EFFICACY OF PERMETHRIN-IMPREGNATED BED NETS ON MALARIA CONTROL IN A HYPERENDEMIC AREA IN IRIAN JAYA, INDONESIA: INFLUENCE OF SEASONAL RAINFALL FLUCTUATIONS

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Abstract. A malaria intervention study was carried out using permethrin impregnated bed nets in the south-central part of Irian Jaya with perennial transmission, from April 1993 to April 1995. Malariometric surveys were carried out periodically for parasite prevalence by species and for spleen rates. Prior to intervention, the percentage of *Plasmodium falciparum* infected inhabitants was significantly higher in Hiripau, where permethrin-impregnated bed nets were used during the study, than in the placebo-treated control village, Kaugapu. After two years of intervention the situation was reversed and figures higher in the control village (RR 0.19, 95% CI 0.10 - 0.36, $p < 0.0001$). Similarly, *P. vivax* infection rates, 12.4% in Hiripau *vs* 5.7% in Kaugapu in April 1993, were reversed in April 1995 (3.6% in Hiripau and 11.3% in Kaugapu, $p < 0.001$). In the treated village, pre-control hyperendemicity was reduced to a low mesoendemic level (spleen rate 12.5%) during two years of intervention, whereas the level was mesoendemic (spleen rate 35.2%) in the control village. Impregnated bed nets were found an effective intervention both in moderate (April 1993 through April 1994, 1,626 mm rainfall) and high (April 1994 through April 1995/1995, 3,321 mm) transmission seasons.

INTRODUCTION

Malaria remains a major public health problem in many tropical areas of the developing world. In Indonesia, the malaria situation is found especially troublesome in Irian Jaya (New Guinea), the easternmost province of the country (Gunawan, 1985; Church *et al*, 1995). In addition to the remote geographical location, the low income and educational level of the inhabitants contribute to malaria being an important disease in this region.

WHO recommended impregnated bed nets for individual protection based on the combination of physical and chemical barrier effects they would provide in reducing disease transmission (WHO, 1983). Trials in many malarious countries showed varying results after evaluation based on short and long-term studies (Rozendaal, 1989). These diverse results were attributed to variations of epidemiological situations, vectors behavior and human population habits. Studies in areas where malaria transmission was relatively low, showed reductions of prevalence of infection, morbidity and mortality (Snow *et al*, 1988; Alonso *et al*, 1993; Wu *et al*, 1993; Luo *et al*, 1994; Luxemburger *et al*, 1994; D' Alessandro *et al*, 1995). On the contrary, several studies in areas with intense malaria transmission were less successful (Rozendaal, 1989; Das *et al*, 1993; Moyou-Somo *et al*, 1995; Binka *et al*, 1996). Continued investigations are required to clarify the potential of impregnated bed nets in areas where malaria transmission is perennial, taking into account that the application of malaria vaccines and new anti-malarials for protection and effective therapy are not yet in sight. Our study site in southern Irian Jaya is an area with perennial transmission with seasonal fluctuations due to variations of rainfall as one of the important ecological factors related to the vectors larval habitats and adult feeding activities (Lindsay and Birley, 1996). Therefore, we specifically considered the influence of local rainfall to evaluate the success of our malaria intervention with impregnated bed nets.

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MATERIALS AND METHODS

Study area and population

The study was carried out from April 1993 until April 1995, in the south-central part of Irian Jaya, in the lowland along coastal areas of East Mimika district, about 20 km west of Timika. A preliminary baseline study was conducted around Timika and Mapurujaya in September 1992, which showed variations of hypo- to holoendemicity based on spleen rates from 4.8% to 92% (Pribadi *et al*, 1998). Two of these villages had a comparable level of endemicity. Hiripau with a spleen rate of 59.4% and Kaugapu of 46.3%. Hiripau showed only a slightly higher overall parasite prevalence of 27.4% *vs* Kaugapu with 22%. Considering also other factors like ethnology, tribal habits, and similar environmental conditions these two villages were chosen for our intervention study.

