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EFFICACY OF CHLOROQUINE, AMODIAQUINE, SULPHADOXINE-PYRIMETHAMINE AND COMBINATION THERAPY WITH ARTESUNATE IN MOZAMBICAN CHILDREN WITH NON-COMPLICATED MALARIA.

Tropical Medicine & International Health: February 2004; 9(2): 200-208.

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This paper reports a two-phase study in Manhiça district, Mozambique: first we assessed the clinical efficacy and parasitological response of *Plasmodium falciparum* to chloroquine (CQ), sulphadoxine-pyrimethamine (SP) and amodiaquine (AQ), then we tested the safety and efficacy in the treatment of uncomplicated malaria, of three combinations: AQ + SP, artesunate (AR) + SP and AQ + AR. Based on the WHO (1996, WHO/MAL/96.1077) *in vivo* protocol, we conducted two open, randomized, clinical trials. Children aged 6-59 months with axillary body temperature ≥ 37.5 °C and non-complicated malaria were randomly allocated to treatment groups and followed up for 21 days (first and second trial) and 28 days (first trial). The therapeutic efficacy of AQ (91.6%) was better than that of SP (82.7%) and CQ (47.1%). After 14 days, 69% of the strains were parasitologically resistant to CQ, 21.4% to SP and 26% to AQ. Co-administration of AQ + SP, AR + SP and AQ + AR was safe and had 100% clinical efficacy at 14-day follow-up. The combination therapies affected rapid fever clearance time and reduced the incidence of gametocytaemia during follow-up. (Author abstract)

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EFFICACY OF MEFLOQUINE AND MEFLOQUINE-ARTESUNATE FOR THE TREATMENT OF UNCOMPLICATED PLASMODIUM FALCIPARUM MALARIA IN THE AMAZON REGION OF BOLIVIA.

Tropical Medicine & International Health: February 2004; 9(2): 217-221.

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We assessed the efficacy of mefloquine monotherapy and mefloquine-artesunate (MQ-AS) combination therapy for the treatment of *Plasmodium falciparum* malaria at four sites in the Bolivian Amazon region. Patients with uncomplicated *P. falciparum* infections between 5 and 60 years of age were randomly assigned to be treated with either MQ (15 mg/kg in a single oral dose) or MQ (15 mg/kg) plus AS (4 mg/kg daily for 3 days). A total of 143 patients were enrolled and followed for 28 days. None of the 73 patients who received MQ alone or the 70 patients who received MQ-AS combination therapy had recurrences of parasitaemia during the 28-day follow-up period. Asexual parasite densities fell significantly more rapidly and the proportion of patients with gametocytes was significantly lower on days 7-28 in patients treated with MQ-AS than in those treated with MQ alone. All patients tolerated the medications well. After this study, the Bolivian Ministry of Public Health changed its treatment policy for uncomplicated *P. falciparum* malaria in the Amazon region to combination therapy with MQ-AS to slow or prevent the development of resistance.
(Author abstract)

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THE NATURALLY DERIVED INSECTICIDE SPINOSAD IS HIGHLY TOXIC TO AEADES AND ANOPHELES MOSQUITO LARVAE.

Medical and Veterinary Entomology: March 2004; 18(1): 50-56.

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Spinosad is a naturally derived biorational insecticide with an environmentally favourable toxicity profile, so we investigated its potency against mosquito larvae (Diptera: Culicidae). By laboratory bioassays of a suspension concentrate formulation of spinosad (Tracer[®]), the 24 h lethal concentration (LC₅₀) against *Aedes aegypti* (L.) third and fourth instars was estimated at 0.025 p.p.m. following logit regression. The concentration-mortality response of third- and fourth-instar *Anopheles albimanus* Weidemann did not conform to a logit model. The LC₅₀ value of spinosad in *Anopheles albimanus* was 0.024 p.p.m. by quadratic linear regression. A field trial in southern Mexico demonstrated that spinosad 1 p.p.m. compared with the standard temephos (Abate[®]) 1% granules 100 g/m³ water prevented *Ae. aegypti* breeding in plastic containers of water for 8 weeks; at 10 p.p.m. spinosad prevented breeding for > 22 weeks. In another field trial, spinosad at 5 p.p.m. and temephos both completely eliminated reproduction of *Ae. aegypti* for 13 weeks. In contrast, the bacterial insecticide *Bacillus thuringiensis* var. *israelensis* (*Bti*, Vectobac[®] AS) performed poorly with just 2 weeks of complete inhibition of *Ae. aegypti* breeding. Spinosad also effectively prevented breeding of *Culex* mosquitoes and chironomids in both trials to a degree similar to that of temephos. We conclude that spinosad merits evaluation as a replacement for organophosphate or *Bti* treatment of domestic water tanks in Mesoamerica. We also predict that spinosad is likely to be an effective larvicide for treatment of mosquito breeding sites. (*Author abstract*)

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USE OF INTERMITTENT PRESUMPTIVE TREATMENT AND INSECTICIDE TREATED BED NETS BY PREGNANT WOMEN IN FOUR KENYAN DISTRICTS.

