onchocerciasis model could not be used for LF because, compared with onchocerciasis, LF is more wide-spread, occurs in areas where different NGDO (with different roles in health delivery) exist, involves more and different drug-distribution systems, and has less powerful lobbyists for its control. The GPELF needs to mobilize NGDO that can generate resources and reach difficult-to-access communities, particularly those in areas of civil unrest where governmental health services are no longer available.

THE ORIGINS OF THE GPELF

The results of just three pieces of research provided the springboard for the start of the global programme. These key investigations: (1) revealed the effects of combinations of drugs on levels of microfilaraemia (Ismail *et al.*, 1998); (2) showed that DEC as a single dose was as effective as multiple dosages in reducing the duration of microfilaraemia (Cao *et al.*, 1997; Meyrowitsch and Simonsen, 1998); and (3) led to the development of a rapid, minimally invasive test for detecting adult-worm antigen in blood samples — the immunochromatographic test, or ICT (Weil *et al.*, 1997). By the time these results were published, the International Task Force for Disease Eradication (WHO, 1992) had already emphasised that LF was eliminable, whilst experience in Korea, Japan, the Solomon Islands, China and Sri Lanka (with *Brugia malayi*) indicated that elimination was possible.

Several meetings held during the 1990s, the first of which was convened, by the WHO's Special Programme for Research and Training in Tropical Diseases (TDR), in Penang (Ottesen and Ramachandran, 1995), set the scene and provided the momentum which led, in 1997, to the WHA resolution (50.97) calling for the elimination of LF as a public-health problem. This resolution, as indicated above, led to the initiation of the GPELF by the WHO, late in 1997. The 'Memorandum of Understanding' between SmithKlineBeecham and the WHO was signed on 5 December 1997, and the first meeting of the newly formed Global Programme Review Group (GPRG), called to review national plans to eliminate LF and recommend the donations of albendazole, took place in July 1998. The donation of Mectizan for the control of LF (in those African communities in hyper- or meso-endemic foci of onchocerciasis that were also at-risk of LF) was officially announced by Merck & Co. Inc. in October 1999. Meetings to define the staged development of MDA and the associated monitoring and evaluation strategies of the GPELF, and to develop manuals to guide the programme managers, then took place (see www.filariasis.org).

By 1999, a strategic plan had been drawn up by the WHO, the result of a consensus-building process with the various partners committed to the elimination of LF (WHO, 1999). This plan, entitled '*Building Partnerships for Lymphatic Filariasis*', formed the foundation on which plans for the next major meeting — the first of the Global Alliance to Eliminate Lymphatic Filariasis, which took place in Santiago de Compostela, Spain, in May 2000 — were built. At about the same time, a technical advisory group (TAG) to the WHO was established and this also met for the first time in May 2000. The TAG's mandate was to review and assess the relevant technical and scientific developments and advise the GPELF accordingly. Whilst the strategic plan was being developed, a small but committed donor base emerged to support the first phase of the programme.

Implementation of the GPELF began in 2000, and since then, as stated above, coverage, both in terms of the number of people covered by MDA and the number of countries in which MDA for the elimination of LF have been initiated, has risen rapidly. The GPRG, which met seven times between July 1998 and February 2001, evolved into six Regional Programme Review Groups (RPRG), which met for the first time during the second half of 2001. At the final meeting of the GPRG, in February 2002, the first round of meetings of the RPRG was reviewed and methods for the phasing out of the GPELF's global-level structures and the decentralization of the programme were discussed.

The Global Alliance, which met for a second time, in New Delhi, in May 2002, was envisioned as a free and unrestricted grouping that brought together the comparative strengths of its many partners — partners who, though they may have different perspectives, roles and mandates, all share the

common goal of eliminating LF by 2020 (WHO, 2000*a*). The prime role of the Alliance is to serve the GPELF, particularly by advocacy and by raising awareness and societal and political commitment, at both international and national levels.

DEVELOPMENTS IN INTERNATIONAL HEALTH

The progress made by the GPELF is detailed below and, to some extent, on the websites maintained by the WHO (www.who.int) and the Global Alliance (www.filariasis.org). It is important that progress is reviewed now, albeit during the programme's infancy, as interest in public–private partnerships (PPP) in health is developing (Buse and Walt, 2000*a*, *b*; Widdus, 2001; Benton *et al.*, 2002; Reich, 2002). The PPP already reviewed include APOC (Benton *et al.*, 2002), the TDR, OCP and the Mectizan Donation Program (Frost *et al.*, 2002; Lucas, 2002) and the International Trachoma Initiative (Barrett *et al.*, 2002). Since 1998, there have been at least eight significant developments in international health that impact on the GPELF, in ways that relate to all of these PPP:

(1) the increased application of sector-wide approaches (SWAP) to health financing in developing countries (Cassels, 1997);
(2) the overt recognition of linkages between poverty and health (Anon., 2000);
(3) the establishment and acceptance of international development targets (IDT);
(4) the analysis of the links between infectious disease and poverty (Gwatkin *et al.*, 1999);
(5) the election of Dr Gro Harlem Brundtland as Director General of the WHO, and her articulation of the need for 'innovative public–private partnerships' to drive forward the global-health agenda;
(6) the involvement of major NGDO in the debate around access to drugs and the questioning of the role of products donated by major pharmaceutical companies to the developing world (Anon., undated);
(7) the creation of the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) and the distribution of the first tranche of funding for national efforts to control these diseases (notwithstanding the initiative of the 'Roll Back Malaria' campaign); and
(8) the publication of the final report of the Macroeconomic and Health Commission (WHO, 2001*a*).

These global developments on the public-health agenda — observations on poverty–health associations, revised public-health priorities, health and social policies, access to and pricing of drugs, funding mechanisms for international aid, and approaches to health financing — have important impacts on disease-specific activities that are frequently considered too 'vertical' by various parties (Anon., undated). Since 1997, the establishment of the Bill and Melinda Gates Foundation, with its massive commitment to global health problems, has provided new hope that much-needed research on the epidemiology and control or prevention of several neglected diseases will be financed. Furthermore, the report of the Macroeconomics and Health Commission (WHO, 2001*a*) clearly identifies the benefits of investment in health, as a way to enhance economic development and help alleviate poverty.

