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MALARIA

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Introduction

This bibliography contains 182 citations and/or abstracts on malaria contained in one of the library database collections of the Environmental Health Project (EHP) of the U. S. Agency for International Development (USAID). The bibliography contains citations/abstracts of documents either held in the EHP Library or available through other sources, e.g., interlibrary loan or document order services.

The main purpose of the bibliography is to provide up-to-date information on malaria to researchers and field staff in developing countries where access to current journals and other publications may be limited or delayed. Due to space limitations the bibliography contains abstracts and not the full text of articles or reports. However, library studies have shown that a detailed abstract can be as useful as the complete text in the majority of cases.

The bibliography focuses on the prevention and control of malaria. It does not include abstracts on such areas as malaria vaccines, clinical treatment of malaria, etc. Since the EDP library began its operations just over a year ago, the vast majority of citations and abstracts were published in 1994 or 1995. We hope to update the bibliography on a periodic basis, and later editions of the bibliography will be cumulative ones.

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The bibliography contains a **Subject List** of the 118 terms or subjects used as keywords, and both a **Subject Index** and an **Author Index**. While either index can stand alone in providing a citation source, the latter contains many abstracts as well as the citations.

To make optimum use of this publication look at the **Subject List** for a keyword or geographic term, then locate that term in the **Subject Index**. If the only information you need is the title, principal author or publisher for an article or publication, then you will find it here in the **Subject Index**. However, if you would like to see if there is an abstract in addition to the citation, then look up the principal author listed alphabetically in the **Author Index**.

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- Morgan, H. G., **Placental Malaria and Low Birthweight Neonates in Urban Sierra Leone.** *Annals of Tropical Medicine and Parasitology* 88, no. 6 (December 1994): 575-80.
- Rasheed, F. N., et al, **Relationships Between Maternal Malaria and Malarial Immune Responses in Mothers and Neonates.** *Parasite Immunology* 17, no. 1 (January 1995): 1-10.
- Schultz, L. J., et al, **Antimalarials During Pregnancy: A Cost-Effectiveness Analysis.** *Bulletin of the World Health Organization* 73, no. 2 (1995): 207-14.
- Schultz, L. J., et al, **The Efficacy of Antimalarial Regimens Containing Sulfadoxine-Pyrimethamine and/or Chloroquine in Preventing Peripheral and Placental Plasmodium Falciparum Infection Among Pregnant Women in Malawi.** *American Journal of Tropical Medicine and Hygiene* 51, no. 5 (November 1994): 515-22.
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F56.10M 2112

ZAIRE

- Karch, S., et al, **Impact of Deltamethrin-Impregnated Bednets on Biting Rates of Mosquitoes in Zaire.** *Journal of the American Mosquito Control Association* 11, no. 2 Part 1 (June 1995): 191-94.

ZOOPROPHYLAXIS

- Bouma, M., et al, **Failure of Passive Zooprophylaxis: Cattle Ownership in Pakistan Is Associated With a Higher Prevalence of Malaria.** *Transactions of the Royal Society of Tropical Medicine and Hygiene* 89, no. 4 (July 1995-August 1995): 351-53.

Achidi, E. A., et al, **A Longitudinal Study of Seroreactivities to Plasmodium Falciparum Antigens in Nigerian Infants During Their First Year of Life.** *Acta Tropica* 59, no. 2 (May 1995): 173-83.

The kinetics of passively transferred maternal antibodies to antigens of Plasmodium falciparum and the dynamics of acquisition of these antibodies during the first year of life was investigated in infants born in a malaria endemic area of south-western Nigeria. Blood samples were collected from the infants at bi-monthly follow-up visits for the analysis of total serum immunoglobulin G, IgM, IgA and antibodies to the antigen Pf155/RESA and against synthetic peptides representing antigenic sequences of the blood stage antigen Pf155/RESA and Ag332 or the circumsporozoite protein (CSP). IgG levels fell from birth till 4 months and a steady rise was observed thereafter till ten months of life. On the contrary mean IgM and IgA levels increased throughout the first year of life. Generally the number of infants positive for antibodies to the antigens under investigation fell from birth and between 4-6 months of age was either low or absent. None of the infants were positive for antibodies to the peptide representing Ag332 during the first year of life. The earliest seroconversion was detected at 6 months of age involving the Pf155/RESA and (NANP)(6) antigens. The results indicate a high level of exposure in this study area to malaria infection early in life. The finding of an active antibody response to malarial antigens in infancy encourages the hope that a malaria Vaccine administered early in life may accelerate the development of naturally acquired immunity and thus protect the population most at risk.

Adagu, I. S., et al, **Antimalarial Drug Response of Plasmodium Falciparum From Zaria, Nigeria.** *Transactions of the Royal Society of Tropical Medicine and Hygiene* 89, no. 4 (July 1995-August 1995): 422-25.

The sensitivity of Zaria strains of Plasmodium falciparum to chloroquine, mefloquine, quinine and sulphadoxine/pyrimethamine was investigated 5 years after the appearance of in vivo/in vitro chloroquine resistance in urban Zaria. Infections in 36/43 children (83.7%) treated with chloroquine were sensitive while those in 7(16.3%) were resistant. 8/13 isolates cultured (61.5%) were sensitive in vitro to chloroquine and 5(38.5%) were resistant. Of the cultured isolates, 13/13(100%), 12/13(92.3%) and 5/7(71.4%) showed mefloquine, quinine and sulphadoxine/pyrimethamine sensitivity, respectively. The results confirmed chloroquine and sulphadoxine/pyrimethamine resistance in urban Zaria and revealed emerging quinine resistance. Resistance to chloroquine and sulphadoxine/pyrimethamine is at RI level and chloroquine should continue to be the first-line drug for the treatment and prevention of P. falciparum infection in the Zaria area of northern Nigeria. We suggest that, while quinine serves as second-line drug mefloquine should be reserved for infections resistant to chloroquine, quinine and sulphadoxine/pyrimethamine.

Aikins, M. K., et al, **Attitudes to Malaria, Traditional Practices and Bednets (Mosquito Nets) As Vector Control Measures.** *Journal of Tropical Medicine and Hygiene* 97, no. 2 (1994): p. 81-86.

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Akanmori, B. D., et al, **A Longitudinal Study of Malaria Infection, Morbidity and Antibody Titres in Infants of a Rural Community in Ghana.** *Transactions of the Royal Society of Tropical Medicine and Hygiene* 89, no. 5 (September 1995-October 1995): 560-561. **TH049**

Akenji, T. N., et al, **Definition of Populations at Risk for Plasmodium Falciparum Infection in Three Endemic Areas of Cameroon.** *Journal of Parasitology* 80, no. 6 (December 1994): 895-99.

Blood samples were collected from 285 individuals attending hospitals in 1 of 3 different regions of Cameroon. Of these, 89 had Plasmodium falciparum parasitemia. Prevalence in the Douala region was drastically reduced above the age of 19. In the Njinikom and Bamenda regions, on the other hand, an appreciable decline in prevalence was not observed until over the age of 49. Enzyme-linked immunosorbent assay (ELISA) values indicate that in Douala, high antibody titers to P. falciparum were present in all age groups tested. In Njinikom and Bamenda, an age dependence was seen in the response, with sera from individuals above 20 having significantly higher ELISA values compared with those below age 20. Generally, individuals with high antibody titers had low or no parasitemia. Results suggest that future malaria control and treatment measures might target high risk populations such as those defined in this study.

Asinas, C. Y., et al, **Evaluation of Selective Spraying of Bendiocarb (Ficam Vc(R)) for the Control of Anopheles-Flavirostris in the Philippines.** *Journal of the American Mosquito Control Association* 10, no. 4 (December 1994): 496-500.

The effectiveness of selective and complete spray applications of bendiocarb for the control of the major malaria vector, Anopheles flavirostris, was compared in an experimental hut trial in the Philippines. Selective spraying involved treatment of the vector's preferred indoor resting sites, namely, the lower wall areas, wall areas immediately surrounding the doors and windows, and eaves. Complete spraying involved treatment of all internal wall and ceiling areas, and the eaves. At intervals over a 6-month period, mosquitoes were released into the huts and recaptured within 13 h, either inside the huts, or within the interior of net traps placed over the huts. Mortality levels differed by <8% between the spray regimes over the posttreatment period, with both regimes giving 75-100% kill of An. flavirostris during the initial 3 months. The time spent spraying and spray volume used during treatment of village houses were respectively 36 and 49% less under the selective spraying regime. Selective application of bendiocarb therefore shows considerable promise, both in terms of efficacy and cost effectiveness, for the control of An. flavirostris in the Philippines.

Astagneau, P., et al, **Antibodies to a Plasmodium Falciparum Blood-Stage Antigen As a Tool for Predicting the Protection Levels of Two Malaria-Exposed Populations.** *American Journal of Tropical Medicine and Hygiene* 53, no. 1 (July 1995): 23-28.

To evaluate the ability of antibodies to Plasmodium, falciparum ring-infected erythrocyte surface antigen (Pf155/RESA) epitopes to discriminate between individuals well protected or poorly protected against malaria, a receiver operating characteristic analysis was performed in two

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populations living in Madagascar and Malawi. The definition of protection was based on longitudinal measurements of clinical malarial attacks during the season of high malaria transmission in the Madagascar study, and on a cross-sectional measurement of parasitemia in the Malawi study. Antibodies to peptides reproducing the 4-mer, 8-mer, and 11-mer of the Pf155/RESA were tested for their reactivities using the Falcon assay screening test-enzyme-linked immunosorbent assay. Maximal detection of poorly protected individuals (specificity = 100%) corresponded to high cutoff antibody titers (range = 1.65-3.0 optical density [OD] units in the Madagascar study and 0.67-1.42 OD units in the Malawi study) and a sensitivity less than 50%. For a given sensitivity of 50%, specificity ranged from 55% to 62% in the Madagascar study, and from 67% to 94% in the Malawi study. The antibody cutoff titers corresponding to minimal misclassification rates ranged from 0.24 to 1.73 OD units in the Madagascar study and from 0.15 to 0.55 OD units in the Malawi study. For each antibody, the highest detectability value as measured by the area under the curve was obtained for anti-R11 in the Malawi study (0.838). In demonstrating such qualities, antibodies to Pf155/RESA epitopes could be used for screening poorly protected populations in which malaria control programs have to be implemented.

Babiker, H. A., et al, **Gene Flow and Cross-Mating in Plasmodium Falciparum in Households in a Tanzanian Village.** *Parasitology* 111, no. Part 4 (November 1995): 433-42.

The diversity of the genes encoding 2 merozoite surface proteins (MSP-1 and MSP-2) of *Plasmodium falciparum* has been examined in parasites infecting members of 4 households in a village in Tanzania. The polymerase chain reaction (PCR) was used to characterize allelic variants of these genes by the sizes and sequences of regions of tandemly repeated bases in each gene. In each household extensive polymorphism was detected among parasites in the inhabitants and in infected mosquitoes caught in their houses. Similar frequencies of the alleles of these genes were observed in all households. Capture-recapture data indicated that both *Anopheles gambiae* and *A. funestus* freely dispersed among households in the hamlet. The results confirm that cross-mating and gene flow occur extensively among the parasites, and are discussed within the context of spatial clustering of natural populations of *P. falciparum*.

Babiker, H. A., et al, **Genetic Changes in the Population of Plasmodium Falciparum in a Sudanese Village Over a Three-Year Period.** *American Journal of Tropical Medicine and Hygiene* 53, no. 1 (July 1995): 7-15.

The prevalence of alleles of genes of the *Plasmodium falciparum* population of Asar village in eastern Sudan was monitored over three consecutive years. The characters studied were parasite surface antigens, proteins detected by two-dimensional polyacrylamide gel electrophoresis, enzymes, and drug response. Fluctuations in allele prevalences from one year to another were detected and are discussed in the context of seasonality of malaria transmission in the region studied.

Baird, J. K., **Host Age As a Determinant of Naturally Acquired Immunity to Plasmodium Falciparum.** *Parasitology Today* 11, no. 3 (March 1995): 105-11.

The usual course of infection by Plasmodium falciparum among adults who lack a history of exposure to endemic malaria is fulminant. The infection in adults living with hyper- to holoendemic malaria is chronic and benign. Naturally acquired immunity to falciparum malaria is the basis of this difference. Confusion surrounds an essential question regarding this process: What is its rate of onset? Opinions vary because of disagreement over the relationships between exposure to infection, antigenic polymorphism and naturally acquired immunity. In this review, Kevin Baird discusses these relationships against a backdrop of host age as a determinant of naturally acquired immunity to falciparum malaria.

Baird, J. K., et al, **Primaquine for Prophylaxis Against Malaria Among Nonimmune Transmigrants in Irian Jaya, Indonesia.** *American Journal of Tropical Medicine and Hygiene* 52, no. 6 (June 1995): 479-84.

A comparison of primaquine versus chloroquine for prophylaxis among nonimmune transmigrants from Java and Bali in the hyperendemic Arso region of Irian Jaya, Indonesia was conducted. Forty-five subjects received 0.5 mg of primaquine base/kg of body weight every other day, and 54 people in the same village received weekly 5 mg of chloroquine base/kg for 16-19 weeks beginning in December 1992. Plasmodium falciparum accounted for 18 of 30 infections with chloroquine, and four of five infections among subjects receiving primaquine. Plasmodium vivax was found in 12 people taking chloroquine but in just one person taking primaquine. The risk of malaria among people taking chloroquine relative to that among subjects taking primaquine was 3.96 (P = 0.014) for P. falciparum and 10.56 (P = 0.012) for P. vivax. Primaquine was better tolerated than chloroquine. The minimal protective efficacy for primaquine prophylaxis was 74% against P. falciparum and 90% against P. vivax among nonimmune children and adults living in Irian Jaya. These findings require confirmation with randomized, double-blinded, and placebo-controlled trials.

Basco, L. K., et al, **In Vitro Activity of Atovaquone Against the African Isolates and Clones of Plasmodium Falciparum.** *American Journal of Tropical Medicine and Hygiene* 53, no. 4 (October 1995): 388-91.

The in vitro activity of atovaquone (566C80) was evaluated and compared with that of chloroquine, quinine, mefloquine, halofantrine, artemether, pyrimethamine, and cycloguanil against African isolates and clones of Plasmodium falciparum using an isotopic, semimicro, drug susceptibility test. Atovaquone was highly active against the chloroquine-susceptible L-3 (geometric mean 50% inhibitory concentration [IC₅₀] = 0.978 nM) and L-16 clones (mean IC₅₀ = 0.680 nM) and against the multidrug-resistant FCM 29 clone (mean IC₅₀ = 1.76 nM). Similar low IC₅₀ values for atovaquone were observed against the chloroquine-susceptible isolates (n = 35; geometric mean IC₅₀ = 0.889 nM) and the chloroquine-resistant parasites (n = 26; geometric mean IC₅₀ = 0.906 nM). The in vitro responses between atovaquone and the other antimalarial drugs were not correlated, indicating the absence of in vitro cross-resistance. The high in vitro

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activity of atovaquone without any in vitro evidence for cross-resistance with other antimalarial drugs against the naturally occurring malaria parasites is a factor that favors further development of the drug for clinical use.

Bayoumi, R. A. L., et al, **Uptake and Efflux of Chloroquine by Chloroquine-Resistant Plasmodium Falciparum Clones Recently Isolated in Africa.** *Acta Tropica* 58, no. 2 (November 1994): 141-49.

In recently isolated African Plasmodium falciparum clones, the intracellular chloroquine concentration at steady-state, under standard culture conditions, could not differentiate chloroquine-sensitive from resistant parasites. However, under an atmosphere of air the chloroquine-resistant P. falciparum clones released pre-accumulated [H-3]chloroquine more rapidly than sensitive clones. The very fast efflux of the preaccumulated drug from chloroquine-resistant (CQR) parasites resulted in a differential in the drug retained by resistant and sensitive parasites. The chloroquine-sensitive parasites retained 2-3 times more chloroquine than resistant parasites. The steady-state uptake of [H-3]chloroquine appeared to be enhanced by verapamil and desipramine in the chloroquine-resistant clones, while the opposite was observed with sensitive clones. This confirmed the suggestion that verapamil inhibits the rapid efflux in CQR parasites resulting in a readily detectable increase in chloroquine accumulation. These observations indicate that the biochemical phenotypes of African chloroquine-resistant P. falciparum are similar to those reported from S.E. Asia and Latin America and are consistent with a common molecular basis for the phenomenon.

Beach, Raymond F., et al, **Effectiveness of Permethrin-Impregnated Bed Nets and Curtains for Malaria Control in a Holoendemic Area of Western Kenya.** *American Journal of Tropical Medicine and Hygiene* 49, no. 3 (1993): p. 290-300.

Beck, Louisa R., et al, **Remote Sensing As a Landscape Epidemiologic Tool to Identify Villages at a High Risk for Malaria Transmission.** *American Journal of Tropical Medicine and Hygiene* 51, no. 3 (1994): p. 271-80.

Bockarie, M. J., et al, **Malaria in a Rural Area of Sierra Leone.III. Vector Ecology and Disease Transmission.** *Annals of Tropical Medicine and Parasitology* 88, no. 3 (1994): pp. 251-62.

Bockarie, M. J., et al, **Vectorial Capacity and Entomological Inoculation Rates of Anopheles Gambiae in a High Rainfall Forested Area of Southern Sierra Leone.** *Tropical Medicine and Parasitology* 46, no. 3 (September 1995): 164-71.

We report the first study of gonotrophic cycle duration, survival rates, pre-gravid rates, vectorial capacity and chromosomal polymorphism of Anopheles gambiae s.s. in Sierra Leone. In the village of Bayama in the Southern Province, An. gambiae was the only species found to be naturally infected with Plasmodium falciparum and it constituted 99.7% of 22,541 anopheline mosquitoes caught. Chromosomal studies revealed only An. gambiae s.s. out of 66 females

examined for chromosomal polymorphism, 61 (92.4%) had the 2LA inversion in the standard arrangement. Other inversions observed in low frequencies included 2Rcu and 2Ru. We estimated a gonotrophic cycle length of three days and survival rate per gonotrophic cycle of 0.59 for this species. The mean daily survival rate of *An. gambiae* was 0.85 and the entomological inoculation rate was 1,235 infective bites/person/year. Blood-meal ELISA tests showed that the species was very anthropophilic and that there were an estimated 35.4 daily inoculations per infective case. The epidemiological significance of these entomological parameters is discussed in the light of parasitological results for nearby villages.

Bouma, M. J., et al, **Prevalence and Clinical Presentation of Glucose-6-Phosphate Dehydrogenase Deficiency in Pakistani Pathan and Afghan Refugee Communities in Pakistan; Implications for the Use of Primaquine in Regional Malaria Control Programmes.**

Transactions of the Royal Society of Tropical Medicine and Hygiene 89, no. 1 (January 1995-February 1995): 62-64.

