The Modern Malaria Handbook

A PSR Guide to Sources and Strategies

A Report by Physicians for Social Responsibility®

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PSR wishes to acknowledge the cooperative effort necessary to develop and produce The Modern Malaria Handbook. In particular, we have sought to produce a handbook that will be accessible to a variety of public health professionals with different technical expertise.

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A. Preface

PSR’s Modern Malaria Control Handbook is meant to serve as a handy, but authoritative introduction and literature review of the best up-to-date studies, information, and practices available in modern malaria control. We hope it will prove useful for medical and public health professionals, for policy-makers and diplomats, and for engaged NGOs and citizens whose participation in international public health campaigns is increasingly important.

Malaria ranks among the world’s great scourges. Despite earlier hopes that it might be eradicated in our time, it still infects 300 million people a year in the world, kills over 1 million of these annually, and leaves millions more sick and debilitated. Most of these are children already suffering disproportionately from poverty and its related ills in Africa and other parts of the developing world. Malaria must be controlled. Physicians for Social Responsibility supports the WHO Rollback Malaria Campaign and every feasible effort to reduce the mortality, morbidity, and further economic stress caused by this dreadful and maddeningly durable disease.

At the same time, PSR is committed to more recent efforts to ban 12 of the most dangerous persistent organic pollutants (POPs) still in use around the globe. These chemicals — DDT, PCBs, dioxin, and the like — cause cancer, interfere with the endocrine system and are linked with a variety of adverse health effects from immune and central nervous dysfunctions to a variety of reproductive health problems. These, too, must be eliminated. And so PSR supports a strong POPs Treaty and the total elimination of persistent organics including the phase-out of DDT.

Since DDT has been highly effective in malaria control in the past and is still permitted under certain controlled circumstances, there remain some practitioners and health officials who have been reluctant to totally eliminate DDT in the face of such widespread suffering. They fear that alternatives may prove too costly, less effective, less feasible, or less acceptable.

Thus, there is good news for all of us in this Modern Malaria Control Handbook. First, it offers a comprehensive, up-to-date medical literature review so that you can decide these issues and review them for yourself. Second, it offers brief introductions that summarize the thrust of the medical literature in each section. These, I am glad to report, show clearly that alternatives to DDT are available, are proven, and are no more costly in a growing number of cases than reliance on DDT. In sum, there are no compelling reasons not to phase-out the production and
use of DDT. Finally, this PSR guide contains a call to action so that medical professionals can mount vigorous campaigns against malaria while eliminating DDT at the same time.

I hope you will join with physicians and health professionals around the world and sign the PSR Physicians Statement on Malaria and DDT. We will use it to tell the world, to any and all who will listen, that we must work simultaneously to battle malaria and to phase-out DDT and other dangerous POPs. Our children and future generations demand no less.

Robert K. Musil, Ph.D.

Executive Director and CEO
August 1999
B. Executive Summary

Under the auspices of the United Nations Environment Programme, a global intergovernmental effort is now underway to phase out the production and use of twelve persistent organic pollutants (POPs), including the pesticide DDT. DDT continues to be used in some countries to control the mosquito carriers of malaria, a disease that today takes a terrible toll on human health and well-being in many parts of the developing world. As public health professionals with an interest in protecting people and ecosystems from the double threat of malaria and DDT exposure, Physicians for Social Responsibility has proposed an integrated approach that combines these two important public health priorities.

Protecting people from malaria demands special care and a significant increase in resources. Malaria continues to impose a tremendous health burden for people living in the tropics, particularly in Africa. It is estimated that half a billion people worldwide are infected with malaria, and between 1.5 to 2.7 million people die of this disease each year. The situation is worsening, as drug-resistant strains of the most virulent form of the malaria parasite, *Plasmodium falciparum*, have spread to most endemic regions. At-risk groups include those in whom immunity has not yet developed (young children in endemic areas, travelers, etc.) and those in whom immunity has waned (pregnant women, the elderly and people from endemic areas who have ceased to be routinely exposed to infection).

In the 1950s and 60s, governments and the World Health Organization (WHO) declared war on malaria and embarked on a mission to eradicate the disease. DDT was a primary weapon in this effort. But the malaria vectors, and the disease-causing parasite itself, proved extraordinarily resilient. After years of futile attempts at eradication, governments and donor agencies wearied of the struggle, and in 1969, WHO abandoned the eradication strategy.

In the ensuing years, the absence of well-designed and funded malaria control programs has allowed the global epidemic of malaria to worsen. Resistance to over-used pesticides and drugs has contributed to the problem. The estimated direct and indirect cost of malaria in Africa was US$1.8 billion in 1995.

While the idea of eradicating mosquitoes is not realistic, many scientists believe that it is possible to reduce and manage the mosquito population below the threshold that would cause disease through a combination of:

- **Alternative chemical vector controls** - Focused use of less persistent, less hazardous insecticides like synthetic pyrethroids. These alternative pesticides can be employed for indoor house spraying as well as for impregnating mosquito bednets, curtains, and clothing.
Ecological vector management - Interfering with the life cycle of mosquitoes through habitat management and the use of beneficial organisms.

Community education and participation - Researchers have reported that many at-risk populations largely do not understand the route by which malaria is transmitted or how to prevent it. Health education and information should be developed and promoted by health officials, local authorities and teachers.

Integrated public health approaches - Such approaches involve focusing both on the disease and on the vectors. A variety of vector control methods are combined with community-based public health strategies that ensure early detection, diagnosis, and prompt treatment of malaria cases to prevent the spread of the disease.

Improved drugs and vaccines - Drug resistant (even multi-drug resistant) parasite strains are not uncommon in many places where malaria is endemic. A number of vaccines have been developed, but none has proved effective. More research and resources are needed in the development and trial of new treatments and vaccines.

Clearly, no single tool—whether pesticide, pharmaceutical, or other—can be relied upon to combat such a complex disease as malaria.

Malaria risk management must be maintained and improved through the development and use of safe, sustainable vector control—including chemical, biological, physical, and environmental methods—as well as increased spending on malaria drug research, treatment, and public health surveillance.

This document represents an initial review of the literature on DDT health effects, alternative malaria control strategies that have shown success, and cost comparisons of switching from DDT. It is by no means exhaustive, nor does it include detailed analysis of the research that is cited. Instead, it is a collection of information sources that can be used in designing successful malaria control programs.

At the end of the document is Physicians for Social Responsibility’s Public Health Statement on Malaria and the Use of DDT. The statement was crafted in collaboration with Kenyan Physicians for Social Responsibility and a number of other African physicians and health professionals. It calls for a DDT phaseout concurrent with increased spending and attention to the malaria crisis, and includes specific recommendations for governments and WHO. Please add your name to the growing list of health professionals endorsing the twin goals of reducing malaria and phasing out the use of DDT.
C. Potential Health Effects of DDT

Introduction

DDT (1,1,1-trichloro-2,2-bis(p-chlorophenyl)-ethane) is an organochlorine-based pesticide that has played a major role in global efforts to combat malaria and other tropical diseases. For decades, it was the weapon of choice against disease-carrying mosquitoes, for its effectiveness at killing insects with few acute effects on people. This led to equally widespread contamination of water, soil, fish, wildlife, and people. DDT is readily metabolized into a stable and equally toxic compound, DDE. Long-range atmospheric transport of DDT into northern countries, is well-documented. DDT has been detected in Arctic air, soil, snow and ice, and virtually all levels of the Arctic food chain (Abstracts 1, 2). The extraordinary persistence of DDT and its tendency to bioaccumulate in body fat raises concerns regarding its chronic effects on human health.

- Breast milk and lactation - For most populations, the primary route of exposure to DDT and its metabolites is through food. DDT and DDE are fat soluble and store well in the adipose tissues of humans and animals. They break down in the body very slowly, and bioaccumulate in food chains. DDT and its metabolites have been found in virtually every breast milk sample tested, including samples taken in tropical areas of Mexico, Canada and South Africa (Abstracts 1, 3-6). Studies have shown an inverse relationship between duration of lactation and the concentration of DDE in breast milk (Abstracts 3, 7, 9). Poor neurological reflexes (using Brozelton Neonatal Behavioral Assessment Scale) has been reported in newborn infants exposed to DDT via breast milk. Long term effects are not known.

- Neurodevelopmental Effects - A major target of acute DDT exposure is the nervous system (Abstracts 12-16). In a study detailing long-term occupational exposure, twenty workers exposed for fourteen years were found to have blood serum levels of DDT that were ten times those of the general population, and showed observable nervous system abnormalities (Abstract 16). The maternal body burden of DDT and its metabolites is stored at the highest concentrations in breast milk and the placenta, creating a hazard for the developmentally vulnerable offspring. Low doses fed to neonatal mice are associated with a permanent hyperactive condition, as well as tremors and paralysis (Abstract 14). Fertilized eggs of killifish exposed to DDT in water suffered a delayed rate of physiological development (Abstract 13).
Carcinogenicity - Due to the carcinogenic activity of DDT in some lab animals, DDT, DDD and DDE are classified by the U.S. EPA as Class B2 probable human carcinogens. A number of studies of the connection between DDT exposure and the incidence of human cancer did not find evidence of a correlation, although results may be obscured due to confounding factors such as smoking and exposure to multiple pesticides. The possible link between DDT exposure and breast cancer is also controversial. Some research has found moderate correlations between breast cancer and body burden of DDT, but other studies have found no such connection. Workplace exposure to DDT found increased risk of pancreatic cancer, liver cancer and multiple myelomas (Abstracts 17-19).

Reproductive Effects - Chronic DDT exposure may also cause health effects related to disruption of the endocrine system (Abstracts 24-26). Some research suggests that DDT and DDE may interfere with normal functioning of certain hormone-mediated processes and may have a multi-generational effect in which contaminants accumulated in fat in the mother are mobilized during the development of the embryo and (for mammals) fetus and during breast feeding of the infant. Thus the offspring could be exposed to higher than ambient levels of DDT or other contaminants during vulnerable periods. Research on rats has also shown that DDT prevents the male hormone, androgen, from binding to its receptor thereby blocking androgen from guiding normal sexual development (Abstract 26). Evidence of the estrogenic properties of DDT and DDE have also been observed in alligators and gulls (Abstracts 24, 25).

Fortunately, other pesticides have been and are being developed which are less persistent and bioaccumulative and appear to be less hazardous to humans and wildlife. These pesticides can be transition chemicals while better and safer methods of vector control are being identified.
DDT Levels in the Arctic

   Regional Centre Monitoring of the Arctic, St. Petersburg, Russia. Under the auspices of Arctic Monitoring and Assessment Programme (AMAP), a Russian-Norwegian co-operation project was established to assess the exposure of delivering women to persistent organic pollutants (POPs) in Arctic areas of Russia. In the period 1993-95 blood and breast milk samples were collected from 94 delivering women in Yamal and Tajmyr Autonomous Regions of Siberia. Concentrations of chlorinated pesticides and polychlorinated biphenyls (PCBs) were determined by high resolution gas chromatography with electron capture detection. The POP levels in maternal plasma among the non-indigenous women were higher than the native population, especially in total PCB, HCHs (hexachlorocyclohexanes) and the DDT-group. The dietary questionnaires showed that the non-indigenous populations consumed considerably less local food items like reindeer meat and fresh water fish. There was no correlation between local food consumption and elevated levels of pollutants. Even if the indigenous groups had lower concentrations of the most important pollutants than the non-indigenous population, they were still higher than the levels measured in the Scandinavian countries of the AMAP-study and up to levels of medical concern. The most important sources of organic pollutants for the Russian Arctic populations of Yamal and Tajmyr seems to be imported food from other areas of Russia and local use of pesticides. It must be a high priority concern to further elucidate.

2. Tenenbaum DJ. **Northern overexposure** Environ Health Perspect 1998 Feb;106(2):A64-9
   The top of the world may look pristine, but the Arctic environment and its inhabitants contain surprisingly high levels of heavy metals, persistent organic pollutants such as pesticides, and nuclear radiation. Although the Arctic has few significant pollution sources, the contaminants are swept northward on ocean currents and winds from industrial regions. Once contaminants arrive, low temperatures and limited sunlight slow their decay, and bioaccumulation concentrates some of them to dangerous levels.

   Concentrations of p,p'-DDT, p,p'-DDE, and p,p'-DDD have been determined in breast milk of mothers residing in two different areas of Kwazulu. Annual intradomiciliary application of DDT was used for the interruption of malaria transmission in one area, while the other served as the control. Milk from mothers living in DDT-treated dwellings had significantly higher mean levels of DDT and metabolites (mean sigma DDT 15.83 mg kg-1 in milk fat) than those from the control area (0.69 mg kg-1). The highest recorded sigma DDT value was 59.3 mg kg-1 (milk fat). Primiparous mothers from the malarious area had significantly more sigma DDT and metabolites (sigma DDT 24.82 mg kg-1) than multiparous mothers from the same area (mean 12.21 mg kg-1). Parity was the best predictor of DDT in breast milk of the exposed group. The percentage DDT and the sigma DDT increased significantly with an increase in parity. The same, but not significant, trend was also found for the control group. It was hypothesized that the increase in percentage DDT that occurred with higher parities was due to the uptake of DDT and elimination via milk. This process was faster than the
uptake and endogenous formation of DDE. Designing predictive models using multiple regression was not very successful. The recorded levels do not represent an appreciable health risk to the mothers. From the literature it was deduced that at the recorded levels, a well-founded risk to the infants, particularly the firstborns, exists in sprayed areas.

4. Bouwman H, Cooppan RM, Reinecke AJ, Becker PJ. 1990. Levels of DDT and metabolites in breast milk from Kwa-Zulu mothers after DDT application for malaria control. *Bull World Health Organ* 68(6):761-8. Concentrations of DDT, DDE and DDD were determined in the breast milk of Kwa-Zulu mothers residing in two different areas—with and without annual intra-domiciliary applications of DDT for the interruption of malaria transmission (exposed and control groups, respectively). While no significant change in levels with time was found in the control group, both DDT and DDE in breast milk of the exposed group increased after DDT application and this continued for three more months, after which it did not decrease appreciably. Percentage DDT increased from 42.57% (sigma DDT = 12.21 mg/kg milk fat) before spraying to 50.87% (sigma DDT = 13.79 mg/kg milk fat) following DDT application. At 6 and 9 months after the application it was 45.85% (sigma DDT = 19.49 mg/kg milk fat) and 43.27% (sigma DDT = 18.34 mg/kg milk fat), respectively. These results suggest a risk to the health of the infants in the exposed group.

5. Bouwman H, Cooppan RM, Becker PJ, Ngxongo S. 1991. Malaria control and levels of DDT in serum of two populations in KwaZulu. *J Toxicol Environ Health* 33(2):141-55. Concentrations of p,p'-DDT, p,p'-DDE, and p,p'-DDD were determined in serum of members of households of two different areas of KwaZulu. Annual intradomiciliary application of DDT is used for the interruption of malaria transmission in one area (the exposed group) while the other served as the control. Demographic differences between the two groups resulted in significantly more females in the control group. The two groups were comparable with respect to age. Serum from household members living in DDT-treated dwellings had significantly higher (p less than .005) levels of sigma DDT and metabolites (mean sigma DDT 140.9 micrograms/l) than those from the control area (mean sigma DDT 6.04 micrograms/l). Percentage DDT was also significantly higher (p less than .05) in the exposed group (28.9%) than the control group (8.3%). sigma DDT for the 3-10 yr age interval (168.6 micrograms/l) was significantly higher (p less than .05) than the 20-29 (60.5 micrograms/l) and 30-39 (84.2 micrograms/l) yr age intervals. There seemed to be two groups with regard to accumulation and elimination. The age group 3-29 appeared to be eliminating DDT, most likely accumulated from contaminated breast milk, faster than they accumulated it. From around 29 yr of age accumulation predominated as the levels increased with age. Regression analysis suggested pharmacokinetic differences for DDE and DDT between the two groups. Liver function parameters between the two groups only differed significantly for gamma-glutamyl transferase (gamma GT) (p less than .001), but the influence of difference in alcohol consumption, which was significantly higher in the exposed group (p less than .0001), offered a better explanation. Those of the exposed group that consumed alcohol had a significantly higher (p less than .05) mean gamma GT level (41.5 IU/l) than those that did not (20.2 IU/l), but were not significantly different for sigma DDT (p greater than .05). The safety of DDT used in malaria control for subjects aged 3 and older was confirmed by the levels of DDT in serum when compared with other studies, which showed lack of any negative effects associated with these levels in adults, and an apparently normal liver function in the exposed and control groups.

6. Bouwman H, Becker PJ, Cooppan RM, Reinecke AJ. 1992. Transfer of DDT used in malaria control to infants via breast milk. *Bull World Health Organ* 70(2):241-50. The transfer of p,p'-DDT (1,1,1-trichloro-2,2-bis(4-chlorophenyl)ethane) and its metabolites to infants via breast-feeding was studied in an area of KwaZulu, South Africa, where DDT is used to interrupt malaria transmission. Samples of whole blood were collected from 23 infants, together with samples of breast milk from their respective mothers. The mean sigma DDT (total DDT) in the whole blood was 127.03 micrograms/l-1 and that in the breast milk, 15.06 mg.kg-1 (milk fat).
DDT of sigma DDT) was significantly higher in the infant blood than in the breast milk (P less than 0.05). A multiplicative regression analysis indicated that sigma DDT increased significantly (P less than 0.01) in infant whole blood with infant age. Multiple regression showed that 70.0% of the variation in sigma DDT was due to the variation in parity of the mother, age of the infant, and the sigma DDT in breast milk. These variables accounted also for 76.3% of the variation in p,p'-DDE but only for 38.2% of that in p,p'-DDT. Organochlorines were therefore largely transferred to the infant from the mother, with DDT in the environment playing a secondary role.


OBJECTIVES. Worldwide declines in the duration of lactation are cause for public health concern. Higher levels of dichlorodiphenyl dichloroethene (DDE) have been associated with shorter durations of lactation in the United States. This study examined whether this relationship would hold in an agricultural town in northern Mexico. METHODS. Two hundred twenty-nine women were followed every 2 months from childbirth until weaning or until the child reached 18 months of age. DDE was measured in breast milk samples taken at birth, and women were followed to see how long they lactated. RESULTS. Median duration was 7.5 months in the lowest DDE group and 3 months in the highest. The effect was confined to those who had lactated previously, and it persisted after statistical adjustment for other factors. These results are not due to overtly sick children being weaned earlier. Previous lactation lowers DDE levels, which produces an artificial association, but simulations using best estimates show that an effect as large as that found here would arise through this mechanism only 6% of the time. CONCLUSIONS. DDE may affect women's ability to lactate. This exposure may be contributing to lactation failure throughout the world.


OBJECTIVES: To estimate infants’ intake of organochlorines (OCs) from their measured intake of breast milk; to compare these with the acceptable daily intakes (ADIs) set by the World Health Organization (WHO). DESIGN: Primiparous nursing mothers were recruited from either an industrial or rural area between January and November 1992. SETTING: Mothers volunteered in response to information displayed at their Infant Welfare Centre. All sampling was undertaken in the subject's home. SUBJECTS: The sole entry criterion was primiparity. Three breast milk samples were collected at one month intervals from each mother. OC levels were measured on a milk fat basis by gas chromatograph-mass spectrometer and individual milk intakes were used to determine the infant's daily OC intake. Of the 23 mothers who entered the study, 17 finished, resulting in 57 samples for intake determination. RESULTS: Some intakes of hexachlorobenzene (HCB), chlordane, dieldrin and heptachlor epoxide (HE) exceeded the ADI. High OC levels in breast milk did not necessarily result in a high intake for the infant. CONCLUSIONS: Assessment of the exposure of infants to OC contaminants in breast milk requires an accurate estimate of OC intake. Intakes estimated using inferred rather than measured values for milk fat and milk intake are not reliable indicators of actual intakes.


The authors measured polychlorinated biphenyls (PCBs) and dichlorodiphenyl dichloroethene (DDE) in maternal serum, cord blood, placenta, and serial samples of breast milk from 868 women. Almost all samples of breast milk showed detectable levels of both chemicals. Overall, values for DDE in this study are within the range of those found previously, whereas those for PCBs are somewhat higher. Possible causes of variation in levels were investigated. For DDE, older women, Black women, cigarette smokers, and women who consumed sport fish...
during pregnancy had higher levels; only age and race showed large effects. For PCBs, older
women, women who regularly drink alcohol, and primiparous had higher levels. In addition, both
chemicals showed modest variation across occupational groupings. Casual exposure to a PCB
spill did not result in chemical levels different from background. In general, women have higher
levels in their first lactation and in the earlier samples of a given lactation, and levels decline both
with time spent breast-feeding and with number of children nursed. These striking declines are
presumably a measure of exposure to the child.

Polychlorinated biphenyls (PCBs) and dichlorodiphenyl dichloroethene (DDE) in human
Oct;77(10):1294-7 We followed 858 children from birth to one year of age to determine whether
the presence of polychlorinated biphenyls (PCBs) and dichlorodiphenyl dichloroethene (DDE) in
breast milk affected their growth or health. Neither chemical showed an adverse effect on weight
or frequency of physician visits for various illnesses, although differences were seen between
breast-fed and bottle-fed children, with bottle-fed children being heavier and having more
frequent gastroenteritis and otitis media. Children of mothers with higher levels of DDE were
breast-fed for markedly shorter times, but adjustments for possible confounders and biases did not
change the findings. In absence of any apparent effect on the health of the children, we speculate
that DDE may be interfering with the mother’s ability to lactate, possibly because of its estrogenic
properties.

Environ 1998 Oct 8;221(2-3):201-4 The monitoring study of 287 human adipose tissue samples
collected from 1988 to 1997 was used to determine the contamination levels of organochlorine
pesticides. The results obtained indicate DDT as dominant. The fluctuation of DDT levels during
the study period reveal a descent tendency and are closely related to the pp’-DDE content. The
results, classified according to the origin of donors, indicate a higher contamination of the
suburban zone. This difference was caused by diminished use of DDT and its substitution by
Malathion and pyrethroids.

Neurodevelopmental Effects

1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane (DDT) and its metabolites,
1,1-dichloro-2,2-bis(p-chlorophenyl)ethene (DDE), 1,1-dichloro-2,2-bis(p-chlorophenyl)ethane
(DDD) and 2,2-bis(p-chlorophenyl) acetic acid (DDA) were comparatively evaluated on humoral
and cell mediated immune (CMI) responses in rats. Rats were given a diet containing 200 ppm of
the various test compounds for 6 weeks and were subsequently immunized with ovalbumin. DDT,
DDE and DDD, all induced differential degrees of humoral and cellular immune suppression.
There were (a) increases in albumin/globulin ratios, (b) suppression of IgM and IgG levels, and
(c) attenuations in ovalbumin induced antibody responses. In CMI studies, there were marked
inhibitions of (a) leucocyte and macrophage migration factors, and (b) delayed type
hypersensitivity (DTH) reaction. Whereas, these effects were most marked with DDE and DDD,
DDA did not elicit such immunomodulatory effects. It is inferred that suppression of immune
responses by immediate DDT metabolites, DDE (and DDD and not DDA) is an important
determinant of the toxicity of DDT (DDE > DDD > DDT) and the influence of this environmental
pollutant in health and disease.
13. Crawford RB, Guarino AM, Effects of DDT in Fundulus: studies on toxicity, fate, and reproduction. Arch Environ Contam Toxicol 1976;4(3):334-8 The toxicity, absorption, distribution, metabolism, and effects on reproduction of DDT was studied using the killifish (Fundulus heteroclitus), a species of economic importance because of its widespread abundance and its presence toward the lower end of the food chain. 14C-DDT was administered by exposure from the ambient water. There was a rapid removal of the radioactive pesticide from the water accompanied by uptake of radioactivity primarily by carcass (primarily muscle tissue) and eggs of the fish. Most (greater than 92%) of the radioactivity in the carcass was shown by TLC methods to be the parent pesticide. One day after a single 24-hr exposure to 14C-DDT, approximately 70% of the administered radioactivity was found in the carcass and the levels of the tissue decayed with a t 1/2 of three days. One day after a single 24-hr exposure to 0.1 ppm of 14C-DDT, the organs that contained the highest concentration of the pesticide (ca. 5 ppm) were intestine and liver. When the pesticide was administered by two 24-hr exposures from water, the intestine, liver and ovaries contained the major concentration of radioactivity (7 to 14 ppm). Untreated Fundulus contained less than 0.2 ppm of total DDT-like compounds. A variety of doses and schedules were tested in an effort to maximize the absorption of DDT, while minimizing the mortality to the fish. An intermittent schedule of 24 hr in 0.1 ppm DDT followed by 24 hr in DDT-free sea water, repeated two times, was found to be optimal. At the levels examined, DDT delayed the rate of normal development of fertilized eggs from Fundulus, but did not appear to cause any observable alterations in the hatched fry. Fertilization of Fundulus eggs was significantly diminished when insemination was carried out in DDT-containing sea water.

14. Eriksson P, Archer T, Fredriksson A, Altered behaviour in adult mice exposed to a single low dose of DDT and its fatty acid conjugate as neonates. Department of Zoophysiology, Uppsala University, Sweden. Brain Res 1990 Apr 23;514(1):141-2, DDT, 1,1,1-trichloro-2,2-bis(p-chlorophenyl)-ethane is one of the best-known insecticides which produces neurotoxic syndrome in mammals. DDT is also a world-wide environmental contaminant which is still used in several countries. We have previously reported on pronounced retention of DDT in the neonatal mouse brain. We have also observed that DDT and a DDT metabolite, DDOH, conjugated to palmitic acid (DDOH-PA), which have been found in DDT-treated female rats, affect the muscarinic cholinergic receptors in the brain of the neonatal mouse. We now report that neonatal exposure to a single low oral dose of DDT and DDOH-PA (1.4 mumol/kg b.wt.) also can lead to a permanent hyperactive condition in the mice as adults.

15. Hall RH A new threat to public health: organochlorines and food. Nutr Health 1992;8(1):33-43 Ambient levels of persistent toxic chemicals, chemicals that persist for decades in the environment, have reached levels high enough to affect the health of children. The organochlorines (PCBs, DDT and the dioxin family) accumulate in human adipose tissue. Pregnant women pass the contamination to their fetuses. The developing nervous system is the most vulnerable. Neurobehavioral deficits, including short-term memory loss, are detected in children born to mothers at the high end of the distribution curve of organochlorines. Humans are not alone in their susceptibility to these subtle effects. Wildlife exposed to the same spectrum of organochlorines as humans suffer a variety of behavioral changes. Rats and Rhesus monkeys fed diets containing the organochlorines under laboratory conditions exhibit behavioral changes that persist into adulthood. For humans, food provides 80 percent of organochlorine contamination. Meat, fish, dairy and commercial fruit are the main sources. A vegetarian diet including unsprayed fruit minimizes contamination. The ultimate solution to this public health problem is elimination of the organochlorines from the environment.

and a persistent chlorinated insecticide (technical hexachlorocyclohexane; HCH; BHC) are reported. Exposure of 160 workers to a combination of pesticides (malathion, parathion, DDT and HCH) resulted in 73% of the workers showing toxic signs and symptoms. Formulators showed marked inhibition of whole blood, plasma and red blood cell cholinesterase (ChE) activity and slightly higher concentrations of DDT and HCH in serum. An interesting observation was that over 25% of the formulators showed ECG aberrations. The ECG changes were not related to whole blood ChE activity. Exposure to the chlorinated insecticide HCH in 19 workers engaged in the manufacture of technical HCH resulted in toxic signs and symptoms in over 90% of the subjects. The HCH concentrations in serum showed a ten-fold increase. Changes in the liver enzymes ornithine carbamyl transferase (OCT), gamma-glutamyl transpeptidase (GGTP), leucine aminopeptidase (LAP) and in immunoglobulin M(IgM) showed possible effects on liver and humoral immunity. ECG monitoring showed evidence of cardiac effects. Exposure of 40 formulators to a highly toxic OP insecticide (phorate) showed that over 60% of the workers suffered from toxic effects in spite of using a complete set of protective clothing. A marked and progressive inhibition in whole blood and plasma ChE activity was found during the two weeks of exposure to phorate. An appreciable recovery in ChE activity was observed 10 days after cessation of exposure. These surveys have established the need to practice and develop biological monitoring techniques to assess exposure and predict health risks in workers occupationally exposed to pesticides.

**DDT and Cancer**

17. Cocco P, Blair A, Congia P, Saba G, Ecca AR, Palmas C. Long-term health effects of the occupational exposure to DDT. A preliminary report. We conducted a proportional mortality study of 1043 deaths among men who took part in an antimalarial campaign in Sardinia, Italy from 1946 to 1950. DDT comprised 94% of the insecticide used during the campaign, and was sprayed over the soil of the entire region at an average concentration of 10 mg/m², as well as in all dwellings and animal shelters. Expected deaths were derived from the proportional mortality rates of the general Italian male population, specific by cause, 5-year age groups, and 5-year calendar periods in the period from 1956 to 1992. The proportional mortality ratio (PMR) for cardiovascular diseases was significantly decreased, while nonmalignant respiratory diseases showed a 22% increase in risk of borderline statistical significance. Significant increases in risk among workers exposed to DDT in application or inspection jobs were observed for liver and biliary tract cancer (PMR = 228; 95% C.I. = 143-345) and multiple myeloma (PMR = 341; 95% C.I. = 110-795). The PMR for myeloid leukemia was also increased (PMR = 189; 95% C.I. = 38-552), although it was not statistically significant. PMRs for liver and biliary tract cancer and myeloid leukemia were also elevated among workers who did not have direct occupational contact with DDT (liver and biliary cancer: PMR = 210; 95% C.I. = 117-346; myeloid leukemia: PMR = 170; 95% C.I. = 19-614). No trends occurred according to length of employment in exposed jobs. These preliminary results are somewhat in agreement with experimental studies in rodents and previous epidemiologic findings. Expansion of the cohort to include all applications, and collection of information to improve exposure assessment is needed to clarify these findings.

18. Eriksson M, Karlsson M. Occupational and other environmental factors and multiple myeloma: a population based case-control study. Br J Ind Med 1992 Feb;49(2):95-103. Epidemiological studies on the aetiology of multiple myeloma are reviewed as a background to this population based case-control study performed in an area with a high incidence of multiple myeloma. The purpose was to identify and evaluate several suspected environmental factors in relation to this disease. A total of 275 confirmed cases diagnosed in four counties in northern Sweden during four years were compared with the same number of control subjects drawn from population registries. The controls were matched for age, sex, county, and vital status. Occupations and work
associated exposures to chemicals and other potential carcinogens were assessed by an extensive questionnaire that also included questions on smoking habits, residential building materials, vicinity to electrical power lines, and leisure time contact with animals, electrical equipment, and chemicals. Information obtained from the questionnaires was completed by telephone interviews when necessary. Univariate analysis and multivariate logistic regression were performed. The study confirmed an association found earlier between farming and multiple myeloma. Some domestic animals (cattle, horses, and goats) and two types of pesticides (phenoxyacetic acids and DDT) were indicated as risk factors within farming. Exposure to electromagnetic fields, asbestos, and organic solvents were negatively associated with myeloma in this study.

19. Garabrant DH, Held J, Langholz B, Peters JM, Mack TM. DDT and related compounds and risk of pancreatic cancer. *J Natl Cancer Inst* 1992 May 20;84(10):764-71. BACKGROUND: A cohort mortality study among 5886 chemical manufacturing workers was completed in 1987 and showed increased mortality due to pancreatic cancer. PURPOSE: We conducted a nested case-control study of pancreatic cancer among these chemical manufacturing workers to identify risk factors for this disease. METHODS: Twenty-eight verified cases of pancreatic cancer and 112 matched controls were studied. Next of kin of each subject were interviewed to determine lifestyle factors, including tobacco, alcohol, and coffee consumption. Written work records and interviews with co-workers were used to determine chemical exposures at the plant under study. RESULTS: DDT was associated with pancreatic cancer (risk ratio [RR] for ever exposed compared with never exposed = 4.8; 95% confidence interval = 1.3-17.6). Among subjects who had a mean exposure to DDT of 47 months, the risk was 7.4 times that among subjects with no exposure. Two DDT derivatives, Ethylan and DDD, were additionally associated with pancreatic cancer (RR = 5.0 and 4.3, respectively); exposures to these two chemicals were correlated, and it was not possible to determine whether each acted independently of the other. Smoking was identified as an independent risk factor, but controlling for smoking (and other potential confounders) in the analyses did not appreciably alter the risks seen for DDT, DDD, or Ethylan. CONCLUSIONS: Exposure to DDT was associated with pancreatic cancer. The association was not explained by exposure to lifestyle factors or other chemicals, and risk increased with both duration of exposure and latency since first exposure. IMPLICATIONS: These results may indicate that DDT can cause pancreatic cancer in humans under circumstances of heavy and prolonged exposure.

