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# Comparison of bednets impregnated with different pyrethroids for their impact on mosquitoes and on re-infection with malaria after clearance of pre-existing infections with chlorproguanil–dapsone

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**Abstract**

Comparisons of bednets treated either with alphacypermethrin or lambdacyhalothrin showed similar effectiveness by various entomological criteria. Lambdacyhalothrin was associated with significantly more reports of nasal irritation than alphacypermethrin. The 2 net treatments were equally effective in reducing incidence of new malaria infections and the treated nets were much more effective than untreated nets. These measurements were made after clearing existing infections with chlorproguanil–dapsone. This drug combination was more than 99% effective in clearing infections 1 week after treatment and a study of children taken to an altitude with no malaria transmission showed that there were very few recrudescences.

**Keywords:** malaria, vector control, impregnated bednets, alphacypermethrin, lambdacyhalothrin, chemotherapy, chlorproguanil–dapsone, Tanzania

## Introduction

So far, WHO-sponsored trials of insecticide-treated nets have used permethrin at a dose of 500 mg/m$^2$. These have produced excellent results on child morbidity and mortality (LENGELER *et al.*, 1996), but the cost of this insecticide treatment is a deterrent to re-treatment when householders are asked to pay for it (CHAM *et al.*, 1997). Lambdacyhalothrin is effective at 10 mg/m$^2$ (NJUNWA *et al.*, 1991; MARBIAH *et al.*, 1998) and this dosage is cheaper than permethrin at the dosage mentioned above (FIELDEN, 1996). LUO DAPENG *et al.* (1994) reported good results with alphacypermethrin at 20 mg/m$^2$ and quoted a price of US$0·06 per net treated, which is much less than with any other pyrethroid so far tested. JAWARA *et al.* (1998) found comparable results with alphacypermethrin, lambdacyhalothrin and permethrin, as assessed by bioassays and number of mosquitoes found alive and dead inside or near nets.

At the request of the WHO Pesticide Evaluation Scheme we carried out a more comprehensive trial of bednets treated with alphacypermethrin (Suspension Concentrate) in comparison with lambdacyhalothrin (Microencapsulated). The work consisted of a questionnaire to ascertain users' perceptions of the advantageous and disadvantageous side-effects of each net treatment, and entomological evaluation by bioassay, in experimental huts, and by impact on mosquitoes in treated hamlets and rooms with treated nets, using the methods that had been employed by CURTIS *et al.* (1998). We also monitored incidence of re-infection with malaria in children whose pre-existing infections had been cleared with chlorproguanil–dapsone (WATKINS *et al.*, 1988; TRIGG *et al.*, 1997; CURTIS *et al.*, 1998). We confirmed the validity of our conclusions regarding malaria re-infection by follow-up trials showing that only small proportions of the effects that we saw were due to: (i) the physical barrier provided by bednets, as distinct from the insecticide on them, and (ii) recrudescence of infections incompletely cured by the drug combination.

## Methods

The work was based at Muheza in north-east Tanzania at the Ubwari Field Station of the Amani Medical Research Centre of the Tanzanian National Institute for Medical Research (NIMR). Ethical clearance was granted by the ethics committees of the NIMR and the London School of Hygiene and Tropical Medicine.

The first method of assessment of the net treatments was use of verandah trap experimental huts, as devised by SMITH & WEBLEY (1969). The huts were those previously used by CURTIS *et al.* (1996) to compare the protection from biting and the insecticidal power of many different net and curtain treatments. In the present trials, nets with 10, 20 and 40 mg alphacypermethrin/m$^2$ and 10 and 20 mg lambdacyhalothrin/m$^2$ were tested, as well as untreated nets. All nets were made of 100-denier polyester fibre and had 6 holes, 4 × 4 cm, cut to simulate damaged nets. They were tested in rotation in 2 huts nightly for 6 weeks and then retested after being hand-washed 5 times in cold water with detergent.