The GPELF does not exist in an isolated environment, and the potential benefits and synergies of linking LF control with many other health programmes (Fig. 1) are only just being appreciated (Molyneux *et al.*, 2000). The Bill and Melinda Gates Foundation recently published the results of an analysis of good practice/governance in such partnerships, entitled '*Developing Successful Global*

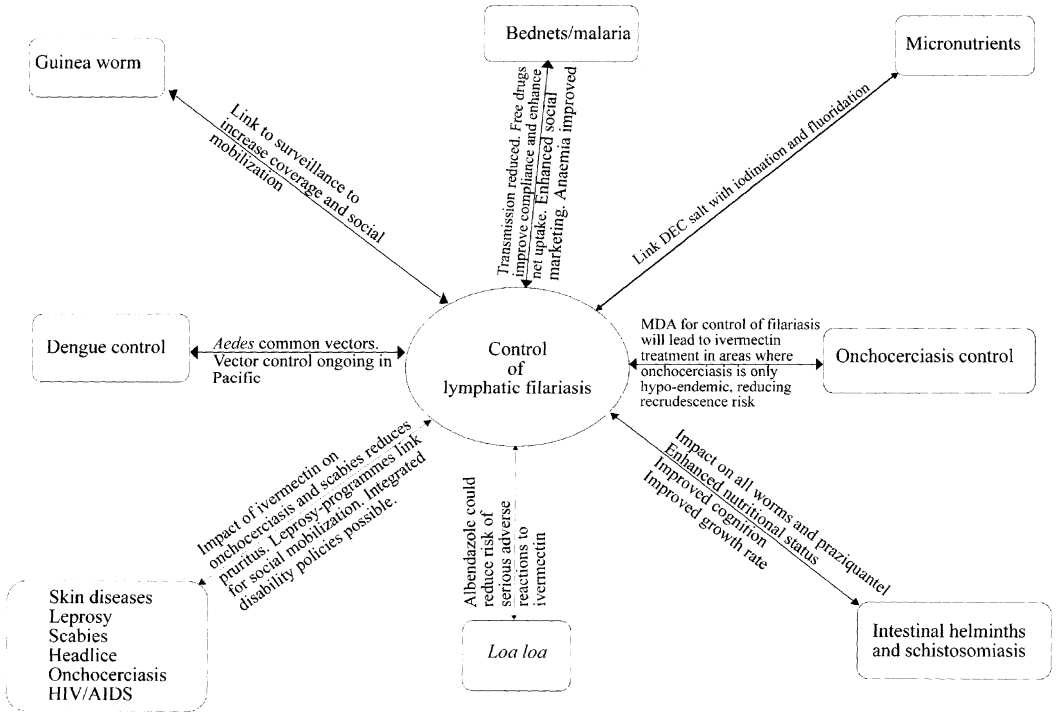

FIG. 1. The multifactorial benefits and linkage potentials of the Global Programme to Eliminate Lymphatic Filariasis, which is based on mass drug administrations (with albendazole–ivermectin or albendazole–dithethylcarbamazine), use of salt fortified with diethylcarbamazine (DEC salt), and, in limited settings, vector control.

Health Alliances' (Anon., 2002), and this has led to the development of an alliance-performance 'scorecard'. The GPELF fits into the framework of poverty alleviation, since it is providing interventions that directly target disadvantaged, low-income units (Tan, 2002) and has the potential to improve significantly the lives of millions, in a relatively short time and at limited cost. As Table 1 illustrates, the poorest countries are often those most affected by LF (WHO, 2001*b*). What follows is an analysis of the progress made, in the various domains of science, public health and policy, since the GPELF started activities at country level in 2000.

TABLE 1. *Poverty in the world and lymphatic filariasis (LF)*

Country group	No. of countries		Population (millions) in:		% of population in endemic countries	Population at-risk of LF (millions)
	In group	Endemic for LF	Group	Endemic countries		
Least developed countries	38	32	643	555	86.0	290
Other low-income countries	21	11	1777	1343	75.6	633
Countries with lower-middle incomes	19	10	2094	90.6	4.3	40
Countries with upper-middle incomes	3	1	573	1.5	0.3	1.3

OVERALL ACHIEVEMENTS 1998–2002

Although the scientific basis for LF elimination had been determined in the decade prior to the GPELF's initiation in 1998, the global programme still had to resolve several key issues before large-scale MDA could be launched. For example, the programme:

(1) had to provide reassurance that both of the two-drug combinations being considered were safe. By 1998, ivermectin, albendazole and DEC, when used alone, each had a unique public-health safety record, with hundreds of millions of treatments already given worldwide. Combinations of these drugs had, however, only been used on a small scale (Horton *et al.*, 2000). The results of analysing the available, published and unpublished data, and independent scrutiny via a WHO pharmacovigilance group, indicated that the drug combinations being considered were safe. At the beginning of the programme, the WHO also set up a system to ensure that there would be active surveillance — of the first 2000 of the at-risk population treated in each implementing country — to evaluate the safety of the drug combination(s) in use. A dedicated database, developed with the help of GSK, was created for storing and analysing the surveillance data. A preliminary analysis of the first 10,000 records provided reassuring results, again indicating that the recommended drug combinations were safe to use.

(2) had to determine the levels of LF endemicity in each area, so that the MDA could be targeted at at-risk populations. Much of the available information on the geographical distribution of the diseases was historic and based on the microscopical examination of smears of blood collected at night. The development of the ICT was a breakthrough in this field (Weil *et al.*, 1997), as it enabled antigen from adult *Wuchereria bancrofti* to be detected in fingerprick samples of blood collected at any time of the day, so obviating the need for inconvenient blood sampling during the night. It also enabled countries to map levels of LF endemicity rapidly and then define implementation units.

(3) had to develop appropriate documentation on programme-management issues. All the documentation — specifically, guidelines for the development of national plans, for drug-administration procedures, for the selection of sentinel sites, and for the procedures and processes of evaluation and monitoring — had to be tailored for use in countries where onchocerciasis was or was not co-endemic.

Significant progress has been made by the GPELF over the past 4 years, in implementation at global, regional, national and sub-national levels. Many of the countries where LF is endemic have engaged with the programme, and the issues of regionalization, safety, operational research, disability prevention, NGDO involvement, logistics, distribution and vector control have been addressed. Such issues are complicated by the unique characteristics of the GPELF. LF, for example, has a global distribution but its epidemiology, causative parasites and mosquito vectors all vary markedly with geographical region. There is also regional and sub-regional variation in the drugs on which the MDA are based: albendazole–DEC; albendazole–ivermectin; or, possibly, salt incorporating DEC. Decentralization has led to the establishment of regional programme review groups that, since they are based on regional epidemiology and operational requirements, cut (sometimes inconveniently) across the borders of the WHO's normal regional groupings. The engagement of the diverse partners on which the GPELF and Global Alliance are based

(including two major pharmaceutical companies, involved in an innovative public–private partnership, who have promised to give albendazole and ivermectin without charge) and the development of successful country partnerships, to facilitate implementation, have had to be rapid. There is the potential of valuable synergy between the GPELF and the efforts to control other diseases (Fig. 1). Programmatic, scientific and training information is being communicated using an information-technology (IT) infrastructure. The academic sector is much involved via the support centres in Liverpool and Atlanta and institutions in endemic countries.

Despite or because of its unique structure, the GPELF has already overcome several important obstacles. For example, donor support was obtained for assessing the safety of the proposed drug combinations (an issue that delayed implementation of the programme). Effective mapping protocols were developed (WHO, 2000*b*, *c*; Gyapong and Remme, 2001; Gyapong *et al.*, 2002) and regionalization of the programme's activities is increasing (WHO, 2001*a*). The need to define implementation units (as a basis for national planning), the potential role of vector control and entomological surveillance (WHO, 2001*a*) and the potential importance of *Wolbachia*, as a chemotherapeutic target (Taylor and Hoerauf, 2001) and cause of adverse side-effects (Cross *et al.*, 2001), have all been recognized recently. A diagnostic test for *Brugia* ('*Brugia* Rapid') has been produced (Rahmah *et al.*, 2001*a*, *b*) and this, or similar methods, is permitting the geographical distribution of *Brugia* to be mapped in detail. Early on in the programme's development, the Cochrane Infectious Disease group was asked to determine and then conduct the most appropriate and useful, evidence-based, systematic reviews and then make regular updates (Addiss *et al.*, 2002); an update of the evidence base for the usefulness of DEC-fortified salt is underway, following the review by Gelband *et al.* (1994). The fact that LF is largely a disease acquired in childhood has been recognized and emphasised (Witt and Ottesen, 2001) and many data on the role of albendazole in the control of LF have been collected (Ottesen *et al.*, 1999).

