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**DEFINING THE ROLES OF VECTOR CONTROL
AND XENOMONITORING IN THE
GLOBAL PROGRAMME TO ELIMINATE
LYMPHATIC FILARIASIS**

**Report of the Informal Consultation
WHO/HQ, Geneva, 29-31 January 2002**



**World Health Organization
Communicable Disease Control, Prevention and Eradication
Parasitic Diseases and Vector Control**

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DEFINING THE ROLES OF VECTOR CONTROL AND XENOMONITORING IN THE GLOBAL PROGRAMME TO ELIMINATE LYMPHATIC FILARIASIS

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Executive summary

The consultation was convened to assess the potential value of vector control to augment the Global Programme to Eliminate Lymphatic Filariasis (GPELF), a mosquito-borne disease affecting about 120 million people in 80 countries. The meeting also provided an opportunity to consider the possible role of monitoring filariasis prevalence in the human population via vector sampling and assays. The term xenomonitoring was introduced for this approach.

The GPELF was launched in 2000, based on two strategies: stopping transmission and alleviation of disability due to the disease. Currently the GPELF depends largely on mass drug administration (MDA) to interrupt transmission of filaria parasites: *Brugia* and *Wuchereria bancrofti*. Integrated vector control activities and environmental sanitation are encouraged while national ELF programmes focus primarily on achieving high rates of MDA coverage.

More than half of the world's burden of lymphatic filariasis (LF) is transmitted by *Culex quinquefasciatus* and other man-biting mosquitoes of the *Culex pipiens* complex, responsible for Bancroftian filariasis transmission in the Americas, Egypt, urban East Africa, the Indian subcontinent, Indonesia and southeast Asia. In about 40 countries (African region and Papuan sub-region), *W. bancrofti* is largely transmitted by *Anopheles* mosquitoes that also vector malaria in rural areas. In most Pacific countries, *W. bancrofti* is vectored by aedine mosquitoes (*Aedes* and *Ochlerotatus*) that also transmit arboviruses, notably dengue. Brugian filariasis, transmitted by *Mansonia* and *Anopheles*, is now limited to only 8 oriental countries.

To provide the GPELF with the option of employing appropriate vector control tools, selectively targeted to prevent transmission, this consultation reviewed the state-of-the-art and current knowledge on proven techniques for controlling mosquitoes responsible for vectoring each type of lymphatic filariasis. Given the rapidity of upscaling MDA coverage in each endemic country, it is essential for GPELF resources to be concentrated on MDA, not dissipated on vector control practices unless there is strong evidence of their cost-benefits. The working papers and presentations indicated that many LF vector scenarios can be tackled effectively, but the cost-effectiveness is seldom clear and needs further analysis in most cases. Even so, there are widespread opportunities for LF vector control to have multi-purpose impact, especially with *Anopheles* control for Roll Back Malaria, with *Aedes* control for dengue fever and dengue haemorrhagic fever prevention and *Culex* control for urban nuisance suppression.

Environmentally acceptable interventions can be effectively employed against mosquito vectors of LF in most, but not all, eco-epidemiological settings. Wherever appropriate (see below), vector management activities can be applied against both mosquito larvae and adults to reduce their density and vector potential. Efforts should be made to optimise the multi-disease impact of vector control operations already underway in other public health programmes. Despite continuing efforts in the affected countries, however, integrated vector management (IVM) is seldom well resourced where LF has to be eliminated.

Wherever malaria and LF are co-endemic and transmitted by the same species of *Anopheles*, anti-malaria vector control practices (i.e. indoor spraying of residual insecticide [IRS] and the use of ITNs — insecticide-treated nets and curtains) tend to have even greater impact on LF transmission, to the point that LF has been eliminated as a by-product of malaria vector control in some situations. This synergy of *Anopheles* control should be further evaluated and optimised. In particular, as *W. bancrofti* is co-endemic with malaria across tropical Africa, participants recommended that African ELF programmes in conjunction with the Roll Back Malaria partnership (RBM) should scale-up ITN coverage in LF endemic districts. Given the RBM 2005 target of 60% coverage with ITNs, there is ample opportunity for developing this synergy in most malarious countries, mediated by respective programme managers in cooperation with endemic district health teams.

Where *W. bancrofti* is transmitted by *Culex* and at least 2/3 of this vector production is from flooded pits (particularly pit latrines and soakage pits), application of expanded polystyrene beads (EPBs) to the pits is recommended for prolonged suppression of vector potential. This approach would be inadequate in situations (areas with monsoon climate) where the majority of vector *Culex* breeding-sites are in flooded ditches, surface pools and water storage containers. Habitual use of ITNs is essential wherever LF remains endemic (being popular against nuisance mosquitoes as well giving substantial protection against malaria and other mosquito-borne diseases), particularly where *Culex* and other mosquitoes are left uncontrolled. Improved sanitation and drainage systems, where affordable, greatly reduce transmission risks of LF as well as other helminth and enteric diseases.

Larviciding is usually not effective or sustainable for filariasis vector control (except in special situations), so this method is generally discouraged as uneconomic and inappropriate for the GPELF. Participants were unable to identify reliable methods for cost-effective control of *Aedes* or *Mansonia* vectors of LF, other than general source reduction and environmental management in conducive situations.

Brugia timori is restricted to islands of Nusa Tenggara (Flores and Timor group) and has only one known vector, *Anopheles barbirostris*, and this is amenable to standard malaria vector control measures (IRS & ITNs). Given the political will and resources, MDA could be augmented by vector control to stop transmission and eliminate *B. timori* (following the example of *W. bancrofti* elimination from Solomons).

Recognising the practical usefulness of PCR assays to detect presence of filaria infection in mosquitoes, participants recommended to standardize and introduce this approach — likely to be more economic than antigen detection — for:

- (a) xenomonitoring of microfilaria prevalence in the human population, and
- (b) verifying interruption of transmission.

A framework for sampling vectors for xenomonitoring was therefore developed by the group.

To facilitate more efficient use of vector control practices intended to interrupt LF transmission, participants identified some priority research questions and issues to be addressed on behalf of the Programme.

1. Introduction and opening remarks

On behalf of the Global Programme to Eliminate Lymphatic Filariasis (GPELF) this informal consultation was convened at WHO Headquarters, Geneva, 29-31 January 2002, to assess the potential value of vector control to augment the Global Programme which is based on mass drug administration (MDA) to interrupt transmission of lymphatic filariasis (WHO, 1999a; 2000a). This meeting also provided an opportunity to consider the possible role of monitoring filariasis prevalence in the human population via vector sampling and assays. The term xenomonitoring was introduced for this approach.

The meeting was opened jointly by Dr Lorenzo Savioli (Coordinator of Strategy Development and Monitoring for Parasitic Diseases and Vector Control) and by Dr Nevio Zagaria (Coordinator of Strategy Development and Monitoring for Eradication and Elimination) on behalf of Dr Maria Neira (Director of Control, Prevention and Eradication) and Dr David Heymann (Executive Director of WHO, Communicable Diseases). After welcoming the participants and introducing relevant staff of the WHO Secretariat (Annex 1), Dr Savioli outlined related WHO activities on vector control, particularly the essential role of vector control in programmes such as Roll Back Malaria (RBM), elimination of Chagas disease, prevention and control of dengue and leishmaniasis and the onchocerciasis control programme (OCP). He also commended the World Health Organization Pesticides Evaluation Scheme (WHOPES) which promotes the development of alternative insecticides for vector control. Dr Savioli then reminded the participants of the main objectives of the consultation, namely to: (1) review and analyse the current status of vector control in lymphatic filariasis control programmes; (2) identify epidemiological situations where vector control can play a critical role in accelerating and enhancing the effect of MDA; (3) define the vector control strategies [in the identified situations] which are cost-effective and sustainable; and (4) define the potential role of xenomonitoring in the GPELF.

Dr Zagaria explained how the Global Programme to Eliminate Lymphatic Filariasis (GPELF) currently emphasises Mass Drug Administration (MDA) to interrupt transmission of infection and alleviation of the disability caused by this disease. He encouraged participants in this consultation to identify ways that vector control might play an additional / supplemental role in the Programme in some situations, to help achieve the local, national and global goals more quickly and cost-effectively. Dr Zagaria explained that the report of the consultation would be formally considered by the Technical Advisory Group (TAG) of the GPELF for recommendation to the Programme. He urged the participants to identify opportunities for multi-disease impact of vector control, especially potential synergies with RBM.

Professor C.P Ramachandran was appointed Chairman, with Dr G B White as Rapporteur of the consultation. After thanking the WHO Secretariat for organizing such a timely meeting, Prof. Ramachandran drew attention to the progress already made in establishing the GPELF since the 1997

Resolution 50.29 by the World Health Assembly "to eliminate lymphatic filariasis as a public health problem." He reported on having recently attended several regional ELF meetings, for example among countries of the Indian sub-continent, the Mekong-plus region, and the Pacific (WHO, 2001b). From these experiences he urged participants to provide clear guidelines on practical and appropriate methods of vector control for potential implementation in the various countries. He remarked that both at the regional and national levels, those responsible for control of communicable diseases are enthusiastic about what the ELF programme can accomplish to decrease the misery caused by lymphatic filariasis. Prof. Ramachandran emphasized that the endemic countries and their administrations have high expectations about the benefits which the programme will bring, noting the attendant challenges and tasks this would bring during the next 10-15 years in order to achieve the objectives of GPELF. He also pointed out that the meeting was the first that sought to define the role of vector control and xenomonitoring in the GPELF and hence was particularly important. Observing that the meeting brought together a critical mass of the world's leading medical entomologists, epidemiologists and other experts, he expressed optimism that relevant conclusions, suggestions and recommendations would be produced for the TAG to review.

2. Background and objectives of the consultation

The GPELF was launched in 2000 and is based on two strategies:

(a) interruption of transmission and (b) alleviation and prevention of disability due to lymphatic filariasis. Currently the GPELF depends largely on MDA to interrupt transmission of *Brugia malayi* and *Wuchereria bancrofti*. This strategy is based on the evidence that single annual doses of drugs or diethylcarbamazine citrate (DEC)-fortified salt can suppress microfilaraemia for prolonged periods of and beyond one year. Although vector control is not advocated as an operational component within GPELF, the programme encourages its application as part of other ongoing integrated vector control approaches. This is primarily to channel the available resources under the national programmes to focus on achieving high drug coverage.

However, it is likely that in some epidemiological settings, the application of appropriate measures against vectors of lymphatic filariasis may accelerate the interruption of transmission when applied in combination with MDA. Effective vector control measures may also reduce the subsequent risk of re-establishment of transmission.

Moreover, current technologies using PCR to detect the presence of specific filarial infection in mosquitoes appears to have a potentially important, but hitherto undefined, role to play in monitoring interruption of transmission during MDA.

For these reasons, the consultation was held, specifically to:

- Review and analyse the current status of vector control in lymphatic filariasis control programmes;
- Identify special epidemiological situations where vector control may play a critical role in accelerating and enhancing the effect of MDA;
- Define the vector control strategies [in the identified situations] which are cost-effective and sustainable;
- Define the potential role of xenomonitoring in the GPELF.

3. Organization of the meeting

The consultation was attended by 20 external scientists (see list of participants, Annex 1), most of whom had prepared working papers on topics for discussion (Annex 2), and 20 members of the WHO Secretariat. Two main themes of the consultation were covered by specially prepared comprehensive documents dealing with (A) the development and evaluation of a sensitive molecular assay for detection of lymphatic filarial parasites in vector mosquitoes (working papers 1-3); (B) a review of control methods for vectors of lymphatic filariasis (working paper 4) and more detailed presentations on this theme (working papers 5-14), plus filariasis modelling, sampling and other research considerations (working papers 15-18). On behalf of the WHO Regional Advisers, Dr Michael Nathan (WHO/CDS/CPE/PVC) distributed the draft Global Framework for Vector Control (WHO, 2001c) so that participants could shape their discussions and recommendations in the context of all vector-borne diseases, bearing in mind the needs to strengthen national capacities for implementation of effective vector control measures (WHA 42.31) and to promote integrated vector control (WHA 50.13).