Glucose-6-phosphate dehydrogenase (G-6-PD) deficiency surveys in Afghan refugees and a local community in the North-West Frontier Province, Pakistan, showed that this trait was most common among Pathan and Uzbek refugees (15.8% and 9.1% respectively). The prevalence among Pakistani Pathans was 7.0%, and that in Tajik and Turkoman refugees was 2.9% and 2.1% respectively. Hospital studies showed that the type of G-6-PD deficiency in Pathans could cause severe haemolytic crises. The potentially fatal side effects of primaquine treatment in the Pathan communities, and the high risk of re-infection, render the anti-relapse treatment policy for *Plasmodium vivax* obsolete. However, epidemic conditions of *P. falciparum* malaria may justify the use of primaquine as a gametocidal drug, administered as a single dose, during the transmission season. These findings necessitate revision of the recommendations for the use of primaquine in the area.

Bouma, M. J., et al, **Fenitrothion Intoxication During Spraying Operations in the Malaria Programme for Afghan Refugees in North West Frontier Province of Pakistan.** *Tropical and Geographical Medicine* 47, no. 1 (1995): 12-14.

During the experimental use of fenitrothion to replace malathion for the control of malaria in North West Frontier Province of Pakistan, serious intoxication of Afghan refugee spraymen occurred. A few weeks after commencement of the spraying operations, cholinesterase levels had fallen to 43.8% in personnel mixing the insecticide, and to 60.7% in spraymen, as measured by tintometry. Most of the personnel reported symptoms of overexposure and the spraying operations had to be discontinued. Intoxication of personnel resulted in poor coverage of the target area. High ambient temperatures during Pakistan's spray season discourage the use of full-protective clothing. Fenitrothion intoxication observed in the Afghan refugee programme, and similar experiences in Pakistan in the past, suggest that this insecticide is too toxic for routine use, when the compliance with safety precautions cannot be effectively supervised.

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- Bouma, M., et al, **Failure of Passive Zooprophylaxis: Cattle Ownership in Pakistan Is Associated With a Higher Prevalence of Malaria.** *Transactions of the Royal Society of Tropical Medicine and Hygiene* 89, no. 4 (July 1995-August 1995): 351-53.
To examine the possibility that domestic cattle kept in house courtyards might protect occupants against malaria through zooprophylaxis, parasite prevalence surveys were conducted of schoolchildren in Pakistani and Afghan refugee villages and analysed according to whether each child's family kept cattle. Parasite prevalence (15.2%) was significantly greater among children of families which kept cattle than among those which did not (9.5%). Comparison of prevalence between different villages revealed a positive correlation between parasite rates and the proportion of families owning cattle. The latter finding supports the prediction of the Sota-Mogi theoretical model that domestic animals can enhance rather than reduce malaria transmission when vectors are zoophilic, the infection rate low, and the human:cattle ratio high. All these conditions applied in the study area.
- Bouwman, H., et al, **Malaria Control and Longitudinal Changes in Levels of DDT and Its Metabolites in Human Serum From KwaZulu.** *Bulletin of the World Health Organization* 72, no. 6 (1994): 921-30.
Blood samples were obtained on four occasions over a 12-month period from individuals living in KwaZulu, South Africa, who had been exposed to DDT (1,1,1-trichloro-2,2-bis(4-chlorophenyl)ethane) as a consequence of its use in their homes to control transmission of malaria. The longitudinal changes in serum DDT and its major metabolites, DDE and DDD, were determined. No additional risk was considered to have been presented by the increases that occurred following application of the pesticide. There were significant increases in DDT, DDE and Sigma DDT (DDT + its metabolites) for the age group greater than or equal to 21 years, but for the age group 3-20 years a reduction in serum levels occurred over 12 months. Two concurrent processes probably govern the increase and decrease in serum levels, and the relative contributions of each interchange as the individual becomes older. The results suggest that children in KwaZulu experience conditions that differ from those of their parents, as well as from those that affect children in developed countries. In consequence, it is desirable that risk assessments of vector control chemicals consider all sectors of a population.
- Bozhao, X. U., et al, **Malaria in Hubei Province, China: Approaching Eradication.** *JNL TROP MED & HYG* 97, no. 5 (1994): pp. 277-81.
- Brabin, Loretta, *Cultural Factors and the Epidemiology of Malaria and Viral Infections in Women: A Study in Madang, Papua New Guinea* (1948). **F56.10M-98**
- Brasseur, P., et al, **Sensitivity of Plasmodium Falciparum to Amodiaquine and Chloroquine in Central Africa: A Comparative Study in Vivo and in Vitro.** *Transactions of the Royal Society of Tropical Medicine and Hygiene* 89, no. 5 (September 1995-October 1995): 528-30.

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A comparative study in vivo of amodiaquine efficacy (35 mg/kg over 3 d) and chloroquine (25 mg/kg over 3 d) was conducted in 1991 and 1992 in Cameroon and Congo in 123 patients with uncomplicated *Plasmodium falciparum* malaria. Amodiaquine was more effective than chloroquine, with parasite clearance by day 7 in 79.7% of the patients compared with 59.4%. Sixteen of 32 (50%) *P. falciparum* Isolates tested in vitro were resistant to chloroquine and only 3 of 34 (9%) were resistant to amodiaquine. 5.3% of patients treated with amodiaquine complained of pruritus and 18.7% of nausea, compared with 15.7% and 5% respectively of those treated with chloroquine.

Bretas, Gustavo, **Geographical Information Systems for the Study and Control of Malaria.** *Geographic Information Systems for Health and the Environment* (June 1995). Z68 2190

Brown, N., **Severe Malaria in Children at Port Moresby General Hospital, Papua New Guinea.**

Tropical and Geographical Medicine 47, no. 3 (1995): 107-10.

The demographic and clinical features of severe malaria in children on the south coast of Papua New Guinea have never been clearly documented. This prospective study sought to define the associations between ethnic origin, domain, age, nutritional status and severe malaria in this group and to assess significant clinical features, evaluate the use of a coma score as a prognostic indicator in cerebral malaria and to determine the ultimate outcome. Twenty patients with severe malaria (17 cerebral malaria and 3 severe anaemia) were studied. Their mean age of 4.96 years was significantly greater than that of matched controls with uncomplicated *Plasmodium falciparum* infection with mean age 3.79 years ($0.02 < p < 0.05$), Nutritional status was not a significant independent risk factor when controlled against inpatients with other diagnoses, Low coma scores (Adelaide scale 4/14 or less) sensitively predicted the risk of dying vs survival, The mortality of 18% was comparable with other series, Current standard treatment with quinine and Fansidar was effective and no early recrudescence was encountered in the survivors. The degree of intermarriage and migration between regions precluded firm conclusions from being drawn as to the relevance of ethnic and geographical factors in the epidemiology of severe malaria in this region.

Burchard, G. D., et al, **Increased Erythropoietin Production in Children With Severe Malarial Anemia.** *American Journal of Tropical Medicine and Hygiene* 53, no. 5 (November 1995): 547-51.

Plasma immunoreactive erythropoietin concentrations were determined in 84 children with *Plasmodium falciparum* malaria in Gabon. There was an inverse log/linear relationship between hemoglobin or hematocrit and plasma erythropoietin, indicating that erythropoietin levels increased exponentially as circulating hemoglobin decreased. These results show that *P. falciparum* malaria does not lead to decreased erythropoietin production, and in turn reduced erythropoietin production does not contribute to the pathogenesis of malarial anemia. There is an adequate response of erythropoietin to anemia in children with *P. falciparum* malaria.

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Burkot, T. R., et al, **The Value of Vector-Based Estimates of Malaria Transmission.** *Annals of Tropical Medicine and Parasitology* 89, no. 2 (April 1995): 125-34.

Estimating malaria transmission in the human is fraught with problems of reconciling clinical illness with parasitological status. It follows that there is a role for entomological assessments as an independent outcome variable and as a process indicator. Advances in DNA technology have expanded our capacity to identify vectors rapidly, while immunoassays allow the inoculation rate to be measured simultaneously in a number of villages with a precision 3-fold greater than measurements of vectorial capacity. The rapid specific identification of parasites in vectors has been utilized to estimate survivorship in mosquitoes per extrinsic incubation period (EIP), circumventing the need for estimates of survivorship per feeding cycle, lengths of feeding cycles or the length of the EIP. While lack of accuracy does not universally preclude the utility of estimates of the components of vectorial capacity in serving as relative estimates of transmission, particularly as process indicators, more accurate estimates of these parameters, particularly for density-dependent variables, may diminish the associated bias in their measurement. When this is accomplished, we will come closer to obtaining true rather than relative estimates of transmission.

Busvine, J. R., *Disease Transmission by Insects: Its Discovery and 90 Years of Effort to Prevent It* (1993). **F56 2475**

Contents. Diseases transmitted by mosquitoes. Diseases transmitted by mites and ticks. Diseases due to viruses. Control measures pre-ddt. The impact of the new pesticides. Modern problems and possibilities.

Chadee, D. D., et al, **Blood-Digestion Kinetics of Four Anopheles Species From Trinidad, West Indies.** *Annals of Tropical Medicine and Parasitology* 89, no. 5 (October 1995): 531-40.

The blood-digestion kinetics of *Anopheles albitarsis*, *An. aquasalis*, *An. bellator* and *An. homunculus* were determined in the laboratory using females collected from two field sites in Trinidad. *Anopheles aquasalis* displayed the highest rate of haemolysis (giving an absorbance of 0.36 at 410 nm), followed by *An. albitarsis* (0.16), *An. bellator* (0.07) and *An. homunculus* (0.05). Trypsin activity peaked 12-24 h after blood feeding and then declined to zero at 60 h in all four species. *Anopheles albitarsis* had significantly higher maximum trypsin activity (0.69 units) than *An. aquasalis* (0.28), *An. bellator* (0.18) or *An. homunculus* (0.12) ($P < 0.01$). Aminopeptidase activity patterns were similar for *An. aquasalis*, *An. bellator* and *An. homunculus*, with peak activity at 18 h. Among the *An. albitarsis* mosquitoes, peak aminopeptidase activity occurred at 24 h. The peritrophic membrane developed 18, 30, 30 and 36 h post-feeding in *An. aquasalis*, *An. albitarsis*, *An. bellator* and *An. homunculus*, respectively. Stage V ovarian follicles Began to mature 36 h after *An. albitarsis* and *An. bellator* fed to repletion and after 48 h in *An. aquasalis* and *An. homunculus*. Ovarian development in the four species was not affected by patterns of erythrocyte haemolysis, proteolytic enzyme activity or peritrophic-membrane development. The inter- and intra-specific variations observed in the

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blood-processing physiology of the four species of *Anopheles* are briefly discussed in terms of phylogeny.

Charlwood, J. D., et al, **A Field Trial With Lambda-Cyhalothrin (ICON) for the Intradomiciliary Control of Malaria Transmitted by *Anopheles Darlingi* Root in Rondonia, Brazil.** *Acta Tropica* 60, no. 1 (September 1995): 3-13.

A two stage field trial comparing the effects of Lambdacyhalothrin (ICON) and DDT when used as residual sprays on the inside surfaces of houses, was conducted in the Machadinho and Jaru areas of Rondonia, Brazil, in 1987 and 1988. In 1987 houses along two 16 km contiguous stretches of a main and a side road were sprayed and the effects on malaria vectors monitored for the succeeding year. In the second stage approximately 55 000 houses in both districts were sprayed with ICON and the effect on malaria incidence measured by passive case detection. Of the eleven species of *Anopheles* caught in indoor and peridomiciliary collections *A. darlingi* was the commonest and is recognised as the most important vector in Brazil, ICON at either of two concentrations in bioassays killed more mosquitoes than DDT at each test from seven to twelve months after spraying. A rise in the number of *A. darlingi* collected eight months after spraying with DDT was not so marked in the ICON areas. Side effects of the insecticide were limited. The number of reported *Plasmodium falciparum* cases in the second phase declined 76% in Machadinho after spraying with ICON to 2851 cases, In Jaru there was a 28% reduction. The observed efficacy of the insecticide, its ready acceptance by the local populace, and its cost effectiveness make it a more useful insecticide for anti-malaria campaigns than DDT.

Cheng, H. L., et al, **Large-Scale Spraying of Bednets to Control Mosquito Vectors and Malaria in Sichuan, China.** *Bulletin of the World Health Organization* 73, no. 3 (1995): 321-28.

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 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.

Choi, H. W., et al, **The Effectiveness of Insecticide-Impregnated Bed Nets in Reducing Cases of Malaria Infection: A Meta-Analysis of Published Results.** *American Journal of Tropical Medicine and Hygiene* 52, no. 5 (May 1995): 377-82.

The use of insecticide-impregnated bed nets to minimize human-vector contact may reduce the incidence. Consequently, several field trials have evaluated their effectiveness as a malaria

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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.

Clark, G. G., **Mosquito Vector Control and Biology in Latin America - A Fifth Symposium - Introduction.** *Journal of the American Mosquito Control Association* 11, no. 3 (September 1995): 343.

The fifth Spanish language symposium presented by the American Mosquito Control Association (AMCA) was held as part of the 61st Annual Meeting in Portland, OR, in March 1995. The principal objective, as for the previous 4 symposia, was to increase and stimulate greater participation in the AMCA by vector control specialists, public health workers, and academicians from Latin America. This publication includes summaries of 20 presentations that were given in Spanish by participants from 6 countries in Latin America and the USA. The symposium included the following topics: ecological and genetic studies of anopheline vectors of malaria, laboratory and field evaluation of chemical and biological control agents for several mosquito species, and community control of *Aedes aegypti*.

Collins, F. H., **Prospects for Malaria Control Through the Genetic Manipulation of Its Vectors.** *Parasitology Today* 10, no. 10 (October 1994): pp. 369-70.

Coosemans, M., et al, **A Hundred Per Cent of Fields Positive in a Thick Film: A Useful Indicator of Relative Changes in Morbidity in Areas With Seasonal Malaria.** *Annals of Tropical Medicine and Parasitology* 88, no. 6 (December 1994): 581-86.

The classical method of estimating the density of *Plasmodium falciparum* in blood, by counting the number of trophozoites per leucocyte, is compared with a method in which the proportion of microscope fields in a thick film that include at least one asexual form is evaluated. Mean densities of 144 and 1920 trophozoites/ μ l blood gave 9.5% and 99.5% positive fields, respectively, and < 5% of slides with 100% positive fields were of blood with < 2000 trophozoites/ μ l. The proportion with high parasitaemia (PHP) in a population, defined as the proportion of individuals with 100% positive fields, is proposed as a simple and reliable indicator of relative changes in malaria morbidity due to seasonal fluctuations or control activities. However, the use of this index is limited to areas with intermediate malaria stability. Data from a

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longitudinal survey in Burundi, presented to illustrate the use of PHP, show that PHP undergoes important fluctuations related to transmission. In contrast to the parasite index, the amplitude of fluctuations in PHP decreases with age as a result of acquired protective immunity. Although two health centres, one in a vector control area and one in an area with no control, reported similar proportions of cases of clinical malaria among their patients, PHP was about three times lower in patients from the vector control area. The estimation of the efficacy of a malaria control programme from simple clinical information appears unreliable. Sentinel health centres, each equipped with a microscope to estimate PHP, may often be better indicators of changes in morbidity.

Cope, S. E., et al, **New Record of the Malaria Vector *Anopheles Sergentii* in the Southern Nile Valley of Egypt.** *Journal of the American Mosquito Control Association* 11, no. 1 (March 1995): 145-46.

Twelve adult female *Anopheles sergentii* were collected from 2 villages in the Nile River Valley in Aswan Governorate, Egypt, in August of 1993. No immature forms were found during limited sampling. This is the first record of this malaria vector in Aswan Governorate and represents the southernmost distribution in northern Africa.

Coxsingham, J., et al, **Assessment of the Association Between Three *Pfmdr1* Point Mutations and Chloroquine Resistance in Vitro of Malaysian *Plasmodium Falciparum* Isolates.** *Transactions of the Royal Society of Tropical Medicine and Hygiene* 89, no. 4 (July 1995-August 1995): 436-37.

Crook, S. E., et al, **The Effect of Permethrin-Impregnated Wall-Curtains on Malaria Transmission and Morbidity in the Suburbs of Maputo, Mozambique.** *Tropical and Geographical Medicine* 47, no. 2 (1995): 64-67.

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 *An. 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 *An. 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.

d'Alessandro, U., et al, **Mortality and Morbidity From Malaria in Gambian Children After Introduction of an Impregnated Bednet Programme.** *Lancet* 345, no. 8948 (February 1995): 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 ail-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 was 38% (0.62 [0.46-0.83], $p=0.001$). A 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.

Defo, B. K., **Epidemiology and Control of Infant and Early Childhood Malaria: A Competing Risks Analysis.** *International Journal of Epidemiology* 24, no. 1 (February 1995): 204-17. Background. Against increasing malaria problems in most tropical countries, very little is known about the socio-epidemiological determinants of this condition. Methods. Using extensive information on a representative sample of 9774 newborns followed for 2 years and multi-state hazards models, this study investigates jointly the determinants of paediatric mortality from malaria and other causes. Results. Malaria contributes to one out of every 10 infant deaths. Malarial mortality covaries with dwelling conditions, antenatal care attendance, parity, infant feeding practices, intercurrent infections, and child's immunization status. Lack of antenatal care, lack of immunization in childhood and sub-standard living conditions of overcrowding are the major risk factors of malanial and non-malarial mortalities, even after correcting for unobserved heterogeneity. Conclusions. These findings suggest that the impact of malaria on infant and early childhood health and survival might be much more important than usually thought. Antenatal care attendance, improved housing conditions and childhood immunization practices are potentially cost-effective strategies for malaria control. The competing risks analysis formulated here is offered as a suitable means of analysing cause-specific mortality differentials.

Demirhan, O., et al, **Bloodfeeding Behavior of Anopheles Sacharovi in Turkey.** *Journal of the American Mosquito Control Association* 11, no. 1 (March 1995): 11-14.

The feeding habits of *Anopheles sacharovi* under natural conditions and in feeding rooms were investigated by use of the gel diffusion technique. Mosquitoes were collected from various villages of Cukurova and also from feeding rooms especially prepared for these experiments. Human, cow, sheep, chicken, horse, and donkey were used as hosts in these rooms. The results showed that *An. sachauovi* is a zoophilic species. The females preferred donkey when human, cow, sheep, chicken, and horse were equally available. Their preference changed to horse, cow, and sheep in the absence of donkey. The host preference index (HPI) was always smaller than 1 for humans in habitats offering a choice of hosts. The human blood index was high only in

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human dwellings. In other habitats numbers of mosquitoes feeding on animals were higher than on humans. Although the human blood index was low, *An. sacharovi* is the principal human malaria vector in Turkey partly because a significant proportion of those resting in human dwellings have fed upon the occupants, and partly because of the uneven distribution of human and animal hosts.

Dietze, R., et al, **The Diagnosis of Plasmodium Falciparum Infection Using a New Antigen Detection System.** *American Journal of Tropical Medicine and Hygiene* 52, no. 1 (January 1995): 45-49.

With the widespread emergence of drug-resistant *Plasmodium falciparum* infection, febrile patients in the tropics can no longer be empirically treated with inexpensive yet effective antimalarials. The substitution of newer and more costly drugs brings with it the need for rapid, accurate, and inexpensive diagnostic procedures so that directed therapy can be used. We report a field trial comparing standard microscopic malaria diagnosis and quantitative buffy coat analysis to a new *P. falciparum* antigen detection system. The ParaSight(TM) F test (PFT) was found to be easy to learn, rapid to perform, and highly accurate. If confirmed, the use of the PFT in endemic areas may aid in the identification of patients requiring therapy for drug-resistant malaria.