That such advances have been made during the GPELF's infancy emphasises the importance of a rigorous scientific process, to provide a strong evidence-base for any subsequent, strategic decisions. The results from the first year or two of implementation highlighted the fact that, whilst LF is widely distributed, regionalization of the programme would best recognize and address the marked regional variations seen in the epidemiology of the disease and in the characteristics of local health systems. Regionalization should also encourage and simplify the involvement of donors who are only concerned with particular geographical areas. For example, the support of the Arab Fund for Social and Economic Development is directed at the Eastern Mediterranean, whereas the Japanese Ministry of Health and Japan International Co-operation Agency support Pacific countries.

If the GPELF is to be successful, it is essential that microfilaraemias are cleared, or at least reduced to very low levels, in almost all of those living in at-risk areas for at least five consecutive years. Both MDA coverage (the percentage of the population of a targeted district who are recorded as having ingested antifilarial drugs during the MDA) and geographical coverage (the percentage of at-risk communities where MDA are regularly conducted) have to be kept high. The implementation of successful MDA (with high treatment coverages) in **all** of the targeted implementation units requires great flexibility in the drug distribution and careful investment of (the frequently scarce) available resources in the most appropriate campaigns of social mobilization (tailored to the local context and to the selected drug distribution mechanisms). A strong system of evaluation and monitoring is also essential.

There are several approaches to drug distribution:

(1) house-to-house delivery by local health workers can be effective in settings where well-functioning health facilities exist (such as semi-urban environments in the Nile Delta of Egypt);
(2) house-to-house deliveries on a designated 'National Filaria Day' can be facilitated with a strong campaign of social mobilization and conducted by a network of community volunteers selected by the communities (as occurs in urban and rural areas of Sri Lanka and Zanzibar);
(3) in areas where LF and onchocerciasis are co-endemic, such as Burkina Faso, albendazole can be added to existing community-directed treatments with ivermectin (Amazigo *et al.*, 2002*a*, *b*), so benefiting from the networks (of NGDO, Ministry-of-Health staff and community healthworkers) already in place for onchocerciasis control; and
(4) distributions from booths or shops on 'Filaria Days', as occurs in French Polynesia and Samoa.

These different approaches require strategies of information, education and communication (IEC) that are culturally specific and appropriate and actively involve political figures and administrative officials who are respected by the at-risk communities. Even such health-related IEC campaigns need not be the sole responsibility of the health sector; every communication model, advocacy tool, media outlet and 'ambassador' should be exploited. The 'ambassadors for health' could be politicians (as used on Tamil Nadu's elimination-campaign poster) but could also be sportsmen (such as the Samoan rugby team) or other local celebrities. Such ambassadors, village heads and local chiefs should be encouraged to take the anti-filarial drugs (and perhaps to wash the feet and legs of those with lymphoedema and elephantiasis) in public, at local ceremonies to launch each MDA campaign. It is important that the comparative impact and cost of each method of mobilization employed are assessed, so that only the most cost-effective methods can be used in the future. In Haiti, radio broadcasts appear to lead to better dissemination of knowledge about the LF-control programme than is achieved using posters (P. J. Lammie, unpubl. obs.). However, such observations should not be extrapolated to all areas, since the most effective method of IEC depends partly on the local environment, health system, social structure, culture, population density and, for the GPELF, method of drug distribution. The ultimate goal of such IEC is behavioural change — the swallowing (and perhaps seeking) of the antifilarial drugs given in MDA (and, for those with lymphoedema, good skin hygiene).

The value of the two donated drugs, albendazole and ivermectin, in providing benefits additional to that of arresting the transmission of the nematodes causing LF should be widely recognized. Each of these two drugs has significant effects not only on filariae but also on a range of other helminths and ectoparasites (Table 2). The de-worming effect of these compounds has important consequences in terms of nutritional status and micronutrient uptake, often leading to general wellbeing and improvements in anaemia status, cognitive function, and skin

TABLE 2. *The broad anti-parasite effectiveness of two of the drugs used to control lymphatic filariasis (Ottesen* et al., *1999)*

	% of cases cured after treatment with:	
Disease/parasite	Ivermectin	Albendazole*
Ascaris	100	100
Strongyloides	95	45
Enterobius	85	85
Trichuris	10–50	40–60
Hookworm	0–20	95
Larva migrans	100	80
Onchocerciasis	95	0
Lice	100	0
Scabies	100	0

*Multiple doses of albendazole are also effective against cysticercosis, echinococcosis, giardiasis, trichomonads, Microsporidia and *Cryptosporidium*.

condition (particularly reducing scabies and onchocercal pruritus). No other drug-donation programme can claim such a multiplicity of ancillary benefits. Many of these benefits are very evident to those who have been treated and lead to higher compliance in subsequent treatment rounds.

LF control is a time-limited intervention; programmes do not need to be sustained indefinitely and costs in Africa for each treatment round should not exceed U.S.$0.10–0.20/person-year. In terms of the disability-adjusted life-years (DALY), costs of individual and community healthcare, and health-system costs ultimately averted, LF elimination based on MDA must be a good health 'buy'. For a total cost of just U.S.$0.5–1.0/person (assuming annual MDA run for 5 years), at-risk communities receive an intervention that provides health improvements for the poorest sectors and prevents generations of children becoming infected with filariae.

The effect the GPELF could have on overall development of local health systems should not be under-estimated. Few programmes offer a greater opportunity for integration into other delivery systems, but possible linkages to several other partnership-orientated programmes for health improvement need to be explored and exploited soon, as the global programme is scaling up (Molyneux *et al.*, 2000). These opportunities should be actively pursued by the national programmes, as considerable synergies could be achieved (Fig. 1).

Given the global nature and complexity of LF control, the regional variation in the epidemiology of LF, and the variation in the partners involved in control in each endemic country, good communication between all the partners is essential. This problem is being largely resolved by the use of IT, with the initiation of on-line or compact-disc-based training programmes at many levels, and enhanced communications between the national and international partnerships, the regional structures and the secretariat of the Global Alliance, which is based in the WHO's headquarters in Geneva.

The Global Alliance's website (www.filariasis.org) offers links to the websites of many partners and to that of *Filaria Journal* (www.filariajournal.com), the newly established electronic journal. Via a one-click approach, the latter site provides access to many filaria-related scientific papers held in the databases of BioMed Central and PubMed Central. The website of the Global Alliance was created to share knowledge and expertise — an important element of a successful programme. It encourages information-sharing amongst (and provision of up-to-date news and information for) the members of the Global Alliance and all of the other players involved in the global effort to eliminate LF. It was recently redesigned, following the distribution of a questionnaire to all interested parties seeking their opinion on a number of issues related to its structure, content and user-friendliness. The site has two sections: public and restricted. The public section displays a wide range of public-health information and documents (covering strategy, policy, project management, and operational and research issues) and has links to the relevant partners. The restricted section (the extranet site) is used for virtual working groups.