More extensive studies were carried out with treated nets provided to all inhabitants of the villages of Songa, Mkulomilo, Tengeni and Enzi which had been the controls in the study of CURTIS *et al.* (1998). Songa and Mkulomilo are situated near Hale, 30 km from Muheza, and Tengeni and Enzi are 5–10 km from Muheza. Songa and Tengeni could each be divided into 4 recognizable hamlets, and 2 hamlets from each of these villages were randomly assigned to testing nets with each of the pyrethroids. Mkulomilo and Enzi had only 2 recognizable hamlets each and, from each of these villages, 1 was randomly assigned to each treatment. Thus there were a total of 6 hamlets with each treatment. Four additional, apparently similar, hamlets were taken into the trial as untreated controls for the entomological studies and the study of untreated nets. In all 16 hamlets malaria transmission is intense, especially in and soon after the rainy seasons.

The methods of assessment in the villages were as follows:

(i) A structured questionnaire was administered to about 100 randomly chosen adults in the hamlets with the alphacypermethrin nets and a similar number in the hamlets with the lambdacyhalothrin-treated nets. The questions concerned whether various types of nuisance insect had existed in the house before provision of the nets and whether they had been eliminated and whether any adverse side-effects of the nets had been noticed.

(ii) Bioassays were carried out with anophelines collected in untreated villages on nets that had been in domestic use before and after washing and re-treatment, the results being assessed in terms of median time for knockdown (WHO, 1996; CURTIS *et al.*, 1998). This method is preferable to a conventional 3-min exposure, followed by 24-h holding, which tends to give nearly 100% mortality with nets varying in insecticidal power and there may be death of controls during the 24-h holding period.

(iii) The mass-killing effect of nets treated with 20 mg alphacypermethrin or 10 mg lambdacyhalothrin/m$^2$ was assessed in 6 hamlets each, in comparison to 4 hamlets with no nets. This was done by monthly light-trapping in

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5 sentinel bedrooms per hamlet equipped with untreated bednets (LINES *et al.*, 1991) and by enzyme-linked immunosorbent assay (ELISA) tests for circumsporozoite protein (CSP) by the method of BURKOT *et al.* (1984) in heads and thoraces of trapped anophelines stored with silica gel until tested. The data allowed estimation of the entomological inoculation rate for an unprotected subject in a treated or untreated hamlet.

(iv) Catches were made with pyrethrum spray and window traps (SERVICE, 1993) in rooms with treated nets in the treated hamlets and in untreated rooms in the hamlets without nets. The proportion of the mosquitoes caught that had blood fed was recorded, the intention being to assess, not only the impact on the mosquito population of the whole hamlet, but also the personal protective effect in individual rooms with treated nets. A water-miscible formulation of pyrethrum (Pycon; Agropharm, High Wycombe, UK) was used for the spray catches rather than the conventional kerosene solution of pyrethrum concentrate.

(v) The rate of incidence of re-infection with malaria parasites was assessed in children aged 1–6 years sleeping under nets with each of the treatments. Pre-existing infections were cleared by 3 doses of 1·25 mg chlorproguanil and 2·5 mg dapsone/kg bodyweight and the children then had bloodslides made weekly until they became positive, or the eighth week after treatment, whichever was the sooner. Results were assessed in terms of the rate of becoming positive per child-week at risk, after week 2 from treatment. Such trials were carried out at different seasons, with cohorts of about 60 children in each hamlet. Each child or the parent/guardian was questioned to check whether the child was sleeping under a treated net.

(vi) To assess the proportion of the effect of the treated bednets on malaria re-infection that can be attributed to the physical barrier presented by the nets, another trial of re-infection after chlorproguanil–dapsone treatment was carried out. This was done in the hamlets with each type of treated net, as well as in 4 hamlets that had not previously had nets but in each of which 60 untreated nets were given out. The children sleeping under these, and a similar number of children without nets (not in the same houses as those provided with the nets), were given the drug combination and monitored weekly for re-infection up to week 8 after treatment.

(vii) To assess the possibility of recrudescence of infections after giving chlorproguanil–dapsone, a group of 41 children from villages near those used for the trials, but without bednets, were treated with the drug combination and taken with their mothers for a 6-week 'vacation' located uninterruptedly at the Gare mission station at an altitude of 1700 m in the west Usambara mountains. They were monitored by weekly bloodslides for recurrence of malaria parasites. A group of 250 of the local highland children were monitored by bloodslide and spleen palpation for evidence of local malaria transmission: none was found. The living accommodation at the mission station was sprayed with lambdacyhalothrin as a precaution against the possibility of initiating an epidemic by infection from the lowland people of any local highland anophelines which may have existed (although searches failed to reveal any).