The working papers and presentation of their key points provided a basis for development of recommendations by working groups and plenary discussion. These papers will be updated and reproduced in a separate publication, with a full bibliography. In addition to a working group which addressed issues related to monitoring and transmission potential, there were five on particular parasite-vector associations:

- *Anopheles* vectors of periodic *B. malayi*, *B. timori* and *W. bancrofti*
- *Aedes* vectors of sub-periodic *B. malayi* and *W. bancrofti*
- *Culex* vectors of nocturnally periodic *W. bancrofti*
- *Mansonia* vectors of periodic/sub-periodic *B. malayi* and *W. bancrofti*
- *Ochlerotatus* vectors of non-periodic *W. bancrofti*

4. Control of mosquito vectors of lymphatic filariasis

The occurrence of filarial disease depends on high rates of transmission to cause incidence of new cases and continued endemicity. It has been calculated that statistically an average of several thousand, probably tens of thousands of bites by **infective** vector mosquitoes (range 2700 to > 100,000) occur before a new human case of infection is established (Southgate, 1984). For *Cx. quinquefasciatus* transmission of *W. bancrofti*, Hairston & DeMeillon (1968) estimated that about 15,500 infective bites would be the average exposure leading to patent microfilaraemia where the mean annual biting rate (ABR) exceeded 80,000 bites/person/year and the microfilaraemia rate among adults of different ethnic groups reached 4 – 11%. Realization that a high proportion of LF cases are contracted during childhood, years before microfilaraemia develops (Witt & Ottesen, 2001), indicates that LF incidence can be caused by far fewer infective mosquito bites than was previously believed necessary.

Even so, in many tropical situations with various vectors it has been observed that, below a critical number of infective bites, LF is not sustained as an endemic disease. For example in cities with good environmental management (e.g. Singapore and Mumbai) and islands such as Cuba, Trinidad, Guam and Mauritius, LF disappeared — apparently as a result of improved sanitation limiting vector density. Moreover in the Solomon Islands, parts of Togo and Papua New Guinea, interruption of filariasis transmission resulted from insecticide house-spraying (IRS = Indoor Residual Spraying) operations by the anti-malaria programme.

Generally, by application of standard methods of mosquito control, it is possible to greatly reduce the risks of filaria transmission, if not to prevent it altogether. The main methods suitable for control of filariasis vectors and personal protection against them are shown in Table 1, based on relevant textbooks and manuals (Feachem, 1983; Curtis, 1991; Rozendaal, 1997). Details of appropriate insecticides, their modes of application and dosages are summarized in WHO documents (e.g. Chavasse & Yap, 1997; Najera & Zaim, 2001) listed on the WHOPES website <http://www.who.int/ctd/whopes>. In many places, mosquito prevention and control can be achieved by environmental management (WHO, 1982, 1988), improved sanitation and other counter-measures by the community, e.g. screening houses and siting them away from mosquito-genic habitats. Communities also benefit from the sum of individual efforts to minimize exposure to mosquito bites, for example by using ITNs (Lengeler *et al.*, 1996, 1997), covering the limbs with clothing at peak biting-times of diurnally active mosquitoes, timely applications of effective mosquito repellents (Barnard, 2000) and customary avoidance of mosquito-infested places. The following sections on each LF vector scenario outline the appropriate (and some inappropriate) uses of general and specific anti-mosquito measures.

Table 1. Summary of control methods for potential use against mosquito vectors of lymphatic filariasis:

+++ most effective; ++ fairly effective; +/- effective for many but not all situations and/or vectors; +/- possibly effective for some species/sites; - not appropriate; X, not applicable; MLOs = mosquito larvicidal oils. Source reduction means preventing potential breeding-sites by drainage, flushing, filling of pools, elimination of water-filled receptacles (discarded cans, tyres etc.) covering of water-storage jars and basins, installation and maintenance of sanitation systems that do not produce mosquitoes.

Mosquito Genus	Peak Time of Biting	Type of Filariasis		Control Method					
				Environmental / physical			Chemical / insecticidal		
		<i>Brugia</i>	<i>Wuchereria</i>	Source Reduction	Larval control	House screening	Bednets curtains	Indoor Residual Spray	Larvicidal chemicals, biopesticides & MLOs
<i>Anopheles</i>	Night	Nocturnally Periodic	Nocturnally periodic	++/-	Predators, e.g. fish	+++	+++	+++	++/-
<i>Culex</i>	Night	Nocturnally Periodic	Nocturnally periodic	+++	expanded polystyrene	+++	+++	++/-	+/-
<i>Mansonia</i>	Night	Nocturnally Periodic	X X	+/-	Clear aquatic vegetation	+++	+++	++/-	-
	Day	Sub-periodic	X X	+/-		++	+/-	+/-	-
<i>Aedes</i>	Day	X X	Sub-periodic	+++	Eliminate containers	+/-	+/-	+/-	+/-
<i>Ochlerotatus</i>	Day & Night	X X	Non-periodic	+/-	Water management	++	+/-	+/-	++

4.1 Control of *Culex* vectors of *W. bancrofti*

About half of the world's burden of lymphatic filariasis is transmitted by *Cx. quinquefasciatus* in India. This and other man-biting forms of the '*Culex pipiens* complex' are responsible for most or all of the bancroftian filariasis transmission in Asian countries, Indonesia, Egypt, urban East Africa and the Americas. These mosquitoes are most unpopular for their persistent biting nuisance, especially bothersome at night in bedrooms. Globally (Annex 5), the majority of *W. bancrofti* is transmitted by *Cx. quinquefasciatus*, known as the tropical house mosquito. This vector bites only in darkness and transmits only nocturnally period *W. bancrofti* in most endemic urban areas (but *Cx. quinquefasciatus* has low susceptibility to *W. bancrofti* in Polynesia and West Africa).

Culex quinquefasciatus typically breeds in stagnant, organically polluted water. In many urban areas, the great majority of *Culex* breeding sites are in flooded pit latrines and soakage pits, which can be targeted for specific control measures (Curtis & Feachem, 1981). In low-lying areas, especially where monsoon climate causes prolonged extensive flooding of ditches and gulleys, source-reduction of *Culex* is virtually unmanageable. Where possible, keeping open drains flowing has been demonstrated to effectively suppress the adult *Cx. quinquefasciatus* biting populations (e.g. in Pondicherry, India, and Tanga, Tanzania), but this needs sustained effort and expenditure. Upgraded sanitation and drainage is undoubtedly the long-term solution to the urban *Culex* problem. Although expensive, the broader benefits to social progress and health (against other enteric diseases and helminth infections) make sanitation systems more cost-effective in the long-run.

Everyone welcomes control of *Culex* biting nuisance. In many towns, however, *Culex* control is not sufficiently feasible at an affordable cost to make a major contribution to the present campaign to eliminate filariasis as a public health problem. This contrasts with more economically advanced situations (e.g. Singapore, Costa Rica, Trinidad) where *Culex* has been readily reduced to levels where LF transmission breaks down.

For larvicidal control of *Cx. pipiens* and *Cx. quinquefasciatus*, extensive use has been made of organophosphate insecticides (e.g. fenthion, temephos), but the widespread development of resistance reduces their effectiveness against *Culex* populations. Oiling is seldom suitable because the lighter 'mosquito larvicidal oils' (MLOs) are readily emulsified by detergents often present in polluted waters preferred by *Cx. quinquefasciatus*, while heavier oils tend to clog soakage pits. To avoid selection pressure on immature stages of mosquitoes (larvae and pupae), pyrethroid insecticides should never be used for larviciding — since pyrethroids are invaluable adulticides. Even so, adult *Culex* mosquitoes are relatively more tolerant than other types of mosquitoes against most insecticide applications, making adulticidal control of *Culex* ineffective. Generally larviciding programmes, with high costs of chemicals, equipment and labour, are uneconomic and unsustainable against *Culex*

vectors of *W. bancrofti*. In situations where *Culex* breed prolifically in flooded drains and sites that cannot be readily treated, larviciding cannot be expected to have sufficient impact to reduce filariasis prevalence, particularly where monsoon climate and periodic flooding cause extensive breeding sites to be unmanageable except by major drainage improvements (WHO, 1982; 1988).

An excellent method of *Culex* control employs floating layers of expanded polystyrene beads (EPBs) which create a physical barrier to egg-laying adult *Culex* while suffocating larvae and pupae. Floating EPBs are extremely durable, giving prolonged suppression of *Culex* populations. EPBs can only be used effectively in habitats where stagnant water is confined within walls, e.g. pit latrines, soakage pits, cess pits, flooded cellars etc. Sustainable control of *Cx. quinquefasciatus* has been demonstrated over several years among communities in Zanzibar, Tanzania (Maxwell *et al.*, 1990, 1999), and Tamil Nadu, India (Reuben *et al.*, 2001; Sunish *et al.*, 2002), where the application of EPBs in all pits found to be breeding-sites of *Cx. quinquefasciatus* virtually eliminated the *Culex* nuisance mosquito problem. One application of EPBs to each pit resulted in several years of control in East African towns. Most importantly, this simple method for sustainable control of *Culex* greatly enhanced the impact of time-limited MDA, by preventing resurgence for a few years after MDA ceased (Sunish *et al.*, 2002). In St. Vincent and the Grenadines, West Indies, this method was applied using shredded waste polystyrene (SWAP) to give long-lasting control of *Cx. quinquefasciatus* in pit latrines (Nathan *et al.*, 1996). Floating carpets of EPBs or SWAP are not suitable for flood-prone areas and exposed breeding-sites from which they may be flushed away. In places where at least 2/3 of *Culex* production is attributed to breeding-sites in pits suitable for polystyrene treatment, the group recommended that this method should be applied to control the filariasis vector population in situations where it is not feasible to improve the sanitation system (e.g. water closet with mains drainage or well maintained mosquito proof septic tanks and cess pits) to prevent breeding of mosquitoes and flies.

Bacillus sphaericus (Bs) can kill *Culex* larvae in polluted water, and may have some recycling potential, whereas *Bacillus thuringiensis israelensis* (Bti) is not effective in such habitats. These 'biopesticides' are commercially available, mainly for use against pest mosquitoes in wetlands of prosperous countries. In practice, for LF vector control, *B. sphaericus* in open breeding sites did not contribute usefully to adult *Culex* suppression beyond what was achieved with EPBs applied to pits in the same areas (of Zanzibar and Tamil Nadu). There have been problems with *B. sphaericus* quality control and rapid development of resistance to it by *Cx. quinquefasciatus*. Enthusiasm for these bioproducts seems to be inappropriate for LF vector control in poor economic situations in developing countries. Among the insect growth regulators (IGRs), pyriproxyfen is most potent (WHO, 2001a) and could be used to suppress immature *Culex* populations, but EPBs would be more cost-effective for prolonged control of LF vectors breeding in flooded pits.

Measures that restrict access of *Cx. quinquefasciatus* into houses, such as the installation of ceilings, or the use of eaves curtains impregnated with insecticides, have been shown to reduce *Culex* biting. Insecticide treated bednets divert *Culex* to bite birds and hence reduce the transmission potential of *W. bancrofti* to humans. The impact of ITNs on LF transmission by *Culex* has not been investigated, although it is well known that careful use of bednets can provide welcome relief from *Culex* biting.

The following methods have been used successfully for sampling *Culex* adult populations (see also Section 5.3 below):

- "Resting collection" of blood-fed mosquitoes per man-hour of searching in rooms (using torches and aspirators or pyrethrum knockdown spray);
- "Landing catch" of human-seeking mosquitoes (N.B. Section 5.3);
- Insecticide-impregnated fabric traps (Das *et al.*, 1997);
- Light-traps (set beside occupied untreated bednets) to catch unfed, host-seeking mosquitoes (Lines *et al.*, 1991);
- "Gravid trap" for collecting females when ovipositing (Reiter, 1987).

4.2 Control of *Anopheles* vectors of *Brugia* and *W. bancrofti*

In addition to their role as vectors of malaria, *Anopheles* mosquitoes transmit lymphatic filariasis in rural areas of tropical Africa and the Papuan sub-region. In 36 African countries where *W. bancrofti* is endemic, it is mostly transmitted by one or two species of *Anopheles*. Several anophelines are vectors of *Brugia malayi* (also transmitted by *Mansonia*) in southeast Asia and Indonesia, while *An. barbirostris* is the only known vector of *Brugia timori*. Fortunately malaria vector control is already a priority for RBM programme managers, with considerable impact on filariasis transmission. This synergy has to be more recognized, advocated and exploited wherever possible.