Hiripau and Kaugapu are located along the Wania river, between 4°30′ and 4°5′ S latitude, about 25 km from the coast. The distance between the two villages is about 2 km, surrounded by thick forest swamps and sago palms. During the study, Hiripau had 657 villagers and 158 households, with 237 children under the age of ten; Kaugapu had 565 inhabitants, 141 households and 201 children under ten. About 90% of the population were local indigenous Irianese from the Kamoro group and the remaining inhabitants were originated from other islands outside Irian Jaya (Maluku Islands, South and North Sulawesi, and Java). Most of the villagers are fishermen and hunters. Sago is the main staple carbohydrate source. Sociological data indicated that most villagers lived under the established poverty line (Bandi, unpublished). Houses are made from wood and placed stilts around 0.5 m above the ground. Mosquitos can easily enter houses from gaps and holes between the boards of floors and walls. Before intervention began, villagers usually slept on the floor or on a mattress without bed nets. Because there was no electricity in this area, adults normally sat outside of the houses in the early evening, particularly during the full moon, before retiring around 22.00 hours. Numbers of domestic animals, dogs, pigs and chickens were similar in both villages.

General and study-independent intervention

For several years prior to and also during the study period, malaria control activities were conducted house to house by the health department of Freeport Indonesia Enterprise (PT Freeport Indonesia), the major employer in the study area, based on an active case detection (ACD) system. Every day, except Sunday, health workers periodically visited and interviewed the inhabitants in the villages of the whole region. Those who presented with fever, headache or other symptoms compatible with malaria were examined for parasitemia by blood slide. Patients with positive blood slides were treated with standard doses of chloroquine (25 mg/kg body weight) and primaquine, 15 mg daily for 3 to 5 days, depending on the malaria species. After one week, blood was examined and if positive, the patients were given a single dose of 3 tablets Fansidar® (combination of 1,500 mg sulfadoxine and 75 mg pyrimethamine).

In limited cases and prior to this study, vector control using bendiocarb fogging was applied in villages experiencing very high endemicity. However, in both study villages, neither DDT nor bendiocarb were used during the period from the beginning of the preliminary study in September 1992 until the end of the intervention study in April 1995.

Once a week, a "free" working day for local residents was organized by PT Freeport to perform vector source reduction activities close to the houses (*eg* draining and clearing ditches filled with rainwater).

A governmental primary health care station in the control village was responsible for medical care for the whole area, including the treated village.

Rainfall measurements

Average 24-hour ambient temperature in the study area was 25° - 30°C throughout the year, with daily period of high humidity of 90-100%. During the years before the study, the rainy season generally lasted from April to September followed by a dry season from October to March (report from Timika's weather station). In our study, rainfall was measured with a simple and calibrated rain gauge device, which was placed in an open field in the control village to collect daily precipitation. Every day, at 07.00 hours the volume of collected rainwater was recorded in millimeters to establish a rainfall profile throughout the study period.

Intervention strategy

Bed nets were made of nylon, rectangular in shape, family-sized (2 m x 2 m x 1.5 m) with 70 cm overlap. For impregnation based on the method of Schreck and Self (1985), 0.5 g/m^2 permethrin (Permanet® 100 EC, PT Bina Guna Kimia, Jakarta) was used. Initially, bed nets were impregnated in Jakarta around 2 weeks prior to the study and afterwards in the study area for further intervention. Six months after initial impregnation, the bed nets should be retreated or replaced, if badly torn. Port and Boreham (1982) found that sleeping under damaged (untreated) bed nets increases the risk of getting mosquito bites. During the survey in August 1993, the study team found 65% of bed nets were badly torn in both villages. Hence, it was decided to replace all nets every four months (instead of retreating torn ones), to provide all inhabitants with the same maximum physical barrier protection thorughout the entire study period.

In April 1993, the treated village (Hiripau) was provided 277 impregnated bed nets (approximately 1.7 per household), while 261 bed nets were distributed in the control village, Kaugapu. Nets in the control village were treated with a milk solution, which produced an appearance similar to the permethrin solution. The study team did this work with the assistance of the local inhabitants. There were two reasons for using milk as a blank formulation instead of the carrier solution without permethrin. Firstly, a possible deterrent effect of the blank emulsion had been reported from a study in The Gambia (Lindsay *et al*, 1991) where milk as placebo did not show deterrent as well as excito-repellent effects. Secondly, the villagers in the control village were not aware (blinded) that their nets had not been treated with insecticide in order to keep up their use compliance. The villagers were instructed to roll up the nets during the day to avoid pets and children damaging the nets.

In both villages, on average, one bed net was used by 0.8 children under ten years old and by 2.3 individuals total. Key persons carried out a house-to-house survey every night for the first three months and twice a week for the rest of the study to encourage compliance in bed net usage by inhabitants. Whenever the team visited the village, all heads of the families were gathered and informed about the importance of nocturnal bed net use while in their houses. With regular health education and awareness, bed net use compliance increased from 63% in the first year to 80% in the second year.

