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A community-directed strategy for sustainable malaria elimination on islands: Short-term MDA integrated with ITNs and robust surveillance

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ABSTRACT

In the Asia Pacific sites with low and unstable transmission, elimination should be feasible with existing tools. On Aneityum island, Vanuatu both *Plasmodium falciparum* and *Plasmodium vivax* malaria were eliminated in 1991 after implementation of a combined intervention package, including mass drug administration (MDA) and insecticide-treated bed nets (ITNs), with high degree of community involvement. Subsequently, community-based surveillance and vector control measures have kept. By reviewing the experiences of the Aneityum project, I intended to examine the roles of community in malaria elimination. To be successful, the program should transfer major intervention components from the external donor-directed initiative to the community-directed approach. Scaling up of community involvement from simple participation to social participation, where communities involve in health planning functions is necessary from malaria control to malaria elimination.

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1. Introduction

A Global Malaria Action Plan, announced at the UN Millennium Development Goals Malaria Summit in New York on 15 September 2008, set the ambitious goals of both reducing malaria burden and to eventually eradicate the disease (Roberts, 2008). In the 1950s scientists and the World Health Organization (WHO) also exuded confidence when they vowed to eradicate malaria. However, this campaign broke down in 1960s. The lessons from the past failure tell us that there are no magic bullets for malaria eradication. The two major defects of the first ambition were a 'one-size-fits-all' approach and resistance of people to interventions as time went by Needham and Canning (2003) and Rieckmann (2006). Today many countries with a lot of outside support have rapidly scaled up their interventions, such as long-lasting insecticide-treated bed nets and artemisinin-based combination therapies. Several countries have reported promising results, with steep reductions in morbidity (Bhattarai et al., 2007; Fegan et al., 2007). This has led to renewed interest in malaria elimination with 39 countries stating their desire to achieve elimination (Feachem and The Malaria Elimination Group, 2009). However an essential question is left unanswered: what happens after aggressive short-term targets are

achieved? How can the malaria-free situation be technically and operationally sustained in a long run (Spielman et al., 1993)?

Islands provide natural ecological experiments and a great potential for intervention studies. Vanuatu with a total population of 186,678 (1999 census) has 68 inhabited islands with a high linguistic diversity. The archipelago belongs to Remote Oceania, a region where Anopheline presence and malaria roughly correspond to the Buxton line. Buxton (1926) mentioned, "The only malarious island outside that area is Aneityum. Malaria occurs on all the inhabited islands of New Hebrides (Vanuatu), except Futuna (Fig. 1a)." Despite different waves of colonization, unstable malaria has continued probably since the first human settlement 4000 years ago (Kaneko et al., 1998). An island community is separated from the next not only by differences of tongue, and of customs, and by the natural barriers of sea and forest, but much more by barriers of fear and of magic (Buxton, 1926). Aneityum, the southernmost island in Vanuatu, is located at the southeast edge of this malaria extension in the Pacific (Fig. 1b). To examine the feasibility of elimination of both *Plasmodium falciparum* and *Plasmodium vivax*, the Aneityum project was initiated in 1991. The strategy was an integrated malaria control program consisting of mass drug administration (MDA) to cover the entire population of 718 inhabitants (1989 census) for a limited period of 9 weeks, insecticide-treated bed nets (ITNs), and larvivorous fish together with malaria surveillance by a community microscopist. Eight years after the project started, we concluded that malaria can be eliminated on islands if there is a high degree of community commitment (Kaneko et al., 2000).

