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Trial of pyrethroid impregnated bednets in an area of Tanzania holoendemic for malaria Part 4. Effects on incidence of malaria infection

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Groups of about 30 children in each of five villages were given pyrimethamine-sulfadoxine to clear their malaria parasitaemia, and they were followed up with fortnightly blood slides Parasitaemia returned rapidly in the absence of vector control, but more slowly when pyrethroid impregnated nets were in use or the houses had been sprayed with DDT Variation between the incidence of malaria infection in these cases seemed to depend more on ecological or social factors than on the particular form of vector control adopted

Key words *Plasmodium falciparum*, Bednets, impregnated, DDT spraying, Malaria incidence, Pyrimethamine-sulfadoxine

Introduction

In areas where malaria is holoendemic and the intervals between infective bites received by a person are short compared with the time taken to recover from an infection, people suffer from 'super-infection', i.e several separate malaria infections at once Very high degrees of vector control are needed to show a marked impact on the prevalence of parasitaemia (Molineaux and Gramiccia, 1980) Under such circumstances it should be easier to show an impact of vector control on the incidence of new infections in people whose pre-existing infections have been cleared by chemotherapy This approach was adopted in short-term trials of permethrin impregnated nets in Sabah, Malaysia (Hii et al , 1987) and Papua New Guinea (Graves et al , 1987) In 1965 a study of re-infection after parasite clearance was carried out in the same area of Tanzania in which we worked (Pringle and Avery-Jones, 1966) The earlier study showed that in the absence of vector control we should expect that 20% of children would become re-infected every week

After it became apparent that it was going to be difficult to show a clear-cut effect on malaria prevalence in the traditional villages in our trial (Lyimo et al., 1991), we decided to carry out a study of malaria incidence on cohorts of children in each of

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our experimental villages The first such trial was in 1988–9 while two of the villages still had no vector control, one had received DDT spraying and two had received permethrin impregnated nets (Njunwa et al , 1991) After all five villages had received permethrin or lambdacyhalothrin treated nets in 1989 the study of malaria incidence was repeated

All children in the experimental villages in which malaria infection was detected were routinely taken for chloroquine treatment (Lyimo et al , 1991) However, resistance to chloroquine is widespread in the area (Kilimali and Mkufya, 1985a) and clearance of parasitaemia could not be relied upon We therefore chose to use pyrimethamine-sulfadoxine (Fansidar^{R}) to attempt to clear the parasitaemia in our cohorts of children Cases of resistance to this drug combination have been reported in East Africa (Hess et al , 1983) and we checked that clearance had occurred a week after treatment before proceeding to follow up the children concerned every two weeks

Methods

Cohorts of about 30 children aged between 1 and 10 were selected for the incidence study from among those regularly seen in each of our five experimental villages They were age-matched with those not included in the incidence study so that those not included in the incidence study could validly continue to be monitored in the ongoing study of malaria prevalence (Lyimo et al , 1991)

Finger-prick thick blood films were taken from the selected cohort at the beginning of the study in October–November 1988 The slides were stained with Giemsa and searched under oil immersion for malaria parasites until 200 white blood corpuscles had been seen After taking the blood slide, pyrimethamine-sulfadoxine was given by a medical assistant according to the following dose schedule age 1–4 half a tablet containing 500 mg sulfadoxine and 25 mg pyrimethamine, 4–8 1 tablet, 9–10 2 tablets

The same children were actively searched for at their homes and elsewhere one week later and fortnightly thereafter for up to 18 weeks However, they were dropped from the cohort if they gave a malaria positive slide or if they reported one night or more away from their home village and were thus exposed to different malaria infection risks

As far as possible the same children were selected for the study cohorts when a second experiment was started in mid-August 1989, after all the villagers had been given impregnated bednets

Results and Discussion

Before the ends of the planned durations of the experiments 32% of the children had spent one or more nights away from their home villages and they had therefore to be removed from the cohorts for further sampling No adverse reactions to pyrimethamine-sulfadoxine were encountered

Figs 1 and 2 show the proportions of the cohorts from each village found to be malaria-free The pre-treatment results were similar to those in the main study (Lyimo