Diop, Mbarack, et al, *Senegal River Basin Health Master Plan Study* (December 1994). **D76.10 850**

Diperri, G., et al, **Pentoxifylline As a Supportive Agent in the Treatment of Cerebral Malaria in Children.** *Journal of Infectious Diseases* 171, no. 5 (May 1995): 1317-22.

In an open, randomized, controlled therapeutic trial, 56 children with cerebral malaria (CM) were randomly assigned to receive standard quinine regimen with or without pentoxifylline (10 mg/kg/day by continuous intravenous infusion), Pentoxifylline exerted an inhibitory effect on the synthesis of tumor necrosis factor (TNF), a possible mediator of CM. The 26 children who received pentoxifylline had significantly shorter comas than controls (median, 6 vs, 46 h; $P < .001$), Pentoxifylline recipients showed a trend toward a lower mortality, with a borderline significant difference ($P = .055$). The better outcome in the pentoxifylline group was associated with a decline in TNF serum levels on the third day of treatment in a few subjects that was not seen in controls. While alternative or concurrent mechanisms of action may be of some relevance, larger double-blind trials are needed to determine whether pentoxifylline has a therapeutic role in CM.

Eamsila, C., et al, **Evaluation of Permethrin-Treated Military Uniforms for Personal Protection Against Malaria in Northeastern Thailand.** *Journal of the American Mosquito Control Association* 10, no. 4 (December 1994): 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

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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.

Easton, E. R., **Urbanization and Its Effects on the Ecology of Mosquitoes in Macau, Southeast Asia.**

Journal of the American Mosquito Control Association 10, no. 4 (December 1994): 540-544.

Recent urbanization in Macau has resulted in the precipitous decline to zero in populations of several anopheline vectors of malaria while providing optimal habitat for the population increase in culicines. Of 18 species of mosquitoes reported in Macau in recent years, 15 species are included here. *Culex quinquefasciatus*, *Culex sitiens*, and *Aedes albopictus* were the most abundant species. Notes are provided for *Anopheles sinensis*, *Armigeres magnus*, *Armigeres subalbatus*, *Culex foliatus*, *Culex fuscus*, *Culex infantulus*, *Culex rubithoracis*, *Culex sumatranus*, *Culex tritaeniorhynchus*, *Mansonia uniformis*, *Toxorhynchites splendens*, and *Tripteroides* sp.

Elhassan, I. M., et al, **High Proportion of Subclinical Plasmodium Falciparum Infections in an Area of Seasonal and Unstable Malaria in Sudan.** *American Journal of Tropical Medicine and Hygiene* 53, no. 1 (July 1995): 78-83.

In the present longitudinal study, a cohort (n = 98) of children and adults 5-30 years of age living in an area of highly seasonal and unstable malaria transmission were followed for malaria morbidity during several successive transmission seasons. Based on morbidity surveillance during 1993 and measurements of antibody titers to the *Plasmodium falciparum* ring-infected erythrocyte surface antigen (Pf155/RESA), the cohort was divided into three groups: those who had at least one episode of clinical malaria (Group 1, n = 31), those who did not suffer from clinical malaria but had (Group 2, n = 63) or had not (Group 3, n = 4) a significant increase in antibody titers against the Pf155/RESA antigen. This increase was defined as equal to or greater than a four-fold increase in antibody titer in samples from same individuals taken at the beginning and the end of the malaria transmission season. Such increases in specific antibody levels suggested that the donors had been exposed to a *P. falciparum* blood-stage infection. Measurements of antibody titers to a peptide derived from the glutamate-rich protein exoantigen gave data parallel to those for Pf155/RESA. A surprisingly high fraction of individuals in the study cohort (approximately 66%) showed evidence of infection without ensuing clinical disease (Group 2).

Feachem, Richard, et al, *Disease and Mortality in Sub-Saharan Africa* (1991). **REF F73.10-12**

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Part I. Patterns of mortality. Infant and child mortality. Adult mortality. Maternal mortality. Part II. Specific diseases. Child malnutrition. Diarrhea. Acute Respiratory Infections. Measles. Tetanus. Polio. Tuberculosis. Malaria. AIDS. Cancer. Part III. Longitudinal diseases. Morbidity and mortality in Kenya and Tanzania. Machakos, Kenya. Kilonbero, Tanzania. Keneba, Gambia. Malumfashi, Nigeria. Danfa Project, Ghana.

Fonseca, L., et al, **Plasmodium Berghei: Selection of Mefloquine-Resistant Parasites Through Drug Pressure in Mosquitoes.** *Experimental Parasitology* 81, no. 1 (August 1995): 55-62.

Mefloquine is an antimalarial drug with schizonticidal activity on blood-stage parasites. Studies of the role of mefloquine on the development of *Plasmodium berghei* ANKA in *Anopheles stephensi* have been carried out that showed a dose-dependent effect on the sporogonic cycle of these parasites, with changes in the numbers of oocysts and the extent of sporozoite invasion of salivary glands. In this study, we show that mefloquine-resistant *P. berghei* ANKA blood stage parasites could be selected through drug pressure during continuous cyclical transmission of *Anopheles gambiae* s.l.

Fryauff, D. J., et al, **Randomised Placebo-Controlled Trial of Primaquine for Prophylaxis of Falciparum and Vivax Malaria.** *Lancet* 346, no. 8984 (November 1995): 1190-1193.

Drug resistance has made malaria prevention difficult and the new agents are too expensive for widespread use, Primaquine, an established drug for treatment, is potentially useful for prevention, Malaria prophylaxis with primaquine was evaluated in Irian Jaya during one year in Javanese men who were not deficient in glucose-6-phosphate dehydrogenase (G-6-PD). 126 volunteers were randomised to receive 0.5 mg/kg primaquine base or placebo daily (double-blinded), or 300 mg chloroquine base weekly (open). The protective efficacy of primaquine relative to placebo was 94.5% (95% confidence interval 57-99) for *Plasmodium falciparum* and 90.4% (95% CI 58-98) for *P. vivax*, Attack rates for either parasite did not differ significantly between the chloroquine and placebo groups. Incidence density of physical complaints not associated with parasitaemia was low (17-18 complaints/person-year) and was about the same in all groups except for cough, which was increased in the primaquine group. Complete blood counts were normal and no evidence of hepatic or renal dysfunction was found with primaquine. However, at 50 weeks the primaquine group had a mean methaemoglobin of 5.8% (range 1.4-13%), which declined by half within 7 days of ending prophylaxis. When used daily for one year by men with normal G-6-PD activity, primaquine was well tolerated and effective for prevention of malaria.

Genton, B., et al, **The Epidemiology of Malaria in the Wosera Area, East Sepik Province, Papua New Guinea, in Preparation for Vaccine Trials. 1. Malariometric Indices and Immunity.** *Annals of Tropical Medicine and Parasitology* 89, no. 4 (August 1995): 359-76.

The epidemiological features of malaria were studied through seven community-based surveys in a population of 4000 in the Wosera area, East Sepik Province, Papua New Guinea. Prevalence of parasitaemia (all species, all ages) was 60%. *Plasmodium falciparum* was the predominant

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species in all surveys (55%), followed by *P. vivax* (25%) and *P. malariae* (20%). The highest prevalence for asexual forms of *P. falciparum* occurred in the 5-9-year age group, whereas *P. falciparum* gametocytaemia and *P. vivax* parasitaemia were observed most frequently in the 1-4-year age group and *P. malariae* in the 10-15-year age group. Mean densities of all species decreased with age except for that of *P. malariae*, which was lower in children aged <1 year than in those aged 1-4 years. The prevalence of enlarged spleen was 57% in children and 10% in adults and closely matched the corresponding age-related parasite rate. Seroprevalence of antibody to the major merozoite surface antigen 2 rapidly increased with age, with >90% of individuals older than 5 years being positive. Malariological indices showed irregular changes over time but there was no clear-cut seasonal pattern. The geographical distribution of these indices and immune responses was not uniform within the study area. Bednet use and drug consumption were negatively correlated with malariometric indices. Identification of significant temporal and local variations in malaria endemicity is important for the design and evaluation of intervention studies, including field trials of an antimalarial vaccine.

Genton, B., et al, **The Epidemiology of Malaria in the Wosera Area, East Sepik Province, Papua New Guinea, in Preparation for Vaccine Trials. 2. Mortality and Morbidity.** *Annals of Tropical Medicine and Parasitology* 89, no. 4 (August 1995): 377-90.

Malaria mortality and morbidity were studied in a rural population of 4000 in the Wosera area, East Sepik Province, Papua New Guinea, Malaria accounted for 4.9% of the 162 deaths investigated by verbal autopsy and for 12.2% of the 49 deaths assessed through medical records. Malaria was the first cause of death in children aged 0.5-4 years. Of the 7795 subjects interviewed and bled during six cross-sectional community-based surveys, children of 1-4 years had the highest malaria-related morbidity. In this age group, point prevalences of fever, fever associated with parasitaemia, and fever plus *Plasmodium falciparum* (Pf) parasitaemia greater than or equal to 10000 parasites/ μ l blood were 5%, 4.1% and 1.5%, respectively. The corresponding figures for adults were 2%, 0.9% and 0.1%, respectively. The calculation of attributable fraction (AF) using a multiple logistic regression model showed that malaria accounted for 0.44 of all fevers in children of 1-4 years and 0.08 of the fevers in adults. Prevalence data derived from the AF estimate were compared with those calculated using different accepted density thresholds. The prevalences which best approximated the results from the logistic regression model were obtained using parasitaemia cut-offs of greater than or equal to 1000 Pf parasites/ μ l in children aged 1-4 years and adults older than 19 years and of greater than or equal to 10000 parasites/ μ l in those aged 5-19 years. Prevalence of fever associated with parasitaemia was highly seasonal, with a peak at the beginning of the wet season. The geographical distribution of malaria morbidity was not uniform. The measurement of malaria-related morbidity, the identification of significant seasonal and local variation as well as the assessment of different methods of defining a clinical episode of PE malaria are crucial for the design and evaluation of intervention studies, including field trials of antimalarial vaccines.

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Genton, G., et al, **The Use of Untreated Bednets and Malaria Infection, Morbidity and Immunity.** *ANN TROP MED & PARASITOL* 88, no. 3 (1994): pp. 263-70.

Glynn, J. R., et al, **Infecting Dose and Severity of Falciparum Malaria.** *Transactions of the Royal Society of Tropical Medicine and Hygiene* 89, no. 3 (May 1995-June 1995): 281-83.

The causes of the wide spectrum of severity in malaria have only partly been elucidated. There are theoretical reasons for thinking that the infecting dose may influence the severity but evidence is scarce. We have analysed the records of 82 non-immune neurosyphilis patients bitten by a known number of mosquitoes infected with one of 3 strains of *Plasmodium falciparum*, whose treatment was delayed. After controlling for strain, the number of mosquitoes was not associated with the prepatent period nor with any of the outcome measures. For one of the main strains, patients with shorter prepatent periods were more likely to receive treatment during the acute phase of the infection, but no other association with measures of severity was found. This study suggests that infecting dose is unlikely to be an important determinant of severity.

Good, M. F., **Development of Immunity to Malaria May Not Be an Entirely Active Process - Point of View.** *Parasite Immunology* 17, no. 2 (February 1995): 55-59.

It has never been explained why it takes so long for humans develop immunity to malaria, although factors such as antigenic variation, antigenic polymorphism, and poor immunological responses to critical antigens are thought to be important. Models of malaria, particularly in rodents, have not been helpful. The course of malaria infection differs considerably between humans and rodents. Mice rapidly develop immunity whereas for most humans it takes several years of exposure for this to occur. Mice typically exhibit high parasitaemias whereas humans typically do not. A significant difference in the immune response of humans and mice to malaria parasites might, in part, explain these differences. Most humans have a pre-existing population of activated malaria parasite-specific T cells (cross-reactive T cells) which we have referred to as 'natural' T cells, but such cells have not been observed in mice. These cells, many of which secrete interferon-gamma, might control parasitaemia early in the infection, but a by-product of their further activation by malaria parasites might be disease symptoms. Development of immunity has been thought of as an active process-acquisition of specific antibody and effector T cell responses. However, it might in part reflect induction of tolerance of this pre-existing population of disease-inducing T cells as a result of chronic parasitaemia. The initial presence of these Th1-like cells may also impede the development of a Th2-like response necessary for the production of protective antibodies. Persistent cross-reactive stimulation may significantly impede this process.

Gravenor, M. B., et al, **The Regulation of Malaria Parasitaemia: Parameter Estimates for a Population Model.** *Parasitology* 110, no. Part 2 (February 1995): 115-22.

Classical studies of non-immune individuals infected with *Plasmodium falciparum* reveal that the infection may be regulated for long periods at a relatively stable parasite density, despite the enormous growth potential of a parasite that continually replicates within host erythrocytes. This

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suggests that the parasite population may be controlled by density-dependent mechanisms, and in theory the most obvious of these is competition between parasites for host erythrocytes. Here we evaluate the role of this mechanism in the regulation of parasitaemia, by modelling the basic population interaction between parasites and erythrocytes in a form that allows all the essential parameters to be estimated from clinical data. Our results show that competition cannot account for the total regulation of *P. falciparum*, but when combined with immune mechanisms it may play a more important role than is generally supposed. Further analysis of the model indicates that in the long term, parasite replication at low parasite densities can contribute significantly to the high degree of anaemia observed in natural infection, a conclusion which is not obvious from simple clinical observation.

Gunawardena, D. M., **Spatial Analysis of Malaria Risk in an Endemic Region of Sri Lanka.** *Geographic Information Systems for Health and the Environment* (June 1995). **Z68 2190**

Hammer, Jeffrey, **The Economics of Malaria Control.** *World Bank Research Observer* 8, no. 1 (1993): p. 1-22. **F56.10M 2119**

Helitzer-Allen, Deborah, et al, **Testing Strategies to Increase Use of Chloroquine Chemoprophylaxis During Pregnancy in Malawi.** *Acta Tropica* 58 (1994): p 255-66. **F56.10M 1316**

Hellgren, U., et al, **Malaria Parasites and Chloroquine Concentrations in Tanzanian Schoolchildren.** *Tropical Medicine and Parasitology* 45, no. 4 (December 1994): 293-97. Subtherapeutic doses of chloroquine (CQ) are considered to promote development of *Plasmodium falciparum* resistance but little is actually known about the drug levels in the population in endemic areas. We have therefore measured blood concentrations of CQ in Tanzanian schoolchildren and related these to parasite microscopy. A total of 163 children (median age 11 years) in a suburb outside Dar es Salaam were followed during four weeks. Thick and thin blood films were obtained once weekly. Parasites were counted in 200 visual fields. CQ and desethyl-chloroquine (DECQ) were determined with HPLC in 100 μ l of capillary blood. During the study *P. falciparum* trophozoites were detected in a mean of 78% of the children, *P. falciparum* gametocytes in 7.7% and *P. malariae* parasites in a mean of 13%. The cumulative prevalence of *P. falciparum* trophozoites and *P. malariae* parasites was 96% and 28% respectively. On day 0 and day 28, CQ was found in 78% and 80% of the children and DECQ in 21% and 31% of them. A total of 19% of all children had a verified CQ intake during the study and 35% had probably taken CQ. With a few exceptions (9% had CQ concentrations > 100 nmol/l) drug levels were not sufficient to affect parasites with a reduced CQ susceptibility but could possibly promote development of resistance by eradicating the most susceptible part of the parasite population.

Hii, J. L. K., et al, **Comparative Effects of Permethrin-Impregnated Bednets and DDT House Spraying on Survival Rates and Oviposition Interval of *Anopheles Farauti* No. 1 (Diptera:**

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Culicidae) in Solomon Islands. *Annals of Tropical Medicine and Parasitology* 89, no. 5 (October 1995): 521-29.

Human-biting, CDC light trap and pig-baited collections were used to monitor changes in the abundance and parity rate of *Anopheles farauti* No. 1 mosquitoes in three Solomon Islands villages for 30 consecutive nights. Houses in one of the villages were sprayed with DDT, another village was unsprayed but its inhabitants used permethrin-treated bednets and the third village was left completely untreated. Mosquitoes collected each day were dissected to determine follicular maturation and parity. In the second year of vector control, survival rates (determined by time-series analysis of the landing catches and biting parous population) were significantly lower in the village using permethrin-treated bednets than in the other two villages. There was no difference in the estimated survival rates between the untreated and DDT-sprayed villages. The oviposition cycle was extended to 4 days in the permethrin-treated village compared with 3 days in the other villages. The expected infective life was 1.75-fold longer in the untreated village than in the permethrin-treated village. The epidemiological implications of replacing DDT spraying with permethrin for malaria control are discussed.

Hogh, B., et al, **Specific and Nonspecific Responses to Plasmodium Falciparum Blood-Stage Parasites and Observations on the Gametocytemia in Schoolchildren Living in a Malaria-Endemic Area of Mozambique.** *American Journal of Tropical Medicine and Hygiene* 52, no. 1 (January 1995): 50-59.

We have observed specific and nonspecific reactivities to the asexual stages and gametocytes of *Plasmodium falciparum* and examined the effect of chloroquine and Fansidar(TM) (pyrimethamine/sulfadoxine) on the dynamics of gametocytemia. Schoolchildren peripheral blood films positive for *P. falciparum* gametocytes were identified in a malaria-endemic area of Mozambique. The children were randomly allocated into two groups to receive chloroquine or pyrimethamine/sulfadoxine, and were followed for 28 days after treatment. In patients harboring drug-sensitive parasites, asexual parasitemias were cleared by day 4, but gametocytes persisted for an additional 17 days. The prevalence of the asexual parasites was 67.6% in the chloroquine-treated group at day 0 and 61.1% at day 28, whereas in the pyrimethamine/sulfadoxine treated group, the initial parasite positive prevalence of 70.7% was reduced to 2.4% at day 28, suggesting a high prevalence of chloroquine-resistant parasites. On day 0, gametocyte prevalence was 59.5% in the chloroquine-treated group and in 68.3% in the pyrimethamine/sulfadoxine-treated group; these values were reduced to 5.6% and 2.4%, respectively, at day 28. Our results suggest strongly that there is no induction of gametocytogenesis by either course of chemotherapy.

Jakobsen, P. H., et al, **Malaria: Toxins, Cytokines and Disease.** *Parasite Immunology* 17, no. 5 (May 1995): 223-31.

In this review the old concept of severe malaria as a toxic disease is re-examined in the light of recent discoveries in the field of cytokines. Animal studies suggest that the induction of TNF by parasite-derived molecules may be partly responsible for cerebral malaria and anaemia, while

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hypoglycaemia may be due to direct effects of similar molecules on glucose metabolism. These molecules appear to be phospholipids and we suggest that when fully characterized they might form the basis of antitoxic therapy for malaria.

Jakobsen, P. H., et al, **The Antimalarial Drug, Ro 42-1611 (Arteflene), Does Not Affect Cytoadherence and Cytokine-Inducing Properties of Plasmodium Falciparum Malaria Parasites.** *Tropical Medicine and Parasitology* 46, no. 2 (June 1995): 88-92.