Malariometric surveys

In April 1993, prior to bed net distribution, a baseline malariometric survey in the two villages was completed including collection of blood samples for microscopy and examination for enlarged, palpable spleens to determine the level of endemicity. The results confirmed those of a preliminary study in September 1992: parasite prevalence and spleen rate were higher in the treated than in the control village (see Results section).

Mass surveys were conducted every 2 to 4 months: finger-stick blood was collected and spleen enlargement examined. Mean coverage rate for the treated village was 54.5% (range 40.6-64.4%) and 46.5% (range 36.1-55.6%) for the control village. The proportion of children under ten out of all surveyed inhabitants was 36.4% (range 34.1-39.5%) in the treated village and 41.8% (range 34.4% - 47.1%) in the control village.

In the field, a member of the study team stained blood films with Giemsa using standard procedures and examined thick smears before declaring them negative. All positive slides were identified to malaria species. Reexamination of the blood slides for 200 fields under 1,000x oil immersion was done in the laboratory by an experienced microscopist, not directly involved in the intervention study in order to provide an objective blinded evaluation. The presented results are based on the laboratory examinations, whereas those in the field were considered preliminary. *P. falciparum* and *P. vivax* were predominated and *P. malariae* accounted for less than 2% of all infections during this study.

Spleen enlargement was determined according to Hackett's grading system (Bruce-Chwatt, 1980). The same experienced physician (except for April 1994) conducted spleen examinations during the study. The April 1994 examination was not considered valid, because of large discrepant values.

Entomological assessment

Anopheles koliensis, An.punctulatus, and *An. farauti* all belonging to the *Anopheles punctulatus* complex (Lee *et al*, 1980) were found in the area, *Anopheles koliensis* and *An. farauti* were considered the primary and secondary vectors, respectively, as determined by a circumsporozoite ELISA (Burkot and Wirtz, 1986). Biting activity of *An. koliensis* was throughout the evening, from 18.00 hours until 06.00 hours with a peak biting activity between 23.00 and 01.00 hours. Mosquitos were found to bite indoors and outdoors.

Standard contact bioassays on the treated and untreated nets were carried out monthly based on prescribed procedures (WHO, 1975). Laboratory-bred *An. farauti* mosquitos were exposed to nets for 30 minutes and held for 24 hours to determine percentage mortality. Results showed effectiveness of between 95% and 100% during the entire period of study. A detailed report on the entomological data will be published separately.

Statistical analysis

Data were analysed using EpiInfo5 (CDC, Atlanta, USA). Chi-square or Fisher's exact tests were used with $p = 0.05$ as the limit of significance and

$p < 0.001$ as that of highly significant difference. Parasite infection rates was calculated as the relative prevalence of various species in the total number of blood samples (Bruce-Chwatt, 1980); parasite formula as the relative prevalence of various species in the total number of positive blood samples. The quotient of *P. falciparum* over *P. vivax* formula is given as a ratio. The spleen rate ratio is the quotient of splenomegaly in 2 to 9 years old children in the treated over splenomegaly in the children of the same age group in the control village.

RESULTS

Rainfall patterns

During the two years of the study, total rainfall in 1994 (3,321 mm) was two-fold higher than in 1993 (1,626 mm). In general, the period from April 1993 to April 1995 was dominated by a long moderate rainy season, which peaked during March to August 1994. Prior to these heavy downpours, rain fall was interrupted by a notable dry period from October 1993 through February 1994 (Fig 1).

Parasite prevalence

Before intervention, the proportion of parasitemic people was significantly higher (by 2.5 fold) in treated than control village (RR 2.49, 95% CI 1.72 - 3.59, $p < 0.001$) (Table 1). This observation was gradually reversed during the first year and a marked change was seen during the high rainy season, from April 1994 through April 1995, when parasite rates became more than two times higher in the control village (RR 0.24 - 0.46, 95% CI 0.14 - 0.69, $p < 0.001$) (Table 1).

Plasmodium falciparum and *P. vivax* infection rates

After four months, the percentage of *P. falciparum* infected persons in the treated village dropped to the level of the control village (RR 1.21, 95% CI 0.64 - 2.27, $p > 0.05$). Two months later, higher infection rates of *P. falciparum* in the untreated village indicated protective efficacy of permethrin impregnated bed nets (RR 0.19 - 0.36, 95% CI 0.08 - 0.76, $p < 0.001$). In both villages, *P. falciparum* infection rates were erratic with peaks in August and October 1994, at the end of heavy rains. However, the heavy rainfalls appear to have had a significantly greater influence on infection rate in the control village (Fig 2).