A filaria-related knowledge-base is also being developed on the Web (www.filariasis.net). It is hoped that an IT-based architecture will soon provide, via an appropriate website, instant access to the evaluation, monitoring and coverage data from all the countries covered by the GPELF (subject to intellectual property rights and country ownership). The GPELF and other disease-elimination programmes can pro-actively use global communications, partnership development and country involvement, as a means to promulgate a new vision of global disease control. Such an approach should make it possible for anyone to access the results of investigations almost as soon as they have been recorded (i.e. open access to 'real time' information), provide distance learning at all levels of the health system (in whatever

medium is deemed the most appropriate), and initiate programme-dedicated communication systems between partners (particularly at national and regional level).

STRENGTHENING OF HEALTH SYSTEMS

Concern has been expressed that to base a general strengthening of health systems on a drug-donation programme (such as the OCP, the APOC, or the GPELF) could lead to distorted priorities and disease-selective healthcare (Anon., undated). However, the data collected from the OCP (Webbe, 1992; Samba, 1994; Molyneux, 1995; Molyneux and Morel, 1998) and the APOC (Richards *et al.*, 2001; Homeida *et al.*, 2002) indicate that, in this respect, the benefits far outweigh the risks. Five years after they had begun, the activities of the APOC were helping to improve health systems generally, even in the poorest and least well-resourced environments and in areas where conflict had disrupted all other systems of healthcare (Homeida *et al.*, 2002). In the 11 African countries covered by the OCP, the programme's activities led to significant strengthening of the national health systems. Most of the improvements occurred after mass distributions of ivermectin began. These mass treatments led directly to general improvements in drug-delivery systems, monitoring and storage. However, they also had many indirect benefits: improvements in communicable-disease surveillance and Ministry-of-Health information systems; better contact between district-level staff and sub-district health providers; better integration of activities at district and sub-district level; capacity-building at post-graduate level; and better recognition of the gender-related inequities that exist in the present systems.

Programmes for the elimination of LF could enhance the development of health systems on an even greater scale. Compared with the onchocerciasis-control programmes, the GPELF offers greater opportunities for: integration with the other campaigns for the control of disease (Fig. 1); the widespread use of IT and improvements in communications between countries and regions; and the integration of the MDA with other, simple interventions (at community and household level) that should reduce the incidence of severe morbidity and help prevent disability.

Drug donations for the control of onchocerciasis and LF provide a basis for the strengthening of health systems in many under-resourced settings, particularly those in sub-Saharan Africa. Such donations provide communities with free products that not only effectively prevent the targeted disabling diseases but also provide many other health benefits and protect generations of children from an adult life of disablement and stigma.

COUNTRY- AND REGIONAL-LEVEL PARTNERSHIPS

The GPELF has several levels of partnership (Table 3). As the programme's mandate is derived from a WHA resolution, the emphasis from the outset has been to place and maintain the full ownership of the programme in the hands of the endemic countries. If the current scaling-up of the field activities of the programme is to be successful, it is essential that effective, long-term, national and global partnerships are developed (www.filariasis.org). Several excellent examples of committed national partnerships already exist. Most of these are based on National Task Forces, are chaired by Ministry-of-Health officials and have a philosophy of free, non-restrictive engagement. The latter provides opportunities for other sectors and interests to be involved, for encouraging strong, local, technical leadership and vision, and for meeting a demand-led impetus from the lower levels of the health systems, politicians and communities.

TABLE 3. *Framework of the Global Programme to Eliminate Lymphatic Filariasis*

Level	Function/activity	Action/partner	Notes
National partnerships	Planning, co-ordination and priority setting	Ministries of Health, National Lymphatic Filariasis Task Forces (NLFTF)	Leading to general improvements in drug distribution and clearance
	Operational/applied research	National academic and research institutes	Leading to general improvements in logistics
	Implementation support	Ministries of Health, Developing Health Technology, national and international non-governmental development organizations (NGDO)	Leading to stronger infrastructures
	School health programmes; information, education and communication (IEC)	Ministries of Education	Encouraging capacity-building
	Environmental control	Ministries of Water and the Environment	Improving cross-sectional awareness
	In-kind support	Private sector, donors via national offices	Strengthening information systems
	Resources and policy: integration/synergy	Ministries of Health, country representation of the World Health Organization (WHO)	Leading to integration of surveillance, monitoring and evaluation
	Co-ordination with other activities; resourcing; links to Regional Programme Review Groups (RPRG)	Disease-control programmes, district medical teams	Leading to integration of control activities and the planning of transportation, distribution, evaluation, health education, and the home-based, long-term care needed to limit filariasis-related disability
Regional programme co-ordination	Co-ordination and monitoring	Countries, regional alliances, programme managers	Involving RPRG and the Pacific, Mekong-plus, Indian sub-continent, Eastern Mediterranean, African and American regionalizations
	Cross-border issues; decision-making on country applications; regional evaluation and cross-border co-ordination; engagement with regional health interests (e.g. South–east Asian Ministers of Education Organization, African Programme for the Control of Onchocerciasis, South Pacific Commission); regional donor interests	Regional Programme Review Groups	Regional donor interests include those of the Arab Fund for Social and Economic Development (in the Eastern Mediterranean), the Japanese Ministry of Health, the Japan International Co-operation Agency and James Cook University (Pacific), Ain Shams University (Egypt), Vector Control Research Centre in Pondicherry (Indian sub-continent) and the NGDO involved in onchocerciasis control (West Africa and other onchocerciasis-endemic regions)
	Regional training	WHO Regional Advisors	
	NGDO recruitment, support of Indian NGDO networks	Academic centres with regional emphasis, NGDO with regional interests	

TABLE 3. *Continued*

Level	Function/activity	Action/partner	Notes
Global programme	Policy and strategy development	WHO [including technical advisory groups (TAG) and the Special Programme for Research and Training in Tropical Diseases (TDR)], countries, regions	Supporting operational research
	Co-ordination, global meeting organization	Global Alliance's secretariat and ad-hoc task force of partners	Encouraging advocacy and fundraising
	Defining and establishing programmatic linkages; website development and maintenance; database management; and global reporting	WHO and Global Alliance (GA) partners	Leading to general improvements in strategic planning and development, communications and training materials
	Basic, operational and implementation research	Academic support centres, TDR, WHO collaborating centres	Leading to development of information-technology infrastructures
	Advocacy and communication; resource mobilization	Global Alliance and its task forces	

Barrett *et al.* (2002) recently described the country-level partnerships in the International Trachoma Initiative, using examples from Tanzania, Morocco, Vietnam, Mali and Ghana. A similar template is being used for several national programmes for LF control. Characteristically, the partnerships on which these national programmes are based are locally specific, involve diverse sectors, have loose (often non-formal) associations and a strong technical and academic component. The technical/academic component, which is usually linked to one of the LF support centres or to a local academic institute or national institute (often supported by TDR), provides a strong creative focus, informing national policy and creating a significant, local, research capacity.