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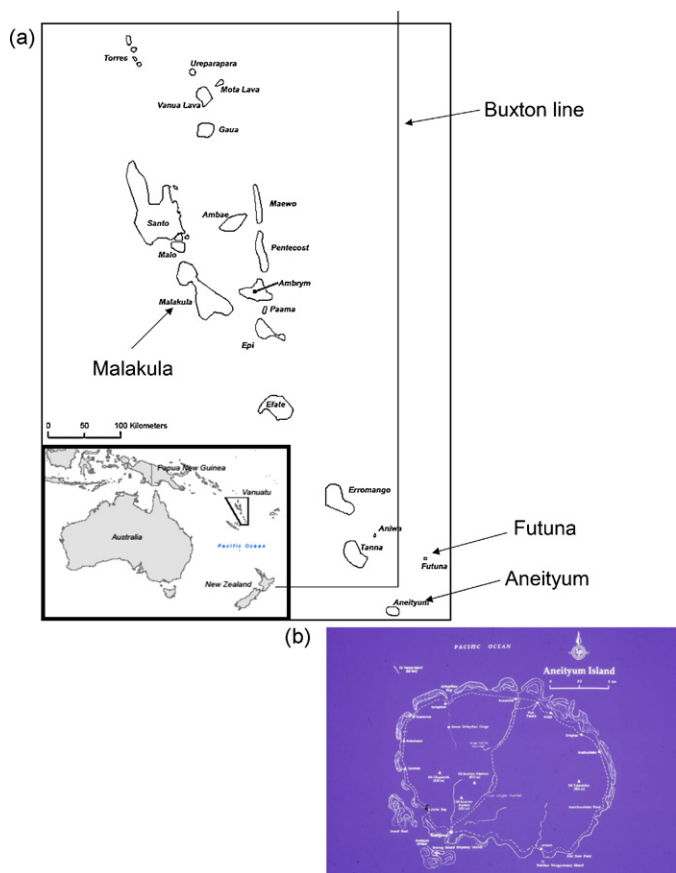


Fig. 1. (a) The Vanuatu archipelago with the Buxton line. (b) The Aneityum island.

I will first review some specific issues of malaria elimination efforts in the Asia Pacific context. Second I will review experiences of the Aneityum project with the intention to propose the roles of community in malaria elimination as a key towards the success of the program.

2. Specific issues of malaria elimination efforts in the Asia Pacific context

In the Asia Pacific sites with low and unstable transmission, elimination should be feasible with existing tools (Feachem and The Malaria Elimination Group, 2009). The unique challenges then have to do with the high proportion of *P. vivax* infections. The existence of a persistent liver stage makes *P. vivax* less vulnerable than *P. falciparum* to elimination efforts.

2.1. *P. vivax* elimination

Although the emphasis on *P. falciparum* malaria is appropriate because of its high mortality in African children, the burden of *P. vivax* malaria should not be underappreciated and exacts a significant toll on almost 40% of the world's population (Price et al., 2007). Control measures for *P. vivax* remain limited in most areas of Asia, South America, and temperate regions of the Middle and Far East. The reemerging *P. vivax* malaria in South Korea also shows the difficulty of its control even with a developed health system in the temperate zone (Han et al., 2006). ACT-treatment-based programs have greater impact on *P. falciparum* than *P. vivax* (Carrara et al., 2006; Nosten et al., 2000). Chloroquine remains inexpensive and effective against *P. vivax* malaria in most areas, including Vanuatu. However the first case of chloroquine-resistant *P. vivax* was

reported in 1989 from Papua New Guinea (Rieckmann et al., 1989). The chloroquine-resistant strains of the parasite are already firmly established in Papua (Ratcliff et al., 2007) and other parts of Indonesia (Baird et al., 1996) and as they spread further afield will impact significantly on the current program (Price et al., 2007). Furthermore multidrug-resistant *P. vivax* associated with severe and fatal malaria has been reported from Papua (Tjitra et al., 2008).

In the era with a new global malaria eradication strategy, it is a remaining challenge how *P. vivax* will be eliminated after *P. falciparum* (Feachem and Sabot, 2008).

2.2. Resurgence after malaria elimination

Malaria resurgence is a major concern after elimination of the disease in an area. Its possibility depends on importation risks (vulnerability: human and mosquito movements) and outbreak risks (receptivity: existence of local vector mosquito and degrees of anti-parasite immunity in human populations).

Adults from hyper-endemic areas seem to require regular contacts with the parasite for immune protection to persist (Nardin et al., 1979). The protective immunity of the population would soon fade if parasites are eliminated from a malaria endemic area (Druilhe and Perignon, 1994). In accordance with this concern, a devastating resurgence after unsustainable success of an attempt to eliminate malaria was previously recorded in various African islands with *P. falciparum* (Arez et al., 1999; Lepers et al., 1988; Loureiro et al., 1996) and Asian countries with *P. falciparum* (Pitt et al., 1998) and *P. vivax* (Wijesundera, 1988). A focal outbreak of malaria caused by a clonal parasite line was previously documented in the outbreak of *P. falciparum* on Santiago island (Arez et al., 1999) and among Amazonian Yanomami Amerindians (Laserson et al., 1999). In a previous study during an epidemic of malaria in the eastern highlands of Papua New Guinea, all *P. falciparum* infections were of a single genotype, suggesting an outside introduction as the source of the epidemics, while *P. vivax* infections were highly diverse, suggesting endemic transmission (Mueller et al., 2002). However, it is a remaining question how *P. vivax* resurgence can occur in relation to species-specific immunity and parasite diversity, and how it can be contained.