The purpose of this study was to investigate the ability of the antimalarial drug, Ro 42-1611 to block parasite mediated cytokine induction in vitro as well as cytoadherence of infected erythrocytes to melanoma cells in vitro. The biological activity of Po 42-1611 was confirmed as it blocked Plasmodium falciparum growth in cultures. Ro 42-1611, had no major effect on TNF IL-alpha or IL-6 cytokine release from mononuclear cells stimulated with malaria antigens or lipopolysaccharide and it did not affect cell viability. Ro 42-1611 only slightly suppressed cytoadherence of infected erythrocytes to melanoma cells. The therapeutic effect of To 42-1611 appears to be confined to its parasite killing activity.

Jamison, Dean, et al, *Disease Control Priorities in Developing Countries* (1993). **REF F73.10-11**

Part 1. Disease control priorities. Causes of death. Part 2. Acute respiratory infection. Diarrheal diseases. Poliomyelitis. Helminth infection. Measles. Tetanus. Tuberculosis. Leprosy. Malaria. Dengue. Hepatitis B. Part 3. Maternal and perinatal health. Micronutrient deficiency disorders. Malnutrition.

Jamjoom, G. A., et al, **Acceptability and Usage of Permethrin-Impregnated Mosquito Bed Nets in Rural Southwestern Saudi Arabia.** *Tropical and Geographical Medicine* 46, no. 6 (1994): 355-57.

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.

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Jana-Kara, B. R., **Deltamethrin Impregnated Bednets Against Anopheles Minimus Transmitted Malaria in Assam, India.** *Jnl Trop Med & Hyg* 98 (1995): p. 73-83. E66 1634

Jelinek, T., et al, **Evaluation of Circumsporozoite Antibody Testing As a Sero-Epidemiological Tool for the Detection of Plasmodium Falciparum Infection in Non-Immune Travelers.** *Tropical Medicine and Parasitology* 46, no. 3 (September 1995): 154-57.

The objective of this investigation was to collect data concerning CS-antibody levels and duration of the immunological response to exposure of non-immune persons to a single malaria infection. For this purpose 156 specimens from 98 patients with confirmed falciparum malaria, 76 specimen derived from 64 patients with vivax malaria and sera from 32 patients who had not been previously to malarious areas were investigated by use of a commercially available ELISA testkit. All specimens from patients with falciparum malaria were also tested for merozoite-antibodies by an indirect fluorescence antibody test (IFAT). Positive levels of merozoite-antibodies were detectable in 89.1% of the specimen in this panel during the period between days 8 and 90 after onset of symptoms and decreased steadily thereafter. The test results were positive for CS-antibodies in 36.4% of the specimens from patients with falciparum malaria during the first 7 days after onset of symptoms. This figure increased to 55.8% during days 8-90 after onset and decreased to 38.9% in specimens which were tested later (91-1898 days). 11 specimens reacted positively to CS-antibody testing but negative in the IFAT. Therefore, the percentage of specimen detected by either IFAT or CS-ELISA was at 51.9% during days 0 and 7 ($p < 0.001$), 95.3% during days 8 and 90 ($p = 0.039$) and 44.4% for testing performed later ($p < 0.001$). CS-antibodies could also be detected in 5.3% of specimen from patients with vivax malaria while none of the sera from the malaria-negative control-group tested positive for CS-antibodies. Mie conclude that CS-antibody testing might prove valuable as an additional method for the determination of merozoite-antibodies in epidemiological surveys. Regardless its low sensitivity it might furthermore become a method for the determination of the efficacy of malaria prevention measures since it detects infection with parasites even without following clinical outbreak of malaria. It should not, however, be considered as a method on which a retrospective diagnosis of malaria could be based exclusively.

Jonkman, A., et al, **Cost-Saving Through Microscopy-Based Versus Presumptive Diagnosis of Malaria in Adult Outpatients in Malawi .** *Bulletin of the World Health Organization* 73, no. 2 (1995): 223-27.

The cost implications of changing from a policy of presumptive diagnosis to one of microscopy-based diagnosis in the management of uncomplicated malaria in an urban hospital adult outpatient clinic in Malawi were studied. Costs were measured in three separate weeks during the rainy season. In weeks I and II all uncomplicated malaria cases were treated on the basis of a presumptive diagnosis. In week II, blood films were taken but the results were not made available and did not affect drug dispensing. In week III, antimalarial drugs were restricted to parasitaemic patients. In week I, a total of 7216 prescriptions were written and dispensed, of which 2883 (39.9%) were for antimalarial drugs, The proportion of antimalarial prescriptions fell

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to 1171/5556 (21.1%) in week II and 357/5377 (6.6%) in week III. We estimate annual savings from microscopy-directed treatment in this setting to be 52 000 Malawi kwacha (US\$ 14 000), This represents 3% of the annual drugs budget for the hospital, and is large enough to justify a change in policy.

Kamugisha, J., et al, **In Vivo Sensitivity of Plasmodium Falciparum to Chloroquine, Amodiaquine and Sulfadoxine-Pyrimethamine in Western Uganda.** *Tropical and Geographical Medicine* 46, no. 6 (1994): 364-65.

In an in vivo study of antimalarial sensitivity in Kabarole District, Western Uganda, 82% of asymptomatic malarial infections and 86% of symptomatic infections were chloroquine sensitive. Of persons with symptomatic malaria, 88% were sensitive to sulfadoxine-pyrimethamine (Fansidar(R)). Amodiaquine cleared parasites in all persons in whom it was used. Over the course of the past five years, there appears to be no substantial increase in the extent of chloroquine resistance in Western Uganda.

Karch, S., et al, **Impact of Deltamethrin-Impregnated Bednets on Biting Rates of Mosquitoes in Zaire.** *Journal of the American Mosquito Control Association* 11, no. 2 Part 1 (June 1995): 191-94.

In a rural area of Zaire, the whole population of a village was protected by deltamethrin-impregnated mosquitoes bednets. A similar village was observed as a control. Biting rates for mosquitoes were recorded in both villages. The principal man-biting species were *Mansonia africana*, *Mansonia uniformis*, and *Aedes aegypti*. In the village protected by the impregnated mosquito bednets, the number of *Mansonia* bites was reduced 96% indoors and at a lesser rate outdoors. Biting rates of *Ae. aegypti* dropped to 0 indoors, but the outdoor biting rate remained unchanged. It is concluded that the reduction in mosquito bites is not only caused by the repellent action of the deltamethrin but also by a reduction in mosquito numbers.

Klein, R. E., et al, **Knowledge, Beliefs, and Practices in Relation to Malaria Transmission and Vector Control in Guatemala.** *American Journal of Tropical Medicine and Hygiene* 52, no. 5 (May 1995): 383-88.

As part of an effort to involve community members in malaria control 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

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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.

Konate, L., et al, **Vectors Bionomics and Transmission of Plasmodium Falciparum, P-Malariae and P-Ovale in a Sudan Savanna Area of West Africa (Dielmo, Senegal).** *Parasite - Journal De La Societe Francaise De Parasitologie* 1, no. 4 (December 1994): 325-33.

From April 1990 to March 1992 a longitudinal entomological study was carried out in Dielmo village, Senegal, an area of Sudan-type savanna. Mosquitoes were sampled by night-bite collections and pyrethrum spray collections. Seven anopheles species were identified: *An. gambiae* s.s., *An. arabiensis*, *An. funestus*, *An. pharoensis*, *An. rufipes*, *An. squamosus* and *An. ziemanni*. Present throughout the year, *An. gambiae* s.l. and *An. funestus* represented more than 98 % of anopheles captured on man. A yearly wave of *An. gambiae* s.l. was observed in the rainy season and *An. funestus* was generally more abundant in the dry season. The sporozoite rate was 1.5 % and 1.3 %, respectively, for these two species. Sporozoite typing by monoclonal antibodies indicated that the proportion of infected salivary glands was 92.7 % *P. falciparum*, 18.2 % *P. malariae* and 8.2 % *P. ovale*. The inoculation rate was calculated to be respectively 111, 21 and 8 infective bites per human for *P. falciparum*, *P. malariae* and *P. ovale* during the first year. Transmission was highest in the second year, with respectively 272, 54 and 25 infective bites per human.

Kremsner, P. G., et al, **Prediction of Accelerated Cure in Plasmodium Falciparum Malaria by the Elevated Capacity of Tumor Necrosis Factor Production.** *American Journal of Tropical Medicine and Hygiene* 53, no. 5 (November 1995): 532-38.

Cytokine regulation was compared in three groups of Gabonese patients with *Plasmodium falciparum* malaria before and after therapy: adults with uncomplicated malaria, children with uncomplicated malaria, and children with severe malaria. Plasma levels of tumor necrosis factor (TNF), interleukin-6 (IL-6), IL-8, TNF receptors (TNF R), and the TNF/TNF R ratios were significantly higher in severe malaria compared with uncomplicated malaria. High plasma levels of all immunoregulatory molecules were associated with slow cure after therapy. In all patients, phytohemagglutinin-induced cytokine production was depressed on admission compared with convalescence. A significant difference was the higher TNF production capacity in patients with severe malaria on day 2 and day 5 compared with that in patients with uncomplicated malaria. In contrast to IL-6 and IL-8, a high TNF production capacity during the acute phase of malaria predicted a rapid clinical and parasitologic cure in the patients. These findings illustrate the dual role of TNF in the protection and pathology of malaria.

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Krishna, S., et al, **Fever in Uncomplicated Plasmodium Falciparum Malaria: Randomized Double-Blind' Comparison of Ibuprofen and Paracetamol Treatment.** *Transactions of the Royal Society of Tropical Medicine and Hygiene* 89, no. 5 (September 1995-October 1995): 507-9. Fever almost invariably accompanies uncomplicated falciparum malaria. In a randomized, double-'blind' study, we compared a single dose of ibuprofen (10 mg/kg, n = 8) with paracetamol (15 mg/kg, n = 8 for the treatment of fever > 38.5 degrees C due to uncomplicated falciparum malaria. Ibuprofen was effective than paracetamol in lowering temperatures throughout the first 4.5 h after dosing (P = 0.016) and should be considered as an antipyretic agent in the management of uncomplicated falciparum infections, providing there is no contraindication to its use.

Kroeger, A., et al, **The Potential for Malaria Control With the Biological Larvicide Bacillus Thuringiensis Israelensis (Bti) in Peru and Ecuador.** *Acta Tropica* 60, no. 1 (September 1995): 47-57.

A study on the efficacy of Bti spraying in mosquito breeding places was undertaken in the Pacific coast of Peru and Ecuador and in the Amazon area of Peru. It was shown that Bti is a powerful larvicide for Anopheles larvae, although it sinks quickly, whereas Anopheles larvae feed at the water surface. The duration of its effect was less than 7 days with the exception of the Amazon area of Peru, where it was approximately 10 days. In two study areas, Bti was sprayed weekly over periods of 10 and 7 weeks, respectively, and the adult mosquito densities were monitored. The Anopheles adult density (bites per person per hour on human baits) was reduced by an average of 70% in one area and by up to 50% in the other. This means that Bti spraying can potentially be an important component of a modified malaria control strategy.

Kroeger, A., et al, **Insecticide-Impregnated Bed Nets for Malaria Control: Varying Experiences From Ecuador, Colombia, and Peru Concerning Acceptability and Effectiveness.** *American Journal of Tropical Medicine and Hygiene* 53, no. 4 (October 1995): 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 peoples' 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

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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.

Kumar, A., **Malaria Control Utilizing *Bacillus Sphaericus* Against *Anopheles Stephensi* in Panaji, Goa.** *Jnl Amer Mosq Control Assoc* 10, no. 4 (1994): p. 534-39.

Kumar, A., et al, **Malaria Control Utilizing *Bacillus-Sphaericus* Against *Anopheles-Stephensi* in Panaji, Goa.** *Journal of the American Mosquito Control Association* 10, no. 4 (December 1994): 534-39.

In a large malaria endemic area in Panaji city, Goa, India, the weekly application of the biolarvicide *Bacillus sphaericus* (Strain 101, Serotype H 5a 5b) at the rate of 1 g/m² in the main *Anopheles stephensi* larval habitats, viz., curing waters, masonry tanks, and sump tanks (under construction), from April to December 1993 resulted in a sharp decline in the habitat positivity (range 0.13-8.0%) as compared with the rest of the Panaji (range 2.2-30.6%) where temephos (Abate) was used as the larvicide. *Bacillus sphaericus* spraying also led to a significant decline in anopheline densities in positive habitats (range 0-7.3/10 dips) as compared with control habitats (range 0.9-53.0/10 dips). Concurrently, malaria incidence observed in the experimental area (slide positivity rate [SPR] range 2.3-7.8%; monthly parasite index [MPI] range 0.18-1.44) was lower than in the control area (SPR range 14.3-25.5%; MPI range 1.75-6.12).

Kumar, A., et al, **Control of *Anopheles Stephensi* Breeding in Construction Sites and Abandoned Overhead Tanks With *Bacillus Thuringiensis* Var *Israelensis*.** *Journal of the American Mosquito Control Association* 11, no. 1 (March 1995): 86-89.

Bacillus thuringiensis (H-14), strain 164 (Bactoculicide) when applied at 1 g/m² surface area successfully controlled *Anopheles stephensi* breeding in construction sites, abandoned overhead tanks, and curing waters. Subsequent to application, no pupal production was observed in these habitats for 3, 18, and 21 days, respectively. Based on these findings, inclusion of Bactoculicide in the bioenvironmental vector control strategy is suggested and fortnightly spraying in construction sites at 1 g/m² surface area is recommended for the containment of vector breeding. However, frequent retreatment of abandoned overhead tanks would be uneconomical and operationally impractical.

Kwiatkowski, D., **Malarial Toxins and the Regulation of Parasite Density.** *Parasitology Today* 11, no. 6 (June 1995): 206-12.

For over a century it has been recognized that many of the clinical symptoms of malaria are caused by toxins released by rupturing schizonts, but it is only in the past few years that the underlying mechanisms have begun to be understood. Dominic Kwiatkowski here focuses on the toxins that cause malaria fever by stimulating host cells to produce tumour necrosis factor alpha

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(TNF) and other pyrogenic cytokines. Both TNF and fever have antiparasite properties, and it is proposed that the release of these toxins plays an important role in the regulation of parasite density within the host. Cerebral malaria is related to excessive TNF production. Recent data indicate that this can be the consequence of genetic variation in the host's propensity to produce TNF.

- Land, K. M., et al, **Anti-Adhesive Antibodies and Peptides As Potential Therapeutics for Plasmodium Falciparum Malaria**. *Parasitology Today* 11, no. 1 (January 1995): 19-23.
The attachment of erythrocytes infected with *Plasmodium falciparum* to the microvessels of the brain leads to a pathological condition known as cerebral malaria. There are no effective therapeutic means for alleviating this. In this review, Kirkwood Land, Irwin Sherman, Jurg Gysin and Ian Crandall discuss the potential of anti-adhesive peptides and antibodies as a means of treating cerebral malaria. Adhesin proteins on the surface of the parasite-infected red blood cell as well as target cell ligand molecules are discussed in the context of anti-adhesion therapy.
- Layton, M., et al, **Mosquito-Transmitted Malaria in New York City, 1993**. *Lancet* 346, no. 8977 (September 1995): 729-31.
In August, 1993, 3 cases of *Plasmodium falciparum* malaria in people without recent travel histories or bloodborne exposure were reported in New York City. An epidemiological investigation confirmed the absence of risk factors for acquisition of malaria in two cases. The third case could not be definitively classified as locally acquired malaria because the patient had travelled to Thailand two years before malaria was diagnosed. The 3 individuals lived in separate houses in the same neighbourhood of Queens, New York and had onset of illness within a day of each other. The investigation consisted of patient interviews, active case finding, reviewing recent New York flight and shipping arrivals, and an entomological survey for anopheline mosquitoes and breeding sites. No other cases were identified. The 3 patients lived several miles from air and sea ports and prevailing winds would have carried any mosquitoes at those sites away from the patients' homes. By the time of the environmental investigation (September, 1993), the area was dry and neither adult nor larval anophelines were found. However, weather conditions at the probable time of infection (July, 1993) were very different. Malaria was probably transmitted to these 2 patients by local anopheline mosquitoes that had fed on infected human hosts. Mosquito-control measures were not implemented because there was no evidence of ongoing transmission. The occurrence of mosquito-transmitted malaria in New York City demonstrates the potential for reintroduction of malaria transmission into areas that are no longer endemic and emphasises the need for continued surveillance and prompt investigations, if cases without risk factors are reported.
- Linhua, Tang, et al, **Social Aspects of Malaria in Heping, Hainan**. *Acta Tropica* 59, no. 1 (March 1995): p. 41-53.

Liu, D. Q., et al, **Changes in the Resistance of Plasmodium Falciparum to Chloroquine in Hainan, China.** *Bulletin of the World Health Organization* 73, no. 4 (1995): 483-86.

In 1979, in view of the widespread resistance of Plasmodium falciparum to chloroquine in the island of Hainan, China, its use as an antimalarial was suspended throughout the island. A longitudinal survey of the chloroquine-sensitivity of P. falciparum was carried out over the period 1981-91 to investigate whether its resistance had changed from the 1979 level. In-vitro assays were carried out every 2-3 years, while in-vivo tests were performed annually over the period 1981-83 and also in 1991. Resistance to chloroquine declined progressively after its use had stopped. The in-vitro tests indicated that the rate of chloroquine-resistant P. falciparum was 97.9% in 1981, but dropped to 60.9% in 1991 (P <0.001). The mean concentration of chloroquine for complete inhibition of schizont formation was 10.4 pmol/ μ l in 1981, but decreased to 3.0 pmol/ μ l in 1991 (P <0.001). The proportion of samples taken from malaria cases that required high concentrations (>6.4 pmol/ μ l) of chloroquine for complete inhibition of schizont formation was 83.3% in 1981, but only 17.4% in 1991 (P <0.001); at low concentrations (<1.6 pmol/ μ l), the corresponding proportions increased from 4.2% in 1981 to 60.8% in 1991 (P <0.001). In the 4-week in-vivo test, the rate of chloroquine-resistant P. falciparum decreased from 84.2% in 1981 to 40% in 1991 (P <0.001). RII + RIII cases represented 59.4% of the total resistant cases in 1981, but decreased to 37.5% in 1991 (0.02 > P > 0.01).

Liu, K. Y., et al, **Identification of Malaria-Infected Dried Mosquitoes by Biotinylated DNA Probe.** *Journal of the American Mosquito Control Association* 11, no. 2 Part 1 (June 1995): 162-66.

Dot-blot hybridization with cloned genomic DNA labeled with photobiotin as a probe is used to detect Plasmodium falciparum sporozoites in dried mosquitoes. The assay is sensitive enough to detect 2 pg Plasmodium parasite DNA, or one infected mosquito in a pool of 40 insects using DNA extraction samples, or one infected mosquito in a pool of 25 insects without DNA extraction. A single mosquito squashed directly on a nitrocellulose filter for the determination of parasites provides a simple method for the detection of sporozoites. The mosquitoes triturated in reduction buffer were efficient for the screening of malaria infection of mosquitoes in a large number of samples. The species specificity, sensitivity, and ease of performance of this assay as well as the stability of the reagents may make it a useful epidemiological tool.