The rapidity with which effective national partnerships have emerged in the field of LF control is both impressive and encouraging. Such strong partnerships emanate from the clear targets of the LF programmes, the limited complexity of the intervention, and the recognition that (1) Ministries of Health should have a leading role in the programme and (2) local institutions should have a critical, supporting role in research support and the engagement of both local and international NGDO (including, in Africa, some associated with onchocerciasis control). The setting up of National Task Forces in endemic countries has been encouraged, as a way of enhancing the creation and consolidation of the necessary partnerships. These partnerships have evolved rather than being formally created. As the problems of LF and its control have been articulated to interested parties, these partnerships have gradually recruited additional partners and they will form the basis of country-level ownership and success.

In 1998, the WHO's regional office for the Western Pacific (WPRO) promoted, through funds provided by the Government of Japan, a sub-regional co-ordination mechanism to implement elimination and associated technical-assistance activities in LF-endemic Pacific islands. Over the last 3 years, this mechanism (PacELF) has ensured that national LF co-ordinators and resource managers have met regularly (annually or bi-annually). At these meetings, logistic and strategic issues linked to the local context, disease epidemiology and health systems have been addressed. Following this successful experience, and in agreement with the main partners of the GPELF, the WHO promoted the regionalization of the Global Programme Review Group. The regional groups so created covered all of the endemic countries and all of the areas that fall within the remit of the WHO's regional offices for South–east Asia and the Western Pacific. The regionalization was allowed to cut across the borders of the WHO's standard regions (Table 4), to permit (1) the clustering of endemic countries which were similar in terms of LF epidemiology and transmission, and (2) each major cross-border focus to be considered in its entirety. This allows the so-called 'Mekong-plus countries' (Cambodia, China, Laos, Malaysia, the Philippines, Vietnam, Indonesia, Myanmar and Thailand) to benefit not only from the experiences of successful programmes in China, Malaysia and Thailand over the last three decades but also from existing health alliances (such as SEAMEO TropMED — the Regional Tropical Medicine and Public Health Network of the South–east Asian Ministers of Education Organization) and the information systems (recently supported by the European Union) developed for malaria control.

The RPRG for the Indian sub-continent links a major endemic country, India, with Nepal, Bangladesh, Sri Lanka and the Maldives. A detailed description of the composition of all six RPRG has already been published (WHO, 2001*c*).

The RPRG are responsible for reviewing national plans for LF control and for recommending (to the manufacturers of albendazole and ivermectin) how many tablets should be donated to each country and when the drugs should be delivered. In

TABLE 4. *National estimates of the numbers of people who will be treated, with albendazole plus ivermectin (AI), albendazole plus diethylcarbamazine (AD), or salt fortified with diethylcarbamazine (DEC salt), in mass drug administrations (MDA) in 2002*

Region and country or territory	Treatment	MDA round	Estimated population at risk (millions)	Population targeted for MDA in 2002	Coverage target (% of those at-risk)
AFRICA					
Burkina Faso	AI	2	12.00	2,612,524	21.7
Benin	AI	1	3.70	419,962	11.4
Comoros	AD	2	0.60	520,156	86.7
Ghana	AI	3	6.57	4,155,933	63.3
Kenya	AD	1	3.00	600,000	20.0
Nigeria	AI	3	80.00	2,167,072	2.7
Togo	AI	3	1.10	871,765	79.1
Uganda	AI	1	6.00	740,000	12.3
Tanzania (excluding Zanzibar)	AI	3	2.60	1,816,421	70.0
Zanzibar, Tanzania	AI	2	0.94	914,094	96.8
All nine countries			116.51	14,817,927	12.7
AMERICAS					
Dominican Republic	AD	1	1.5	510,795	34.0
Guyana	DEC salt	1	0.65	650,000	100.0
Haiti	AD	2	6.0	500,000	8.3
All three countries			8.15	1,660,795	20.4
EASTERN MEDITERRANEAN					
Egypt	AD	3	2.41	2,395,000	99.5
Yemen	AI	1	14.50	153,580	1.0
Both countries			16.91	2,548,580	15.1
MEKONG-PLUS					
Indonesia	AD	1	110.0	912,179	0.8
Myanmar	AD	2	46.50	9,424,088	20.3
Philippines	AD	3	23.50	11,861,103	50.6
Thailand	AD	1	9.00	125,000	0.1
Vietnam	AD	1	10.00	900,000	9.0
All five countries			199	23,222,370	11.6
INDIAN SUB-CONTINENT					
Bangladesh	AD	2	34.00	5,147,000	15.1
India	AD	2	454	21,000,000	4.6
Maldives	AD	1	0.25	25,000	10.0
Sri Lanka	AD	2	9.50	9,000,000	94.7
All four countries			497.75	35,172,000	7.1
PACIFIC					
American Samoa	AD	3	0.06	64,100	106.7
Cook Islands	AD	3	0.02	18,700	100.0
Fiji	AD	1	0.90	824,700	91.1
French Polynesia	AD	3	0.23	233,000	101.3
Kiribati	AD	2	0.09	90,700	104.7
Niue	AD	3	0.002	1900	95.0
Samoa	AD	3	0.170	169,200	99.4
Tonga	AD	2	0.10	100,200	100.0
Tuvalu	AD	2	0.01	9900	91.0
Vanuatu	AD	3	0.19	199,800	106.4
Wallis and Futuna	AD	1	0.02	14,166	70.0
All 11 countries			1.78	1,726,366	96.4
All 34 countries			840.11	79,148,038	9.4

addition, they play an important role in monitoring the progress of the national programmes, in identifying critical issues which still need to be addressed (in terms of operational research), and finally in promoting the LF-elimination initiative, by making innovative approaches to advocacy and resource mobilization.

MAPPING DISEASE DISTRIBUTION

At the time the GPELF was initiated, estimates of the global burden posed by LF and of the total number of individuals at-risk had been made (WHO, 1992; Michael *et al.*, 1996; Michael and Bundy, 1997). However, these estimates are far too general to permit identification of those communities that, because of their moderate or high levels of endemicity, will most benefit from MDA. Before the GPELF is implemented in any country, it is therefore necessary to identify the geographically identifiable units where transmission of the filariae causing LF is established. In each area for which no relevant parasitological data are available, parasitological surveys, generally based either on the ICT (in areas where *Wu. bancrofti* is endemic) or microscopical examination of smears of blood collected during the night (in areas where *B. malayi* or *B. timori* is endemic), have to be carried out. When many samples have to be investigated, the short period (after a sample has been tested) when an ICT result can be validly read becomes a problem. The manufacturer of the test cards is currently trying to make them more 'user-friendly', by prolonging the period over which valid readings can be taken; this would also facilitate cross-checking of the readings.

The current target is to complete the initial assessment and mapping of all implementation units for MDA in all endemic countries by the end of 2005 (WHO, 2000*a*). Encouraging progress has already been made in the West African sub-region. All of the mapping information gathered is stored and graphically displayed using HealthMapper (a software package for integrated database management and mapping, developed by the WHO, which is available free of cost to all LF-control programmes). HealthMapper helps users to choose implementation units (IU), draw preliminary maps of the distribution of LF based on existing data, select sample villages for survey, enter and analyse the survey data, overlay prevalence contour maps or other relevant layers, classify each IU as endemic, non-endemic or 'uncertain' (Fig. 2), prepare a plan of action, and monitor both the coverage and impact of MDA. Use of the HealthMapper software, like that of several other tools provided in the context of the GPELF, need not be confined to the control of LF. Once a country has the software, it can be used to make useful analyses of any geographical, demographic, environmental, disease-related or health-system-related data available.