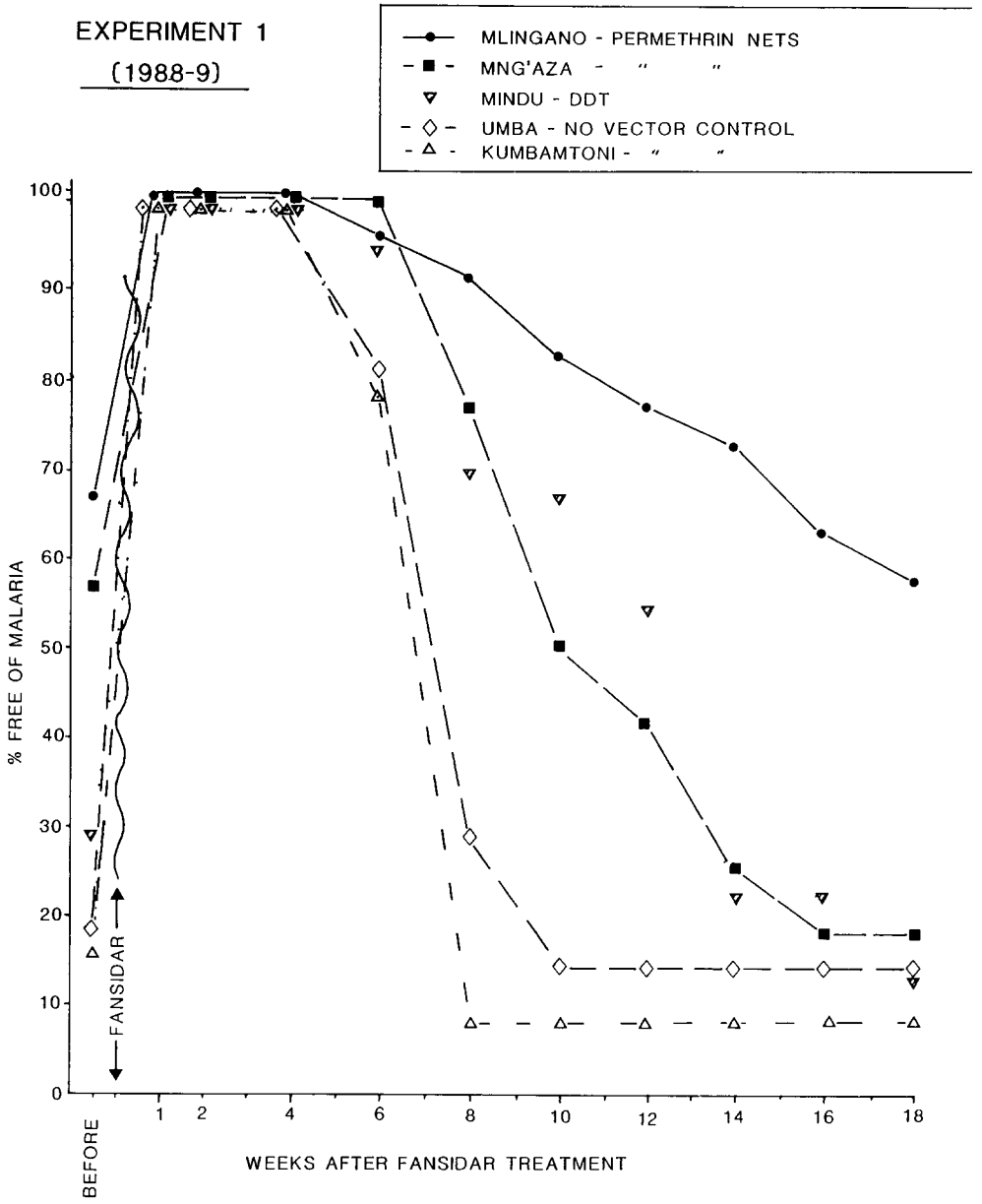

Fig 1 Percentage of cohorts of about 30 children free of malaria before, and over the 18 weeks after, treatment with pyrimethamine-sulfadoxine The data are from experiment 1 started in October 1988 when Kumbamtoni and Umba still were without vector control

et al , 1991), i e more were malaria-free in Mlingano where the bednets were most successful

The drug treatment was 100% successful in eliminating parasitaemia within one week, i e there was no evidence for drug resistance, as also found in a smaller sample in this area by Kilimali and Mkufya (1985b) There was no reversion to positivity