## Results and Discussion

*Experimental hut trials*

Table 1 shows the results of collecting mosquitoes entering experimental huts with untreated nets or nets treated with either of the insecticides at various dosages and unwashed or 5 times washed. The numbers of mosquitoes on different nights were not normally distributed and Kruskall–Wallace non-parametric tests were therefore used. There were significant reductions in the proportion of mosquitoes blood feeding on the sleepers using any of the treated nets compared with the untreated nets, i.e., the pyrethroid deposit generally repelled or killed host-seeking mosquitoes before they found the holes in the treated nets, but with the untreated nets they readily found the holes. The treated nets caused significant mortality among the anophelines compared to the untreated nets. As reported by CURTIS *et al.* (1996), the treated nets caused very little mortality of *Culex quinquefasciatus*.

Compared with lambdacyhalothrin, alphacypermethrin was significantly better at preventing feeding but significantly worse at killing anophelines. There were no consistent dose effects and repeated washing caused no significant effects on ability of a net to protect the user against biting but had slight but significant effects on mosquito mortality. The slightness of the effects of washing conforms with evidence for good wash resistance of lambdacyhalothrin and was in marked contrast to earlier data with permethrin assessed by 3-min bioassays (NJUNWA *et al.*, 1991; MILLER *et al.*, 1995; CURTIS *et al.*, 1996).

*Questionnaire to net users*

As previously reported by NJUNWA *et al.* (1991) and JAWARA *et al.* (1998), some users noticed nasal irritation (which they described by the Swahili word for a common cold) from the nets treated with 10 mg lambdacyhalothrin/$m^2$. In the present trial of 105 users of these nets who were questioned, 19 reported this irritation. Of 117 users with 20 mg alphacypermethrin/$m^2$, only 3 reported this sensation—significantly fewer than with lambdacyhalothrin. There were only a few other adverse effects perceived, with no difference in frequency between the 2 insecticides.

As frequently reported before, the pyrethroid-treated nets were observed to be highly effective against bedbugs (141 infestations reported to be eliminated from 146 initially reported). All 17 initially reported head-louse infestations were reported to be eliminated. The treated nets were also found moderately effective against fleas, cockroaches and ants. These beneficial side-effects were observed equally frequently with the 2 insecticides.

*Bioassays on nets in village use*

Table 2 shows that in bioassays of nets in domestic use there was no significant difference in speed of knockdown due to nets treated with 20 mg alphacypermethrin or 10 mg lambdacyhalothrin/$m^2$, but there was an almost significant effect of washing of nets (one or more times) by their users which caused slower knockdown than with unwashed nets. Re-impregnation after 8 months of net use markedly increased the speed at which the nets caused knockdown. There was no evidence for loss of knockdown power with months of domestic use of nets. However, a small effect of this kind might have been obscured by the fact that among the wild-collected mosquitoes used for these tests only *Anopheles funestus* was available for testing in the later stages of the trial and this species is slightly more susceptible to knockdown than *An. gambiae* (CURTIS, 1996).

*Light-trapping in untreated rooms in treated hamlets*

Monitoring the hamlet populations of anophelines by light-traps set beside untreated nets showed major fluctuations between the cool dry season in August–October 1997 on the one hand, and peaks in and after the normal rainy season in May and the months following the exceptional rains associated with El Niño in December 1997. The species composition differed markedly between these 2 peak seasons, with mainly *An. gambiae s.s.* in mid-1997 and large numbers of *An. funestus*, *An. arabiensis*, *An. gambiae s. s.* and members of the *An. marshallii* group being caught in early 1998, some individuals from each of these species being found positive for circumsporozoite protein (C.F. Curtis *et al.*, paper in preparation). In almost every month, catches were larger in the hamlets without nets than in those with treated nets (monthly data not shown), and the 2