Tropical Medicine & International Health: February 2004; 9(2): 255-261.

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The roll back malaria (RBM) movement promotes the use of insecticide-treated bednets (ITNs) and intermittent presumptive treatment (IPT) of malaria infection as preventive measures against the adverse effects of malaria among pregnant women in Africa. To determine the use of these preventive measures we undertook a community-based survey of recently pregnant women randomly selected from communities in four districts of Kenya in December 2001. Of the 1814 women surveyed, only 5% had slept under an ITN. More than half of the 13% of women using a bednet (treated or untreated) had bought their nets from shops or markets. Women from rural areas used bednets less than urban women (11% vs. 27%; $P < 0.001$), and 41% of the bednets used by rural women had been obtained free of charge from a research project in Bondo or a nationwide

UNICEF donation through antenatal clinics (ANCs). Despite 96% of ANC providers being aware of IPT with sulphadoxine-pyrimethamine (SP), only 5% of women interviewed had received two or more doses of SP as a presumptive treatment. The coverage of pregnant women with at least one dose of IPT with SP was 14%, though a similar percentage also had received at least a single dose as a curative treatment. The coverage of nationally recommended strategies to prevent malaria during pregnancy during 2001 was low across the diverse malaria ecology of Kenya. Rapid expansion of access to these services is required to meet international and national targets by the year 2005. The scaling up of malaria prevention programmes through ANC services should be possible with 74% of women visiting ANCs at least twice in all four districts. Issues of commodity supply and service costs to clients will be the greatest impediments to reaching RBM targets. (*Author abstract*)

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Laxminarayan, Ramanan

DOES REDUCING MALARIA IMPROVE HOUSEHOLD LIVING STANDARDS?

Tropical Medicine & International Health: February 2004; 9(2): 267-272.

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Living in malaria-endemic regions places an economic burden on households even if they do not actually suffer an episode of malaria. Households living in endemic malarial regions are less likely to have access to economic opportunities and may have to modify agricultural practices and other household behaviour to adapt to their disease environment. Data from Vietnam demonstrate that reductions in malaria incidence through government-financed malaria control programmes can contribute to higher household income for all households in endemic areas. Empirically, the roughly 60% decline in malaria cases over the 1990s in Vietnam translated to a \$12.60 average improvement in annual consumption of *all* households, or a roughly \$180 million annual economic benefit in the form of improved living standards. (*Author abstract*)

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SHORT COMMUNICATION: AN ASSESSMENT OF THE USE OF MALARIA RAPID TESTS BY VILLAGE HEALTH VOLUNTEERS IN RURAL LAOS.

Tropical Medicine & International Health: March 2004; 9(3): 325-329.

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Rapid malaria diagnosis, a key component of malaria control strategies, is hampered by the expense and training requirements of reliable microscopy. Rapid malaria antigen tests may improve the diagnosis of malaria in the rural tropics. After 1 h training 64 village health volunteers (VHVs) from rural Laos, with no previous laboratory experience, performed two malaria rapid diagnostic tests (ParacheckPfTM and OptiMALTM) accurately. The reliability of six VHVs was assessed longitudinally, over 10 months with different frequencies of retraining. Compared with microscopy, error rates in dipstick interpretation were low (<2%) for both tests and were not associated with retraining frequency ($P > 0.2$). Previously untrained Lao VHVs performed malaria rapid tests reliably with high sensitivity and specificity after minimal training. (*Author abstract*)

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ARTEMETHER-LUMEFANTRINE FOR UNCOMPLICATED MALARIA: A SYSTEMATIC REVIEW.

Tropical Medicine & International Health: February 2004; 9(2): 192-199.

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BACKGROUND: The World Health Organization (WHO) is promoting artemether-lumefantrine for treating uncomplicated malaria. The objective of this review is to summarize available evidence of its effects compared with other antimalarial regimens.

METHODS: We sought randomized and quasi-randomized studies comparing artemether-lumefantrine with any other antimalarial drug regimen. Databases searched were MEDLINE (to February 2003), EMBASE (to February 2003), and the Cochrane Controlled Trials Register (issue 1, 2003). Conference proceedings and reference article lists were searched and malaria researchers and the drug

manufacturer were contacted. Two reviewers independently applied inclusion criteria and extracted data.