Apparently it is because *Anopheles* females bite only at night that microfilariae are nocturnally periodic to ensure uptake by the vector. After blood-feeding, the female *Anopheles* usually rest indoors for 1 to 4 days while their eggs develop. Hence spraying indoors with residual insecticide (IRS = indoor residual spraying) is designed to limit the likelihood of these vectors surviving. Since the transmission of filaria larvae is less efficient than for malaria sporozoites, house-spraying has even greater impact on filariasis transmission. Thus filariasis disappeared from the Solomon Islands and some other places as a result of anti-malaria spraying programmes (Webber, 1979). This dividend should be encouraged wherever LF is co-endemic with malaria having the same vectors.

Likewise the use of insecticide-treated bednets and curtains (ITNs) for protection against malaria transmission (Lengeler *et al.*, 1996) also limits exposure to filariasis vector *Anopheles*, with significant reductions in potential transmission rates of filariae (Fig. 1). In view of rapidly expanding ITN coverage as a major intervention of the RBM programme in most malarious countries (WHO, 2001a), the consequences should be investigated epidemiologically to

assess the impact on LF incidence, prevalence and clinical symptoms. Even the use of untreated bednets appears to cut filariasis prevalence. For example, a survey in Papua New Guinea (Bockarie et al., 2002) found that habitual users of bednets show significantly lower rates of microfilaraemia and hydrocoele.

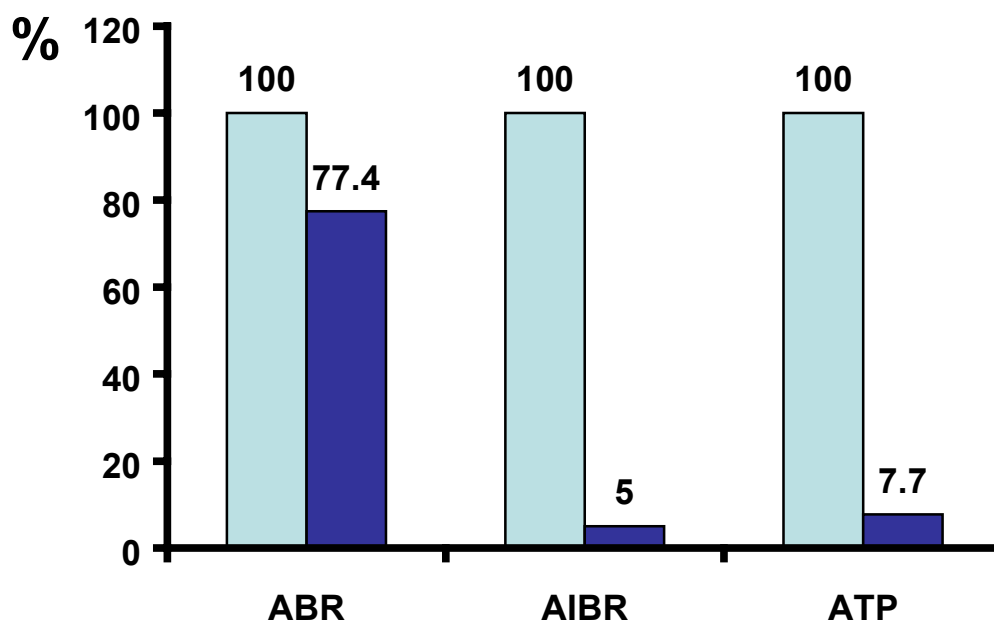


Figure 1. Relative reduction in transmission potential of *Wuchereria bancrofti* in a Kenyan village after intervention with impregnated bednets (Mukoko et al., 2002).

ABR = annual biting rate of *An. funestus*, *An. gambiae* & *Cx. quinquefasciatus*;
AIBR = annual infective biting rate of these vectors combined;
ATP = annual transmission potential.

Other methods of vector control, such as larviciding and source reduction, are inappropriate for use against most species of anopheline vectors, mainly due to their vast and scattered breeding habitats. In a few cases, it may be practical to eliminate the breeding-sites nearest to villages (e.g. *An. funestus* in Africa; *An. barbirostris* and *An. subpictus* in Indonesia), but most *Anopheles* species are not ecologically amenable to environmental control. These vectors breed in obscure small pools (e.g. *An. farauti*, *An. gambiae*), seaside lagoons (*An. sudaicus*), swamps (*An. campestris*, *An. donaldi*), streams (*An. flavirostris*, *An. minimus*), riversides (*An. leucosphyrus*, *An. nili*) and irrigated rice-fields (*An. sinensis*), so that each local situation would require much understanding and resources to be dealt with environmentally. Targetting the female adult *Anopheles* mosquito population, to reduce their survival rates (mainly by IRS) and to limit their contact with humans, has greatest impact on vectorial capacity according to the Macdonald model (Garrett-Jones & Grab, 1964).

A peculiar disadvantage of filaria larvae in *Anopheles* vectors is known as the phenomenon of 'facilitation', whereby the female mosquito has armatures that damage a high proportion of ingested microfilariae (presumably as a defense mechanism for the mosquito). At low microfilaria densities, few survive, whereas a progressively greater proportion of larvae develop in female *Anopheles* that ingest a high microfilaria intake. This is attributed to the protection of some microfilariae by others as they pass over the armatures lining the pharynx and cibarium of the mosquito gut lumen. Fortunately, therefore, the reduction of microfilaria density by successful MDA should be conducive to lower vector competence of *Anopheles*. As filaria-infected *Anopheles* may have reduced life expectancy and activity, due to their load of filaria larvae, the reduction of LF may give rise to increased malaria vectorial capacity of *Anopheles*. This would be worth careful investigation but, in most co-endemic areas, the likely increase in entomological inoculation rate (EIR) of malaria would be unlikely to make much difference to the prevailing high endemicity of malaria. Conversely, any reduction of vectorial capacity resulting from vector control interventions would impact more on lymphatic filariasis.

4.3 Control of *Mansonia* vectors of *B. malayi* and *W. bancrofti*

Brugian filariasis prevalence is declining steadily in most endemic countries (3 in SEARO & 5 in WPRO) through effective chemotherapy and environmental improvements. Elimination of nocturnally periodic *B. malayi* from Sri Lanka, Korea and China was hastened by effective vector control in some areas, whereas southeast Asian communities inhabiting swamp-forest areas not amenable to control of *Mansonia* have to rely on MDA alone. Emphasis on control of *Mansonia* vectors of Brugian filariasis through income generating schemes in Kerala, South India, was encouraging and its augmentation with MDA was useful in achieving total interruption in transmission.

Considering the feeding and breeding habits of *Mansonia* vectors of sub-periodic *B. malayi*, especially in the swamp-forest ecotype, most conventional vector control methods cannot cope with their densities coming from extensive breeding areas and biting outdoors during daytime. Residual insecticide spraying of houses and animal shelters has been shown to reduce vectorial capacity of nocturnally active *Mansonia* vectors, as well as *Anopheles* vectors, of nocturnally periodic Brugian filariasis, but there is no significant impact on vectors of sub-periodic *B. malayi*. Operational research with use of house-screening, ITNs and behavioural and personal protection measures (e.g. use of repellents when working in exposed situations) to reduce vector-human contact might devise appropriate methods to limit risks of Brugian filariasis transmission, particularly needed against zoonotic strains that cannot be eliminated by MDA. For national ELF Programmes of countries with zoonotic *Brugia*, as MDA proceeds, it will be necessary to investigate the amount of human infection coming from reservoir hosts via *Ma. bonneae/dives* and other vectors of sub-periodic strains. If this proves to be a persistent problem, specific counter-measures and modified local tactics may be needed.

Unlike other mosquitoes, an essential biological requirement of *Mansonia* is for the larvae and pupae to attach their breathing tubes to underwater roots, stems and leaves of floating aquatic plants. Therefore, removal of host plants by herbicides or mechanically can be very effective to prevent *Mansonia* production. However, to avoid contamination of the aquatic environment by chemical herbicides and the potentially adverse effect on the ecosystem, large-scale suppression of aquatic vegetation is considered unsuitable for routine vector control. Furthermore, the floating mats of host plants (*Eichornia*, *Pistia*, *Salvina* etc.) soon reinvade due to their high rate of vegetative growth.

Permanent prevention of *Mansonia* breeding is best achieved by environmental manipulation as demonstrated in Kresek, Indonesia. Density of *Ma. indiana* and BF cases decreased following an irrigation development programme, even without drug treatment or insecticide application. Chemical larviciding is unsatisfactory against *Mansonia*, due to the inaccessibility of most breeding areas and large volumes of water to be treated in places with monsoon climate. In circumscribed breeding-sites such as domestic ponds, application of granular insecticide formulation can prevent *Mansonia* breeding for up to a month. Immature stages of *Mansonia* can be killed by systemic insecticide applied to leaves of the host plant, but this is impractical except for ornamental situations. Swamp drainage may eliminate *Mansonia* sources as a side-effect of development schemes. Replacement of natural swamps by irrigated crops should not be allowed to produce new vector problems due to *Anopheles* (LF or malaria) or *Culex* (JE and other arboviruses). For such reasons, the control of *Mansonia* and Brugian filariasis cannot be separated from inter-sectoral issues of water and environmental management, as well as developments in agriculture and forestry.

4.4 Control of aedine vectors of *W. bancrofti*

In some situations, bancroftian filariasis is transmitted by aedine mosquitoes that bite during daytime: accordingly the microfilariae of *W. bancrofti* are sub-periodic where reliant on these vectors. The main vectors involved — with several million people exposed — are several species of *Ochlerotatus* subgenus *Finlaya* breeding in plant axils, bamboo stumps etc., notably *Oc. poicilius* associated with abaca plantations in The Philippines and *Oc. niveus* [also a vector of zoonotic dengue] in forested parts of eastern Myanmar, western Thailand and Nicobar Islands of India.

Of great concern for the population of about one million inhabitants in the affected island nations of Melanesia and Polynesia, several members of the *Aedes* (*Stegomyia*) *scutellaris* group — notably the most widespread species *Ae. polynesiensis* are responsible for highly efficient transmission among the "at risk" populations inhabiting hundreds of islands. These vectors are very voracious biters coming from breeding-sites in various types of water-filled containers (natural and artificial), plant axils and tree stumps, crab-holes, rock pools and water-storage cisterns. Dengue is also transmitted by *Ae. polynesiensis*, *Ae. pseudoscutellaris* and possibly others of the

Ae. scutellaris group. Operational guidelines for combating such *Aedes* (*Stegomyia*) vectors of LF and dengue are available from WPRO (WHO, 1995) and SEARO (WHO, 1999d).

Generally these aedine mosquito vectors have proved to be intractable and no specific control methods have been devised. Laborious source-reduction within a radius of 100-200 metres from houses can limit the problem, as these vectors usually do not fly far. Elimination of water-containers such as discarded receptacles (e.g. cans & tyres) is an important way to prevent the production of these LF vectors from peri-domestic breeding-sites, also to reduce risks of dengue/DHF outbreaks (WHO, 2000d). For that reason, enforcement of legislation for a weekly 'dry day' when all containers of water must be emptied has been practiced successfully. Containers may be stored under shelter to prevent inadvertent flooding by rainfall. Constant vigilance against breeding of *Aedes* (*Stegomyia*) is strictly maintained by municipalities such as Mumbai, Singapore and Hong Kong where LF has been eliminated.

Larvicidal treatments have to be efficiently applied regularly with good coverage rates to make any impact and this cannot be effective during the rainy season. Filling and poisoning of crab-holes can eliminate such sources of *Aedes* for years, but is uneconomical and only possible in limited areas. Use of biological control methods (predators and pathogens) gives disappointing results. Determined campaigns of environmental sanitation against these species of *Aedes* subgenus *Stegomyia* [including the more widespread dengue vectors *Ae. aegypti* and *Ae. albopictus* — that do not transmit lymphatic filariasis], have proved to be unsustainable in most Pacific islands. This is no excuse for complacency over vector control in such situations, but precludes any easy recommendations for dealing efficiently with such difficult vector species. As they bite during daytime, both indoors and outdoors, personal protection methods (i.e. covering legs and arms with clothes, use of repellents) are unrealistic in places with such humid climate. House-screening and air-conditioning provide some protection, but these species of *Aedes* subgenus *Stegomyia* often breed indoors where suitable receptacles occur. Ovitrap baited with insecticide may help to limit the domestic breeding of these species, requiring well-coordinated community participation. Zahar *et al.* (1980) comprehensively reviewed information about the eco-epidemiology of sub-periodic *W. bancrofti* and its vectors, giving many examples of experimental control successes with insecticides and environmental modification. Upscaling of these methods to reliable sustainability remains elusive.