2.3. MDA to interrupt malaria transmission

MDA was previously recognized as an important method of malaria control (Macdonald et al., 1968; Onori, 1972; Molineaux and Gramiccia, 1980; Garfield and Vermund, 1983). In recent years, however, it has not been recommended for malaria control programmes because of compliance problems and the risks of selection for resistant parasites (Wernsdorfer, 1992). The MDA on Aneityum in 1991 resulted in a decade of malaria freedom and this duration should be appreciated to be long enough in terms of cost-effectiveness. MDA to eliminate *P. vivax* could be justified in the following circumstances: the expected high prevalence of hypnozoites in young populations, asymptomatic profiles of most of *P. vivax* cases, which seemed to transmit gametocytes through mosquitoes before they reach clinical thresholds, and the high risk of relapse without primaquine therapy, particularly Melanesian strains (99%, Baird and Hoffman, 2004). MDA using primaquine is necessary to eliminate *P. vivax* hypnozoites. MDA can be species- and age-specifically applied as shown in the following two examples on Aneityum.

The 1st MDA to cover the entire population on Aneityum island (718 inhabitants) was done from September to November 1991, prior to the rainy season, once a week for 9 weeks to eliminate different stages of the malaria parasites (i.e., the blood sexual and asexual stages, the liver stage, and possibly the stages in vector mosquitoes). To achieve a parasite-free status in human and vector

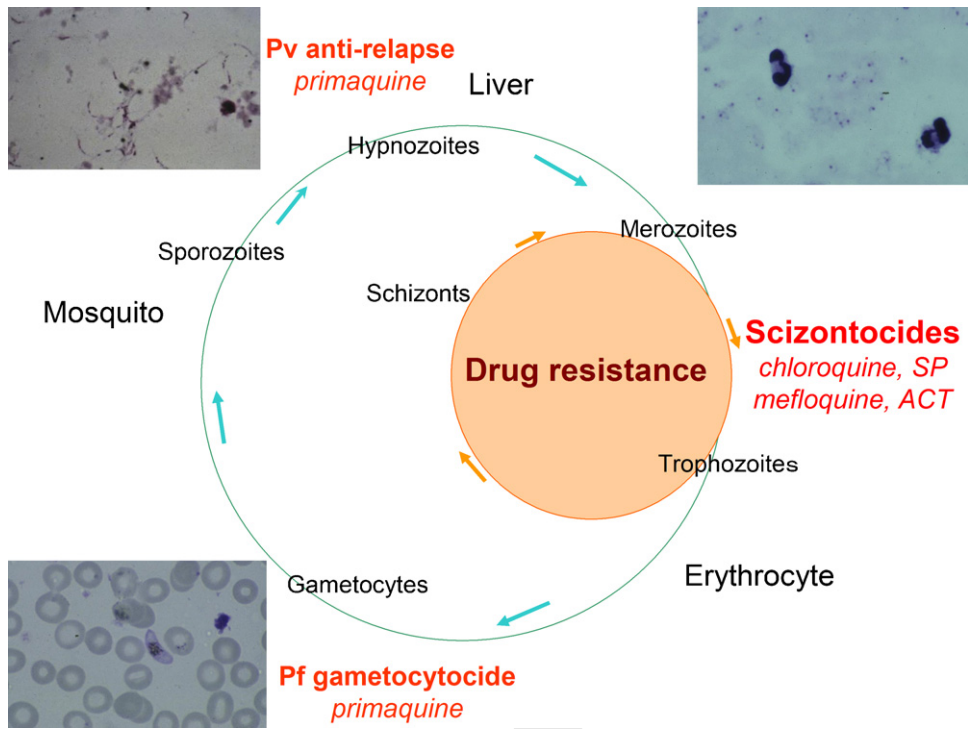


Fig. 2. The life cycle of malaria parasites with species- and stage-specific efficacies of antimalarial drugs. Pv: *P. vivax*. Pf: *P. falciparum*. SP: sulfadoxine-pyrimethamine. ACT: artemisinin-based combination therapy.