Long, G. W., **Simple Method for Diagnosis of Plasmodium Falciparum Malaria by Polymerase Chain Reaction From Dried Blood Spot Samples (Vol 52, Pg 344, 1995).** *American Journal of Tropical Medicine and Hygiene* 53, no. 2 (August 1995): 216.

Luxemburger, C., et al, **Oral Artesunate in the Treatment of Uncomplicated Hyperparasitemic Falciparum Malaria.** *American Journal of Tropical Medicine and Hygiene* 53, no. 5 (November 1995): 522-25.

Patients with uncomplicated hyperparasitemic falciparum malaria are usually given parenteral antimalarial treatment to prevent a progression to vital organ dysfunction and death. Since the

oral artemisinin derivatives are more rapidly effective than other antimalarial drugs, we compared oral artesunate (4 mg/kg/day for three days with mefloquine 25 mg/kg on the second day) with an intravenous quinine loading dose (20 mg of salt/kg initially then 10 mg/kg every 8 hr, followed by mefloquine 25 mg/kg) in an open paired randomized trial in 60 patients with acute falciparum malaria and greater than 4% parasitemia, but no evidence of vital organ dysfunction. There were no deaths and none of the patients progressed to develop severe malaria. Oral artesunate treatment resulted in shorter median [range] times to fever clearance (19 hr [4-45] versus 47 hr [4-107]) ($P < 0.0001$), parasite clearance (36 hr [18-61] versus 82 hr [36-140]) ($P < 0.0001$), and discharge from the hospital (25 hr [12-44] versus 58 hr [24-115]) ($P < 0.0001$). There was no toxicity attributable to artesunate. The cure rates by day 28 were 70% (19 of 27) and 39% (11 of 27) in the artesunate and quinine groups, respectively (relative risk = 1.7; 95% confidence interval = 1.0-3.0). Oral artesunate was simpler, cheaper, safer, and more effective than intravenous quinine for the treatment of uncomplicated hyperparasitemia.

Mabeza, G. F., et al, **Predictors of Severity of Illness on Presentation in Children With Cerebral Malaria.** *Annals of Tropical Medicine and Parasitology* 89, no. 3 (June 1995): 221-28.

The presenting features of 195 children with cerebral malaria were analysed to determine which correlated with severity of coma and anaemia. The children, who came from a single community in southern Zambia, were enrolled in an ongoing blinded drug trial in 1992 and 1993. Children with deep coma (scoring 0-2) had significantly longer duration of coma before presentation ($P=0.019$) and were more likely to have been treated with chloroquine ($P=0.022$) than children with light coma (scoring 3 or 4 on the Blantyre coma scale). Children with severe anaemia (haematocrit 18%) were younger ($P=0.005$), had been febrile longer ($P=0.005$), had splenomegaly ($P<0.005$) and hypoglycaemia ($P<0.008$) more often and were more likely to have been treated with chloroquine ($P<0.005$) than those without severe anaemia. The counts of asexual parasites in the peripheral blood were not significantly correlated with depth of coma or severity of anaemia. The observed widespread and uncontrolled use of chloroquine has probably led to the development of resistant malaria and of many severe complications despite early consultation. While early treatment of febrile illnesses in young children and immediate medical attention for altered consciousness must be emphasized in the community approach to severe malaria, our data indicate that effective public health measures will be difficult to develop in the face of a high prevalence of chloroquine resistance.

Manguin, S., et al, **Biochemical Systematics and Population Genetic Structure of Anopheles Pseudopunctipennis, Vector of Malaria in Central and South America.** *American Journal of Tropical Medicine and Hygiene* 53, no. 4 (October 1995): 362-77.

An electrophoretic survey of 42 populations of *Anopheles pseudopunctipennis* collected throughout its known geographic distribution was performed to clarify the taxonomic status of this important malaria vector species. The results indicated strong differences in the allele frequencies of three enzyme loci (glycerol dehydrogenase, 6-phosphogluconate dehydrogenase, and phosphoglucomutase) of the 33 loci analyzed. No fixed electromorphic differences separate

the populations of *An. pseudopunctipennis*. The populations of *An. pseudopunctipennis* showed little genetic divergence, with Nei distances ranging from 0 to 0.079. A comparison of *An. pseudopunctipennis* data with either one of three other *Anopheles* species showed a high genetic distance of 0.335 with a closely related species, *An. franciscanus*; 0.997 with *An. crucians*, and 2.355 with *An. (Nyssorhynchus) albimanus*. Geographic populations of *An. pseudopunctipennis* were classified into three clusters; one cluster included populations collected in North America (United States and Mexico) and Guatemala, one cluster included populations from Belize and South America (Colombia, Ecuador, Peru, Chile, and Argentina); and one cluster was represented by populations from the Island of Grenada (type-locality of *An. pseudopunctipennis*). Based on our isozyme analyses, we defined these clusters as three geographic populations of *An. pseudopunctipennis*. Of the two mainland populations, one extends from the southern United States south through Mexico and Guatemala, and the other extends north from southern South America through Central America to Belize. These two geographic populations converge in southern Mexico and northern Central America. One part of the convergence zone was identified in the area of eastern Guatemala and southern Belize.

Mapaba, E., et al, **Susceptibility of Plasmodium Falciparum to Quinine in Vitro: Effects of Drug Concentrations and Time of Exposure.** *Transactions of the Royal Society of Tropical Medicine and Hygiene* 89, no. 1 (January 1995-February 1995): 85-89.

We have studied the relationship between quinine concentrations ranging from 0.16 to 332 $\mu\text{mol/L}$ in a blood-medium mixture and the time of exposure (12-168 h) needed for inhibition of *Plasmodium falciparum* (F32 strain) in continuous culture. When we exposed the parasites for 12 h, only brief inhibition was observed. After 24 h of exposure, parasites were inhibited for 2-3 d at quinine concentrations greater than or equal to 10.4 $\mu\text{mol/L}$. With 48 and 72 h of exposure, the inhibition lasted for 6-8 d at concentrations greater than or equal to 1.3 $\mu\text{mol/L}$ and for 8-11 d at concentrations between 2.6 and 166 $\mu\text{mol/L}$. After 96 h of exposure, parasites were inhibited for 11-17 d at concentrations greater than or equal to 0.65 $\mu\text{mol/L}$. With 168 h of exposure, parasites were inhibited at all quinine concentrations greater than or equal to 0.65 $\mu\text{mol/L}$ during 28 d of post-exposure cultivation. After reappearance, parasites multiplied on average 7.6 fold during each parasite schizogony cycle. The calculated parasite elimination rate in the presence of effective concentrations of quinine was 99.7-99.9% per cycle. We conclude that the elimination rate of the parasites is concentration-dependent at low concentrations of quinine in vitro. As soon as a threshold concentration of 0.65-2.6 $\mu\text{mol/L}$ is attained, only the exposure time determines parasite elimination. These experiments suggest that it might be preferable to reduce each dose rather than the duration of treatment in areas where *P. falciparum* is susceptible to quinine.

Marlarthan, et al, **Development of Resistance to Chloroquine by Plasmodium Vivax in Myanmar.** *Transactions of the Royal Society of Tropical Medicine and Hygiene* 89, no. 3 (May 1995-June 1995): 307-8.

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Fifty patients with *Plasmodium vivax* infection were treated with the standard regimen of chloroquine phosphate (1500 mg over 3 d) followed by primaquine (45 mg immediately and then weekly for 8 weeks); 43 patients had sensitive infections but recrudescences of parasitaemia occurred between days 3 and 14 with RI, RII and RIII patterns in one, 3 and 3 patients, respectively. All the chloroquine-resistant cases were again treated with chloroquine (1500 mg) and no further recrudescence or relapse was detected on days 21 and 28. This study indicates that chloroquine is losing its efficacy against *P. vivax* in Myanmar.

Marsh, K., et al, **Indicators of Life-Threatening Malaria in African Children.** *New England Journal of Medicine* 332, no. 21 (May 1995): 1399-404.

Background. About 90 percent of the deaths from malaria are in African children, but criteria to guide the recognition and management of severe malaria have not been validated in them. **Methods.** We conducted a prospective study of all children admitted to the pediatric ward of a Kenyan district hospital with a primary diagnosis of malaria. We calculated the frequency and mortality rate for each of the clinical and laboratory criteria in the current World Health Organization (WHO) definition of severe malaria, and then used logistic-regression analysis to identify the variables with the greatest prognostic value. **Results.** We studied 1844 children (mean age, 26.4 months) with a primary diagnosis of malaria. Not included were 18 children who died on arrival and 4 who died of other causes. The mortality rate was 3.5 percent (95 percent confidence interval, 2.7 to 4.3 percent), and 84 percent of the deaths occurred within 24 hours of admission. Logistic-regression analysis identified four key prognostic indicators: impaired consciousness (relative risk, 3.3; 95 percent confidence interval, 1.6 to 7.0), respiratory distress (relative risk, 3.9; 95 percent confidence interval, 2.0 to 7.7), hypoglycemia (relative risk, 3.3; 95 percent confidence interval, 1.6 to 6.7), and jaundice (relative risk, 2.6; 95 percent confidence interval, 1.1 to 6.3). Of the 64 children who died, 54 were among those with impaired consciousness (n = 336; case fatality rate, 11.9 percent) or respiratory distress (n = 251; case fatality rate, 13.9 percent), or both. Hence, this simple bedside index identified 84.4 percent of the fatal cases, as compared with the 79.7 percent identified by the current WHO criteria. **Conclusions.** In African children with malaria, the presence of impaired consciousness or respiratory distress can identify those at high risk for death.

Martens, W. J. M., et al, **Potential Impact of Global Climate Change on Malaria Risk.**

Environmental Health Perspectives 103, no. 5 (May 1995): 458-64.

The biological activity and geographic distribution of the malarial parasite and its vector are sensitive to climatic influences, especially temperature and precipitation. We have incorporated General Circulation Model-based scenarios of anthropogenic global climate change in an integrated linked-system model for predicting changes in malaria epidemic potential in the next century. The concept of the disability-adjusted life years is included to arrive at a single measure of the effect of anthropogenic climate change on the health impact of malaria. Assessment of the potential impact of global climate change on the incidence of malaria suggests a widespread increase of risk due to expansion of the areas suitable for malaria transmission. This predicted

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increase is most pronounced at the borders of endemic malaria areas and at higher altitudes within malarial areas. The incidence of infection is sensitive to climate changes in areas of Southeast Asia, South America, and parts of Africa where the disease is less endemic; in these regions the numbers of years of healthy life lost may increase significantly. However, the simulated changes in malaria risk must be interpreted on the basis of local environmental conditions, the effects of socioeconomic developments, and malaria control programs or capabilities.

Martin, P. H., et al, **Malaria and Climate: Sensitivity of Malaria Potential Transmission to Climate.** *Ambio* 24, no. 4 (June 1995): 200-207.

Malaria, according to the World Health Organization, is one of the most serious and complex health problems facing humanity in the 20th century. In the past, climatic changes have greatly affected its geography. Its seriousness and complexity are therefore likely to be compounded by an anthropogenic greenhouse effect. The Malaria Potential Occurrence Zone (MOZ) model was designed to calculate first-order estimates of climate change impacts on malaria. MOZ focuses on the climatic determinants of the life cycles of malaria parasites and vectors. It does not take epidemiology into account. MOZ predicts receptivity, or potential transmission, rather than actual occurrence. MOZ indicates that the intensity and the extent of malaria potential transmission significantly change under the climate change scenarios generated by five atmospheric general circulation models. All five simulations reveal an increase in seasonal malaria at the expense of perennial malaria. This is cause for great concern. Indeed, seasonal malaria is most likely to lead to epidemics among unprepared or nonimmune populations. Moreover, climate change may trigger massive migrations of environmental refugees. Such population movements would likely put national and international health infrastructures under severe stress. Today, malaria is a developing country issue but could spread to higher latitudes. The results obtained with MOZ suggest that malaria could become a public-health problem for developed countries within decades.

Matteelli, A., **Malaria and Anaemia in Pregnant Women in Urban Zanzibar, Tanzania.** *ANN TROP MED & PARAS* 88, no. 5 (October 1994): pp. 475-84.

Mbogo, C. N. M., et al, **Relationships Between Plasmodium Falciparum Transmission by Vector Populations and the Incidence of Severe Disease at Nine Sites on the Kenyan Coast.** *American Journal of Tropical Medicine and Hygiene* 52, no. 3 (March 1995): 201-6.

The transmission of *Plasmodium falciparum* was studied in relation to the incidence of severe malaria infections at nine sites in the Kilifi District in Kenya. Intensive mosquito sampling during a one-year period yielded *Anopheles gambiae* s.l., *An. funestus*, *An. coustani*, *An. squamosus*, *An. nili*, and *An. pharoensis*. *Anopheles gambiae* s.l. was the predominant vector, comprising 98.4% of the total anophelines collected. Overall, 3.5% of 2,868 *An. gambiae* s.l. collected indoors and 0.8% of 261 collected outdoors contained *P. falciparum* sporozoites. Transmission was detected during 10 months, with peak periods from June to August and

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December to January. In eight of the nine sites, entomologic inoculation rates (EIRs) averaged only four infective bites per year (range 0-18); an annual EIR of 60 was measured for the site with the highest intensity of transmission. The incidence of severe malaria infections, ranging from 8.6 to 38.1 per 1,000 children (0-4 years), was not associated with EIRs. At these sites on the coast of Kenya, a high incidence of severe disease occurs under conditions of very low levels of transmission by vector populations. With respect to conventional approaches for vector control in Africa, decreases in transmission, even to levels barely detectable by standard approaches, may not yield corresponding long-term reductions in the incidence of severe disease.

Mcdermott, J. M., et al, **Mortality Associated With Multiple Gestation in Malawi.** *International Journal of Epidemiology* 24, no. 2 (April 1995): 413-19.

Background. Multiple gestation is associated with increased maternal, perinatal, and infant mortality. The prevalence of multiple gestation varies widely with the highest rates reported among populations in Africa. There have been few population-based studies of the impact of multiple gestation on pregnancy outcomes in sub-Saharan Africa. Methods. Data from a 1987-1990 prospective study of the effect of malaria chemoprophylaxis among pregnant women on birthweight and mortality of their infants in a rural area of Malawi were used to estimate the prevalence of multiple gestation and to quantify the risk of mortality associated with multiple gestation compared with single gestation. Results. There were 88 (2.2%) multiple gestations among 4049 women. Mortality was high; only 38% of mothers were known to have all their infants survive to 1 year, compared with 74% in singleton gestations. The increased mortality associated with multiple gestation was due to two factors: a higher frequency of low birthweight and a fourfold increase in perinatal mortality among the infants with birthweights greater than or equal to 2500 g and among infants with unknown birthweight. We estimated that multiple gestation contributes to 5.5% of the perinatal, 1.2% of the postperinatal, and 11.5% of the maternal deaths in this population. Conclusion. Multiple gestation in Malawi contributed to increased perinatal and maternal mortality, but did not increase the risk of mortality after the perinatal period.

Mcelroy, P. D., et al, **Predicting Outcome in Malaria: Correlation Between Rate of Exposure to Infected Mosquitoes and Level of Plasmodium Falciparum Parasitemia.** *American Journal of Tropical Medicine and Hygiene* 51, no. 5 (November 1994): 523-32.

The level of Plasmodium falciparum parasitemia at clinical presentation has repeatedly been shown to correlate with severity of disease. Using data collected in western Kenya over 21 months, we examined associations between exposure variables, especially exposure to infective mosquitoes, and prevalence and density of P. falciparum parasitemia among 1,007 children six months to six years of age. The prevalence of P. falciparum infection was similar at all exposure levels, but there was a correlation between exposure to sporozoite-infected mosquitoes over the previous 28-day period, and geometric mean parasite density of each cohort (Spearman rank coefficient = 0.724, P = 0.002). The relative odds of having a parasite density greater than or equal to 5,000/mu l was increased almost two-fold among individuals exposed to more than 10

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infective bites during the prior 28-day period. Children enrolled during the highest incidence period were 80% more likely to have a density greater than or equal to 5,000/mu l relative to individuals enrolled during periods of lower incidence. The data suggest that measures, such as malaria vaccines, that reduce parasite densities by limiting numbers of sporozoites reaching the liver, or merozoites released from the liver, will reduce malaria-associated morbidity and mortality, even when they do not prevent all infections.

Meek, S. R., **Vector Control in Some Countries of Southeast Asia: Comparing the Vectors and the Strategies.** *Annals of Tropical Medicine and Parasitology* 89, no. 2 (April 1995): 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. sudaicus*, 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.

Mendis, K. N., et al, **Clinical Disease and Pathogenesis in Malaria.** *Parasitology Today* 11, no. 5 (May 1995): PT11-PT116.

This is the report of a meeting held in Ahungalla, Sri Lanka, 16-19 January 1994, under the sponsorship of the Rockefeller Foundation, Health Sciences Division. The meeting was initiated jointly by the Rockefeller Foundation and the TDX Special Programme of the World Health Organization in order to bring together scientists with a wide spectrum of experience relating to malarial disease and pathogenesis. The objective was to generate interdisciplinary discussion ranging from the clinical pictures of malarial infections and their impact in different parts of the

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world, to current investigations on mechanisms of pathogenesis and clinical immunity and the genetic determinants in human and parasite populations affecting the nature of the disease.

Menendez, C., **Malaria During Pregnancy: A Priority Area of Malaria Research and Control.**

Parasitology Today 11, no. 5 (May 1995): 178-83.

More than 2000 million people live in areas where malaria transmission occurs and are therefore at risk of being infected. It follows that 1000 million people are exposed to the risks of malaria when pregnant. Although the special features of malaria during pregnancy have been recognized for nearly a century(1), it is only recently that it is being considered as a priority for malaria research and control, as discussed here by Clara Menendez.

Menendez, C., et al, **The Effects of Iron Supplementation During Pregnancy, Given by Traditional Birth Attendants, on the Prevalence of Anaemia and Malaria.**

Transactions of the Royal Society of Tropical Medicine and Hygiene 88, no. 5 (September 1994-October 1994): 590-593.

A randomized, double-blind, placebo-controlled community-based trial of oral iron supplementation (200 mg ferrous sulphate daily) administered to multigravid pregnant women by traditional birth attendants (TBAs) was carried out in a rural area of The Gambia. Iron supplementation led to a significant reduction in the prevalence of anaemia and of iron deficiency. Iron supplementation was not accompanied by increased susceptibility to malaria infection; there was no difference in the prevalence and severity of peripheral blood or placental malaria infection between the 2 groups of women. The birth weight of children born to women who received iron prophylaxis was increased by an average of 56 g. It is concluded that oral iron prophylaxis can be successfully delivered through TBAs integrated into a primary health care programme. This simple intervention can produce significant beneficial effects on the health of the mother without inducing increased susceptibility to malaria and has the potential for reducing perinatal mortality by increasing birth weight.