To make matters worse, these *Aedes* are unusually efficient carriers of filaria larvae. This is due to a phenomenon known as 'limitation' whereby when microfilaria densities are low nearly all of them develop successfully after ingestion by these vector *Aedes*. Hence transmission risks remain significant even when the microfilaria rate has been suppressed in humans after MDA. Moreover, blood-seeking *Ae. polynesiensis* is strongly attracted to humans (other hosts are relatively scarce in Pacific islands). Thus transmission potential can be relatively high even where vector densities are low. Actually,

Oc. poicilius in The Philippines as well as *Ae. polynesiensis* and other members of the *Ae. scutellaris* group in Pacific islands are often locally so abundant as to be regarded as serious biting pests. For this reason their control is always desirable, despite the difficulty. Community action for integrated vector control (i.e. combination of all appropriate methods) can ameliorate the problem.

In Fiji and Samoa, nocturnally active species of *Ochlerotatus* subgenus *Finlaya* contribute locally to sub-periodic *W. bancrofti* transmission. As they bite at night, the use of bednets and house-screening can be helpful against them. Clearance of vegetation (e.g. *Freycinetia*, *Pandanus*) from village periphery can reduce their densities. Fogging of larvicidal temephos into clumps of vegetation with breeding-sites of *Oc. samoanus* has been shown to stop its breeding for a month or more (Samarawickrema *et al.*, 1992); this method might be useful against *Ochlerotatus* (*Finlaya*) species generally but would be costly and harmful to non-target arthropods. Formerly, periodic *B. malayi* was transmitted by *Oc. kiangsiensis* in China and *Oc. togoensis* in Japan and Korea, but these vectors have ceased to be of any importance following DEC campaigns to eliminate LF. In Papua New Guinea *Oc. kochi* contributes to transmission of nocturnally periodic *W. bancrofti* for which anophelins are the main vectors in most areas and the same control methods are applicable (section 4.2).

Among the biological agents often advocated for mosquito control, *Toxorhynchites* predatory mosquito larvae have little impact on *Aedes* biting densities, while larvivorous fish and parasitic *Romanomermis* nematodes are unsuited to breeding sites in containers and phytotelmata. Copepods are the most promising biocontrol agents employed against *Aedes* (*Stegomyia*) vectors of dengue, but *Mesocyclops aspericornis* had disappointing impact on biting densities of *Ae. polynesiensis* in French Polynesia. Following field trials of several species of *Mesocyclops* and *Macrocylops* in various countries and larval habitats, successful community use of copepods against *Ae. aegypti* and *Ae. albopictus* has begun in Honduras, Mexico and especially Viet Nam, so there is a good case for further evaluation of such predators against *Ae. polynesiensis* and other LF vectors.

In Australasian coastal marshy areas, the aedine mosquito *Ochlerotatus vigilax* bites at all times of day and night, and is the only known vector of non-period *W. bancrofti* in New Caledonia. Occasional outbreaks of arboviruses (e.g. Barmah and Ross River) are also transmitted by *Oc. vigilax*. To control this pest and vector, therefore, salt-marsh management (runnelling) and larviciding are practiced in Australia and could be usefully applied in New Caledonia, if found to be cost-effective.

Considering that these aedine mosquitoes cause much discomfort and are vectors of other diseases as well as LF, they cannot be ignored. To tackle the many difficulties of their control justifies further specific investigations (e.g. prevention of breeding in crab-holes: section 6.1). Dangers of human bait collection warrant the development of alternative sampling procedures for

xenomonitoring (see section 5.3). While general vector control expertise should be maintained in the countries concerned, this approach cannot be considered as cost-effective against vectors of filariasis, unless the relative cost-benefits are recalculated in the event that the ELF programme goal is not achieved by 5 years of MDA (Burkot & Ichimori, 2002).

5. Monitoring

5.1 Monitoring filaria prevalence and transmission potential

Standard methods for monitoring LF prevalence in the human population (WHO, 1987) are based on blood slide examination or filter sampling of microfilaraemia, supported by immunodiagnostic tests and now the ICT card test (Weil *et al.*, 1997).

Risk of LF transmission in any situation is indicated by 'transmission potential' — based on the number of third-stage filaria larvae (L3) to which a person is exposed by the bites of infective vectors during a specified period of time. Transmission potential takes into account the vector biting density and number of infective larvae per mosquito, fluctuating seasonally. This is expressed as annual or monthly transmission potential (MTP):

$$\text{MTP} = \frac{\text{total number of infective larvae}}{\text{number of mosquitoes dissected}} \times \text{number of bites / person / month}$$

The Annual Transmission Potential (ATP) is the sum of twelve MTPs in a year, as originally employed for monitoring the Onchocerciasis Control Programme (OCP) in West Africa (WHO, 1977), based on control of *Simulium* vectors of *Onchocerca volvulus*. Operational criteria for OCP were set to keep the ATP below 100 L3/person/year and the annual biting rate (ABR) of *Simulium* below 1000/person/year (irrespective of infection).

When applied to filaria vector mosquitoes, the ATP is a potentially useful indicator of LF transmission risk, but has not been evaluated in detail with respect to LF incidence and transmission efficiency of each species of filaria by its different vectors. To quantify LF risk in terms of ATP would involve much laborious (and unacceptably hazardous) field-work that cannot be observed directly. For reasons of the many contrasts between life-cycles of LF and *Onchocerca* it is invalid to adopt the ABR and ATP values from OCP as control threshold targets for LF. Moreover, due to variable competence and transmission efficiency of the different LF vector genera (facilitation by *Anopheles*, limitation by *Aedes*, intermediate effects by *Mansonia* and *Culex*) the model of LF transmission dynamics and risk remains unresolved. Certainly the critical level of transmission control to prevent incidence of new LF patent infections will vary according to the vector species involved.

The most important parameter for calculating ATP is the human-biting or landing rate. Landing collections of mosquitoes on human bait are cumbersome, expensive, ethically unacceptable in some countries and not feasible to carry out in a large-scale programme. There is a need to find an alternate way of collecting the biting population. Quantitatively, at least for indoor-resting (endophilic) female mosquitoes, there is a significant correlation between resting and biting density (Subramanian *et al.*, 1989). However, qualitatively resting and biting mosquitoes differ in terms of age structure, infection and infectivity. On the other hand, significant correlation was found between hand catch and insecticidal trap collections (Das *et al.*, 1997) in terms of mosquito density, abdominal condition, age distribution, infection and infectivity status. Therefore, trap collections can be used for collecting adult mosquitoes. Methods for mosquito sampling and collection are reviewed by WHO (1975) and Service (1993).

Relative values of transmission may be compared by the Transmission Intensity Index (TII) using data generated by trap collections (Das *et al.*, 1997). By setting up traps in large numbers, one can cover larger areas and more houses with ease and rapidity and at a lower cost, without the risks and ethical problems of using human-bait. Of particular suitability is the method of employing a CDC light-trap beside an untreated mosquito net used by an overnight sleeper, for sampling *Anopheles* and *Culex* attracted to the human host (Lines *et al.*, 1991). Applicability of the bednet entry-trap recently developed in Kenya for anopheline collection should be investigated for other mosquitoes. In view of the many productive alternative methods for mosquito collection, participants in the consultation strongly discourage the use of human-bait collections for LF vector sampling.

In measuring filaria infection and infective rates of female mosquitoes, it is important to distinguish clearly between (a) blood-fed mosquitoes in which microfilariae will be detected and which provide a proxy measure of prevalence in human blood; (b) unfed mosquitoes in which filarial L1, L2 and L3 larvae are detectable. The procedure of knocking-off the heads of batches of mosquitoes, and testing heads only, should provide an approximation of the infective rate.

5.2 PCR assays for filaria detection in vectors

Molecular detection of filarial DNA in humans or mosquitoes can best be done with polymerase chain reaction (PCR) assays to detect specific DNA sequences. A repeat sequence (188 bp) designated *Sspl*, identified from a *W. bancrofti* genomic library was found to characterize *Wuchereria* (Zhong *et al.*, 1996) as distinct from *Brugia* and other filariae. A PCR assay was developed to amplify this *Sspl* family of repeated DNA elements using specific primers (NV-1 and NV-2). The assay was shown to be sensitive enough to detect 0.1 pg of *W. bancrofti* genomic DNA, representing less than 1% of one infective larval DNA within its mosquito host (Chanteau *et al.*, 1994). Recently, several research groups in African countries started using this sensitive PCR mosquito-pool-screening approach in preference to the classical method of

dissecting mosquitoes to determine their filarial infection and transmission potential. Also in India, VCRC workers have devised a simpler, quicker and less expensive PCR assay procedure for screening mosquitoes to detect *W. bancrofti* parasites.

The PCR approach to detect *W. bancrofti* can be used for diagnosis of infection in the human host and, more importantly, detection of filarial DNA in the mosquito vector (Farid *et al.*, 2001). A reliable, sensitive, specific and faster immunochromatographic (ICT) card format for rapid diagnosis of *W. bancrofti* active infection in humans is also available (Weil *et al.*, 1997), but is more costly (now ~ \$ 1.50/test). Thus, compared to ICT card tests or mosquito dissection, the PCR technique is economical, can be applied to humans and has more practical value for xenomonitoring by detection of filarial DNA in mass screening of mosquito vectors. The PCR method has the advantage of detecting a single worm in a pool of wild-caught mosquitoes (Ramzy *et al.*, 1997), being very cost-effective for field application. Thus, screening of pools of wild caught mosquitoes by PCR, a non-invasive means, could be used for identifying endemic regions, but would be particularly useful for monitoring transmission in areas where mosquito infection rates are very low, e.g. during active control programmes.

In applying this assay to field collected samples, experiences of the DNA diagnostics laboratory of the Onchocerciasis Control Programme (OCP) in West Africa may prove to be a helpful model in overcoming this obstacle. For the past nine years, the OCP's laboratory has been using a PCR assay based on the amplification of a 150 bp repeat sequence family to monitor infection in the *Simulium damnosum* complex vectors of African onchocerciasis. Initially, the OCP laboratory's efforts were primarily directed towards identifying individual parasites dissected by the OCP's field teams, but the laboratory has been successfully applying a pool screening approach to monitor infection in the vector population since 1996. Similarly, the Onchocerciasis Elimination Program of the Americas (OEPA) has been applying this technology to monitor transmission in the Americas since 1999.

Because PCR assays are not quantitative, it is impossible to determine if a positive pool contains one or more than one infected mosquito. However, it is possible to state that pools that produce negative results do not contain any infected mosquitoes. This observation has been used to develop a method to calculate the prevalence of infection in the vector population, based upon the size and number of negative pools. This algorithm has been incorporated into a simple computer program, called *Poolscreen*, which is available to interested investigators by contacting Dr Thomas Unnasch¹.

In addition to the development of practical ways to employ the PCR detection techniques in specific field situations, additional research is needed to develop and apply similar PCR assays specific for *B. malayi* and *B. timori* (without cross-reactions to other enzootic *Brugia* species) for xenomonitoring prevalence

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via vectors. Also, for measuring transmission potential and monitoring the impact of transmission control, specific PCR assays that detect only the L3 infective larvae would be useful.

5.3 Sampling for xenomonitoring of LF prevalence in human populations

Within an LF elimination programme, **xenomonitoring** is the use of wild-caught mosquitoes to detect microfilaraemia in a community. Clearly the 'sampling frame' for mosquito collection is of critical importance. Optimally sampling will be geared to collecting mosquitoes that have recently taken a human blood meal. For this reason, xenomonitoring is best suited to areas where there are vectors which rest indoors after blood-feeding. Hence xenomonitoring will be suitable for the whole of the Americas, Africa and India, for example, where the vectors of lymphatic filariasis are endophilic *Cx. quinquefasciatus*, *Anopheles* or *Mansonia* (Table 2). Even in LF zones with diurnally active vectors, it may be possible to sample indoor-resting *Culex* blood-fed females for xenomonitoring, but the validity of this needs to be verified.

