The PacELF programme: will mass drug administration be enough?

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The Pacific Programme to Eliminate Lymphatic Filariasis is a regional, mass drug administration-based campaign in 22 countries and territories with the aim of eliminating filariasis transmission and alleviating the suffering caused by *Wuchereria bancrofti.* The challenges to filariasis elimination campaigns based on mass drug-administration alone are reviewed in this article. These challenges together with the previous successes of mosquito control campaigns in eliminating filariasis from regions in the Pacific argue for inclusion of entomology components in the control of filariasis and the monitoring of filariasis elimination programs.

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The argument for an integrated campaign which includes entomology in the control and monitoring of the Pacific Programme to Eliminate Lymphatic Filariasis (PacELF) are discussed here with a summary of the progress to date.

A fifth of the world's population is at risk from lymphatic filariasis, with an estimated 120 million people infected. Lymphatic filariasis is caused primarily by *Wuchereria bancrofti* and *Brugia malayi*. The pathology resulting from lymphatic filariasis has profound social and economic repercussions with 43 million infected people officially recognized as being disabled [1]. In the Pacific, an estimated 1.8 million people were infected with *W. bancrofti* in 1997, accounting for a prevalence of 29% [2].

Recently, lymphatic filariasis was identified by the International Taskforce for Disease Eradication (ITDE) as one of six diseases with the potential for eradication [3]. This assessment was based on the absence of animal reservoirs and the availability of new tools for surveillance and control of the disease [4]. New surveillance tools included the development of polymerase chain reactions (PCR) for detecting worms in mosquitoes [5] and, more importantly, the development of rapid antigen-detection tests such as the immunochromatographic test (ICT) for identifying infections in humans [6]. The ICT was particularly noteworthy because it eliminated the need for night-time surveys for periodic filariasis.

For control of filariasis, combinations of drugs are now being used, in particular, the combination of diethylcarbamazine (DEC) and albendazole which eliminates 99% of microfilariae (Mf) for one year (compared with DEC alone which eliminates 90% of Mf for a year) [4]. This drug combination became economically viable following the generous donation of albendazole by GlaxoSmithKline for use in filariasis elimination programmes [7].

Furthermore, new control measures to interrupt transmission of filariasis by mosquitoes were developed, including the use of insecticide-impregnated bednets against night-time biting mosquitoes, biocides and polystyrene beads against larval mosquitoes.

Based on these developments, in 1997, the World Health Assembly adopted Resolution WHA50 29, which called for the elimination of lymphatic filariasis as a global health problem. This worldwide filariasis elimination programme is the first elimination programme based on drugs rather than on vaccines or behaviour modification [3]. In March 1999, consecutive meetings between the Ministers and Directors of Health of Pacific Island countries and territories endorsed a resolution to develop and implement a comprehensive strategy to eliminate lymphatic filariasis from the Pacific. Following this resolution, PacELF was formed [8] with assistance from the Secretariat of the Pacific Community (funded by the Australian Agency for International Development) and the WHO. PacELF is responsible for the co-ordination of antifilariasis programmes in the following Pacific island countries and territories: American Samoa, Cook Islands, Federated States of Micronesia, Fiji, French Polynesia, Guam, Kiribati, Marshall Islands, Nauru, New Caledonia, Niue, Northern Mariana Islands, Palau, Papua New Guinea (PNG), Pitcairn Island, Samoa, Solomon Islands, Tonga, Tokelau Islands, Tuvalu, Vanuatu, and Wallis and Futuna. The twin goals of PacELF are to stop transmission of filariasis and to alleviate the suffering caused by the disease.

The primary strategy of PacELF is mass drug-administration (MDA) of DEC (6 mg kg^{-1} body weight and albendazole (400 mg per person) in a single, annual dose with health education and clinical care of infected cases. Pacific island countries, particularly Samoa and French Polynesia, have a long history of MDA campaigns using DEC to control lymphatic filariasis. In 1999, Samoa became the first Pacific Island country to implement the PacELF strategy using DEC plus albendazole. In the same year, Nigeria and Egypt also began their filariasis elimination programs. In 2000, French Polynesia, Vanuatu, Niue and American Samoa began their MDA campaigns and by 2002, 13 Pacific Island countries will have begun the PacELF MDA regimen.

Whereas the small size of most Pacific island countries simplifies the logistics of implementing the MDA-based elimination campaign, the frequent travel of Pacific islanders between and within countries requires co-ordination of the campaign among all countries in the region. For example, Mf