RESULTS: Six trials (1698 participants) studied the four-dose regimen. Fever and parasite clearance tended to be shorter with artemether-lumefantrine, but parasitological failure on day 28 was more common with artemether-lumefantrine in comparison with mefloquine (one trial, n = 233), halofantrine (one trial, n = 86) and mefloquine-artesunate (one trial, n = 537); but less common with chloroquine (two trials, n = 378). For the six-dose regimen, two studies compared artemether-lumefantrine with mefloquine-artesunate, but there was insufficient data to demonstrate any meaningful comparative effects for day 28 parasitaemia, and no difference in parasite or fever clearance time was detected. There were 11 parasitological failures with artemether-lumefantrine and none with mefloquine-artesunate.

CONCLUSION: There is no evidence to demonstrate the four-dose regimen of artemether-lumefantrine results in a higher cure rate than other antimalarial regimens against which it has been tested, apart from chloroquine in areas with high chloroquine resistance. Artemether-lumefantrine has potential advantages over non-artemisinin regimens because of the faster clearance time and gametocyte clearance. There is insufficient evidence about the six-dose regimen to know whether it is less or more effective than current antimalarial drug regimens. (*Author abstract*)

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EFFICACY OF SULPHADOXINE-PYRIMETHAMINE ALONE OR COMBINED WITH AMODIAQUINE OR CHLOROQUINE FOR THE TREATMENT OF UNCOMPLICATED FALCIPARUM MALARIA IN UGANDAN CHILDREN.

Tropical Medicine & International Health: February 2004; 9(2): 222-229.

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The rapid development of falciparum resistance to sulphadoxine-pyrimethamine (SP) in East and Central Africa has raised concerns as to the efficacy of combining it with another drug. In 2002, we assessed the efficacy of SP alone

and combined with amodiaquine (AQ/SP) or chloroquine (CQ/SP) in Ugandan children with uncomplicated falciparum malaria. At day 14, adequate clinical response was 100% (84/84) for AQ/SP, 93% (92/101) for CQ/SP and 91% (73/80) for SP. At day 28, parasitological failure (RI-RIII) occurred in 16% (13/80) of children treated with AQ/SP, in 48% (48/100) of those treated with CQ/SP and in 61% (48/79) of those treated with SP alone. Compared with the AQ/SP arm, the odds for parasitological failure at day 28 were five times higher (95% CI, 2-10) in the CQ/SP group and sevenfold higher (95% CI, 3-17) in that of SP alone. CQ/SP does not offer any significant added benefit over SP alone while AQ/SP is an efficacious low-cost combination. These findings have important policy implications for Uganda and other resource-constrained African countries faced with the problematic choice of a new first-line antimalarial treatment in a context of high CQ resistance. (*Author abstract*)

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MALARIA TRANSMISSION AND MAJOR MALARIA VECTORS IN DIFFERENT GEOGRAPHICAL AREAS OF SOUTHEAST ASIA.

Tropical Medicine & International Health: February 2004; 9(2): 230-237.

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During the last decade, major progress in malaria control has been achieved in Vietnam, Laos and Cambodia. However, malaria is still a potentially fatal disease in some hilly-forested areas and continues to be endemic in a few coastal foci. To estimate the risk that stems from the major vectors after a decade of intensive malaria control, an entomological study based on human landing collections was conducted between April 1998 and November 2000 in six study villages (four in Vietnam, one in Cambodia and one in Laos) located in different physio-geographical areas. Five villages were selected in places where new cases of malaria still occurred. In the sixth village, in the northern hilly area of Vietnam, no case of malaria was detected during the past 3 years. In three study villages of the hilly forested areas of Cambodia and central Vietnam, *Anopheles dirus* A still played an important role in malaria transmission and maintain perennial transmission inside the villages despite its low density. *Anopheles minimus* A was found in all study villages except in the southern coastal village of Vietnam. Its role in malaria transmission, however, varied between localities and surveys. In one study village of central Vietnam it was almost absent (one specimen