Mills, A., **The Household Costs of Malaria in Nepal.** *Tropical Medicine and Parasitology* 44, no. 1 (1993): p. 9-13.

Mills, A., et al, **Financing Mechanisms for Village Activities in the Gambia and Their Implications for Financing Insecticide for Bednet Impregnation.** *Jnl Trop Med & Hygiene* 97, no. 6 (1994): p. 325-32.

Mishra, S. K., et al, **Effectiveness of Alpha, Beta-Arteether in Acute Falciparum Malaria.**

Transactions of the Royal Society of Tropical Medicine and Hygiene 89, no. 3 (May 1995-June 1995): 299-301.

With the emergence of widespread chloroquine resistance and a world-wide scarcity of quinine, a search for newer antimalarial drugs has become imperative. Different derivatives of qinghaosu have been successfully tried. alpha, beta-Arteether, an ethyl derivative of qinghaosu, was administered to 51 patients with Plasmodium falciparum malaria, in a dose of 150 mg

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intramuscularly once a day on 3 consecutive days. Complete parasite clearance from the peripheral blood was observed in 80% of the patients at 48 h and in 98% at 72 h. The median parasite clearance time was 2 d (range 1-4 d). 65% of the patients became afebrile within 48 h and 81% by 72 h. The mean fever clearance time was 52.04 h (standard deviation 27.09). No side effect was seen. Patients were followed-up for 4 weeks; 7 were readmitted with *P. falciparum* infection but it could not be ascertained definitely whether these cases were reinfections or recrudescences. alpha-beta Arteether was a safe, effective and convenient drug for treating *P. falciparum* malaria. This is the first clinical study with arteether in *falciparum* malaria.

Mnyika, K. S., et al, **Self-Medication With Antimalarial Drugs in Dar Es Salaam, Tanzania.** *Tropical and Geographical Medicine* 47, no. 1 (1995): 32-34.

A hospital-based cross-sectional study was conducted in Dar es Salaam, Tanzania, using a questionnaire to assess the extent of self medication with antimalarial drugs and malaria treatment seeking behaviour among patients attending out-patient treatment at Mnazi mmoja dispensary. It was found that 15.3% of respondents admitted to having ever used malaria chemoprophylaxis while 8.0% reported to be current users of chemoprophylaxis. Among the current users of malaria chemoprophylaxis, some reported having used quinine and Fansidar(R). While 71.7% reported having treated themselves with home kept antimalarial drugs for a suspected malaria fever, 14.7% consulted traditional healers, The data suggest the need for increasing Public awareness on malaria and appropriate use of antimalarial drugs.

Mnzava, A. E. P., et al, **Host Blood Meals and Chromosomal Inversion Polymorphism in Anopheles-Arabiensis in the Baringo District of Kenya.** *Journal of the American Mosquito Control Association* 10, no. 4 (December 1994): 507-10.

Studies were carried out in the villages of Kapkuikui and Maji-Ndege in the Lobo area of Baringo District, Kenya, to obtain baseline data on species identification of the *Anopheles gambiae* group, their feeding and resting behavior, and their frequencies of chromosomal inversions. This was carried out towards predicting the effect of introducing permethrin-impregnated cloths or other intervention measures. In this study, *Anopheles arabiensis* was identified as the only species of the *An. gambiae* group. This species contained 2 inversions, 2Rb and 3Ra, occurring at frequencies ranging from 55 to 60%, and from 5 to 11%, respectively. There was no evidence for nonrandom mating. Indoor- and outdoor-collected samples were significantly different in respect of inversion 3Ra in one village and in the distribution of the different sources of blood meals in both areas. In these villages, 37% of indoor-resting mosquitoes fed outside before entering houses to rest.

Mockenhaupt, F. P., **Mefloquine Resistance in Plasmodium Falciparum.** *Parasitology Today* 11, no. 7 (July 1995): 248-53.

Mefloquine resistance in *Plasmodium falciparum*, the most dangerous of the four pathogenic malaria parasites of humans, is established in several endemic regions of the world. After a promising start, resistance has developed to disturbing extents in some areas, whereas in many

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regions it remains an effective drug. In this article, Frank Mockenhaupt reviews the factors that are likely to influence the development of mefloquine resistance, its possible mechanism and its geographical spread.

Monlun, E., et al, **Cardiac Complications of Halofantrine: A Prospective Study of 20 Patients.** *Transactions of the Royal Society of Tropical Medicine and Hygiene* 89, no. 4 (July 1995-August 1995): 430-433.

Halofantrine, increasingly used for treatment of *Plasmodium falciparum* malaria, is a normally well-tolerated amino-alcohol with very few side-effects, but torsades de pointes ventricular tachycardia due to halofantrine has been reported in a few patients with a congenital long QT interval (Romano-Ward syndrome). We performed a prospective study of the cardiac effect of halofantrine in 20 patients with 48 h ambulatory electrocardiographic (ECG) monitoring; the halofantrine levels in their serum were also determined. Minimal ECG changes were noted, with lengthening of the QT interval without clinical symptoms. This effect was dose-dependent and can be very severe in cases of pre-existing cardiopathy; it also occurs in patients without any pre-existing cardiopathy. In order to reduce the likelihood of such incidents, which are admittedly rare, we suggest performing electrocardiography on all patients before initiating treatment with halofantrine.

Morgan, H. G., **Placental Malaria and Low Birthweight Neonates in Urban Sierra Leone.** *Annals of Tropical Medicine and Parasitology* 88, no. 6 (December 1994): 575-80.

The birthweights of 768 singleton neonates were assessed in a study carried out over a 3-year period among indigenous, parient women in Freetown, where malaria is mesoendemic. About 18.5% of placentae were found infected with malaria and the dominant species was *Plasmodium falciparum*. The proportion of low birthweight (LBW) babies from infected placentae (22.5%) was significantly greater than the proportion from the uninfected ($P < 0.01$) and, among the infected, the proportion from primiparae (38.9%) was significantly greater than that from the multiparae ($P < 0.05$). The mean weight of babies from infected mothers was 265 g lower than that of babies from uninfected mothers ($P < 0.001$) and the babies of primiparae were, on average, 156 g lighter than those of the multiparae ($P < 0.001$). Although infection significantly lowered mean birthweight in both parity groups ($P < 0.001$), the reduction was larger in the primiparae (294 g) than in the multiparae (240 g). The LBW risk ratio for primiparae compared with multiparae was 2.3 for both infected and uninfected groups. The proportions of attributable risk indicated that parity accounted for about 57% of all cases of LBW in primiparae, irrespective of infection. Infection enhanced the risk of producing LBW babies in the primiparae by 11.6%. LBW frequency and relative risk were inversely related to parity of mothers and were higher for infected placentae.

Mulla, M. S., **Mosquito Control Then, Now, and in the Future.** *Journal of the American Mosquito Control Association* 10, no. 4 (December 1994): 574-84.

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This is a memorial lecture honoring the late Professor Stanley B. Freeborn of the University of California. In the spirit of his life-long academic and research interests in mosquitoes and mosquito-borne diseases, I am presenting here the evolution of vector control technology, especially that pertaining to mosquitoes and mosquito-borne diseases during the 20th century. Vector control technology in the first half of this century was relatively simple, utilizing source reduction, larvivorous fish, petroleum hydrocarbon oils, and some simple synthetic and botanical materials. During the 2nd half of this century, however, various classes of synthetic organic chemicals, improved petroleum oil formulations, insect growth regulators, synthetic pyrethroids, and microbial control agents were developed and employed in mosquito control and control of other disease-vectoring insects. Among these groups of control agents, petroleum oil formulations have endured to be used through the whole century. It is likely that petroleum oil formulations, insect growth regulators, and microbial control agents will provide the main thrust against vectors at least during the first quarter of the 21st century. It is also possible that effective tools through the development of vaccines and molecular entomology techniques might become available for the control of vectors and vector-borne diseases during this period of the 21st century.

Mwensei, Halima, et al, **Child Malaria Treatment Practices Among Mothers in Kenya**. *Soc Sci Med* 40, no. 9 (1995): p. 1271-77. **F56.10M 1706**

Nakazawa, M., et al, **Differential Malaria Prevalence Among Villages of the Gidra in Lowland Papua New Guinea**. *Tropical and Geographical Medicine* 46, no. 6 (1994): 350-354. Antibody titres against Plasmodium falciparum and P. vivax were examined using the indirect fluorescent antibody test (IFAT) for 183 Gidra-speaking adults and adolescents in four ecologically different villages of lowland Papua New Guinea. The findings highlight that 1) in Gidraland P. falciparum was more prevalent than P. vivax, 2) the proportion of antibody titres of 1:64 or higher markedly differed among the villages, ranging from 35.3% to 100% for males and from 31.6% to 100% for females, and 3) in the two villages with high prevalences, these were higher among males than females. The inter-village and sex differences can be largely explained by microenvironmental conditions and behavioural patterns of the population. The population-based analyses of this study intend to contribute to a better understanding of the prevalence of malaria in human-environment settings and thus to the planning of malaria prevention.

Nakazawa, S., et al, **A Correlation Between Sequestered Parasitized Erythrocytes in Subcutaneous Tissue and Cerebral Malaria**. *American Journal of Tropical Medicine and Hygiene* 53, no. 5 (November 1995): 544-46.

Sequestered parasitized erythrocytes were found in microvessels of subcutaneous tissues in a comatose patient with cerebral malaria even though the blood smears were negative after quinine treatment. This situation reflects the continued presence of sequestered parasites in the brain and suggests that negative parasitemia in peripheral blood does not necessarily mean the end point of malarial treatment has been reached. Our findings suggest that biopsy of subcutaneous tissue

from severe malaria patients may be useful for determining the severity and prognosis of malaria patients.

Neill, A. L., et al, **Effects of Endotoxin and Dexamethasone on Cerebral Malaria in Mice.**

Parasitology 111, no. Part 4 (November 1995): 443-54.

CBA/T6 and DBA/2J mice inoculated with *Plasmodium berghei* ANKA (PbA) develop cerebral involvement 6-8 days post-inoculation, from which the CBA mice almost invariably die and the DBA mice recover. Dexamethasone (DXM; 80 mg/kg) given to inoculated CBA mice twice, on day 3 and again within 48 h, reduced the cerebral symptoms and prevented death from cerebral malaria. Plasma tumour necrosis factor (TNF) levels, which increased at the time of the cerebral symptoms, were also reduced in these DXM-treated mice. Intravenously administered Evans Blue, a dye which binds to albumin, diffused extensively across the blood-brain barrier only during the period of cerebral symptoms, in proportion to the severity of the cerebral symptoms and the disease. In PbA-infected CBA mice, cerebral symptoms and the amount of Evans Blue diffusing into the brain tissue were both reduced by DSM treatment, but only if the steroid was given on day 3 and again within 48 h. Endotoxin injected intravascularly into PbA-infected DBA mice after day 5 resulted in an exaggeration of cerebral symptoms and death between days 6 and 9. Plasma TNF and the amount of Evans Blue in the brain parenchyma increased above normal levels in these mice. Endotoxin injections had only minor effects on the severity of the cerebral symptoms in PbA-infected CBA mice and did not cause the animals to die sooner.

Ntoumi, F., et al, **Age-Dependent Carriage of Multiple *Plasmodium falciparum* Merozoite Surface Antigen-2 Alleles in Asymptomatic Malaria Infections.** *American Journal of Tropical*

Medicine and Hygiene 52, no. 1 (January 1995): 81-88.

Genetic diversity of the merozoite surface antigen-2 gene of the human malaria parasite *Plasmodium falciparum* has been analyzed in a Senegalese village where malaria is holoendemic. A cross-sectional survey of 65 residents was performed in 1992 during the high transmission season. *Plasmodium falciparum* was detected both by microscopy (77% positive samples) and DNA amplification using a single (29% or 38% positive samples, depending on the primers used) or nested polymerase chain reaction (PCR) (78% positive samples). The overlap between the positive nested PCR and microscopic examination was not complete. The PCR fragments were analyzed for size polymorphism on agarose gels, and were subsequently assigned to the major allelic families 3D7 or FC27 by hybridization with family-specific probes. Both allelic families were found, with a slightly higher prevalence for FC27. Chimeric alleles that failed to hybridize under stringent conditions to the reference probes were also observed. Some were typed using a novel PCR approach, using hybrid pairs of primers, consisting of a family-specific sense oligonucleotide combined with an antisense oligonucleotide specific for the other family. Combining typing techniques, 82% of the positive PCR results yielded more than one band. Both the overall number of fragments and the number of allelic types per carrier were markedly reduced around the age of 15 years. The number of DNA fragments decreased abruptly from an average of four per carrier before the age of 15 years to an average of two in individuals more

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than 15 years of age. Similarly, the number of individuals carrying more than one allelic type decreased with age, with a cutoff at the age of 15 years. This parallels the observed decrease in prevalence and parasite density in this village. There was, however, no age-dependent carriage of any particular allele, with the various alleles being detected in all age groups. The results, therefore, indicate that acquiring anti-parasite immunity not only results in decreasing parasite load, but also in decreasing the complexity of the infections.

Pan American Health Organization, *Health Conditions in the Americas: Volume I* (1994). **REF F54.10 659 v.I**

Chapters: Health and living conditions. Population. Health of population groups. Health and the environment. Diseases.

Pelletier, D. L., et al, **The Effects of Malnutrition on Child Mortality in Developing Countries.**

Bulletin of the World Health Organization 73, no. 4 (1995): 443-48.

Conventional methods of classifying causes of death suggest that about 70% of the deaths of children (aged 0-4 years) worldwide are due to diarrhoeal illness, acute respiratory infection, malaria, and immunizable diseases. The role of malnutrition in child mortality is not revealed by these conventional methods, despite the long-standing recognition of the synergism between malnutrition and infectious diseases. This paper describes a recently-developed epidemiological method to estimate the percentage of child deaths (aged 6-59 months) which could be attributed to the potentiating effects of malnutrition in infectious disease. The results from 53 developing countries with nationally representative data on child weight-for-age indicate that 56% of child deaths were attributable to malnutrition's potentiating effects, and 83% of these were attributable to mild-to-moderate as opposed to severe malnutrition. For individual countries, malnutrition's total potentiating effects on mortality ranged from 13% to 66%, with at least three-quarters of this arising from mild-to-moderate malnutrition in each case. These results show that malnutrition has a far more powerful impact on child mortality than is generally appreciated, and suggest that strategies involving only the screening and treatment of the severely malnourished will do little to address this impact. The methodology provided in this paper makes it possible to estimate the effects of malnutrition on child mortality in any population for which prevalence data exist.

Philips, Margaret, et al, *Guidelines for Cost-Effectiveness Analysis of Vector Control* (1993). **G14.30-6**

Chapters: 1. Planning a cost-effectiveness study. 2. Estimating the costs of vector control. 3. Estimating the effectiveness of vector control. 4. Analysis and presentation of data. 5. Case studies.

Pickard, J., et al, **8. Cost-Effectiveness of Bed Net Impregnation Alone or Combined With Chemoprophylaxis in Preventing Mortality and Morbidity From Malaria in Gambian Children.** *Transactions of the Royal Society of Tropical Medicine and Hygiene* 87, no. Supplement 2 (1993): p. 53-57.

- Plowe, C. V., et al, **Pyrimethamine and Proguanil Resistance-Confering Mutations in Plasmodium Falciparum Dihydrofolate Reductase: Polymerase Chain Reaction Methods for Surveillance in Africa.** *American Journal of Tropical Medicine and Hygiene* 52, no. 6 (June 1995): 565-68.

As chloroquine resistance spreads across Africa, the dihydrofolate reductase (DHFR) inhibitors pyrimethamine and proguanil are being used as alternative first-line drugs for the treatment and prevention of Plasmodium falciparum malaria. Resistance to these drugs is conferred by point mutations in parasite DHFR. These point mutations can be detected by polymerase chain reaction (PCR) assays, but better methods for sample collection, DNA extraction, and a diagnostic PCR are needed to make these assays useful in malaria-endemic areas. Here we report methods for collecting fingerstick blood onto filter paper strips that are air-dried, then stored and transported at room temperature. Cell lysis and DNA extraction are accomplished by boiling in Chelex-100. We also report a nested PCR technique that has improved sensitivity and specificity. These procedures readily detect mixed infections of parasites with both sensitive and resistant genotypes (confirmed by direct sequencing) and are reliable at parasite densities less than 250/mm³ in field surveys.

- Pous, E., et al, **Mefloquine-Induced Grand Mal Seizure During Malaria Chemoprophylaxis in a Non-Epileptic Subject.** *Transactions of the Royal Society of Tropical Medicine and Hygiene* 89, no. 4 (July 1995-August 1995): 434.

- Premji, Z., et al, **Anaemia and Plasmodium Falciparum Infections Among Young Children in an Holoendemic Area, Bagamoyo, Tanzania .** *Acta Tropica* 59, no. 1 (March 1995): 55-64.

Although the aetiology of anaemia in tropical areas is multifactorial, Plasmodium falciparum malaria is commonly associated with anaemia in children living in holoendemic malaria areas. Such an association was examined in a population based study of 338 children 6 to 40 months of age living in the Bagamoyo area of Tanzania. Stepwise regression analysis showed that fever and parasitaemia were effective in predicting anaemia and that the anaemic condition was age dependent. The majority of the children were iron deficient, followed by normochromic macrocytic anaemias. There was strong evidence in this age group that the anaemia was associated with malaria and not geohelminth infection. The importance of malaria and anaemia as a cause of childhood morbidity in Africa is discussed. This condition has taken on new significance with the realization that blood transfusions commonly used to treat severe anaemia are a major vehicle for Human Immunodeficiency Virus (HIV) transmission.

- Premji, Z., et al, **Changes in Malaria Associated Morbidity in Children Using Insecticide Treated Mosquito Nets in the Bagamoyo District of Coastal Tanzania.** *Tropical Medicine and Parasitology* 46, no. 3 (September 1995): 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 implementers. 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 malariometric 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.

Price, R. N., et al, **Artesunate Versus Artemether in Combination With Mefloquine for the Treatment of Multidrug-Resistant *Falciparum* Malaria.** *Transactions of the Royal Society of Tropical Medicine and Hygiene* 89, no. 5 (September 1995-October 1995): 523-27.

To compare the therapeutic efficacy of oral artesunate and artemether in combination with mefloquine for the treatment of multidrug resistant malaria, a trial was conducted in 540 adults and children on the Thai-Myanmar border. Three regimens were compared: artesunate (4 mg/kg/d for 3 d), artemether (4 mg/kg/d for 3 d), both in combination with mefloquine (25 mg/kg), and a single dose of mefloquine (25 mg/kg). The artesunate and artemether regimens gave very similar clinical and parasitological responses, and were both very well tolerated. There was no significant adverse effect attributable to the artemisinin derivatives. Fever and parasite clearance times with mefloquine alone were significantly longer ($P < 0.001$). After adjusting for reinfections the failure rates were 13.9% for the artesunate combination, 12.3% for the artemether combination and 49.2% for mefloquine alone ($P < 0.0001$; relative risk 3.8 [95% confidence interval 2.6-5.4]). Mefloquine should no longer be used alone for the treatment of multidrug resistant *falciparum* malaria in this area. Three-day combination regimens with artesunate or artemether are well tolerated and more effective.