20. Hunter DJ, Hankinson SE, Laden F, Colditz GA, Manson JE, Willett WC, Speizer FE, Wolff MS. Plasma organochlorine levels and the risk of breast cancer. *N Engl J Med* 1997 Oct 30;337(18):1253-8. BACKGROUND: Exposure to "environmental estrogens" such as organochlorines in pesticides and industrial chemicals has been proposed as a cause of increasing rates of breast cancer. Several studies have reported higher blood levels of 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene (DDE) and polychlorinated biphenyls (PCBs) in patients with breast cancer than in controls. METHODS: We measured plasma levels of DDE and PCBs prospectively among 240 women who gave a blood sample in 1989 or 1990 and who were subsequently given a diagnosis of breast cancer before June 1, 1992. We compared these levels with those measured in matched control women in whom breast cancer did not develop. Data on DDE were available for 236 pairs, and data on PCBs were available for 230 pairs. RESULTS: The median level of DDE was lower among case patients than among controls (4.71 vs. 5.35 parts per billion, P=0.14), as was the median level of PCBs (4.49 vs. 4.68 parts per billion, P=0.72). The multivariate relative risk of breast cancer for women in the highest quintile of exposure as compared with women in the lowest quintile was 0.72 for DDE (95 percent confidence interval, 0.37 to 1.40) and 0.66 for PCBs (95 percent confidence interval, 0.32 to 1.37). Exposure to high levels of both DDE and PCBs was associated with a nonsignificantly lower risk of breast cancer (relative risk for women in the highest quintiles of both DDE and PCBs as compared with women in the lowest, 0.43; 95 percent confidence interval, 0.13 to 1.44). CONCLUSIONS: Our data do not support the hypothesis that exposure to DDT and PCBs increases the risk of breast cancer.
21. Siddiqui MK, Saxena MC, Mishra UK, Murti CR, Nag D. Long-term occupational exposure to DDT, *Int Arch Occup Environ Health* 1981;48(3):301-8, Blood serum of twenty workers occupationally exposed to DDT for an average duration of 14 years was analysed for organochlorine pesticides by gas-liquid chromatography with an electron capture detector. Significant levels of BHC, p,p'-DDT, p,p'-DDD and p,p'-DDE were detected. A higher incidence of total DDT equivalent, about 10 times, was observed in DDT exposed workers when compared with a comparable sample of unexposed persons from the general population. Levels of DDT in serum of occupationally exposed workers were more than the permitted level of 200 ppb. The daily intake was computed to be about 10 mg/man/day as against 0.25 mg--the acceptable daily intake. Abnormal nerve conduction was encountered in a few cases of DDT sprayers. No significant correlation was observed between the total DDT equivalent in serum and duration of occupational exposure in workers. Levels of BHC in controls was 2.3 times the level in exposed workers, possibly due to induction of hepatic drug metabolising enzymes by high levels of DDT in the latter group. Findings are discussed in the light of existing knowledge of the bio-chemical effects evoked due to residual intoxication of DDT during occupational exposure.

22. Wolff MS, Weston A. Environ Health Perspect 1997 Jun;105 Suppl 4:891-6 Breast cancer risk and environmental exposures. Although environmental contaminants have potential to affect breast cancer risk, explicit environmental links to this disease are limited. The most well-defined environmental risk factors are radiation exposure and alcohol ingestion. Diet is clearly related to the increased incidence of breast cancer in developed countries, but its precise role is not yet established. Recent studies have implicated exposure to organochlorines including DDT as a risk factor for breast cancer in the United States, Finland, Mexico, and Canada. Other investigations have discovered associations between breast cancer risk and exposures to chemical emissions and some occupational exposures. Several points must be considered in evaluating the relationship of environmental exposure to breast cancer. Among these considerations are the mechanism of tumorigenesis, timing of environmental exposure, and genetic modulation of exposure. Epidemiologic and ecologic investigations must take into account the very complex etiology of breast cancer and the knowledge that tumorigenesis can arise from different mechanisms. Thus crucial exposures as well as reproductive events related to breast cancer may occur years before a tumor is evident. Moreover, environmental contaminants may alter reproductive development, directly or indirectly, and thereby effect the course of tumorigenesis. Such alterations include change in gender, change in onset of puberty, and inhibition or promotion of tumor formation. Timing of exposure is therefore important with respect to mechanism and susceptibility. Finally, genetic polymorphisms exist in genes that govern capacity to metabolize environmental contaminants. Higher risk may occur among persons whose enzymes either are more active in the production of procarcinogens or fail to detoxify carcinogenic intermediates formed from chemicals in the environment.

23. The human health effects of DDT (dichlorodiphenyltrichloroethane) and PCBS (polychlorinated biphenyls) and an overview of organochlorines in public health. Organochlorines are a diverse group of persistent synthetic compounds, some of which are detectable in nearly everyone. Many organochlorines are endocrine disruptors or carcinogens in experimental assays. p,p'-DDE (dichlorodiphenyl-dichloroethene) and PCBs (polychlorinated biphenyls) comprise the bulk of organochlorine residues in human tissues. We reviewed relevant human data cited in the 1991-1995 Medline database and elsewhere. High-level exposure to selected organochlorines appears to cause abnormalities of liver function, skin (chloracne), and the nervous system. Of more general interest, however, is evidence suggesting insidious effects of background exposure. Of particular concern is the finding of neonatal hypotonia or hyporeflexia in relation to PCB exposure. The epidemiologic data reviewed, considered in isolation, provide no convincing evidence that organochlorines cause a large excess number of cancers. A recent risk assessment that considered animal data, however, gives a cancer risk estimate for background exposure to
dioxin and dioxin-like compounds (e.g. some PCBs) with an upper bound in the range of 10\(^{-4}\) per year.

**Endocrine Disruption**


Injection of DDT [1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane] into gull eggs at concentrations comparable to those found in contaminated seabird eggs in 1970 induces abnormal development of ovarian tissue and oviducts in male embryos. Developmental feminization of males is associated with inability to breed as adults and may explain the highly skewed sex ratio and reduced number of male gulls breeding on Santa Barbara Island in southern California.


The reproductive development of alligators from a contaminated and a control lake in central Florida was examined. Lake Apopka is adjacent to an EPA Superfund site, listed due to an extensive spill of dicofol and DDT or its metabolites. These compounds can act as estrogens. Contaminants in the lake also have been derived from extensive agricultural activities around the lake that continue today and a sewage treatment facility associated with the city of Winter Garden, Florida. We examined the hypothesis that an estrogenic contaminant has caused the current failure in recruitment of alligators on Lake Apopka. Supporting data include the following: At 6 months of age, female alligators from Lake Apopka had plasma estradiol-17 beta concentrations almost two times greater than normal females from the control lake, Lake Woodruff. The Apopka females exhibited abnormal ovarian morphology with large numbers of polyovular follicles and polyanuclear oocytes. Male juvenile alligators had significantly depressed plasma testosterone concentrations comparable to levels observed in normal Lake Woodruff females but more than three times lower than normal Lake Woodruff males. Additionally, males from Lake Apopka had poorly organized testes and abnormally small phalli. The differences between lakes and sexes in plasma hormone concentrations of juvenile alligators remain even after stimulation with luteinizing hormone. Our data suggest that the gonads of juveniles from Lake Apopka have been permanently modified in ovo, so that normal steroidogenesis is not possible, and thus normal sexual maturation is unlikely.


Reproductive Toxicology Branch, US Environmental Protection Agency, Research Triangle Park, North Carolina 27711, USA. The increase in the number of reports of abnormalities in male sex development in wildlife and humans coincided with the introduction of ‘oestrogenic’ chemicals such as DDT (1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane) into the environment. Although these phenotypic alterations are thought to be mediated by the oestrogen receptor, they are also consistent with inhibition of androgen receptor-mediated events. Here we report that the major and persistent DDT metabolite, p,p'-DDE (1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene), has little ability to bind the oestrogen receptor, but inhibits androgen binding to the androgen receptor, androgen-induced transcriptional activity, and androgen action in developing, pubertal and adult male rats. The results suggest that abnormalities in male sex development induced by p,p’-DDE and related environmental chemicals may be mediated at the level of the androgen receptor.
D. Alternative Chemical Vector Control

Introduction

Indoor house spraying with an insecticide can be an effective way to reduce malaria transmission because many of the important vector species like to rest on walls or ceilings (endophilic) and tend to feed on humans indoors (endophagic). Mosquitoes landing on sprayed surfaces will contact the insecticides with their feet and either die or be irritated sufficiently to leave the house, usually breaking the transmission cycle. House spraying programs are more likely to be effective where the principle vectors are endophilic and endophagic, and where strong financial support can ensure timely applications by well-trained operators using appropriate equipment and insecticides (Abstracts 31, 33).

Many different insecticides could be suitable for indoor residual spraying. An appropriate insecticide should be highly toxic to the insect, safe for humans and non-target organisms, persistent on the wall or ceiling surface, acceptable to the inhabitants of the house, easy to apply and fairly cheap. While DDT was previously the only effective, affordable insecticide that could be used for indoor house spraying against malaria without acute toxicity, this is no longer the case. Synthetic pyrethroids offer several benefits over DDT and other insecticides (Abstracts 27-29, 31-33). They are less persistent than DDT, less acutely toxic than carbamate and organophosphate insecticides, and tend not to bioaccumulate. In addition, synthetic pyrethroids are cost-competitive in many instances.

In the late 1970s, synthetic pyrethroids were developed to mimic natural insecticidal compounds found in chrysanthemums. Pyrethroids are widely used as household insecticides and are effective against mosquitoes.

The pyrethroids, including the natural pyrethrins, have been subdivided in two types:

- **Type I:** without an alpha-cyano group (e.g. bioallethrin, permethrin)
- **Type II:** containing a cyano substituent (e.g. deltamethrin, fenvalerate)

Their main biological effect is the modification of the kinetic of voltage-dependent sodium channels in nervous tissue.

Of course, the development of resistance to any particular insecticide can occur (Abstract 30). Acceptable solutions will have to be determined in conjunction with the people involved and could include finding alternative insecticides in anticipation of this happening and promoting scheduled shifts in the insecticides used.
Selected Bibliography on Alternative Chemical Vector Control

27. Ansari, M.A. et al. 1990. Field evaluation of deltamethrin against resistant Anopheles culicifacies in Distt. Ghasiabad (U.P) India. Indian Journal of Malariology 27:1-12. A large-scale field experiment involving over 100 villages tested the efficacy of house spraying with the pyrethroid deltamethrin against A. culicifacies mosquitoes exhibiting high levels of resistance to DDT and HCH. The mosquitoes were controlled and malaria transmission was much lower in villages treated with deltamethrin than in the control villages receiving the usual HCH treatment.

28. Arrendondo-Jimenez, J.I. et al. 1993. Indoor low-volume insecticide spray for the control of Anopheles albimanus in southern Mexico. Village scale trials of bendiocarb, deltamethrin and cyfluthrin. Journal of the American Mosquito Control Association 9:210-220. The authors compared the efficacy of low-volume spraying of houses with several different insecticides. The low-volume approach lowered both insecticide costs and spray time significantly. However, while both bendiocarb and deltamethrin spraying reduced the incidence of malaria by about 50% when compared to the untreated control, low-volume sprays of cyfluthrin did not reduce malaria.

29. Bouma, M. J., S. D. Parvez, R. Nesbit, and A. M. Winkler. 1996. Malaria control using permethrin applied to tents of nomadic Afghan refugees in northern Pakistan. Bull World Health Organ 74, no. 4: 413-21. Malaria control among nomadic populations has, in the past, posed serious logistic difficulties. Presented in this article are the results of a pilot study in which permethrin was sprayed on the tents of over 26000 nomadic Afghan refugees in an area of Pakistan where seasonal malaria outbreaks occur. In this area Anopheles culicifacies and A. stephensi are the malaria vectors. Population surveys in the year of the study, before and at the end of the transmission season, showed that the increase in the Plasmodium falciparum prevalence among the Afghan nomads was on average significantly less (increase from 6.4% to 15.3%) than that among the resident Pakistani population (from 3.2% to 45.6%). Surveys at the end of the transmission season among primary schoolchildren the year before and the year of the permethrin trial showed that the P. falciparum prevalence among nomadic children decreased significantly (from 46.9% to 16.3%), whereas an increase was observed among the local Pakistani children. The results show that spraying tents with permethrin was a safe and culturally acceptable intervention for the Afghan refugees and that the findings warrant further investigation.

30. Chandre F, Darrier F, Manga L, Akogbeto M, Faye O, Mouchet J, Guillet P Bull World Health Organ 1999;77(3):230-4 Status of pyrethroid resistance in Anopheles gambiae sensu lato. The present study confirms the presence of pyrethroid resistance among Anopheles gambiae s.l mosquitoes in Cote d'Ivoire and reports the observation of such resistance in two other countries in West Africa (Benin and Burkina Faso). Malaria vector populations from Cameroon (Central Africa), Senegal (West Africa) and Botswana (southern Africa) were found to be susceptible to pyrethroids. In the most resistant mosquito populations, resistance to permethrin was associated with reduced mortality, not only with respect to this compound but also towards deltamethrin. Moreover, a significant increase in knockdown time was observed in some mosquito populations before any decrease in mortality, suggesting that knockdown time could be a good indicator for the early detection of pyrethroid resistance. In view of the current extension of such resistance, there is an urgent need to set up a network in Africa to evaluate its development. It is also vital that the impact of this resistance on pyrethroid-impregnated bednets be assessed.
31. Hewitt, S., M. Rowland, N. Muhammad, M. Kamal, and E. Kemp. 1995. Pyrethroid-sprayed tents for malaria control: an entomological evaluation in Pakistan. *Med Vet Entomol* 9, no. 4: 344-52. Field trials were undertaken in the North West Frontier Province of Pakistan to determine the effects of pyrethroid-sprayed tents on feeding success, mortality and biting-rates of wild mosquitoes attracted to bait cows confined within the tents. Under natural conditions, endophagic mosquitoes rested only briefly in untreated tents during the night, followed by complete exodus at dawn. In tents sprayed on the interior surface with permethrin 0.5 mg/m² or with deltamethrin 0.03 g/m² the biting rate of Anopheles stephensi was reduced by about 40%; deterrency against culicines and other anophelines was much less. Mortality-rates of bloodfed mosquitoes from the treated tents were 75% An.stephensi, 65% An.subpictus but only 10% of culicines. Outer fly-sheets prolonged the effective life of the treatment; bioassays on the sprayed inner-sheets showed that insecticidal efficacy remained high for over a year, whereas on tents without fly-sheets permethrin residual efficacy declined rapidly 20-40 weeks post-treatment. It is concluded that tent-spraying with fast-acting photostable residual pyrethroid insecticide would probably provide effective protection against malaria transmission for the inhabitants of tents in any part of the world where the vector mosquitoes are endophilic and susceptible to pyrethroids.


33. Roberts, D. R., and R. G. Andre. 1994. Insecticide resistance issues in vector-borne disease control. *Am J Trop Med Hyg* 50, no. 6 Suppl: 21-34. Vector-borne diseases are an increasing cause of death and suffering worldwide. Efforts to control these diseases have been focused on the use of chemical pesticides, but arthropod resistance (whether physiological, biochemical, or behavioral) to pesticides is now an immense practical problem. The pharmacokinetic interactions of pesticides with arthropods, mechanisms of resistance, and the strengths and shortcomings of different resistance test methods are briefly reviewed. Using malaria control as an example, the differences between the efficacy of insecticide-sprayed houses in reducing malaria transmission, and the actual effect of such treatments on vectors are discussed. Reduced malaria transmission as a result of spraying house walls occurs through some combination of killing vectors that land on sprayed walls (insecticidal effect) and by preventing vectors from entering or remaining inside long enough to bite (behavioral effects). Both insecticidal and behavioral effects of insecticides are important, but the relative importance of one versus the other is controversial. Field studies in Africa, India, Brazil, and Mexico provide persuasive evidence for strong behavioral avoidance of DDT by the primary vector species. This avoidance behavior, exhibited when malaria vectors avoid insecticides by not entering or by rapidly exiting sprayed houses, should raise serious questions about the overall value of current physiological and biochemical resistance tests. The continued efficacy of DDT in Africa, India, Brazil, and Mexico, where 69% of all reported cases of malaria occur and where vectors are physiologically resistant to DDT (excluding Brazil), serves as one indicator that repellency is very important in preventing indoor transmission of malaria. This experience with DDT has implications for future control efforts because pyrethroids also stimulate avoidance behaviors in arthropods. Each chemical should be studied early (before broad-scale use) to define types of action against vector species by geographic area, especially for impregnated bed net applications. The problems for vector control created by use of insecticides in agriculture and the potential for management of resistance in both agriculture and vector-borne disease control are discussed.
34. Yadava, R. L., C. K. Rao, and H. Biswas. 1996. **Field trial of cyfluthrin as an effective and safe insecticide for control of malaria vectors in triple insecticide resistant areas. J Commun Dis** 28, no. 4: 287-98. Cyfluthrin (Solfac**) 10 wp, a synthetic pyrethroid was evaluated for its efficacy in malaria control through primary health centre approach, and for its acceptance by the community and effect on human health, and non target organisms, in predominantly tribal areas of Maharashtra and Gujarat from 1988 to 1990. Two dosage schedules; 2 rounds of indoor residual spraying a year, at 25 mg/sq. m2 in Maharashtra, and 3 rounds a year at 15 mg/sq. m2, in Gujarat were followed. There was significant reduction in per man hour densities of *An. culicifacies* the principal malaria vector, and collaterally of *C. quinquefasciatus* also. Significant reductions in slide positivity rates and slide falciparum rates were observed in both the areas as compared to the controls. The community acceptance of Cyfluthrin in terms of room coverage was 96% in Gujarat, and 89% in Maharashtra, as against average 68.5% and 55% in case of DDT and Malathion respectively. There were no reported ill-effects on humans or non-target organisms.
E. Impregnated Bednets and Other Physical Barriers

Introduction

Insecticide impregnation of mosquito bednets has become one of the most promising avenues for limiting the number of deaths caused by malaria. More than 60 studies of insecticide-treated nets (ITNs) and other physical barriers have been conducted in malaria endemic areas of the world (Abstracts 35-98). Most studies have documented a reduction in malaria disease rates between 20% and 90% (Abstracts 36, 38, 41, 42, 47, 60, 77, 83). Disease reduction is achieved mainly through the reduced biting rate of the malaria vector (Abstract 44). A meta-analysis conducted in 1995 found that ITNs decreased the incidence ratio of malaria by approximately 50% (Abstract 36). Studies on children and infants have been particularly encouraging (Abstracts 35, 47). In one of the areas where ITNs were tested in the Gambia, they cut the child mortality rate by 25% (Abstract 47). The findings of these studies confirm the efficacy of insecticide-treated nets for improving child survival and provide strong evidence of their specific role in reducing severe, life-threatening illness from malaria morbidity. According to the International Development Research Center (IDRC), studies in Kenya and Ghana suggest that using insecticide treated bednets “could save the lives of as many as 500,000 children each year who would normally die from the direct or indirect effects of malaria.”

African studies evaluating the success of bednets have been conducted in Kenya (36, 58, 60-62), Ghana (39), Burkino Faso (68), Mozambique (43), Tanzania (71), Cote d’Ivoire (49), Cameroon (51), Zaire (52), Sierra Leone (33), Madagascar (47), and the Congo (74). For pregnant women, ITNs may be particularly important. A study in Gambia found that fewer babies were classified as premature, and the mean birth weight was higher in villages where treated bednets were used (Abstract 46).

Successful use of impregnated bednets has occurred in China and Saudi Arabia (80) in the Middle East and India (76), Thailand (77), Afghanistan (89), China (75), Malaysia (85), the Solomon Islands (83), the Philippine Islands (92), and Myanmar in Asia (92). One study found bednets associated with a reduction in maternal malaria-associated anemia in the Thai-Burmese border area (Abstract 77).

The World Health Organization has given its approval to the use of pyrethroids in general and of permethrin in particular for the treatment of bednets. In addition to bednets, a number of studies have looked at the possibility of spraying or impregnating curtains, fabric wall hangings, sisal eaves, and even clothing with insecticides for malaria vector control. Based on this review of studies, bednets appear to provide the best and most consistent results.
Selected Bibliography on Impregnated Bednets & Other

Physical Barriers

Africa

35. Alonso, P. L., S. W. Lindsay, J. R. Armstrong, M. Conteh, A. G. Hill, P. H. David, G. Fegan, A. de Francisco, A. J. Hall, F. C. Shenton, and a. l. et. 1991. The effect of insecticide-treated bed nets on mortality of Gambian children. Lancet 337, no. 8756: 1499-502. Insecticide treatment of bed nets ("mosquito nets") may be a cheap and acceptable method of reducing the morbidity and mortality caused by malaria. In a rural area of The Gambia, bed nets in villages participating in a primary health-care (PHC) scheme were treated with permethrin at the beginning of the malaria transmission season. Additionally, children aged 6 months to 5 years were randomised to receive weekly either chemoprophylaxis with maloprim or a placebo throughout the malaria transmission season. We measured mortality in children in PHC villages before and after the interventions described, and compared this with mortality in villages where no interventions occurred (non-PHC villages). About 92% of children in PHC villages slept under insecticide-treated bed nets. In the year before intervention, mortality in children aged 1-4 years was lower in non-PHC villages. After intervention, the overall mortality and mortality attributable to malaria of children aged 1-4 in the intervention villages was 37% and 30%, respectively, of that in the non-PHC villages. Among children who slept under treated nets, we found no evidence of an additional benefit of chemoprophylaxis in preventing deaths. Insecticide-treated bed nets are simple to introduce and can reduce mortality from malaria.

36. Beach, R. F., T. K. Ruebush 2d, J. D. Sexton, P. L. Bright, A. W. Hightower, J. G. Breman, , Mount DL, and A. J. Oloo. 1993. Effectiveness of permethrin-impregnated bed nets and curtains for malaria control in a holoendemic area of western Kenya. Am J Trop Med Hyg 49, no. 3: 290-300. The effectiveness of village-wide use of permethrin-impregnated bed nets or eave, window, and door curtains as control measures for Plasmodium falciparum malaria was evaluated during two successive high-transmission seasons in western Kenya. Pairs of villages were assigned to one of three study groups: bed net, curtain, or control. Clinical, parasitologic, and entomologic measures were made from March to July 1990 and again 12 months later. When compared with the controls in 1990 and 1991, we observed a marked reduction in the incidence of P. falciparum infections in children less than six years old in the bed net villages (reduced by 40% and 48%) and a smaller but still significant reduction in the curtain villages (10% and 33%). Significant reductions were also seen in the incidence of P. falciparum parasitemias greater than 2,500/mm3 in the bed net group (reduced by 44% and 49%) and curtain group (16% and 32%). Additionally, we observed significant reductions in the incidence of documented fevers in association with P. falciparum parasitemia in bed net (reduced by 63%) and curtain villages (53%) when compared with controls. Entomologic inoculation rates in both bed net and control villages decreased by more than 50% below control values during both high transmission seasons. The results of this study, together with a 1988 study in the same area during the low transmission season, show that bed nets offer greater year-round of protection against P. falciparum infection than curtains. However, during the high transmission season, this technique reduces the frequency of P. falciparum infection rather than preventing it entirely.
37. Bermejo, A., and H. Veeken. 1992. Insecticide-impregnated bed nets for malaria control: a review of the field trials. Bull World Health Organ 70, no. 3: 293-6. Insecticide-impregnated bed nets act as a physical barrier to repel and kill mosquitoes. Community intervention trials suggest that these nets are effective in preventing malaria-related mortality and morbidity—but not malaria infection—in areas of low and moderate transmission; the results from areas of high transmission are not so encouraging. Comparison of the results from these trials and their interpretation are difficult because of variations in the epidemiology of malaria and several methodological flaws. Problems such as defining appropriate health indicators, monitoring bed-net usage, introducing bed nets randomly, selecting adequate controls, performing statistical analysis, and comparing bed nets with other available interventions are considered. Further community intervention trials are needed, paying attention to the methods and to assessment of their impact on malaria.

38. Binka, F. N., A. Kubaje, M. Adjuik, L. A. Williams, C. Lengeler, G. H. Maude, G. E. Armah, B. Kajihara, J. H. Adiamah, and P. G. Smith. 1996. Impact of permethrin impregnated bednets on child mortality in Kassena-Nankana district, Ghana: a randomized controlled trial [see comments]. Trop Med Int Health 1, no. 2: 147-54. A community-based randomized, controlled trial of permethrin impregnated bednets was carried out in a rural area of northern Ghana, between July 1993 and June 1995, to assess the impact on the mortality of young children in an area of intense transmission of malaria and no tradition of bednet use. The district around Navrongo was divided into 96 geographical areas and in 48 randomly selected areas households were provided with permethrin impregnated bednets which were re-impregnated every 6 months. A longitudinal demographic surveillance system was used to record births, deaths and migrations, to evaluate compliance and to measure child mortality. The use of permethrin impregnated bednets was associated with 17% reduction in all-cause mortality in children aged 6 months to 4 years (RR = 0.83; 95% CI 0.69-1.00; P = 0.05). The reduction in mortality was confined to children aged 2 years of younger, and was greater in July-December, during the wet season and immediately after (RR = 0.79; 95% CI 0.63-1.00), a period when malaria mortality is likely to be increased, than in the dry season (RR = 0.92, 95% CI 0.73-1.14). The ready acceptance of bednets, the high level of compliance in their use and the subsequent impact on all-cause mortality in this study has important implications for programmes to control malaria in sub-Saharan Africa.

39. Binka, F. N., and P. Adongo. 1997. Acceptability and use of insecticide impregnated bednets in northern Ghana. Trop Med Int Health 2, no. 5: 499-507. A district-wide study was undertaken in a rural population of northern Ghana to identify factors influencing the acceptance and use of insecticide-impregnated bednets (IIBNs). A series of focus group discussions were conducted during 2 years of implementation of IIBNs to gauge community reactions to the introduction of the nets and a structured questionnaire was administered to approximately 2000 randomly selected individuals. Although the IIBNs were accepted and used because they provided protection from mosquito bites, seasonal factors, patterns of use, and questions of cost were key factors likely to influence the dissemination and effectiveness of bednets. Use of the bednets was highly seasonal. Almost all recipients used their IIBNs in the rainy season (99%), corresponding to the period of high mosquito density and 20% used them in the dry seasons, the period of low mosquito density. Mothers with young children were more likely to wash the bednets frequently (because the children soiled the bednets with faeces and urine), resulting in no protection from the insecticide. Provision of wider bednets, or the provision of plastic sheets with the bednets or possible incorporation of the insecticide in washing soaps could improve protection for young children. The success of the promotion of IIBNs in malaria control programmes will depend on the cost of the package and the time of year that it is delivered. Financing mechanisms for individual and village groups are discussed. Social research effectively monitored the intervention in this study, and it should be included as an important component of national malaria control programmes.
Carnevale, P., P. Bitsindou, L. Diomande, and V. Robert. 1992. **Insecticide impregnation can restore the efficiency of torn bed nets and reduce man-vector contact in malaria endemic areas.** *Trans R Soc Trop Med Hyg* **86**, no. 4: 362-4. Three trials with torn bed nets impregnated with permethrin and deltamethrin were made under field conditions at the Soumouso Field Station and the Vallee du Kou rice-field area, both in Burkina Faso, and the Djoumouna fish pond area in the Congo Republic. Even a considerably torn correctly impregnated bed net could be an useful method for limiting human-anopheline contacts. But bed nets in poor condition, i.e. too little impregnated and too much torn, cannot protect the users against anopheline bites. Protection increases with insecticide concentration, but at a high dosage insecticide could have more a repellent than a killing effect. Therefore a balance has to be found for the optimum rate of insecticide treatment of bed nets to obtain a real reduction in malaria transmission and morbidity, in every epidemiological situation.

Carnevale, P., V. Robert, R. Snow, C. Curtis, A. Richard, C. Boudin, L. H. Pazart, J. M. Halna, and J. Mouchet. 1991. **[The impact of impregnated mosquito nets on prevalence and morbidity related to malaria in sub-Saharan africa].** <Original> L'impact des moustiquaires impregnees sur la prevalence et la morbidite liee au paludisme en Afrique sub-saharienne. *Ann Soc Belg Med Trop*; **71** Suppl 1 127-50. Insecticide treated bed nets (permethrin, deltamethrin and lambda cyathothrin) were used for malaria control in The Gambia, Burkina Faso and Tanzania where Anopheles gambiae (and An.funestus in Burkina Faso) is the main vector. Treated mosquito nets are efficient when used on a large scale and not on an individual level. Such a large scale use, acting on longevity and infectivity of vectors, always induced a decrease of malaria transmission by more than 90%. Treated bed nets had no significant effect on the overall parasite rate, showing that malaria transmission was not stopped. But it was usually found that there was a significantly smaller number of children with parasitemia higher than a critical threshold, a sensitive parameter of malaria morbidity. Indeed, in the three situations studied, malaria morbidity (fever + high parasitemia greater than critical level in the concerned area) has generally shown a similar drop of 60%. These data demonstrate that treated bed nets are useful to reduce transmission and morbidity. Advised as a new way for reduction of nuisance, treated bed nets were always welcomed by the populations and this method may be considered as a complementary weapon in public health.

Choi, H. W., J. G. Breman, S. M. Teutsch, S. Liu, A. W. Hightower, and J. D. Sexton. 1995. **The effectiveness of insecticide-impregnated bed nets in reducing cases of malaria infection: a meta-analysis of published results.** *Am J Trop Med Hyg* **52**, no. 5: 377-82. The use of insecticide-impregnated bed nets to minimize human-vector contact may reduce the incidence of malaria. Consequently, several field trials have evaluated their effectiveness as a malaria prevention strategy. A meta-analysis of published reports of field trials that measured the incidence of infections was performed to provide a measure of the effectiveness of insecticide-treated bed nets in preventing clinical malaria. Subsetted analyses were performed on the 10 field trials to calculate pooled incidence rate ratios of infection among the study groups. For the studies comparing insecticide-impregnated bed nets with untreated bed nets, the summary incidence rate ratio for acquiring malarial infections was 0.757 (95% confidence interval [CI] = 0.612-0.938), representing a reduction of 24%. For the studies comparing permethrin-impregnated bed nets with controls without bed nets, the summary incidence rate ratio was 0.497 (95% CI = 0.417-0.592) (Rothman-Boice heterogeneity statistics = 17.27 [P = 0.004] and 23.55 [P = 0.0003], respectively). These data suggest that insecticide-impregnated bed nets are effective in preventing malaria, decreasing the incidence rate ratio by approximately 50% in field trials performed to date.
43. Coene, J. 1991. Prospects for malaria control in urban and rural Kinshasa. *Ann Soc Belg Med Trop; 71 Suppl 1 P103-12*. Malaria is a major cause of paediatric illness and death in Kinshasa, and all 3 million inhabitants are at risk. In view of the increasing chloroquine-resistance of *Plasmodium falciparum*, the early treatment of fever cases as the sole malaria control measure is no longer acceptable. The prospects for vector control are determined by the effectiveness, the acceptability and the practicability of the various methods in the local conditions of Kinshasa. Pronounced differences in the level of endemicity exist between the various parts of the town. These differences, and the ecological and socio-economic factors that underlie them, must be taken into account when estimating the potential of a control method. The reduction of man-vector contact through personal protection with impregnated bednets is the only realistic goal at this moment, but even a very marked decrease of the inoculation rate will produce little apparent effect in the highly endemic (semi-)rural districts at the periphery of town. In the urbanized center of Kinshasa, where the moderate to low intensity of transmission is more susceptible to a critical reduction, the same method may have an impact on malaria morbidity. Moreover, the big nuisance from non-vector mosquitoes in the urban area is an important motivating factor for the acceptance and the use of bednets. A mass effect, on the other hand, only is to be expected in isolated villages. Field trials are needed to evaluate the short- and long-term effect on malaria transmission and on its’ clinical expression, as well as on the build-up of natural immunity, in the epidemiologically distinct areas. However, the final outcome of a large scale implementation of malaria control with impregnated mosquito nets will equally depend on health education, on the availability of bednets at low cost, on the creation of the appropriate structures for the (re)impregnation and distribution of the nets, and finally on the sustainability of the whole effort.