collected over 480 man nights), and in another village sporozoite positive specimens (2.8%) were only observed during the first two surveys whereas this species disappeared from the collections from November 1998 onwards (six surveys: 360 man nights). In the northern study site *An. minimus* A and C were found in all collections, but no local malaria transmission occurred. However, the constant presence of these two species associated with a high longevity (parous rate up around 80% and 65%, respectively), suggests that transmission can occur at almost any time if parasite reservoirs are reintroduced in the area. The proper management of malaria cases and population movement is, therefore, important to prevent outbreaks and the reintroduction of malaria in northern Vietnam. In the study site of the Mekong delta, *An. sudaicus* occurred at high densities (up to 190 bites/man/night). The recent changes in land use from rice cultivation to shrimp farming probably explains the increase of this brackish water breeding species during the study period. However, none of the 11 002 specimens was positive for *Plasmodium* circumsporozoite protein (CSP). The relative low survival rate as estimated by the parous rate (around 47 %) may reflect its low vectorial status that could explain the very low malaria incidence (1.9 case/100 persons/year) in this study site. A calculated sporozoite rate of maximum 1/300 000 is enough to explain this low malaria incidence. Despite the successes in malaria control, the vector *An. dirus* A continues to play an important role in malaria transmission, whereas *An. minimus* A showed temporal and spatial variation in its role as vector. The role of *An. sudaicus* as vector could not be confirmed because of the low incidence in the coastal study village. Other *Anopheles* species may be locally involved, but in the five study villages where malaria is still present they probably do not contribute significantly to malaria transmission. The study also points towards the fact that in Southeast Asia it will become increasingly difficult to incriminate *Anopheles* species in malaria transmission while the risk for malaria transmission still persist.
(Author abstract)

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COMBATING TROPICAL INFECTIOUS DISEASES: REPORT OF THE DISEASE CONTROL PRIORITIES IN DEVELOPING COUNTRIES PROJECT.

Clinical Infectious Diseases: March 15, 2004; 38(6): 871-878.

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Infectious diseases are responsible for >25% of the global disease toll. The new Disease Control Priorities in Developing Countries Project (DCPP) aims to decrease the burden of these diseases by producing science-based analyses from demographic, epidemiologic, disease intervention, and economic evidence for the purpose of defining disease priorities and implementing control measures. The DCPP recently reviewed selected tropical infectious diseases, examined successful control experiences, and defined unsettled patient treatment, prevention, and research issues. Disease elimination programs against American trypanosomiasis (Chagas disease), onchocerciasis, lymphatic filariasis, leprosy, trachoma, and measles are succeeding. Dengue, leishmaniasis, African trypanosomiasis, malaria, diarrheal diseases, helminthic infections, and tuberculosis have reemerged because of inadequate interventions and control strategies and the breakdown of health delivery systems. Application of technologies must be cost-effective and intensified research is essential if these and other scourges are to be controlled or eliminated in the 21st century.

(Author abstract)

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DEPRESSED NATURAL KILLER CELL CYTOTOXICITY AGAINST PLASMODIUM FALCIPARUM-INFECTED ERYTHROCYTES DURING FIRST PREGNANCIES.

Clinical Infectious Diseases: February 1, 2004; 38(3): 342-347.

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We measured natural killer (NK) cell cytotoxicity and cortisol and prolactin concentrations in peripheral venous blood samples obtained from pregnant Gabonese women at the time of delivery. The NK cell-mediated cytotoxicity against Plasmodium falciparum-infected erythrocytes in vitro was lower in samples obtained from primiparous women than in samples obtained from multiparous women; cortisol concentrations were significantly higher in primiparous women than in multiparous women, and prolactin concentrations were significantly lower. The highest cortisol concentrations were found in the plasma of P. falciparum-infected primiparous women. A positive correlation was found between cortisol concentration and parasite load; an inverse correlation was found between the magnitude of the NK cell cytolytic effect and cortisol production. A positive correlation was found between this effect and prolactin

production. Thus, depressed NK cell cytotoxicity against *P. falciparum* infected erythrocytes is correlated with high cortisol concentrations and may contribute to increased susceptibility to malaria during pregnancy. (*Author abstract*)

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Onwujekwe, Obinna^{1,2}; Hanson, Kara³; Fox-Rushby, Julia^{3,4}

INEQUALITIES IN ACQUISITION OF MOSQUITO NETS AND WILLINGNESS TO PAY FOR INSECTICIDE-TREATED NETS IN NIGERIA: CHALLENGES TO SUCCESSES OF MALARIA CONTROL INTERVENTIONS.

Malaria Journal: March 16, 2004, 3:6. (*published online*)

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OBJECTIVE: To explore the equity implications of insecticide-treated nets (ITN) distribution programmes that are based on user charges.

METHODS: A questionnaire was used to collect information on previous purchase of untreated nets and hypothetical willingness to pay (WTP) for ITNs from a random sample of householders. A second survey was conducted one month later to collect information on actual purchases of ITNs. An economic status index was used for characterizing inequity.