Ramasamy, R., et al, **Dynamics of Natural Antibody Responses to Malaria Parasite Surface Proteins in the Intermediate Rainfall Zone of Sri Lanka.** *Indian Journal of Medical Research* 101 (February 1995): 66-74.

Antibodies against repetitive epitopes on *Plasmodium falciparum* and *P. vivax* circumsporozoite (CS) proteins and epitopes on the 45 kDa and 185-200 kDa *P. falciparum* merozoite surface proteins were measured by radioimmunoassay in a two year longitudinal study in Nikawehera

village located in the intermediate rainfall zone of Sri Lanka. The prevalence and concentrations of specific antibodies were in many, but not all instances, greater in adults than in children who were aged 7-15 yr at the beginning of the study. The concentrations and prevalence of antibodies were associated with malaria transmission levels previously determined from entomological and hospital admission data in the area. Antibody responses to epitopes on different *P. falciparum* antigens, two different epitopes within the 185-200 kDa merozoite surface protein and between the *P. falciparum* and *P. vivax* CS repeats were significantly correlated. Antibody concentrations against a conserved epitope in the 185-200 kDa protein were significantly higher in *P. falciparum* infected individuals than in non-parasitaemic subjects. Antibody concentration and prevalences in Nikawehera were lower than at Weheragala, a site located 70 km away in the dry zone of Sri Lanka. It is postulated that lower levels of immunity in the population in areas such as Nikawehera, that are adjacent to more highly malaria endemic areas, may promote epidemics when conditions favour transmission.

Rasheed, F. N., et al, **Relationships Between Maternal Malaria and Malarial Immune Responses in Mothers and Neonates.** *Parasite Immunology* 17, no. 1 (January 1995): 1-10.

Immune responses of 97 Gambian women and their neonates were studied. New methods distinguished between active and previous placental malaria, were used to examine relationships between maternal malaria and neonatal immune responses. Many placentas (61%) had active or previous malarial infection. Maternal and cord malarial IgG levels correlated ($P < 0.001$). Malarial IgG was raised in cord blood in active placental malaria; IgM was not detected. Mean lymphoproliferation and the proportion of responders to soluble *P. falciparum* antigens (F32) and conserved regions of p190 expressed on trophozoites and schizonts (190L and 190N) were higher in neonates than mothers. There was no clear relationship between maternal malaria and neonatal mean lymphoproliferation to malarial antigens, although fewer neonates responded when mothers were actively infected. Matched maternal and neonatal lymphoproliferation responses did not correlate. However, first born neonatal lymphoproliferation to PPD and malarial antigens appeared lower than other neonates, in agreement with lower lymphoproliferation in primigravidae compared with multigravidae. Also in common with mothers, autologous plasma suppressed neonatal lymphoproliferation to PPD and malarial antigens, suggesting common immunoregulation. Higher cortisol or other circulating factors in first pregnancies may be implicated. The relevance of cell-mediated malarial immune responses detected at birth remains to be established.

Redd, Stephen, et al, **Risk Factors for Anemia in Young Children in Rural Malawi.** *Am J Trop Med Hyg* 51, no. 2 (1994): p. 170-174.

Rejmankova, E., et al, **Predictions of Adult Anopheles Albimanus Densities in Villages Based on Distances to Remotely Sensed Larval Habitats.** *American Journal of Tropical Medicine and Hygiene* 53, no. 5 (November 1995): 482-88.

Remote sensing is particularly helpful for assessing the location and extent of vegetation formations, such as herbaceous wetlands, that are difficult to examine on the ground. Marshes that are sparsely populated with emergent macrophytes and dense cyanobacterial mats have previously been identified as very productive *Anopheles albimanus* larval habitats. This type of habitat was detectable on a classified multispectral Systeme Probatoire d'Observation de la Terre image of northern Belize as a mixture of two isoclasses. A similar spectral signature is characteristic for vegetation of river margins consisting of aquatic grasses and water hyacinth, which constitutes another productive larval habitat. Based on the distance between human settlements (sites) of various sizes and the nearest marsh/river exhibiting this particular class combination, we selected two groups of sites: those located closer than 500 m and those located more than 1,500 m from such habitats. Based on previous adult collections near larval habitats, we defined a landing rate of 0.5 mosquitoes/human/min from 6:30 PM to 8:00 PM as the threshold for high (greater than or equal to 0.5 mosquitoes/human/min) versus low (< 0.5 mosquitoes/human/min) densities of *An. albimanus*. Sites located less than 500 m from the habitat were predicted as having values higher than this threshold, while lower values were predicted for sites located greater than 1,500 m from the habitat. Predictions were verified by collections of mosquitoes landing on humans. The predictions were 100% accurate for sites in the > 1,500-m category and 89% accurate for sites in the < 500-m category.

Robert, V., et al, **Detection of Falciparum Malarial Forms in Naturally Infected Anophelines in Cameroon Using a Fluorescent Anti-25-KD Monoclonal Antibody.** *American Journal of Tropical Medicine and Hygiene* 52, no. 4 (April 1995): 366-69.

Anopheles gambiae s.s. and *An. funestus* were sampled in houses located in a Plasmodium falciparum-holoendemic site in southern Cameroon. The midguts of female mosquitoes in half-gravid or gravid stages of blood digestion were incubated with a fluorescent monoclonal antibody directed against the *P. falciparum* zygote/ookinete surface protein Pfs25 and examined using a fluorescent light microscope. Malarial forms were detected in 11.6% of the half-gravid mosquitoes and in 0.0% of the gravid ones ($P = 0.012$). No difference in infections or the occurrence of malarial forms between *An. gambiae* and *An. funestus* was observed. Overall, 127 malarial forms were counted and distributed among round forms, retorts, and ookinetes in 77.2%, 9.5%, and 13.4%, respectively. Round forms include macrogametes, activating microgametocytes, and zygotes. The mean number of malarial forms per infected midgut was 2.16 and the maximum number observed was 13. In four anophelines, round forms, retorts, and ookinetes were simultaneously observed. Sporozoite rates were 5.7% for *An. gambiae* and 3.8% for *An. funestus*. In the human population, the gametocyte index for *P. falciparum* was 38% with a mean density of 1.11 gametocytes per microliter of blood. Differences concerning malarial forms in mosquito midguts were observed between houses (range percentage = 4.7-21.3%; mean range of forms per positive anopheline = 1.1-3.1). In each house, relationships existed between infected vectors and the gametocyte reservoir of their inhabitants. The role in transmission of people with very low gametocytemia, approximately one per microliter, as a reservoir of falciparum malaria in highly endemic areas, is emphasized.

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Rogier, C., et al, **Malaria Attacks in Children Exposed to High Transmission: Who Is Protected?** *Transactions of the Royal Society of Tropical Medicine and Hygiene* 87, no. 3 (1993): p. 245-46.

Ruebush, T. K., et al, **Self-Treatment of Malaria in a Rural Area of Western Kenya.** *Bulletin of the World Health Organization* 73, no. 2 (1995): 229-36.

Reported are the results of a study of residents' knowledge about malaria and antimalarial drugs and of their treatment-seeking behaviour in a rural area of western Kenya. The study subjects were generally well-informed about the symptoms of the disease. Malaria was perceived as a relatively mild illness, much less severe than acquired immunodeficiency syndrome (AIDS), measles, difficulty in breathing, and diarrhoea. Self-treatment was extremely common: of 138 episodes of febrile illness, 60% were treated at home with herbal remedies or medicines purchased at local shops, and only 18% received treatment at a health centre or hospital; no treatment was sought by the remainder. Commercially available chloroquine preparations were perceived as more effective than either antipyretics or herbal remedies for the treatment of malaria, and injections were regarded as more effective than oral medications. 4-Aminoquinolines were used to treat 58% of febrile illnesses but in only 12% of the cases was a curative dose of greater than or equal to 25 mg/kg body weight employed. Even attendance at a health centre did not ensure adequate treatment because of the common practice of sharing medication among family members. Greatly increased attention should be paid to the role of home treatment of malaria when policies are being developed for the management of febrile illnesses in sub-Saharan Africa.

Sauerborn, R., et al, **The Economic Costs of Illness for Rural Households in Burkina Faso.** *Tropical Medicine and Parasitology* 46, no. 1 (March 1995): 54-60.

Analyses of the health costs in developing countries have mainly dealt with provider costs. This is in spite of the fact that the bulk of illness related costs is borne by households. Where studied, household time and financial costs have not been treated in a comprehensive way. However, an incomplete cost assessment will lead to an underestimation of household costs. Using data from a household interview survey in a rural area of Burkina Faso, the authors carried out an exhaustive assessment of the economic cost of illness that households incur. Financial costs included out-of-pocket expenditures for drugs, fees, transport to the treatment site, lodging and food for accompanying household members. Time costs, in turn, were comprised of production foregone both by the sick person and by healthy household members, who tended to the sick. Time costs amounted to by far the largest proportion (73 %) of total household costs. Of the total amount of illness related time loss of the average household, 45 % was due to the fact that healthy household members tended to or accompanied their sick kin. Of the financial cost items, expenditures for drugs or traditional products represented 62 %. When Western type services were sought, expenditures for transport, food etc., exceeded those for treatment fees. Total cost of illness was 4,002 F CFA/month for the average household. This amounted to 3.7 % of household income and to 6.2 % of household expenditures in the reference month. The authors discuss policy measures aimed to reduce household time costs. They point to the substantial underestimation of the financial burden that health care imposes on households, when these costs

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are assessed in an incomplete way. Finally, they call for great caution in taking the households' "ability-to-pay" for health care for granted.

Schultz, L. J., et al, **Antimalarials During Pregnancy: A Cost-Effectiveness Analysis.** *Bulletin of the World Health Organization* 73, no. 2 (1995): 207-14.

Antenatal clinics (ANC) provide an avenue for interventions that promote maternal and infant health. In areas hyperendemic for *Plasmodium falciparum*, malaria infection during pregnancy contributes to low birth weight (LBW), which is the greatest risk factor for neonatal mortality. Using current data and costs from studies in Malawi, a decision-analysis model was constructed to predict the number of LBW cases prevented by three antimalarial regimens, in an area with a high prevalence of chloroquine (CQ)-resistant malaria. Factors considered included local costs of antimalarials, number of ANC visits, compliance with dispensed antimalarials, prevalence of placental malaria, and LBW incidence. For a hypothetical cohort of 10 000 women in their first or second pregnancy, a regimen consisting of one dose of sulfadoxine-pyrimethamine (SP) in the second trimester followed by a second dose at the beginning of the third trimester would prevent 205 cases of LBW at a cost of US\$9.66 per case of LBW prevented. A regimen using a treatment dose of SP followed by CQ 300 mg (base) weekly would prevent 59 cases of LBW at a cost of \$62 per case prevented, compared with only 30 cases of LBW prevented at a cost of \$113 per case when the regimen involves initial treatment with CQ (25 mg/kg) followed by CQ 300 mg (base) weekly. In areas hyperendemic for CQ-resistant *P. falciparum*, a two-dose SP regimen is a cost-effective intervention to reduce LBW incidence and it should be included as part of the antenatal care package.

Schultz, L. J., et al, **The Efficacy of Antimalarial Regimens Containing Sulfadoxine-Pyrimethamine and/or Chloroquine in Preventing Peripheral and Placental *Plasmodium falciparum* Infection Among Pregnant Women in Malawi.** *American Journal of Tropical Medicine and Hygiene* 51, no. 5 (November 1994): 515-22.

To define an effective and deliverable antimalarial regimen for use during pregnancy, pregnant women at highest risk of malaria (those in their first or second pregnancy) in an area of Malawi with high transmission of chloroquine (CQ)-resistant *Plasmodium falciparum* were placed on CQ and/or sulfadoxine-pyrimethamine (SP). Of 38 pregnant women who received CQ treatment followed by weekly CQ prophylaxis (CQ/CQ) for at least 45 days prior to delivery, 32% had placental malaria infection, compared with 26% of 50 pregnant women who received a treatment dose of SP followed by weekly CQ prophylaxis (SP/CQ), and only 9% of 71 pregnant women who received a two-dose SP regimen (SP/SP; given once during the second trimester and repeated at the beginning of the third trimester) ($P = 0.006$, by chi-square test). During the peak transmission season from April to July, 47% of the women who received CQ/CQ had placental malaria infection at delivery, as compared with 37% of the women who received SP/CQ, and 10% of women who received SP/SP ($P = 0.004$, by chi-square test). Among women in their first or second pregnancy, two treatment doses of SP were highly effective in decreasing the proportion of women with placental malaria infection at delivery.

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- Service, Michael W., *Demography and Vector Borne Diseases* (1989). **R11-40**
Chapters. Problems of human mobility and diseases. Vector borne diseases introduced into new areas due to human movements. Chagas disease and human behavior. Economic analysis of schistosomiasis control projects. Vector borne diseases among displaced Kampucheans. Developments in the Senegal River Basin on the spread of schistosomiasis. Vector borne diseases associated with dams and other development schemes. Effect of malaria on demographic patterns and human behavior. Migration and malaria. Demographic aspects of the epidemiology of onchocerciasis in West Africa.
- Sexton, John D., **Impregnated Bed Nets for Malaria Control: Biological Success and Social Responsibility.** *American Journal of Tropical Medicine and Hygiene* 50, no. 6 (1994): p. 72-81.
- Sharma, V. P., **Cost Effectiveness of Environmental Management for Malaria Control in India.** *Sixth Meeting of the WHO/FAO/UNEP Panel of Experts on Environmental Management for Vector Control* (1994). **G14.30-434**
- Sims, Jacqueline, *Women, Health & Environment, An Anthology* (1994). **R14.30 1332**
- Slutsker, L., et al, **In-Hospital Morbidity and Mortality Due to Malaria-Associated Severe Anaemia in Two Areas of Malawi With Different Patterns of Malaria Infection.** *Transactions of the Royal Society of Tropical Medicine and Hygiene* 88, no. 5 (September 1994-October 1994): 548-51.
We examined the relative contribution of malaria-associated severe anaemia (parasitaemia and haematocrit less than or equal to 15%) to malaria-related morbidity and mortality among children admitted at 2 hospitals in areas with different seasonal patterns of malaria infection in Malawi. The prevalence of malaria-associated severe anaemia was 8.5% among admissions at the hospital in an area with sustained, year-round infection (Mangochi District Hospital [MDH]), compared to 5.2% at the hospital in an area with a fluctuating pattern of infection (Queen Elizabeth Central Hospital [QECH]). Infants at MDH were nearly twice as likely to have malaria-associated severe anaemia as were those at QECH. Parasite density on admission was not related to the risk of severe anaemia at MDH, but if was at QECH. A similar proportion of all deaths was attributed to malaria at MDH (17.5%) and QECH (20.4%). However, malaria-associated severe anaemia accounted for 54% of malaria-related deaths at MDH compared to only 32% at QECH. Malaria-associated severe anaemia contributed significantly to morbidity and mortality at both sites, but its impact was more marked in the area with a sustained pattern of infection. These findings suggest that seasonal fluctuations in malaria infection may contribute to differences in patterns of malaria disease.

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Smith, T., et al, **Mapping the Densities of Malaria Vectors Within a Single Village.** *Acta Tropica* 59, no. 1 (March 1995): 1-18.

Small scale spatial variation and temporal heterogeneity in mosquito densities can have important consequences for disease transmission, but the extreme variation which is observed in populations of malaria vectors makes it difficult to obtain good predictions of densities for short time periods over limited areas. We have applied Bayesian techniques derived for use in cancer epidemiology in order to map densities of *Anopheles gambiae* al. and *A. funestus* in a Tanzanian village where there is intense transmission of *Plasmodium falciparum* malaria. Estimates derived in this way should prove useful in vector population biology and in improving estimates of exposure-response relationships of the human host to malaria. The same methods can be applied in other fields of animal ecology.

Smith, T., et al, **Relationships Between Plasmodium Falciparum Infection and Morbidity in a Highly Endemic Area.** *Parasitology* 109, no. Part 5 (December 1994): 539-49.

A total of 736 outpatients diagnosed as having malaria using clinical criteria at a health centre in a highly endemic area of Papua New Guinea were investigated parasitologically. *Plasmodium falciparum*-attributable fractions were determined using a logistic regression model to compare parasite densities in cases with those of healthy individuals in community surveys. Thirty-seven percent of presumptive cases were found to have raised *P. falciparum* parasitaemia. This corresponds to an average reporting rate for the population of 0.53 attributable episodes per annum. Whilst the maximum prevalence of parasitaemia in the community was in children aged 5-9 years, the maximum age-specific incidence of attributable cases at the outpatient clinic was 2 cases per annum in the 2- to 4-year-old age group. The procedure for estimating attributable fractions makes it possible to compare morbidity rates between age groups, and to examine how the relationship between morbidity risk and parasite density changes with age, without diagnosing individual episodes. The average tolerance of parasites in an age group was measured by considering the level of parasitaemia associated with a given risk of malaria-attributable morbidity. In contrast to anti-parasite immunity, tolerance of parasites declines with age since at parasite isodensity the probability of being symptomatic increases with age.

Snow, R. W., et al, **Will Reducing Plasmodium Falciparum Transmission Alter Malaria Mortality Among African Children?** *Parasitology Today* 11, no. 5 (May 1995): 188-90.

There have been few attempts to examine the relationship between the intensity of transmission and the ensuing burden of disease or mortality from *Plasmodium falciparum* in Africa. Bob Snow and Kevin Marsh here present the available data on malaria-specific mortality and severe morbidity among African children in relation to estimates of annual rates of *falciparum* inoculation. These data suggest that cohort mortality from malaria may remain similar between areas experiencing over 100-fold differences in transmission pressure. The authors raise doubts about the possible long-term benefits to children living in areas of high transmission of control strategies aimed at sustained reduction in human-vector contact, for example insecticide-treated bednets.

Somboon, P., et al, **Entomological Evaluation of Community-Wide Use of Lambdacyhalothrin-Impregnated Bed Nets Against Malaria in a Border Area of North-West Thailand.**

Transactions of the Royal Society of Tropical Medicine and Hygiene 89, no. 3 (May 1995-June 1995): 248-54.

This paper reports 2 studies. (i) After a year of baseline data collection, lambdacyhalothrin-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 3 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. Both studies, especially the second, suggested that the community-wide use of treated bed nets did not generally reduce the vectorial capacity of vectors in this area, probably because of the biting behaviour of the mosquitoes.

Soto, J., et al, **Efficacy of Permethrin-Impregnated Uniforms in the Prevention of Malaria and Leishmaniasis in Colombian Soldiers.** *Clinical Infectious Diseases* 21, no. 3 (September 1995): 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.

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Sowunmi, A., et al, **Open Comparison of Mefloquine, Mefloquine/Sulfadoxine/Pyrimethamine and Chloroquine in Acute Uncomplicated Falciparum Malaria in Children.** *Transactions of the Royal Society of Tropical Medicine and Hygiene* 89, no. 3 (May 1995-June 1995): 303-5.