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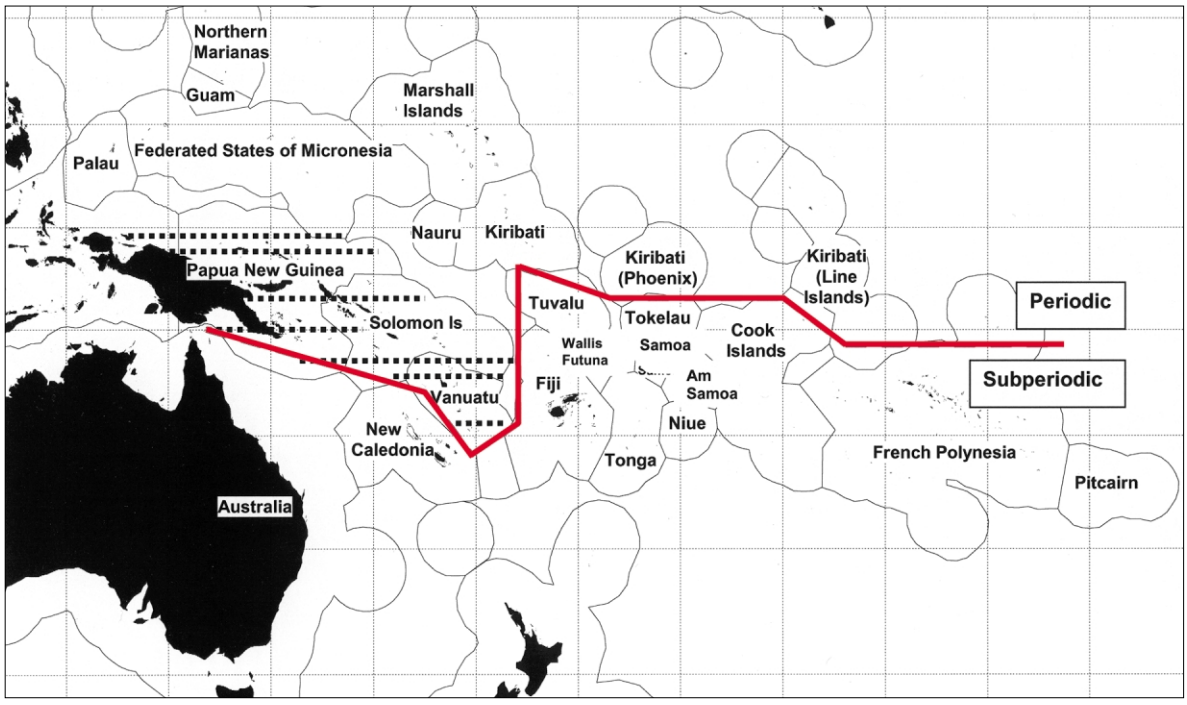

Fig. 1. Epidemiology of the Pacific island countries and territories participating in Pacific Programme to Eliminate Lymphatic Filariasis (PacELF) (Australia and New Zealand are not PacELF countries). The red solid line separates areas of periodic filariasis (north of the line) from areas with subperiodic filariasis (south of the line). Anopheline transmission (either historical or present) occurs only in the area denoted by the black dotted lines. Transmission by *Culex quinquefasciatus* occurs thoughout the Pacific, and *Aedes* and *Ochlerotatus* are vectors in the non-anopheline areas.

prevalence rates increased in some Samoan villages after DEC-based MDA treatment as a result of people movement, indicating that the mobility of a human population can threaten filariasis elimination [9]. In a PNG study, 39% of all migrants were positive for Mf [10]. Hence, the simultaneous implementation of an elimination campaign in all geographic areas in the Pacific is a necessity.

Filariasis control programmes have a long history in the Pacific. The successes and failures of these earlier programmes present questions and challenges for the PacELF. Can we learn anything from the earlier campaigns that will facilitate the success of the PacELF campaign?

Table 1. Lymphatic filariasis vectors in the Pacific

Vector	Country
Aedes cooki	Niue
Aedes fijiensis	Fiji
Aedes horrensces	Fiji
Aedes kochi	Papua New Guinea
Aedes marshallensis	Kiribati
Aedes oceanicus	Tonga
Aedes polynesiensis[a]	American Samoa, Samoa, Cook Islands, Tokelau, Tuvalu, French Polynesia, Wallis and Futuna, Fiji
Aedes pseudoscutellaris	Fiji
Aedes rotumae	Rotuma Island in Fiji
Aedes samoanus	Samoa
Aedes tabu	Tonga
Aedes tutuilae	Samoa
Aedes upolenis	Samoa
Ochlerotatus vigilax[a]	New Caledonia, Fiji
Anopheles punctulatus complex[a,b]	Papua New Guinea, Solomon Islands[c], Vanuatu
Culex annulirostris	Irian Jaya
Culex quinquefasciatus[a]	Kiribati, Pelau, Federated States of Micronesia, Papua New Guinea, Fiji (and several other Pacific Island countries)
Mansonia uniformis	Papua New Guinea

[a]Species names denote major vectors in the four zones as described in Ref. [11].
[b]The *Anopheles punctulatus* complex is now believed to comprise >11 species. All three morphological species (*An. faurauti*, *An. koliensis* and *An. punctulatus*) have been implicated as vectors of lymphatic filariasis in Papua New Guinea.
[c]Evidence suggests that filariasis has been eradicated from the Solomon Islands [14,15].