The sampling unit will be the household (or cluster of houses) within the sentinel areas/sites. Sampling of indoor-resting mosquitoes will require sampling of considerable numbers of houses for which aspirator collections would be most suitable. During the initial period of MDA, survey samples of perhaps 1000 mosquitoes will be required, subsequently rising to probably 10,000 per survey. The precise numbers of households and of mosquitoes per household will change as the programme develops, with sampling rates conforming to GPELF guidelines (WHO, 1999b,c). Initially we recommend collection of 10-50 mosquitoes per house and a minimum of 100-250 households per sentinel site, per sample period, with typically one sample point per year.

Xenomonitoring will not be suitable where there is a well-integrated, effective vector control programme, since this depletes the availability of blood-fed adult mosquitoes. The interpretation of xenomonitoring requires validation against direct human blood surveys, using ICT tests and night blood films in the different epidemiological settings. Countries well suited for these evaluation and validation studies must be identified and enlisted for collaboration in a multi-centre exercise.

Sentinel sites for xenomonitoring should be selected to represent the ELF implementation units, see section 7 of Programme Manager's guidelines (WHO, 2000 b,c). These sites can be selected randomly, or on the basis of factors such as areas of high prevalence and/or with high vector densities: two sentinel sites for each MDA district of the ELF programme

For base-line LF prevalence data in each site, using standard methods (WHO, 1987), examine at least 500 individuals for microfilaraemia and filarial disease before each round of MDA. Calculate the microfilaria prevalence and mean microfilaria density for the people at each sentinel site.

For each sentinel site, mosquito samples (collected as above) should be processed by the following simple procedures:

- sort and count by vector species;
- dry in the sun;
- store in tubes labelled by locality, household, date, species etc;
- pool by household for PCR assays.

After reducing prevalence below 1% detected by xenomonitoring, and/or following five yearly rounds of MDA, survey 3000 children/unit with ICT cards (and perhaps other confirmation tests) to validate successful outcome.

Table 2. Mosquito Sampling for Xenomonitoring

ATP = annual transmission potential (total L3 from infective bites/person/year)

VECTOR	BITING PEAK	SAMPLING PRIORITY & COLLECTION METHOD	
		XENODIAGNOSIS Freshly blood-fed female mosquitoes	TRANSMISSION RISK (ATP)
<i>Culex</i>	Night	Indoors: early morning aspirator collection from resting-sites (e.g. bedrooms)	Light trap + bednet
<i>Anopheles</i>	Night		
<i>Mansonia</i>	Night		
<i>Ochlerotatus</i>	Day	Outdoors: late afternoon aspirator collection from resting-sites outdoors (e.g. tree-trunks, box-shelters)	Gravid traps
<i>Aedes (Finlaya)</i>			
<i>Aedes (Stegomyia)</i>	Day	or by vacuum collector from vegetation	* landing (not biting) on human bait

* human bait collection discouraged for reasons of ethics and safety

6. Suggestions for research on filaria vectors

During this consultation, on behalf of the GPELF, many uncertainties were perceived to justify further investigations on LF vector control, ecology and sampling. Specially prepared working papers (Annex 2) adequately summarised the available knowledge, but also pointed to gaps of information and methods not available from current experience nor from the background documents, references and sources (Annex 3). As these issues are not covered by TDR, the following topics and questions were recorded as worthy of attention to assist the GPELF in specific ways, in addition to the Main Recommendations of this consultation (Section 8).

6.1 Studies where lymphatic filariasis is transmitted by aedines

- for control of specific aedine vectors (species of *Aedes* or *Ochlerotatus*), trials of a wide range of control methods should aim to determine which, if any, can effectively reduce LF transmission; this is particularly needed for ecotopes where the vectors breed in crab-holes (e.g. insecticidal baits to be foraged by land-crabs) or in water-filled plant axils and tree-holes (e.g. spraying of vegetation with larvicides).
- in LF zones with diurnally active vectors which are difficult/dangerous to collect, it may be possible to sample indoor-resting *Culex* blood-fed females for xenomonitoring, but the validity of this has to be verified;
- mosquito trapping and sampling methods (e.g. CO₂ baited traps, odour-baited vacuum traps, power-aspirator collections) should be evaluated and standardized as alternatives to human bait and landing collections for xenomonitoring in zones with day-active vectors of sub-periodic LF.

6.2 Studies where lymphatic filariasis is transmitted by *Anopheles*

To investigate the impact of ITN programmes on LF, as an RBM by-product, WHO/AFRO plans to coordinate 16 countries participating in a multi-centre study with standardized protocol (in preparation). After measuring base-line LF prevalence, prior to MDA, each country will study longitudinal epidemiological indicators of LF in 2 or 3 districts with good ITN coverage. Assuming that ITNs show beneficial impact on LF as well as malaria, this study could demonstrate several favourable outcomes:

- Rational utilization of resources (human & materials)
- Avoidance of duplication of IEC & implementation
- Social mobilization by appreciation of reduced mosquito densities & disease
- Community acceptance leading to improved compliance
- Partnership approach (community, MoH, NGOs etc)
- Cost recovery/revolving funds
- Decentralised health policy.

Evaluation is an inbuilt component in this approach, including ITN effects on other vector-borne diseases (e.g. arboviruses) and human ectoparasites (e.g. head-lice) in addition to LF and malaria. It is also intended to undertake systematic financial evaluation, so as to make cost-effectiveness analysis of these ITN programmes in Africa. Similar exercises may be useful for co-endemic countries of the Papuan sub-region (i.e. Indonesia, Philippines, PNG, Vanuatu) in SEARO & WPRO Regions of the WHO. This would be particularly appropriate for communities with *B. timori* in East Timor (where

many agencies are currently active) and the Indonesian Nusa Tenggara Timur (Flores, West Timor, etc.).

6.3 Studies where lymphatic filariasis is transmitted by *Culex*

- Analyse, in typical settings, the incremental cost-effectiveness of combining *Culex* control with MDA, for both short-term acceleration of ELF and to minimise the risk of filariasis resurgence thereafter;
- Measure the impact on LF transmission potential (and on LF endemicity in conjunction with MDA) of insecticide-treated bednets and curtains, and of mosquito-proof house modifications, e.g. screening of windows and eaves, installation of ceilings for bedrooms etc;
- Characterize (district-wise) the relative productivity of major breeding-sites of vector *Culex* where these are inadequately known (e.g. Guyana, Haiti, India, Indonesia) to facilitate rational judgements on appropriate vector control interventions (e.g. to apply EPBs or not);
- Assess the practicality (logistics, economics, acceptability) of collecting and shredding waste polystyrene (SWAP) and its routine application for control of *Culex* breeding in pit latrines and soakage pits in places where upgrading the sanitation system is impractical;
- Investigate the role of *Cx. quinquefasciatus* in LF transmission across Africa; how widespread is its "refractoriness" (non-usceptibility) to *W. bancrofti*, as reported in West Africa; how and where might this mechanism be employed for genetic control?
- Evaluate the relative operational impact of the IGR pyriproxyfen in comparison with other methods (i.e. *B. sphaericus*, EPBs, OPs, oils, sanitation) of suppressing *Culex* in each major type of breeding-site.
- Develop social mobilization and communications for combined control of vectors of various diseases (malaria, LF, dengue) and of nuisance biting.
- Where RBM activities are implemented in co-endemic areas, measure the collateral effects of ITNs (and/or IRS) on LF incidence/prevalence, and analyse the cost-benefits of multi-disease impact (reinforces 6.2 above).

6.4 Studies where lymphatic filariasis is transmitted by *Mansonia*

- In situations with periodic (non-zoonotic) *B. malayi*, assess the relative proportions of transmission by *Anopheles/Mansonia*, so as to interpret their degrees of importance and control implications (c.f. sections 4.2. 4.3 & 6.2);

- In situations with sub-periodic *B. malayi*, identify/assess the zoonotic origins and implications for control and obstacles for ELF.
- For Brugian filariasis control apart from environmental management, develop the use and assess the efficacy of house-screening, ITNs and personal protection measures (e.g. use of repellents when working in exposed situations) to reduce vector-man contact, particularly needed against zoonotic strains that cannot be eliminated by MDA.

7. General discussion and global issues

To provide the GPELF with the option of employing appropriate vector control tools, selectively targeted in situations where MDA may need augmentation, this consultation reviewed the state-of-the-art and current knowledge on proven techniques for controlling mosquitoes responsible for vectoring each type of lymphatic filariasis. The working papers and presentations gave convincing evidence that many LF vector scenarios can be tackled effectively, but the cost-benefits are seldom clear and need further analysis in most cases. Even so, there are widespread opportunities for LF vector control to have multi-disease impact, especially with *Anopheles* control for RBM, and also *Aedes* control for dengue fever and dengue haemorrhagic fever prevention.

Important advances have been made, on various scales, demonstrating the power and value of vector control in arresting filariasis transmission in most — but not all — circumstances. Vector management activities can generally be integrated in two ways: by complementary implementation of mosquito control practices against both larvae and adults (Table 1); also by adding effective vector control operations to the range of public health programmes also underway. Integrated vector control programmes are rarely well resourced in developing countries where LF has to be eliminated. Given the rapidity of upscaling MDA for the ELF in each country, it is essential for limited resources to be concentrated on the MDA and other priorities and not dissipated on vector control practices unless there is strong evidence of their cost-effectiveness to expedite ELF goals.

The following key points were recognized:

- Environmentally acceptable and effective control methods are available for use against mosquitoes that transmit lymphatic filariasis in the endemic countries in specific eco-epidemiological situations.
- More than half the global LF burden is vectored by the tropical house mosquito *Cx. quinquefasciatus* breeding in polluted water (e.g. latrine pits, stagnant drains) that can be minimized by simple sanitation improvements or application of expanded polystyrene beads to prevent breeding in select locations.

- Wherever malaria and LF are co-endemic, *Anopheles* control practices (mainly IRS and use of ITNs) tend to have greater impact on LF transmission, to the point that LF has sometimes been eliminated as a side-effect of malaria vector control. This vector control synergy should be further evaluated and optimised.
- *B. timori* is restricted to a few islands and has only one known vector, *An. barbirostris*, that is amenable to standard malaria vector control measures (section 3.2). Given the political will and resources, MDA could be augmented by vector control to interrupt *B. timori* transmission in Flores and Timor islands (following the example of *W. bancrofti* elimination from the Solomon Islands).
- Special problems confront the control of aedine vectors of *W. bancrofti* sub-periodic and aperiodic strains (*Oc. niveus* in some Asian forest habitats; *Ae. polynesiensis* and others in Polynesia; *Oc. samoanus* in Samoa; *Oc. poicilius* in The Philippines; *Oc. vigilax* in New Caledonia), due to their inaccessible breeding sites and aggressive biting behaviour (outdoors at times when people cannot be readily protected). Currently available methods (source reduction, personal protection, larviciding, biological control) do not give satisfactory results against these vectors. However, the combined burden of filariasis transmitted by these vectors is relatively small and MDA is going well in most of the countries involved (notably PacELF).

Given these important eco-epidemiological differences, the potential contribution of vector control to the elimination of LF is likely to differ in relation to the scale and likely impact of the intervention; the cost-effectiveness and cost-benefit of the intervention; and the availability of appropriate vector control methods in space and time. Moreover, the contribution will differ in relation to community microfilaria load, vector/parasite combinations and force of infection, and insecticide susceptibility of the vector species.

In addition to the technical considerations, the role of vector control in national ELF programmes will be determined by other factors, including:

- Human and financial resources available to national VC programme(s)
- Coordination between LF programme managers and VC programmes at central and district levels
- Capacity to integrate an acceptable and effective VC element into LF programmes which are expanding more rapidly than the human and financial resources available to the vector control element of GPELF
- Ability to mobilize communities when appropriate
- Integrating role of NGOs and the ITN community
- Efficiency of the monitoring and evaluation systems

As *W. bancrofti* is co-endemic with malaria across tropical Africa and is transmitted by the same *Anopheles* vectors in rural areas of most African countries, the group recommended that African national ELF programmes should seek ways of cooperation with RBM to scale-up ITN coverage in LF endemic districts. Given the RBM 2005 target of covering 60% of vulnerable groups there is ample opportunity for developing this synergy in most malarious countries. Such an approach should be mediated by respective national programme managers, in cooperation with endemic district health teams. This combined effort should be evaluated and documented, as in the pilot studies being undertaken by AFRO vector control unit in 16 countries (see section 3.2). Thus LF and RBM together provide a common focus for national vector control staff. These activities should be seen as closely linked to national health financing, donor input and the opportunity for support from the Global Fund for Health interventions.