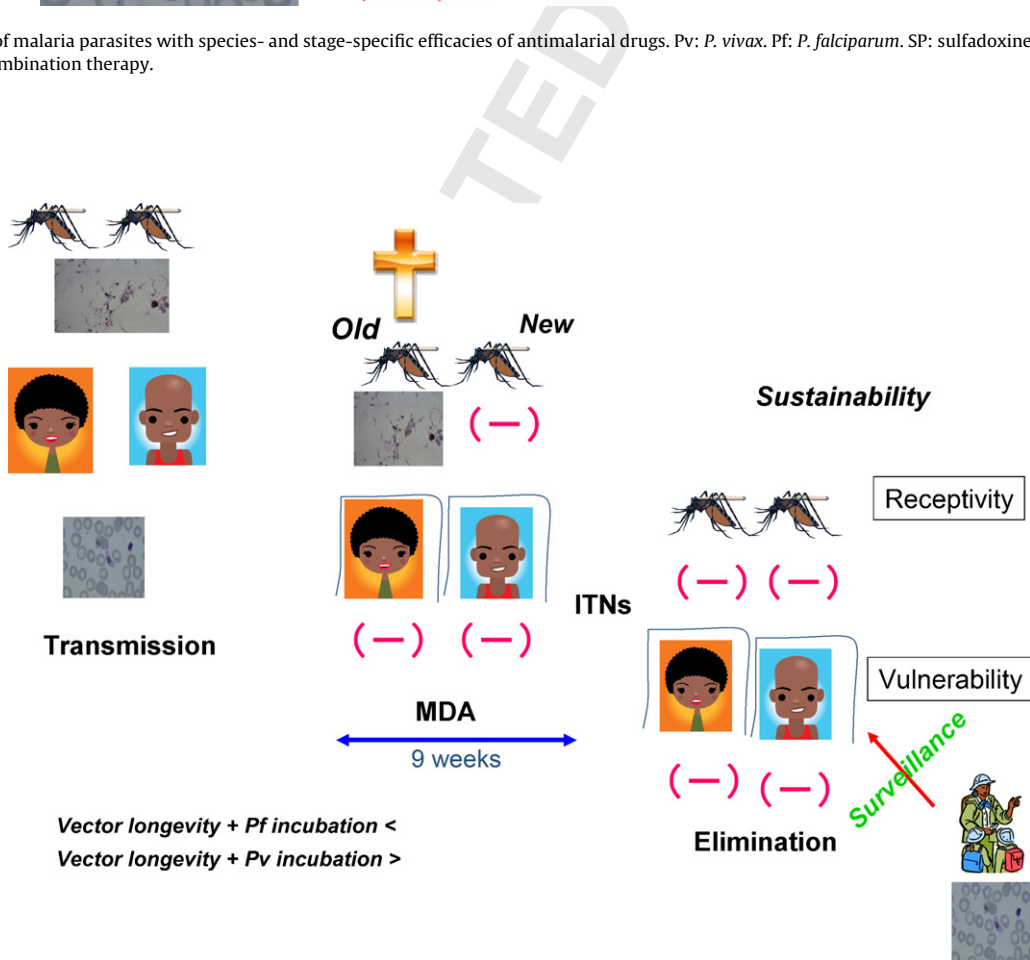


Fig. 3. A strategy for sustainable malaria elimination on islands: MDA integrated with ITNs and a robust surveillance system. Since the maximum longevity of vector mosquito is estimated to be less than 5 weeks, a 9-week drug administration period to keep the target human population free of parasites (–) is considered sufficient for *P. falciparum* (Pf) with a short incubation period to result in a parasite-free (–) vector population, because old mosquitoes are dying (†) and new mosquitoes have no chance to get parasites during the MDA period. However this period may not be long enough for *P. vivax* (Pv) considering its extended incubation period. Therefore it is quite important for the target human population to be completely prevented from mosquito bites by ITNs particularly during the MDA period (short-term ITNs). After malaria elimination is achieved, it is also important to minimize potential resurgence risks by a robust surveillance system and continuous vector control efforts (long-term ITNs).