By contrast, a reduction of *P. vivax* infection rate was only observed in the second year of study,

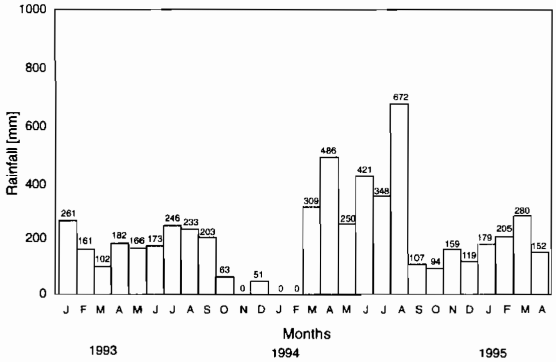

Fig 1–Rainfall profile in the study area (January 1993 - April 1995).

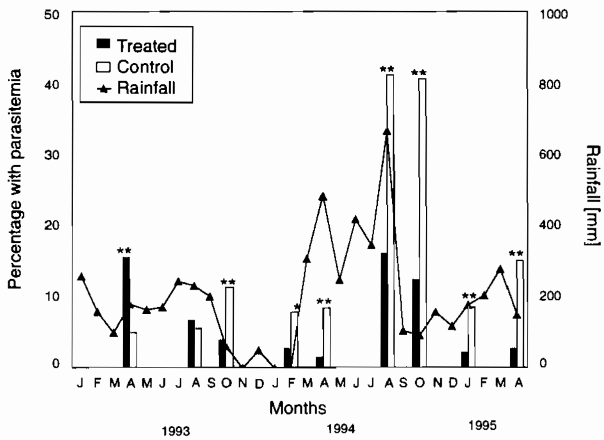

Fig 2–*P. falciparum* infection rate by survey months and rainfall pattern.
* significantly different ($p < 0.05$)
** highly significant ($p < 0.001$)

presumably because of secondary relapses. Significant differences in both villages at the beginning and at the end of the study period gave some evidence that *P. vivax* reinfection was also prevented by impregnated bed nets (treated *vs* control villages: April 1993 12.4% *vs* 5.7%; April 1995 3.6% *vs* 11.3%; $p < 0.001$) (Fig 3).

In the beginning, the ratio of *P. falciparum* over *P. vivax* was greater in the treated village (around 1 in both villages), then decreased to 0.5 after six months of intervention with impregnated bed nets indicating reduced transmission in the treated village. Although the ratio increased again during the heavy rainfalls in 1994, it always remained lower than in the control village, until the end of the study.

Gametocyte rates clearly increased in both villages during the peak of rainy season. However, treated bed nets appeared to have decreased the overall

Table 1
Overall parasite prevalence during two years of intervention in the treated and control sites.

Survey month	Treated (%)	Control(%)	p-value	RR and 95 % CI[a]
April 1993	27.7 (74/267)	11.1 (35/314)	<0.0001[b]	2.49 (1.72-3.59)
August 1993	13.9 (43/310)	10.8 (31/286)	0.2621	1.28 (0.83-1.97)
October 1993	15.8 (67/423)	18.4 (50/272)	0.3818	0.86 (0.62-1.20)
February 1994	14.4 (51/355)	15.9 (43/270)	0.5889	0.90 (0.62-1.31)
April 1994	4.6 (17/371)	19.3 (43/223)	<0.0001[b]	0.24 (0.14-0.41)
August 1994	22.6 (67/296)	49.1 (115/234)	<0.0001[b]	0.46 (0.36-0.59)
October 1994	18.7 (70/375)	52 (140/269)	<0.0001[b]	0.36 (0.28-0.46)
January 1995	6.4 (26/404)	14.7 (43/292)	0.0003[b]	0.44 (0.28-0.69)
April 1995	6.6 (28/422)	26.5 (54/204)	<0.0001[b]	0.25 (0.16-0.38)

% : number of infected persons/total number of people examined
[a] : RR = risk ratio with 95% confidence intervals
[b] : highly significant ($p < 0.001$)

Table 2
Splenomegaly prevalence during two years of intervention in the treated and control sites.