With regard to xenomonitoring of LF prevalence by application of PCR assays to blood-fed mosquitoes — before, during and after MDA — this promising new approach requires field trials and standardization for each vector in comparison with ICT tests and other base-line LF data.

8. Main conclusions and recommendations

- 1) Whereas MDA can be generally expected to reduce or interrupt transmission of LF, the goal of GPELF could be achieved more rapidly through additional vector control in some situations. Where MDA coverage rates or duration are limited, the added impact of effective vector control can most usefully augment the GPELF, especially where uncontrolled and efficient vector populations might sustain transmission or contribute to its resurgence.
- 2) National ELF programme managers should establish links with other vector-borne disease control programmes (e.g. RBM, dengue), wherever they exist, in order to maximise synergies and use of limited resources, including social mobilization and community-based approaches to their delivery.
- 3) Where *W. bancrofti* is mainly vectored by *Culex* (this is the most widespread vector-parasite combination), transmission should be reduced by improved sanitation and, where appropriate in flooded pits, application of expanded polystyrene beads.
- 4) Where *Brugia* or *W. bancrofti* are mainly vectored by anophelines, the risks of transmission can be reduced by use of insecticide treated materials (e.g. pyrethroid-impregnated bednets) and/or indoor residual spraying (IRS) and appropriate housing design/modification.

- 5) Where *W. bancrofti* is mainly vectored by *Aedes*, the risks of transmission should be reduced by personal and household protection and, where feasible, by elimination of nearby breeding sites.
- 6) Where *Brugia* or *W. bancrofti* are mainly vectored by *Mansonia*, the risks of transmission should be reduced by personal and household protection and, where feasible, elimination of the floating vegetation on which the aquatic stages are entirely dependent.
- 7) As the use of indoor residual spraying (IRS) and bednets (especially ITNs) for malaria control also impact on filariasis, these interventions should be implemented with optimal coverage and evaluated for control of both diseases in co-endemic areas.
- 8) Participants in the consultation collectively endorsed, in principle, the draft global framework for vector control (WHO, 2001d), in response to WHA 42.31 and 50.13, to optimize synergies of vector control for each national ELF programme to achieve its goal in response to WHA 50.29.
- 9) To augment the GPELF, vector control activities are practical in most epidemiological settings. The value of environmental management should be emphasised as the underlying principle of such measures.
- 10) Local cost-benefit analyses of existing and potential filariasis vector control activities should be carried out in a representative range of situations, so that decisions based on cost-efficacy may justify the value of specific vector control practices for the GPELF — and the value to the GPELF of such interventions by other agencies pursuing operations that impact (positively or negatively) on LF vectors.
- 11) The standardised PCR protocol for detecting *W. bancrofti* filarial infection (DNA) in mosquitoes should be finalised and evaluated for GPELF xenomonitoring in parallel with antigen and microfilaria prevalence.
- 12) Similar PCR assays specific for *B. malayi* and *B. timori* are needed for xenomonitoring prevalence via vectors. Also for measuring transmission potential, specific PCR assays that detect only the L3 infective larvae would be useful.
- 13) The status and role of each LF vector species should be kept under review in all LF endemic zones (c.f. Annexes 4 & 5), in order to improve the targeting and cost-benefits of LF vector control operations that may be considered useful/wasteful in support of the GPELF.

- 14) For standardised sampling of mosquitoes to be used for xenomonitoring, indoor-resting collection of blood-fed females is considered most appropriate. Such samples of *Anopheles*, *Culex* or *Mansonia* can be readily obtained in most situations, with bloodmeals representing the human population in the majority of epidemiological settings.

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Annex 2. List of working papers

1. The Mosquito PCR Diagnostic Project to develop a rapid assessment tool for the detection of *W.bancrofti* infected mosquitoes
S. Williams, T. Unnasch, E. Ottesen
2. PCR Detection of Lymphatic Filarial Parasites in Mosquitoes
Report of a Meeting, 15-16 November 2001, LF Support Center, Emory University, USA
3. Field application of PCR assays for monitoring *Wuchereria bancrofti* infection in Africa
R. Ramzy
4. Potential role of vector control in the Global Programme to Eliminate Lymphatic Filariasis
M. Bockarie
5. The PacELF Programme: will mass drug administration be enough?
T. Burkot and K. Ichimori
6. Operational issues in control of *Brugia* vectors
Chang Moh Seng
7. Cost-effectiveness of vector control and mass drug administration, alone or in combination
K. Krishnamoorthy & R. Reuben
8. Vector control, lymphatic filariasis, health sector policy and strategic issues
D. Molyneux
9. Impact of insecticide treated materials on filariasis transmission by different vectors
E.M. Pedersen & D. Mukoko
10. Use of floating layers of polystyrene beads to control filaria vector *Culex quinquefasciatus* populations
C.F. Curtis, M. Malecela-Lazaro, R. Reuben & C.A. Maxwell
11. Biological control of vectors of filariasis and dengue with larvivorous fish, bacterial larvicides and copepods
F. Lardeux
12. *Wolbachia* as a potential tool for suppressing filariasis transmission
H. Townson
13. Issues and Comments on vector control synergies between RBM and GPELF in the African Region
L. Manga

14. Issues and Comments on vector control synergies between RBM and GPELF in the South-east Asian Region
C. Prasittisuk
15. Sampling protocols for estimating annual transmission potential (ATP)
P.K. Das
16. Limitation and facilitation in filariasis vectors and other aspects of the dynamics of transmission: the need for vector control against *Anopheles*-transmitted filariasis
G. Pichon
17. TDR's research strategy for lymphatic filariasis
H. Remme
18. Modelling lymphatic filariasis epidemiology, transmission and control
P.K. Das

Annex 3. Background documents, references and sources

Barnard, D.R. (2000). Repellent and toxicants for personal protection. Position paper, Global Collaboration for Development of Pesticides for Public Health. Document WHO/CDS/WHOPES/GCDPP/2000.5. 40 pp.

Bockarie, M.J., Tavul, L., Kastens, W., Michael, E. & Kazura, J.W. (2002). Impact of untreated bednets on prevalence of *Wuchereria bancrofti* transmitted by *Anopheles farauti* in Papua New Guinea. *Medical & Veterinary Entomology*, 16, 116-119.

Bögh, C., Pedersen, E. M., Mukoko, D. A. & Ouma, J. H. (1998). Permethrin-impregnated bednet effects on resting and feeding behaviour of lymphatic filariasis vector mosquitoes in Kenya. *Medical & Veterinary Entomology*, 12, 52-59.

Burkot, T.R., Garner, P., Paru, R., Dagoro, H., Barnes, A., McDougall, S., Wirtz, R.A., Campbell, G. & Spark, R. (1990). Effects of untreated bed nets on the transmission of *Plasmodium falciparum*, *P. vivax* and *Wuchereria bancrofti* in Papua New Guinea. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 84, 773-779.

Burkot, T. & Ichimori, K. (2002). The PacELF Programme: will mass drug administration be enough? *Trends in Parasitology*, 18, 109-115.

CDC (1993). Recommendations of the International Task Force for Disease Eradication. *Morbidity and Mortality Weekly Report*, 42, 1-38.

Chanteau, S., Luquiaud, P., Failloux, A. & Williams, S.A. (1994). Detection of *Wuchereria bancrofti* larvae in pools of mosquitoes by the polymerase chain reaction. *Transactions of the Royal Society of Tropical Medicine & Hygiene*, 88, 665-666.

Curtis, C.F. (1991). *Control of Disease Vectors in the Community*. Wolfe, London. 233 pp.

Curtis, C.F. & Feachem, R.G. (1981). Sanitation and *Culex pipiens* mosquitoes: brief review. *Journal of Tropical Medicine and Hygiene*, 84, 17-25.

Das, P.K., Sivagnaname, N. & Amalraj, D.D. (1997). A comparative study of a new insecticide impregnated fabric trap for monitoring adult mosquito populations resting indoors. *Bulletin of Entomological Research*, 87, 397-403.

Farid, H.A., Hammad, R.E., Hassan, M.M., Morsy, Z.S., Kamal, I.H., Weil, G.J. & Ramzy, R.M.R. (2001). Detection of *Wuchereria bancrofti* in mosquitoes by the polymerase chain reaction: a potentially useful tool for large-scale control programs. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 95, 29-32.

Feachem, R. (1983). *Sanitation and Disease: Health Aspects of Excreta and Wastewater Management*. John Wiley, Chichester.

Garrett-Jones, C. & Grab, B. (1964). The assessment of insecticidal impact on the malaria mosquito's vectorial capacity, from data on the proportion of parous females. *Bulletin of the World Health Organization*, 31, 71-86.

Kamal, I.H., Fischer, P., Adly, M., El Sayed, A.S., Morsy, Z.S., & Ramzy, R.M.R (2001). Evaluation of a PCR–ELISA to detect *Wuchereria bancrofti* in *Culex pipiens* from an Egyptian village with a low prevalence of filariasis. *Annals of Tropical Medicine & Parasitology*, 95, 833-842.

GPELF, the Global Programme to Eliminate Lymphatic Filariasis:
<http://www.filaria.org/>

Hairston, N.G. & De Meillon, B. (1968). On the inefficiency of transmission of *Wuchereria bancrofti* from mosquito to human host. *Bulletin of the World Health Organization*, 38, 935-941.

Lengeler, C., Cattani, J. & de Savigny, D., eds (1996). *Net Gain. A new method for preventing malaria deaths*. IDRC, Ottawa & WHO/TDR, Geneva. 189 pp.

Lengeler, C., Cattani, J. & de Savigny, D., eds (1997). *Un mur contre la malaria. Du nouveau dans la prevention des deces dus au paludisme*. IDRC, Ottawa & WHO/TDR, Geneva. 220 pp.

Lines, J.D., Curtis, C.F., Wilkes, T.J. & Njumka, K.J. (1991). Monitoring human-bait mosquitoes (Diptera: Culicidae) in Tanzania with light-traps hung beside mosquito nets. *Bulletin of Entomological Research* 81, 77-84.

Maxwell, C.A., Curtis, C.F., Haji, H., Kisumku, S., Thalib, A.I. & Yahya, S.A. (1990). Control of Bancroftian filariasis by integrating therapy with vector control using polystyrene beads in wet pit latrines. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 84, 709-714.

Maxwell, C.A., Mohammed, K., Kisumku, U. & Curtis, C.F. (1999). Can vector control play a useful role against bancroftian filariasis? *Bulletin of the World Health Organization*, 77, 138-143.

Michael, E. & Bundy, D.A.P. (1997). Global mapping of lymphatic filariasis. *Parasitology Today* 13, 472-476.

Michael, E., Bundy, D.A. & Grenfell, B.T. (1996). Re-assessing the global prevalence and distribution of lymphatic filariasis. *Parasitology* 112, 409-428.

Mukoko, D.A.N., Pedersen, E.M., Masese, N.N., Lindsay, S.W., Estambale, B. & Ouma, J.H. (2002). The effect of permethrin impregnated bednets on the transmission of Bancroftian filariasis in Kwale District, Coast Province, Kenya.

Nathan, M.B., Toney, S., Bramble, S. & Reid, V. (1996). Control of *Culex quinquefasciatus* in pit latrines, using shredded, waste polystyrene. *Annals of Tropical Medicine and Parasitology*, 90, 207-212.

Ottesen, E. A. (2000). The Global Programme to Eliminate Lymphatic Filariasis. *Tropical Medicine and International Health* 5, 591-594.

Ottesen, E.A., Duke, B.O.L., Karam, M. & Behbehani, K. (1997). Strategies and tools for the control/elimination of lymphatic filariasis. *Bulletin of the World Health Organization*, 75, 491-503.

Ramzy, R.M.R., Farid, H.A., Kamal, I.H., Ibrahim, G.H., Morsy, Z.S., Faris, R., Weil, G.J. & Williams, S.A. (1997). A polymerase chain reaction-based assay for detection of *Wuchereria bancrofti* in human blood and its mosquito vector in Egypt. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 91, 156-160.

RBM, the Roll Back Malaria partnership: <http://www.rbm.who.int>

Reiter, P. (1987). A revised version of the CDC gravid mosquito trap. *Journal of the American Mosquito Control Association*, 3, 325-327.