RESULTS: The lower economic status quintiles were less likely to have previously purchased untreated nets and also had a lower hypothetical and actual WTP for ITNs.

CONCLUSIONS: ITN distribution programmes need to take account of the diversity in WTP for ITNs if they are to ensure equity in access to the nets. This could form part of the overall poverty reduction strategy. (*Author abstract*)

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Chilundo, Baltazar^{1,2}; Sundby, Johanne²; Aanestad, Margunn³

ANALYSING THE QUALITY OF ROUTINE MALARIA DATA IN MOZAMBIQUE.

Malaria Journal: March 3, 2004; 3:3. (*published online*)

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BACKGROUND: In Mozambique, malaria is the principal cause of morbidity and mortality. Efforts are being made to increase control activities within communities. These activities require management decisions based on evidence of malaria incidence. Although some data generated are of poor quality, there is little research towards improving the reporting systems.

METHODS: An analysis of the quality of routine malaria data was performed in selected districts in Southern Mozambique from August to September 2003. The aim was to assess the quality of the source data in terms of completeness, correctness and consistency across management levels.

RESULTS: Analysis revealed primary data to be of poor quality. The diversity of reporting systems with limited coordination give rise to redundancies and wastage of resources. There was evidence of “invention” of data in health facilities contributing to an incorrect representation of malaria incidence. Large, “non-clinical”, time-based variations of malaria cases due to reporting delays were also noted, contributing to false alerts of outbreaks. Furthermore, targets established in the national strategic plan for malaria cannot be calculated through the existing systems; this is the case, for example, for data related to pregnant women and children under-five years.

DISCUSSION AND RECOMMENDATIONS: The existing reporting system for malaria is currently not satisfying the information needs of managers. It is suggested that one standardized system, including the creation of one form to include the essential variables required for the calculation of key indicators by age, gender and pregnancy status, and to establish a national database that maps malaria by location. (*Author abstract*)

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INTER-ALLELIC RECOMBINATION IN THE PLASMODIUM VIVAX MEROZOITE SURFACE PROTEIN 1 GENE AMONG INDIAN AND COLOMBIAN ISOLATES.

Malaria Journal: March 5, 2004; 3:4.

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BACKGROUND: A major concern in malaria vaccine development is the polymorphism observed among different Plasmodium isolates in different geographical areas across the globe. The merozoite surface protein 1 (MSP-1) is a leading vaccine candidate antigen against asexual blood stages of malaria parasite. To date, little is known about the extent of sequence variation in the Plasmodium vivax MSP-1 gene (Pvmsp-1) among Indian isolates. Since P. vivax accounts for >50% of malaria cases in India and in Colombia, it is essential to know the Pvmsp-1 gene variability in these two countries to sustain it as a vaccine candidate. The extent of polymorphism in Pvmsp-1 gene among Indian and Colombian isolates is described.

METHODS: The sequence variation in the region encompassing the inter-species conserved blocks (ICBs) five and six of Pvmsp-1 gene was examined. PCR was carried out to amplify the polymorphic region of Pvmsp-1 and the PCR products from twenty (nine Indian and 11 Colombian) isolates were sequenced and aligned with Belem and Salvador-1 sequences.

RESULTS: Results revealed three distinct types of sequences among these isolates, namely, Salvador-like, Belem-like and a third type sequence which was generated due to interallelic recombination between Salvador-like sequences and Belem-like sequences. Existence of the third type in majority (44%) showed that allelic recombinations play an important role in PvMSP1 diversity in natural parasite population. Micro-heterogeneity was also seen in a few of these isolates due to nucleotide substitutions, insertions as well as deletions.

CONCLUSIONS: Intergenic recombination in the Pvmsp-1 gene was found and suggest that this is the main cause for genetic diversity of the Pvmsp-1 gene.
(Author abstract)

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FOSMIDOMYCIN-CLINDAMYCIN FOR PLASMODIUM FALCIPARUM INFECTIONS IN AFRICAN CHILDREN.

The Journal of Infectious Diseases: March 1, 2004; 189(5): 901-908.

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BACKGROUND: Fosmidomycin is a new antimalarial drug with a novel mechanism of action. Studies in Africa that have evaluated fosmidomycin as monotherapeutic agent demonstrated its excellent tolerance, but 3-times-daily treatment regimens of ≥ 4 days were required to achieve radical cure, prompting further research to identify and validate a suitable combination partner to enhance its efficacy.