Survey month	Treated (%)	Control(%)	p-value	RR and 95 % CI[a]
April 1993	39.3 (105/267)	37.7 (118/313)	0.6888	1.04 (0.85-1.28)
August 1993	28.1 (87/310)	37.8 (108/286)	0.0117[b]	0.74 (0.59-0.94)
October 1993	28.4 (120/423)	27.9 (76/272)	0.9026	1.02 (0.80-1.30)
February 1994	14.6 (52/355)	23.1 (62/268)	0.0066[b]	0.63 (0.45-0.88)
April 1994	ND	32.7 (73/223)	ND	ND
August 1994	16.6 (49/296)	30.3 (69/228)	0.0001[c]	0.55 (0.40-0.76)
October 1994	18.1 (68/375)	32.6 (86/264)	<0.0001[c]	0.56 (0.42-0.73)
January 1995	15.8 (64/404)	34.8 (100/287)	<0.0001[c]	0.45 (0.35-0.60)
April 1995	13.3 (56/422)	28.1 (57/203)	<0.0001[c]	0.47 (0.34-0.66)

% : numbers of people with spleen enlargement/ total number of people examined
ND : no data
[a] : RR=risk ratio with 95% confedence intervals
[b] : significantly different ($p < 0.05$)
[c] : highly significant ($p < 0.001$)

source of potential transmission, indicated by lower gametocyte rates in the treated village throughout intervention.

Level of endemicity

The reduction in proportion of splenomegaly started in February 1994, nearly one year after the use of impregnated bed nets was begun (RR 0.47 - 0.63, 95% CI 0.34 - 0.88, $p < 0.05$) (Table 2). This changed the level of defined endemicity in the treated village from hyperendemic to low mesoendemic by the end of the study. Differences between the treated and control villages became highly significant from August 1994 until April 1995 ($p < 0.001$). Splenomegaly prevalence did not fluctuate during the heavy rainy season in 1994 (Table 2).

In general, spleen rates in children (2 - 9 years old) gave similar results, although slightly correlated with rainfall. The ratio of spleen rates in the treated over control village was greater than 1 in 1993, then decreased to around 0.5 during 1994 until April 1995 (data not presented).

Acute malaria cases

From May 1993 to February 1994, survey of acute fever cases was also included in this study. Fig 4 depicts the number of fever cases with *P. falciparum* parasitemia. Differences between the two villages were observed at the end of the rainy season during September through November 1993. When rainfall decreased, acute parasitemic fever cases rose in the untreated village, whereas they declined in

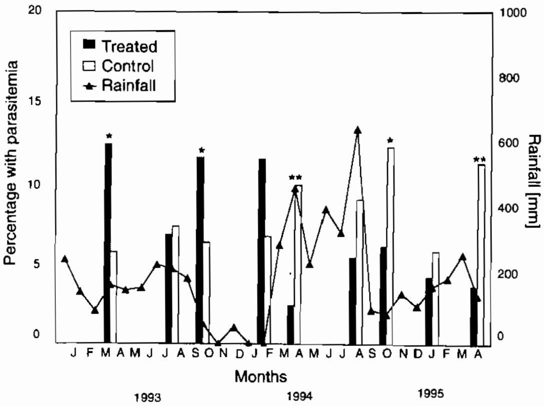

Fig 3–*P. vivax* infection rate by survey months and rainfall pattern.

* significantly different ($p < 0.05$)

** highly significant ($p < 0.001$)

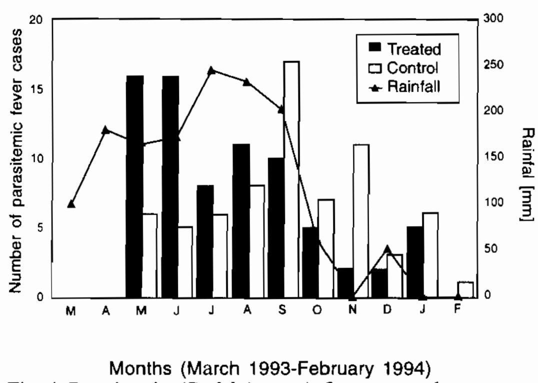

Fig 4–Parasitemic (*P. falciparum*) fever cases by survey months and rainfall pattern (March 1993 - February 1994).

the treated village (Fig 4). In general, the proportion of fever cases having active parasitemia was low (<30%) and the values similar in both villages.

DISCUSSION

In malaria areas with high levels of endemicity, clear differentiation between persistent and new infections is often difficult. This phenomenon is due to a longer period of time required to recover from one infection than potentially to acquire another new infection. Evaluation of intervention programs in such areas was ideally conducted on the incidence of "true new infectionu" from the blood of all participants in the study. Because of the logistic of following the large number of participants (hundreds of villagers), the uncertainty about anti-malarial therapy, patients' compliance, and drug resistance in the study area (Pribadi *et al*, 1998), measures of true incidence could not be obtained in this study.

