



Bulletin 172 | 28 July 2008

From K&S Consulting

The first three weeks of August there will be no MalariaWorld. We will include reference to articles published in this period toward the end of August. The summer editions of MalariaWorld will mainly cover publications and will not include News items.

Publications

Open access | Exported Proteins Required for Virulence and Rigidity of Plasmodium falciparum-Infected Human Erythrocytes

Alexander G. Maier et al.

Cell, Volume 134, Issue 1, 11 July 2008, Pages 48-61

A major part of virulence for Plasmodium falciparum malaria infection, the most lethal parasitic disease of humans, results from increased rigidity and adhesiveness of infected host red cells. These changes are caused by parasite proteins exported to the erythrocyte using novel trafficking machinery assembled in the host cell. To understand these unique modifications, we used a large-scale gene knockout strategy combined with functional screens to identify proteins exported into parasite-infected erythrocytes and involved in remodeling these cells.

Open access | Febrile Plasmodium falciparum Malaria 4 Years after Exposure in a Man with Sickle Cell Disease

Tatiana Greenwood, Tomas Vikerfors, Maria Sjöberg, Gunnar Skeppner, and Anna Färnert
Clinical Infectious Diseases 15 August 2008, Vol. 47, No. 4: e39-e41

We report a case of symptomatic Plasmodium falciparum malaria that manifested 4 years after a visit to an area of endemicity in an 18-year-old male patient with sickle cell disease. The exceptionally long incubation time raises the questions of how and where P. falciparum parasites can reside for several years before suddenly causing disease.

Open access | Dispatch: Cluster of Falciparum Malaria Cases in UK Airport

A.J. Rodger et al.

EID, Volume 14, Number 8–August 2008

cluster of 6 cases of Plasmodium falciparum malaria occurred in a UK airport among 30 travelers returning to the United States from East Africa. Molecular genotyping analysis indicated that all had been exposed to different parasites. The travelers' use of chemoprophylaxis was poor; their perception of risk was limited.

Open access | Letter: Plasmodium falciparum in Ancient Egypt

A.G. Nerlich et al.

EID, Volume 14, Number 8–August 2008

In this report, we describe the unambiguous identification of ancient DNA (aDNA) for P. falciparum in ancient Egyptian mummy tissues from »4,000 years ago. This report adds another infectious disease to the spectrum of paleomicrobiology in ancient Egypt, thereby further explaining the previously postulated influence of infectious diseases on the low life expectancy for ancient Egyptian populations (10). Molecular detection of pathogen aDNA can be used not only to identify a certain disease, but it may also provide information on disease frequency, evolutionary origin, and pathways.



Open access | The effect of water turbidity on the near-surface water temperature of larval habitats of the malaria mosquito *Anopheles gambiae*

K. P. Paaïjmans, W. Takken, A. K. Githeko and A. F. G. Jacobs

International Journal of Biometeorology, Online first

Here we show that at midday (1300 hours) the upper water layer (thickness of 10 mm) of the water pool with the highest turbidity was on average 2.8°C warmer than the same layer of the clearest water pool. Suspended soil particles increase the water temperature and furthermore change the temperature dynamics of small water collections during daytime, exposing malaria mosquito larvae, which live in the top water layer, longer to higher temperatures.

Open access | A central role for free heme in the pathogenesis of severe malaria: the missing link?

Ana Ferreira, József Balla, Viktória Jeney, György Balla and Miguel P. Soares

Journal of Molecular Medicine, Online first

Using well-established rodent models of malaria infection, we found that survival of a *Plasmodium*-infected host is strictly dependent on the host's ability to up-regulate the expression of heme oxygenase-1 (HO-1 encoded by the gene *Hmox1*).

Open access | A physiological time analysis of the duration of the gonotrophic cycle of *Anopheles pseudopunctipennis* and its implications for malaria transmission in Bolivia

Frederic J Lardeux, Rosenka H Tejerina, Vicente Quispe, Tamara K Chavez

Malaria Journal 2008, 7:141 (26 July 2008)

Useful data on egg development of this South American malaria vector, which have been used to develop a mathematical model to explain the variation in population parameters and the malaria transmission potential of this vector in different parts of its geographical range.

Open access | Epochal changes in the association between malaria epidemics and El Nino in Sri Lanka

Lareef Zubair, Gawrie N Galappaththy, Hyemin Yang, Janaki Chandimala, Zeenas Yahiya, Priyanie Amerasinghe, Neil Ward, Stephen J Connor

Malaria Journal 2008, 7:140 (24 July 2008)

An assessment of the relationship between El Nino climatic variations and malaria epidemics in Sri Lanka over a very long time period.

Open access | Establishment of the 1st World Health Organization International Standard for *Plasmodium falciparum* DNA for nucleic acid amplification technique (NAT)-based assays

David J Padley, Alan B Heath, Colin Sutherland, Peter L Chiodini, Sally A Baylis

Malaria Journal 2008, 7:139 (24 July 2008)

It was highly relevant and important to set an international standard for the molecular detection of malaria parasites. This paper describes the process of standardization.

Open access | Efficacy of local neem extracts for sustainable malaria vector control in an African village

Rebecca L Gianotti, Arne Bomblies, Mustafa Dafalla, Ibrahim Issa-Arzika, Jean-Bernard Duchemin, Elfatih AB Eltahir

Malaria Journal 2008, 7:138 (23 July 2008)

The study addresses the potential impact of using crushed neem seeds spread on the surface of larval habitats to reduce vector abundance. The intervention uses local resources and is an affordable addition to other control measures.