populations in the target area, it is necessary to combine different classes of antimalarial chemotherapeutic agents in consideration with the levels of drug resistance in parasites (Fig. 2). Since the maximum longevity of *Anopheles farauti* is estimated to be less than 5 weeks, a 9-week drug administration period is considered sufficient for *P. falciparum* with a short incubation period to result in a parasite-free vector population, because old mosquitoes are dying and new mosquitoes have no chance to get parasites during the MDA period (Fig. 3). However this period may not be long enough for *P. vivax* considering its extended incubation period. Therefore it is quite important for the target human population to be completely prevented from mosquito bites by ITNs particularly during the MDA period (short-term ITNs). After malaria elimination is achieved, it is also important to minimize potential resurgence risks by a robust surveillance system and continuous vector control efforts (long-term ITNs). The MDA schedule on Aneityum in 1991 was weeks 1, 5, and 9—45 mg primaquine and 600 mg chloroquine and three tablets of 75 mg pyrimethamine plus 1500 mg sulfadoxine; weeks 2–4 and 6–8—45 mg primaquine plus 300 mg chloroquine. Due to the increased degrees of drug resistance particularly in *P. falciparum* malaria parasites, sulfadoxine–pyrimethamine should be replaced by alternative drugs such as mefloquine or artemisinin-based combination therapy.

After a small outbreak of *P. vivax* was detected on Aneityum in 2002, the 2nd MDA of weekly chloroquine for 4 weeks and daily primaquine for 14 days was additionally carried out on the population borne after 1982 before the onset of the rainy season in December 2002 in concert with re-strengthening of the community-based provisions of ITNs and larvivorous fish.

In the above-mentioned MDA regimes primaquine has quite important roles as *P. vivax* hypnozoitocide and *P. falciparum* gametocytocides (Fig. 2). Glucose-6-phosphate dehydrogenase (G6PD) deficiency potentially results in haemolytic reactions after primaquine administration, although previous surveys detected no individuals with this on Aneityum or two other southern islands of Vanuatu (Kaneko et al., 1998). It is an important subject in Asia

Pacific how to screen and manage G6PD deficient subjects (homozygous male, homozygous female, and heterozygous female?) in endemic areas in the context of primaquine administration.

A well-adjusted short-term MDA should be considered as an important tool combined with vector control methods to interrupt malaria transmission in an isolated endemic area. However its application totally depends on local epidemiological conditions and health systems of the target area. It is important that any MDA should not be applied in a top-down manner. I believe community commitment is an important requirement in the success of MDA (see the latter chapter).

3. The Aneityum project in the context of community involvement

By reviewing the experiences on Aneityum island since 1991 (Kaneko et al., 2000), I intend to examine the role of the community in malaria elimination in the belief that community involvement is a key factor towards the success of the program.

3.1. Aneityum island and its malaria prevalence

Aneityum is a circular island of volcanic origin, and mountainous with wooded peaks rising to 850 m. Aneityum has abundant streams and swampy valleys, which serve as larval habitat for *A. farauti* (Fig. 1b). The total population of 718 live in and around three major villages: Analgaut, Port Patrick, and Unmet (Kaneko et al., 2000).

The age- and species-specific parasite rates (PRs) and the spleen rates (prevalence of palpable spleen among children aged 2–12 years) of Aneityum and two comparison islands, mesoendemic Malakula and nonendemic Futuna, at the beginning and 7 years later are presented in Fig. 4. Before the intervention the malaria situation on Aneityum showed a pattern similar to that of Malakula. The PRs generally decreased with age. The prevalence of *P. vivax* decreased in individuals older than 5 years of age whereas the