44. Crook, S. E., and A. Baptista. 1995. The effect of permethrin-impregnated wall-curtains on malaria transmission and morbidity in the suburbs of Maputo, Mozambique. *Trop Geogr Med 47*, no. 2: 64-7. The effect of nylon-netting wall-curtains impregnated with 0.5 g permethrin/m2 upon the biting rate of malaria vectors (*Anopheles gambiae* s.l. and *A. funestus*) and on the *Plasmodium falciparum* parasite rate, and morbidity due to malaria in children under five and between five and fourteen years was tested in the Maputo area. The curtains significantly lowered biting rates of both vector species inside curtained houses, but reduced inside resting and outside biting only in *A. funestus*. The percentage of children with falciparum parasitaemia fell significantly in curtained houses, and among their neighbours. However, parasite load and malaria morbidity in under fives was unaffected but malaria morbidity fell throughout the experimental area in 5 to 14-year-olds. This led to the speculation that malaria vectors inhibited from feeding in the vicinity of the curtains might have gone to feed in the adjacent control area.

45. Curtis, C. F., J. Myamba, and T. J. Wilkes. 1992. Various pyrethroids on bednets and curtains. *Mem Inst Oswaldo Cruz; 87 Suppl 3 P363-70*. Verandah trap huts in a Tanzanian village were used to assess the effectiveness of impregnated bednets and curtains in preventing hut entry and feeding by, and in killing of, *Anopheles gambiae* and *A. funestus*. Permethrin, deltamethrin, lambdacyhalothrin and pyrethrum were used for impregnation of damaged or undamaged bednets, sisal eaves curtains or bed curtains made of polypropylene fibre. The performance of the three synthetic pyrethroids did not differ statistically significantly, except that on a damaged net permethrin was better at preventing feeding. Sisal eaves curtains deterred mosquitoes from hut entry but did not kill those that had entered. In assessing damaged nets and curtains it must be recognised that anything less than the best vector control may have no appreciable impact on holoendemic malaria.
46. D'Alessandro, U., P. Langerock, S. Bennett, N. Francis, K. Cham, and B. M. Greenwood. 1996. The impact of a national impregnated bed net programme on the outcome of pregnancy in primigravidae in The Gambia. *Trans R Soc Trop Med Hyg* 90, no. 5: 487-92. In 1992, the Gambian national impregnated bed net programme (NIBP) introduced insecticide treatment of bed nets into half of the primary health care villages in The Gambia. One component of the evaluation of this programme was the determination of whether it had any impact on the outcome of pregnancy in primigravidae. From February 1992, 651 primigravidae were recruited into the study. Less than 50% of them used an insecticide-treated bednet. During the rainy season the prevalence of *Plasmodium falciparum* among primigravidae was lower, fewer babies were classified as premature, and the mean birth weight was higher in villages where treated bed nets were used than in control villages. Therefore, during the rainy season, despite the low use of insecticide-treated bed nets by Gambian primigravidae, the NIBP had some impact on the outcome of pregnancy, particularly on the percentage of premature babies, and this was probably due to the decreased risk of malaria infection achieved during this period.

47. D'Alessandro, U., B. O. Olaleye, W. McGuire, P. Langerock, S. Bennett, M. K. Aikins, M. C. Thomson, M. K. Cham, B. A. Cham, and B. M. Greenwood. 1995. Mortality and morbidity from malaria in Gambian children after introduction of an impregnated bednet programme. *Lancet* 345, no. 8948: 479-83. After the success of a controlled trial of insecticide-treated bednets in lowering child mortality, The Gambia initiated a National Insecticide Impregnated Bednet Programme (NIBP) in 1992 with the objective of introducing this form of malaria control into all large villages in The Gambia. Five areas (population 115,895) were chosen as sentinel sites for evaluation of the NIBP. During the first year of intervention a 25% reduction was achieved in all-cause mortality in children 1-9 years old living in treated villages (rate ratio 0.75 [95% CI 0.57-0.98], p = 0.04). If one area where the programme was ineffective was excluded, the reduction was 38% (0.62 [0.46-0.83], p = 0.001). A decrease in rates of parasitaemia and high-density parasitaemia, an increase in mean packed-cell volume (rate ratio 0.75 [95% CI 0.59-0.98], p = 0.04) and an improvement in the nutritional status of children living in treated villages were also detected. In a country such as The Gambia, where nets were widely used and which has a good primary health care system, it is possible to achieve insecticide-treatment of bednets at a national level with a significant reduction in child mortality; but at a cost which the country cannot afford.

48. D'Alessandro, U., B. O. Olaleye, W. McGuire, M. C. Thomson, P. Langerock, S. Bennett, and B. M. Greenwood. 1995. A comparison of the efficacy of insecticide-treated and untreated bed nets in preventing malaria in Gambian children. *Trans R Soc Trop Med Hyg* 89, no. 6: 596-8. An evaluation of the Gambian national insecticide bed net programme, which has introduced insecticide treatment of bed nets into all primary health care (PHC) villages in The Gambia, provided an opportunity to compare the individual risk of malaria in children who slept under untreated or insecticide-treated bed nets. 2300 children 1-4 years old were selected for a survey at the end of the 1992 rainy season, 1500 from PHC villages and 800 from non-PHC villages. All maliariometric indices were lower, and the mean packed cell volume was higher, in children who slept regularly under treated or untreated bed nets than in those who did not use a net. This study suggested that untreated bed nets provide some individual protection against malaria, although not as efficiently as that provided by insecticide-treated bed nets which were particularly effective at preventing infections accompanied by high parasitaemia.

49. Dossou-yovo, J., J. M. Doannio, F. Riviere, and G. Chauvancy. 1995. Malaria in Cote d'Ivoire wet savannah region: the entomological input. *Trop Med Parasitol* 46, no. 4: 263-9. A two years study has been carried out in Alloukouko, a traditional wet savannah village in the central region of Cote d'Ivoire. The productive breeding sites of malaria vectors are natural puddles and some

-30-
man-made shelters around the village. 576 man-nights of capture have identified Anopheles gambiae s.l. and An. funestus as vectors of malaria in the study area. The low densities of An. phaoensis and An. coustani implies that their possible role in transmission is very negligible. An. gambiae s.l. was the predominant species throughout the year with a mean of 19.2 b/m/n in 1991 and 13.6 b/m/n in 1992. The densities of An. funestus increased gradually during the rainy season and reached its peak values towards the end of the season. An. gambiae s.l. assures transmission throughout the year. An. funestus maintains a seasonal transmission which is spread over seven months. In 1991, each person would have received an average of 264.5 infected bites altogether with 204.5 infected bites from An. gambiae s.l. and 62 infected bites from An. funestus. In 1992, there would have been 196.5 infected bites per man with 160 and 36.5 infected bites respectively from An. gambiae s.l. and An. funestus. This study has shown that in wet savannah areas, the rainy season spreading almost all over the year, allows the breeding sites to retain water much longer and thus, to keep alive a more important residual vector populations capable to ensure malaria transmission even during the dry season. The great majority of infected glands (96.7%) were observed between 11 p.m. and 04 a.m. So, the large scale use of treated bednets has been therefore strongly recommended as key measure against malaria transmission in this area.

50. Githeko, A. K., N. I. Adungo, D. M. Karanja, W. A. Hawley, J. M. Vulule, I. K. Seroney, . Ofulla AV, F. K. Atieli, S. O. Ondijo, I. O. Genga, P. K. Odada, P. A. Situbi, and J. A. Olo. 1996. Some observations on the biting behavior of Anopheles gambiae s.s., Anopheles arabiensis, and Anopheles funestus and their implications for malaria control. Exp Parasitol 82, no. 3: 306-15. Studies were carried out in three villages in western Kenya on the biting behavior of Anopheles gambiae s.s., Anopheles arabiensis, and Anopheles funestus. Blood feeding behavior and departure from houses were studied under the impact of permethrin-impregnated eaves-sisal curtains. Only 2-13% of the female vector population was collected biting before 2200 hr. Over 90% of the villagers went to bed by 2100 hr. An. funestus was 6.6-8.2 times more likely to bite people indoors than outdoors, while An. gambiae s.l. females were only 2 times as likely. Under the influence of permethrin-impregnated sisal curtains placed under the eaves of village houses, there was a marked egress of blood-fed An. funestus and An. gambiae s.s. Permethrin seems to have induced exophily of half-gravid female An. gambiae s.s. While An. gambiae s.s. remained highly anthropophagic under the impact of permethrin, An. funestus shifted to feeding more on cattle. An arabiensis were largely zoophilic. Our results underline the difficulties of controlling An. gambiae s.s., the principal African malaria vector. New strategies must be found to control this vector.

51. Le Goff, G., V. Robert, E. Fondjo, and P. Carnevale. 1992. Efficacy of insecticide impregnated bed-nets to control malaria in a rural forested area in southern Cameroon. Mem Inst Oswaldo Cruz; 87 Suppl 3 P355-9. Due to current spreading of chemoresistant strains of Plasmodium falciparum malaria control must incorporate vector control programmes. Due to well known constraints house sprayings cannot be performed as before. Personal protection can be developed and a large scale use of insecticide treated bed-nets appeared to be very useful to reduce man-vector contact in Asia, South America and West and East Africa. No trial has been done in forest Central Africa where transmission is permanent. We performed such a trial in the southern part of Cameroon (using deltamethrin, at 25 mg/m2) and obtained similar data to those observed in The Gambia, Burkina Faso and Tanzania with a noteworthy reduction of both transmission and high parasitaemia of P. falciparum (respectively 78% and 75%) meaning a drop of malaria morbidity.

Kinshasa, Zaire, where malaria is stable, three villages have been selected for a trial of malaria control using bednets impregnated with deltamethrin at 25 mg per square meter from February to November 1991. One village (3,000 inhabitants) has been provided 800 impregnated bednets and another one (2,900 inhabitants) kept 800 non impregnated bednets. The third village (900 inhabitants) served as a control and has remained without nets. Anopheles gambiae was the main and nearly exclusive vector of malaria. Its biting density was reduced by 94% in the village protected by impregnated bednets and the inoculation rate dropped from 182 infective bites/man/year to 3.7 a decrease of 98%. The longevity of the vector expressed by its expectation of life decreased from 11.02 days to 3.64 days. In the village where inhabitants were protected by non impregnated nets, as well as in the control, the entomological indexes did not change. In the village protected with impregnated nets the malaria prevalence decreased by 50%, five months after the beginning of the experiment. The high parasitemia, above 10,000 and 20,000 parasites per mm3 decreased by 77% and 83% in the 0-7 year age group and by 67% and 65% in the 8-14 year group in the protected village. These high parasitemias are good markers of the clinical malaria risk. The experiment can be considered as very satisfactory on the point of view of public health.

53. Lengeler, C., and R. W. Snow. 1996. From efficacy to effectiveness: insecticide-treated bednets in Africa. Bull World Health Organ 74, no. 3: 325-32. Insecticide-treated bednets and curtains (ITBC) have proven in recent large-scale trials to have a high efficacy in reducing morbidity and mortality from malaria in African children. However, it is unlikely that the efficacy measured in trials can be entirely sustained under programme conditions. This has important implications for the cost-effectiveness of the intervention. Furthermore, there is a need to assess the long-term impact of ITBC. This article traces the history of ITBC and the different phases of their assessment, especially the determination of efficacy in randomized controlled trials (phase III assessment). It then outlines the reasons for continued assessment of their effectiveness under programme conditions (phase IV assessment). The methodologies for measuring effectiveness are discussed, and a critical review of the issues reveals that it is impractical to measure effectiveness directly. A simple effectiveness model, allowing for differentiation between individual and community effectiveness, provides a useful conceptual framework. First, individual effectiveness is measured through a case-control study. This estimate is then combined with a coverage indicator to estimate community effectiveness. This approach could provide programme managers with a powerful tool to monitor the impact of health interventions at the community level.

54. Lindsay, S. W., J. H. Adiamah, J. E. Miller, and J. R. Armstrong. 1991. Pyrethroid-treated bednet effects on mosquitoes of the Anopheles gambiae complex in The Gambia. Med Vet Entomol 5, no. 4: 477-83. The response of Anopheles gambiae complex mosquitoes to men sleeping under insecticide-impregnated or untreated bednets in six verandah trap huts was studied during the dry season in The Gambia. With this type of hut it was possible to collect live and dead indoor-resting mosquitoes and estimate the number of wild mosquitoes which entered, bloodfed on man, and exited each night. Bednets were treated with emulsions targetted to leave deposits of 25 mg/m2 lambda-cyhalothrin, or 5, 50 or 500 mg/m2 permethrin, diluted from emulsifiable concentrates (EC), or a blank formulation similar to the EC except that the permethrin was omitted; the sixth net was left untreated. Nets and sleepers were rotated between huts on different nights, the design being based on a series of Latin squares and conducted double-blind. Permethrin-impregnated bednets deterred mosquitoes from entering the huts. The degree of deterrence was proportional to the dosage of permethrin. This effect was also caused by the blank formulation and therefore attributed to other components of the formulation, rather than to the permethrin itself. The net impregnated with 500 mg permethrin per square metre gave the best individual protection, reducing mosquito bloodfeeding by 91% compared with untreated nets. However, lambda-cyhalothrin was proportionately more insecticidal than permethrin at doses of equivalent
deterrency. At this stage of research, it remains conjectural whether chemical deterrency or killing of malaria vectors is better for community protection.

55. Lyimo, E. O., F. H. Msuya, R. T. Rwagoshora, E. A. Nicholson, A. E. Mnzava, J. D. Lines, and . Curtis CF. 1991. Trial of pyrethroid impregnated bednets in an area of Tanzania holoendemic for malaria. Part 3. Effects on the prevalence of malaria parasitaemia and fever. Acta Trop 49, no. 3: 157-63. Children aged 1-10 in five villages were contacted fortnightly. Their axillary temperatures, reports of fevers and blood slides were taken. Following the introduction of permethrin impregnated nets into two estate villages the slide positivity for falciparum malaria declined markedly. In traditional villages the introduction of impregnated nets had less convincing effects than in the estate villages and DDT spraying had no perceptible effect on malaria. Over all villages there was a clear relationship between axillary temperature greater than 37.4 degrees C, reports of fever and high parasitaemia. We defined malaria fever in this way, and found in some cases significant reductions in occurrence of such fever following some time after introduction of permethrin impregnated nets. No such effects were found with lambdacyhalothrin nets or with DDT spraying.

56. Magbity, E. B., N. T. Marbiah, G. Maude, C. F. Curtis, D. J. Bradley, B. M. Greenwood, . Petersen E, and J. D. Lines. 1997. Effects of community-wide use of lambdacyhalothrin-impregnated bednets on malaria vectors in rural Sierra Leone. Med Vet Entomol 11, no. 1: 79-86. The effect of community-wide use of bednets treated with lambdacyhalothrin 10 mg/m2 on the malaria vector Anopheles gambiae (forest form) was evaluated in Sierra Leone. Sixteen similar villages near the town of Bo were randomly allocated either to remain without nets or to receive treated bednets for all inhabitants, with effect from June 1992. Mosquitoes were sampled using human biting catches on verandas, light-trap catch (beside an occupied untreated bednet), window exit-trap catch and pyrethrum spray collections. During the first year of intervention (June 1992 to July 1993) the treated bednets provided personal protection for people sleeping under them, but had very little impact on densities of An.gambiae collected on human bait. The human blood index (HBI) of An.gambiae was not affected (HBI = 99% in villages with and without nets). An.gambiae parous rates were significantly reduced in all intervention villages, but malaria sporozoite rates fell in only some of the villages. These results are intermediate between those obtained from other projects in Tanzania and Burkina Faso, where treated bednets reduced man-biting, parity and sporozoite rates, versus The Gambia where treated bednets had no significant impact on any of these factors. Possible reasons for these contrasted findings are discussed.

57. Manga, L., V. Robert, and P. Carnevale. 1995. [Effectiveness of coils and mats for protection against malaria vectors in Cameroon]. Efficacite des serpentins et des diffuseurs en plaquettes dans la protection contre les vecteurs du paludisme au Cameroun. Sante 5, no. 2: 85-8. The evaluation of the effectiveness of coils and mats on mosquitoes, especially malaria vectors was carried out in the Southern Cameroon. The study was performed in the Nsimalen village from November 1993 to August 1994. Two brands of coils: Timor and Moon Tiger containing 0.15% W/W of esbiothrin and two brands of mats: ARS MATS (containing d-allethrin) and Moon Tiger (with S biothrin and diethyl-toluamide) were tested. The evaluation was based on night catches on human bait inside houses. A catcher was sitting at two meters of a coil or a mat. Mosquitoes were caught during five consecutive nights per month in five houses. Two of the five houses were protected with the coils, two others with the mats and the fifth was used as control. Each night, coils and mats were rotated in such a way that at the end of the five nights, each house has been protected twice with coils, twice with mats and had served once as control. The composition of the mosquito samples collected was analyzed and the reduction rate of bites was calculated for each method. A thousand and twenty nine mosquitoes were caught in all. Two hundred and fifty nine
mosquitoes in houses with coils, 180 in those with mats and 590 in the houses which served as control. Anopheles moucheti and Mansonia s.p. accounted more than 90% of the samples; Anopheles gambiae s.s. represented 4 to 9%. Coils reduced malaria vectors bites by 82.8% and mats by 90.5%. Mansonia bites were reduced by 66% only.

58. Mbogo, C. N., N. M. Baya, A. V. Ofulla, J. I. Githure, and R. W. Snow. 1996. The impact of permethrin-impregnated bednets on malaria vectors of the Kenyan coast. Med Vet Entomol 10, no. 3: 251-9. The effects of introducing permethrin-impregnated bednets on local populations of the malaria vector mosquitoes Anopheles funestus and the An.gambiae complex was monitored during a randomized controlled trial at Kilifi on the Kenyan coast. Pyrethrum spray collections: inside 762 households were conducted between May 1994 and April 1995 after the introduction of bednets in half of the study area. All-night human bait collections were performed in two zones (one control and one intervention) for two nights each month during the same period. PCR identifications of An.gambiae sensu lato showed that proportions of sibling species were An.gambiae sensu stricto > An.merus > An.arabiensis. Indoor-resting densities of An.gambiae s.l. and the proportion of engorged females decreased significantly in intervention zones as compared to control zones. However, the human blood index and Plasmodium falciparum sporozoite rate remained unaffected. Also vector parous rates were unaltered by the intervention, implying that survival rates of malaria vectors were not affected. The human-biting density of An.gambiae s.l., the predominant vector, was consistently higher in the intervention zone compared to the control zone, but showed 8% reduction compared to pre-intervention biting rates-versus 94% increase in the control zone. Bioassay, susceptibility and high-performance liquid chromatography results all indicated that the permethrin content applied to the nets was sufficient to maintain high mortality of susceptible vectors throughout the trial. Increased rates of early outdoor-biting, as opposed to indoor-biting later during the night, were behavioural or vector composition changes associated with this intervention, which would require further monitoring during control programmes employing insecticide-treated bednets.

59. Moyou-Somo, R., L. G. Lehman, S. Awahmukalah, and P. Ayuk Enyong. 1995. Deltamethrin impregnated bednets for the control of urban malaria in Kumba Town, South-West Province of Cameroon. J Trop Med Hyg 98, no. 5: 319-24. This study was conducted from January to December 1992 in Kumba, a town situated in the rain forest region of the South-West Province of Cameroon, and consisted of a longitudinal survey including parasitological and clinical studies. Forty households were chosen for the study and randomly divided into two groups, each with approximately 240 inhabitants aged < or = 15 years. One group received deltamethrin impregnated bednets and the other group had no nets (control). For the months of April, June and August (rainy season), deltamethrin impregnated bednets did not reduce malaria prevalence significantly, but the overall malaria prevalence for all months of the study was significantly reduced (chi 2 MH = 9.17, P = 0.002). Enlarged spleen rates (chi 2 MH = 6.73, P = 0.009) and spleen sizes (P = 0.0002) were also significantly reduced by the nets. However, the reduction in the geometric mean parasite density (GMPD) was not significant. Even though some of these reductions were statistically significant, they were relatively low in a global context compared with previous work done mainly in rural areas. In an urban environment, parents and children usually stay up late, and probably receive many mosquito bites before going to sleep.

2,000 houses resulted in significantly lower rates of malaria parasite prevalences with an overall reduction rate of 73% (P < 0.001) in the treated area. Control areas had an initial increase in rate of malaria parasite prevalence of 30% and later a reduction of 31%. There was a slight reduction in spleen rates in the control and treated areas but it was not significant for either between the surveys or among the villages.

61. Mutinga, M. J., D. M. Renapurkar, D. W. Wachira, C. M. Mutero, and M. Basimike. 1992. Evaluation of the residual efficacy of permethrin-impregnated screens used against mosquitoes in Marigat, Baringo district, Kenya. *Trop Med Parasitol* 43, no. 4: 277-81. Insecticide-impregnated screens and bednets are gradually finding wider use in malaria control programmes. The efficacy of these devices is dependent on the method of application, the acceptability by the people and effectiveness of the insecticide used. The present studies were carried out to determine the duration of the effectiveness of a permethrin-impregnated wall cloth (Mbu cloth) used in the Marigat area of Baringo District, Kenya in order to ensure its effective use. Cotton cloth impregnated with permethrin was hung inside an experimental house in Marigat and small pieces cut off each month for bioassay against mosquitoes over a twelve month period. The wall cloth remained effective for 6, 4 and 10 months against Anopheles gambiae s.l. the known vector of malaria, Culex quinque-fasciatus and Aedes aegypti, respectively.

62. Nevill, C. G., E. S. Some, V. O. Mung'ala, W. Mutemi, L. New, K. Marsh, C. Lengeler, and . Snow RW. 1996. Insecticide-treated bednets reduce mortality and severe morbidity from malaria among children on the Kenyan coast [see comments]. *Trop Med Int Health* 1, no. 2: 139-46. New tools to prevent malaria morbidity and mortality are needed to improve child survival in sub-Saharan Africa. Insecticide treated bednets (ITBN) have been shown, in one setting (The Gambia, West Africa), to reduce childhood mortality. To assess the impact of ITBN on child survival under different epidemiological and cultural conditions we conducted a community randomized, controlled trial of permethrin treated bednets (0.5 g/m2) among a rural population on the Kenyan Coast. Between 1991 and 1993 continuous community-based demographic surveillance linked to hospital-based in-patient surveillance identified all mortality and severe malaria morbidity events during a 2-year period among a population of over 11000 children under 5 years of age. In July 1993, 28 randomly selected communities were issued ITBN, instructed in their use and the nets re-impregnated every 6 months. The remaining 28 communities served as contemporaneous controls for the following 2 years, during which continuous demographic and hospital surveillance was maintained until the end of July 1995. The introduction of ITBN led to significant reductions in childhood mortality (PE 33%, CI 7-51%) and severe, life-threatening malaria among children aged 1-59 months (PE 44%, CI 19-62). These findings confirm the value of ITBN in improving child survival and provide the first evidence of their specific role in reducing severe morbidity from malaria.

63. Oloo, A. J., J. V. Mudegu, D. K. Ngare, R. O. Ogutu, S. O. Ondijo, P. S. Odada, N. I. Adungo, . Githeko AK, W. S. Ekisa, and S. Mahadevan. 1993. The effect of permethrin impregnated sisal curtains on vector density and malaria incidence: a pilot study. *East Afr Med J* 70, no. 8: 475-7. Impregnation of bednets and curtains with suitable pyrethroids may reduce entomological inoculation rates (EIR) and malaria incidence. We conducted a quasi-experimental pilot study over 3 months in Western Kenya on 20 houses with 54 children. Ten houses in the experimental site received sisal curtains treated with permethrin at either 0.5g/m2 or 0.1g/m2. Control houses had untreated curtains or none. Mosquito vector density (MVD), man biting rates (MBR), and residual insecticidal effects (RIE) of permethrin were determined every two weeks. MVD was reduced by 97.7% and 98.7% in houses from the 2 experimental groups with a 60% reduction with unimpregnated curtains. MBR varied from 6.4 (no curtains), 1.7 (unimpregnated), 0.7
0.4 (1.0g/m² curtains). RIE begun to decline after the fourth month. Malaria incidence remained similar at the two sites. **We conclude that covering of eaves and windows with permethrin impregnated sisal curtains can reduce MVD and the number of mosquito bites to individuals sleeping in protected houses.**

64. Oloo, A., A. Githeko, N. Adungo, D. Karanja, J. Vulule, I. Kisia-Abok, I. Seroney, J. Ayisi, S. Ondijo, D. K. Koech, and M. S. Abdullah. 1996. **Field trial of permethrin impregnated sisal curtains in malaria control in western Kenya.** *East Afr Med J* 73, no. 11: 735-40. A trial to determine the effectiveness of sisal eaves-curtains impregnated with permethrin for malaria control was conducted in the malaria holoendemic western Kenya between 1991 and 1993. Indoor resting densities of *Anopheles gambiae* s.l. and *Anopheles funestus* were reduced by 90.9% and 93.8% respectively in protected houses. The entomological inoculation rate (EIR) was reduced by 72% in the intervention village. There was no significant reduction in vector longevity or survival as shown by the sustained high sporozoite rates. Monthly bioassays for retained insecticidal potency of permethrin on the fibre indicated vector mortality rates above 95% over the period. Of 283 and 240 children followed up from the intervention and control villages, a mean malaria prevalence of 43.2% and 52.2% respectively was observed over the trial period (p < 0.01). The prevalence rose to 73.5% and 75.7% (p = 0.541) respectively after the removal of the curtains. No significant differences were observed in the mean parasite density between the groups or between the proportions with parasite density exceeding 2,500 per microliter and with or without fever. The prevalence of splenomegaly was significantly lower in the intervention group compared to the control, both during (p = 0.005) and after the intervention (p < 0.001). There was no significant difference in the mean change in haematocrit at the end of the intervention. **We observe that permethrin impregnated sisal curtains effectively retain permethrin, alter favourably the indoor vector density and EIR, and could provide a reduction in malaria prevalence.**

65. Petersen, E., N. T. Marbiah, E. Magbiti, J. D. Lines, G. H. Maude, B. Hogh, C. Curtis, B. Greenwood, and D. Bradley. 1993. **Controlled trial of lambda-cyhalothrin impregnated bed nets and Maloprim chemosuppression to control malaria in children living in a holoendemic area of Sierra Leone, west Africa. Study design and preliminary results.** *Parassitologia*; 35 Suppl P81-5. The effect of lambda-cyhalothrin impregnated bed nets and maloprim/placebo was studied in approximately 1,500 children living in 17 villages in a rural area of Sierra Leone, approximately 150 miles south east of Freetown, 30 miles north of the town of Bo. Villages were selected randomly amongst villages with impregnated bed nets and villages with no nets at all. Within these villages, children with ages ranging between 3 months to 6 years were chosen to receive maloprim or a double-blind distributed placebo fortnightly. In the villages randomised to receive nets, all beds have received nets. Malaria morbidity is estimated from weekly active case detection, and the impact on the Anopheles vector is being estimated by indoor spray catching, exit trap catching, human night landing catches and light trap catches. During the first 8 weeks of the intervention there was a significant reduction in slide positive rates, reported fever rates and children with temperature > or = 37.5 degrees C in the villages with impregnated bed nets.

66. Pietra, Y., P. G. Procacci, G. Sabatinelli, S. Kumlien, L. Lamizana, and G. Rotigliano. 1991. [**Impact of utilization of permethrin impregnated curtains on malaria in a rural zone of high transmission in Burkina Faso.**] *Bull Soc Pathol Exot* 84, no. 4: 375-85. The efficacy of permethrin impregnated curtains as a malaria control measure was evaluated in a rice field area nearby Ouagadougou (BF). Two groups of children aged 1-5 years matched for age, sex and malaria exposure, were followed through the rainy season of 1987 for illness and febrile episodes. One group of 118 children lived in houses
protected with impregnated curtains, the other in houses without curtains. All children were examined for parasitaemia spleen index packed cell volume (PCV) and antisporozoites antibodies at the beginning and the end of the rainy season. During rainy season no difference could be found in the number of clinical episode between the two groups. A reduction in the prevalence of splenomegaly and parasitaemia and an increase in the PCV was observed during the dry season.

67. Premji, Z., P. Lubega, Y. Hamisi, E. Mchopa, J. Minjas, W. Checkley, and C. Shiff. 1995. Changes in malaria associated morbidity in children using insecticide treated mosquito nets in the Bagamoyo district of coastal Tanzania. Trop Med Parasitol 46, no. 3: 147-53. A community based malaria control intervention using insecticide treated mosquito nets (IMN) has been implemented and tested in 13 villages of the Yombo Division, Bagamoyo District in the Coastal Region, Tanzania, an area holoendemic for P. falciparum malaria. Following extensive sociological research into local perceptions of malaria, the programme was implemented. It was decided by consensus that village mosquito net committees would be the appropriate local level implementors. These were formed and provided with IMN's which were sold to villagers at subsidised cost. The income was invested for use by the committees for sustaining the activity. Use patterns were determined and high coverages were obtained among the community, particularly after promotions e.g. plays, school meetings etc. Malaria morbidity was measured among children 6-40 months of age in 7 index villages prior to the intervention in 1992 and in a comparison study between 3 villages using nets and 4 villages not using nets in 1993. Examination of the 7 cohorts of children was done from June to October each year covering the period of most severe transmission. The children using nets showed marked improvement in several malarialmetric indices. Following an initial clearance of parasitaemia with sulphadoxine/pyrimethamine, when compared with unprotected children, those with nets were slower to become re-infected (Relative Risk 0.45), had lower parasitaemias and showed marked improvement in anaemia (RR 0.47). Use of IMN's produced a 54% reduction in the prevalence of anaemia among young children. Attempts are being made to ensure that the programme is locally sustained.

68. Procacci, P. G., L. Lamizana, V. Pietra, C. Di Russo, and G. Rotigliano. 1991. [Utilization of permethrin-impregnated curtains by the inhabitants of a rural community in Burkina Faso]. Utilisation de rideaux impregnes de permethrine par les habitants d'une communauterurale du Burkina Faso. Parasitologia 33, no. 2-3: 93-8. The degree of utilisation of permethrin-impregnated curtains was assessed in a rural community near Ouagadougou, Burkina Faso. Results showed that in the first half of the night, until 11-11.30 p.m., curtains were only partially used by the community. Indeed by this time around 50% of houses had doors well protected by curtains and, over 35% of the community, children and adults, were staying outside. A very marked pattern of this behavior was found, wrong utilisation of curtains being higher in the warm season and lower in the cold season. On the one hand, this situation decreased the potential action of curtains as a barrier to avoid mosquito-man contact and, on the other hand, facilitated the exposure of community to the risk of outdoor infection. These findings may explain the variable level of efficacy showed by curtains in the prevention of malaria morbidity, which seems to be higher in the period between January and February, the winter season in Burkina Faso. The possible application of impregnated curtains as a community-based vector control method is discussed.

Madagascar. *Sante* 7, no. 1: 39-45. To evaluate the efficacy of deltamethrin impregnated curtains on malaria morbidity in a low transmission area, we studied volunteer families in the village of Ankazobe in the Madagascar Highlands from February 1993 to June 1994. After randomization, we provided 46 houses having 244 inhabitants with impregnated curtains (I) and 45 others having 257 inhabitants with nonimpregnated curtains (NI) as controls. We first estimated the number of mosquito bites in the protected versus nonprotected households. Every month, we captured mosquitos on humans in 6 houses per night for 4 nights. For the I group compared to the NI group, the number of bites by the Anopheles funestus vector per human per night was reduced by 64% in 1993 and 39% in 1994. We also analyzed the malaria morbidity. Malaria morbidity was defined as patients having both temperatures greater than 37.5 degrees C and Plasmodium falciparum parasitemia greater than 1500/microliter with clinical symptoms. From February to July 1993, we observed no significant difference in morbidity; there were 103 cases of malaria among 244 inhabitants of the I group and 117 cases among 257 inhabitants of the NI group. However, during the period of highest transmission from March to May in 1993, there were significantly fewer cases in the I group (68) than in the NI group (94). From January to June 1994, the difference was clear: only 35 malaria cases were observed among the 208 inhabitants of the I group as compared to 65 cases among the 223 inhabitants of the NI group (Chi square = 9.17, p = 0.0024). Inhabitants of the I group could have been contaminated before the curtains were set up. After treatment of the cases and use of curtains during the second year, we observed a reduction in the number of mosquito bites and malaria cases. The small size of the trial made the interpretation of the data difficult. Nonetheless, the results tentatively support the use of impregnated curtains as an antimalaria tool in an integrated control program.