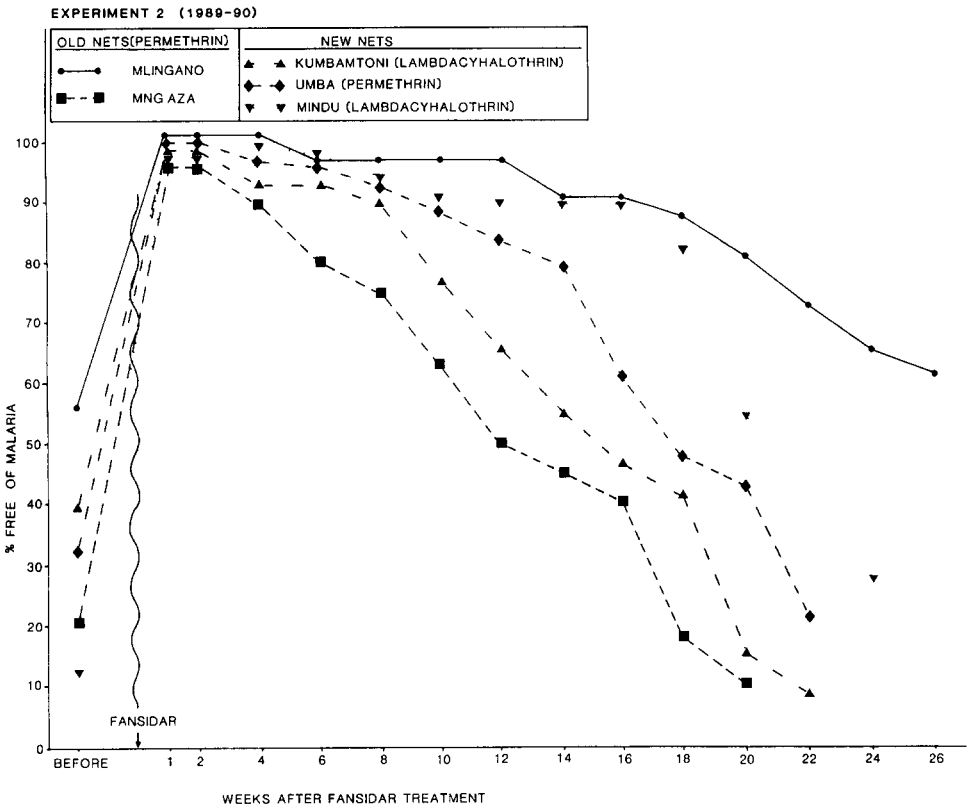

Fig 2 Data from the second experiment with pyrimethamine-sulfadoxine treatment started in August 1989 when all five villages had impregnated nets

within 4 weeks in experiment 1 as also found in a recent study of children near Dar es Salaam given pyrimethamine-sulfadoxine (Hellgren et al , 1990)

In the villages without vector control in experiment 1 (Kumbamtoni and Umba), after infections began to appear at week 6 it took only another 2–4 weeks for almost all the children to become re-infected Of the three children who remained uninfected in these villages until the end of the trial at least one was sleeping under a bednet which we had provided to be used in conjunction with one of our mosquito light traps (Magesa et al., 1991) Discounting these three children and the period between weeks 4 and 6, when the rate of re-infection seems to have been reduced by lingering effects of the prophylaxis, a total of 18 re-infections were observed in 20 unprotected child-fortnights, clearly more frequent blood sampling would have been necessary to measure this rate accurately. It was certainly higher than the average of 0 22 per child-week observed in nearby villages by Pringle and Avery-Jones (1966) over 20 years ago. Those authors estimated the sporozoite inoculation rate to average about 0 3 per person per week, whereas our data for the relevant months in the two unprotected villages would indicate an inoculation rate of about 6 per week (Magesa et al , 1991)

In experiment 1 the children at Mlingano and Mng'aza, with permethrin impregnated bednets, and those at Mindu, where DDT had been sprayed 5 months before,

showed much lower rates of conversion than the unprotected controls, the rate being particularly low at Mlingano

In the second trial the children in Kumbamtoni and Umba, who had by then been provided with impregnated bednets, showed a much lower rate of conversion to positivity than they had in experiment 1