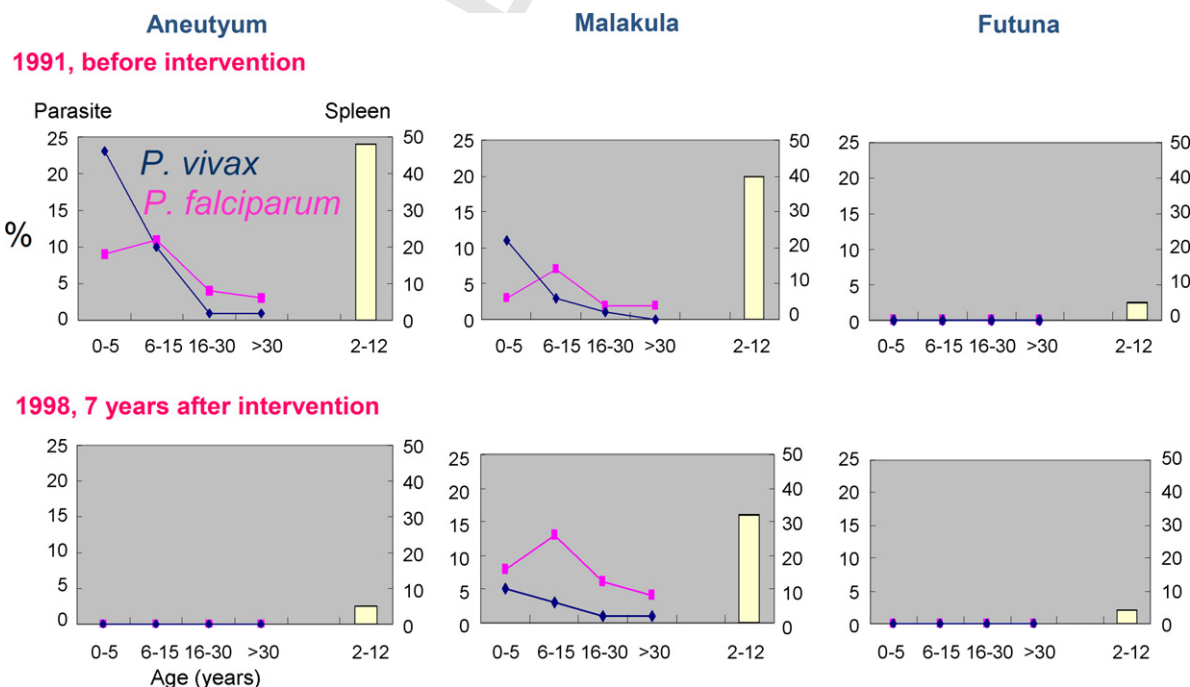


Fig. 4. Age- and species-specific parasite rates and spleen rates in children on Aneityum (intervention), Malakula (mesoendemic), and Futuna (nonendemic): red lines represent *P. falciparum* parasite rates, blue lines *P. vivax* parasite rates, and yellow bar spleen rates in children aged 2–12 years. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.)

prevalence of *P. falciparum* decreased in individuals older than 15 years of age. *P. falciparum* gametocytes were detected in all age-groups but with a higher prevalence in the younger age-groups (data not shown). Seven years later the situation on Aneityum, however, has become similar to that of Futuna (Kaneko et al., 2000).

3.2. MDA

The above-mentioned 1st MDA plan was formulated by the malaria control program in the Vanuatu Department of Health. The district malaria supervisor in the southern district took a key operational role. There were several meetings with community in early 1991 to explain the purposes and procedures of MDA and to get a full commitment of the community to eliminate malaria from the island by MDA. At the same time 12 village volunteers were selected and trained as MDA staff. Each dose was administered under close supervision by the staff. The villagers were asked about possible side-effects of the previous week's drug intake before the next round of treatment. The drugs were provided free of charge. The compliance rate was defined as the percentage of the appropriate, age-scaled doses that were successfully administered. The 718 inhabitants of Aneityum were registered in the records of MDA logbook kept by the district malaria supervisor during the drug intervention period. Of 6462 scheduled drug doses, 509 (7.9%) were not administered because of villagers' absence from the island, and the intake of a further 247 (3.8%) doses was not properly recorded and could not be confirmed. Of the remaining 5706 scheduled doses, 5038 were successfully administered during the nine MDA rounds, resulting in an overall calculated compliance rate of 88.3%. The main reasons for non-compliance were because the villagers were working some distance from the study centre. The compliance rate of around 90% during the first three mass drug administration rounds dropped to 79% in the fourth round. Some villagers reported vomiting after taking the tablets and others complained that the tablets per dose were too numerous (13 tablets for an adult in the first round). In response to these complaints, a meeting to provide additional information and respond to questions was held with the villagers and resulted in the removal of chloroquine from the scheduled drug regimen from the fifth and the ninth rounds without any replacement drugs. This modification to the protocol was well received and compliance improved in the further rounds (86–92%). Side-effects were seldom reported in the latter part of the programme.

3.3. Vector control

Impregnated bed nets: In October, 1991 the population of Aneityum was provided with 680 impregnated bed nets (0.94 nets per villager), consisting of 423 single nets, 157 double nets, and 100 family-size nets. Because many of these bed nets accommodate more than one person, our estimate of coverage is conservative. Some families requested and received extra nets to be used by returning relatives or visitors. They were treated with permethrin (500 mg/m²). Dipping and dripping of the bed nets with permethrin solution was done by village volunteers under the supervision of the district malaria supervisor. The bed nets were provided free of charge to mothers and small children less than 5 years of age, at a cost of US\$4 to adults and US\$2 to schoolchildren. The bed nets were treated in the same way with permethrin once a year. The villagers were asked to wash their nets 1 day before re-treatment. The cost of re-treatment was US\$1 per family.