Filariasis in the Pacific

Filariasis in the Pacific is caused solely by *W. bancrofti*. The Pacific can be divided into four epidemiological zones based on periodicity of the parasite and the importance of the vector species [11]. Both periodic and subperiodic forms of the parasite are present, with nocturnally periodic *W. bancrofti* being historically found in the Melanesian zone (PNG, Solomon Islands and Vanuatu) (Fig. 1). A great diversity of mosquito spp. in the genera *Aedes*, *Anopheles*, *Culex* and *Mansonia* are capable of acquiring and supporting the development of Mf to infectious third-stage larvae (L3) in the Pacific (Table 1). These include members of the *Anopheles punctulatus* (or *farauti*) complex in PNG and Vanuatu (and previously in Solomon Islands); *Ochlerotatus vigilax* in New Caledonia, *Culex quinquefasciatus* in Micronesia and *Aedes polynesiensis* from Fiji to French Polynesia [11,12]. Not all mosquito species that can be infected and can transmit L3, however, are important vectors of filariasis. Whereas *Cu. quinquefasciatus* is widely distributed throughout the Pacific, a significant contribution to filariasis transmission by this mosquito is doubtful in many areas.

The evolution of filariasis control in the Pacific

Vector control was once advocated as the primary tool to control filariasis because effective antifilarial drugs were unknown and MDA campaigns were believed to be too labour-intensive. Success in the control and elimination of filariasis based only on anti-vector

Box 1. The concepts of proportionality, limitation and facilitation

The term 'proportionality' is used to describe mosquitoes in which the proportion of microfilaria (Mf) that develop into infectious third-stage larvae (L3) is independent of the number of Mf ingested. With respect to limitation, there is an inverse relationship between ingested Mf and L3. Mosquitoes that demonstrate facilitation show an increased rate of Mf developing into L3 with increased numbers of Mf ingested. Mosquito vectors that exhibit limitation are the most challenging for filariasis control programs because the efficacy of transmission will increase when Mf densities decrease.

activities has been demonstrated. In PNG and Solomon Islands, where *Anopheles* spp. were the vectors of malaria and filariasis, filariasis was eliminated from areas where DDT spray campaigns to control malaria were undertaken [13–15]. Similarly, *W. bancrofti* was eliminated from Australia, primarily by sanitation campaigns against *Cu. quinquefasciatus* [16].

In the 1960s and 1970s, there was a shift in the control strategy to MDA-based campaigns, which often achieved significant reductions in Mf prevalences and densities [17–19]. In Samoa, five extensive campaigns using DEC were implemented. The first two campaigns began in 1966 and 1971 using 12–18 DEC treatments [17]. The DEC treatments consisted of weekly doses of 5 mg kg^{-1} body weight for six weeks followed by monthly treatments with DEC at 5 mg kg^{-1} body weight. Single, annual doses of DEC at 6 mg kg^{-1} body weight were then administered in 1982, 1983 and 1986. These efforts reduced the Mf prevalence from 21% in 1964 to 2.3% in 1987. It should be noted that Mf prevalences had declined to 0.14% in 1974, following the second DEC campaign, but rebounded to 2.1% within two years [17].

An even more intensive effort was expended on filariasis control in Maupiti, French Polynesia. Since 1955, excluding the years 1960–1967 and 1970–1974, twice-yearly DEC chemotherapy with 6 mg kg^{-1} body weight was administered to an average of 85% of the population in Maupiti [18]. In addition, mosquito control using DDT from 1955–1957 and destruction of larval-breeding sources from 1955–1970 were implemented. Despite these efforts, 0.4% of residents were positive for Mf with 4.6% having antigenaemia in the year 2000 [18].

Thus, after cessation of the MDA campaigns in Samoa and French Polynesia, Mf prevalences often rose rapidly [9,17,18]. Whereas these extensive campaigns succeeded in minimizing filariasis temporarily as a public health problem by significantly reducing the number of clinical cases, the elimination of the parasite was not achieved.

The evidence that the DEC plus albendazole combination will be successful against adult worms includes the decrease in adult-worm antigen levels [20] and clinical reactions in infected humans after receiving the drug combination [21]. Twenty-four months following a single DEC plus albendazole treatment, filarial antigen levels had decreased to 30% of pre-treatment levels in a trial in Sri Lanka [22]. Furthermore, the DEC plus albendazole combination is more effective against Mf than DEC alone. Can this drug combination approach only targeting the worm succeed? Or, is there a role for anti-vector interventions in the PacELF campaign?

The rationale for entomology in the PacELF programme

The persistence of lymphatic filariasis in the Western Pacific, despite several MDA campaigns, urges some caution to the hope that an MDA campaign alone will eliminate filariasis. The success of any MDA-based antifilariasis campaign depends on the efficacy of the drugs to kill or sterilize adult worms. Field and laboratory studies have shown that DEC alone does not kill or sterilize all *W. bancrofti* adults. Individuals have remained Mf positive following repeated treatment with DEC in French Polynesia* [18] and Samoa [17,23].

A significant proportion of adult worms are insensitive to DEC [24,25]. Noroes and colleagues [24,25] estimated that only 42% of adult worms are sensitive to DEC. Although all nodules contained damaged and degenerating adult worms following DEC ingestion, the continued presence of Mf suggested that adult worms have differential susceptibilities to DEC [24]. The observation that DEC plus albendazole fails to eliminate all Mf [21] is consistent with the hypothesis that not all adult worms are susceptible to this drug combination.