70. Robert, V., and P. Carnevale. 1991. *Influence of deltamethrin treatment of bed nets on malaria transmission in the Kou valley, Burkina Faso*. *Bull World Health Organ* 69, no. 6: 735-40. A 3-year entomological study was carried out on the transmission of malaria in a village of 900 inhabitants in a rice-growing area of Burkina Faso. In the study area inhabitants use bed nets to protect themselves from mosquito bites. In the first year of the study, baseline data were collected; in the second year, the village was divided in two parts and all the bed nets in the southern part were sprayed with deltamethrin (25 mg/m2); and in the third year, all the bed nets in both parts of the village were sprayed. The inoculation rate was estimated by hand collection of mosquitos on human volunteers who were not protected by bed nets. The overall inoculation rate in the first year was 55 infected bites per person and was higher in the southern than in the northern part of the village. During the second year the rate increased to 70 bites per person on average (but was slightly lower than this in the southern part of the village). During the third year, the inoculation rate fell to three infected bites per year, i.e., a reduction of 94% compared with the first year. This reduction arose primarily because of a marked decrease in the sporozoite index and a lower density of vectors. Thus, use of pyrethroid-impregnated bed nets by all members of the community appears to be a major tool in preventing transmission of malaria.

71. Thomson, M., S. Connor, S. Bennett, U. D'Alessandro, P. Milligan, M. Aikins, . Langerock P, M. Jawara, and B. Greenwood. 1996. *Geographical perspectives on bednet use and malaria transmission in The Gambia, West Africa*. *Soc Sci Med* 43, no. 1: 101-12. Insecticide-impregnated bednets are now widely accepted as an important tool in reducing malaria-related deaths in children in Africa. Defining the circumstances in which net treatment programmes are likely to be effective is essential to a rational development of this control strategy. In The Gambia a National Impregnated Bednet Programme was introduced into the primary health care system in 1992. Prior to its introduction baseline epidemiological and entomological studies were conducted throughout the country. These studies showed that in areas where mosquito biting nuisance was high, people protected themselves with bednets and that where mosquito densities (and therefore bednet usage)
was low malaria prevalence rates were relatively high. Since the national programme is designed to assist only those people who already own a bednet (by providing the insecticide) an understanding of the factors which determine bednet ownership is needed to help evaluate the programme’s effectiveness and provide guidelines for increasing bednet usage. Village scale bednet usage rates and malaria prevalence rates obtained from the baseline survey were correlated with certain geographical variables: dominant ethnic group, area, habitat, distance from the River Gambia and distance from the 'bluffline' (the interface between the sandstone soils and alluvial soils which border the river system). In a multiple regression analysis, bednet usage was independently associated with area (P < 0.001), ethnic group (P = 0.010), habitat (P = 0.006) and distance from the river (P = 0.013). A negative association of bednet usage with malaria prevalence persisted after allowing for the other variables. Malaria prevalence was not independently associated with area, ethnic group, habitat or distance from the river. Our analysis showed that the impregnated bednet programme is likely to be most effective in villages which are sited near to or on the alluvial soils in the middle and lower river zones. These villages, which were originally settled for easy access to the river (for transport) and its swampy margins (for rice production) are within the flight distance of mosquitoes that have their breeding sites on the poorly drained alluvial soils. Variation in malaria prevalence rates (after bednet usage has been taken into account) may be related to factors such as poverty and access to health care, and/or to localized differences in the ecology of The Gambia, which determine the duration and intensity of transmission. If the National Bednet Programme is to be effective throughout The Gambia it is vital to develop promotional activities which will encourage bednet usage in areas where nuisance biting by mosquitoes is low.
83.8% say to do something about it. Among the latter, 43.5% spend money for their protection: incense coils (85.6%), insecticide sprays (55.5%), bednets (38.6%). In May 1990, families have spent a median sum of US$ 5.00, which was at that time about the price of an impregnated bednet. 89.5% of the surveyed families said they would agree to buy an impregnated bednet if the price was acceptable (median sum of US$ 4.00 is judged as acceptable). Impregnated bednets being an efficient method of malaria control, financially accessible and acceptable, their utilization should be further encouraged by the national programme of malaria control and primary health care.

74. Zoulani, A., P. Carnevale, and L. Penchenier. 1994. [Influence of mosquito nets impregnated with deltamethrin on the aggressivity cycle of Anopheles gambiae in Djoumouna, Congo]. <Original> Influence des moustiquaires impregnees de deltamethrine sur le cycle d'agressivite d'Anopheles gambiae a Djoumouna, Congo. Ann Soc Belg Med Trop 74, no. 2: 83-91. Several studies recently done in Africa south of the Sahara have clearly demonstrated that pyrethroid impregnated bednets should actually reduce malaria inoculation rate due to Anopheles gambiae and therefore high Plasmodium falciparum parasitaemia and malaria morbidity, even mortality. Nevertheless some concerns were recently raised on an eventual shift in the usual behavior of this species induced by the presence inside the house of bednets treated with pyrethroid insecticide known to have a deterrent or excito-repellent effect, and which could therefore lead to a biting behavior earlier than usual. The current limited study, done in Djoumouna, a place well known for the very high density of An. gambiae, has shown that the temporary presence inside a house of a bednet impregnated with deltamethrin (12.5 or 25 ma a.i./m2) has not induced any shift in the biting cycle of this species, but it actually reduced by some 50% its biting rate noticed on human beings. It is worth underlining that all sporozoite infected specimens were actually caught after midnight. This biting behavior of An. gambiae could explain why impregnated bednets are so efficient in reducing man-vector contact and malaria.

Asia

75. Cheng, H., W. Yang, W. Kang, and C. Liu. 1995. Large-scale spraying of bednets to control mosquito vectors and malaria in Sichuan, China. Bull World Health Organ 73, no. 3: 321-8. Since 1987, up to 2.42 million bednets owned by rural householders in over 40 counties in seven prefectures of Sichuan Province, China, have been sprayed annually with deltamethrin at a dose of about 10 mg/m2. Data for the years 1987-89 indicate that there were marked reductions in the biting populations and survival of the two vector species Anopheles anthropophagus and A. sinensis. Extensive tests in 1992 in areas where bednet spraying had been carried out for 5 years showed that mortality was 100% with the WHO-recommended discriminating dose of deltamethrin, i.e., there was no indication of resistance. Malaria data obtained by passive surveillance of reported cases, mass blood surveys of schoolchildren, and active surveillance of reported blood slides from fever cases all indicated marked reductions after introduction of the net spraying. In contrast, in the control areas, where the nets were not treated, the situation remained static or deteriorated slightly.

76. Das, P. K., L. K. Das, S. K. Parida, K. P. Patra, and P. Jambulingam. 1993. Lambdacyhalothrin treated bed nets as an alternative method of malaria control in tribal villages of Koraput District, Orissa State, India. Southeast Asian J Trop Med Public Health 24, no. 3: 513-21. A village scale trial was carried out to evaluate the efficacy of bed-nets impregnated with lambdacyhalothrin, at the dose of 0.025 g/m2, in reducing malaria transmission in villages of Koraput District of Orissa,
India, inhabited by tribals. The nets were distributed before peak transmission season. There was an overall decline in the parasite rate in all the age groups, six months after the supply of impregnated nets while the same increased in control village and in a village where untreated nets were supplied. The vector densities (resting and man landing) were lower in the treated village as compared to untreated and control villages throughout the study period. The reduction in the parasite rate was consistent when the reimpregnation was done at six monthly interval and the same tend to increase when the gap between the two impregnations was increased to one year. Though malaria incidence was reduced, transmission was not completely interrupted during the study period, due to outdoor transmission. The insecticidal effect of bednets was retained up to six months. Washing of bednets by the community did not affect the efficacy. The acceptance and usage was better with impregnated nets as compared to ordinary nets.

77. Dolan, G., F. O. ter Kuile, V. Jacoutot, N. J. White, C. Luxemburger, L. Malankirii, T. Chongsuphajaisiddhi, and F. Nosten. 1993. Bed nets for the prevention of malaria and anaemia in pregnancy. Trans R Soc Trop Med Hyg 87, no. 6: 620-6. A prospective comparison of the antimalarial efficacy of bed nets was conducted with 341 pregnant women living in a mesoendemic malarious area of the Thai-Burmese border. Women in 3 adjacent study sites were allocated at random to receive either a single size permethrin-impregnated bed net (PIB), a non-impregnated bed net (NIB), or to a control group who used either their own family size non-impregnated bed net (FNIB) or no net. In one study site, but not the other 2, PIB significantly reduced parasite densities and, together with FNIB, reduced the incidence of malaria in pregnancy from 56% to 33% (relative risk = 1.67, confidence interval = 1.07-2.61, P = 0.03, allowing for parity). Anaemia proved a more sensitive marker of bed net antimalarial efficacy than parasite rates. The incidence of anaemia (haematocrit < 30%) at all study sites was significantly lower at delivery in the PIB (27%) and FNIB groups (21%) than in the NIB group (41%) or those using no net (56%). This suggests that a significant proportion of the malaria in pregnancy in this mesoendemic area was sub-patent. Both patent Plasmodium falciparum parasitaemia and anaemia were associated with a reduction in birth weight. Infant mortality was high (16%) and strongly associated with prematurity, low birth weight and maternal anaemia. PIB were well tolerated and had no apparent adverse effect on the pregnancy or infant development. Although the overall effect of bed nets on patent parasitaemia was marginal, they were associated with a significant reduction in maternal malaria-associated anaemia.

78. Eamsila, C., S. P. Frances, and D. Strickman. 1994. Evaluation of permethrin-treated military uniforms for personal protection against malaria in northeastern Thailand. J Am Mosq Control Assoc 10, no. 4: 515-21. A trial to compare the effect of military clothing treated by high-pressure spray with permethrin or placebo on the incidence of malaria in Royal Thai Army troops was conducted in northeastern Thailand. Bioassays of treated clothing using laboratory-reared Anopheles dirus females showed permethrin remained in the treated fabric for up to 90 days. Both permethrin- and placebo-treated uniform shirts provided > 84% protection from biting An. dirus in laboratory bioassays for the duration of the study. In laboratory tests, knockdown of An. dirus exposed to permethrin-treated cloth fell to < 20% after 3 hand washes, despite the presence of 28.7-59.9% of the original dose of permethrin. The use of permethrin-treated uniforms without adjunct application of topical repellents did not reduce malaria in Thai troops in an operational setting where incidence during 6 months was as high as 412 cases/1,000 in spite of chemoprophylaxis and use of untreated bednets.

undertaking a specific intervention, in four cross-sectional community-based surveys in 10 villages of a highly endemic area of Papua New Guinea. Over half (55%) of the villagers interviewed reported that they had used a bednet on the previous night. In general and after adjustment for age, village and housing characteristics, bednet users, particularly children, had lower parasite prevalences and spleen rates and less enlarged spleens than non-users. However, users were similar to non-users in terms of fever reported for the previous week, axillary temperature, parasite density and haemoglobin level. The prevalence of antibody to the ring erythrocyte surface antigen and the major merozoite surface antigen 2 was lower in users than non-users. The association with malarial indices and immune responses remained significant when bednet users were compared with non-users in houses without bednets. Thus, untreated bednets do not reduce malaria transmission sufficiently to decrease morbidity. They might paradoxically increase the risk of clinical malaria by lowering the development of humoral immunity.

80. Jamjoom, G. A., A. A. Mahfouz, I. A. Badawi, M. S. Omar, O. S. al-Zoghaibi, O. M. al-Amari, M. Ibrahim, and I. Siam. 1994. Acceptability and usage of permethrin-impregnated mosquito bed nets in rural southwestern Saudi Arabia. Trop Geogr Med 46, no. 6: 355-7. In 1989 a total of 2,320 sets of locally-made durable permethrin-impregnated bed nets and support frames were provided for the first time to 410 families (2,485 individuals) in Al-Fateeha area in the malarious region of Tihamat Asir, southwestern Saudi Arabia. In interviews carried out with a sample of the heads of the families two years later, most of them said to have used bed nets regularly (78.3%) and a majority started using them shortly after sunset (73.9%). Most heads of families expressed willingness to encourage their friends and neighbours to get bed nets (94.4%) and use them regularly (92.9%). Public requests for bed nets were received from neighbouring areas. These results indicate that impregnated bed nets can be successfully integrated into a malaria control programme provided that they are of a durable type and accompanied with support devices to facilitate their use while sleeping outdoors. Records of the primary health care centre serving the trial area indicated that the incidence of malaria decreased progressively from 277.4 per thousand in 1988 to 124.4 in 1991. The possible contribution of mosquito nets--as a major newly introduced variable--to this decrease is suggested but was not directly measured.

81. Jana-Kara, B. R., W. A. Jihullah, B. Shahi, V. Dev, C. F. Curtis, and V. P. Sharma. 1995. Deltamethrin impregnated bednets against Anopheles minimus transmitted malaria in Assam, India. J Trop Med Hyg 98, no. 2: 73-83. Of the 20 Anopheles species caught in villages in Sonapur, Assam, only An. minimus was incriminated as a malaria vector by finding sporozoites in the salivary glands. It was found to be endophagic and endophilic in Assam and because its biting peaked after midnight it was a suitable target for insecticide impregnated bednets. After the withdrawal of DDT spraying and collecting a year's baseline data, deltamethrin impregnated nets were distributed in 3 villages, untreated nets were distributed in 6 villages and 3 were held as untreated controls. The population of each of these groups of villages was about 1700. The nets were well received by the local tribal population. Human landing catches with baits unprotected or under partially lifted nets showed that the nets provided a high degree of personal protection against all the local species of human biting mosquito. In addition, there was evidence for suppression of the An. minimus population in a village with treated nets. Malaria was monitored by weekly active surveillance in all the villages. In the untreated control villages the slide positivity rate and monthly parasite index rose significantly during the trial. In the villages with untreated nets, these parameters showed no significant change, but in the villages with treated nets they declined significantly. On the basis of these results, the widespread distribution of impregnated nets was recommended to the state health authorities.
82. Kamol-Ratanakul, P., and C. Prasittisuk. 1992. The effectiveness of permethrin-impregnated bed nets against malaria for migrant workers in eastern Thailand. Am J Trop Med Hyg 47, no. 3: 305-9. A randomized, double-blind, field trial was carried out to compare the effectiveness of permethrin-treated nets with that of untreated nets as a method of malaria control for migrant workers in eastern Thailand. The study was conducted using 261 subjects in eastern rural areas that are known to be highly endemic for multidrug-resistant Plasmodium falciparum infection. One hundred twenty-six subjects used treated nets, while 135 used untreated nets. During the 35 weeks of observation, 23 subjects using treated nets and 33 workers using untreated nets developed 28 and 51 episodes of malaria, respectively (P = 0.029). The reduction in risk per subject due to treated nets was 0.06. The residual effects of permethrin were tested using a World Health Organization standard bioassay. Anti-mosquito activity was found to be present in the nets for more than 16 months. We conclude that because of the failure of the development of safe, effective, long-lasting prophylactic agents, integrating the use of impregnated nets with large-scale primary health care programs may be a partially effective method for controlling malaria in eastern Thailand.

83. Kere, N. K., A. D. Parkinson, and W. A. Samrawickerema. 1993. The effect of permethrin impregnated bednets on the incidence of Plasmodium falciparum, in children of north Guadalcanal, Solomon Islands. Southeast Asian J Trop Med Public Health 24, no. 1: 130-7. The effect of permethrin impregnated bednets was studied for the first time amongst a large community in North Guadalcanal, Solomon Islands. The community was divided into two; one covered 23 villages with 860 people who were given bednets impregnated at 0.5 g/m2, and the other 20 villages with 520 people was used as control. Parasitological data were collected by regular prevalence surveys and examination of records of malaria patients who have sought treatment in clinics. Entomological data by landing catches using human bait. The entomological results showed a 71% reduction of Anopheles farauti. Even though there was no significant reduction observed with An.punctulatus, as the density was already very low, the number biting indoor was much lower than those outdoor of houses with treated bednets. Parasitologically there was a steady decline in the incidence between surveys with Plasmodium falciparum in the under 10 years old. Even though there was no significant reduction in the other variables measured, there was a steady increase in the clearance rate between surveys which might also be due to easy accessibility to chemotherapy. The study showed the significant beneficial effect of permethrin impregnated bednets, which was found to be still effective up to twelve months, against stable P. falciparum malaria in children.

84. Kere, N. K., A. Arabola, B. Bakote'e, O. Qalo, T. R. Burkot, R. H. Webber, and B. A. Southgate. 1996. Permethrin-impregnated bednets are more effective than DDT house-spraying to control malaria in Solomon Islands. Med Vet Entomol 10, no. 2: 145-8. A field trial compared DDT house-spraying with permethrin-impregnated bednets for malaria control in Solomon Islands from 1987 to 1991. Mortality-rates of malaria vector Anopheles farauti in exit window traps were 11.6% from an untreated hut, 10.1% from a hut sprayed with DDT 2 g/m2, and 98% of those from a hut in which the occupants used bednets treated with permethrin 0.5 g/m2. Since bioassays of the DDT-sprayed walls (15 min exposure in W.H.O. standard test cones) gave 77% mortality of An.farauti, it was concluded that the insignificant impact of DDT could be explained by the exophilic behaviour of endophagic vectors, whereas the greater impact of permethrin was attributed to the more effective exposure of An.farauti females to the impregnated bednets-attracted by the occupants. The parous rate was higher indoors, except in the area with permethrin-impregnated bednets. It was therefore concluded that permethrin-impregnated bednets reduced the mean longevity of An.farauti and hence its vectorial capacity. The circumsporozoite (CS) antigen positivity rate of An.farauti in the DDT area was 0.18% outdoors, significantly less than 1.42% indoors. In the comparison area CS rates were 0.65% outdoors and 0.75% indoors. CS
antigen was not detected in An.farauti from the bednet area, indicating the apparent prevention of malaria transmission. As DDT spraying was so much less effective, it was discontinued in 1993 and permethrin-impregnated bednets are now the principal malaria control method in Solomon Islands.

85. Leake, D. W. Jr, and J. L. Hii. 1994. Observations of human behavior influencing the use of insecticide-impregnated bednets to control malaria in Sabah, Malaysia. *Asia Pac J Public Health* 7, no. 2: 92-7. Observational and survey methodologies were used to probe human behavioral factors influencing the use of insecticide-impregnated bednets to control malaria in rural Sabah, Malaysia. One aim was to investigate why a field trial of such nets in an interior area yielded disappointing results. A second aim was to gather baseline data prior to a field trial proposed for a coastal area. Interior villagers reported a significantly higher net usage rate than that observed directly, suggesting that subject self-reports need to be validated in some way. The poor results of the interior field trial appeared related to reluctance to regularly use nets, which were not in wide use previously. Prospects for reducing malaria transmission through bednets appeared better for the coastal area since nearly half of observed villagers were sleeping in them. However, significantly more coastal than interior villagers were observed watching television at night, an activity that may increase malaria risk by keeping villagers awake and out of bednets.

86. Nguyen, T. V., D. B. Bui, V. S. Mai, V. T. Ta, T. Q. Nguyen, N. Tan, and T. Nguyen. 1996. *Evaluation of malaria vector control measures in central Vietnam (1976-1991)*. (<Original> Evaluation des mesures antivectorielles contre le paludisme dans le centre du Viet-nam (1976-1991). *Sante* 6, no. 2: 97-101. Activities used to control malaria transmission in the pilot station of Vanh Canh in the Binh Dinh Province of central Vietnam from 1976 to 1991 have been evaluated. These activities were: spraying DDT in and around the houses in the villages and the settlements in the fields; spraying lambdacyhalothrin in the houses; and use of bed-nets impregnated with permethrin. Their efficacy was measured by the number of fever episodes due to malaria infections among the population. The spraying of DDT in the houses was followed by a reduction of malaria infection by more than 90%. However, spraying of the settlements was not disadvantageous. The termination of DDT spraying was not followed by an increase of malaria infections. Spraying with lambdacyhalothrin was slightly more effective than with pyrimiphos and DDT. The use of pesticide-impregnated bed-nets was efficient, especially in the villages far away from the forest. Thus, these activities can contribute to the control of the malaria endemic in central Vietnam.

87. Prasittisuk, M., C. Prasittisuk, V. Pothichiti, B. Aum-aung, and P. Mongklangkul. 1996. The effect of pyrethroid impregnated mosquito nets on field malaria vector populations in experimental huts and in individual local houses. *Southeast Asian J Trop Med Public Health* 27, no. 3: 610-6. Studies were carried out in Tak Province, northwest Thailand to determine repellency and killing effects of four commercially available pyrethroids etofenprox, deltamethrin, lambdacyhalothrin and permethrin treated mosquito nets on field malaria vector populations in experimental huts and local houses. The studies reveal that all four test pyrethroids have a highly repellency effect. Repellency ratio between lifted and torn nets also showed some different among the four pyrethroids. Mosquito net treated with 0.3 g/m2 permethrin was most toxic to mosquito followed by 0.02 g/m2 deltamethrin, etofenprox 0.3 g/m2 and 0.02 g/m2 lambdacyhalothrin. However, careful consideration for future use should also include problem of cross-resistance, persistence of chemicals and also type of mosquito net material.

impact of permethrin-impregnated curtains on the incidence of malaria episodes, parasitaemia and splenomegaly was assessed during a 22 month period in 2 groups of children aged 0.5-6 years. One group lived in houses where permethrin-impregnated curtains had been installed, the other group lived in houses without curtains. A significant reduction of incidence of malaria episodes, mean parasite density, parasite prevalence and splenomegaly was consistently observed in the intervention group towards the end of the period of moderate transmission, whereas no clear-cut impact could be demonstrated during the high transmission period. The influence of malaria pressure and community utilization on the protective efficiency of curtains is discussed. Because of their acceptability and the ease of reimpregnation, curtains proved to be a suitable technique for integration into primary health care.

89. Rowland, M., M. Bouma, D. Ducornez, N. Durrani, J. Rozendaal, A. Schapira, and E. Sondorp. 1996. Pyrethroid-impregnated bed nets for personal protection against malaria for Afghan refugees. Trans R Soc Trop Med Hyg 90, no. 4: 357-61. A field trial of permethrin-impregnated bed nets (PIBs) was conducted in 2 Afghan refugee villages in Pakistan. Nets were issued to only 10% of families (= 1398 people); this simulated a situation in which bed nets are gradually adopted by villagers in Afghanistan. A further 10% lacking bed nets were selected as controls from the same villages. An initial survey showed that 86% of household heads were aware that malaria was transmitted by mosquito bites, but only 2% had used bed nets before. Trial families were encouraged to attend the village health centres if they fell ill. Microscopy records showed that, between July and December 1991, 22.4% of the control group became infected with Plasmodium vivax and 13.0% contracted P. falciparum while in the intervention group only 9.9% contracted P. vivax (relative risk 0.58, confidence interval [CI] 95% 0.49-0.68) and only 3.8% contracted P. falciparum (relative risk 0.39, 95% CI 0.29-0.53). A single treatment of the nets with permethrin at 0.5g/m2 remained protective throughout the 6 months' transmission season. 73% of families claimed to use their nets every night; members of families who claimed to use nets less regularly showed an incidence similar to that of the control group. There was no sex or age difference in net use or protective efficacy. Headlouse infestation rates were reduced in PIB users. Few nets were washed, given away or sold. The prospect for PIBs as personal protection appears good, despite people's lack of previous experience.

90. Rowland, M., S. Hewitt, N. Durrani, P. Saleh, M. Bouma, and E. Sondorp. 1997. Sustainability of pyrethroid-impregnated bednets for malaria control in Afghan communities. Bull World Health Organ 75, no. 1: 23-9. Between 1992 and 1995 a series of studies was undertaken to assess the long-term suitability of pyrethroid-impregnated bednets (PIBs) for malaria control in Afghan refugee communities in two villages in North-West Frontier Province, Pakistan. During 1992, 86% of bednet owners volunteered to have their bednets re-impregnated, and a further 15% of families purchased nets at two-thirds of cost price. From 1992 onwards, 27% of the villagers returned to Afghanistan, and annual house spraying campaigns were introduced to protect those still resident but sleeping without bednets. Within 3 years, these campaigns, together with PIBs, reduced the annual incidence of malaria by 87%, from 597 to 78 cases per 1000 population. Nevertheless, 65% of resident families continued to re-impregnate their nets annually with permethrin. To assess whether PIBs were still being used and were still protective, in view of these reduced transmission rates, we carried out a case--control study in 1994 on febrile or otherwise symptomatic patients presenting at village health centres. Comparison of the slide-positivity rates of PIB users and those without bednets showed that regular usage reduced the odds of contracting falciparum and vivax malaria to 0.22 (95% confidence interval (CI): 0.09-0.55) and 0.31 (95% CI: 0.19-0.51), respectively. There was no evidence of a sex- or age-bias in bednet use or in protective effect. The results indicate that a community-based PIB programme is an appropriate malaria control measure in areas where management or security problems make traditional house-spraying campaigns impossible. A relevant finding for those involved in the monitoring of bednet distribution projects.
is that the local coverage of bednets and the local impact on malaria, even when introduced to remote areas, can be estimated very cheaply by health centre microscopists who simply catalogue blood film diagnoses according to patients' bednet use practices.

91. Somboon, P., J. Lines, A. Aramrattana, U. Chitprarop, S. Prajakwong, and . Khamboonruang C. 1995. Entomological evaluation of community-wide use of lambda cyhalothrin-impregnated bed nets against malaria in a border area of north-west Thailand. *Trans R Soc Trop Med Hyg* 89, no. 3: 248-54. This paper reports 2 studies. (i) After a year of baseline data collection, lambda cyhalothrin-treated bed nets were introduced into 3 of 5 villages in north-west Thailand, the remaining 2 being treated with placebo. Human bait collections were carried out in each village on 2 nights per month, for 8 months of each year, and the biting densities were compared between the first year and the second year. The treated bed nets did not have any significant impact on the density or parous rates of Anopheles sawadwongporni and A. maculatus s.s. populations. The results for A. dirus s.l. were not conclusive because of the low number caught. Significant reductions in biting and parous rates of A. minimus species A were observed in only one of the 3 treated villages, and there was no overall difference between treated and control groups. However, the trial suffered from the washing of nets by villagers and the low rate of reimpregnation. (ii) A short-term study involved 4 villages in a cross-over design, and lasted 48 d. For the first 24 d, residents of 2 villages were given new treated nets while the other 2 villages retained their own untreated nets. For the second 24 d, this situation was reversed. Daily light-trapping revealed no significant difference in the indoor densities or parous rates of A. minimus species A between the periods with treated or untreated nets.

92. Torres, E. P., N. P. Salazar, V. Y. Belizario, and A. Saul. 1997. Vector abundance and behaviour in an area of low malaria endemicity in Bataan, the Philippines. *Acta Trop* 63, no. 4: 209-20. The vectorial importance of known and potential vectors in Morong, Bataan, Philippines was assessed based on human and animal baited collections of adult mosquitoes and on larval collections. Anopheles flavirostris, the principal vector in the Philippines, was the most abundant among human landing catches, followed by An. maculatus sensu lato (s.l.). Both showed similar seasonal abundance with a peak during the early drier part of the year, which coincided with the peak in malaria cases. Both An. flavirostris and An. maculatus s.l. fed throughout the night with the broad peak of capture from 00:00 to 04:00 and from 22:00 to 00:00, respectively. The two species had similar parous rates (0.76 and 0.72, respectively) giving an average life span equivalent to four feeding cycles. Neither vector was abundant with average human landing rates on collectors of 0.6 and 0.4 mosquitoes per person per night, respectively over the study period. An. maculatus s.l. showed a stronger preference for outdoor feeding compared to An. flavirostris. An. maculatus s.l. was markedly zoophilic with a biting rate on water buffalo 50 times the human landing rate. An. flavirostris was less zoophilic with a corresponding ratio of 7.5. It was concluded that in this area, An. flavirostris is the principal vector. The combination of localised transmission, late night biting pattern and localised breeding sites of An. flavirostris suggest that the use of bed nets and environmental management are relevant control measures that can be implemented through community participation.

93. Tun-Lin, W., M. M. Thu, S. M. Than, and M. M. Mya. 1995. Hyperendemic malaria in a forested, hilly Myanmar village. *J Am Mosq Control Assoc* 11, no. 4: 401-7. A 1-year longitudinal study of hyperendemic malaria was carried out at Tha-byewa village, Oktwin township, situated in the forested Bago mountain range in south-central Myanmar. Mosquito infectivity was assayed using specific, sporozoite enzyme-linked immunosorbent assays. Anopheles dirus was the predominant vector in the postmonsoon season (October); during the cool-dry season (January), both An. dirus and Anopheles minimus were vectors. Members of the Anopheles culicifacies complex were
caught in the hot-dry season (April) but none was infective. The entomological inoculation rate was estimated to be at least 13.7 infective bites/person/year. Infective An. dirus were caught feeding on cattle as well as on humans. Three of the 4 positive An. dirus and both positive An. minimus were caught biting humans indoors in the second quarter of the night when most people were sleeping. This suggests that use of insecticide-impregnated bednets in this area could interrupt transmission.

94. Vythilingam, I., L. C. Foo, G. L. Chiang, S. T. Chan, K. L. Eng, S. Mahadevan, J. W. Mak, and Singh KI. 1995. The impact of permethrin impregnated bednets on the malaria vector Anopheles maculatus (Diptera: Culicidae) in aboriginal villages of Pos Betau Pahang, Malaysia. Southeast Asian J Trop Med Public Health 26, no. 2: 354-8. The effect of permethrin impregnated bednets on Anopheles maculatus Theobald was studied in four villages in Pos Betau, Pahang, Malaysia from August 1990 to July 1992. Collections of mosquitoes were carried out indoors and outdoors from 1900 to 0700 hours. All mosquitoes were dissected for sporozoites and parity. In May 1991 two villages received bednets impregnated with permethrin at 0.5 g/m2 and two villages received placebo bednets. There was a significant difference in the sporozoite and parous rates between the treated and control villages after the distribution of bednets (p < 0.05). There was no significant difference in the bites/man/night of An. maculatus between the pre and post treatment periods in the control villages. However there was a significant difference in bites/man/night between pre and post treatment in the treated villages (p < 0.001).

95. Wu, N., L. Qin, G. Liao, W. Zhou, W. Geng, Y. Shi, Y. Tan, and K. Zhao. 1993. Field evaluation of bednets impregnated with deltamethrin for malaria control. Southeast Asian J Trop Med Public Health 24, no. 4: 664-71. Trials were undertaken in a hypoendemic area of malaria in an area bordering Vietnam, in Napo County of Guangxi Zhuang Autonomous Region, China. The aim was to compare the relative cost effectiveness of DDT residual spraying and of bednets impregnated with deltamethrin in the malaria control program. The trials were divided into three subgroups: (1) two farming areas and one coal mining area with a total population > 20,000, where the trial consisted of mass bednets impregnated with deltamethrin 15 mg/m2 net surface once a year, (2) one farming area with a population of approximately 3,600 where DDT residual spraying at 2g/m2 was carried out twice a year in May and August; (3) one farming area and one coal mining village with a population of > 4,000 were used as a control. The malaria vector population consisted mainly of Anopheles minimus and An. anthropophagus with a small contribution from An. sinensis. After bednets were impregnated with deltamethrin the mosquitoes resting on the surface of the bednets decreased significantly, although there was less effect on the total vector population. The results showed that malaria incidence decreased significantly both in areas where impregnated bednets were used and in areas where residual spraying was undertaken. The positive IFAT rates of residents who slept under impregnated bednets decreased significantly in farming areas, especially in that area where bednet impregnation as a vector control measure had been undertaken for two years, but there was no change in the IFAT rate in DDT sprayed or control areas.
96. Kroeger, A., M. Mancheno, J. Alarcon, and K. Pesse. 1995. *Insecticide-impregnated bed nets for malaria control: varying experiences from Ecuador, Colombia, and Peru concerning acceptability and effectiveness*. Am J Trop Med Hyg 53, no. 4: 313-23. Between 1991 and 1994, an intervention program with permethrin- and lambda-cyhalothrin-impregnated bed nets was carried out over a period of nine months in each of five endemic, malarious areas of Ecuador, Peru, and Colombia. This program was evaluated through household surveys, blood sampling, in-depth longitudinal studies, and entomologic analysis. Eighty-four communities (including approximately 35,000 individuals) were paired according to malaria incidence, size, and coverage with bed nets and then randomly allocated to intervention and control groups. The results showed that people's acceptance of the measure was related to their perception of an immediate protective effect against insects. The effectiveness of the bed nets, measured as a reduction of malaria incidence in intervention communities as against control communities, showed large variations between and within the study areas. The protective efficacy varied between 0% and 70% when looking only at the postintervention differences between intervention and control groups. The average protection was 40.8% when considering a four-month incidence of clinical malaria attacks and 28.3% when considering a two-week malaria incidence. Important factors for the success of the bed net program were insect susceptibility to pyrethroids, high coverage with impregnated bed nets, high malaria incidence, good community participation, high mosquito densities when people go to bed, and a high proportion of Plasmodium falciparum. In one area, where DDT spraying in the control communities was executed, the effectiveness of bed net impregnation was slightly better than that of spraying.