METHODS: We conducted a randomized, controlled, open-label study to evaluate the efficacy and safety of fosmidomycin combined with clindamycin ($n = 12$; 30 and 5 mg/kg body weight every 12 h for 5 days, respectively), compared with fosmidomycin alone ($n = 12$; 30 mg/kg body weight every 12 h for 5 days) and clindamycin alone ($n = 12$; 5 mg/kg body weight every 12 h for 5 days) for the clearance of asymptomatic *Plasmodium falciparum* infections in schoolchildren in Gabon aged 7-14 years.

RESULTS: Asexual parasites were rapidly cleared in children treated with fosmidomycin-clindamycin (median time, 18 h) and fosmidomycin alone (25 h) but slowly in children treated with clindamycin alone (71 h; $P = .004$). However, only treatment with fosmidomycin-clindamycin or clindamycin alone led to the radical elimination of asexual parasites as measured by day 14 and 28 cure rates of 100%. Asexual parasites reappeared by day 28 in 7 children who received fosmidomycin (day 14 cure rate, 92% [11/12; day 28 cure rate, 42% [5/12]). All regimens were well tolerated, and no serious adverse events occurred.

CONCLUSION: The combination of fosmidomycin and clindamycin is well tolerated and superior to either agent on its own with respect to the rapid and radical clearance of *P. falciparum* infections in African children. (*Author abstract*)

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THE DEFORMABILITY OF RED BLOOD CELLS PARASITIZED BY *PLASMODIUM FALCIPARUM* AND *P. VIVAX*.

The Journal of Infectious Diseases: January 15, 2004; 189(2): 190-194.

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Red blood cells (RBCs) must deform considerably during their multiple passages through the microvasculature and the sinusoids of the spleen. RBCs infected with *Plasmodium falciparum* (Pf-IRBCs) become increasingly rigid as they mature but avoid splenic clearance by sequestering in venules and capillaries. In contrast, RBCs infected with *P. vivax* (Pv-IRBCs) do not sequester. We compared the effects of *P. vivax* and *P. falciparum* infection on RBC deformability in a laminar shear flow system. Pf-IRBCs became more rigid as the parasite matured, but equivalent maturation of Pv-IRBCs resulted in a doubling of flexibility. Coincidentally, the IRBC surface area increased from $56.7 \pm 1.3 \mu\text{m}^2$ to $74.7 \pm 0.6 \mu\text{m}^2$ to $90.9 \pm 1.1 \mu\text{m}^2$ in ring-, trophozoite-, and schizont-stage Pv-IRBCs, respectively, whereas Pf-IRBCs did not increase in size. *P. vivax* increases the deformability of IRBCs and thereby avoids splenic entrapment. (*Author abstract*)

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Alves, Maria José Chinelatto Pinheiro, Mayo, Renata Caporalle; Donalisio, Maria Rita

HISTORY, EPIDEMIOLOGY AND CONTROL OF MALARIA IN CAMPINAS REGION, SÃO PAULO STATE, BRAZIL, 1980 TO 2000.

Revista da Sociedade Brasileira de Medicina Tropical: January-February, 2004: 37(1): 41-45.

It is a retrospective descriptive study about 3314 notified cases of malaria in Superintendência de Controle de Endemias, Campinas, an area that covers 88 cities and 5.366.081 inhabitants, during 80's and 90's. The region data were compared to national statistics looking at disease history and control program impact in endemic areas. It was observed a decrease in notified cases in Campinas region, while over the same period incidence in Amazonia was increasing. The highest prevalence was in men (83%) between 20 and 49 years old, mainly from Rondônia, Pará and Mato Grosso State; 59% were diagnosed in three first days of symptoms. It was suggested the impact of educational campaigns addressed to risk population and health professionals in the Campinas region. In no endemic areas, early diagnostic and treatment are a great challenge because it may extend patient access and proper health care decreasing lethality and impeding local transmission. It can also facilitate

integration among vector control, epidemiologic surveillance and attendance to patients. (*Author abstract*)

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Leal, Osvaldo; Leal, Elaine Azevedo Soares; Borges, Jr., Franklin Roberto Pereira; *et al.*

CLINICAL-PARASITOLOGICAL RESPONSE TO TREATMENT WITH QUININE ASSOCIATED TO DOXYCYCLINE IN UNCOMPLICATED FALCIPARUM MALARIA.

Revista da Sociedade Brasileira de Medicina Tropical: November-December 2003; 36(6): 751-754.

The response of patients with uncomplicated falciparum malaria to quinine plus doxycycline was studied in an open clinical trial. The majority (76.2%; n = 16) had plasmodia sensitive to the treatment, and 23.8% (n = 5) were resistant. This therapeutic scheme appears to be a good option in uncomplicated falciparum malaria. (*Author abstract*)

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Doerig, Christian

PROTEIN KINASES AS TARGETS FOR ANTI-PARASITIC CHEMOTHERAPY.