**Table 1. Mean numbers of mosquitoes collecte on replicate nights of testing untreated or treated nets (unwashed or washed) in verandah-trap experimental huts and significance of differences**

| Net treatment | | | *An. gambiae* and *An. funestus* | | | *Cx. quinquefasciatus* | | |
|---|---|---|---|---|---|---|---|---|
| Insecticide ($mg/m^2$) | Times washed | Replications | Total[a] | Fed (%) | Dead (%) | Total[a] | Fed (%) | Dead (%) |
| None | 0 | 18 | 50·9 | 69·8 | 4·4 | 31·6 | 81·1 | 0·6 |
| Alphacypermethrin (10) | 0 | 5 | 27·6 | 18·5 | 59·5 | 8·6 | 13·5 | 5·1 |
| Alphacypermethrin (10) | 5 | 3 | 36·7 | 32·9 | 24.8 | 16.7 | 26.1 | 0 |
| Alphacypermethrin (20) | 0 | 10 | 40·1 | 31·5 | 63·4 | 28.3 | 52·2 | 1·6 |
| Alphacypermethrin (20) | 5 | 11 | 41·3 | 33·3 | 43·8 | 21·9 | 33·8 | 0 |
| Alphacypermethrin (40) | 0 | 8 | 45·1 | 20·6 | 50·1 | 18·0 | 40·8 | 3·8 |
| Alphacypermethrin (40) | 5 | 12 | 28·4 | 20·8 | 43·5 | 15·6 | 36·2 | 0 |
| Lambdacyhalothrin (10) | 0 | 10 | 33·8 | 36·7 | 71·4 | 26·4 | 49·8 | 2·0 |
| Lambdacyhalothrin (10) | 5 | 8 | 34·7 | 45·2 | 61·3 | 17·5 | 25·8 | 2.1 |
| Lambdacyhalothrin (20) | 0 | 11 | 34·3 | 36·7 | 74·8 | 23·4 | 29·1 | 1·7 |
| Lambdacyhalothrin (20) | 5 | 11 | 39·2 | 37·7 | 56·0 | 16·3 | 24·6 | 6·8 |
| **Comparison** | | | *P* values from Kruskall–Wallace tests | | | | | |
| Untreated vs all treated | | | 0·06 | <0·001 | <0·001 | <0·01 | <0·001 | NS |
| 5 × washed vs unwashed | | | NS | NS | <0·01 | NS | 0·06 | <0·05 |
| Alphacypermethrin vs lambdacyhalothrin | | | NS | <0·01[b] | <0·01[b] | NS | NS | NS |
| 3 doses of alphacypermethrin | | | NS | 0·06[c] | NS | <0·05[c] | 0·08[c] | NS |
| 2 doses of lambdacyhalothrin | | | NS | NS | NS | NS | NS | NS |

[a]Total = numbers dead or alive, fed or unfed, found in hut + window trap + twice numbers found in verandah traps on 2 sides of the hut (CURTIS *et al.*, 1996); this total is assumed to be approximately the number entering the hut during the night.
[b]More fed and more dead with lambdacyhalothrin than with alphacypermethrin.
[c]More *Anopheles* and *Culex* fed and more *Culex* in total with the middle dose than with the highest or the lowest.
NS, not significant.

**Table 2. Bioassays on nets treated with 20 mg alphacypermethrin/m² or 10 mg lambdacyhalothrin/m² and in regular domestic use**

| Months since net treatment | $KT_{50}$ (seconds) | | | |
|---|---|---|---|---|
| | Alphacypermethrin | | Lambdacyhalothrin | |
| | Unwashed | Washed | Unwashed | Washed |
| 4–7 after 1st treatment (g) | 361 (5) | 410 (6) | 379 (6) | 464 (6) |
| 1–4 after retreatment (gf) | 253 (12) | 294 (3) | 218 (8) | NT |
| 6–7 after retreatment (f) | 259 (3) | 263 (4) | 217 (4) | 260 (1) |

Data are based on observed median times for knockdown of blood-fed anophelines collected from untreated villages. (Numbers in parentheses indicate number of nets tested.)
NS, not significant; NT, not tested.
(g), Tests with *An. gambiae s.s.*; (gf), tests with mixture of *An. gambaie s.s.* and *An. funestus*; (f), tests with *An. funestus* (species used according to seasonal availability).

**Results of analysis of variance for data 4–7 months after 1st treatment**

| | d.f. | *F* | |
|---|---|---|---|
| Between insecticides | 1 | 0·81 | NS |
| Washed vs unwashed | 1 | 3·34 | $0.05 < P < 0.1$ |
| Interaction | 1 | 0·22 | NS |
| Within subgroups | 20 | | |

*t*-Tests between the insecticides
1–4 months after re-treatment: $t = 1.57$, d.f. = 18, NS
6–7 months after re-treatment: $t = 3.06$, d.f. = 5, $0.02 < P < 0.05$.