97. Richards, F. O. Jr, R. E. Klein, R. Z. Flores, S. Weller, M. Gatica, R. Zeissig, and . Sexton J. 1993. *Permethrin-impregnated bed nets for malaria control in northern Guatemala: epidemiologic impact and community acceptance*. Am J Trop Med Hyg 49, no. 4: 410-8. Permethrin-impregnated bed nets were evaluated as a control measure for malaria in northern Guatemala. Twelve hundred forty participants were allocated to one of three experimental groups (impregnated bed nets [IBN], untreated bed nets [UBN], and controls) and followed up for a period of 13 months. The incidence density of malaria was significantly lower in both IBN (86 cases/1,000 person-years) and UBN groups (106/1,000) compared with that in controls (200/1,000). No difference in malaria incidence was noted between the IBN and UBN groups. Complaints of fever and chills were less frequent in the IBN group compared with controls. The participants were enthusiastic about the nets, which they saw as a means for avoiding nuisance insects more than for preventing malaria. Most (85%) wanted to wash their nets every 4-12 weeks, a practice known to shorten the duration of residual insecticide action. Larger studies are needed to determine whether or not impregnated bed nets offer an advantage over untreated nets in this setting.

98. Soto, J., F. Medina, N. Dember, and J. Berman. 1995. *Efficacy of permethrin-impregnated uniforms in the prevention of malaria and leishmaniasis in Colombian soldiers*. Clin Infect Dis 21, no. 3: 599-602. We determined the efficacy of the use of permethrin-impregnated uniforms for prevention of malaria and leishmaniasis in a double-blind, randomized study of Colombian soldiers on patrol. In the study of malaria, soldiers were issued impregnated uniforms (i.e., a shirt, an undershirt, pants, socks, and a hat) or uniforms washed in water; the soldiers wore the uniforms day and night...
for a mean of 4.2 weeks and were observed for an additional 4 weeks. Three (3%) of 86 soldiers wearing impregnated uniforms contracted malaria, whereas 12 (14%) of 86 soldiers wearing control uniforms contracted malaria (P = .015). In the study of leishmaniasis (soldiers were in the area of endemicity for 6.6 weeks and were observed for 12 weeks thereafter), 4 (3%) of 143 soldiers wearing impregnated uniforms and 18 (12%) of 143 soldiers wearing control uniforms acquired disease (P = .002). In the leishmaniasis study, and presumably in the malaria study, breakthrough infections in the treated group were primarily due to bites in unclothed regions of the body (face and hands). Permethrin-treated uniforms were virtually nontoxic (there were only two cases of mild skin irritation among 229 subjects), and impregnation is quick and inexpensive. Impregnation of clothing with permethrin is suggested for nonimmune populations who are likely to be exposed to malaria or leishmaniasis over a period of 1-2 months.
F. Potential Health Effects of Pyrethroid Insecticides

Introduction

At the current time, the pyrethroids appear to be the safest alternative to DDT because they and are less persistent and bioaccumulative and can be used in significantly smaller amounts (Abstract 104). While pyrethroids are generally less toxic to humans when compared to carbamates and organophosphates, they are highly toxic to aquatic life. If periodic exposure exceeds an organism's ability to metabolize these chemicals, concentrations will build up (Abstract 105). Pyrethroids' established toxicity for fish and other aquatic organisms has important consequences for the disposal of net treatment and washing liquids (Abstract 103). In order to avoid adverse impacts on non-target species, burial or pit latrines have been identified as the best disposal method.

Despite their low toxicity, a number of the pyrethroids have also been found to have endocrine disrupting properties (Abstracts 101, 102). However, the limited research conducted to date on synthetic pyrethroids is insufficient to fully assess exposure to them. Further study is needed to determine the endocrine disruption potential and other possible health effects of synthetic pyrethroids, and this research should continue throughout and beyond a DDT phaseout period.

Currently, pyrethroids appear to be the safest transition pesticide for use in malaria vector control when considering the stronger endocrine disrupting properties of DDT (Abstracts 12-16).
Anadon A, Martinez-Larranaga MR, Diaz MJ, Bringas P. 1991. Toxicokinetics of permethrin in the rat. Toxicology and Applied Pharmacology 110:1-8. The toxicokinetics of permethrin after single 460mg/kg oral and 46 mg/kg intravenous doses were studied in male Sprague-Dawley rats. Serial blood samples after oral and intravenous dosage, and brain, medulla oblongata, sciatic nerve, and liver samples after oral administration were collected. Plasma, hypothalamus, cerebellum, frontal cortex, caudate putamen, hippocampus, medulla oblongata, sciatic nerve, and liver concentrations of permethrin and its metabolites, m-phenoxybenzyl alcohol and m-phenoxybenzoic acid, were determined by a high-performance liquid chromatographic assay. The permethrin plasma profile could be adequately described by a two-compartment open model. For permethrin, the elimination half-life (t1/2 beta) and the mean residence time from plasma were 8.67 and 11.19 hr after i.v. and 12.37 and 17.77 hr after po administration. The total plasma clearance was not influenced by dose concentration or route and reached a value of 0.058 liter/hr. After the single oral dose, permethrin was absorbed slowly with a Tmax of 3.52 hr. The maximum plasma concentration was 49.46 micrograms/ml. The oral bioavailability of permethrin was found to be 60.69%. The plasma concentration-time data for permethrin metabolites as well as the tissue concentration-time data for permethrin and its metabolites after an oral dose of permethrin were found to fit a one-compartment open model. The elimination half-life (t1/2el) of permethrin was greater for the hippocampus, medulla oblongata, frontal cortex, and sciatic nerve (23.10, 22.36, 13.86, and 16.27 hr, respectively) than for plasma (t1/2 beta, 12.37 hr). The maximum amounts of permethrin in cerebellum, hippocampus, caudate putamen, frontal cortex, hypothalamus, and sciatic nerve were about 1.5, 2, 2, 2.7, 4.8, and 7.5 times higher than in plasma, respectively, indicating an accumulation of pyrethroid by nervous tissue itself. Nervous tissue accumulation of permethrin was also reflected by the area under the concentration curve ratios of tissue/plasma (1.16, 3.71, 1.57, 4.27, 3.48, and 8.77, respectively). The metabolites of permethrin, m-phenoxy-benzyl alcohol and m-phenoxybenzoic acid, were detected in plasma and in all selected tissues for 48 hr after dosing, suggesting that a combination of metabolism by the tissues and diffusion into it from the blood may be present.

100. Anadon A, Martinez-Larranaga MR, Fernandez-Cruz ML, Diaz MJ, Fernandez MC, Martinez MA. 1996. Toxicokinetics of deltamethrin and its 4'-HO-metabolite in the rat. Toxicology and Applied Pharmacology 141:8-16. The toxicokinetics of deltamethrin and its metabolite 4'-HO-deltamethrin after single doses of 26 mg of deltamethrin/kg (oral) or 1.2 mg of deltamethrin/kg (intravenous) were studied in male Wistar rats. Serial blood samples were obtained after oral and intravenous administration. Brain, vas deferens, and anococcygeus tissue samples were also obtained after oral administration. Plasma, hypothalamus, cerebellum, frontal cortex, caudate putamen, hippocampus, medulla oblongata, vas deferens, and anococcygeus concentrations of deltamethrin and 4'-HO-deltamethrin were determined by a high-performance liquid chromatographic assay. The deltamethrin and 4'-HO-deltamethrin plasma profiles could be adequately described by a two-compartment open model. For deltamethrin and 4'-HO-deltamethrin, the elimination half-lives (t1/2 theta) from plasma were 33.0 and 25.67 hr after iv and 38.50 and 30.13 hr after po administration of deltamethrin parent compound. The apparent volume of distribution [V
alpha(area) and volume of distribution at steady state [V d(m)] for deltamethrin were 5.33 and 2.04 liters, respectively, after iv administration, suggesting a considerable diffusion of the pyrethroid into tissue. The total plasma clearance of deltamethrin was the same for both the oral and the iv routes-0.11 liter/hr. After the single oral dose, deltamethrin was rapidly absorbed with a Tmax of 1.83 hr. The maximum plasma concentrations of deltamethrin and 4'-HO-deltamethrin were 0.46 and 0.26 microgram/ml. The maximum plasma concentration of 4'-HO-deltamethrin was achieved at 3.29 hr. The oral bioavailability of deltamethrin was found to be 14.43%. The tissue concentration time data for deltamethrin and its metabolite 4'-HO-deltamethrin were found to fit a one-compartment open model. Considerable concentrations of deltamethrin and 4'-HO-deltamethrin were found in the hypothalamus, cerebellum, frontal cortex, caudate putamen, hippocampus, medulla oblongata, vas deferens, and anococcygeus tissues. The elimination half-lives (t1/2 el) for both deltamethrin and 4'-HO-deltamethrin were somewhat smaller for the cerebellum, frontal cortex, caudate putamen, medulla oblongata, vas deferens, and anococcygeus tissues (range, 18-33 hr for deltamethrin and 15-28 hr for 4'-HO-deltamethrin) than for plasma (t1/2 el, 38.50 and 30.13 hr, respectively). Exceptions were seen for the hypothalamus and hippocampus in which the t1/2et's for deltamethrin were 40.76 and 38.50 hr, respectively. Nervous tissue accumulation of deltamethrin and its metabolite 4'-HO-deltamethrin was evidenced by the tissue/plasma area under the concentration (AUC) versus time curve ratios. The ratios of AUCtissue/AUCplasma for deltamethrin were 2.32 in medulla oblongata, 295.30 in hypothalamus, and intermediate in other tissues.

101. Garey J; Wolff MS. Estrogenic and antiprogestagenic activities of pyrethroid insecticides, Biochem Biophys Res Commun, 251(3):855-9 1998 Oct 29 Many pesticides possess hormonal activity and have thus been classified as endocrine disruptors. Pyrethroids are commonly used insecticides worldwide, but little has been done to characterize their hormone agonist/antagonist potential. We tested four frequently encountered pyrethroids, fenvalerate, sumithrin, d-trans allethrin, and permethrin, for estrogen and progesterone agonist/antagonist activities using the Ishikawa Var-I human endometrial cancer cell line and the T47D human breast cancer cell line. Both cell lines produce alkaline phosphatase as an indicator of hormonal activity. Fenvalerate and sumithrin demonstrated significant estrogenicity; at concentrations of 10 &mgr;M, these compounds achieved maximal activities comparable to that of 10 nM 17alpha-ethynylestradiol in Ishikawa Var-I cells. None of the four compounds showed statistically significant estrogen antagonist activity or acted as progestins. However, fenvalerate and d-trans allethrin significantly antagonized the action of progesterone in T47D cells. Through these hormonal pathways, exposure to certain pyrethroids may contribute to reproductive dysfunction, developmental impairment, and cancer.

102. He F, Sun J, Han K, Wu Y, Yao P, Wang S, Liu L. Effects of pyrethroid insecticides on subjects engaged in packaging pyrethroids. Br J Ind Med 1988 Aug;45(8):548-51 A health survey was conducted on 199 workers engaged in dividing and packaging pyrethroids. The subjects were exposed to fenvalerate at 0.012-0.055 mg/m3 and deltamethrin at 0.005-0.012 mg/m3 in the air with simultaneous skin contact for 0.5-4.5 months. Burning sensations and tightness or numbness on the face appeared in two thirds of the subjects and one third had sniff and sneezes. Abnormal facial sensations, dizziness, fatigue, and miliary red papules on the skin were more evident in summer than in winter. Neither abnormalities in other organs or systems nor symptoms or signs of acute pyrethroid poisoning were found by interviews, examinations, and laboratory tests. There was no significant difference in plasma levels of NA, cAMP, and cGMP between the examined subjects and the control group. The urine concentration of fenvalerate in the study group ranged from 1.02 to 18.6 micrograms/l; deltamethrin in the urine was present in trace amounts.
103. Mittal PK, Adak T, Sharma VP Acute toxicity of certain organochlorine, organophosphorus, synthetic pyrethroid and microbial insecticides to the mosquito fish Gambusia affinis (Baird and Girard). *Indian J Malariol* 1991 Sep;28(3):167-70 acute toxicity of certain organochlorine, organophosphorus, synthetic pyrethroid and microbial insecticides to the mosquito fish Gambusia affinis were determined to collect baseline data for selecting the resistant strains of the fish. The synthetic pyrethroid, Lambdacyhalothrin was most toxic to the fish (LC50 = 0.0022 ppm), followed by deltamethrin, cypermethrin and fenvalerate. Organochlorine insecticides, DDT and gamma-HCH, were less toxic than the pyrethroids, and these were followed by organophosphorus insecticides, malathion, fenthion, monocrotophos and temephos. The last two insecticides were least toxic among the different chemical insecticides (LC50 greater than 80 ppm ai). The microbial insecticide ABG-6262 ( Vectolex 2.5 AS), a Bacillus sphaericus preparation, was totally harmless to the fish at 2500 microliters/l up to one week.

104. Miyamoto J, Kaneko H, Tsuji R, Okuno Y Pyrethroids, nerve poisons: how their risks to human health should be assessed. Sumitomo Chemical Co., Ltd., Osaka, Japan The extensive worldwide efforts of structural modification of natural pyrethrins for better performances have resulted in successful development of a wide variety of synthetic pyrethroids with tremendously high efficacy, knock-down activity or vapor action, and/or with acceptable environmental stability and safety. Currently these pyrethroids including their preferentially manufactured stereoisomers are widely used in agriculture, and for public health as well as household insect control. The detailed toxicology and metabolism studies intended to attain human risk assessment have revealed that with voltage-dependent sodium channel as target site pyrethroids induce pronounced repetitive activity characterized grossly by tremor, hypersensitivity, choleoathetosis, and salivation. In addition, so-called cyano-pyrethroids cause transient skin paresthesia in workers. With regard to tumorigenicity, mutagenicity, teratogenicity and developmental toxicity, no significant findings have been reported. Pyrethroids are eliminated from the animals quite rapidly and completely, undergoing oxidation and ester hydrolysis followed by various conjugations, with low tissue residues. Thus, overall, sound scientific bases exist for human risk assessment under the present usage conditions.

105. Scherb H, Weigelt E [Statistical description of health complaints after pyrethroid exposure]. *Gesundheitswesen* 1994 Nov;56(11):622-8 [Article in German] In 96 pyrethroid-exposed persons data on subjective health impairment were collected by means of a questionnaire. The present explorative statistical analysis is restricted to a subgroup of 51 out of the 96 persons for which pyrethroid concentrations in dust samples from residential dwellings or from work places could be determined. Since measurements were taken from dwellings or work places, there is in some cases only one common measured value for families or teams. In total, we have 34 independent measurements. Based on the type of measured exposures, the 51 participants can be divided into 3 groups: 26 cases exposed to permethrin and tetramethrin (type-I pyrethroids), 13 cases exposed to deltamethrin, cyfluthrin or cypermethrin (type-II pyrethroids), and 12 cases with mixed exposure to the mentioned type-I and type-II pyrethroids. For the 3 groups we computed weighted mean values of pyrethroid concentrations, each independent measurement being weighted with the number of corresponding persons. The mean values are 425.7, 56.1, and 958.9 mg pyrethroid/kg dust for the groups in the above order. After combining the two highly exposed groups into one new group with now 38 members and a mean pyrethroid concentration of 594.1 mg/kg, an increased frequency of health complaints was found as compared to the group exposed only to type-II pyrethroids.

development, senescence, and carcinogenesis. Pyrethroid insecticides are now the most widely used agents for indoor pest control, providing potential for human exposure. Using the MCF-7 human breast carcinoma cell line, we studied the estrogenic potential of several synthetic pyrethroid compounds in vitro using pS2 mRNA levels as the end point. We tested sumithrin, fenvalerate, d-trans allethrin, and permethrin. Nanomolar concentrations of either sumithrin or fenvalerate were sufficient to increase pS2 expression slightly above basal levels. At micromolar concentrations, these two pyrethroid compounds induced pS2 expression to levels comparable to those elicited by 10 nM 17β-estradiol (fivefold). The estrogenic activity of sumithrin was abolished with co-treatment with an antiestrogen (ICI 164,384), whereas estrogenic activity of fenvalerate was not significantly diminished with antiestrogen co-treatment. In addition, both sumithrin and fenvalerate were able to induce cell proliferation of MCF-7 cells in a dose-response fashion. Neither permethrin nor d-trans allethrin affected pS2 expression. Permethrin had a noticeable effect on cell proliferation at 100 μM, whereas d-trans allethrin slightly induced MCF-7 cell proliferation at 10 μM, but was toxic at higher concentrations. Overall, our studies imply that each pyrethroid compound is unique in its ability to influence several cellular pathways. These findings suggest that pyrethroids should be considered to be hormone disruptors, and their potential to affect endocrine function in humans and wildlife should be investigated.

107. Zhang ZW, Sun JX, Chen SY, Wu YQ, He FS Levels of exposure and biological monitoring of pyrethroids in spraymen. Br J Ind Med 1991 Feb;48(2):82-6 To assess the exposure response relation of pyrethroids in spraymen, 50 adult male cotton growers were selected and divided into three groups, one group to spray pyrethroids for one day, two groups to spray for three days. Deltamethrin, fenvalerate, and a deltamethrin methamidophos mixture were sprayed by appropriate subgroups for five hours a day. Exposure levels were evaluated by measuring the air concentration, dermal exposure concentration, and urinary content of pyrethroids by gas chromatography. Air concentrations of deltamethrin at the breathing zone were 0.01-0.89 microgram/m3 in the deltamethrin exposed group. For fenvalerate, air concentrations were 0.06-1.98 micrograms/m3. Dermal exposure, particularly on the legs, feet, and hands was appreciable and indicated that this was the main route of absorption. In those spraying for one day, urinary deltamethrin was not detectable by 12 hours after the beginning of exposure whereas fenvalerate was still detectable up to 24 hours after first exposure. Both pyrethroids could be detected two days after the end of three day spraying. Health effects were investigated by interview and physical examination. Twenty nine spraymen complained of abnormal facial sensations that developed mostly two to three hours from the start of pyrethroid spraying and that disappeared by 24 hours after exposure ceased. Some had dizziness, headache, and nausea, but no subject was diagnosed as having acute pyrethroid poisoning. The symptoms showed no significant correlation with urinary pyrethroid excretion. Blood cholinesterase activity of spraymen using the pyrethroid methamidophos mixture did not change.
G. Environmental Management of Malaria Vectors

Introduction

Environmental management of vector insects can dramatically reduce pesticide use and associated costs while contributing to sustained disease reduction (Abstracts 108-121). Techniques include reducing breeding habitat through improved drainage or water flow, biological control of larvae using larvivorous fish or the microbial insecticide *Bacillus thuringiensis israelensis*, and improved housing and sanitation to reduce human-vector contact (Abstracts 108, 112, 115). For example, vector population reduction through habitat modification played a major role in reducing malaria transmission in the southeastern United States (Abstract 112). Increased malaria transmission has often been associated with particular land management and development projects such as road-building, dams and irrigation (Abstracts 110, 114). These negative effects may be prevented by improved project design, thus reducing the need for more chemically-based vector control (Abstract 109). In recent years, the use of GIS (geographic information system) has become a useful tool for malaria surveillance (Abstracts 111, 120).

In an effort to reduce mosquito populations, scientists are enhancing the distribution and density of natural enemies to malaria. This approach has the advantage of sustaining itself without human help in the field. However, the introduction of non-native “predators” may pose a threat to biodiversity. In the case of larvivorous fish, the WHO recommends that they originate from the same areas where biological control is to be used.

- **Larvivorous fish** - This strategy is most effective at the larval stage; animals that eat the larvae of mosquitoes and other vectors are often labeled *larvivorous*. Central American “mosquito fish (*Gambusia affinis*), South American gruppies (*Poecilia reticulata*), African *Tilapia*, and other larvivorous fish have been introduced into artificial and natural wetlands and bodies of water as part of disease control programs in many countries (Abstract 117).

- **Fungus** - The *Lagenidium giganteum* fungus, developed to control mosquitoes in California farm fields, is already approved for use in pastures, soybean and rice fields. These fields are major sources of mosquitoes. A pesticide version of the fungus is nearing the market (Abstract 113).
Blue-green alga - In a related effort, genes from a strain of \textit{Bacillus thuringiensis}, another well-known insect killer, have been moved into a blue-green alga. While scientists at University of Memphis try to persuade the transgenic alga to produce higher amounts of toxin, researchers in Hawaii are exploring out how to grow the plant commercially (Abstract 120).

Environmental management is especially appropriate to vector control in urban areas where controlling the larval populations may be more feasible economically and more environmentally sound than focusing on adult insect control. However, in many rural areas, environmental management alone may not be effective or affordable. With good information about local vector biology, an integrated, sustainable disease prevention program can be developed that includes a mixture of chemical and non-chemical methods of reducing human-vector contact.
Environmental management: a re-emerging vector control strategy. Am J Trop Med Hyg 1994;50(6 Suppl):35-49 Vector control may be accomplished by environmental management (EM), which consists of permanent or long-term modification of the environment, temporary or seasonal manipulation of the environment, and modifying or changing our life styles and practices to reduce human contact with infective vectors. The primary focus of this paper is EM in the control of human malaria, filariasis, arboviruses, Chagas' disease, and schistosomiasis. Modern EM developed as a discipline based primarily in ecologic principles and lessons learned from the adverse environmental impacts of rural development projects. Strategies such as the suppression of vector populations through the provision of safe water supplies, proper sanitation, solid waste management facilities, sewerage and excreta disposal systems, water manipulation in dams and irrigation systems, vector diversion by zooprophylaxis, and vector exclusion by improved housing, are discussed with appropriate examples. Vectors of malaria, filariasis, Chagas' disease, and schistosomiasis have been controlled by drainage or filling aquatic breeding sites, improved housing and sanitation, the use of expanded polystyrene beads, zooprophylaxis, or the provision of household water supplies. Community participation has been effective in the suppression of dengue vectors in Mexico and the Dominican Republic. Alone or combined with other vector control methods, EM has been proven to be a successful approach to vector control in a number of places. The future of EM in vector control looks promising.

Environmental management of vector insects can dramatically reduce pesticide use (and associated costs) while contributing to sustained disease reduction. Techniques include reducing breeding habitat through improved drainage or water flow, biological control of larvae using larvivorous fish or the microbial insecticide *Bacillus thuringiensis israelensis*, and improved housing and sanitation to reduce human-vector contact.

Malariometry in district Ratnagiri during 1988-1993. Indian J Public Health 41(2):36-42. Ratnagiri, a coastal district situated in the western part of Maharashtra, is stratified as 'Non-Problem District' as far as Malaria is concerned based on API, topography, rainfall, vector species, Vulnerability etc. Konkan rail project was launched in 1991 and 6 out of 9 blocks of districts Ratnagiri are penetrated by the rail-line. The local ecology of the district is disturbed on account of the project, which is expected to favor malarial transmission. A study based on secondary data was undertaken with following objectives: To assess various operational indicators under NMEP during 1988-93 in the district with respect to their quantitative and qualitative fulfillment. To assess API in the district during same period in the context of inception of Konkan rail. It disclosed that the operational indicators like SPR, SFR & Pf Percentage showed upward trend since 1991 i.e. the year of inception of the Konkan rail project. With ABER consistently above 10% & concordance of the cross-checking results above 96%, the estimate of API becomes more meaningful. Though API shows upward trend, it was never above 2 during 1988-93. Less number of positive cases were found in Active Surveillance during 1988 to 1993. The contribution of Drug Distribution Centres (DDCs) is almost negligible in the district. In-depth analysis of positive cases revealed that the immigrants suffered more and May to July was the...
season for malaria transmission in the district during the said period. More people above 15 yrs. and more males were found malaria positive which may be because of more outdoor life of this group. Block wise analysis revealed that Mandanged & Khed Blocks showed API more than 2 since 1992. Paradoxically, Mandangad is a coastal block without rail-line, while Khed block is situated away from seashore but has rail-line. More irrigation, less adequate surveillance because of staff vacancy & nonfunctional Drug Distribution Centres (DDCs), more losses to radical treatment are the probable factors responsible for higher API in Mandangad and Khed blocks as compared with the rest of the blocks from the District Ratnagiri.

111. Kitron U. 1998. Landscape ecology and epidemiology of vector-borne diseases: tools for spatial analysis. *J Med Entomol* 35(4):435-45. Geographic information systems (GIS), global positioning systems (GPS), remote sensing, and spatial statistics are tools to analyze and integrate the spatial component in epidemiology of vector-borne disease into research, surveillance, and control programs based on a landscape ecology approach. Landscape ecology, which deals with the mosaic structure of landscapes and ecosystems, considers the spatial heterogeneity of biotic and abiotic components as the underlying mechanism which determines the structure of ecosystems. The methodologies of GIS, GPS, satellite imagery, and spatial statistics, and the landscape ecology--epidemiology approach are described, and applications of these methodologies to vector-borne diseases are reviewed. Collaborative studies by the author and colleagues on malaria in Israel and tsetse flies in Kenya, and Lyme disease, LaCrosse encephalitis, and eastern equine encephalitis in the north-central United States are presented as examples for application of these tools to research and disease surveillance. Relevance of spatial tools and landscape ecology to emerging infectious diseases and to studies of global change effects on vector-borne diseases are discussed.

112. Kitron U. and A. Spielman. 1989. Suppression of transmission of malaria through source eduction: Antianopheline measures applied in Israel, the United States, and Italy. *Reviews of Infectious Diseases* 11:391-406. The authors reviewed three successful antimalarial campaigns that occurred largely before DDT became available. The primary method of control was the modification or elimination of aquatic habitats to reduce mosquito breeding.

113. Lacey LA, Lacey CM. *J Am Mosq Control Assoc* Suppl 1990 Jun;2:1-93 Published erratum appears in J Am Mosq Control Assoc Suppl 1990 Dec;6(4):762 The medical importance of riceland mosquitoes and their control using alternatives to chemical insecticides. The medical importance, ecology and control of riceland mosquitoes using alternative strategies is reviewed. Over 135 pest and vector anopheline and culicine mosquito species found in association with riceland habitats and their medical importance are presented. Malaria and Japanese encephalitis are the two most serious human diseases transmitted by riceland mosquitoes, but they have been incriminated as vectors of dozens of arboviruses and other parasites and pathogens including the causal agents of West Nile and Rift Valley Fevers and lymphatic filariasis. Control of vector and pest mosquitoes using chemical pesticides has generated several problems including: insecticide resistance, safety risks for humans and domestic animals, and other environmental concerns. These problems and the high cost and sustainability of programs based predominantly on conventional insecticides have stimulated increased interest in integrated control measures in ricelands. The integrated pest management (IPM) strategy for mosquito control, also known as integrated vector control (IVC), is an ecologically based approach that may involve several complementary interventions used in combination or singly. Environmental management, and chemical, biological and mechanical control, comprise the elements of IVC proposed for use in or near riceland habitats. Some of the elements of environmental management include the use of intermittent irrigation; flushing of fields; use of rice cultivars that require less water; shifting of planting schedules to avoid optimal mosquito breeding conditions; relocation of communities or use of dry belt farming around
them; and zoonoprophylaxis and other personal protection methods, especially use of insecticide-impregnated bed nets. Biological control agents that have been used successfully in rice fields include several species of larvivorous fish, a mermithid nematode (Romanomermis culicivorax), a fungus (Lagenidium giganteum) and bacteria (Bacillus thuringiensis var. israelensis and Bacillus sphaericus). The mermithid and the entomopathogens have demonstrated little or no adverse effects on populations of vertebrate and invertebrate nontarget organisms. The successful use of any particular method or combination of interventions for the control of riceland mosquitoes will depend on in-depth ecological studies on the target species and nontarget organisms, sound geographic reconnaissance and effective routine sampling and evaluation. When biological control agents are considered, additional background on the environmental factors limiting their efficacy will also be needed. In addition to the technical components of the various interventions employed in integrated control, sustained suppression of riceland mosquitoes and the diseases they transmit will require a greater sociocultural supportive background, particularly in developing countries.

114. Mouchet J, Carnevale P. 1997. [Impact of changes in the environment on vector-transmitted diseases] [Original in French]. Sante 7(4):263-9. We have defined the relationship between infectious diseases and environmental conditions and considered the development of this relationship to its current situation, where human intervention is occurring more often and is becoming more aggressive. The increase in the transport of freight and passengers by air has allowed parasite vectors to spread quickly and easily over large distances. Every country can now be reached from any other country within a couple of days. Usually, foreign species are unable to establish themselves and to persist in the new environment; but the recent arrival of Aedes albopictus in Albania, Italy and the Americas is a cause for concern. Demographic pressure has increased the need for land and the exploitation of new areas leads to large changes in the vegetation. The classic example of this man-made damage is the destruction of tropical forest in Western Africa, but the destruction of herbaceous vegetation, such as papyrus, in East Africa, could also have serious epidemiological consequences. Streams and rivers have been managed for power production and irrigation. The use of dams, both large and small, and the culture of rice in paddy-fields produces large expanses of water which are suitable breeding grounds for mosquitoes and snails, the vectors of human diseases such as malaria and schistosomiasis in sub-Saharan Africa. They are, however, of lesser importance in Asia and the Americas. Urbanization imposes a set of very similar structures on a specific rural environment. The effect of these two factors on each other determines the pathologies associated with each town. The suburban area is a specific environment where both urban and rural diseases occur and are made worse by poor hygiene conditions (waste, sewage, etc.). However, not all man-made changes to the environment cause a deterioration in public health. Urban and agricultural development projects must consider these issues and should use medical and environmental studies to avoid causing epidemic-prone conditions or spreading endemic diseases. Currently, most studies are limited to listing the specific diseases in the target area and very few attempt to assess the possible consequences of changing the environment. Forecasting the consequences of changes in environmental management is of great importance, but it requires the development of multi-disciplinary teams in the field who must be involved in the planning and implementation of the projects.
115. Sharma, V.P. and R.C. Sharma. 1989. **Community based bioenvironmental control of malaria in Kheda District, Gujarat, India.** *Journal of the American Mosquito Control Association* 5:514-521. A study on the bioenvironmental control of malaria was launched in 1983 with the help of village communities. A variety of techniques helped to suppress the mosquito population and significantly reduced malaria transmission in large rural areas. When compared with the residual spraying of insecticides under the National Malaria Eradication Programme, the alternate strategy was found feasible, socially acceptable, cost effective and brought about environmental improvement and awareness in the rural areas.