Whilst the results of ICT-based population surveys provide an excellent mapping tool to define overall prevalence at the level of the IU (Onapa *et al.*, 2001; Ngwira *et al.*, 2002), the predictive modelling of the distribution of LF is also possible (Lindsay and Thomas, 2000; Gyapong *et al.*, 2002). Thomson *et al.* (2000) provided a model for predicting the risk of *Loa loa* prevalence, based on data from $>14{,}000$ patients in Cameroon. This model, together with the rapid-assessment technique for loiasis (WHO, 2001*d*), should enable accurate delineation of the areas where, because onchocerciasis and loiasis are co-endemic, severe adverse reactions to ivermectin treatment might occur (Gardon *et al.*, 1997). In these areas, which all probably lie within the Central African countries of Cameroon, the Central African Republic, Sudan, Gabon, Congo and the Democratic Republic of the Congo, distribution of ivermectin will cease.

Comparison of the independently derived maps for malaria endemicity (Kleinschmidt

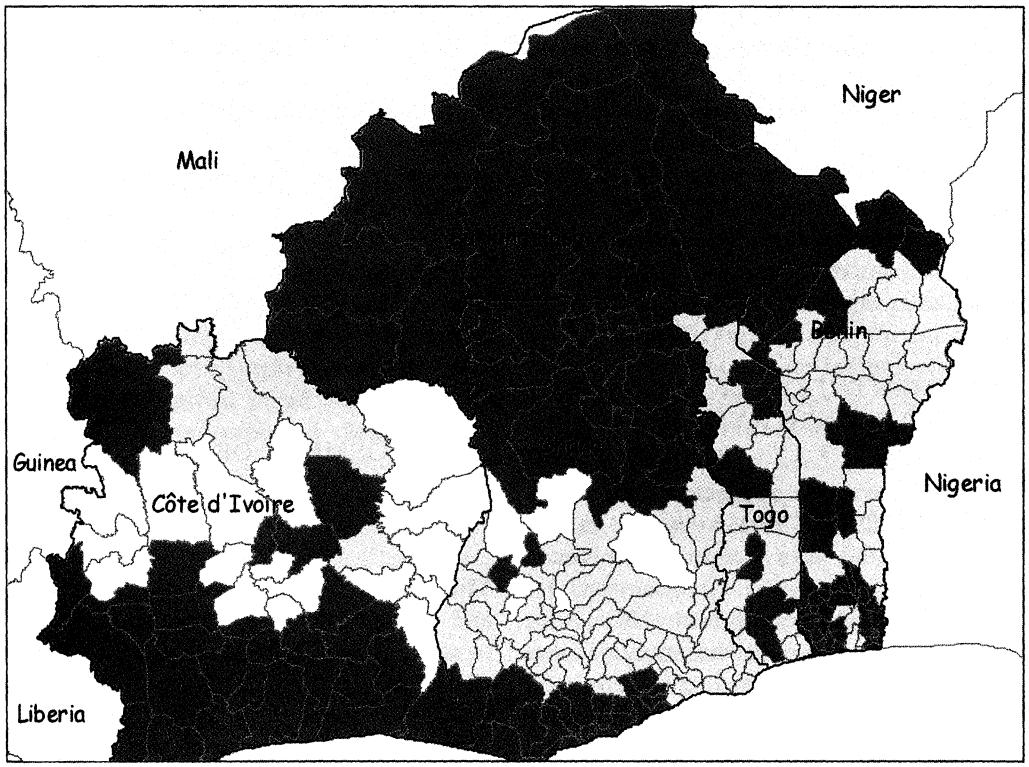

FIG. 2. A map of five West African countries, showing the implementation units where the level of endemicity of lymphatic filariasis remains unknown ( ), and those where the disease is known to be endemic (■) or non-endemic ( ). Produced by the World Health Organization's Public Health Mapping Team, from data collected for the Global Programme to Eliminate Lymphatic Filariasis (© World Health Organization, September 2002).

et al., 2001) and LF endemicity (Gyapong *et al.*, 2002) in West Africa highlight unexpected inverse relationships between the two diseases, which merit further analysis.

Progress in the Initial Assessment and Mapping of Implementation Units

A list of countries and territories where LF is endemic has been published (WHO, 2002) and is also available on the Global Alliance's website (www.filariasis.org).

The distribution of LF has recently been reviewed in eight countries (Cambodia, Laos, Indonesia, Malaysia, Myanmar, the Philippines, Thailand and Vietnam), based on pre-existing data from parasitological or questionnaire-based surveys. Implementation units, as defined by each of these countries, have already been categorized as endemic, non-endemic or 'uncertain'. Further serological surveys (to detect filarial antigenaemia) or parasitological surveys, to eliminate the 'uncertain' category, are either planned or in progress in these countries.

The first results of antigenaemia surveys in four West African countries (Benin, Burkina Faso, Ghana and Togo) were completed in 2000 (Gyapong *et al.*, 2002). Spatial analysis of the data was used to create contour maps showing the varying levels of endemicity. Draft plans for implementing and monitoring MDA in those units which were thus identified as having LF transmission have been prepared.

Mapping workshops — to promote a standardized methodology for LF mapping, facilitate the compilation of existing information on LF prevalence, assist in developing plans for LF mapping in each endemic country, and provide training in the use of the HealthMapper software and in monitoring and evaluating the implementation of MDA — have been provided in all LF-endemic regions

IMPLEMENTATION OF MASS DRUG ADMINISTRATIONS

As stated above, the number of individuals treated in MDA in 2001 (only the second year that MDA had been implemented) reached 26 million (in 22 countries) — almost a 10-fold increase from 2000. This growth was in line with the strategic plan (WHO, 1999). The target of covering 50 million of those at-risk by the end of 2002, as envisaged in the plan, will be exceeded, as >40 million people had already been treated by July 2002. A revised target of 80 million has been set for 2002, as several countries will soon commence MDA.

Of the three drugs used in the programme, the free supplies of albendazole from GSK and ivermectin from Merck and Co. Inc. are ensured to be of high quality. Applications from countries for ivermectin and albendazole are reviewed by the MDP and RPRG; drug policies are reviewed by the Mectizan Expert Committee and the Albendazole Committee. The DEC (or DEC citrate) has to be purchased, either directly from a manufacturer, via the established mechanism for drug purchase in the country involved, or indirectly, via a request to the WHO. To ensure that national programmes use DEC of good quality, the WHO, in collaboration with all the relevant national and state regulatory authorities, has carried out on-site audit visits of the manufacturers of DEC tablets or DEC starting material. During these visits, each manufacturing company has been investigated to see if it follows good manufacturing practices and good (quality control) laboratory practices. Currently, only two manufacturers are qualified for the supply of DEC tablets, although the process of approving additional manufacturers is ongoing. A new HPLC-based assay for checking the purity of DEC starting material and DEC tablets has been developed, validated and incorporated in the latest *United States Pharmacopoea* (USP 25); efforts are being made to incorporate it into the other standard pharmacopoeias.

