Review TRENDS in Parasitology Vol.23 No.1

Parasitology in Japan

Lymphatic filariasis elimination in the Pacific: PacELF replicating Japanese success

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Japan successfully eliminated lymphatic filariasis and other parasitic diseases through community-driven, integrated nationwide campaigns undertaken during the 1960s and 1970s. The campaigns also created a cadre of experienced clinicians, scientists and public health workers with excellent technical and operational knowledge and a positive attitude towards filariasis elimination. These factors, and the humanitarian desire to improve health in neighbouring nations, influenced Japan to support filariasis control efforts overseas, starting in the 1970s and continuing through to the inception of the Pacific Programme to Eliminate Lymphatic Filariasis (PacELF) in 1999. The unique community-driven, self-help approach of Japan to disease control and health improvement profoundly influenced the activities of PacELF. PacELF is demonstrating that the successful national disease-elimination model in Japan can be extended to the regional level.

Winning battles but not yet the disease-elimination war

The Pacific region has a high prevalence of lymphatic filariasis. Control campaigns instituted in several countries or parts of countries in the 1950s were partially successful but did not succeed in eliminating the disease. In Japan, post-World War II (WWII) conditions for its 70 million inhabitants mirrored those seen in many developing nations today. Yet lymphatic filariasis was successfully eliminated from Japan following a 15-year integrated programme of disease detection, drug treatment and prevention coupled with extensive health education. Subsequently, Japanese clinicians, parasitologists and entomologists have been influential in filariasis elimination campaigns overseas, campaigns that have also been strongly supported financially by the Japanese government. This review explores historical reasons why this influence has been so strong and how it has shaped current practices of the Pacific Programme to Eliminate Lymphatic Filariasis (PacELF: http://www.pacelf.org), itself a pathfinder disease-elimination initiative operating on a regional basis.

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Available online 28 November 2006.

Priority setting

Currently, most international assistance to control infectious diseases goes to fight so-called 'killer diseases' such as HIV/AIDS, tuberculosis and malaria. However, it is widely recognized that there are other diseases, like lymphatic filariasis, that are not fatal but which cause serious disability and psychological suffering for patients and impose intolerable burdens on mostly impoverished communities [1]. Lymphatic filariasis, one of the so-called 'neglected diseases' [2], is a highly disfiguring, disabling parasitic disease caused by helminth worms transmitted by mosquitoes. Severe symptoms such as elephantiasis of limbs and swelling of the scrotum can develop in some infected people. In poor communities throughout developing countries, the social burden of filariasis is massive – a major source of pain and suffering, social stigmatization and reduction in productivity that creates or exacerbates poverty. On the socioeconomic front, lymphatic filariasis is estimated to cost $3 billion annually in lost productivity, with control investments likely to produce a highly respectable economic rate of return of 27% over the period 2000–2029, according to the International Task Force for Disease Eradication [3].

Filariasis in Japan

When the Japanese nationwide elimination campaign began in 1962, there were estimated to be over one million people infected with filariasis in the country [4]. The highest prevalences (over 20% in some islands) were in the southern Amami and Ryukyu archipelagos of Okinawa prefectures. Kyushu island also had high endemicity, and cases were found throughout two of the other main islands: Honshu and Shikoku [4,5]. Only the most northern main island, Hokkaido, was disease-free. All infections were caused by *Wuchereria bancrofti*, transmitted by the *Culex pipiens* group, except for one small island where *Brugia malayi* was transmitted by *Aedes togoi* [4].

Filariasis elimination in Japan

The filariasis control project in Japan was preceded by ten years of research and pilot studies in addition to diverse community-driven interventions to control many other

 1471-4922/$ – see front matter doi:10.1016/j.pt.2006.11.005

parasitic diseases. After the discovery of the effects of diethylcarbamazine (DEC) hydrochloride on filarial worms by Hewitt in 1947, Japanese scientists synthesized Supatonin (DEC citrate) in 1950 [6] and used it to conduct important dose–response and adverse effect studies; it was also used to control ascariasis. These studies helped to determine the survey methodology (three linear blood smears of 20 μl each from the whole population) and the dose of DEC to be used in the control campaign (6 mg kg^{-1} once a day for 12 days), and to demonstrate the relationship between microfilarial load and adverse effects of treatment. This information helped to improve community participation by informing and reassuring individuals about the likelihood and duration of adverse effects from DEC treatment. Extensive health education campaigns had to be carried out to overcome the reluctance to participate in mass drug administration (MDA) among those who developed post-treatment fevers resulting from accumulation of dead worm tissue in their bodies.