**Table 3. Estimates of infective biting populations of *An. gambiae s.l.*, *An. funestus* and *An. marshallii* and populations of *Cx. quinquefasciatus* in hamlets with nets treated with alphacypermethrin or lambdacyhalothrin or no nets**

| | Alphacypermethrin | Lambdacyhalothrin | No nets |
|---|---|---|---|
| No. of hamlets | 6 | 6 | 4 |
| Total no. of light-trap catches | 292 | 287 | 189 |
| Mean catch of anophelines over all seasons | 15·23 | 14·34 | 75·22 |
| No. of anopheline bites/unprotected person/night[a] | 22·84 | 21·51 | 112·83 |
| Reduction due to treated nets in hamlets | 79·8% | 80·9% | – |
| CSP +ve/no. of mosquitoes ELISA-tested (%) | 17/2529 (0·67%) | 13/1995 (0·65%) | 50/1739 (2·87%) |
| Infective bites/unprotected person/night | 0·153 | 0·140 | 3·24 |
| Reduction due to treated nets in hamlets | 95·3% | 95·7% | – |
| Mean catch of *Cx. quinquefasciatus* | 9·30 | 15·12 | 3·21 |

Estimates are based on monthly light trapping in 5 rooms with untreated nets in each hamlet and on ELISA tests of anophelines for circumsporozoite protein (CSP).
[a]Light-trap catch × 1·5 (LINES *et al.*, 1991).

treatments had similar effects. This is seen more clearly in the average catches of both vector species (Table 3) and also in the rates of CSP positivity whose reduction in the treated hamlets can be attributed mainly to shortening of the mean lifespan as a result of killing of anophelines attracted to the treated nets (MAGESA *et al.*, 1991). The overall effect of the reduced numbers and CSP rate was a reduction in the entomological inoculation rate into unprotected people in the treated hamlets by 95–96% due to either insecticide on the nets. There was no reduction in numbers of *Cx. quinquefasciatus*, in conformity with the lack of killing of this species seen in the experimental huts: the markedly larger numbers of this species in the treated hamlets may have been due to a programme of installation of pit latrines in Songa and Mkulomilo which probably provided breeding places for these mosquitoes.

*Resting and exit trap catches from treated rooms*

Table 4 also shows major and similar reductions due to each insecticide, compared to the controls, in numbers of fed mosquitoes in, and exiting from, treated rooms. Taking into account the reduction in CSP rate, it can be estimated that the number of infective bites on a person under either type of treated net would have been reduced by about 99%. As with the light-trap data, there was no sign of a reduction in the population of *Cx. quinquefasciatus* due to the treated nets. In all hamlets the pyrethrum-spray catches were less than the light-trap catches; it is now suspected that the water-miscible pyrethrum which was used may be less effective than the conventional kerosene solution and this is being investigated.

*Malaria incidence*

As in our previous trials (TRIGG *et al.*, 1997; CURTIS *et al.*, 1998) chlorproguanil–dapsone was more than 99% effective in clearing pre-existing asexual parasitaemia at week 1 after treatment. Within each of the trials there were very similar mean rates of incidence of re-infection in children sleeping under nets treated with each insecticide (Table 5). Analysis of variance showed no significant difference between the effects of the 2 insecticides, but a significant difference between the rates of re-infection at different seasons, with the maximum in the long rains in April–May when vector populations were maximal. No untreated control children were included in the first 2 of these trials, but, in comparison with results for

**Table 4. Data from pyrethrum-spray collections of mosquitoes indoors and in exit traps on windows of rooms with alphacypermethrin- or lambdacyhalothrin-treated nets or no nets**

| | Alphacypermethrin | Lambdacyhalothrin | No nets |
|---|---|---|---|
| Total no. of spray and exit-trap collections | 213 | 204 | 109 |
| Mean catch of *An. gambiae s.l.*, *An. funestus* and *An. marshallii s.l.* | | | |
| Mean total catch | 0·582 | 0·903 | 16·345 |
| Mean total no. fed | 0·288 | 0·511 | 11·122 |
| Reduction in no. fed due to treated nets | 97·4% | 95·4% | – |
| Estimated infective bites/room/night[a] | 0·0019 | 0·0033 | 0·319 |
| Reduction in infective bites due to treated nets | 99.4% | 99.0% | – |
| Mean catch of *Cx. quinquefasciatus* | | | |
| Mean total catch | 3·538 | 2·508 | 3·305 |
| Mean total no. fed | 1·610 | 1·276 | 2·256 |

[a]From the circumsporozoite protein-positive rate from Table 3, and classification of mosquitoes as fed or unfed.