In experiment 2, especially in Mindu, there were signs of an unexplained increase in the rate of re-infection in the later stages of the experiment This makes it difficult accurately to test the significance of the apparent differences in the rates mentioned above Nevertheless, the data were re-arranged to show the number of conversions to positivity per child per fortnight at risk (Fig 3) and approximate confidence limits were attached from the binomial distribution Comparing experiment 2 with experiment 1 the rates were lower, but not significantly so, in Mlingano and Mng'aza (where the nets were the same) and in Mindu (where impregnated nets had replaced DDT spraying) The reductions following introduction of impregnated nets at Kumbamtoni and Umba were significant

Following net introduction the sporozoite inoculation rates, calculated for people outside their nets, were greatly reduced and this represents the 'mass effect' of widespread use of insecticidal nets (Magesa et al , 1991) Only in Mng'aza were there sufficient mosquitoes after net introduction to calculate the sporozoite inoculation rate accurately figures of 0 86 and 0 48 per person per night were obtained in April–September 1988 and 1989 (Magesa et al , 1991) The rates of re-infection shown in Fig 3 equate to average rates of only 0 014–0 017 per child per night. The discrepancies between these estimates and those for the sporozoite inoculation rates presuma-

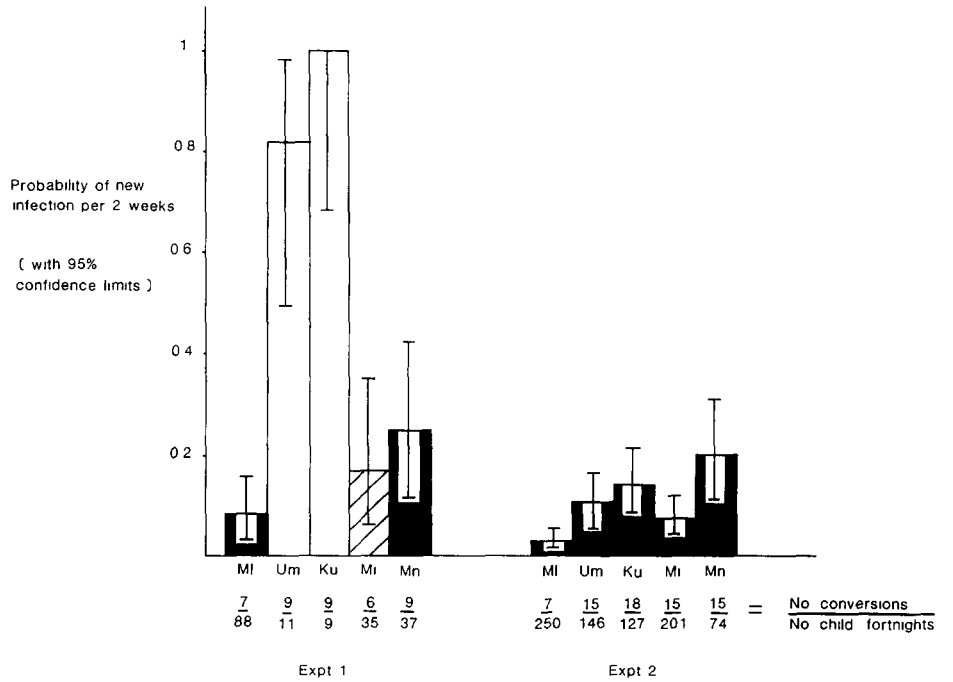

Fig 3 Probability of conversion of a child to malaria positivity per two week period in each village and experiment, with 95% confidence limits attached from the binomial distribution

bly at least partly reflect the 'personal protection' component of the benefit which it is hoped that impregnated nets would provide

In experiment 2 the results in the villages with lambdacyhalothrin impregnated nets (Kumbamtoni and Mindu) fell between the extremes for those with permethrin impregnated nets in Mlingano and Mng'aza, which differed in vector population density (Magesa et al , 1991) and probably also in the likelihood that parents would treat their children with chloroquine at the first signs of fever (Lyimo et al , 1991) Thus the ecological and social circumstances appear to be more important than the particular pyrethroid which is chosen in determining the impact on malaria transmission

In future trials of vector control in holoendemic areas it is desirable that studies are carried out on malaria incidence as well as prevalence These should be carried out in the period of baseline data collection as well as after intervention has started

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