The Japanese strategy involved mass screening and DEC treatment of positive cases, supplemented by spraying with dichlorodiphenyltrichloroethane (DDT) or malathion insecticides to kill vector mosquitoes. The highest prevalence area of the Ryukyu islands, comprising Miyako, Yaeyama and Okinawa, saw commencement of a control campaign in 1964, followed by the Yaeyama region in 1967 and the Okinawa region in 1969 [4]. Infection rates in all prefectures fell to almost zero by 1971 and elimination was finally achieved in 1978 [5]. A monument commemorating the achievement was erected on Miyako island in 1988.

Success factors in Japan

In Japan, communities worked together to eliminate diseases nationwide, coordinated by central authorities and sharing scant resources. A multifaceted approach was taken, using interventions generated by local communities that were best suited to the prevailing environment and conditions. The group was invariably favoured over the individual. The Japanese filariasis elimination programme worked in a collaborative way, engaging the affected communities themselves to achieve high coverage of screening and MDA [5]. From the start there was a realization that local knowledge of the disease was lacking and so a large investment was made in health education. The health providers (local doctors and nurses, including public health nurses) worked closely and cohesively with local governments and communities. The strategy of an integrated programme (MDA together with vector control) was based on strong scientific and technical input from pilot studies and close participation and collaboration between research and control specialists. Consequently, academic, industrial, medical and local civil society interests all worked harmoniously and expeditiously towards a common goal.

As an example, a particular feature of Miyako island society is the 'Araragama spirit' of community-based pride and competition [5]. The 'Araragama spirit' had a crucial role in filariasis elimination, with communities trusting the scientific evidence of filariology and sincerity of the administrative sectors. People wanted to improve their health by taking upon themselves the responsibility to combat the disease; thus, elimination required the total understanding and commitment of the community, with support from central authorities and external resources where necessary. Prior experience and manpower available from the malaria eradication programme in this region was an extremely advantageous factor, as was the positive morale and motivation of public health nurses and other staff.

The Japan-style, community-based, self-help approach is much broader in scope than what is termed 'community health' and can be viewed as a form of social dynamism. This way of working has strongly influenced the PacELF programme, which has harnessed key components of the Japanese approach and elements of inspirational and altruistic spirit in designing the 'PacELF Way' strategy [7]. This involves:

- A regional collaborative approach to benefit the entire Pacific family.
- Pacific island country ownership.
- Operational flexibility.
- A simple core package of activities.
- Effective coordination and integration into existing health services.
- Focus on the positive outcome.

Filariasis in the Pacific

The prevalence of filariasis and elephantiasis in the Pacific used to be among the highest in the world. Before the 1950s, measures to control filariasis in the Pacific consisted of sporadic vector control and environmental management to curtail mosquito numbers but this resulted in little overall sustained impact. In several instances, subsequent post-WWII MDA campaigns using DEC in a few countries, usually vertical programmes orchestrated by ex-colonial powers, effectively controlled the disease only for it to return within a short timeframe. American Samoa introduced MDA using DEC in the 1960s [8], which reduced infection levels to ~1% but this had climbed back up to an antigen prevalence of 16.5% by the time of the PacELF baseline study in 1999. A similar situation was observed in the Cook Islands, where MDA in Aitutaki in the 1960s resulted in an antigen prevalence of 0.9%, which had risen to 8.6% by the time of the baseline study in 1999 [7]. Fiji initiated MDA with DEC in the 1950s and cut microfilaremia prevalence to <1% in some areas [9] but the nationwide antigen prevalence was 16.6% by the time of the PacELF baseline study. Similarly, French Polynesia started MDA in 1949 and, following a decades-long programme, reduced the infection rate to low levels [10], only to record an antigen prevalence of 13% during the baseline study. Samoa has a history of implementing successful measures to control filariasis and set up a Filariasis Control Department in its Ministry of Health in 1964. MDA started in 1965–1967 and was followed by seven subsequent programmes (for a review, see Ref. [11]). Although disease prevalence was diminished markedly, Samoa never controlled the disease completely or on a long-term basis, recording 4.5% antigen prevalence in its baseline study [7]. Several other countries were simply unaware of the existence of lymphatic filariasis among their populations or were unable to

attack the disease because of other more pressing public health needs, such as malaria control.