116. Shililu JI, Maier WA, Seitz HM, Orago AS. **Seasonal density, sporozoite rates and entomological inoculation rates of Anopheles gambiae and Anopheles funestus in a high-altitude sugarcane growing zone in Western Kenya.** An entomological study was conducted on vectors of malaria and their relative contribution to Plasmodium falciparum transmission in Mumias, a high-altitude site and large-scale sugarcane growing zone in Kakamega district, western Kenya. Anopheles gambiae s.l., the predominant vector species, represented 84% (n=2667) of the total Anopheles mosquitoes collected with An. funestus comprising only 16%. Polymerase chain reaction (PCR) identified all 600 specimens of the An. gambiae complex tested as An. gambiae sensu stricto, an indication that it is the only sibling species represented in the high-altitude sites in western Kenya. Plasmodium falciparum sporozoite rates of 6.3% (133/2118) for An. gambiae s.l. and 9.5% (38/402) for An. funestus by ELISA were obtained in Mumias. None of 1600 mosquitoes tested for P. malariae sporozoites was positive. ELISA tests of mosquito blood meals indicated a high tendency of anthropophagy, a behaviour contributing significantly to malaria transmission by the vector species, with 95.9%, 4.86% and 0.2% having taken at least one blood meal on human, bovine and avian hosts, respectively. Malaria transmission intensity was low as revealed by the low entomological inoculation rates (EIR) recorded. The EIR values for An. gambiae s.l. were 29.2 infective bites per person per year (ib/p/year) and 17.5 ib/p/year for An. funestus in Mumias. The highest inoculation rate for both vector species was 7.0 ib/p/month in July. Plasmodium falciparum parasite rate among asymptomatic children was 55.4% and 44% in the wet (July-September) and dry (December-February) seasons, respectively. These results indicate that malaria transmission intensity in the high-altitude site is low but perennial, with transmission being maintained by An. gambiae s.s. and An. funestus.

117. Tadei WP, Thatcher BD, Santos JM, Scarpassa VM, Rodrigues IB, Rafael MS. **Ecologic observations on anopheline vectors of malaria in the Brazilian Amazon.** Human intervention in the Brazilian Amazon region promotes contacts between humans and vectors that may favor the propagation of anopheline mosquitoes and the spread of malaria in the absence of planning and infrastructure to control this disease. Vector ecology studies were carried out to determine the risk areas. These data should help in designing appropriate malaria control measures. Data from 14 different regions are reported. Vectors are able to adapt to different environments, which made it necessary to study each area. The parameters studied were Anopheles breeding sites, species distribution, incidence, feeding preferences, hours of maximum activity of adult mosquitoes, seasonality, resting places, and the presence of Plasmodium. Species complexes were also studied. Anopheles darlingi may be responsible for maintaining malaria in human populations in this region. A reduction in the population density of A. darlingi in a particular geographic area can sometimes cause the disappearance of malaria. This species feeds at night but has a peak of activity at the beginning of the evening and another at dawn. Other species are mainly crepuscular and all anophelines.
demonstrated pronounced exophilia. The timing of feeding activities was found to vary in areas altered by human intervention and also depended on the time of the year and climatic conditions. The larvae were more abundant in the rivers with a less acidic pH and rural areas showed the highest larval index.

118. Thomson MC; Connor SJ; Milligan PJ; Flasse SP. The ecology of malaria--as seen from Earth-observation satellites, *Ann Trop Med Parasitol*, 90(3):243-64. Data from sensors on board geostationary and polar-orbiting, meteorological satellites (Meteosat and NOAA series) are routinely obtained free, via local reception systems, in an increasing number of African countries. Data collected by these satellites are processed to produce proxy ecological variables which have been extensively investigated for monitoring changes in the distribution and condition of different natural resources, including rainfall and vegetation state. How these data products (once incorporated, along with other data, into a geographical information system) could contribute to the goals of monitoring patterns of malaria transmission, predicting epidemics and planning control strategies is the subject of the present review. By way of illustration, an analysis of two of these products, normalized difference vegetation index (NVDI) and cold-cloud duration (CCD), is given in conjunction with epidemiological and entomological data from The Gambia, a country where extensive studies on malaria transmission have been undertaken in recent years. Preliminary results indicate that even simple analysis of proxy ecological variables derived from satellite data can indicate variation in environmental factors affecting malaria-transmission indices. However, it is important to note that the associations observed will vary depending on the local ecology, season and species of vector. Whilst further quantitative research is required to validate the relationship between satellite-data products and malaria-transmission indices, this approach offers a means by which detailed knowledge of the underlying spatial and temporal variation in the environment can be incorporated into a decision-support system for malaria control.

**Biological Monitoring**

119. Federici BA J Am Mosq Control Assoc 1995 Jun;11(2 Pt 2):260-8 The future of microbial insecticides as vector control agents. Insect vectors of human diseases are subject to diseases of their own caused by viruses, bacteria, fungi, protozoans, and nematodes. Over the past 30 years, many members of these groups have been evaluated as vector control agents, particularly for mosquito control. Most pathogens and nematodes occur primarily in larvae, and are only effective against this stage. The principal candidate control agents studied include iridescent and nuclear polyhedrosis viruses, the bacteria Bacillus thuringiensis and Bacillus sphaericus, the fungi Lagenidium giganteum, Culicinomyces clavosporus, and species of the genus Coelomomyces, the protozoan Nosema algerae, and the mermithid nematode Romanomermis culicivorax. Of these, the only one considered an operational success is the bacterium, Bacillus thuringiensis subsp. israelensis (B.t.i.), which has proven useful for control of both mosquito and blackfly larvae in programs where larviciding has been traditionally employed as a vector control tactic. The reasons for the success of B.t.i. are its cost-effectiveness and relative ease of use, which are due, respectively, to the ability of B.t.i. to be grown on artificial media and the development of formulations that can be applied using conventional insecticide application technology. Because few microbial insecticides are cost-effective, and those that are are only effective against larvae, these agents will likely play only a minor, but in some cases important, role in most future vector control programs.
120. Heckel DG, Gahan LJ, Liu YB, Tabashnik BE. Proc Natl Acad Sci U S A 1999 Jul 20;96(15):8373-7. **Genetic mapping of resistance to bacillus thuringiensis toxins in diamondback moth using biphasic linkage analysis.** Transgenic plants producing environmentally benign Bacillus thuringiensis (Bt) toxins are deployed increasingly for insect control, but their efficacy will be short-lived if pests adapt quickly. The diamondback moth (Plutella xylostella), a worldwide pest of vegetables, is the first insect to evolve resistance to Bt toxins in open-field populations. A recessive autosomal gene confers resistance to at least four Bt toxins and enables survival without adverse effects on transgenic plants. Allelic variants of this gene confer resistance in strains from Hawaii, Pennsylvania, and the Philippines. Here we exploited the biphasic nature of Lepidopteran genetic linkage to map this gene in diamondback moth with 207 amplified fragment length polymorphisms as DNA markers. We also cloned and sequenced an amplified fragment length polymorphism marker for the chromosome containing the Bt resistance gene. The results provide a powerful tool for facilitating progress in understanding, monitoring, and managing resistance to Bt.

121. Robert V, Awono-Ambene HP, Thioulouse J. 1998. *Ecology of larval mosquitoes, with special reference to Anopheles arabiensis (Diptera: Culicidae) in market-garden wells in urban Dakar, Senegal.* J Med Entomol 35(6):948-55. The urban area of Dakar, Senegal, contains > 5,000 market-garden wells that provide permanent sites for mosquito larvae, in particular Anopheles arabiensis Patton, the major vector of malaria. A study of the biocology of mosquito larvae was conducted over 1 yr with a monthly visit to 48 of these wells. Overall, 9,589 larvae were collected of which 80.1% were Culicinae and 11.9% Anophelineae. Larvae from stages III and IV (n = 853) were identified to 10 species. An. arabiensis represented 86% of the anophelines collected and An. ziemanni Grunberg 14%. The most common Culicinae species included Aedeomyia africana Neveu-Lemaire, Culex quinquefasciatus Say, and Mimomyia splendens Theobald. Maximum anopheline abundance was observed at the end of the dry season in June, whereas maximum Culicinae abundance was observed at the end of the rainy season in September. Most wells (67%) did not harbor any An. arabiensis larvae and in the remaining 33% the larval abundance was low, averaging 0.54 larvae in stages III-IV per tray sample. To identify factors that determine the abundance of larvae in these wells, a co-inertia (multivariate) analysis was carried out to account for physicochemical variables (depth, turbidity, temperature, pH, conductivity, Na+, Cl-, HCO3-, CO3--, and NO3- concentrations) and biological variables (abundance of mosquito species, predators [e.g., fish, Dytiscidae, Notonectidae, odonates], molluscs [Bulinus and Biomphalaria], and surface plants [water lettuce, Lemna, and filamentous algae]). The co-inertia analysis indicated that the abundance of An. arabiensis was associated with Cx. quinquefasciatus and Cx. decens for the physicochemical data but was not associated with other mosquito species for floro-faunistic data. The conditions associated with abundant An. arabiensis were warm temperature (28-30 degrees C), clear and not too deep water (< 0.5 m), elevated concentrations of HCO3- and CO3--, low concentrations of NO3- and NaCl, low populations of larvivorous fish and invertebrate predators (notably odonates), the presence of water lettuce, and an absence of Lemna. These results indicate that many contributing factors influence the ecology of the immature stages of An. arabiensis.
H. Community Education and Participation in Malaria Control

Introduction

Studies have shown that the effectiveness of any malaria control strategy is increased with the active and informed participation of the intended beneficiaries (Abstracts 124, 128-130). Particularly in remote rural areas of Africa, researchers have reported that people do not understand the route of malaria transmission (Abstracts 122, 123). Community education efforts that explain the role of mosquitoes as disease vectors, and their preferred breeding habitats and feeding behaviors, improve the success rates of vector control programs (Abstracts 124, 129). For example, when people understand where disease-carrying mosquitoes breed, they are more careful to change or remove these potential habitats. Similarly, studies indicate that when parents understand how treated bednets can protect their sleeping children from malaria, they are more likely to acquire, use, and care for them properly (Abstract 136).

Women in particular have been shown to be critical targets of education efforts in vector control programs (Abstracts 125, 136, 138). The International Development Research Center reported on a project in Benin that is examining community participation in the local production, distribution and use of bednets, as well as variables pertaining to the process of periodically treating the bednets with insecticides. At the Centre de promotion sociale de Savalou [Savalou Social Advancement Centre], seamstresses make bednets out of polyethylene tulle, while other women dip the new mosquito nets into a large tub of insecticide. "In the African family, it is the woman who takes care of the family's health," says Solange Laleye, who is the group animator. According to her, the project is seen as important and, therefore, enhances the esteem accorded to women. She also believes the initiative has contributed significantly to the emancipation of Savalou women. "In the beginning, their husbands were not too pleased because women spent less time at home. Afterwards, however, they realized that it was also to their advantage. There is less family illness. They have the benefit of the additional income of their wives and the bikes that are made available to them. Now, no husbands are bitterly opposed to the project. They are the ones reminding their wives that it is time to go. Some of them even drive their wives to work!"

Researchers also recommend that health education and information be developed and promoted by health officials, local authorities and teachers. As in vector control projects, public health programs to identify and treat malaria cases are aided by a knowledgeable community.
122. Aikins, M. K., H. Pickering, P. L. Alonso, U. D’Alessandro, S. W. Lindsay, J. Todd, and B. M. Greenwood BM. 1993. A malaria control trial using insecticide-treated bed nets and targeted chemoprophylaxis in a rural area of The Gambia, west Africa. 4. Perceptions of the causes of malaria and its treatment and prevention in the study area. Trans R Soc Trop Med Hyg; 87 Suppl 2 P25-30. Perceptions of the causes of malaria, its treatment and prevention were studied among 996 adults, selected randomly from 73 villages and hamlets in a rural area of The Gambia. Structured questionnaires and other interview techniques were used for data collection. Malaria has no specific name in the study area; it is referred to commonly as Fula kajewo (Fula fever). Only 28% of the respondents knew that mosquitoes transmitted malaria. However, most people believed correctly that August to October was the main malaria season. Eighty-six per cent of the subjects were bed net users. The majority of nets were produced locally, usually white in colour and made of sheeting fabrics. Usage of nets was correlated with ethnic group, age and polygamy but not with education, income, occupation or ownership of certain items which indicate high social status. Analysis of expenditure on mosquito coils indicated that non-users of nets spent 43% more on coils than did users. Bed nets have been used for a long time in the study area; 98% of users saw their parents using them during their childhood.

123. Aikins, M. K., H. Pickering, and B. M. Greenwood. 1994. Attitudes to malaria, traditional practices and bednets (mosquito nets) as vector control measures: a comparative study in five west African countries. J Trop Med Hyg 97, no. 2: 81-6. Five West African communities were visited to assess the knowledge of the cause of malaria and to document traditional ways of treating and preventing the infection. Knowledge of the cause of malaria was low in the five communities visited. People were more concerned about mosquitoes being a nuisance than a cause of the infection. Various herbs were used as mosquito repellents. Malaria was treated by a number of traditional practices, including herbal remedies. Bednets were used to a varying extent, from 44% Ghana to 86% Gambia, in each community to protect against mosquito bites but also for other purposes such as privacy, decoration and protection from roof debris dropping on the bed.

124. Akogbeto, P. M., and A. Nahum. 1996. [Impact of deltamethrin impregnated mosquito nets on the transmission of malaria in the coastal lagoon area, Benin]. <Original> Impact des moustiquaires impregnees de deltamethrine sur la transmission du paludisme dans un milieu cotier lagunaire, Benin. Bull Soc Pathol Exot 89, no. 4: 291-8. We have measured the entomological impact of insecticide treated nets on malaria transmission at Ganvie, a village in the coastal and lagoon area of Benin. The nets we have impregnated belong to the population of this village. Men and women of Ganvie used the nets everyday against nuisance biting. Then, the nets we have impregnated are not experimental nets introduced in the village. We have treated 3,230 nets, that means 79% of the nets of this village which counts 20,000 inhabitants. After treating the nets, the inoculation rate due to Anopheles gambiae s.s. and A. melas has decreased from 11 to 4.6 infected bites per man/year, that represents 58.5% of reduction of malaria transmission. We have also observed that the parturity rate of anophes has decreased from 45.3 to 38.8%. We are sure that the entomological performances due to the impregnation will increase more if the inhabitants of Ganvie change their behaviours. They must reduce the frequency of impregnated net wash and repair the teared nets.
The Blue Nile Health Project (BNHP 1980-1990) was launched in 1980 mainly for control of water associated diseases in central Sudan. The BNHP model was chosen to conduct this work. The study showed that women were actively involved in the implementation of the BNHP strategies as health instructors (murshidat) who constituted 75% of the staff of BNHP unit of health education, as members of village health committees (VHC) where they constituted 40% of the VHC members and also as recipients of the project services. All murshidat were interviewed whereas multistage random sampling for VHC members and recipient women in 40 villages was used to select a sample which was interviewed. The results showed that the murshidat and VHC women members played a major role in the motivation, organization and health education of local communities prior to campaigns of environmental sanitation and vector control. Household commitments and difficulties in communication with the public were the main gender-related factors that contributed negatively to women's activities. Cases of malaria have more considerable socio-economic impact than other common diseases, especially with regard to women's household commitments and work. Recipient women were more concerned with aspects of self protection, management of family cases of malaria and health education programmes. They were less involved in drying mosquito breeding sites and spraying activities of insecticides which had been reluctantly accepted because of allergy and bad odour. Although the majority of women considered antimalarials to be less harmful than effects of malaria itself on pregnancy, they did not realize the role of malaria chemoprophylaxis during pregnancy. This needs more health education. The study showed that the BNHP programme was very successful in recruiting women in control and management programmes. Therefore, health planners are urged to persuade the subordinated communities of women in many African countries like Sudan to play a more active role in the health programmes and welfare of their communities.

The adopted strategy for malaria control results from preliminary epidemiological studies. The recommended measures are the improvement of medical care and vector control. The latter is based on indoor spraying of malathion, once a year. Malathion is only active during the period (2 months) of highest transmission, which occurs at the end of the rainy season. Occasionally other insecticides are used. Impregnated bed-nets with deltamethrin and village draining are complementary methods. In villages of the rice-growing area with good participation of the community, vector control activities have a considerable impact on malaria prevalence. About 70% before the intervention, the prevalence does not exceed 10% in 1990. High parasitaemia (greater than 2000 troph./microliters), and hence morbidity, decreased considerably (35% in 1983 to less than 5% in 1990). In villages with poor community participation, the decrease of prevalence is less spectacular (from 70% to 25%). Drains are not kept in repair and constitute new breeding places of vectors in the populated areas. The use of mosquito bed-nets is not common, a better information campaign should overcome this unpopularity. In peri-urban villages, inhabitants are complaining about indoor spraying, but the results are satisfactory. This programme demonstrates that reducing malaria prevalence and
morbidity with conventional measures is feasible in particular biotopes. Health education activities in the Imbo Centre must be pursued and adapted according to the professional activities of the community.

127. Binka, F. N., and P. Adongo. 1997. **Acceptability and use of insecticide impregnated bednets in northern Ghana.** Trop Med Int Health, 2, no. 5: 499-507. A district-wide study was undertaken in a rural population of northern Ghana to identify factors influencing the acceptance and use of insecticide-impregnated bednets (IIBNs). A series of focus group discussions were conducted during 2 years of implementation of IIBNs to gauge community reactions to the introduction of the nets and a structured questionnaire was administered to approximately 2000 randomly selected individuals. Although the IIBNs were accepted and used because they provided protection from mosquito bites, seasonal factors, patterns of use, and questions of cost were key factors likely to influence the dissemination and effectiveness of bednets. Use of the bednets was highly seasonal. Almost all recipients used their IIBNs in the rainy season (99%), corresponding to the period of high mosquito density and 20% used them in the dry seasons, the period of low mosquito density. Mothers with young children were more likely to wash the bednets frequently (because the children soiled the bednets with faeces and urine), resulting in no protection from the insecticide. Provision of wider bednets, or the provision of plastic sheets with the bednets or possible incorporation of the insecticide in washing soaps could improve protection for young children. The success of the promotion of IIBNs in malaria control programmes will depend on the cost of the package and the time of year that it is delivered. Financing mechanisms for individual and village groups are discussed. Social research effectively monitored the intervention in this study, and it should be included as an important component of national malaria control programmes.

128. Cai, X., D. Deng, K. Wu, L. Tang, C. Lan, Z. Gu, Y. He, K. Wang, D. Wu, and J. Du. 1995. [A study on human behavior and socioeconomic factors affecting malaria transmission and control in Qiongzhong, Hainan]. Chung Kuo Chi Sheng Chung Hsueh Yu Chi Sheng Chung Ping Tsa Chih; 13. This study was conducted in Heping District of Qiongzhong County, a hyperendemic mountainous area, in August-September 1992. The comparative surveys between the village and state-run farm, Li and Miao nationalities and Han nationality were carried out by using the sociological method together with the epidemiological methods. Gray relational analysis was conducted between the aforementioned 7 socioeconomic human behavioral factors and IFA rates. The result showed that their degrees of relation (r) were in the following order: (1) percentage of persons who had stayed in the mountain overnight (r = 0.8690); (2) percentage of bed net users (r = 0.7990); (3) percentage of households seeking medical service (r = 0.7990); (4) number of mosquito nets per person (r = 0.7867); (5) percentage of householders knowing malaria transmission route (r = 0.7798); (6) percentage of households with tile-roofed houses (r = 0.6767) and (7) income per capita (r = 0.6636). It indicates that staying in the mountain, using bed net and seeking medical service were three discriminating factors affecting local malaria transmission and control. Therefore, it is suggested that carrying out health education, changing the stay-in-mountain behavior, increasing the utilization of mosquito nets and reinforcing the primary health care should be taken as the fundamental measures for malaria control programme.

129. Garfield RM; Prado E; Gates JR; Vermund SH. **Malaria in Nicaragua: community-based control efforts and the impact of war.** Int J Epidemiol, 18(2):434-9 1989 Jun This descriptive study of temporal trends and geographical distribution examines the effects of prolonged low-intensity warfare on the community-based malaria control efforts. Nicaragua's post-1979 malaria control programme is based on community participation in health education and in mosquito breeding site drainage, expanded case finding, and increased availability of chemotherapy. Mosquito resistance and increasing costs have forced a reduction in the use of residual pesticides. The number of reported malaria cases in the country fell from 25,465 in 1980 to 15,702 in 1984, while the ratio of blood smears to total population increased from 86 to 137 per 1000 people. Malaria incidence in the eight states of the
country under heaviest military attack in the current war was compared to incidence in the eight states least affected by the war. In the war zone there was a 17% excess in cases from August 1983-April 1985 above a 1974-82 baseline average, while there was a 62% decline in the number of cases in the non-war zone.

130. Ghebreyesus TA; Alemayehu T; Bosman A; Witten KH; Teklehaimanot A. 1996. Community participation in malaria control in Tigray region Ethiopia. Acta Trop, 61(2):145-56. During the Ethiopian civil war from 1974 to 1991, the Tigrean People's Liberation Front established a primary health care system in Tigray in which community residents helped to plan and implement health services through health committees and community health workers (CHWs). To strengthen and update this system, a Community-Based Malaria Control Programme was initiated in 1992. The primary objectives of the Programme are to reduce malaria morbidity and mortality and to prevent malaria in pregnant women through early diagnosis and treatment of cases, chemoprophylaxis during pregnancy, and vector control by environmental management. A secondary objective is to introduce a cost-sharing scheme for eventual development of a village revolving fund. A total of 681 volunteers chosen by their communities have received malaria training and serve a rural population of 1,682,319 (CHW/population ratio 1:2,500). The principal success of the programme at this stage is that a significant proportion of the rural population at risk for malaria is now being treated at the village level. During the last major transmission season from September through November 1993, each CHW treated a mean of 45178 clinical malaria cases per month. Under-utilization of treatment services by women and children under 5 years and low chemoprophylaxis coverage of pregnant women have been documented. After focus group discussions with community members and CHWs to identify the reasons for these problems, changes in programme policies were made to improve coverage of these groups. Since 1992, considerable progress toward meeting programme objectives has been made, and continued evaluation will allow for interventions that should further strengthen the malaria control efforts in the region.

131. Hewitt, S. E., M. Farhan, H. Urhaman, N. Muhammad, M. Kamal, and M. W. Rowland. 1996. Self-protection from malaria vectors in Pakistan: an evaluation of popular existing methods and appropriate new techniques in Afghan refugee communities. Ann Trop Med Parasitol 90, no. 3: 337-44. Experimental huts were used to measure the impact of several techniques for self-protection from malaria vectors in Pakistan. An electric fan, pyrethrum coils, untreated curtains, pyrethroid-vaporizing mats and permethrin-impregnated curtains reduced the total catches of blood-fed Anopheles stephensi by 27%, 36%, 47%, 56% and 65%, respectively. The most marked effect of all the interventions was in reducing the numbers of mosquitoes entering the huts, although all the techniques, except for the untreated curtain, also reduced the proportion of mosquitoes inside the hut which fed. Although the trends seen were similar for both anopheline (all An. stephensi) and culicine mosquitoes, they were more pronounced in the culicines. Social surveys were conducted on current self-protection practices. The social and economic constraints associated with each of the various techniques are discussed. All the strategies were shown to offer a degree of protection and their use should be encouraged. Impregnated curtains seem especially promising. Pyrethroid-impregnated bednets have been widely promoted in eastern Afghanistan since 1991 and have the advantage of providing protection when people sleep outside during the summer. However, surveys show that some owners stop using their nets in late autumn, despite the continued risk of malaria. People should be encouraged to use their bednets as impregnated curtains rather than putting them into storage.

activities, we studied knowledge, beliefs, and practices of residents of both the Pacific coastal plain and northeastern Guatemala related to malaria transmission and Anopheles albimanus control. Most residents recognized the role of mosquitoes in malaria transmission, but few knew how mosquitoes acquired their infections or understood the risk of having an untreated person in their midst. If this were more widely known, residents might put greater pressure on infected patients to seek timely and appropriate antimalarial treatment. Seventy-three percent of families owned one or more bed nets; however, even though most informants believed that bed nets help protect against malaria, the major reason for using them was to prevent nuisance mosquito bites. It is concluded that efforts should be made to promote bed net use by seeking ways to make them more affordable and by emphasizing their effectiveness as a barrier to nuisance mosquitoes. Although residents have a very positive opinion of the National Malaria Service spray teams, it is proposed that cooperation might be improved if malaria workers would emphasize the fact that house spraying reduces the numbers of nuisance mosquitoes and other pest insects, rather than focusing solely on malaria prevention, which most informants believed was less important. This study emphasizes the importance of understanding community beliefs and practices when planning or evaluating vector control activities.

133. Kroeger A; Meyer R; Mancheno M; González M, Health education for community-based malaria control: an intervention study in Ecuador, Colombia and Nicaragua. Trop Med Int Health, 1(6):836-46 1996 Dec A malaria study was undertaken in 98 rural communities of the Pacific coast of Ecuador (n = 14), Colombia (n = 22) and Nicaragua (n = 62). In-depth interviews on people's knowledge and practice regarding malaria aetiology, symptoms and treatment were conducted and complemented by formal household interviews. On the basis of this information, an educational programme was set up which included the training of village health promoters and community workshops organized by the health workers and used a set of methods of interactive learning. After the baseline survey the communities were paired and randomly allocated to the intervention and control groups. Malaria education took place only in the intervention communities. At the start of the project people's knowledge about malaria-transmitting mosquitoes and malaria symptoms was correct and widespread in those areas where the community exposure to formal health services was pronounced. However, knowledge of the recommended dose of chloroquine was poor everywhere, and self-treatment of malaria episodes deficient. The educational intervention achieved a high level of participant satisfaction which was expressed in a high and continuous attendance rate at the monthly workshops. The knowledge of malaria aetiology and symptoms was 33-61% better in the intervention group than in the control group. Knowledge of the recommended doses of chloroquine increased significantly (34% in Ecuador, 93% in Colombia but not in Nicaragua) and correct use of chloroquine in the treatment of malaria episodes also improved (26% in Ecuador, 85% in Colombia). In Nicaragua the results were less satisfactory due to the short period of promotional activities and the health services' policy of delivering only supervised treatment to the population. It is concluded that health education should play a major role in malaria control.

134. Louis, J. P., G. Le Goff, A. Trebucq, R. Migliani, F. J. Louis, V. Robert, and . Carnevale P. 1992. [Feasibility of mosquito control using insecticide-impregnated bednets in rural areas of Cameroon]. <Original> Faisabilite de la strategie de lutte par moustiquaires de lit impregnees d'insecticide remanent en zone rurale au Cameroun. Ann Soc Belg Med Trop 72, no. 3: 189-95. The feasibility of using impregnated bednets in a malaria control strategy has been evaluated in a rural area of Cameroon. The benefit is well perceived by the population in terms of protection against nuisance but not in terms of prevention of the disease. The correct use of bednets is, however, unsatisfactory. The material should be adapted to the various sleeping accommodations, and efforts for education and information directed towards the potential users should be intensified.
Mfaume, M. S., P. J. Winch, A. M. Makemba, and Z. Premji. 1997. Mosques against malaria. *World Health Forum* 18, no. 1: 35-8. In a community-based malaria control project covering a predominantly Muslim population in the United Republic of Tanzania, difficulty was encountered in motivating people to have their mosquito nets reimpregnated with insecticide at six-monthly intervals. Education on this subject was therefore provided in mosques during Friday noon prayers. People who attended these services considered them an appropriate forum for discussing health concerns and viewed them as a credible source of information.

Pagnoni, F; Convelbo N; Tiendrebeogo J; Cousens S; Esposito F. 1997. A community-based programme to provide prompt and adequate treatment of presumptive malaria in children. *Trans R Soc Trop Med Hyg*, 91(5):512-7. A community-based programme to ensure prompt and adequate treatment of presumptive episodes of clinical malaria in children has been established in a rural province of Burkina Faso. The implementation strategy was based on training a core group of mothers in every village and supplying community health workers with essential antimalarial drugs specially packed in age-specific bags containing a full course of treatment. Drugs were sold under a cost-recovery scheme. The programme was run in 1994 by the national malaria control centre (CNLP), and in 1995 it was developed to the provincial health team (PHT). Knowledge and awareness of malaria increased with the intervention. Drug consumption by age group was compatible with the distribution of disease, and no major problem of misuse emerged. The actual implementation costs of the intervention were US$ 0.06 per child living in the province. An evaluation of the impact of the intervention on the severity of malaria, using routine data from the health information system and taking as an indicator the proportion of malaria cases which were recorded as severe in health centres, was performed. In 1994, when the intervention was implemented on a provincial scale by CNLP, this proportion was lower than the average of the 4 preceding years (3.7% vs. 4.9%). In 1995, when the programme was implemented by the PHT, the proportion of severe cases was lower in health centres achieving a programme coverage of > or = 50% in their catchment area compared with the others (4.2% vs. 6.1%). Our experience shows that a low-cost, community-based intervention aimed at providing children with prompt and adequate treatment of presumptive episodes of clinical malaria is feasible, and suggests that it may lead to a reduction in the morbidity from severe malaria.

Van Bortel, W., M. Barutwanayo, C. Delacollette, and M. Coosemans. 1996. Motivation to acquire and use impregnated mosquito nets in a stable malaria zone in Burundi. *Trop Med Int Health* 1, no. 1: 71-80. In Burundi, the purchase, acceptance and utilization of impregnated bed nets sold at a promotion price (2 $US) were evaluated in a stable malaria area (South-Imbo, district of Nyanza Lac) where this method of protection was previously unknown to the inhabitants. The sale of the impregnated nets differed between the administrative subdivisions (so-called 'collines') of the area with a coverage varying from 10 to 70% of families. Moreover, in one of these collines with a high overall coverage rate (62%) a difference was also found between the three administrative regions (so-called 'sous-collines') which were socially and economically similar. However, these sous-collines (SC) differed in their geographical location and were found at different altitudes. The real coverage corresponding with the percentage of families showing at least one installed bed net, was calculated for each SC. This coverage was 77% in the SC-1 situated in the low wet area and decreased gradually to 14% in the SC-3 at the highest altitude. The purchase of a bed net does not necessarily mean that people will use them. About 30% of the bed nets bought at the promotion price could not be found and most of them were resold in the neighbouring country (Tanzania). Between 7 (SC-1) and 47% (SC-3) of the bed nets were still packed and not in use. The motivation for buying and using impregnated nets appears to depend essentially on the nuisance level caused by mosquitoes, as shown by the abundance of the mosquitoes in the SC-1 situated in the low wet area (75 bites/man/night) compared to that observed in the SC-2 located at a higher
altitude (i bite/man/night). The authors conclude that appropriate health education and information should be developed and promoted by health staff, local authorities and teachers in order not only to improve comfort by decreasing the insect nuisance, but also to decrease the considerable malaria burden in the community.

138. Winch, P. J., L. S. Lloyd, L. Hoemeke, and E. Leontsini. 1994. Vector control at the household level: an analysis of its impact on women. Acta Trop 56, no. 4: 327-39. The home is the setting where many vector-borne diseases are transmitted. Strategies for their control consequently have to involve the active participation of householders. In this paper we propose that low rates of participation in control activities frequently are related to the negative impact they have on women's power and authority within the domestic domain. This can arise from intrusion into domestic space by male vector control personnel, reorganization of the domestic environment as part of control activities, and promulgation of the idea that disease originates from within the home. In addition, women may need to make significant investments of both time and money in order to carry out the recommended control measures. Very little is known about the impact of vector control measures on women. This subject will assume increasing relevance as planners seek to involve householders, rather than the personnel of vertically-organized control programmes, in the implementation of vector control measures.

139. Ziba C, Slutsker L, Chitsulo L, Steketee RW Use of malaria prevention measures in Malawian households. Trop Med Parasitol 1994 Mar;45(1):70-3 Community Health Sciences Unit, Ministry of Health, Lilongwe, Malawi. Information on malaria prevention practices in households was obtained in a nation-wide knowledge, attitudes, and practice survey in Malawi. Of the 1,531 heads of household questioned, 55% were able to identify mosquitoes as the cause of malaria. Use of any type of malaria prevention method was reported by 52% of respondents. Among users, 47% used commercial products (insecticide, mosquito coils, bednets), and 64% used natural measures (burning leaves, dung, or wood); 11% used both. The most common commercial measure used was mosquito coils (16%) followed by insecticide spray (11%) and bednets (7%). Increasing household income and educational level of the household head were strongly correlated with use of commercial methods to prevent malaria; households with an income ranked moderate or greater were eight times more likely to have used a purchased product. Use of natural measures was correlated with lower income and educational level. Thirty-six percent of respondents reported having heard or seen information on malaria in the previous year. Use of household malaria preventive measures in Malawi is very low and income-dependent. Educational messages are required to improve understanding and use of affordable measures.
I. Cost of Alternative Vector Control

Introduction

The areas where malaria is most prevalent are often the poorest regions of the world. Families may spend considerable portions of their disposable income on health care, often for malaria treatment. However, the cost-effectiveness of malaria control is well established when taking into account lost productivity (Abstracts 140, 142, 143, 152). Family members can be more productive, have fewer bouts of illness, and do not have to spend hard earned money on a variety of prevention methods and treatments. The results provide ample economic justification for malaria control.