Elimination of filariasis using MDA will require an efficient drug distribution system and high compliance by the population for an extended period because estimates of the life span of *W. bancrofti* adults range from 5 to 40 years [26,27]. In the 1958 MDA campaign using DEC in Tahiti, only 58% of people received treatment†. A four-year campaign (1974–1978), using a single annual dose of DEC, achieved only 69% coverage in Tahitian villages [19].

One potential cause of non-participation in MDA could be adverse reactions following DEC ingestion, particularly among asymptomatic Mf-positive individuals after the initial MDA treatment. When treated with DEC at 6 mg kg^{-1} per person, 57% of Mf-positive people in Samoa reported adverse effects, whereas only 33% of Mf-negative people did [9]. A significant drop in drug ingestion compliance among Mf-positive individuals would represent a serious threat to the goal of filariasis elimination in the Pacific.

*4th World Health Organization/South Pacific Commission Seminar on Filariasis and Vector Control (1974) Apia, Western Samoa.
†Laigret, Rapport Annuel, Institut de Recherches Medicales de la Polynesie, (1958).

Table 2. Important biological characteristics of the filariasis vectors in the Pacific

Characteristic	*Anopheles punctulatus* complex	*Culex quinquefasciatus*	*Ochleratatus vigilax*[a]	*Aedes polynesiensis*
Breeding sites	Brackish water, swamps, streams, puddles	Pools, domestic water supplies, septic tanks (prefers high organic content in water)	Salt water marshes	Tyres, drums, wells, cisterns, tins, crab holes, tree holes
Biting time	Night (peaks between 2200 and 0200 hrs)	Night (dusk and first part of the night)	Day and night (peaks in the evening)	Day
Biting location	Indoor and outdoors	Indoors	Outdoors	Outdoors
Resting habits	Indoors (<12 hrs), then outdoors	Outdoors	Outdoors	Outdoors
Infection mode	Facilitation	Proportion or limitation	NK	Limitation
Blood meal hosts	*An. punctulatus* and *Anopheles koliensis* are more anthropophilic than *Anopheles farauti*	Humans (up to 85% human blood index)	Opportunistic on available hosts	Opportunistic on available hosts
Flight range	2–3 km	Up to 5 km	>10 km	100 m

[a]Abbreviation: NK, not known

Another challenge to PacELF is the efficacy of *Ae. polynesiensis* as a filariasis vector. Drug treatment lowers the density of Mf in infected individuals, but might not eliminate Mf. *Aedes polynesiensis* has an increased efficiency at acquiring infections when feeding on individuals with low densities of Mf, a process termed limitation [27,28,29] (Box 1). The ability of filariasis to rebound in Samoa and French Polynesia after years of MDA is a tribute to the efficacy of *Ae. polynesiensis* as a vector [17,18].

A strong reason for implementing vector control with MDA is that mosquito control has proven effective against filariasis transmission in some epidemiological situations, particularly where *Anopheles* and *Culex* transmit filarial worms. Untreated [30] and insecticide-treated [31] bednets, in addition to residual indoor insecticide-sprays [13–15] can significantly impact filariasis transmission. A 70% reduction in L3 prevalence in mosquitoes was found after introduction of untreated bednets into a village where *An. punctulatus* was the filariasis vector [30]. Residual insecticides appear to have eliminated filariasis from Solomon Islands [14,15] and parts of PNG [13]. Sanitation measures succeeded in eradicating filariasis from Australia where it was transmitted by *Culex* [16]. Reductions of up to 98% of *Cu. quinquefasciatus* were documented in Africa [32] and India [33] when using *Bacillus sphaericus* and polystyrene beads to control the larval stages.

These are strong arguments for incorporating vector control strategies in any filariasis elimination programme. However, a key question remains: are we in a better position today to monitor and control the vectors of filariasis in the Pacific than when the vertically organized anti-mosquito campaigns were abandoned?

The challenge of Pacific vectors of lymphatic filariasis

New tools, in particular PCR, for detecting worms in mosquitoes should facilitate vector surveillance, and insecticide-impregnated mosquito nets, biocides and polystyrene beads offer new options for mosquito control. The development of PCR to detect a single *W. bancrofti* L3 in a pool of 50 mosquitoes [5] offers significant labour savings, but the test cannot distinguish between stages of *W. bancrofti*. Hence, PCR can tell us that mosquitoes are infected, but cannot distinguish infected from infectious mosquitoes. PCR data can confirm that transmission is still occurring (e.g. that Mf-positive individuals still exist) but cannot determine when transmission has truly ended. The usefulness of detecting pathogens in mosquitoes as a surveillance tool diminishes when the parasite prevalence in the human population drops because it becomes increasingly difficult to find infected mosquitoes.