After the successful elimination of filariasis transmission from Japan, many Japanese experts turned their attention to the problems of other countries. This was exemplified by Manabu Sasa, who compiled his comprehensive global review in the book 'Human Filariasis' in 1976 [4], covering all available knowledge of filariasis distribution worldwide in addition to treatment and control strategies.

In the 1980s, Eisaku Kimura and other Japanese scientists (including one of the authors of this review, K.I.) began assisting the Samoan MDA programme [12,13]. This work included the discovery that annual, single-dose DEC was as effective as repeated doses [14], along with extensive research on the mosquito vectors [11,15–17], which would prove beneficial in supplemental vector control. Single-dose versus multiple-dose studies were repeated in Fiji [18,19] and provided further evidence to support a strategy of annual single doses, which is in use today in PacELF [20] and in the Global Filariasis Elimination Programme. In the mid-1990s, discovery of the greater impact of combination therapy and the donation of the drug albendazole by GlaxoSmithKline (http://www.gsk.com) revolutionized MDA programmes and offered the distinct hope of eliminating the disease, not only from the entire Pacific region but also globally.

PacELF

The World Health Organization (WHO: http://www.who.int) recognizes lymphatic filariasis as a potentially eradicable disease. In May 1997, the World Health Assembly resolved to eliminate the disease as a public health problem (WHA50.29) and WHO drafted a plan to eliminate lymphatic filariasis globally by 2020. In response to the WHA resolution, health ministers from all countries in the Pacific region met in Palau in 1999, where they agreed to work with the WHO Western Pacific Regional Office (WHO/WPRO) to eliminate lymphatic filariasis from the Pacific by 2010, ten years earlier than the global target, and established PacELF to achieve this goal. WHO/WPRO created a PacELF office in Fiji and is implementing a programme to eliminate lymphatic filariasis in the 22 countries and territories of the Pacific (Figure 1) using annual MDA of DEC and albendazole [21]. There is also an underlying policy to integrate PacELF activities into ongoing national disease and vector control programmes wherever possible.

Originally established with WHO and Australian government support, and supported extensively since then by Japanese aid, PacELF aims to interrupt transmission through MDA and to alleviate suffering caused by the disease (Table 1). Each country has ownership, choosing its own MDA strategy and carrying out its own customized

Table 1. PacELF summary[a]

Component	Statistic
PacELF countries	22
Nationwide baseline surveys completed[b]	22
Total population (2005 estimated)	8.8 million
Population at risk	8.0 million
Population covered by MDA (2005)	1.6 million
MDA treatment coverage (2005)	63%

[a]Abbreviation: MDA: mass drug administration of diethylcarbamazine and albendazole combination.
[b]Of which 11 are endemic and five are partially endemic.