Cellular & Molecular Biology Letters: 2003; 8(2A): 524-525.

also published in Biochimica et Biophysica Acta - Proteins & Proteomics: March 11, 2004; 1697(1-2): 155-168. <http://www.sciencedirect.com/>

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Parasitic protozoa infecting humans have a staggering impact on public health, especially in the developing world. Furthermore, several protozoan species are major pathogens of domestic animals and have a considerable impact on food production. In many instances, the parasites have developed resistance against available chemotherapeutic agents, making the search for alternative drugs a priority.

In line with the current interest in protein kinases inhibitors as potential drugs against a variety of diseases, the possibility that protein kinases may represent targets for novel anti-parasitic agents is being explored. Research into parasite protein kinases has benefited greatly from genome and EST sequencing

projects, with the genomes of a few species fully sequenced (notably that of the human malaria parasite *Plasmodium falciparum*) and several more under way.

The overall picture that emerged from research in this area shows that the phylogenetic isolation of parasitic protozoa is reflected by atypical structural and functional properties of many of their protein kinase homologues. Likewise, evidence is emerging, which suggests that the organisation of some otherwise well-conserved signal transduction pathways is divergent in some parasitic species. The differences between protein kinases of a parasite and their homologues in its host cell suggest that specific inhibition of the former can be achieved. The development of anti-parasitic drugs based on protein kinase inhibition is being pursued following two avenues: one consists of screening chemical libraries on recombinant enzymes; several protein kinases from parasitic protozoa are now available for this approach.

The second approach relies on the identification of the molecular targets of kinase inhibitors which display anti-parasitic properties. This has led to promising developments in a few instances, in particular regarding PKG as a drug target against *Eimeria* and *Toxoplasma*, and purvalanol B, a purine-based CDK inhibitor which appears to affect unexpected targets in several protozoan parasites.

The recent resolution of the structure of a *Plasmodium* protein kinase complexed with small inhibitory molecules opens the way to a rational approach towards the design of anti-parasitic drugs based on kinase inhibition. (*Author abstract*)

PMID: 15023358

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Richter, Joachim¹; Harms, Gundel²; Müller-Stöver, Irmela¹; Göbels, Klaus¹; Häussinger, Dieter¹

PERFORMANCE OF AN IMMUNOCHROMATOGRAPHIC TEST FOR THE RAPID DIAGNOSIS OF MALARIA.

Parasitology Research: April 2004; 92(6): 518-519.

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The immunochromatographic test (ICT) for the rapid diagnosis of malaria has been marketed for several years. In a study in which three Centres of Tropical Medicine participated and data were pooled, performance of the test varied considerably when comparing the results between each centre. The sensitivity of ICT in 2,343 patients tested in our services was 100% and the specificity

99.74%. Moreover, two patients with a positive ICT would initially have been missed by expert microscopy, with *Plasmodium falciparum* malaria being confirmed microscopically some hours later. The principal reasons for the better performance of the test in our series appear to be blood collection in EDTA vials and considerable experience with handling and interpreting the ICT test. (*Author abstract*)

PMID: 15007639

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Christopher V Plowe¹, James G Kublin¹, Fraction K Dzinjalama², Deborah S Kamwendo², Rabia A G Mukadam², Phillips Chimpeni², Malcolm E Molyneux³, Terrie E Taylor⁴

SUSTAINED CLINICAL EFFICACY OF SULFADOXINE-PYRIMETHAMINE FOR UNCOMPLICATED FALCIPARUM MALARIA IN MALAWI AFTER 10 YEARS AS FIRST LINE TREATMENT: FIVE YEAR PROSPECTIVE STUDY.

British Medical Journal: February 2004, 328: 545-550.

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Please refer also to the related editorial by Dr. Brian Greenwood, below.

OBJECTIVE: To measure the efficacy of sulfadoxine-pyrimethamine treatment of falciparum malaria in Malawi from 1998 to 2002, after a change from chloroquine to sulfadoxine-pyrimethamine as first line treatment in that country in 1993.

DESIGN: Prospective open label drug efficacy study.

SETTING: Health centre in large peri-urban township adjacent to Blantyre, Malawi.

PARTICIPANTS: People presenting to a health centre with uncomplicated *Plasmodium falciparum* malaria.

MAIN OUTCOME MEASURES: Therapeutic efficacy and parasitological resistance to standard sulfadoxine-pyrimethamine treatment at 14 days and 28 days of follow up.