MANAGEMENT OF SIDE-EFFECTS AND SURVEILLANCE FOR SEVERE ADVERSE EVENTS

The results of closely monitored, hospital and community-based trials indicated that treatment with albendazole–ivermectin or albendazole–DEC did not lead to any severe adverse events or to a higher incidence of the side-effects seen when each drug was used alone (Horton *et al.*, 2000). Although these results led to national programmes of MDA based on these drug combinations, each implementing country was encouraged actively to follow-up 1000–2000 people (representative of the population covered) who had been treated. For this follow-up, a standard questionnaire on which all possible adverse drug reactions (ADR) could be recorded was provided. The data collected on these questionnaires, assimilated by the GPELF at the WHO's headquarters, show that both drug combinations are safe and offer little cause for concern over the wide-scale use of either combination. The side-effects seen were all mild, consistent with past experience with the combinations and individual drugs, and seem to be related to the therapeutic effects of the drugs (Horton *et al.*, 2000).

Countries that are implementing MDA for the control of LF are encouraged to establish a system for the detection and reporting of any serious adverse experiences (SAE) that follow and are attributable to

the drug combination(s) used in the MDA. A standard SAE-reporting form has been developed, in consultation with the two donor pharmaceutical companies (GSK and Merck & Co., Inc.). Any reports of SAE are required to be forwarded to the appropriate drug-regulatory authorities within 15 days. The WHO receives such reports, at the same time as the pharmaceutical companies concerned, and interacts closely with the companies and local health authorities. Encouragingly, not a single SAE attributable to a treatment given in an MDA for the control of LF was reported during 2001, although almost 26 million people were given albendazole with either ivermectin or DEC in that year.

PREVENTING OR LIMITING DISABILITY

The GPELF's primary method of preventing disabilities caused by LF is the interruption of filarial transmission, through the MDA; once transmission ceases there will be no new infection and no subsequent lymphatic filariasis. The results of a recent study have demonstrated that four rounds of annual treatment, with DEC alone or DEC–ivermectin at coverages of 77%–86%, not only reduced the prevalences of *W. bancrofti* microfilaraemia but also those of hydrocoele and leg lymphoedema (Bockarie *et al.*, 2002). However, before this goal is reached, much can be done to improve the lives of many of those who already have the clinical manifestations of LF. Filariasis-attributable disability can be severe, and even relatively mild disability can lead to social and economic deprivation. One of the GPELF's aims is to educate those already affected by LF in simple techniques for the management and limitation of their disability. Regular skincare, good hygiene, limb exercises (to prevent a lymphostasis) and the wearing of protective footwear are to be encouraged. To be effective, these methods of disability limitation must be carried out for many years (until death, in most cases). In most endemic areas, such long-term healthcare is only feasible if it is carried out in the LF case's home, either by the case or, if the case is severely debilitated, by the case's family or community. Surgery remains the recommended treatment for hydrocoeles but needs to be made available closer to the home and, if possible, at the second level of care, with, for the most difficult cases, a functioning system of referral to tertiary-care institutions. Community-health providers, both from the health sector and the community, need to be trained to screen for hydrocoele, to refer scrotal swellings to primary-health-care physicians, and to advise on lymphoedema care. Training of the communities, in the simple techniques of disability limitation, requires effective health education and mass communication. A comic book, produced to educate schoolchildren and their families on LF (with emphasis on these simple methods), is already in use in Egypt. A similar book is planned for India. The focus of the health education is on the thorough washing and careful drying of the affected part of the body, wound care, exercise (but not during acute attacks), elevation of any affected limb, and the wearing of comfortable footwear (i.e. open sandals rather than constricting shoes or bare feet).

Health staff need to understand the reasons why LF cases may fail to follow advice on hygiene and care, and they must be educated to listen to, observe, train and encourage patients. Much can be done at the peripheral level, and much can be achieved in disability prevention, at little financial cost per patient, by using locally-available materials. Protective footwear is the most expensive item but it is relatively durable. It is important that health personnel make the best possible use of locally-available resources and guide their patients to do likewise. The early recognition and prompt treatment of entry lesions, the referral of patients with lymphoedema who

do not respond to treatment at home, and the referral of patients with hydrocoele for surgery should all be promoted.

The training of physicians and other health workers on the principles of alleviating and preventing the disability associated with LF has commenced in Bangladesh, Haiti, India, Nigeria, the Philippines, Sri Lanka, Togo, and Tanzania. In Sri Lanka, where 1876 hydrocoelectomies have been performed, >2500 patients with lymphoedema have been treated at regional centres and another 6500 at village health centres.

TRAINING

Capacity-building is an essential component of the global programme. Programme managers, the trainers of drug distributors and the personnel involved in disability-prevention activities and social mobilization all need to be trained, in order to ensure the success of the LF-elimination campaigns. Training workshops have therefore been organized at regional and country level, in collaboration with national institutes, using training modules and packages that have been developed and improved as a result of extensive field-testing and feedback. Following their training, the programme managers were provided with grants to enable them to organize workshops at district level in their respective countries, and so disseminate the information to the lower levels of their health systems.

SOCIAL MOBILIZATION AND ADVOCACY

Social mobilization is a planned process which enlists the support of any or all sectors of society that can play a role in achieving an agreed social objective. Although, to be sustainable, the process must be rooted in the community, strong political and administrative commitment will encourage the population to participate actively. Planning for social mobilization begins with a situation analysis and identification of the behavioural change required to achieve the health goal; in the context of the GPELF this goal is most frequently high treatment coverage. The analysis identifies potential allies and points of resistance, ways to improve the knowledge and motivation of the beneficiaries, the most effective media, and the potential for community participation. The greatest challenge in transforming the commitment of the GPELF into action for the benefit of local communities is to have the full involvement and participation of the at-risk communities themselves, in order to reach and sustain high coverage for 4–6 years. The lower the coverage, the longer the period necessary to achieve interruption of transmission will be. Sustained high coverage requires intense social mobilization, and this needs advocacy and effective communication (through interpersonal or group contacts or via the mass media). In order to participate in MDA, those in at-risk communities must believe that, by taking the antifilarial drugs, they are acting in their own interests. To make this a common perception will require innovative and pro-active interventions that go beyond traditional health education, advocacy and community-mobilization initiatives. The communication-for-behavioural-impact (COMBI) approach — social mobilization directed at influencing societal and personal behaviour, so as to prompt individual and family action — represents one such initiative. It blends strategically a variety of communication interventions, all of which are aimed at drawing the attention of individuals and families to recommended healthy behaviour and encouraging them to adopt and maintain that behaviour.

Pamphlets for advocacy purposes have been produced in collaboration with country officers and adapted to local situations. An advocacy film package, consisting of four videos, has also been developed. The films show MDA and education and social-mobilization activities in India, the Philippines and Africa, and provide an overview of the

GPELF and the Global Alliance, at national and global level. Adaptation of these films to make them country-specific is being encouraged.

A recommendation was made, by several of those participating in the second meeting of the Global Alliance, in New Delhi in May 2002, that a resource compact-disc (CD) be produced for use by all those working towards the goal of LF elimination at national and global level. It was suggested that this CD could contain all the documents and materials produced by the partners of the Global Alliance: technical documents, films, and advocacy, iconographic and training materials. The WHO, as secretariat of the Global Alliance, is currently co-ordinating the compilation of such a CD.

ACTIVITIES IN REGIONS AND COUNTRIES

Table 4 summarizes the overall implementation of MDA campaigns by country and by region and provides the targeted total populations for 2002.