**Table 5. Rates of re-infection with asexual malaria parasites after treatment with chlorproguanil–dapsone of c.60 children per hamlet sleeping under nets treated with alphacypermethrin or lambdacyhalothrin, untreated nets or no nets**

| | Apr–May 1997 | Nov 1997–Jan 1998 | Feb–Mar 1998 |
|---|---|---|---|
| **Alphacypermethrin nets** | | | |
| No. of hamlets (total no. of child-weeks) | 6 (1506) | 6 (1576) | 4 (1318) |
| Mean | 11·41% | 8·31% | 4·17% |
| SD | 4·91% | 6·77% | 3·14% |
| Protection | 73·0% | 70·6% | 80·8% |
| **Lambdacyhalothrin nets** | | | |
| No. of hamlets (total no. of child-weeks) | 6 (1283) | 6 (1458) | 4 (1310) |
| Mean | 11·69% | 7·13% | 3·66% |
| SD | 6·70% | 4·45% | 2·71% |
| Protection | 72·3% | 74·8% | 83·2% |
| | Apr–May 1995 | Nov–Dec 1996 | Feb–Mar 1998 |
| **No nets** | | | |
| No. of hamlets (total no. of child-weeks) | 12 (492) | 2 (281) | 4 (832) |
| Mean | 42·28% | 28·32% | 21·75% |
| SD | 10·09% | 20·7–35·9% | 4·42% |
| **Untreated nets** | | | |
| No. of hamlets (total no. of child-weeks) | – | – | 4 (920) |
| Mean | – | – | 14·61% |
| SD | – | – | 4·77% |
| Protection | – | – | 32·8% |

Data shown are means and SD of the rates of re-infection in each hamlet with each treatment of numbers of children becoming positive per 100 child-weeks at risk.

| **Analysis of variance** (arcsin transformed) | d.f. | *F* | *P*-value |
|---|---|---|---|
| Between the 2 insecticides and 3 seasons | | | |
| Insecticides | 1 | 0·01 | NS |
| Seasons | 2 | 7·07 | <0·01 |
| Interaction | 2 | 0·15 | NS |
| Within subgroups | 26 | | |
| Between net treatments and no net, Feb–Mar 1998 | | | |
| Nets/treatments | 3 | 19·5 | <0·001 |
| Within groups | 12 | | |
| Treated vs untreated | | 23·3 | <0·001 |
| Untreated vs no nets | | 4·3 | 0·06 |

such controls at the same season in earlier years, reductions in incidence of about 72% resulted from each treatment.

The third trial (Table 5, column 4) was conducted to establish how much of the reduction in incidence was due to the physical barrier presented by the bednets. For this purpose untreated nets were provided for some of the children in the hamlets used as controls for the entomological work. There was again no difference between children with the 2 insecticide treatments and an estimated protection factor of about 81% compared with contemporary data on children with no nets. There was a highly significant difference between those with treated and untreated nets, but a not quite significant difference between those with untreated and with no nets (estimated protection factor of untreated nets about 33%).

The greater importance of the insecticide than the physical barrier presented by the net implied by these results is consistent with the major reduction in entomological inoculation rate outside nets in hamlets with treated nets (Table 3) and the relatively small additional personal protection factor indicated in rooms with treated nets (Table 4). Previously, JANA-KARA *et al.* (1995) and D'ALESSANDRO *et al.* (1995) had shown intermediate results of untreated nets compared with treated ones and no nets, but it was difficult from their