RESULTS: Therapeutic efficacy remained stable, with adequate clinical response rates of 80% or higher throughout the five years of the study. Analysis of follow

up to 28 days showed modest but significant trends towards diminishing clinical and parasitological efficacy over time within the study period.

CONCLUSION: Contrary to expectations, sulfadoxine-pyrimethamine has retained good efficacy after 10 years as the first line antimalarial drug in Malawi. African countries with very low chloroquine efficacy, high sulfadoxine-pyrimethamine efficacy, and no other immediately available alternatives may benefit from interim use of sulfadoxine-pyrimethamine while awaiting implementation of combination antimalarial treatments. (*Author abstract*)

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Greenwood, Brian

TREATING MALARIA IN AFRICA: SULFADOXINE-PYRIMETHAMINE MAY STILL HAVE A FUTURE DESPITE REPORTS OF RESISTANCE.

BMJ: March 6, 2004; 328: 534-535.

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Please refer also to the related article by Dr. Christopher V. Plowe, et al., above.

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NEW BOOK(s)

MALARIA PARASITES: GENOMES AND MOLECULAR BIOLOGY

A.P. Waters; C.J. Janse, Editors.
Leiden University Medical Centre, Leiden, The Netherlands

March 2004
List Price: \$230 ; £115
Hardbound: 558 pages.
ISBN: 0954246462
Publisher: Caister Academic Press

The completion of the *Plasmodium falciparum* genome sequence in late 2002 heralded a new era in malaria research. The search began in earnest for new drugs and vaccines to combat malaria, a disease which afflicts up to 500 million people worldwide and is responsible for the deaths of more than one million people each year. The new genomic data is aiding a greater understanding of the living parasite and its interaction with the insect vector and human host.

In this book internationally renowned experts provide up-to-date reviews of the most important aspects of post-genomic malaria research. Topics covered include: the *P. falciparum* genome and model parasites, bioinformatics and genome databases, microsatellite analysis, analysis of chromosome structure, cell cycle to RNA polymerase I and II mediated gene expression, role of the nuclear genome, the parasite surface and cell biology, and much more.
(*Publisher description*)

Chapters:

Introduction: The *Plasmodium falciparum* Genome Project

- D.J. Carucci, P.M. Goodwin, M. Gottlieb, V. McGovern

Chapter 1: The Genome of *Plasmodium falciparum*

- Neil Hall, Malcolm Gardner

Chapter 2: The Genome of Model Malaria Parasites, and Comparative Genomics

- Jane Carlton, Joana Silva, Neil Hall

Chapter 3: Getting the Most out of Bioinformatics Resources

- Jessica C. Kissinger, David S. Roos

Chapter 4: Manipulating the *Plasmodium* Genome

- Teresa Gil Carvalho, Robert Ménard

Chapter 5: *Toxoplasma gondii* a Model Organism for the Apicomplexans?

- Dominique Soldati, Markus Meissner

Chapter 6: Microsatellite Markers and Population Genetics in *Plasmodium falciparum*

- Deirdre Joy, Jianbing Mu, Xin-zhuan Su

Chapter 7: Chromosome Structure and Dynamics of *Plasmodium* Subtelomeres

- Artur Scherf, Luisa M. Figueiredo, Lúcio H. Freitas-Junior

Chapter 8: Gene Expression

- Kirk W Deitsch

Chapter 9: Regulation of rRNA Transcription and Processing During the *Plasmodium* Life Cycle

- Thomas F. McCutchan, Rosalinda van Spaendonk, Chris Janse, Jun Fang, Andrew P. Waters

Chapter 10: Cell Cycle Control in *Plasmodium falciparum*: A Genomics

Perspective

- Christian Doerig, Debopam Chakrabarti

Chapter 11: The Apicoplast

- Ross F. Waller, Geoff I. McFadden

Chapter 12: The Surface of the *Plasmodium falciparum*-infected Erythrocyte

- Joseph D. Smith, Alister G. Craig

Chapter 13: Merozoite Cell Biology

- Agnieszka E. Topolska, Lina Wang, Casilda G. Black, Ross L. Coppel

Chapter 14: Sexual Development of Malaria Parasites

- C.J. Janse, A.P. Waters

Chapter 15: Ookinete Cell Biology

- R.E. Sinden, Y.I.H. Alavi, G.A. Butcher, J.T. Dessens, J.D. Raine, H.E. Trueman

Chapter 16: Molecular and Cellular Biology of Chloroquine Resistance in *Plasmodium falciparum*

- Karena L. Waller, Sylvia Lee, David A. Fidock

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