Following MDA with DEC in Samoa in 1984, 0.06% of mosquitoes were infected with filarial worms [17]. If the next round of MDA was 87% effective (as stated in Ref. [34]), the collection and analysis of 23 115 mosquitoes will be required to achieve 90% probability of finding a significant effect at the 5% level. Hence, using mosquito numbers to evaluate the efficacy of an MDA campaign in eliminating filariasis could only be practical during the early stages of intervention when the mosquito infection rate is relatively high. If an antimosquito campaign to reduce transmission by reducing mosquito numbers was also implemented, the usefulness of any parasite detection system would be further limited by the potential difficulty of collecting adequate numbers of mosquitoes for a meaningful statistical analysis.

Despite these operational hurdles, information from vector infection rates could provide valuable data not presently available from the ICT. The reason for this is that antigen prevalences based on ICT testing of human blood remain high for up to three years following DEC treatment [6]. Thus, data from vector infection rates could provide faster feedback on the progress of a MDA campaign than that is possible from antigen prevalences derived from humans.

A prerequisite for the design and implementation of a successful control strategy against a vector of lymphatic filariasis is knowledge of the biology of the vector. Important characteristics of the major vectors in the four Pacific filariasis zones are summarized in Table 2. The relative importance of a mosquito as a vector and the potential impact of a particular control strategy are dependent on the biology of each vector

species. Of particular importance is whether the vector demonstrates limitation, proportion or facilitation with respect to filarial infections [28]. There are proven effective strategies against the members of the *An. punctulatus* complex (residual insecticide spraying and bednets) and *Cu. quinquefasciatus* (bednet and polystyrene beads) which are based on exploiting weaknesses in the biology of these vectors.

Unfortunately, detailed knowledge on aspects of the biology of *Ae. polynesiensis*, the most important vector of filariasis from Fiji to French Polynesia, is lacking. Although *Ae. polynesiensis* rarely flies >100 m and will avoid open areas with strong sunlight, it is uncertain where *Ae. polynesiensis* transmits *W. bancrofti* (e.g. in the village or in the bush) (reviewed by Iyengar[‡]). Part of this uncertainty stems from the imprecision in how to measure filariasis transmission (a function of human-biting rates and proportion of mosquitoes infected with L3). Generally, L3 prevalences in *Ae. polynesiensis* are higher near villages, but human-biting rates are greater in plantation or bush areas. Most likely, the relative importance of transmission in the village or in the bush will vary in different ecological settings. Recent work in Fiji argues that filariasis transmission by *Ae. polynesiensis* is greater in the bush as a result of either higher mosquito-mortality rates in the village or the fact that older mosquitoes take more blood meals away from the villages [35]. Resolution of this debate is needed in order to determine where anti-*Ae. polynesiensis* control measures should be implemented.

Mosquito surveillance and control is already part of many Pacific island countries' filariasis control plans. Unfortunately, the efficacy of antimosquito interventions has rarely been evaluated for its impact on a population level. For example, *Mesocyclops aspericornis*, a predacious copepod, reduced the number of *Ae. polynesiensis* larvae breeding in treated crab-holes by 98%. Despite the treatment of >14 000 crab holes in one study, there was no measurable impact on the numbers of *Ae. polynesiensis* biting [36].

The minimal impact of insecticide fogging and spraying campaigns on *Ae. polynesiensis* biting rates is particularly noteworthy. In three field trials, *Ae. polynesiensis* biting rates were reduced by <64% following insecticide fogging or spraying[§].

Whereas some larval-source reduction campaigns were highly effective against *Ae. polynesiensis*, many of these campaigns were conducted by the US military during World War II in a manner that could be difficult to duplicate as effectively today. Some studies lamented the rapidity of the reappearance of the breeding sites after clean-up campaigns. Less than five months after destroying 3906 containers, 2040 breeding sites were found [37]. After the destruction of 2544 tree holes, 388 additional tree holes were discovered at a post-treatment inspection [38]. Environmental clean up campaigns often necessitated extensive removal of bushes and other vegetation to locate *Ae. polynesiensis* breeding sites with only 77% of breeding sites being amenable to destruction. On economic grounds, Hairston[¶] felt that it was not feasible for a vertical programme to undertake a mosquito control programme based on breeding-site elimination, but left the possibility that communities might be able to undertake this task.

The biology of *O. vigilax* presents a different set of challenges for effective control. The long flight-range (up to 50 km) and the outdoor biting-behaviour by *O. vigilax* will render this species not very amenable to control by insecticide applications. Furthermore, larval source-reduction is difficult because *O. vigilax* breeds in salt marshes. Whereas runnels (ditches designed to allow flushing of salt marshes by tides) can impact larval numbers in salt marshes [38], the impact of runnels on adult mosquito-biting rates is unknown.

It has been estimated that 9 and 11–12 years of vector control would be necessary to eliminate filariasis from foci where *Anopheles* and *Culex*, respectively, are the vectors [33]. More time might be required in areas where *Aedes* transmit *W. bancrofti*. Furthermore, because the biology of many Pacific vectors of filariasis did not make them susceptible to control by any of the available options at the launch of PacELF, vector control was not stressed in the present PacELF campaign.

Where are we now?