In general, nets cost between US$5.00 - $10.00 and between US$.50 - $1.00 per year thereafter to re-treat with the insecticide according to the International Development Research Center. Polyester nets can last up to 5 years and have to be re-dipped every 6 months according to most studies. At present, families who can afford it are paying for anti-malarial drugs, insecticide sprays, coils, or traditional control methods (Abstracts 72, 145). In absolute terms, studies in the Solomon Islands and elsewhere found bednets to be cheaper than DDT spraying (Abstracts 144, 150). In the long term, treated nets are expected to be more cost effective as the nets are durable and can be re-dipped in insecticide locally. In fact, local industries can be created around the manufacturing of these nets.

Various financing mechanisms for bednets are being investigated, including village fundraising, private sector supply and governmentally supported free and reduced-cost bednet programs (Abstracts 141, 148, 151). It has been suggested that nets can be made more affordable to individual households through changes in trade policies, encouraging local mass production, providing community credit, and other financial schemes. As with other public health programs and control methods, governments and donor agencies contribute to the costs (Abstract 142). With these significant results, additional donor support is needed to ensure the results are implemented quickly.

For indoor house spraying, DDT generally remains the cheapest insecticide to apply, but the cost differences are no longer as great as they once were. As synthetic pyrethroids have come down in price, the price of DDT is now going up. In addition, the market for DDT is shrinking, and only three known producers remain (India, China, and Mexico--the latter is now phasing out its production). The price of synthetic pyrethroids can be expected to go down as demand increases.

A 1999 cost comparison by the U.S. Environmental Protection Agency shows that indoor house spraying with pyrethroid insecticides is becoming competitive with DDT spraying (Personal Communication, K. Walker, U.S. EPA --pp. 78-80). Estimated product cost per house treated with DDT ranges from US$1.60 - $4.27, with similar bottom of range costs for synthetic pyrethroids: permethrin, $2.10 - $8.40; cyfluthrin, $3.30 - $7.73; lambda-cyhalothrin, $3.76 - $7.52; and deltamethrin, $4.00 - $8.00.
Selected Bibliography on Cost of Alternative Vector Control

140. Asenso-Okyere WK, Dzator JA. Household cost of seeking malaria care. A retrospective study of two districts in Ghana. Soc Sci Med 1997 Sep;45(5):659-67. Although malaria or fever (as it is commonly referred to) is a major cause of morbidity and mortality in Ghana, the cost of treating the disease in the country has not been well documented. Knowledge about the cost of treating malaria can affect the health care seeking behaviour of people and justify increased expenditure for malaria control. This study used data collected from 1289 households in two districts in Ghana to estimate the direct and indirect costs of malaria treatment. Malaria was ascertained not by parasitological tests but through symptoms described by the respondents using a recall period of one month. It was found that substantial amount of time was spent in seeking malaria care and taking care of the sick, which makes the indirect cost per case of fever represent 79% of the total cost of seeking treatment in the survey area. The results provide ample economic justification for malaria control. The average cost of treating an episode of the disease including direct costs and the opportunity costs of travel and waiting time amounted to $8.67 or 3.7 days of male output or 4.7 days of female output. When compared with the average five days loss of output for the patient due to malaria morbidity and caretaking, it can be concluded that the cost of controlling malaria is lower than lost earnings or the value of output.

141. Binka, F. N., and P. Adongo. 1997. Acceptability and use of insecticide impregnated bednets in northern Ghana. Trop Med Int Health 2, no. 5: 499-507. A district-wide study was undertaken in a rural population of northern Ghana to identify factors influencing the acceptance and use of insecticide-impregnated bednets (IIBNs). A series of focus group discussions were conducted during 2 years of implementation of IIBNs to gauge community reactions to the introduction of the nets and a structured questionnaire was administered to approximately 2000 randomly selected individuals. Although the IIBNs were accepted and used because they provided protection from mosquito bites, seasonal factors, patterns of use, and questions of cost were key factors likely to influence the dissemination and effectiveness of bednets. Use of the bednets was highly seasonal. Almost all recipients used their IIBNs in the rainy season (99%), corresponding to the period of high mosquito density and 20% used them in the dry seasons, the period of low mosquito density. Mothers with young children were more likely to wash the bednets frequently (because the children soiled the bednets with faeces and urine), resulting in no protection from the insecticide. Provision of larger bednets, or the provision of plastic sheets with the bednets or possible incorporation of the insecticide in washing soaps could improve protection for young children. The success of the promotion of IIBNs in malaria control programmes will depend on the cost of the package and the time of year that it is delivered. Financing mechanisms for individual and village groups are discussed. Social research effectively monitored the intervention in this study, and it should be included as an important component of national malaria control programmes.

142. Brinkmann, U., and A. Brinkmann. 1995. Economic aspects of the use of impregnated mosquito nets for malaria control. Bull World Health Organ 73, no. 5: 651-8. The use of pyrethroids to impregnate mosquito nets has had a good impact on the incidence of morbidity and mortality from malaria. These nets are therefore likely to be used on a large scale as an important strategy of malaria control in the future. Published information on the cost and effectiveness of mosquito nets is presented and
analysed. In two examples, from Malawi and Cameroon, the per household expenditure to purchase and use impregnated mosquito nets compares favourably with the costs of malaria. Thus, we expect that the economic losses from malaria would be reduced by 37.3% over a 3-year period in Malawi. Even if the impact of malaria on productivity is not taken into account, the introduction of nets will result in gains, as shown in Cameroon; savings of 9.3% and 11.2% in two places resulted as a consequence of a diminished need for case treatment. The role of government programmes in the promotion of bednets is indirect and concerned mainly with facilitation and the dissemination of information. Much depends on the capability of the private sector and the willingness of the target population to buy the nets for a programme to be effective. Specific studies by health economists on this subject are lacking.

143. Kamol-Ratanakul, P., B. Dhanamun, C. Prasittisuk, and J. A. Grisso. 1993. **Economic analysis of malaria control for migrant workers in eastern Thailand.** *Southeast Asian J Trop Med Public Health* 24, no. 2: 216-20. A randomized, double-blind field trial was carried out to compare the economic impact of permethrin-treated nets with that of untreated nets as a method of malaria control. The study was conducted in 261 long-term migrant workers and 138 seasonal agricultural migrant workers in the eastern rural areas known to be highly endemic for multidrug-resistant *Plasmodium falciparum* infection. One hundred and twenty-six long-term migrants and 59 seasonal migrants used treated nets, while 135 and 79, respectively, used untreated nets. The impregnated-nets program was cost-saving as well as offering improved effectiveness. The net benefit of using a treated net was US$1.17 per worker from the Malaria Division's perspective and US$1.61 per worker from the worker viewpoint. The use of impregnated nets with large-scale primary health care programs likely will be the most cost-effective and cost-beneficial method for controlling malaria in eastern Thailand.

144. Kere, J.F. and N.K. Kere. 1992. **Bed-nets or spraying? Cost analyses of malaria control in the Solomon Islands.** *Health Policy and Planning* 7:382-386. The authors compared the costs of two different malaria controls employed in the Solomon Islands - DDT spraying versus providing permethrin-impregnated bednets. They found that bednets were significantly cheaper (SI$3.85 per person) than DDT spraying (SI$8.53).

145. Kroeger, A., A. Gerhardus, G. Kruger, M. Mancheno, and K. Pesse. 1997. **The contribution of repellent soap to malaria control.** *Am J Trop Med Hyg* 56, no. 5: 580-4. A study about the acceptability, protective efficacy, effectiveness, and cost of a repellent soap containing 20% diethyltoluamide and 0.5% permethrin was carried out on the Pacific coast of Ecuador and Peru, where malaria is endemic and the transmission is seasonal. The malaria vectors were *Anopheles albimanus*, *An. punctimacula*, and *An. pseudopunctipennis* in Ecuador and *An. albimanus* in Peru. Comparing the hourly mosquito bites on human subjects with and without the protection of the repellent soap, it showed that inactive, protected subjects were bitten 94.2% less than unprotected controls 2 hr after application of the soap. This protective efficacy was reduced to 81% after 6 hr. In persons physically active for 3 hr after application, the efficacy of the soap was 67% in the fourth hour after application and 52% in the sixth hour after application. Sweating decreased the protective efficacy of the soap even more. In a community-based malaria control program, the soap was introduced by community health promoters. Acceptance was good when it was given free of charge but reduced dramatically when it was sold. People used the soap mainly because of the nuisance of mosquitoes. The application was generally done correctly. However, no significant impact on the incidence of malaria episodes could be shown when comparing intervention communities with control communities, either in Ecuador, where the proportion of *Plasmodium falciparum* cases was high, or in Peru, where *P. vivax* was the only species of *Plasmodium* seen. This can probably be explained by the limited use of soap and the shift of mosquito bites from users to nonusers of the repellent soap. The cost of a soap program...
would be $4.60 (USA) per person per year, which seems to be quite high in terms of cost of soap and its distribution related to people's low cash income. The implications of the introduction of repellent soap into a control program are discussed.

146. Luo, D., D. Lu, R. Yao, P. Li, X. Huo, A. Li, L. Wen, C. Ge, S. Zhang, H. Huo, and a. l. et. 1994. Alphamethrin-impregnated bed nets for malaria and mosquito control in China. *Trans R Soc Trop Med Hyg* 88, no. 6: 625-8. A community-based intervention trial was carried out to evaluate the effectiveness of alphamethrin-impregnated bed nets for control of Plasmodium vivax malaria and its vector in an area of moderate endemicity in southern Henan province, central China in 1990. Malaria incidence was significantly lower in the intervention group than in the comparison group (2.03 vs. 3.57 per 100 person-years at risk). The protective efficacy for malaria incidence was 43%. The prevalence of malaria parasitaemia among children under 10 years old in the intervention group was about one-quarter of that in the comparison group (0.93% vs. 3.25% and 0.71% vs. 1.96% after one and 4 months use of impregnated nets, respectively). Alphamethrin-impregnated bed nets had a mass killing effect on vector mosquitoes. The outdoor person-biting density of Anopheles anthropophagus and A. sinensis decreased by 70.3% and 29.3% respectively. The density of these 2 mosquito species found resting inside treated nets was close to zero. No side effect was found among users of impregnated bed nets. Impregnation with alphamethrin was more effective on polyester than on cotton netting and residual effects lasted at least one year. Use of alphamethrin is less expensive than permethrin and deltamethrin.

147. Mills, A. 1992. The economic evaluation of malaria control technologies: the case of Nepal. *Soc Sci Med* 34, no. 9: 965-72. This paper illustrates the methodological issues arising from the use of economic evaluation in a developing country context, and how economic evaluation can be applied in developing countries to draw conclusions of relevance to policy-makers. The paper reports research on the cost-effectiveness of the malaria control programme in Nepal. It outlines the hierarchy of choices presented by malaria control and concentrates on the evaluation of the mix of routine strategies employed by the programme, particularly for vector control and case detection and treatment. A social perspective is taken, and emphasis placed on identifying costs falling on households, namely private expenditure on treatment and loss of days of work. Conclusions are drawn relating to the application of economic evaluation methodology to disease control programmes in developing countries.

148. Mills, A., J. Fox-Rushby, M. Aikins, U. D'Alessandro, K. Cham, and B. Greenwood. 1994. Financing mechanisms for village activities in The Gambia and their implications for financing insecticide for bednet impregnation. *J Trop Med Hyg* 97, no. 6: 325-32. The recent enthusiasm for impregnated bednets as a malaria control measure leaves unresolved the question of how to finance them. The National Impregnated Bednet Programme in The Gambia faced the question of how to obtain funds from villages to finance the cost of insecticide, but knew very little about current village fundraising for development purposes. A survey was conducted of such fundraising, and questions also asked about willingness to pay for insecticide and preferred means of paying. All 53 villages surveyed paid taxes/rates, but 34% of villages reported no voluntary fundraising. The most common reason for collecting money was for the maintenance of wells (40% of villages). Collective farming was used as a means of raising money in 32% of villages. There was some variation in the type and extent of fundraising by region and also by the predominant ethnic groups of the village. Villages with voluntary fundraising activities seemed to have well established collective mechanisms for agreeing on sums to be collected and their use, and for collecting and recording income and expenditure. Non-payment was rare, and misuse of funds was not reported. Respondents were asked how much compounds might be willing to pay for insecticide impregnation: the most frequently cited maximum amounts were D5 and 10, and minimum D1 and 5 (D15 = 1 pound).
paper discusses payment options for insecticide, such as whether the village should be allowed to decide itself how to raise funds, and whether the payment should be made only by households with nets or by a village-wide mechanism such as collective farming.

Following the success of a controlled trial of insecticide-impregnated bednets in reducing mortality in children. The Gambia started a National Impregnated Bednet Programme (NIBP) in 1992. The objectives of this programme were to introduce impregnated bednets into all primary health care (PHC) villages and to establish a system of cost recovery over a three-year period. During the initial phase of the programme, when insecticide was given out free, a high uptake was achieved. However, after small user charges were introduced in 1993, coverage dropped to a low level. In 1994, different systems of insecticide distribution and permethrin formulations were tried in an attempt to improve coverage. A nationwide cross-sectional survey carried out during the 1994 rainy season measured coverage by distribution channel, as well as the knowledge, attitudes and practices of health workers and villagers during the intervention. Overall, only 16% of bednets were impregnated in 1994, compared to 80% when the insecticide was offered free of charge in previous years. Lack of money was the major reason given by villagers for not impregnating their bednets in 1994. Use of impregnated bednets was higher in areas where the sale of permethrin emulsion by village health workers was supplemented by the sale of insecticide in individual packages through shops. In villages where insecticide was distributed free to women with small children through governmental mother and child health (MCH) services, higher levels of coverage were achieved among women and young children than in villages where other distribution systems were used. We conclude that the sale of insecticide through the private sector may increase bednet impregnation rates in African communities, and that the free distribution of insecticide through MCH services may be an effective way of targeting young children, the group most at risk of malaria.

150. Neng, W. et al. 1993. Field evaluation of bednets impregnated with deltamethrin for malaria control. Southeast Asian Journal of Tropical Medicine and Public Health 24:664-671. Researchers compared the effects of DDT house sprays vs. providing deltamethrin-impregnated bednets on the incidence of malaria in a large-scale experiment involving over 25,000 people. While both the house spraying and the bednets significantly reduced incidence of malaria, DDT spraying was more than 6 times more expensive per person per year than providing the bednets.

151. Njunwa, K. J., J. D. Lines, S. M. Magesa, A. E. Mnzava, T. J. Wilkes, M. Alilio, K. Kivumbi, and C. F. Curtis 1991. Trial of pyrethroid impregnated bednets in an area of Tanzania holoendemic for malaria. Part 1. Operational methods and acceptability. Acta Trop 49, no. 2: 87-96. In five Tanzanian villages, nets impregnated with permethrin or lambdacyhalothrin were given out. The people received them enthusiastically and brought their nets for re-impregnation at six monthly intervals. Bioassays showed that the insecticidal power of permethrin impregnated nets remained adequate for six months unless the nets were washed. Nets with 30 mg lambdacyhalothrin/m2 retained high insecticidal power despite washing, but this dose caused temporary cold-like symptoms in those sleeping under freshly treated dry nets. Methods by which durable bednets might be made affordable by Tanzanian villagers are discussed.
Cost comparison of insecticides used for indoor spraying (per house per 6 months - US$)

DDT
Permethrin
Cyfluthrin
Lambdacyhalothrin
Deltamethrin
Malathion
Fenitrothion
Bendiocarb
Propoxur

0 5 10 15

20-50

* The cost ranges reflect variability both in insecticide costs and spray dosages.
* Other insecticides appropriate for indoor spraying include pirimiphos-methyl, cypermethrin, and etofenprox. Not listed due to insufficient price data.

Kathleen Walker, Ph.D., AAAS Fellow, USEPA

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152. Picard, J., M. Aikins, P. L. Alonso, J. R. Armstrong Schellenberg, B. M. Greenwood, and Mills A. 1993. *A malaria control trial using insecticide-treated bed nets and targeted chemoprophylaxis in a rural area of The Gambia, west Africa.* 8. Cost-effectiveness of bed net impregnation alone or combined with chemoprophylaxis in preventing mortality and morbidity from malaria in Gambian children. *Trans R Soc Trop Med Hyg; 87 Suppl 2 P53-7.* In The Gambia, insecticide impregnation of bed nets, used alone or combined with Maloprim, reduced morbidity and mortality from malaria amongst children between one and 4 years of age. Taking expenditure of both time and money by public authorities and village volunteers into account, the costs and cost-effectiveness of each intervention were estimated. Bed net impregnation alone and the combined strategy cost US $5.65 and US $7.49 per child-year protected respectively (1990 figures). Insecticide (and drugs) accounted for more than 80% of the costs of each intervention strategy. They were both highly cost-effective. Estimated costs per death and per clinical episode of malaria averted were US $188 and US $28 for bed net impregnation and US $257 and US $19 for impregnation combined with chemoprophylaxis. Estimated costs per healthy year of life saved, discounted at 3%, were US $7.90 and US $10.84.
Cost comparisons of insecticides for indoor house spraying
(excluding operational costs)\textsuperscript{1, 2}

EPA, Personal Communication, Walker

<table>
<thead>
<tr>
<th>Insecticide</th>
<th>Dosage (gm active ingred. per m\textsuperscript{2}) per spray</th>
<th>Number of sprays per six month period</th>
<th>Formulation</th>
<th>Cost (US per kg or liter of product)</th>
<th>Product cost per house per 6 months - 200 m\textsuperscript{2} per house</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>DDT</td>
<td>2</td>
<td>1</td>
<td>75% WP 50% WP</td>
<td>3.00 4.23 5.90 8.00 1.60 2.26 3.15 4.27</td>
<td>2.00 - 4.00 2.55 3.20 - 6.40 4.08</td>
<td>WHO 1990  A-J et al. 1993 K. and K. 1992 Borja 1999</td>
</tr>
<tr>
<td>malathion (Fyfanon)</td>
<td>2</td>
<td>2</td>
<td>50% WP 50% EC</td>
<td>7.50 12.00</td>
<td>Cheminova 1998 WHO 1998</td>
<td></td>
</tr>
<tr>
<td>fenitrothion</td>
<td>2</td>
<td>2</td>
<td>50% WP</td>
<td>50.00 5.00 - 10.00</td>
<td>A-J et al. 1993</td>
<td></td>
</tr>
<tr>
<td>bendiocarb (Ficam)</td>
<td>0.2 - 0.4</td>
<td>2</td>
<td>80% WP</td>
<td>9.30 37.20</td>
<td>WHO 1990 Bayer 1998</td>
<td></td>
</tr>
<tr>
<td>propoxur (Baygon)</td>
<td>2</td>
<td>2</td>
<td>20% EC 50% WP</td>
<td>35.00 28.00 - 56.00</td>
<td>WHO 1990 Bayer 1998</td>
<td></td>
</tr>
<tr>
<td>lambda-cyhalothrin</td>
<td>0.03 0.025 - 0.05</td>
<td>1</td>
<td>10% WP</td>
<td>75.00 75.20 4.50 3.76 - 7.52</td>
<td>Zeneca 1999 WHO 1998</td>
<td></td>
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<tr>
<td>(ICON)</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>deltamethrin</td>
<td>0.025 0.025 - 0.05</td>
<td>1</td>
<td>2.5% WP 2.5% EC</td>
<td>25 -28.00 20.00 4.00 - 8.00 5.00 - 5.60</td>
<td>WHO 1990 WHO 1998</td>
<td></td>
</tr>
<tr>
<td>K-Othrin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>permethrin</td>
<td>0.125 0.125 - 0.5</td>
<td>2</td>
<td>25% WP 50% EC</td>
<td>30.00 21.00 6.00 2.1 - 8.40</td>
<td>WHO 1990 WHO 1998</td>
<td></td>
</tr>
<tr>
<td>cyfluthrin (Solfac)</td>
<td>0.03 0.03 - 0.05</td>
<td>1</td>
<td>10% WP</td>
<td>128.82 55.00 7.73 3.30 - 5.50</td>
<td>A-J et al. 1993 Bayer 1998</td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{1} Description of Columns:

**Insecticides:** The insecticides listed include some of the products recommended by WHO in place of DDT. Product trade names are in parentheses.

**Dosage and number of sprays:** The application rates here are those provided by the information sources cited. If this information was not available, spray rates were taken from Chavasse, D. and H. Yap, Chemical methods for the control of vectors and pests of public health importance, World Health Organization 1997.

**Formulation:** Insecticides are generally not applied in their pure form. Instead, a percentage of the pesticide (active ingredient) is mixed with a wetting agent. WP is a wettable powder. EC is an emulsifiable concentrate.

**Cost:** These costs are averages quoted by the references. The price paid by a particular country may depend upon the amount ordered and the packaging (small containers are more expensive per kilo than large drums). Shipping costs (not included in most of the prices listed) can also raise the price of older, bulkier products such as DDT and malathion.
2 Price information sources:

World Health Organization: These prices do not include shipping charges.


Insecticide manufacturers: These prices are averages and do not include shipping charges.


Published papers: These prices are wholesale local prices and include shipping charges) in the Solomon Islands in 1988-90 and in Mexico in 1993-4.


J. Integrated Public Health Approaches to Malaria Control

Introduction

Integrated public health programs are the most successful approaches to reducing malaria (Abstracts 153-161). Techniques include reducing breeding habitat through improved drainage or water flow, biological control of larvae using natural predators, improved housing and sanitation through community education and participation and drug treatment. While an integrated public health approach to disease may have several components, a comprehensive malaria control strategy described by the Environment & Health Project of US Agency for International Development included three interdependent components: (1) case management, (2) surveillance, and (3) prevention.

- **Case management** - Accurate diagnosis and prompt, appropriate treatment are fundamental to malaria control. Incorrect diagnosis can lead to inappropriate treatment, flawed surveillance, and misguided preventive activities (Abstract 157).

- **Surveillance** - Surveillance is real-time monitoring of the occurrence or increase of a disease in a specified area. National, continental, or global geographical data make it possible to observe large-scale trends, but, to be useful in program design and implementation, surveillance must be local as well. Local surveillance and assessment of site-specific malaria problems is essential before embarking on any control activity. Surveillance and assessment information should also include information on underlying risk factors relating to predisposing human behaviors and environmental conditions. GIS (geographic information system) mapping has become a useful tool for surveillance (Abstract 161).

- **Prevention** - Malaria prevention is often viewed as personal protection: use of bednets, protective clothes, and insect repellents. However, a variety of community-wide preventive malaria control measures are available and can be used effectively to reduce mosquito populations (Abstracts 154,155,158).
The following are examples of a full range of malaria prevention activities. Their appropriateness depends on the local situation, which should be carefully assessed before a program is developed. They include:

1. *Land planning and environmental management*: cross-sector activities to ensure that major development projects are assessed for their potential to create new vector breeding areas; changing natural habitats and human habitation to reduce the abundance of target vectors.

2. *Targeted residual spraying*: most appropriate where vectors breed only part of the year and only one vector may transmit malaria; organically based pyrethroid insecticides of low mammalian and avian toxicity have been used successfully.

3. *Personal protection*: insecticide-impregnated bednets and other materials, repellents, and vector avoidance must be considered, like all other control measures, in the social and economic contexts in which they might be used.

4. *Larval control, including larvicides and biological control agents*: quite successful in areas with limited, identifiable breeding places.

5. *Health education*: programs in the community and the schools; includes training of control staff, raising of community awareness, and interdisciplinary curricula, which can all be linked to community-based programs.
A malaria control trial using insecticide-treated bed nets and targeted chemoprophylaxis in a rural area of The Gambia, west Africa. 6. The impact of the interventions on mortality and morbidity from malaria. Trans R Soc Trop Med Hyg; 87 Suppl 2 P37-44. The effects of insecticide-impregnated bed nets on mortality and morbidity from malaria have been investigated during one malaria transmission season in a group of rural Gambian children aged 6 months to 5 years. Sleeping under impregnated nets was associated with an overall reduction in mortality of about 60% in children aged 1-4 years. Mortality was not reduced further by chemoprophylaxis with Maloprim given weekly by village health workers throughout the rainy season. Episodes of fever associated with malaria parasitaemia were reduced by 45% among children who slept under impregnated nets. The addition of chemoprophylaxis provided substantial additional benefit against clinical attacks of malaria; 158 episodes were recorded among 946 children who slept under impregnated nets but who also received chemoprophylaxis. Chemoprophylaxis reduced the prevalence of splenomegaly and parasitaemia at the end of the malaria transmission season by 63% and 83% respectively. Thus, insecticide-impregnated bed nets provided significant protection in children against overall mortality, mortality attributed to malaria, clinical attacks of malaria, and malaria infection. The addition of chemoprophylaxis provided substantial additional protection against clinical attacks of malaria and malaria infection but not against death.

A malaria control trial using insecticide-treated bed nets and targeted chemoprophylaxis in a rural area of The Gambia, west Africa. Design and implementation of the trial. Trans R Soc Trop Med Hyg; 87 Suppl 2 P31-6. A large-scale malaria intervention programme using insecticide-treated bed nets and chemoprophylaxis administered to children was introduced into a rural area of The Gambia. The operation was carried out using the existing primary health care (PHC) service in the region. Training of the village health workers, sensitization of the communities, and implementation of net impregnation and the drug delivery programme are described. This delivery system resulted in over 90% of nets being treated with insecticide and 80% of children receiving over 90% of their tablets during the rainy season. There was considerable variation in the distribution of permethrin on a bed net and between individual nets, which is likely to facilitate the spread of insecticide resistance in the local mosquito populations. Bed nets made from heavier fabrics tended to absorb more insecticide than those made from lighter materials. Four months after dipping, 89% of the insecticide had been lost from treated nets. This was probably due mainly to women washing their nets, an activity carried out on average once every 2 months during the rainy season. The high number of insecticide-treated bed nets in the study area demonstrated that a malaria control programme operated through a PHC system can be implemented successfully.

Malaria: current and future prospects for control. Annu Rev Entomol; 40 P195-219. Malaria is the most important insect-transmitted human disease, but progress in its control has been slow, especially in Africa where approximately 90% of the infections occur. Several factors have contributed to the problem. Parasites and vectors have developed resistance to antimalarial drugs and insecticides; differences in the biology of major
malaria vectors preclude the development of simple, universally applicable strategies for malaria control; and the cost of available malaria-control tools often exceeds the public health resources in the most malarious parts of the world. New tools are desperately needed. Current efforts include the testing of tools such as insecticide-impregnated bed nets that could become available in the near term, as well as long-term projects such as the development of malaria vaccines and mosquito-targeted genetic control strategies. The success or failure of any of these approaches will depend ultimately on understanding the natural patterns of malaria transmission in the field.

156. Coosemans, M., M. Wery, J. Mouchet, and P. Carnevale. 1992. Transmission factors in malaria epidemiology and control in Africa. Mem Inst Oswaldo Cruz; 87 Suppl 3 P385-91. Genetic and environmental components of factors contributing in malaria transmission are reviewed. Particular attention is given to density dependent regulation of vector populations in relation to the survival rate of anophelines. The expectation of vector control activities are different according to the epidemiological characteristics of malaria, mainly its stability. In areas with perennial and high transmission (stable malaria) vector control could reduce malaria related morbidity and mortality, without any effect on the endemicity. However this need further investigations. In areas where the transmission period is very short (unstable malaria), vector control will have an important impact on the disease and on the endemicity. Control projects using indoor spraying with insecticide and impregnated bed nets are discussed.

157. Ghebreyesus TA; Alemayehu T; Bosman A; Witten KH; Teklehaimanot A. 1996. Community participation in malaria control in Tigray region Ethiopia. Acta Trop, 61(2):145-56. During the Ethiopian civil war from 1974 to 1991, the Tigrean People's Liberation Front established a primary health care system in Tigray in which community residents helped to plan and implement health services through health committees and community health workers (CHWs). To strengthen and update this system, a Community-Based Malaria Control Programme was initiated in 1992. The primary objectives of the Programme are to reduce malaria morbidity and mortality and to prevent malaria in pregnant women through early diagnosis and treatment of cases, chemoprophylaxis during pregnancy, and vector control by environmental management. A secondary objective is to introduce a cost-sharing scheme for eventual development of a village revolving fund. A total of 681 volunteers chosen by their communities have received malaria training and serve a rural population of 1,682,319 (CHW/population ratio 1:2,500). The principal success of the programme at this stage is that a significant proportion of the rural population at risk for malaria is now being treated at the village level. During the last major transmission season from September through November 1993, each CHWs treated a mean of 45,178 clinical malaria cases per month. Under-utilization of treatment services by women and children under 5 years and low chemoprophylaxis coverage of pregnant women have been documented. After focus group discussions with community members and CHWs to identify the reasons for these problems, changes in programme policies were made to improve coverage of these groups. Since 1992, considerable progress toward meeting programme objectives has been made, and continued evaluation will allow for interventions that should further strengthen the malaria control efforts in the region.

158. Kanda, T., D. Bunnag, V. Deesin, T. Deesin, S. Leemingsawat, N. Komalamisra, Thimasam K, and S. Sucharit. 1995. Integration of control measures for malaria vectors in endemic areas of Thailand. Southeast Asian J Trop Med Public Health 26, no. 1: 154-63. Various vector control measures were applied in different endemic areas in two provinces, Saraburi and Chanthaburi, with comparison among different control measures. Application of IGR (insect growth regulator, pyriproxyfen) was introduced at Wat Tam Pra Pothisat, Tab-Kwang District, Saraburi Province. Some integration measures were performed at villages 6 and 8, Patavee, Makham District, Chanthaburi Province. In Tab-Kwang District with low malaria endemicity at the study site
predators were not able to be released due to rapid velocity of running water. IGR could effectively control malaria compared to the basin released predators. Another endemic areas villagers 6 and 8, Patavee, Makham, Chanthaburi Province was chosen. Highly endemic multidrug resistant malaria has been prevalent for many years in this area. Integration of Kanda’s trapping system, application of IGR, use of both residual spraying and impregnated bed-net methods with etofenprox successfully interrupted malaria infection. The application of these methods as an integrated control system could be adjusted to environmental conditions. The results of this study suggest rapid effective vector control.

159. Meek, S. R. 1995. Vector control in some countries of Southeast Asia: comparing the vectors and the strategies. Ann Trop Med Parasitol 89, no. 2: 135-47. The use of information on malaria vector behaviour in vector control is discussed in relation to the area of Southeast Asia comprising Cambodia, Laos, Myanmar, Thailand and Vietnam. The major vectors in the region are Anopheles dirus, An. minimus, An. maculatus and An. sundaicus, of which An. dirus is the most important. Options for vector control and the biological features of mosquitoes, which would make them amenable to control by these measures, are listed. The methods with the greatest potential for controlling each of the four vector species are described. Experiences of vector control by residual spraying, insecticide-treated nets and larva control and of personal protection against the four vectors are outlined, and it is noted that choice of control strategy is often determined by epidemiological, economic and political considerations, whilst entomological observations may help to explain failures of control and to indicate alternative strategies. Future research needs include basic entomological field studies using the most appropriate indicators to detect changes related to rapidly changing environmental conditions, such as loss of forest and climate change. Further studies of the efficacy of insecticide-treated mosquito nets, with greater attention to study design, are needed before it can be assumed that they will work in Southeast Asia. At the same time, research to improve sustainable utilization of nets is important, bearing in mind that nets are not the only means to control malaria and should not drain resources from supervision and training, which improve access to diagnosis and treatment of malaria and other diseases. Research is needed to make decisions on whether vector control is appropriate in different environments, and, if so, how to carry it out in different health systems. Researchers need to play a greater role in making operational research (entomological, epidemiological, social, economic and health systems research) of good quality an integral component of implementation programmes.

160. Msuya, F. H., and C. F. Curtis. 1991. Trial of pyrethroid impregnated bednets in an area of Tanzania holoendemic for malaria. Part 4. Effects on incidence of malaria infection. Acta Trop 49, no. 3: 165-71. 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.