Three different interventions were simultaneously conducted: impregnated bed nets to decrease human-vector contact, environmental sanitation to diminish larval breeding sites, and diagnosis/treatment of acute malaria cases to eliminate parasite source. Two of these prescribed general control measures in the study area were not conducted or monitored by the study team. Hence, evaluation of the relative contribution and the impact on these interventions on our study with impregnated bed nets would appear difficult. However, because both villages were covered similarly, any significant differences in malaria rates would presumably be the result of reduced vector contact by impregnated bed nets.

On the other hand, acute malaria cases in the study area were not predominant, with an average of 7 - 8 cases/month in either village (Fig 4) declining by the end of the study to one febrile case in the control and none in the treated village. Moreover, known resistance to antimalarials (Pribadi *et al*, 1998) would further reduce efficacy and the impact of this kind of intervention. Comparison of the two health care systems offered in the study areas (governmental primary health station in Kaugapu and PT Freeport health services) gave evidence that villagers preferred the company's assistance, which was free of charge.

The second general intervention, reduction of larval breeding sites by draining ditches around the houses, and eliminating small sites of standing water, may have made a minor contribution to malaria control in this area, but native forests and swamps around the villages still provide breeding sites, especially during increased rainfall.

In the treated village, parasite prevalences were similar after the first and the second year of intervention (4.6% in April 1994 and 6.6% in April 1995). However, in the second year infection rates were considerably higher, especially in the surveys of August and October 1994 (Table 1). Comparing the two villages, the differences indicate efficacy of permethrin also during the second year. Although *P. falciparum* infection rate followed the pattern of rainfall, the peak of malaria infection in August/ October 1994 was much lower in the treated than in the control village. This is cautiously interpreted as a direct impact of the use of impregnated bed nets. Permethrin may exert toxic as well as excito-repellent effects (Lindsay *et al*, 1991) and both properties would potentially reduce infected mosquitos contact with humans and lower infection rates. Availability of alternative host species in the study area, primarily dogs, might divert mosquitos to bite animals instead of humans. In Papua New Guinea, Burkot *et al* (1990) reported greater diversion of *An. punctulatus* to biting dogs when people were using nets.

In the treated village, *P. vivax* infection decreased only one year after intervention with impregnated bed nets. In Papua New Guinea, Graves *et al* (1987) did not observe reduction of *P. vivax* prevalence and incidence in children after 10 weeks of impregnated bed net use. In the Solomon Islands, Kere *et al* (1996) also showed a delayed disappearance of *P. vivax* over *P. falciparum* cases during three years of intervention. However, in a mesoendemic area in China, Luo *et al* (1994) showed a reduction of *P. vivax* infection in children after sleeping under treated bed nets for only one month. Tropical strains of *P. vivax* (Chesson) from Irian Jaya, Papua New Guinea and Solomon Islands relapse more rapidly (Graves *et al*, 1987) than temperate strains from China.

In the hyperendemic area of our study, splenomegaly in children decreased after one year of using bed nets, more slowly with placebo-treated ones and much more pronounced with impregnation. Several studies in Africa documented a reduction in the proportion and degree of splenomegaly in children after several months of using impregnated bed nets (Snow *et al*, 1988; Alonso *et al*, 1993; Moyou-Somo *et al*, 1995). However, in Papua New Guinea, no reduction of splenomegaly in children was observed after several weeks of using impregnated nets (Graves *et al*, 1987) or after one year of using untreated bed nets (Burkot *et al*, 1990).

Completely replacing old and torn nets with new ones every four months in both villages certainly played an important role in the observations in this study. Das *et al* (1993) showed a reduction in efficacy of bed nets on malaria incidence and prevalence when nets were retreated after longer intervals. Alonso *et al* (1993) reported increasing parasite prevalence and splenomegaly in children who slept under damaged bed nets. To answer the question, whether bed net replacement every 4 to 6 months is practicable as a general measure in malaria control is beyond the aims of this study. Certainly, regular replacement contributed to high compliance of routine use (80%) during the second year and to the success of malaria reduction in the treated group.

The results of this study revealed significant differences between the treated and the control villages concerning essential parameters of malaria epidemiology. There are good indications that impregnated bed nets are an effective intervention strategy in a highly endemic area with seasonally fluctuating malaria, both in moderate and high rainfall seasons.

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