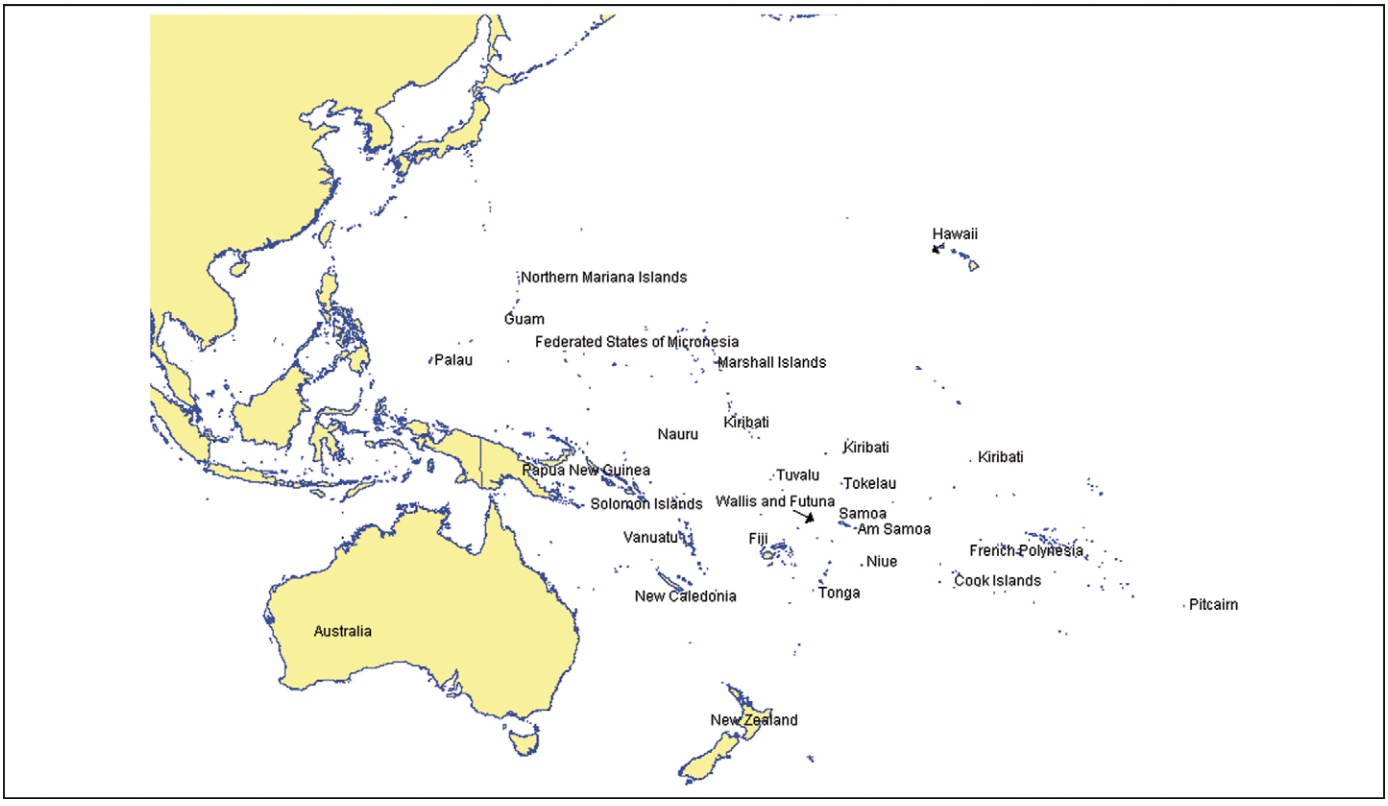

Figure 1. Map of the Pacific ocean showing Japan and the Pacific islands involved in PacELF. Reproduced, with permission, from the South Pacific Applied Geoscience Commission (http://www.sopac.org).

Table 2. Antigen prevalence after mass drug administration[a]

Location	Baseline survey			Nationwide survey (after five rounds)			
	Examined	Positives	% positive	Examined	Positives	% positive	% reduction
Cook Islands	1884	162	8.6	2606	33	1.3	85.3
Niue	1794	56	3.1	1285	3	0.2	93.5
Samoa	7006	317	4.5	12 719	144	1.1	75.6
	Baseline survey			Sentinel site survey (after one to three rounds)			
	Examined	Positives	% positive	Examined	Positives	% positive	% reduction
American Samoa	350	61	17.4	602	64	10.6	39.0
Fiji	234	90	38.5	345	78	22.6	41.2
Tonga	4002	108	2.7	3896	96	2.5	8.7
Tuvalu	574	128	22.3	3800	483	12.7	43.0
Vanuatu	627	151	24.1	1171	92	7.9	67.4

[a]Diethylcarbamazine and albendazole combination.

social mobilization and information, education and communication activities. PacELF coordinates drug procurement, storage and supply, in addition to providing technical advice, health-promotion guidance, surveillance guidelines and data management, and functioning as a liaison among all associated partners and donors. Reflecting the altruistic Araragama spirit, six of the 22 member states are non-endemic but still contribute to the overall goal as equal partners. Owned by the 22 member states, PacELF encompasses the fundamental Japanese success components of government commitment, policy formulation based on solid evidence, a community-based public health approach, private sector involvement, engagement of women's groups and fundamental and cohesive participation by research scientists and control programme managers.

All the endemic countries (American Samoa, Cook Islands, Fiji, French Polynesia, Kiribati, Niue, Papua New Guinea, Samoa, Tonga, Tuvalu and Vanuatu) and one partially endemic country (Wallis and Futuna) have started MDA and five of them completed five rounds by 2005. A total of 6.2 million people are targeted to receive at least five rounds of MDA by the end of the programme. During the last five years, MDA has reached 69–75% of the population in the region.