161. Xu, B., H. Li, and R. H. Webber. 1994. Malaria in Hubei Province, China: approaching eradication. J Trop Med Hyg 97, no. 5: 277-81. In the last six years, there has been a steady reduction of Plasmodium vivax malaria in Hubei Province with an API (annual parasite incidence) of 0.134 per thousand by 1992. This is especially so in the south, east, west and north-west parts of the province. Much of this reduction has been produced by a policy of repeated radical treatment in the non-malaria season. In the centre of Hubei, where Anopheles anthropophagus is the chief vector, malaria is still a problem. The key factors in destabilizing malaria are a sudden increase in the number of An. anthropophagus, introduction of non-immunes into the endemic area, and the village doctors' diminished interest in malaria surveillance activities. Impregnated bed nets are possibly the best strategy for reducing malaria, but where the prevalence is reduced to a sufficiently low level efficient case finding and detection are able to contain malaria and produce a continued reduction.
K. New Malaria Treatments

Introduction

In the past, malaria prophylaxis was not a major problem, as all *plasmodium* species, which cause malaria in humans, were sensitive to *Chloroquine*, a well tolerated and safe drug. The drug remains effective in areas where malaria is not resistant to it, such as North Africa, most countries in the Middle East, portions of China, Haiti and the Dominican Republic, west of the Panama Canal, and temperate South America. Although it does not actually prevent infection, it limits the extent of infection and suppresses the symptoms.

Today, however, numerous countries no longer have Chloroquine-sensitive malaria (Abstracts 164, 165, 166, 167). In some cases, the resistance is due to the plasmodium species developing resistance to drugs and in other instances because of the inappropriate use of Chloroquine as a prophylactic (Abstract 163). A new antimalarial drug, CGP 56697, shows promise as a safe and effective antimalarial drug in African children (Abstract 169). However, researchers say that the development of new, effective drug treatments should be a high priority (Abstract 165).

In addition to anti-malarial drug treatments, recent studies have looked at the role of nutrient deficiencies that could impair the development of immunity against *P falciparum* or exacerbate the disease. Vitamin A, often deficient in individuals living in malaria endemic areas, is essential for normal immune function, and studies suggest it could play a part in potentiating resistance to malaria (Abstract 168). In a study of young children in Papua New Guinea, Shankar et al report a 30% decrease in mortality from malaria in those who received vitamin A compared to a control group. The study goes on to compare this effect with other intervention methods: 48% reduction in episodes seen with insecticide-treated bednets and an overall 23% reduction achieved with Spf66 malaria vaccine. Based on a cost comparison of vaccines and bednets done by others, the authors suggest that vitamin A supplementation ranks among the more cost-effective non-pharmacological interventions for malaria (Abstract 168).
Selected Bibliography on New Malaria Treatments

162 Ambroise-Thomas P. 1995. For new antimalarial drugs: the methods of fundamental research. Med Trop (Mars), 55(4 Suppl):23-6. Research in new antimalarial drugs has too long been limited to a only pharmacological approach with its four main modalities: isolation of compounds from medicinal plants, oriented or not screening of varied molecules, molecular ingeniery modifying structure of wellknown drugs in order to improve their efficacy, products reversing resistance to antimalarial drugs (anti-Pfmdr). Important success has been obtained by these ways but the possibility of new discoveries seems to be limited. It is time certainly to concentrate efforts no more on the drug itself but on the real target i.e. Plasmodium or malaria disease. Our knowledge of Plasmodium biology and of pathophysiological mechanisms in malaria are still very limited. This kind of study comes up against many difficulties (plasmodial intracellular parasitism, parasitic specificity of Plasmodium parasites in Man, etc). Nevertheless, only a huge effort in fundamental research will open new perspectives in antimalarial therapeutics by identifying possible targets for new compounds from which pharcaceutical industry will be able to develop new medicines.

163 Djimde A; Plowe CV; Diop S; Dicko A; Wellems TE; Doumbo O. 1998. Use of antimalarial drugs in Mali: policy versus reality. Am J Trop Med Hyg, 59(3):376-9. Inappropriate use of antimalarial drugs undermines therapeutic efficacy and promotes the emergence and spread of drug-resistant malaria. Strategies for improving compliance require accurate information about current practices. Here we describe Knowledge-Attitude-Practice surveys conducted among health providers and consumers in two Malian villages, one rural and one periurban. All sanctioned providers limited their first choices of antimalarial drug to those recommended by the national malaria control program and reported using correct dosing regimens. However, the majority of consumers in the two villages chose non-recommended treatments for malaria and reported suboptimal treatment regimens when they did use recommended drugs. Antimalarial drugs were also widely available from unsanctioned sources, often accompanied by erroneous advice on dosing regimens. This study demonstrates that even when the most peripheral health providers are well-trained in correct use of antimalarial drugs, additional measures directly targeting consumers will be required to improve drug use.

164 Ekvall H; Premji Z; Bjorkman A. 1998. Chloroquine treatment for uncomplicated childhood malaria in an areas with drug resistance: early treatment failure aggravates anaemia. Trans R Soc Trop Med Hyg, 92(5):556-60. Childhood anaemia is a major public health problem in malaria holoendemic areas. We assessed the effects of antimalarial treatment in an area with drug-resistant falciparum malaria on haemoglobin levels in small children by applying the 1996 World Health Organization in vivo method for the evaluation of standard chloroquine treatment at the community level. In Fukayosi village, coastal Tanzania, 117 children aged 5-36 months with clinical malaria episodes were treated with chloroquine syrup (25 mg/kg). Early treatment failure (ETF) occurred in 20% and late treatment failure (LTF) in 22% of cases. Age > 1 year and malnutrition were protective factors against ETF. The evidence that chloroquine treatment could not prevent an exacerbation of anaemia was (i) the fact that the fall in haemoglobin level after 72 h was significantly greater in ETF than in children with LTF and an adequate clinical response, and (ii) the absence of any haematological improvement at follow-up in children receiving chloroquine alone, even in true treatment successes. In contrast, pyrimethamine/sulfadoxine administered to treatment failures
improved the haemoglobin level significantly > 21 d after treatment started (mean difference 14 g/L, 95% confidence interval 2.1-27). We conclude that, when chloroquine treatment of childhood malaria is associated with a 20% ETF rate, the haemoglobin response is unsatisfactory and there is a need to change the recommended first-line treatment.

165. Gomes M; Wayling S; Pang L. 1998. Interventions to improve the use of antimalarials in south-east Asia: an overview. *Bull World Health Organ*, 76 Suppl 1:9-19. There are few drugs for malaria, and those which are available for use are subject to rapid development of resistance. Curiously, little effort has been made to improve drug use in malaria-endemic countries and to assess the benefits of such improvements. Advances can be made in public understanding of the value of ingesting a full regimen of antimalarials, in order to achieve complete cure, and in improving simple technologies (blister packaging) to achieve the same result. Better efforts can be made to reduce the availability of fake or substandard drugs in the marketplace. In this article, we describe the outcome of a concerted effort to improve drug compliance and drug quality in an area of multidrug resistance for malaria. These research efforts, guided by the Task Force for Improved Use of Antimalarials, characterized the problems in drug compliance in South-East Asia, and developed interventions to improve drug use in the various countries. Interventions involved drug packaging, public information campaigns, and assessments of drug quality. Results show that blister packaging worked best to improve drug compliance and that the increased cost of packaged medication did not limit its use. Drug quality was a major problem in unregulated countries and should be improved.

166. Hastings IM; Mackinnon MJ. 1998. The emergence of drug-resistant malaria. *Parasitology*, 117(5):411-7. Stochastic processes play a vital role in the early stages of the evolution of drug-resistant malaria. We present a simple and flexible method for investigating these processes and understanding how they affect the emergence of drug-resistant malaria. Qualitatively different predictions can be made depending on the biological and epidemiological factors which prevail in the field. Intense intra-host competition between co-infecting clones, low numbers of genes required to encode resistance, and high drug usage all encourage the emergence of drug resistance. Drug-resistant forms present at the time drug application starts are less likely to survive than those which arise subsequently; survival of the former largely depends on how rapidly malaria population size stabilizes after drug application. In particular, whether resistance is more likely to emerge in areas of high or low transmission depends on malaria intra-host dynamics, the level of drug usage, the population regulation of malaria, and the number of genes required to encode resistance. These factors are discussed in relation to the practical implementation of drug control programmes.

167. Hien TT; VinhChau NV; Vinh NN; Hung NT; Phung MQ; Toan LM; Mai PP; Dung NT; HoaiTam DT; Arnold K. 1997. Management of multiple drug-resistant malaria in Viet Nam. *Ann Acad Med Singapore*, 26(5):659-63. Malaria is still the most common infectious cause of mortality and morbidity in Viet Nam as it is in many developing countries in the tropics. The presence of resistance to available antimalarials and compliance in the target population are factors that influence the choice of drugs and regimens. In order to develop an ideal treatment for malaria, we conducted several clinical trials in patients with the disease in different settings. The results of these trials suggest that a combination of single dose artemisinin (or its derivatives) and mefloquine is the most effective, safe and practical treatment for acute non-complicated malaria due to multidrug-resistant Plasmodium falciparum. Concerning severe and complicated malaria, parenteral or rectal multi-doses of artemisinin or analogues are recommended due to their rapid parasite clearance time and other possible anti-cytoadherence effects. With its rapid parasite clearance, very early treatment of uncomplicated cases with artemisinin (and derivatives), especially at a health post level may help to prevent the development of complications, consequently reducing the number of severe cases and the malaria mortality rate.
168. Shankar AH, Genton B, Semba RD, Baisor M, Paino J, Tamja S, Adiguma T, Wu L, Rare L, Tielsch JM, Alpers MP, West KP Jr. Effect of vitamin A supplementation on morbidity due to Plasmodium falciparum in young children in Papua New Guinea: a randomised trial. Lancet 1999 Jul 17;354(9174):203-9. BACKGROUND: Many individuals at risk of malaria also have micronutrient deficiencies that may hamper protective immunity. Vitamin A is central to normal immune function, and supplementation has been shown to lower the morbidity of some infectious diseases. We investigated the effect of vitamin A supplementation on malaria morbidity. METHODS: This randomised double-blind placebo-controlled trial of vitamin A supplementation took place in a P. falciparum endemic area of Papua New Guinea. Of 520 potentially eligible children aged 6-60 months, 480 were randomly assigned high-dose vitamin A (n=239) or placebo (n=241), every 3 months for 13 months. Malaria morbidity was assessed through weekly community-based case detection and surveillance of patients who self-reported to the health centre. Cross-sectional surveys were also done at the beginning, middle, and end of the study to assess malariometric indicators. Analyses were by intention to treat. FINDINGS: The number of P. falciparum febrile episodes (temperature > or = 37.5 degrees C with a parasite count of at least 8000/microL) was 30% lower in the vitamin A group than in the placebo group (178 vs 249 episodes; relative risk 0.70 [95% CI 0.57-0.87], p=0.0013). At the end of the study P. falciparum geometric mean density was lower in the vitamin A than the placebo group (1300 [907-1863] vs 2039 [1408-2951]) as was the proportion with spleen enlargement (125/196 [64%] vs 148/207 [71%]); neither difference was significant (p=0.093 and p=0.075). Children aged 12-36 months benefited most, having 35% fewer febrile episodes (89 vs 141; relative risk 0.65 [14-50], p=0.0023), 26% fewer enlarged spleens (46/79 [58%] vs 67/90 [74%], p=0.0045), and a 68% lower parasite density (1160 [95% CI 665-2022] vs 3569 [2080-6124], p=0.0054). Vitamin A had no consistent effect on cross-sectional indices of proportion infected or with anaemia. INTERPRETATION: Vitamin A supplementation may be an effective low-cost strategy to lower morbidity due to P. falciparum in young children. The findings suggest that clinical episodes, spleen enlargement, and parasite density are influenced by different immunological mechanisms from infection and anaemia.

169. Von Seidlein L; Jaffar S; Pinder M; Haywood M; Snounou G; Gemperli B; Gathmann I; Royce C; Greenwood B. 1997. Treatment of African children with uncomplicated falciparum malaria with a new antimalarial drug, CGP 56697. J Infect Dis, 176(4):1113-6. New antimalarial drugs are urgently needed. The use of short courses of the new antimalarial drug artemether as monotherapy has been limited by secondary malaria episodes following parasite clearance. Therefore, a new antimalarial drug, CGP 56697, has been developed, which combines artemether with a longer-acting antimalarial agent, benflumetol. A safety trial was undertaken in 60 Gambian children 1-6 years old with uncomplicated Plasmodium falciparum malaria. All children treated with CGP 56697 cleared their parasites 72 h after the start of treatment. No neurologic, cardiac, or other adverse reactions were observed. Second episodes of falciparum malaria were recorded in 16 (27%) of the children. Second infections were more frequent during the rainy season than during the dry season. Molecular epidemiologic studies suggested that 12 of the 14 second episodes of malaria in children treated with CGP 56697 were due to new infections. CGP 56697 proved to be a safe and effective antimalarial drug in African children.
L. Development of an Effective Malaria Vaccine

Introduction

Since many of the poorest nations of the world are afflicted with malaria, a successful drug intervention must be inexpensive, cost-effective, and relatively easy to administer and maintain (Abstract 170). Historically, vaccines have been among the most cost-effective and easily administered means of controlling infectious diseases. As yet no licensed vaccine exists for malaria. Compared to vaccines for most bacterial diseases, development of malaria vaccines present formidable obstacles. Malaria parasites have complex life cycles and, thus, distinct developmental stages, each of which may have multiple antigens that could serve as targets of an immune response. An effective vaccine will probably need to incorporate multiple components that will induce an immune response to the different stages of the malaria infection (Abstract 172). Nevertheless, there are reasons to believe that protective immunity against malaria can be elicited because human populations residing in malaria endemic areas have been observed to acquire immunity to clinical disease naturally over time. While vaccines based on live, attenuated or killed malaria parasites are economically and technically impracticable, there is hope that recombinant or synthetic subunit vaccines may induce potent and perhaps long-term cellular immunity against malaria.

In 1987, Dr. Manuel Elkin Patarroyo developed the world's first synthetic vaccine, the first vaccine against a parasite and the first vaccine against *Plasmodium falciparum* (the most common and deadly malaria parasite). Still under development, the vaccine has not yet proven to reduce deaths in Africa. While the first trial of the vaccine in Tanzania in 1993 was shown to be safe and immunogenic, a later trial in the Gambia was not successful in reducing mortality (Abstract 173). There is much controversy surrounding the SPf66 vaccine. Many have criticized the manner in which the trials have been conducted and the fact that it is not understood how SPf66 mediates protection. SPf66 will most likely not be the answer to the malaria burden, but it has given several research teams valuable experience in conducting malaria vaccine trials that can be helpful during the next generation of trials (Abstract 171).

The ideal vaccine for malaria today encompasses the following three essential characteristics: First, it is multi-stage, incorporating antigenic characteristics at multiple stages of *P. falciparum*’s life cycle. Second, it would be multi-valent, which would help overcome genetic restriction and allelic and antigenic variation, problems plaguing single antigen-based vaccines. Lastly, it would be multi-immune, inducing more than one type of immune response, including
cell-mediated and humoral (antibody production) (Abstracts 172, 178). Consequently, the focus of current malaria is on DNA technology, which can meet these requirements. The results of recent trial of a DNA vaccine in humans is of special interest. The results, while preliminary demonstrated the feasibility of inducting specific cellular immunity in humans with use of a DNA vaccine (Abstract 178).

While a multi-component DNA vaccine offers the best prospects for protection against malaria, there are some safety issues associated with them. RA Seder and S Gurunathan in a New England Journal of Medicine editorial postulate that DNA vaccines could provoke a strong cellular immune response not only against the parasite but also against the host’s own antigens, thereby causing more harm than good. Despite these caveats, a multi-component vaccine would increase the probability of a more sustainable and effective host response.

On a different front, a group of insect geneticists, genome researchers and funding officials have recently put forth a plan to sequence the genome of the Anopheles gambiæ, the mosquito primarily responsible for malaria (Abstract 177). To enter its human host, the malaria parasite needs the help of the Anopheles mosquito, which injects the parasite into the host’s bloodstream while ingesting blood. What some researchers call the ‘Holy Grail’ of malaria control would be to create a genetically modified mosquito incapable of transmitting Plasmodium, an aim that would be greatly aided by knowing the sequence of the mosquito’s genome. The human genome is already being sequenced and so is Plasmodium.

While current research on a malaria vaccine holds a great deal of promise, many scientists estimate it could take seven to 15 years before an effective vaccine is available.
Selected Bibliography on the Development of an Effective Malaria Vaccine

170. Graves PM Comparison of the cost-effectiveness of vaccines and insecticide impregnation of mosquito nets for the prevention of malaria. *Ann Trop Med Parasitol* 1998 Jun;92(4):399-410 The cost-effectiveness of two different methods of prevention of morbidity and mortality due to *Plasmodium falciparum* malaria, vaccination and impregnation of mosquito nets with permethrin, was compared. The analysis was performed with reference to the cohort of all children born in The Gambia in 1990 and protected for 5 years, using estimates of costs from studies in The Gambia. The vaccine was assumed to be given in three doses before the age of 6 months, through the Expanded Programme of Immunization, and to remain effective up to the age of 5 years. The bednets were assumed to be impregnated at 6-monthly intervals over the 5-year period. The expected number of deaths and attacks due to *P. falciparum* in the first 5 years of the 1990 cohort's lives were estimated from published literature. The numbers of deaths and attacks averted by the two strategies were then estimated by decision analysis, using the best estimates of effectiveness available in the literature. The vaccine strategy would have averted an estimated 743 deaths and 50,502 malaria attacks, whereas the net impregnation would have averted 1537 deaths and 69,415 attacks. The estimated cost per death averted was U.S. $252 for the vaccine and U.S. $711 for net impregnation. The estimated cost per *P. falciparum* attack averted was U.S. $3.71 for the vaccine and U.S. $15.75 for net impregnation. Sensitivity analysis, examining the effect of varying the vaccine cost or insecticide cost, the efficacy of the vaccine or net impregnation, and the percentage coverage of the population, confirmed the greater cost-effectiveness of the vaccine strategy for either of the outcomes examined under the conditions of the model. However, limitations on the absolute number of deaths and malaria attacks which can be averted by currently available vaccines demonstrate that a vaccine of higher efficacy would be highly desirable.

171. Kitua AY Field trials of malaria vaccines. *Indian J Med Res* 1997 Aug;106:95-108 Malaria due to *Plasmodium falciparum* is probably the most important infectious disease in the tropical world. About 2000 million people live in areas exposed to malaria and 300 million individuals are infected every year. In Africa south of the Sahara alone, over 1 million children die annually as a result of malaria. It is a difficult parasitic disease both to diagnose and control. It does not provide sterile immunity even after long exposure periods. However, acquisition of partial immunity allows over 60 per cent of individuals with long exposure to carry the parasite in their blood without symptoms, posing difficulties for case definition, malaria attributable morbidity and deaths. Further, it is extremely difficult to establish the extent to which malaria has influence over the adverse outcome of other infectious disease like measles and malnutrition. The complex life cycle of the parasite involving human and vector mosquitoes as well as its allelic diversity and antigenic variations makes the development and implementation of effective malaria control intervention problematic. It is now becoming evident that multi-intervention approach may be the most appropriate way of combating malaria in view of the increasing resistance of the parasite to antimalarial drugs as well as vector mosquitoes to insecticides. Malaria vaccines will therefore play a major role in future malaria interventions. New malaria vaccine candidates will require testing in malaria endemic countries. Sufficient sites for testing potential malaria vaccines must be prepared. In this paper we discuss the necessary preparations required for field testing of malaria vaccines in tropical countries.

Malaria remains the most prevalent and devastating parasitic disease worldwide. Vaccination is considered to be an approach that will complement other strategies for prevention and control of the disease in the future. In the last 10 years, intense studies aimed at the development of a malaria vaccine have provided important knowledge of the nature of the host immunological mechanisms of protection and their respective target antigens. It became well established that protective immune responses can be generated against the distinct stages of *Plasmodium*. However, in general, protective immune responses are directed at stage-specific antigens. The elucidation of the primary structure of these antigens made possible the generation of synthetic and recombinant proteins that are being extensively used in experimental immunizations against the infection. Today, several epitopes of limited polymorphism have been described and protective immunity can be generated by immunization with them. These epitopes are being tested as primary candidates for a subunit vaccine against malaria. Here we critically review the major roadblocks for the development of a malaria vaccine and provide some insight on how these problems are being solved.

**Spf66**


The Gambia. In 1994, 630 Gambian infants were immunized with three doses of the synthetic polypeptide malaria vaccine Spf66 or with a control vaccine. No significant protection against first or total attacks of malaria was observed among the children who received Spf66. However, the period of follow-up was short. Thus, 532 children were followed for a second malaria transmission season during which 291 episodes of malaria were detected. Protective efficacies of Spf66 against first attacks of malaria and against all attacks of malaria were 8% [95% CI-20%, 30%] and 2% [95% CI-26% 24%] respectively. Spf66 did not provide any significant degree of protection to Gambian infants during a second year of follow-up.


In preparation for a recently reported, independent field trial of Spf66 malaria vaccine efficacy in Thailand, we first established the safety and immunogenicity of two clinical lots of U.S. manufactured lots of Spf66 in a series of overlapping Phase I studies. The vaccine was produced in approved laboratories using good manufacturing practices. Two clinical lots of alum-adsorbed Spf66 were evaluated in a combined, open-label, Phase I clinical trial involving 50 healthy, malaria-experienced Karen adults and children. Volunteers were grouped by age and immunized sequentially. Group 1 had 30 adults. Group 2 had 10 children 8-15 years of age, and Group 3 had 10 children 2-6 years of age. The Spf66 vaccine was well tolerated in this malaria-experienced population. The most common side effects were erythema, induration, warmth, and tenderness at the site of injection, which typically resolved within 24-48 hr. One adult volunteer developed an acute urticarial rash following the third dose. Among adults, and to a lesser extent older children females had more local reactions than their male counterparts. Seroconversion to Spf66 by enzyme-linked immunosorbent assay occurred in 76% of volunteers receiving two or three doses. This vaccine was safe and immunogenic in malaria-experienced Karen adults and children. This study establishes the comparability of U.S.-manufactured Spf66 with that of Colombian origin, and is important for interpreting the efficacy results of U.S.-manufactured Spf66 in the same study population.
175. **Urdaneta M, Prata A, Struchiner CJ, Tosta CE, Tauil P, Boulos M** Evaluation of Spf66 malaria vaccine efficacy in Brazil. *Am J Trop Med Hyg* 1998 Mar;58(3):378-85 This paper reports the efficacy results of the randomized, placebo-controlled, field trial of Spf66 malaria vaccine in Costa Marques, Rondonia, Brazil. This region is characterized by the seasonal distribution of Plasmodium falciparum and P. vivax infections, and the recent occupation by migrants from nonendemic areas. A total of 800 individuals of both sexes, ranging in age from seven to 60 years, were included in the study. Of the initial cohort, 572 participants completed the vaccination schedule. Clinical and parasitologic evaluations were obtained by active and passive searches on a periodic basis. The overall protective efficacy against P. falciparum infections was -1.6% (-32.9% to 22.4%), and 14.1% (-17.0% to 36.9%) for the first episode. The overall protective efficacy for P. vivax infections was -19.7% (-44.8% to 1.03%), and -10.8% (-41.1% to 12.8%) for the first episode. No statistical evidence of an overall significant protective effect of Spf66 malaria vaccine against P. falciparum and P. vivax malaria was obtained in this trial.

**DNA Vaccines**

176. Ambroise-Thomas P, [Vaccination against malaria. Disappointments and hopes]. [Article in French] *Bull Acad Natl Med* 1997 Nov;181(8):1637-48; discussion 1648-50 After the first in vitro cultivation of Plasmodium falciparum 21 years ago, the prospect of anti-malarial vaccination arose many hopes, but, in the end, it so far has mainly given rise to doubts and disappointments. Technically, the problem is particularly difficult. Plasmodium falciparum has a very complex antigenic structure with several hundreds, if not several thousands, of different epitopes for each of the four main evolutive stages of the parasite (sporozoites, merozoites, gametocytes, ookinete) which correspond to different phase of the infection and could be a target for vaccination. Many of these epitopes are stage-specific and some of them vary from one strain to another. Adjuvants also play a major role and can qualitatively modify the type of immune response. The immune mechanisms also differ according to the final goal: anti-Plasmodium infection or anti-disease vaccine. Over the last few years, the first clinical assays have been carried out with the Spf66 vaccine, a synthetic complex protein directed against sporozoites and merozoites. In adults and children, the first results in South America and in East Africa were modest but encouraging. Unfortunately they were not confirmed by further studies in West Africa and South-East Asia. Two new types of vaccines are under preliminary clinical evaluation. One is directed against ookinete of Plasmodium falciparum (Pfs25 and Pfs28) and can stop the transmission from the mosquito. The other is an anti-sporozoite vaccine with a new immunogen (RTS,S) in which the circumsporozoite protein is fused to the hepatitis B surface antigen and can protect against infestation. New prospects and improvements are offered by the technique of DNA vaccines and will probably also result from better knowledge of cellular and molecular biology of the parasite which is being extensively studied (genomic structure). If new promising perspectives exist, it is particularly important to be careful to avoid such disappointments as those caused, in the past, by a too-optimistic and over-publicized presentation of some preliminary results. It is now certain that one or several malaria-vaccines will be available, but no one can seriously say when, for whom and how. In any case, it is unrealistic to hope that vaccine(s) alone will be able to eradicate such an epidemiologically complex disease as malaria. It is probable that only the coordinated use of all the techniques available (anti-vectorial protection and fight, chemoprophylaxis and chemotherapy, vaccination) will lead to success.

177. Michael Balter **Gene Sequencers Target Malaria Mosquito** Volume 285, Number 5427 Issue of 23 Jul 1999, pp. 508 - 509 A group of insect geneticists, genome researchers, and funding officials has put together a plan to open a new front in the war against malaria: the sequencing of the genome of
Anopheles gambiae, the mosquito primarily responsible for spreading the disease in Africa. The participants will submit proposals to major biomedical agencies in Europe and the United States to fund the project, which would take an estimated 5 years and cost between $50 million and $90 million. Malaria researchers hope that sequencing the genome will help them genetically engineer a mosquito that is resistant to the malaria parasite.

178. Wang R, Doolan DL, Le TP, Hedstrom RC, Coonan KM, Charoenvit Y, Jones TR, Hobart P, Margalith M, Ng J, Weiss WR, Sedegah M, de Taisne C, Norman JA, Hoffman SL. Induction of antigen-specific cytotoxic T lymphocytes in humans by a malaria DNA vaccine. Science 1998 Oct 16;282(5388):476-80 CD8+ cytotoxic T lymphocytes (CTLs) are critical for protection against intracellular pathogens but often have been difficult to induce by subunit vaccines in animals. DNA vaccines elicit protective CD8+ T cell responses. Malaria-naive volunteers who were vaccinated with plasmid DNA encoding a malaria protein developed antigen-specific, genetically restricted, CD8+ T cell-dependent CTLs. Responses were directed against all 10 peptides tested and were restricted by six human lymphocyte antigen (HLA) class I alleles. This first demonstration in healthy naive humans of the induction of CD8+ CTLs by DNA vaccines, including CTLs that were restricted by multiple HLA alleles in the same individual, provides a foundation for further human testing of this potentially revolutionary vaccine technology.
Public Health Statement on Malaria and the Use of DDT

As physicians and public health professionals, we recognize the continuing and even increasing threat posed in much of the world by malaria. The disease now causes clinical symptoms in 300 million to 500 million people each year. Between 1.5 million and 2.7 million die annually – mostly children under five years of age.\(^1\) Somewhere in the world, someone dies of malaria every 15 seconds. More than 40% of the world’s population, in 100 countries, is currently at risk for the disease.\(^2\) Aided by climatic changes like El Niño and global warming, malarial mosquitoes may actually be expanding their geographic ranges.

We know that malaria is both an effect of, and a contributor to extreme poverty in many places in the developing world. This is particularly true in the countries of sub-Saharan Africa, where 90% of the world’s malaria occurs,\(^3\) but where its victims are usually too poor to afford medical treatment or preventive measures. Worldwide, the direct and indirect economic costs of malaria are estimated at $2 billion each year.\(^4\)

Despite the staggering human and economic toll taken by malaria, the war against this disease is woefully underfunded. Research on malaria receives a fraction of the amount spent on other diseases. While the worldwide expenditure for asthma is estimated at U.S. $789, only $65 is currently spent for each malaria death.\(^5\) Drugs that were once effective are often inadequate due to

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\(^1\) World Health Organization.

\(^2\) Id.

\(^3\) World Health Organization, Division of Control of Tropical Disease.


\(^5\) Id.
the increasing resistance of the parasite that causes malaria. A vaccine has not yet been developed. Far from being eradicated, the disease and the vectors that carry it are stronger than ever.

For decades, the pesticide DDT was the weapon of choice against disease-carrying mosquitos, for its effectiveness at killing insects with few acute effects on people. Although many countries have since banned DDT, it is still used.

Over the last ten years, the World Health Organization (WHO), a primary source of expertise and guidance for national public health programs, has taken an ever stronger stand against the use of DDT because of growing concerns about human health effects. The tendency of DDT to concentrate in breast milk and, therefore, in the bodies of infants was identified as a potential health problem. In 1997, the WHO Assembly adopted a resolution that endorsed the use of DDT in government-sponsored public health programs only and urged that strong steps be taken to ensure that DDT was not diverted to private sector entities. Unfortunately, DDT continues to be used by the private sector in many countries.

As physicians and health professionals, we believe that DDT is no longer an appropriate tool in the fight against malaria. This extremely persistent pesticide poses a threat to the environment and, potentially, to public health globally. Although it has been banned or severely restricted in much of the world for years, its persistence and ability to travel long distances on air and water currents have made it a ubiquitous pollutant. It bioaccumulates in food chains and concentrates in species at the top, including humans. In wildlife, DDT and its metabolites have been linked with reproductive failures. In a strain of laboratory mice, DDT has induced cancer-like tumors. In humans, the possibility of longer-term effects cannot be excluded. Furthermore, some mosquito populations have grown increasingly resistant to DDT over the years, reducing its longer term effectiveness as an antimalarial tool and lending additional urgency to the need for its replacement by alternatives.

Alternatives to house spraying with DDT include the use of synthetic pyrethroid insecticides, which break down faster and tend not to bioaccumulate; biological controls such as the stocking of ponds and streams with mosquito larva-eating fish; and the use of barriers like bed nets and screens. Such methods are safe and environmentally sustainable, and have proven to be effective in a number of places, but they require community participation and a shift in thinking by local and national governments as well as intergovernmental aid organizations.
In 1997, Heads of State and Government of the 53 countries of the Organization for African Unity adopted the Harare Declaration on Malaria Prevention and Control, committing their countries to a renewed effort to control malaria. In 1998, the WHO’s Director General, Gro Harlem Brundtland pledged to “Roll Back Malaria” worldwide. And in the same year, nearly 100 governments began meeting under the auspices of the United Nations Environment Programme to negotiate a global agreement to eliminate 12 persistent organic pollutants, among them DDT.

As these efforts go forward, we offer the following recommendations for reducing malaria occurrence and facilitating the elimination of DDT:

1. **That all governments commit to the phase out and eventual elimination of DDT use and production as part of a global agreement on persistent organic pollutants (POPs) while ensuring that malarial risk management is maintained and improved using alternative means of vector control.**

2. **That the development and implementation of safe, sustainable alternative methods of mosquito control be a priority for all governments.** These should include targeted use of safer larvicides (biological control and non-persistent chemical control), and, where appropriate, safer chemical pesticides like synthetic pyrethroids for residual spraying.

3. **That, beginning immediately and while DDT use is being phased out, the following steps be taken by governments and aid organizations to ensure that its elimination does not compromise the health of people in malaria-endemic zones—**

   (a) **Implementation — by aid organizations as well as health agencies in malaria-endemic zones — of traditional public health and public education measures for controlling the spread of malaria.** These may include epidemiological surveillance, early and aggressive case detection and treatment, the distribution of bed nets and screens, and the mobilization of communities to eliminate vector breeding sites.

   (b) **Development of improved and affordable drugs for the treatment of malaria, and of an effective, affordable vaccine for the disease.** This must be a high priority of both the pharmaceutical industry and governments.
(c) *Commitment of increased spending by industrialized country governments toward research on malaria.* Given the new global economy and the possibility of increasing mosquito ranges due to climatic changes, it is in the interest of all countries to renew their commitment to the treatment and prevention of malaria.

(d) *Analysis of the efficacy and cost of varying control methodologies.* Respected practitioners believe it is necessary to adequately assess programs as they are implemented in order to speed the transition to non-DDT programs.