**Table 6. Percentage positivity of children for asexual malaria parasites before and 1 week after treatment with chlorproguanil–dapsone and percent conversion to positivity in relation to nets used**

| Date | Net | Wk 0 (a) | Wk 1 (b) | Wk 1–2 (c) | Wk 2–4 (c) | Wk 4–6 (c) | Wk 6–8 (c) | Wk 2–8 (c) | Cor[d] pf[e] |
|---|---|---|---|---|---|---|---|---|---|
| Apr–May 1997 | tr. | 66.3% | 0.43% | 3.2% | 12.6% | 11.2% | 10.1% | 11.5% | 10.2% |
| | | (703) | (464) | (686) | (1222) | (882) | (685) | (2789) | 75% |
| Nov 1997–Jan 1998 | tr. | 43.3% | 0.33% | 0.3% | 6.6% | 9.3% | 8.4% | 8.0% | 6.4% |
| | | (695) | (301) | (676) | (1277) | (1007) | (750) | (3034) | 76% |
| Feb–Mar 1998 | tr. | 34.4% | 0 | 0 | 3.0% | 4.6% | 4.2% | 3.9% | 2.6% |
| | | (477) | (477) | (477) | (938) | (908) | (782) | (2628) | 87% |
| Feb–Mar 1998 | untr. | 74.5% | 0.86% | 6.1% | 14.3% | 16.8% | 13.4% | 14.7% | 13.4% |
| | | (236) | (232) | (230) | (446) | (327) | (201) | (974) | 34% |
| Feb–Mar 1998 | no | 81.3% | 1.6% | 3.0% | 24.2% | 18.5% | 19.8% | 21.7% | 20.4% |
| | | (246) | (241) | (235) | (451) | (270) | (111) | (832) | – |
| Mar–Apr 1998 | hi[f] | 76.2% | 0 | 0 | 3.7% | 0 | 0 | 1.3% | – |
| | | (42) | (34) | (42) | (82) | (78) | (77) | (237) | |

Numbers in parentheses used as denominators:
(a), total number of children sampled initially;
(b), number positive for parasites at week 0 minus number lost to follow-up;
(c), number of child-weeks sampled based on number negative at beginning of time interval minus number lost to follow-up and number of weeks in the time interval.
[d]Corrected for recrudescence rate found in the highlands.
[e]Protection factor compared with children with no nets at same season.
[f]In highlands with no local transmission.
tr., treated; untr., untreated.

**Note**: above data refer to asexual stages only—gametocytes were not cleared, as also reported by TRIGG *et al.* (1997). Mean prevalences of gametocytes were 7·2% and 3·9% at weeks 1–3 and 4–6, respectively, many of the same individuals being positive at successive weeks.

results to assess the relative importance of the net and the insecticide.

It might be thought that untreated nets would give an indication of the effect of treated nets against a pyrethroid-resistant mosquito population. However, this indication would be inexact because it leaves out the irritant effect of pyrethroids which still exists, although to a reduced extent, with at least some types of pyrethroid resistance (HODJATI & CURTIS, 1997).

*Tests for recrudescence and residual effect of chlorproguanil–dapsone*

Other workers have measured malaria incidence in high-transmission areas from infant parasite conversion rates (MACDONALD, 1950; SNOW *et al.*, 1996) without the need for use of drug treatment. However, we doubted whether we could find sufficient infants who had not yet had any experience of malaria and whether their mothers would agree to repeated blood sampling from such young babies. Furthermore, babies sleep close to their mothers to whom most mosquito biting is diverted (BRYAN & SMALLEY, 1978).

We appreciated that our measures of incidence after clearance of pre-existing infections in children over the age of 1 year could be seriously erroneous if (i) there was a residual effect of the treatment of chlorproguanil–dapsone in the period when incidence was being measured, and/or (ii) some infections, although not patent at week 1 after treatment, had not been completely cured and could recrudesce. From the shapes of the graphs of recurrence of infections (CURTIS *et al.*, 1998) it seems that from week 2 after treatment delayed effects of this drug combination have waned. A more detailed examination of the pattern of recurrence of asexual infections (Table 6) supports this: from initial high prevalence of infection, especially in villages without nets, the elimination in the first week is almost complete. Recurrence in the next week is remarkably slow for a drug combination with a short half-life. However, it is known that chlorproguanil, but not dapsone, can act on the liver stages (see PETERS, 1970) and, if infections progressing through the liver are eliminated, a lag time would be expected after treatment before new infections would become patent. In any of the trial cohorts, the rate of recurrence from week 2 until week 8 was approximately constant and appears to reflect the risk of receiving an infective bite, which varies with season and presence of treated, untreated or no nets.