In 2000, the 22 Pacific island countries and territories in PacELF had a population of >7.6 million. The PacELF programme has so far distributed 41 000 ICT tests, and random testing for lymphatic filariasis was conducted on 35 638 people in 14 Pacific island countries. This represented sampling between 0.2 and 94% of the populations in those countries** (i.e. 0.2% of the 448 000 people in the Solomon Islands were ICT-tested whereas 94% of the 1900 residents of Niue were ICT-tested). Guam, the Marshall Islands, the Northern Mariana Islands, Palau, Pitcairn Island and the Solomon Islands appear to be non-endemic for filariasis. Positive antigen rates range up to 22% in

[‡]An Annotated Bibliography of Filariasis and Elephantiasis Part 2. South Pacific Commission Technical Paper No. 88, (1956).
[§]Chow, C.Y. (1974) Filariasis vectors and their control in the South Pacific. Paper presented at the 4th Joint World Health Organization/South Pacific Commission Seminar on Filariasis and Vector Control, p. 3; WPR/Fil/9, Apia, Western Samoa; Suzuki T. and Sone, F. eds (1976) Laboratory and field tests of insecticides against vector mosquitoes of subperiodic filariasis in Western Samoa, unpublished report to World Health Organization; and Suzuki, T and Sone, F. (1980) Breeding habits and vector mosquitoes of filariasis and dengue fever in Samoa, abstract no. 208 in Zahar, A.R. and Chow, C.Y. (1980) A review and an annotated bibiography on subperiodic bancroftian filariasis with special reference to its vectors in Polynesia, South Pacific.

[¶]Assessment of filariasis in Western Samoa. Assignment report submitted to World Health Organization/WPRO (1973).
**World Health Organization Report to the Workshop on Field Operations for Filariasis Elimination in the Pacific presented in Brisbane, Australia (2000).

Tuvalu. Based on antigen prevalences, ~123 000 people were infected with lymphatic filariasis across 14 Pacific island countries and territories. MDA programmes in nine Pacific island countries have begun with 11 million and 1.7 million tablets of DEC and albendazole, respectively, having been distributed (Ichimori, unpublished). These data does not include PNG which has extensive areas with Mf prevalences as high as 68% [30,39–41] and filarial antigen prevalences up to 98% [42]. Overall, non-random testing in PNG indicates an antigen prevalence as high as 56% [39] suggesting that up to 2.7 million people could be infected with filarial parasites in PNG. Because of the magnitude of filariasis in PNG, the campaign there is presently trying to assess the level of endemicity [10].

One of the obstacles to the success of any filariasis elimination programme based on MDA was earlier identified as participation of the populations in ingesting the drugs. With the exception of American Samoa, dissemination of DEC plus albendazole in the six other PacELF countries for which data is available has been greater than 80%. The low coverage (17%) in American Samoa necessitated a re-evaluation and relaunch of the campaign. Drug dissemination coverage for Vanuatu and Samoa was 83% and 90%, respectively. Based on direct observations, 81% and 94% of the populations of the Cook Islands and Niue, respectively, received and ingested DEC plus albendazole in the last round of MDA.

In the present PacELF campaign in French Polynesia, 93% of individuals surveyed reported having received DEC and albendazole with 88% ingesting the medication [43]. Of people receiving the drugs in French Polynesia, 73% ingested the drug the day it was received whereas 13% consumed it the following day. Four percent of people reported waiting four or more days before consuming the drug.

Adverse reactions are commonly reported by individuals, particularly by microfilariaemic individuals following the first round of MDA with DEC. In French Polynesia, 29% of the population reported adverse effects: 39% suffered effects if the drugs were taken before meals compared with 21% if taken after meals. The most common adverse affects were fatigue (15%), dizziness (10%), nausea (9%) and headaches (8%). Adverse reactions lasted a day or less for 80% of people affected. However, adverse reactions were of sufficient severity to affect activities of 4% of the population, with an additional 4% requiring confinement to bed. Data on side effects have been obtained from >5000 individuals in Samoa, American Samoa, Niue and Vanuatu in 1999 and 2000. This data is still being analyzed.

Similar to earlier DEC-based MDA campaigns in Samoa (1966, 1971, 1982,1983 and 1986) [17] and French Polynesia (1955 to the present) [18], the DEC plus albendazole-based PacELF MDA campaign is showing a dramatic immediate impact on filarial prevalence in humans. Before the implementation of the first round of MDA in Samoa, 13% of 659 people in three villages were filarial-antigen positive. After two annual MDA rounds, the antigen prevalence dropped to 8% in these villages. Antigen positives decreased by 17%, 23% and 67% in the villages of Matatufu, Lepale and Apai, respectively. A clearer indication of the impact of MDA will be obtained in 2002 when the mid-campaign evaluation will be conducted in Vanuatu and Samoa.

Conclusions

Several hurdles remain for the PacELF to succeed in eliminating filariasis. The present PacELF campaign relies on MDA using DEC plus albendazole for filariasis elimination and on the ICT test for monitoring the progress of the campaign. The primary obstacle for an MDA-based strategy to eliminate filariasis is the uncertainty of DEC plus albendazole treatment for eliminating adult worms. This uncertainty necessitated the design of a five-year campaign requiring a high compliance of drug ingestion in the target population. The efficacy of mosquito control in eliminating filariasis from Solomon Islands, Australia and parts of PNG highlights the potential usefulness of mosquito control as part of an antifilariasis programme in the Pacific.