Since the initial bed net distribution, several batches of nets were repeatedly distributed to maintain the entire coverage. In 2001, we further provided 1000 bed nets to the community as a stock in the dispensary, from which bed nets were regularly

supplied to villagers upon their requests. From 2000 up to 2006, averaged 510 nets were re-impregnated with permethrin each year with the assistance of the villagers (annual re-impregnation rate: 75%). The original affordable charging strategy to bed net users was maintained since 1991 till 2006, when the population was provided with a total of 716 long-lasting impregnated bed nets (0.87 nets per villager). Aggressive health education resulted in sustained compliance with the bed net programme even though the number of malaria infections decreased over time.

Larvivorous fish: The larvivorous fish (*Gambusia* spp.) were introduced into a large swamp behind Analgaut and several small ponds that were identified as breeding places of *A. farauti* in 1991 by the district malaria supervisor with village volunteers. Additional fish have been maintained in a stock pond. These sites have been monitored by community at least once a year and confirmed that the fish have become established

3.4. Surveillance by community microscopists

There are two flights to Aneityum every week with about ten passengers per flight. These flights depart from the malaria-free capital Port Vila and from the neighbouring Tanna island with a low malaria endemicity. In recognition of the risk of reintroduction from even this limited flow of visitors to Aneityum, one village volunteer was selected by the local health committee in 1992 to be trained for malaria microscopy. This community microscopist has been working with the registered nurse of the island dispensary to guard against malaria reintroduction by examining all passengers on arrival and any febrile cases in the villages. A new microscopy facility attached to the local dispensary was constructed by the community in 2004. A total of 6 village volunteers have actively maintained this community microscopist until now.

3.5. *P. vivax* outbreak and containment

There was a malaria upsurge in Vanuatu in the early 2000, recorded in the passive case detection data of the Vanuatu Department of Health. The southern TAFEA province consists of 5 islands. In 2001, *P. vivax* cases firstly started increasing on Tanna (1999 population census: 25840). Then, in 2003, devastating *P. falciparum* increases appeared on Tanna, Erromango and even on Aniwa, where no case had been recorded in the last 5 years. Only Futuna was completely exempted from this malaria outbreak, confirming no Anopheles condition on this island.

On Aneityum, *P. falciparum* cases had never appeared during this period, although *P. vivax* cases appeared in 2002. Importantly the unusual increase of cases on Aneityum was first recognized by the community microscopists and quickly reported to us, while those on other islands were retrospectively recognized in the passive case detection data. I believe that the prevention of *P. falciparum* in Aneityum were triggered by the surveillance of the community microscopists, which could enable the project to take effective counter-actions quick enough, including the investigation of the outbreak, the age-selected MDA specifically to eliminate *P. vivax* parasites (see the above-mentioned Section 2.3), and the strengthening of community-based vector control activities and surveillance by community microscopists itself. However it seemed that this surveillance system was not robust enough to prevent the reintroduction of *P. vivax* to Aneityum, suggesting quite a high vulnerability of the island. The epidemic quickly waned from Aneityum after the 2nd MDA except for a few asymptomatic infections of *P. vivax* detected in three population-wide surveys, 2003–2005. We are now preparing a separate report of these longitudinal courses on Aneityum.

4. Community-directed malaria elimination process

4.1. Community-directed approach

Sen (1999) defined development as freedom. To be free of malaria in once endemic area is a kind of freedom, which can become a reality with better tools, if the people desire to have it. However there is a serious concern that maintenance of intensive intervention will be difficult once malaria is no longer a major public-health threat and populations and donors lose interest (Feachem and Sabot, 2008). Thus, the internalization of the malaria problem by ways of community education seems to play a key-role as shown in other settings (Yasuoka et al., 2006). The upsurge of malaria in Vanuatu in 2002–2004 shows the risk of elimination programs that are externally funded in weak economies (Singer and de Castro, 2007). While control strategies during 1940s led to the elimination of malaria in several places, mostly countries where programs were not based on external funds achieved a long-lasting elimination (Spielman et al., 1993). Community-directed intervention (CDI) approach was recently shown to be much more effective than currently used delivery approaches for various interventions including malaria (WHO/TDR, 2008). There is the difference between “participation” as used to denote the community simply accepting action that has been decided for them elsewhere, and the concept of participation as a process of community involvement in the planning, organization, operation, and control of health care as called for in the Declaration of Alma-Ata (WHO, 1984). CDI refers to the latter. To ensure a long-term sustainability after a short-term push towards elimination, the program should transfer major intervention components from the donor-directed initiative to the community-directed approach.