Reuben, R., Rajendran, R., Sunish, I.P., Mani, T.R., Tewari, S.C., Hiriyan, J., & Gajanana, A. (2001). Annual single dose diethylcarbamazine (DEC) plus ivermectin(IVR) for control of bancroftian filariasis: comparative efficacy with and without vector control. *Annals of Tropical Medicine and Parasitology* 95, 361-378.

Rozendaal, J.A. (1997). *Vector Control. Methods for Use by Individuals and Communities*. WHO, Geneva. xiii + 412 pp.

Samarawickrema, W.A., Sone, F., Self, L.S., Cummings, R.F. & Paulson, G.S. (1992). Distribution of breeding and control of the filariasis vector *Aedes samoanus* in leaf axils of *Pandanus* in Samoa. *Medical and Veterinary Entomology*, 17, 367-370.

Sasa, M. (1976). *Human Filariasis. A Global survey of epidemiology and control*. University of Tokyo Press. 819 pp.

Service, M. W. (1993). *Mosquito Ecology: Field Sampling Methods* (2nd edn.). Elsevier Applied Science, London and New York, 988 pp.

Southgate, B.A. (1984). Recent advances in the epidemiology and control of filarial infections including entomological aspects of transmission. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 78, 19-28.

Subramanian, S., Vanamail, P., Ramaiah, K.D., Pani, S.P. & Das, P.K. (1989). A single deterministic model for host-parasite relationship in *Wuchereria bancrofti* and its relevance to regulation of parasite in human host. *Indian Journal of Medical Research*, 89: 411-417.

Sunish, I.P., Rajendran, R., Mani, T.R., Munirathinam, A., Tewari, S.C., Hiriyan, J., Gajanana, A. & Satyanarayana, K. (2002). Resurgence in filarial transmission after withdrawal of mass drug administration and the relationship between antigenaemia and microfilaraemia - a longitudinal study. *Tropical Medicine and International Health*, 7: 59-69.

Webber, R.H. (1979). Eradication of *Wuchereria bancrofti* infection through vector control. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 73, 722-724.

Weil, G.J., Lammie, P.J. & Weiss, N. (1997). The ICT Filariasis Test: a rapid format antigen test for diagnosis of Bancroftian filariasis. *Parasitology Today*, 13, 401-404.

WHA 42.31. Disease vector control. Resolution 42.31 of the World Health Assembly, May 1989.

WHA 50.13. Promotion of chemical safety, with special attention to persistent organic pollutants. Resolution 50.13 of the World Health Assembly, May 1997.

WHA 50.29. Elimination of lymphatic filariasis as a public health problem. Resolution 50.29 of the World Health Assembly, May 1997.

WHO (1975). *Manual on Practical Entomology in Malaria*.

Part I. Vector Bionomics and Organization of Anti-Malaria Activities. 160pp.

Part II. Methods & Techniques. 191pp. World Health Organization, Geneva.

WHO (1977). The biometrical criteria for resettlement in the Volta Basin Onchocerciasis Control Programme Area (OCP). *Report of a Scientific Advisory Panel Working Group*. Document OCP/SAP/77.1.

WHO (1982). *Manual on environmental management for mosquito control, with special emphasis on malaria vectors*. WHO Offset Publication No. 66, 283 pp.

WHO (1984). Lymphatic Filariasis. Fourth Report of the WHO Expert Committee on Filariasis. WHO TRS 702, 112 pp.

WHO (1987). Control of Lymphatic Filariasis. A manual for health personnel. WHO, Geneva. 89 pp.

WHO (1988). *Environmental management for vector control*. Training & Information Materials on Vector Biology & Control. Slide Set Series. 90 slides + 40 pp.

WHO (1989). Geographical distribution of arthropod-borne diseases and their principal vectors. Document WHO/VBC/89.967. 134 pp.

WHO (1991). *Personal protection and community action for vector and nuisance control*. Training & Information Materials on Vector Biology & Control. Slide Set Series. 79 slides + 40 pp.

WHO (1992). Lymphatic Filariasis: the diseases and its control. Fifth Report of the WHO Expert Committee on Filariasis. WHO TRS 821. 71 pp.

WHO (1995). *Guidelines for dengue surveillance and control*. Western Pacific Education in Action Series No. 8, WHO/WPRO Manila. 104 pp.

WHO (1999a). Building Partnerships for Lymphatic Filariasis. Strategic Plan. September 1999. Document WHO/FIL/99.198. 64 pp.

WHO (1999b). Report of a WHO informal consultation on epidemiologic approaches to lymphatic filariasis elimination: initial assessment, monitoring, and certification. Atlanta, Georgia, USA, 2-4 September 1998. Document WHO/FIL/99.195. 35 pp.

WHO (1999c). Guidelines for certifying lymphatic filariasis elimination (including discussion of critical issues and rationale). Document WHO/FIL/99/197. 16 pp.

WHO (1999d). Prevention and control of dengue and Dengue Haemorrhagic Fever. WHO Regional Publication, SEARO No. 29. Delhi. 134pp.

WHO (2000a). Eliminate Filariasis: Attack Poverty. The Global Alliance to Eliminate Lymphatic Filariasis. Proceedings of the First Meeting, Santiago de Compostela, Spain, 4-5 May 2000. Document WHO/CDS/CPE/CEE/2000.5. 41 pp.

WHO (2000b). Preparing and implementing a national plan to eliminate lymphatic filariasis (in countries where onchocerciasis is not co-endemic). Document WHO/CDS/CPE/CEE/2000.15. 65 pp.

WHO (2000c). Preparing and implementing a national plan to eliminate lymphatic filariasis (in countries where onchocerciasis is not co-endemic). Document WHO/CDS/CPE/CEE/2000.16. 67 pp.

WHO (2000d). Strengthening implementation of the global strategy for dengue fever/dengue haemorrhagic fever prevention and control. Report of the informal consultation, 18-20 October 1999. WHO HQ Geneva. Document WHO/CDS/(DEN)/IC/2000.1. 21 pp.

WHO (2000e). *Health Systems: Improving Performance*. The World Health Report 2000. WHO Geneva. 215 pp.

WHO (2001a). Report of the Fourth WHOPES Working Group Meeting, Geneva, 4-5 December 2000. Review of: IR3535, KBR3023, (RS)-methoprene 20% EC, pyriproxyfen 0.5% GR, lambda-cyhalothrin 2.5% CS. Document WHO/CDS/WHOPES/2001.2. 102 pp.

WHO (2001b). Insecticide-Treated Netting Materials. Report of the third meeting of the Technical Support Network. Geneva 12-13 March 2001. Roll Back Malaria. Document WHO/CDS/RBM/2001.36.

WHO (2001c). Pacific Programme to Eliminate Lymphatic Filariasis (PacELF). Annual Meeting Report, Nadi, Fiji, 24-29 September 2001. WHO Office of the Representative in the South Pacific, Suva, Fiji. 32 pp.

WHO (2001d). Draft Global Strategic Framework for Vector Control, 4pp. Annex to Report of the Meeting with WHO Regional Advisors, Geneva, 11-13 June 2001.

WHOPES, the World Health Organization Pesticides Evaluation Scheme: <http://www.who.int/ctd/whopes>

Witt, C. & Ottesen, E.A. (2001). Lymphatic filariasis: an infection of childhood. *Tropical Medicine & International Health*, 6, 582-606.

Zahar, A.R., King, M. & Chow, C.Y. (1980). A review and annotated bibliography on subperiodic bancroftian filariasis with special reference to its vectors in Polynesia, South Pacific. WHO/AFRO Manila, Philippines. 491 pp.

Zhong, M., McCarthy, J., Bierwert, L., Lizotte-Waniewski, M., Chanteau, S., Nutman, T.B., Ottesen, E. & Williams, S.A. (1996). A polymerase chain reaction assay for detection of the parasite *Wuchereria bancrofti* in human blood samples. *American Journal of Tropical Medicine and Hygiene*, 54, 357-363.

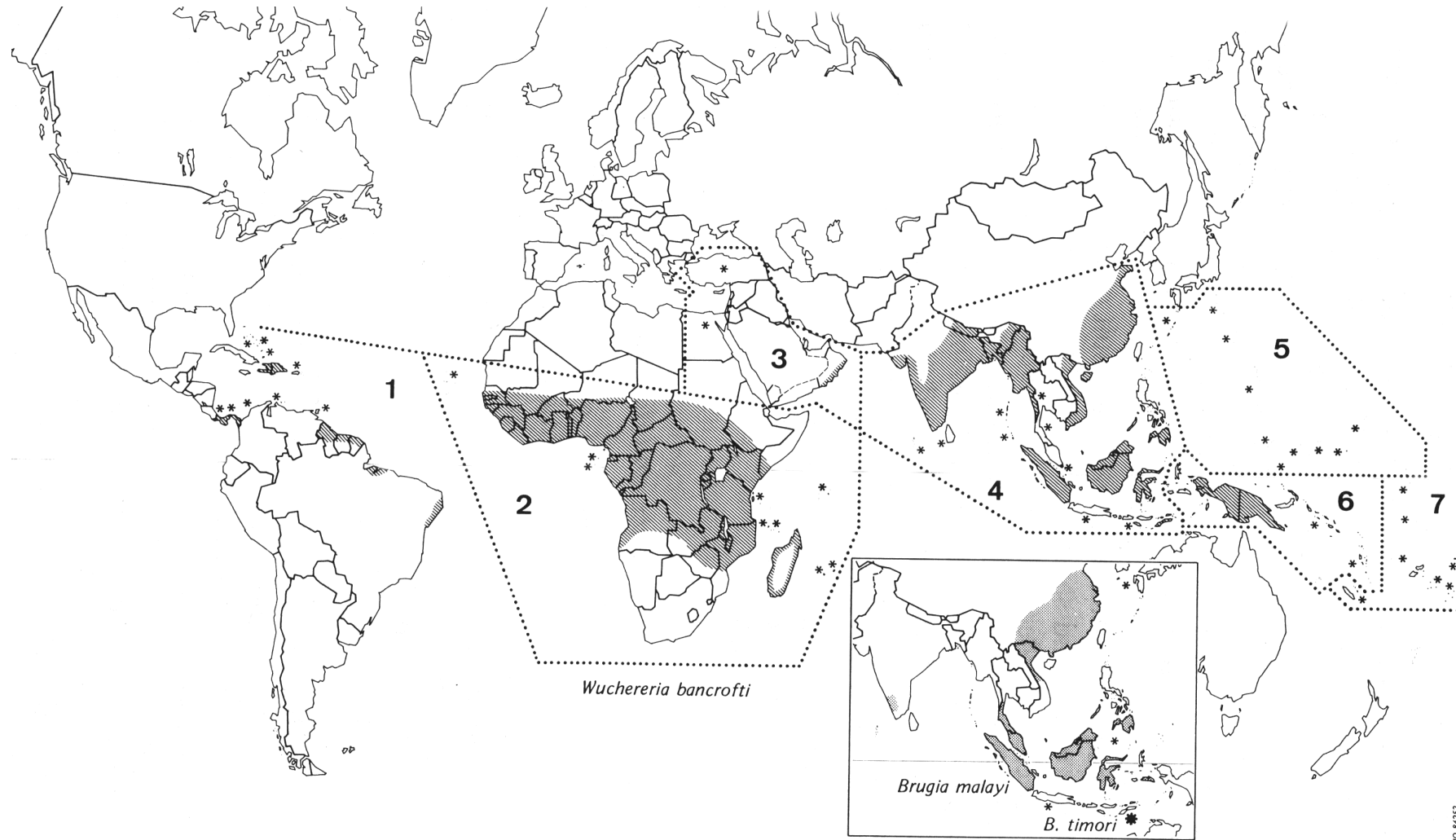
Annex 4. Mosquito vectors of lymphatic filariasis, based on published reports for LF epidemiological regions (See map, Fig. 2) with contrasted LF types due to different vector characteristics. Species names in parenthesis are those regarded as no longer involved in LF transmission: square brackets = LF eliminated from species range; wavy brackets = species eliminated from LF range; curved brackets = species doubtfully/rarely implicated in LF transmission. List updated from documents previously issued by WHO (1984, 1989, 1992). For mosquito nomenclature and taxonomy see <http://wrbu.si.edu>