Integration of mosquito control as part of the PacELF campaign will require additional, basic ecology research on the important vectors, particularly on the daytime feeding behaviour by *Ae. polynesiensis*, and operational research on cost-effective implementation of control strategies based on knowledge of vector biology.

Monitoring programmes success requires careful evaluation of the status of ongoing transmission. The ICT test enabled rapid assessment of filariasis prevalence. However, the persistent filarial antigenaemia following MDA minimizes the usefulness of the ICT test for monitoring the campaign. Alternative ways of estimating transmission and prevalence in humans are needed. Filarial infection rates in mosquitoes and filarial-specific antibodies could be suitable approaches to monitor filariasis elimination programmes.

Similar to the earlier DEC-based MDA programmes in Samoa and French Polynesia, the PacELF strategy of DEC plus albendazole MDA is having a dramatic impact on filariasis prevalence. Whereas this approach might succeed in minimizing filariasis as a public health problem in the short term, failure to eliminate the parasite could lead to an eventual resurgence of the disease. In order to prevent this from happening, the present strategy of reliance on MDA alone needs to be re-examined. GlaxoSmithKline and the WHO recognized that 'drugs alone will not provide the answer' [7]. We need to address operational research questions on effective sustainable anti-vector strategies if their implementation is needed in the next generation of filariasis elimination programmes.