4.2. Community-directed malaria elimination

Community involvement in the malaria elimination process has, to my knowledge, been relatively poorly documented and described. Although community participation in malaria control has been extensively promoted by the WHO and the RBM partnership, I was not able to find recommendations related to community participation in elimination programs in any of the more recent WHO guidelines. In Vanuatu, however a high degree of community participation was identified as a key factor in the success of the elimination program, initiated in 1991. High community involvement, as measured by compliances of mass drug administration, bed net provision and re-impregnation, and surveillance by community microscopist, resulted in sustained interruption of malaria transmission on Aneityum island (Kaneko et al., 2000). Importantly, regardless of the malaria situations, the community continuously kept the initial high commitment during the whole period. Expanded elimination efforts on islands in the South-west Pacific are planning to have strong community involvement based on the above-mentioned results in Vanuatu (Pacific Malaria Initiative, 2007).

A community-directed malaria elimination initiative should be developed. This is an initiative that is undertaken at the community level under the direction of the community itself. The health services and its partners introduce in a participatory manner the range of possible intervention(s), and the means by which the community-direction concept can ensure community ownership from the onset. From then on, the community takes charge of the process, usually through a series of community meetings for decision-making on implementation. The following activities proposed by RBM (WHO, 2002) can be integrated in the community-directed malaria elimination process.

Activities that can be achieved with community-directed malaria elimination process:

- To improve recognition of malarial illness, diagnosis (microscope and RDT) and provision of early treatment by caregivers.
- To strengthen the capacity of health systems, particularly at community level (aid posts), including access to antimalarial drugs.
- To improve health-seeking behaviour of caregivers, family and community so they can recognize signs of illness and seek appropriate care quickly.
- To conduct mass drug administration.
- To improve access to insecticide-treated nets, and to promote their regular and proper use and re-treatment.
- To promote intermittent preventive treatment for pregnant women.
- To promote vector control, including larvivorous fish and environmental management wherever appropriate.
- To strengthen community self-monitoring and decision-making with key indicators including the numbers of households with ITNs, fever and malaria cases treated, ponds with larvivorous fish, and people going out and coming in.

4.3. Roles of community and health services in malaria elimination

The following roles of community and health services/partners are adapted from the previous CDI study (WHO/TDR, 2008).

4.4. Role of community

- Community members collectively discuss malaria elimination from their own perspective, as well as possible interventions, taking into account relevant community knowledge, tradition and additional information provided to them.
- Community members collectively decide whether they want malaria elimination initiatives to be delivered at the community level and if they want to take the responsibility for its implementation.
- Community members collectively design the approach to implementing the intervention in the community and identify the resources within the community.
- Community members collectively plan how, when, where and by whom the intervention will be implemented, as well as how it will be supervised, what support shall be provided to the implementers, and how the process will be monitored.
- Community-directed implementers execute the intervention.
- Following its execution, community members collectively discuss the results of the intervention in light of monitored results, financial balances in the community account, and adjust the implementation strategy accordingly.

4.5. Role of health services/partners

- Introduce to the community the concept of community-directed malaria elimination and technical aspects of the intervention(s).
- Provide and facilitate capacity-building and technical support.
- Provide supervision on the basis of procedures agreed upon with the community.
- Ensure adequate provision of the necessary supplies, i.e., drugs, diagnostics, ITNs, larvivorous fish and other intervention materials.
- Generate health policies for community-directed malaria elimination and clear policy guidelines for the integration of specific interventions in the community-directed intervention package.

5. Conclusion

To ensure high compliance of available tools and long-term sustainability towards the ultimate goal, malaria elimination, the program should transfer major intervention components from the external donor-directed initiative to the community-directed approach. Scaling up of community involvement from simple participation to social participation, where communities involve in health planning functions is necessary from malaria control to malaria elimination.

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