African Region

LF is endemic in 39 of the 46 countries in the WHO's African Region. Filaria control is relatively new to this region. Approximately 420 million people are considered to be at-risk. *Wuchereria bancrofti* is the only species causing LF in the region and is mostly transmitted by anopheline and culicine mosquitoes. Filariasis and onchocerciasis are co-endemic in 28 countries. At national or sub-national level, there is clearly the potential for synergy between the activities of the GPELF in this region and the promotion of insecticide bed-nets (by the 'Roll Back Malaria' campaign; Manga, 2002) or the ivermectin-based control of onchocerciasis (organized by the APOC).

In 2001, six of the 39 endemic countries initiated MDA and more than 3.3 million people were covered by MDA based on albendazole–ivermectin (Burkina Faso, Ghana, Nigeria, Togo and Tanzania) or albendazole–DEC (Comoros). During 2002, Benin, Kenya, Uganda have initiated MDA.

American Region

Seven countries in the American Region are considered LF-endemic (Brazil, Costa Rica, Dominican Republic, Haiti, Guyana, Suriname, and Trinidad and Tobago) with a total of 7.6 million people at-risk. This number of individuals represents $<1\%$ of the global burden of LF. Any LF in Costa Rica, Suriname, and Trinidad and Tobago is no longer a public-health problem but there has yet to be a validation of the absence of filarial transmission in these three countries. Haiti and the Dominican Republic and Guyana undertook MDA in 2002. Guyana plans to use DEC-fortified salt in its endemic areas.

Eastern Mediterranean Region

The population at-risk in the Eastern Mediterranean Region, like that in the American Region, represents $<1\%$ of the global burden of LF. In this region, LF is only endemic in three countries: Egypt, Yemen and Sudan. Sudan and Yemen are also endemic for onchocerciasis. Although many other countries of the region have filarial infections in immigrant populations, they probably have no indigenous transmission, although this needs verification. The Arab Fund for Social and Economic Development supports activities in the Arab countries. Egypt is now in its third year of MDA and targeted the entire at-risk population from the outset. Yemen has initiated MDA in pilot areas and is ready to scale-up.

Mekong-Plus Region

The 11 endemic countries that form the Mekong-plus Region were grouped together for epidemiological and operational reasons. These countries bear 25% of the global burden of LF and have all three parasite species that cause LF in humans: *Wu.*

bancrofti, *B. malayi* and *B. timori*. China, Indonesia, Malaysia and Thailand have a long history of implementing control programmes. As it has reduced the prevalence of microfilareamia to $<1\%$ in all of its previously endemic regions, China has already achieved the basic elimination criterion. Endemic areas have been greatly reduced in Malaysia and Thailand and are now limited to a few identified foci. Cross-border migration and transmission, particularly between Myanmar and Thailand and between Indonesia and Malaysia, remain a problem.

Indian Sub-continent Region

Almost half of the global population at-risk of LF live in five countries on the Indian subcontinent: Bangladesh, India, the Maldives, Nepal and Sri Lanka. Many of those with filarial infection have the chronic manifestations of LF, and LF is wide-spread in each endemic country. The causative parasite is predominantly *Wu. bancrofti*, transmitted by *Culex quinquefasciatus*, but *B. malayi* occurs in some pockets in India (although it no longer occurs in Sri Lanka). There is a long history of control measures in India, the Maldives and Sri Lanka. Bangladesh, India and Sri Lanka have initiated MDA, and Nepal and the Maldives plan to start in 2002.

Pacific Region

The population at risk in the Pacific Region is estimated to number 4.13 million, distributed in 16 endemic countries or territories (American Samoa, Cook Islands, Marshall Islands, Fiji, French Polynesia, Kiribati, Micronesia, New Caledonia, Niue, Palau, Papua New Guinea, Samoa, Tonga, Tuvalu, Vanuatu, and Wallis and Futuna). Papua New Guinea is the country with the highest estimated at-risk population: around 2 million (50% of the total population at risk in the region). In 2001, nine out of the 16 countries at-risk in this region implemented MDA and other LF-elimination activities (Burkot *et al.*, 2002). By the end of 2001, at least 850,000 people were covered by MDA. A diversity of vectors occurs in the different island groups of the Pacific (Burkott and Ichimori, 2002). *Aedes* vectors are particularly efficient transmitters of the diurnally sub-periodic strain of *Wu. bancrofti* and, given their abundance and vector competence, present a great challenge for the PacELF programme (Esterre *et al.*, 2001; Burkot *et al.*, 2002). It is generally agreed that LF elimination in areas where *Anopheles* transmitting the nocturnally periodic strain of *Wu. bancrofti* will be relatively easy to achieve (Burkott and Ichimori, 2002; Burkot *et al.*, 2002).

GENERAL DISCUSSION

The ambitious decision to target the global elimination of LF as a public-health problem by 2020 presents a significant challenge to the community of partners involved in the GPELF, and particularly to the endemic countries. However, since the programme commenced, there has been rapid engagement of countries that have a limited or no previous history of LF control. LF was considered an eliminable problem once it became clear that effective and safe drug combinations and a rapid, easy, sensitive and specific diagnostic test (for bancroftian filariasis) were available and that the impact on microfilaraemia of a single dose of DEC (at 6 mg/kg) was similar to that of multiple doses. The long-term commitment of GSK to provide albendazole and the extension of Merck's Mectizan Donation Program to include LF elimination were important steps in mobilizing the support of additional donors and the engagement of NGDO. Whilst these developments enabled the transmission-control elements of the programme to evolve, parallel studies on the disease itself provided hope for existing cases of LF. Once the role of bacterial and fungal infection in acute attacks of dermato-adenolymphangitis had been made clear (Dreyer *et al.*, 1999), the potential for limiting disability by routine skincare became apparent. Comprehensive

studies on symptom alleviation have been completed and now permit the introduction of a strategy to prevent disability through a community-oriented approach. Within national programmes, the mutual interaction between transmission control and disability limitation is a key element in enhancing compliance.

In the earliest phases of the GPELF, it became clear that the problems of the programme's extent and diversity could best be resolved by the decentralization of most activities. However, a globally standardized system of reporting (albeit one with sufficient flexibility to cope with the differences in settings, health systems and drug-distribution mechanisms) was promoted, since this would produce results that could be easily compared and interpreted by all of the partners.

Lymphatic filariasis has been eliminated as a public-health problem in a few countries and limited application of a control intervention, such as selective treatment with DEC, is likely to clear the disease soon from several other countries (e.g. Suriname, Costa Rica and Trinidad and Tobago). The role of vector control in the GPELF will largely be as an auxiliary activity, linked to the vector component of other disease-control programmes (such as the use of bednets against the *Anopheles* vectors of malarial parasites, or the control of the *Aedes* vectors of dengue virus in the Pacific) where this is relevant.

This review is designed to highlight the progress made in the GPELF and the challenges which still have to be met before the ultimate target, of global elimination, is achieved. The 'side-benefits' and cost-effectiveness of the programme are so great that this goal will almost certainly be reached **if** the international community and the endemic countries can jointly assure the financial, logistic and societal support necessary for the scaling-up of operations. Although realistic, the medium-term goal — to cover 350 million of those at risk by the end of 2005 — can only be reached through a huge, focused and concerted effort by all of the interested 'actors' and partners.

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