Japanese support to PacELF

Japan, the major resource provider, is collaborating with WHO and has donated ¥110 million ($1 million) annually to PacELF since 2000. As bilateral assistance, Japan also provides drugs and equipment such as DEC tablets, diagnostic testing kits and insecticide-impregnated mosquito nets. In addition to direct assistance in the form of supplies, Japan has dispatched a regular flow of volunteers to Pacific island nations.

Japanese volunteers in Samoa cooperate with the staff at the Ministry of Health to carry out blood testing, distribution of medicines, management of supplies sent from the PacELF office, and reporting and training. The measures to control filariasis in Samoa are rooted in local communities and work within established social institutions. For example, on the day of blood testing, the village women's associations set up the testing centres and notify the villagers, reflecting the predominant role that women had in improving the overall health of Japan during the 1950s and 1960s. It was also found that, in American Samoa, the church could have a key role in initial MDA activities and plans were adjusted to take advantage of this fact accordingly. Volunteers working in Vanuatu, Fiji and Tonga work with national staff and local populations on similar tasks.

The PacELF family receives additional non-Pacific support from the Atlanta-based Centers for Disease Control and Prevention (http://www.cdc.gov) and Emory University (http://www.emory.edu) (which work in American Samoa and other US territories in the region), from the Liverpool School of Tropical Medicine (http://www.liv.ac.uk/lstm) in the UK, from GlaxoSmithKline and through assistance from the UK and UN volunteer corps.

PacELF results

Disease distribution has been mapped throughout the region [7], peaking at 22% prevalence in Tuvalu. Public awareness of the disease has been dramatically raised region-wide and sentinel sites for monitoring and evaluation have been identified on all islands. Based on mid-term results from nine countries, prevalence fell by an average of 38% after two rounds of MDA. A dramatic reduction averaging 85% in filarial antigen prevalence was seen after five rounds of MDA in three countries: Cook Islands, Niue and Samoa (Table 2). Antigen prevalence was reduced to 1.3% in the Cook Islands, 0.2% in Niue and 1.1% in Samoa. The antigen test overestimates by two- to fourfold the number of microfilaria carriers, which was reduced from 1.1% to 0.4% in 175 000 eligible inhabitants of Samoa. In addition to these three countries, five others observed reduction in antigen prevalence between initial and follow-up surveys conducted in sentinel sites after MDAs [21]. The relatively low percent reduction in prevalence in Tonga (8.7% after three MDA rounds) could be cause for concern. However, dramatic reductions in antigen prevalence between the midterm sentinel site survey (after two or three MDA rounds) and final nationwide survey (after five rounds) have been the norm. For example, the reduction in prevalence in the Cook Islands went from 18.9% reduction (after three MDAs) to 85.3% reduction after five MDAs. Monitoring and evaluation has, however, shown that in some cases, more than the originally envisaged five rounds of MDA might be required to achieve elimination.

Concluding remarks

Filariasis transmission in many Pacific islands and territories is different from that observed in Japan, most notably in Polynesian countries, which have the sub-periodic form of *W. bancrofti* transmitted by *Aedes polynesiensis* and *Aedes scutellaris* mosquitoes [22,23]. However, Japan has an unparalleled recent history in exploiting its expertise

and best practices developed during successful national disease-elimination activities and transferring them to other nations where they can be refined and applied to suit local conditions. Moreover, Japan has also helped to ensure maximum impact by concurrently transferring resources in the form of funds and skilled individuals. The latest example of this is the Health and Development Initiative, a global $5 billion aid programme announced in mid-2005, which will have a strong regional component focusing on health improvements in Africa [24].

There are still many challenges that need to be overcome to achieve elimination of lymphatic filariasis in some of the remote islands and areas of the Pacific and, thus, free millions of people from the threat of infection and assist the 500 000 already infected. Nevertheless, Japan is committed to provide financial support and volunteers, in addition to technical and operational advice, to overcome these challenges and make progress towards the 2010 PacELF elimination target.

Acknowledgements

We are grateful to Tom Burkot for useful discussions. We thank the Ministries and Departments of Health in the 22 countries and territories that form PacELF for their enthusiasm and cooperation.

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