The susceptibility in vivo of Plasmodium falciparum to mefloquine, mefloquine/sulfadoxine/pyrimethamine and chloroquine was investigated in 115 children with acute uncomplicated falciparum malaria. Susceptibility of P. falciparum isolates to mefloquine and chloroquine in vitro was also investigated. Mefloquine alone and mefloquine/sulfadoxine/pyrimethamine showed similar response rates and both reduced parasitaemia and fever more rapidly than chloroquine. Mefloquine also promptly reduced parasitaemia and fever within 48 h in all chloroquine treatment failures. In vitro, 10% of isolates showed reduced susceptibility to mefloquine and 18% were resistant to chloroquine. These results suggest that the addition of sulfadoxine/pyrimethamine does not have a significant therapeutic advantage over mefloquine alone in the treatment of acute uncomplicated falciparum malaria in children from this endemic area.

Sowunmi, A., et al, **Artemether Treatment of Sulfadoxine/Pyrimethamine-Resistant Plasmodium Falciparum Malaria in Children.** *Transactions of the Royal Society of Tropical Medicine and Hygiene* 89, no. 4 (July 1995-August 1995): 435-36.

Sowunmi, A., et al, **Falciparum Malaria Presenting As Psychosis.** *Tropical and Geographical Medicine* 47, no. 5 (1995): 218-19. **TC215**

A 15 year-old male presented on three occasions with fever, aggressive behaviour, poor sleep acid mixed affective and schizophreniform symptoms in association with falciparum malaria, The symptoms resolved promptly following antimalarial treatment. Prophylaxis with proguanil prevented recurrence of the illness.

Stephens, C., et al, **Knowledge of Mosquitos in Relation to Public and Domestic Control Activities in the Cities of Dar Es Salaam and Tanga.** *Bulletin of the World Health Organization* 73, no. 1 (1995): 97-104.

A study of community awareness of mosquitos and related subjects in the residential areas of two Tanzanian cities (Dar es Salaam and Tanga) showed that residents were well aware of mosquitos. Almost all claimed to use some form of domestic mosquito control product for their personal protection, and many spend a significant portion of the household income on this. The problems of nuisance-biting and malaria transmission are usually not separated and are considered to be the result of poor environmental hygiene, for which both residents and local authorities are responsible. Although Cuter mosquitos are not a primary target of the Urban Malaria Control Project (UMCP), the persistence of nuisance-biting has made residents sceptical and dissatisfied with insecticide spraying. The residents' priorities are evidently not the same as those of the health authorities, yet mutual cooperation is essential. In order to maintain community support campaigns aimed at malaria vectors should consider the need for additional measures to control Cuter mosquitos, such as those now being tried by the UMCP. Mosquito breeding sites are non-

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specifically associated with rubbish and standing water of all kinds, and so the actions that the community considers necessary for mosquito source reduction tend to be poorly targeted. Residents do not recognize that some sources produce malaria mosquitoes while others produce nuisance mosquitoes. The environmental anti-mosquito measures currently promoted by health education and other forms of propaganda are also poorly targeted. While some of them are directed at important *Culex* breeding sites, others are aimed at sites of little importance for mosquitoes of any kind. Almost no attention is paid to the most productive breeding sites for *Anopheles* malaria vectors.

Tanariya, P., et al, **Clinical Response and Susceptibility in Vitro of Plasmodium Vivax to the Standard Regimen of Chloroquine in Thailand.** *Transactions of the Royal Society of Tropical Medicine and Hygiene* 89, no. 4 (July 1995-August 1995): 426-29.

The clinical effectiveness of the standard regimen of chloroquine (CQ) (a total dose of 1500 mg, given over 48 h at 0, 6, 24 and 48 h) for the treatment of *Plasmodium vivax* malaria in Thailand was investigated in 57 patients in an endemic area of Thailand (Chantaburi Province, eastern Thailand). For radical treatment, an additional course of a tissue schizontocidal agent, primaquine, was given following the complete course of CQ. With this regimen, satisfactory whole blood concentration-time profiles of CQ and its major metabolite desethylchloroquine (DECQ) were achieved. Mean whole blood levels of CQ and DECQ always much exceeded the reported therapeutic level of CQ (90 ng/mL) during the first 7 d of treatment. All patients responded well, to the treatment; in most cases, complete and rapid clearance of parasitaemia was observed within the first 48 h. No reappearance of the parasitaemia was detected in peripheral blood films of any patient within 14 d of the evaluation period. In 6 patients, however, reappearance of *P. vivax* parasitaemia was observed after 30 d; 2 of them had not completed the course of primaquine. There was no difference in whole blood concentrations of CQ and DECQ, admission parasitaemia, susceptibility of the isolates to chloroquine in vitro, and parasite clearance time between patients with or without reappearance of parasitaemia. A prominent trend of deteriorating sensitivity of the parasite to the drug was, however, suggested.

Tang, L. H., et al, **Social Aspects of Malaria in Heping, Hainan.** *Acta Tropica* 59, no. 1 (March 1995): 41-53.

This paper presents findings from a study conducted in Heping Town, Qiongzong County, Hainan Province, China. The study, conducted in 1992, used qualitative as well as quantitative methods to gather social, cultural and behavioural data associated with the acquisition, transmission and prevention of malaria, and the diagnosis and treatment of disease. These methods included focus groups, key informant and other in-depth interviews, and observations, a household survey and tests of school children of knowledge of malaria. The study is among the first to our knowledge that has utilized this broad mix of methods for tropical disease research in China.

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Tauil, Pedro Luiz, **Economic Aspects of Malaria Prevention and Control by Means of Environmental Management in Resource Development Projects in the Brazilian Amazon Region.** *Sixth Meeting of the WHO/FAO/UNEP Panel of Experts on Environmental Management for Vector Control* (1994). **G14.30-434**

Taylor-Robinson, A. W., **Regulation of Immunity to Malaria: Valuable Lessons Learned From Murine Models.** *Parasitology Today* 11, no. 9 (September 1995): 334-42.

A major advance in immunology has been the establishment of a framework for analysing how certain immune responses dominate following exposure to a particular pathogen or antigen. CD4(+) T helper (Th) cells can be separated into two major subsets which mediate qualitatively distinct cell-mediated (Th1) and humoral (Th2) immune responses. Immunity to most pathogens can be broadly categorized into a predominant protective response of either type. A characteristic of murine malaras is that primary infections with asexual erythrocytic parasites (the pathogenic stage of the malaria life cycle) generate a host protective immune response with a broad spectrum of Th1- and Th2-type CD4(+) T-cell involvement and so can be examined as models of the interaction of Th1 and Th2 cells during an immune response to an infectious agent. Andrew Taylor-Robinson here describes recent events in the dissection of the mechanisms responsible for the generation of protective immunity to *Plasmodium chabaudi chabaudi* and other experimental malaras in mice.

Thomson, M. C., et al, **Entomological Evaluation of the Gambia's National Impregnated Bednet Programme.** *Annals of Tropical Medicine and Parasitology* 89, no. 3 (June 1995): 229-41.

Entomological studies were conducted in paired study villages in three of the five study areas used for the epidemiological assessment of the Gambia's National Impregnated Bednet Programme. Baseline data collected in 1991 were compared with post-intervention data from 1992, when one of each village pair (from areas II, III and V) was included in the treatment programme in which villagers' nets were dipped in permethrin. In a longitudinal study, indoor-resting densities of *Anopheles gambiae* s.l. in the treated villages were significantly reduced, when compared with their paired untreated village, in areas II ($t=3.32$, 13 degrees of freedom, $P=0.006$) and III ($t=3.71$, 13 degrees of freedom, $P=0.003$). However, this was not associated with higher outdoor-biting rates in the evenings in the treated villages than in the controls. The reduction in vector population was most evident in area II, where the treated village was relatively isolated and 74% of the population slept under a treated net. *Anopheles gambiae* s.l. were also collected during two fortnightly periods in area V, where the sporozoite rates in 1991 had been relatively high (7.65% and 6.07%). There was no significant decrease in the sporozoite rate in the treated village in area V in 1992, despite the fact that this village was over 5 km from its nearest neighbouring village. However, the proportion of villagers sleeping under a treated net in this village was <50%. No clear evidence for an epidemiologically significant 'mass killing effect', resulting from the village-wide use of treated nets, emerges in this or any other study undertaken in The Gambia. However, such an effect is indicated by results from Salikene, where the village mosquito population was relatively isolated and where the majority of the population

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slept under a treated net. This situation is unlikely to be repeated in most Gambian villages in the primary-health-care scheme, since treated and untreated villages are generally interspersed and the mosquito populations move freely between them. We must therefore conclude that, on a national scale, the nets provide an exceptionally high level of personal rather than community protection. The mechanisms underlying the personal protection are, however, still unclear.

Touze, J. E., et al, **Human Pharmacokinetics of Chloroquine and Proguanil Delivered in a Single Capsule for Malaria Chemoprophylaxis.** *Tropical Medicine and Parasitology* 46, no. 3 (September 1995): 158-60.

Two antimalarial prophylactic regimens were compared in 17 healthy volunteers. Regimen A consisted of daily ingestion of a single capsule containing 100 mg base chloroquine (CQ) and 200 mg proguanil (PG). Regimen B consisted of daily ingestion of separate tablets of CQ (100 mg base) and PG (two 100 mg tablets). Both treatments lasted for 12 days. Effective chloroquine levels were reached after 72 hours with both regimens (49.9 ng/ml for treatment A and 36.7 ng/ml for treatment B). Proguanil and cycloguanil plasma levels were significantly lower on sampling obtained at H3 (three hours later) and H6 (six hours later) on day 1 in the regimen A ($p < 0.002$). Thereafter there were no significant difference between the two regimens. Both regimens were well tolerated, but regimen A using the capsule appeared better accepted and facilitates compliance.

Trape, Jean-Francois, **The Dielmo Project: A Longitudinal Study of Natural Malaria Infection and the Mechanisms of Protective Immunity in a Community Living in a Holoendemic Area of Senegal.** *Am J Trop Med Hyg* 51, no. 2 (1994): p. 123-37.

Findings suggest that sterile immunity and clinical protection are never fully achieved in humans continuously exposed since birth to intense transmission.

Trape, Jean-Francois, et al, **Malaria Morbidity Among Children Exposed to Low Seasonal Transmission in Dakar, Senegal and Its Implications for Malaria Control in Tropical Africa.** *American Journal of Tropical Medicine and Hygiene* 48, no. 6 (1994): p. 748-56.

U.S. Agency for International Development, *Addressing the Challenges of Malaria Control in Africa* (n.d). **F56.10M 766**

Weiss, W. R., et al, **Daily Primaquine Is Effective for Prophylaxis Against Falciparum Malaria in Kenya: Comparison With Mefloquine, Doxycycline, and Chloroquine Plus Proguanil.** *Journal of Infectious Diseases* 171, no. 6 (June 1995): 1569-75.

Primaquine was tested as a prophylactic drug against Plasmodium falciparum in a region in western Kenya in which malaria is holoendemic. Children 9-14 years old were randomized to receive regimens of daily primaquine, daily doxycycline, daily proguanil plus weekly chloroquine, daily vitamin plus weekly mefloquine, or daily vitamin alone. Primaquine, doxycycline, and mefloquine were equally effective in preventing both symptomatic and

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asymptomatic malarial infections. Chloroquine plus proguanil was the least effective regimen, There was no toxicity from daily primaquine during the 11 weeks of the study, Findings show that primaquine can be successfully used as a causal prophylactic regimen against falciparum malaria in western Kenya; chloroquine plus proguanil was not as efficacious as the three other preventive regimens; most Kenyan children receiving standard doses of mefloquine and doxycycline had lower than expected serum trough drug levels; and some volunteers with adequate mefloquine or doxycycline levels at trough developed asymptomatic parasitemias and clinical malaria.

Wernsdorfer, W. H., et al, *Malaria: Principles and Practice of Malariology* (1988). **F56.10M-37**
Volume 2 Chapters. Epidemiology. Mathematical models. Environmental management.
Imagociding. Larviciding. Biological control. Global distribution. Animal models.
Chemotherapy.

Wernsdorfer, W. H., et al, **Chloroquine Resistance of Plasmodium Falciparum: A Biological Advantage?** *Transactions of the Royal Society of Tropical Medicine and Hygiene* 89, no. 1 (January 1995-February 1995): 90-91.

The response in vitro of Plasmodium falciparum to chloroquine, mefloquine and quinine was studied in a hyperendemic peri-urban area of Accra, Ghana, during the fourth quarter of 1991, yielding a total of 159 valid tests. Schizont maturation in drug-free controls and effective chloroquine concentrations were strongly correlated. This was not seen with mefloquine or quinine. Higher mean parasitaemia in untreated oligosymptomatic carriers of overtly chloroquine-resistant P. falciparum than in carriers of more sensitive parasites was another indication of higher viability and biological advantage of chloroquine-resistant P. falciparum that may conceivably have clinical implications.

Wijeyaratne, Pandu, *Gender, Health and Sustainable Development: A Latin American Perspective, Proceedings of a Workshop Held in Montevideo, Uruguay, 26-29 April 1994* (1994). **R14.30-159**
C.2

Chapters. Gender and occupational health in Chile. Gender and occupational health in Venezuela. Socioeconomic and cultural factors of Chagas Disease. Socioeconomic impact and gender differentials of cholera. Prevalence of malaria in Costa Rica.

Wijeyaratne, Pandu, *Gender, Health and Sustainable Development: Proceedings of a Workshop Held in Nairobi, Kenya, 5-8 October 1993* (1993). **R14.30-159**

Chapters. Gender issues in the control and prevention of malaria and schistosomiasis in Cameroon. Gender and tropical diseases in Nigeria. Gender and impregnated mosquito bednets for malaria control. Gender issue in the prevention and control of visceral leishmaniasis: kala-azar and malaria. Refugees, gender and health.

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Wijeyaratne, Pandu, et al, *Women and Tropical Diseases* (1993). **R14.30-83**

Chapters. Leprosy in Women. Women and schistosomiasis. Women and malaria. Leprosy. Does schistosomiasis infection impair the health of women. Clinicopathologic and socioeconomic impact of Chagas disease on women: a review. Materno-fetal malaria.

Wildling, E., et al, **Malaria Epidemiology in the Province of Moyen Ogoov, Gabon.** *Tropical Medicine and Parasitology* 46, no. 2 (June 1995): 77-82.

In the course of epidemiological and immunological baseline studies parasitological surveys were conducted, in 1992, in three localities situated in our near rain forest in the area of Lambarene, Gabon, western Central Africa. *Anopheles gambiae* s.s. and *A. funestus* are considered to be the main vectors of malaria. The three localities represent strata with obvious differences in the intensity of malaria transmission. The lowest parasite rates were recorded in the village around the Albert-Schweitzer-Hospital where environmental sanitation and easy access to diagnostic and therapeutic facilities afford a fair measure of malaria control. The villages of Bellevue and Tchad show a much higher prevalence of *Plasmodium falciparum*, followed by *P. malariae* and *P. ovale*. In all three villages parasite rates and geometric mean parasite densities of *P. falciparum* showed the age pattern typical for areas with stable, hyperendemic malaria. Analysis by season showed the period of the long rains to be the epidemiologically calmest while the dry season and even more the short rainy season produced an increase of parasite rates and densities. In Tchad, the most affected of the three villages, the parasite rates in female adults were significantly lower than in male adults. This was accompanied by lower parasite densities in female adults.

Wirima, Jack, *Malaria Prevention in Pregnancy: The Magochi Malaria Research Project* (n.d). **F56.10M 2112**

World Health Organization, *Antimalarial Drug Policies: Data Requirements, Treatment of Uncomplicated Malaria and Management of Malaria in Pregnancy* (1994). **F56.10M 1344**

World Health Organization, *Entomological Field Techniques for Malaria Control: Part I, Learner's Guide* (1992). **G14.30-55 part I**

Chapters. Malaria and its control. Role of entomological work. Recognition of anopheline mosquitoes. Collection of mosquitoes.

World Health Organization, *Entomological Field Techniques for Malaria Control: Part II: Tutor's Guide* (1992). **G14.30-56 part II**

Chapters. Malaria and its control. Recognition of anopheline mosquitoes. Collection of mosquitoes.

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- World Health Organization, *Implementation of the Global Malaria Control Strategy* (1993). **F56.10M-3**
Ch 4. Disease management. 5. Disease prevention. 6. Health information systems. 7. Program management.
- World Health Organization, *Manual on Environmental Management for Mosquito Control* (1982).
G14.30-44
Chapters. Environmental management. Environmental modification. Environmental manipulation. Reduction of man and mosquito contact. Guidelines for the vector control worker.
- World Health Organization, *Parasitic Diseases in Water Resources Development: The Need for Intersectoral Negotiation* (1993). **F56-5**
Ch. 2. Parasitic diseases and water resources development. 3. Adverse health effects of water development schemes. 4. Health effects of small village dams. 5. Disease control. 6. Policy critique of health aspects of water development projects. 7. Intersectoral negotiating strategies for health authorities.
- World Health Organization, **World Malaria Situation in 1992: Part I**. *Weekly Epidem Rec* 69, no. 42 (October 1994): pp. 309-13.
- World Health Organization, **World Malaria Situation in 1992: Part II**. *Weekly Epidemiological Record* 69, no. 43 (October 1994): p. 317-24.
- World Health Organization, **World Malaria Situation in 1992: Part III**. *Weekly Epidemiological Record* 69, no. 44 (November 1994): p. 325-30.
- Yeo, A. E. T., et al, **A Statistical Analysis of the Antimalarial Activity of Proguanil and Cycloguanil in Human Volunteers**. *Annals of Tropical Medicine and Parasitology* 88, no. 6 (December 1994): 587-94.
Proguanil, an orally administered antimalarial drug, was given to 36 individuals (200 mg daily for 3 days). The antimalarial activity in plasma samples collected after the drug administration was then determined by bioassay. Concentrations of proguanil and cycloguanil (the principal active metabolite) in these samples were also measured by high performance liquid chromatography. A regression analysis was then performed on these variables to determine if the antimalarial activity of the samples was due to proguanil alone or to proguanil and cycloguanil together. The analysis indicated that cycloguanil is the main determinant of antimalarial activity after proguanil administration and that the activity of cycloguanil is not influenced by the presence of proguanil.
- Yeo, A. E. T., et al, **Increased Antimalarial Activity of Azithromycin During Prolonged Exposure of Plasmodium Falciparum in Vitro**. *International Journal for Parasitology* 25, no. 4 (April 1995): 531-32.

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The minimum inhibitory concentration, MIC, of azithromycin was determined for 2 isolates of *Plasmodium falciparum* at 48 and 96 h. The MIC at 48 h for the K1 and FC isolates were 6.2 and 8.7 µg/ml, respectively. At 96 h, the MIC decreased to 0.08 µg/ml for the K1 isolate and 0.04 µg/ml for the FC isolate. The marked reduction in the MIC values between the first and second asexual erythrocytic cycles suggests that the drug acts slowly and that it may have to be used in combination with a faster acting drug.

Zahar, A. R., *Applied Field Studies: Vector Bionomics, Malaria Epidemiology and Control by Geographical Areas* (1990). **F56.10M 819**

Ziba, C., et al, **Use of Malaria Prevention Measures in Malawian Households.** *Trop Med Parasitol* 45 (1994): p 70-73. **F56.10 1138**