Filaria type	Endemic Region (map zone number)	Vector species	
		Major and widespread	Local or subsidiary
<i>Brugia malayi</i> periodic	(4) South Asia	<i>Anopheles (Anopheles) barbirostris</i> <i>Anopheles (Anopheles) campestris</i> <i>Anopheles (Anopheles) donaldi</i> <i>Mansonia (Mansonioides) annulata</i> <i>Mansonia (Mansonioides) annulifera</i> <i>Mansonia (Mansonioides) uniformis</i>	[<i>Anopheles (Anopheles) anthropophagus</i>] [<i>Anopheles (Anopheles) kweiyangensis</i>] <i>Anopheles (Anopheles) nigerrimus</i> [<i>Anopheles (Anopheles) sinensis</i>] <i>Mansonia (Mansonioides) bonneae</i> <i>Mansonia (Mansonioides) dives</i> <i>Mansonia (Mansonioides) indiana</i> [<i>Ochlerotatus (Finlaya) kiangsiensis</i>] [<i>Ochlerotatus (Finlaya) togoi</i>]
<i>Brugia malayi</i> sub-periodic	(4) South Asia	<i>Mansonia (Mansonioides) annulata</i> <i>Mansonia (Mansonioides) bonneae</i> <i>Mansonia (Mansonioides) dives</i>	<i>Coquillettidia (Coquillettidia) crassipes</i> <i>Mansonia (Mansonioides) uniformis</i>
<i>Brugia timori</i> periodic	(4) Flores, Timor	<i>Anopheles (Anopheles) barbirostris</i>	
<i>Wuchereria bancrofti</i> periodic	(1) Americas	<i>Culex (Culex) quinquefasciatus</i>	(<i>Anopheles (Nyssorhynchus) albimanus</i>) { <i>Anopheles (Nyssorhynchus) aquasalis</i> } { <i>Anopheles (Nyssorhynchus) darlingi</i> } (<i>Mansonia (Mansonia) titillans</i>) (<i>Ochlerotatus (Ochlerotatus) scapularis</i>) (<i>Ochlerotatus (Ochlerotatus) taeniorhynchus</i>)

	(2) Afrotropical	<i>Anopheles (Cellia) funestus</i> <i>Anopheles (Cellia) gambiae</i> <i>Culex (Culex) quinquefasciatus</i>	<i>Anopheles (Cellia) arabiensis</i> <i>Anopheles (Cellia) hancocki</i> <i>Anopheles (Cellia) melas</i> <i>Anopheles (Cellia) merus</i> <i>Anopheles (Cellia) nili</i> <i>Anopheles (Cellia) pauliani</i> (<i>Anopheles (Cellia) wellcomei</i>) (<i>Culex (Culex) antennatus</i>) (<i>Mansonia (Mansonioides) uniformis</i>)
	(3) Middle East	<i>Culex (Culex) pipiens molestus</i> <i>Culex (Culex) quinquefasciatus</i>	<i>Culex (Culex) antennatus</i>
	(4) South Asia	<i>Culex (Culex) quinquefasciatus</i>	[<i>Anopheles (Anopheles) anthropophagus</i>] <i>Anopheles (Anopheles) barbirostris</i> <i>Anopheles (Anopheles) donaldi</i> [<i>Anopheles (Anopheles) kweiyangensis</i>] <i>Anopheles (Anopheles) letifer</i> <i>Anopheles (Anopheles) leucosphyrus</i> <i>Anopheles (Anopheles) nigerrimus</i> <i>Anopheles (Anopheles) sinensis</i> <i>Anopheles (Anopheles) vagus</i> <i>Anopheles (Anopheles) whartoni</i> <i>Anopheles (Cellia) aconitus</i> <i>Anopheles (Cellia) balabacensis</i> <i>Anopheles (Cellia) dirus</i> <i>Anopheles (Cellia) flavirostris</i> <i>Anopheles (Cellia) jeyporiensis</i> <i>Anopheles (Cellia) maculatus</i> { <i>Anopheles (Cellia) minimus</i> } <i>Anopheles (Cellia) philippinensis</i> <i>Anopheles (Cellia) subpictus</i> <i>Anopheles (Cellia) tessellatus</i> (<i>Culex (Culex) bitaeniorhynchus</i>) (<i>Culex (Culex) sitiens</i>) <i>Ochlerotatus (Finlaya) poicilius</i>

	(5) Far East	<i>Culex (Culex) quinquefasciatus</i>	[<i>Anopheles (Anopheles) bancrofti</i>]
	(6) Papuan	<i>Anopheles (Cellia) farauti</i> <i>Anopheles (Cellia) koliensis</i> <i>Anopheles (Cellia) punctulatus</i>	(<i>Culex (Culex) annulirostris</i>) (<i>Culex (Culex) bitaeniorhynchus</i>) [<i>Culex pipiens pallens</i>] <i>Mansonia (Mansonioides) uniformis</i> <i>Ochlerotatus (Finlaya) kochi</i>
<i>Wuchereria bancrofti</i> sub-periodic	(4) Nicobar, Thailand	<i>Ochlerotatus (Finlaya) niveus</i> <i>Ochlerotatus (Finlaya) harinasutai</i>	
	(7) Polynesia	<i>Aedes (Stegomyia) polynesiensis</i>	<i>Aedes (Stegomyia) cooki</i> <i>Aedes (Stegomyia) horrescens</i> <i>Aedes (Stegomyia) kesseli</i> <i>Aedes (Stegomyia) marshallensis</i> <i>Aedes (Stegomyia) pseudoscutellaris</i> <i>Aedes (Stegomyia) rotumae</i> <i>Aedes (Stegomyia) tabu</i> <i>Aedes (Stegomyia) tongae</i> <i>Ochlerotatus (Finlaya) fijiensis</i> <i>Ochlerotatus (Finlaya) oceanicus</i> <i>Ochlerotatus (Finlaya) samoanus</i> <i>Ochlerotatus (Finlaya) tutuilae</i> <i>Ochlerotatus (Finlaya) upolensis</i> <i>Ochlerotatus (Ochlerotatus) vigilax</i>

Fig. 2 Mosquito vectors of lymphatic filariasis based on published reports for LF epidemiological regions



Annex 5. Global proportions of lymphatic filariasis vectors

- A. Crude estimates of global proportions of LF vectors in relation to LF disease burden, expressed as lost disability-adjusted life years (DALYs x 1000), split by WHO Region (WHO, 2000e) (see map, fig. 3).

Region	DALYs	<i>Anopheles</i>	<i>Culex</i>	aedine	<i>Mansonia</i>
AFRO	1834	1651	183	0	0
AMRO	8	0	8	0	0
EMRO	11	1	10	0	0
SEARO	2788	250	2370	28	140
WPRO	278	28	222	14	14
Total	4918	1930	2793	42	154
Proportion	100%	39%	57%	1%	3%

Notes:

Assumptions of vector proportions determined after the consultation by discussion among expert participants:

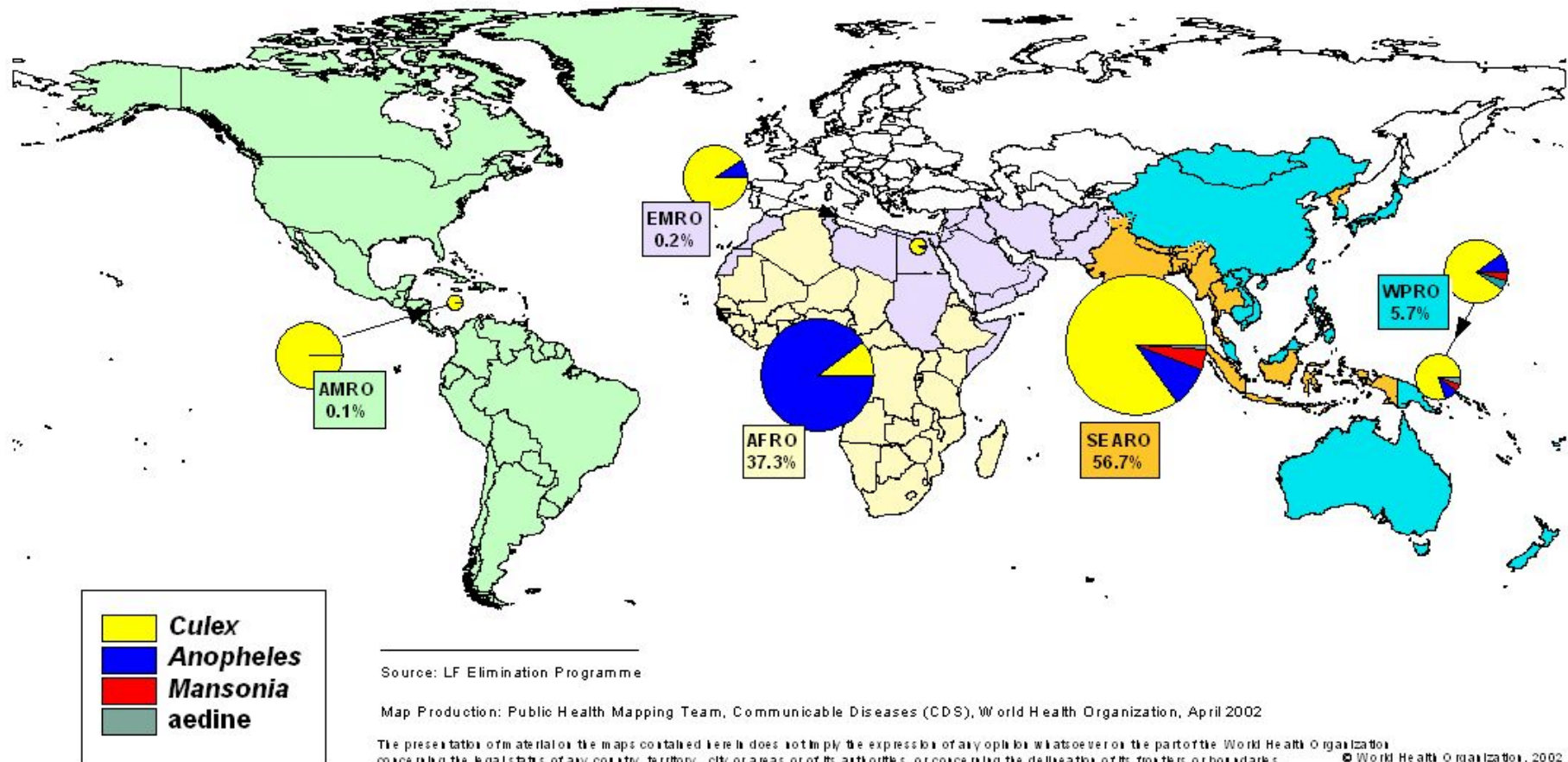
AFRO assumes 90% *Anopheles*, 10% *Culex* vectors of *W. bancrofti*.

EMRO assumes 10% *Anopheles*, 90% *Culex* vectors of *W. bancrofti*.

SEARO assumes 10% *Brugia* comprising 5% *Anopheles*, 5% *Mansonia* transmission; 90% *W. bancrofti* comprising 1% *Aedes*, 4% *Anopheles*, 85% *Culex* transmission.

WPRO assumes 5% *Brugia/Mansonia*; 5% *W. bancrofti/aedines*; 10% *W. bancrofti/Anopheles*; 80% *W. bancrofti/Culex*.

Fig. 3 Regional proportions (%) of LF transmitted by different vectors based on WHO Regional estimates of DALYs lost



B. Lost DALYs (x 1000) due to lymphatic filariasis and other major diseases transmitted by arthropods and/or caused by helminths, per WHO Region (WHO, 2000e). * M = Millions. X = present but none included by WHO (2000e).

Disease	AFRO	AMRO	EMRO	EURO	SEARO	WPRO	TOTAL	%
Malaria	36,838	76	2,774	2	3,071	2,235	44,998	71.4
Lymphatic filariasis	1,834	8	11	0	2,788	278	4,918	7.8
Trypanosomiasis	1,991	678	56	0	0	0	2,724	4.3
Gut Nematodes	860	294	149	3	1,228	119	2,653	4.2
Leishmaniasis	256	50	210	X	1,467	0	1,983	3.2
Schistosomiasis	1,637	133	98	15	18	30	1,932	3.1
Trachoma	434	0	237	0	62	505	1,239	2.0
Onchocerciasis	1,083	2	X	0	0	0	1,085	1.7
Jap encephalitis	0	0	1	0	218	828	1,046	1.7
Dengue	24	X	1	0	440	X	465	0.7
Total DALYs x1000	44,957	1,241	3,537	20	9,292	3,995	63,043	100
Human Population*	616M	813M	485M	872M	1,508M	1,667M	5,961M	100