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References

1 Cox, F.E.G. (2000) Elimination of lymphatic filariasis as a public health problem. *Parasitol. Today* 16, 135
2 Michael, E. and Bundy, D.A.P. (1997) Global mapping of lymphatic filariasis. *Parasitol. Today* 13, 477–480
3 Dean, M. (2000) At last, the fight against lymphatic filiariasis begins. *Lancet* 355, 385
4 Ottesen, E.A. *et al.* (1997) Strategies and tools for the control/elimination of lymphatic filariasis. *Bull. WHO* 75, 491–503
5 Chanteau, S. *et al.* (1994) Detection of *Wuchereria bancrofti* larvae in pools of mosquitoes by the polymerase chain reaction. *Trans. R. Soc. Trop. Med. Hyg.* 88, 665–666
6 Schuetz, A. *et al.* (2000) Evaluation of the whole blood filariasis ICT test for short-term monitoring after antifilarial treatment. *Am. J. Trop Med. Hyg.* 62, 502–503
7 Sharp, D. (1998) Another tropical drug donation. *Lancet* 351, 388
8 Dean, M. (2000) Launching a lymphatic filariasis campaign in the Pacific Islands. *Lancet* 356, 143
9 Kimura, E. *et al.* (1985) The efficacy of annual single-dose treatment with diethycarbamazine citrate against diurnally subperiodic bancroftian filariasis in Samoa. *Bull. WHO* 63, 1097–1106
10 Alexander, N.D.E. *et al.* (2001) Migration and dispersal of lymphatic filariasis in Papua New Guinea. *Trans. R. Soc. Trop. Med. Hyg.* 95, 277–279
11 Hawking, F. and Denham, D.A. (1976) The distribution of human filariasis throughout the world. Part I. The Pacific Region including New Guinea. *Trop. Dis. Bull.* 73, 347–372
12 Raghavan, N.G.S. (1961) The vectors of human infections by *Wuchereria* species in endemic areas and their biology. *Bull. WHO* 24, 177–195
13 Bockarie, M. (1994) Can lymphatic filariasis be eradiated in Papua New Guinea? *P. N. G. Med. J.* 37, 61–64
14 Webber, R.H. (1977) The natural decline of *Wuchereria bancrofti* infection in a vector control situation in the Solomon Islands. *Trans. R. Soc. Trop. Med. Hyg.* 71, 396–400
15 Webber, R.H. (1979) Eradication of *Wuchereria bancrofti* infection through vector control. *Trans. R. Soc. Trop. Med. Hyg.* 73, 722–724
16 Boreham, P.F.L. and Marks, E.N. (1986) Human filariasis in Australia: introduction, investigation and elimination. *Proc. R. Soc. Queensland* 97, 23–52
17 Ichimori, K. (2001) Entomology of the filariasis control programme in Samoa, *Aedes polynesiensis* and *Ae. samoanus*. *Med. Entomol. Zool.* 52, 11–21
18 Esterre, P. *et al.* (2001) The impact of 34 years of massive DEC chemotherapy on *Wuchereria bancrofti* infection and transmission: the Maupiti cohort. *Trop. Med. Int. Health* 6, 190–195
19 Laigret, J. *et al.* (1980) Chimiotherapie de masse par la diethylcarbamazine end doses espacees: effets obtenus a Tahiti sur la microfilaremie a *Wuchereria bancrofti*, var. *pacifica*. *Bull. WHO* 58, 779–783
20 Ismail, M.M. *et al.* (1998) Efficacy of single dose combinations of albendazole, ivermectin and diethylcarbamazine for the treatment of bancroftian filariasis. *Trans. R. Soc. Trop. Med. Hyg.* 92, 94–97
21 Ottesen, E.A. *et al.* (1999) The role of albendazole in programmes to eliminate lymphatic filariasis. *Parasitol. Today* 15, 382–386
22 Ismail, M.M. *et al.* (2001) Long-term efficacy of single dose combinations of albendazole, ivermectin and diethylcarbamazine for the treatment of bancroftian filariasis. *Trans. R. Soc. Trop. Med. Hyg.* 95, 332–335
23 Suzuki, T. and Sone, F. (1975) Filarial infections in vector mosquitoes after mass drug administration in Western Samoa. *J. Trop. Med. Hyg.* 16, 147–156
24 Figueiredo-Silva, J, *et al.* (1996) Histological evidence for adulticidal effects of low doses of diethylcarbamazine in bancroftian filariasis. *Trans. R. Soc. Trop. Med. Hyg.* 90, 192–194
25 Noroes, J. *et al.* (1997) Assessment of the efficacy of diethylcarbamazine on adult *Wuchereria bancrofti in vivo*. *Trans. R. Soc. Trop. Med. Hyg.* 91, 78–81
26 Vanamail, P. *et al.* (1996) Estimation of the fecund life span of *Wuchereria bancrofti* in endemic areas. *Trans. R. Soc. Trop. Med. Hyg.* 90, 119–121
27 Carme, B. and Laigret, J. (1979) Longevity of *Wuchereria bancrofti* var *pacifica* and mosquito infection acquired from a patient with low levels of parasitaemia. *Am. J. Trop. Med. Hyg.* 28, 53–55
28 Southgate, B.A. (1992) The significance of low density microfilaremia in the transmission of lymphatic filariasis parasites. *J. Trop. Med. Hyg.* 95, 79–86
29 Bryan, J.H. and Southgate, B.A. (1976) Some observations on filariasis in Western Samoa after mass administration of diethylcarbamazine. *Trans. R. Soc. Trop. Med. Hyg.* 70, 39–48
30 Burkot, T.R. *et al.* (1990) Effects of untreated bed nets on the transmission of *Plasmodium falciparum*, *P. vivax* and *Wuchereria bancrofti* in Papua New Guinea. *Trans. R. Soc. Trop. Med. Hyg.* 84, 773–779
31 Charlwood, D. and Dagoro, H. (1987) Impregnated bednets for the control of filariasis transmitted by *Anopheles punctulatus* in rural Papua New Guinea. *P. N. G. Med. J.* 30, 199–202
32 Maxwell, C.A. *et al.* (1999) Can vector control play a useful supplementary role against bancroftian filariasis? *Bull. WHO* 77, 138–143
33 Ramaiah, K.D. *et al.* (1994) Estimation of permissible levels of transmission of bancroftian filariasis based on some entomological and parasitological results of a 5-year vector control programme. *Acta Trop.* 56, 89–96
34 Maxwell, C.A. *et al.* (1990) Control of bancroftian filariasis by integrating therapy with vector control using polystyrene beads in wet pit latrines. *Trans. R. Soc. Trop. Med. Hyg.* 74, 709–714
35 Rakai, I.M. (1974) Mosquitoborne infections in Fiji. IV. Biting times for village mosquitoes and human filaria transmission potential of *Aedes polynesiensis* and *Aedes pseudoscutellaris*. *J. Med. Entomol.* 11, 588–594
36 Lardeux, F. *et al.* (1992) Release of *Mesocyclops aspericornis* (Copepoda) for control of larval *Aedes polynesiensis* (Diptera: Culicidae) in land crab burrows on an atoll of French Polynesia. *J. Med. Entomol.* 29, 571–576
37 Burnett, G.F. (1960) Filariasis research in Fiji, 1957–1959. *J. Trop. Med. Hyg.* 63, 156–162
38 Dale, P.E.R. *et al.* (1993) Runnelling to control saltmarsh mosquitoes: long-term efficacy and environmental impacts. *J. Am. Mosq. Control Assoc.* 9, 174–181
39 P. Pisters. Prevalence of filarial antigenaemia in Papua New Guinea – Results of surveys by School of Public Health and Tropical Medicine, James Cook University. *P. N. G. Med. J.* (in press)
40 Cattani, J. *et al.* (1983) Malaria and filariasis in the Ok Tedi Region of the Star Mountains, Papua New Guinea. *P. N. G. Med. J.* 26, 122–126
41 Kazura, J.W. *et al.* (1984) Parasitologic and clinical features of bancroftian filariasis in a community in East Sepik Province, Papua New Guinea. *Am. J. Trop. Med. Hyg.* 33, 1119–1123
42 Tisch, D.J. *et al.* (2001) Ecologic and biologic determinants of filarial antigenemia in bancroftian filariasis in Papua New Guinea. *J. Infect. Dis.* 184, 898–904
43 Hubert, B. *et al.* (2001) Evaluation de la campagne de lutte contre dal filariose-Avril 2000. *Bull d'Informations Sanitaires et Epidemiologiques* 2, 1–4