To test for recrudescence, 41 children were treated with the usual 3 doses of chlorproguanil–dapsone after they had been taken to a highland location where there was no evidence for local malaria transmission, as judged by blood surveys and spleen palpation of local highland children. Three of the treated lowland children showed recurrence of asexual parasites at week 3 after treatment. On detailed enquiry it transpired that one of these had vomited after each of the treatments and therefore must have been under-dosed. Also, 1 of the 3 had been among the 9 children who appeared negative for parasites when the treatment was given. Accepting all 3 as cases of recrudescence, and since no more recurrences occurred in the 6 weeks in the highlands and in the week after return to the lowlands, our best estimate of the probability of recrudescence is 1·3% per child-week. The estimates for re-infection over weeks 2–8 in the lowlands (Table 6) may be corrected for the small fraction of the recurrent parasitaemias which is now considered to be recrudescence. This correction has relatively more effect where the rate of recurrence of infection is low; it thus slightly increased the estimates of the protection factors due to the treated nets. However, the correction is insufficient to explain the discrepancy between these estimated protection factors and those expected from the entomological data (Tables 3 and 4). This is true also of several comparisons reported by CURTIS *et al.* (1998) of reductions of entomological inoculation rate and incidence of re-infection with malaria (now corrected for the rate of recrudescence after chlorproguanil–dapsone treatment). This discrepancy has been so consistently found that we believe it to be real, even though it would be difficult to attach statistical confidence limits to any one of the estimates of reduction in entomological inoculation rate (e.g., those in Tables 3 and 4), as these are composites of several different parameters. A similar discrepancy between entomological and malaria incidence data was noted by CHARLWOOD *et al.* (1998) without being able to offer any obvious explanation.

The data in Table 6 support other evidence (e.g., from AMUKOYE *et al.*, 1997) that chlorproguanil–dapsone is very promising for routine treatment of malaria as well as being a useful and valid means of setting up studies on the impact of vector control on malaria incidence in areas of intense transmission.

## Conclusions

1. The 2 pyrethroids tested had a similar impact on mosquitoes and malaria incidence. There were more reports of nasal irritation with lambdacyhalothrin and if alphacypermethrin can be obtained cheaply as suggested by the report of LUO DAPENG *et al.* (1994), this could be the pyrethroid of choice for net treatment
2. Chlorproguanil–dapsone gives very high rates of clearance of parasitaemia with little recrudescence.

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## Book Review

**Malaria Research in The Solomon Islands.** A. Ishii, N. Nihei & M. Sasa (editors). Tokyo: Inter Group Corporation, 1998. xii+192pp. Price ¥3500E. ISBN 4-901070-00-2.

This soft-back book comprises several sections: General; Diagnosis; Pathophysiology; Vector Mosquitoes; Epidemiology and Control, and an Annex and Postscript. Altogether there are 26 papers covering this wide range of topics.

As the editors state in their Preface, 'This is a compilation of reports of work carried out in the Solomon Islands by research groups between 1990 and 1995'. The original book was published in Japanese 3 years after the project commenced, but because it was unable to reach a wider readership the current volume was produced in 1998, and included additional work carried out in the final 2 years of the project.

Despite the comment that the book is a compilation of reports, each report is presented in the form of a peer-reviewed paper. The editors hope that this publication will contribute to the advancement of research and assist in solving the problems associated with the prevention and treatment of malaria, not only in the Solomon Islands, but also in other places. My personal opinion is that whilst the work provides a solid foundation for future malaria workers in the Solomon Islands and the surrounding area, it is unlikely to be of significant relevance to much of the rest of the malaria endemic world. Having said that, the list of references provides a good introduction to the field with, naturally, a preponderance of Japanese papers.

At the beginning of the book are 4 pages of excellent quality colour photographs, which are later reproduced, in the appropriate papers, in black and white. The maps, drawings and graphs are clear, but the photographs of the gels leave much to be desired.

The results of using polymerase chain reaction for malaria diagnosis show clearly that it is more sensitive than microscopy, but as the authors state its main drawback is the high cost which limits its wider application. In a similar vein, following the comparison of clinical diagnosis with that of microscopy, the authors point to the need for a good diagnostic test without microscopy—a not uncommon observation.

My overall perception was that this book could be a useful reference and provider of source material for anyone in the South West Pacific area starting out in any of the specialities of malaria research covered in this publication. However, I suggest that readers may wish to draw their own conclusions from the results, as frequently the authors' conclusions and discussions are rather shallow.

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