Open access | Plasmodium falciparum variant STEVOR antigens are expressed in merozoites and possibly associated with erythrocyte invasion

Ayman Khattab, Insa Bonow, Nadine Schreiber, Michaela Petter, Christel Schmetz, Mo-Quen Klinkert

Malaria Journal 2008, 7:137 (23 July 2008)

The paper describes results with antibodies raised against synthetic peptides based on one STEVOR protein, with identification of a STEVOR protein in merozoites and evidence for STEVOR 'release' during erythrocyte invasion.

Open access | Dynamics of transmission of Plasmodium falciparum by Anopheles arabiensis and the molecular forms M and S of Anopheles gambiae in Dielmo, Senegal

Mamadou Ousmane Ndiath, Cecile Brengues, Lassana Konate, Cheikh Sokhna, Christian Boudin, Jean Francois Trape, Didier Fontenille

Malaria Journal 2008, 7:136 (23 July 2008)

No difference was observed either in host preference or in Plasmodium falciparum infection rates between sympatric M and S populations, but they present different dynamics of population. These variations are probably attributable to different breeding conditions.

Open access | Prospects, achievements, challenges and opportunities for scaling-up malaria chemoprevention in pregnancy in Tanzania: the perspective of national level officers

Godfrey M Mubyazi, Ib C Bygbjerg, Pascal Magnussen, Oystein Olsen, Jens Byskov, Kristian S Hansen, Paul Bloch

Malaria Journal 2008, 7:135 (22 July 2008)

A study of the feasibility of IPTp programmes in the context of antenatal care guidelines.

Open access | The impact of HIV-1 on the malaria parasite biomass in adults in sub-Saharan Africa contributes to the emergence of antimalarial drug resistance

Jean-Pierre Van geertruyden, Joris Menten, Robert Colebunders, Eline Korenromp, Umberto D'Alessandro

Malaria Journal 2008, 7:134 (22 July 2008)

The leading hypothesis of this paper, as developed in the discussion part is very logical and probably true : HIV-1 induced immunosuppression increases incidence of clinical malaria and parasite density. As a result, there is increased incidence of fever empirically treated by anti-malarial drugs, hence an increased risk of emergence of antimalarial drug resistance.

Open access | Malaria in pregnant women in an area with sustained high coverage of insecticide-treated bed nets

Abdunoor M Kabanywany, John R MacArthur, Wilma A Stolk, J Dik F Habbema, Hassan Mshinda, Peter B Bloland, Salim Abdulla, S Patrick Kachur

Malaria Journal 2008, 7:133 (21 July 2008)

This study of a group of pregnant women who have not taken IPTp with SP during their pregnancy shows that malaria remains a problem even in an area with high bed net coverage.

Open access | Presumptive treatment of fever cases as malaria: help or hindrance for malaria control?

Roly D Gosling, Christopher J Drakeley, Alex Mwita, Daniel Chandramohan

Malaria Journal 2008, 7:132 (16 July 2008)



In this opinion paper, the authors propose a hypothesis to explain the apparent decrease in malaria cases in endemic countries over the last decade.

Open access | Competency of *Anopheles stephensi mysorensis* strain for *Plasmodium vivax* and the role of inhibitory carbohydrates to block its sporogonic cycle

Hamid R Basseri, Soghra Doosti, Kamran Akbarzadeh, Mehdai Nategpour, Miranda MA Whitten, Hossein Ladoni

Malaria Journal 2008, 7:131 (15 July 2008)

An interesting and appealing article, addressing the conditions of infection of *Anopheles stephensi* with *Plasmodium vivax*.

Open access | MalHaploFreq: A computer programme for estimating malaria haplotype frequencies from blood samples

Ian M Hastings, Thomas A Smith

Malaria Journal 2008, 7:130 (15 July 2008)

The paper describes an algorithm to estimate multiplicity of infection, and the algorithm has been developed into a free-standing computer programme to estimate haplotype frequencies.

Open access | Evaluation of immunoglobulin purification methods and their impact on quality and yield of antigen-specific antibodies

Elke S Bergmann-Leitner, Ryan M Mease, Elizabeth H Duncan, Farhat Khan, John Waitumbi, Evelina Angov

Malaria Journal 2008, 7:129 (14 July 2008)

This comparison demonstrated that overall polyethylene glycol purification of human serum/plasma samples and protein G Sepharose purification of rabbit sera are optimal for recovering functional Ag-specific antibodies. Consequently, critical consideration of the purification method is required to avoid selecting non-representative populations of recovered Ig, which could influence interpretations of vaccine efficacy, or affect the search for immune correlates of protection.

Open access | Performance of self-diagnosis and standby treatment of malaria in international oilfield service employees in the field

Anna H Roukens, Johannes Berg, Alex Barbey, Leo G Visser

Malaria Journal 2008, 7:128 (14 July 2008)

This survey demonstrated that a comprehensive programme targeting malaria prevention in expatriates can be effectively implemented and that it significantly increased malaria awareness.

Open access | Amodiaquine-artesunate vs artemether-lumefantrine for uncomplicated malaria in Ghanaian children: a randomized efficacy and safety trial with one year follow-up

George O Adjei, Jorgen AL Kurtzhals, Onike P Rodrigues, Michael Alifrangis, Lotte CG Hoegberg, Emmanuel D Kitcher, Ebenezer V Badoe, Roberta Lamptey, Bamenla Q Goka

Malaria Journal 2008, 7:127 (11 July 2008)

AS+AQ and AM-L were efficacious for treatment of children with uncomplicated malaria in Ghana and drug-related adverse events were rare in treated subjects during one year of follow-up. The high prevalence of potentially AQ resistant parasites raises questions about the utility of AQ as a partner drug for ACT in Ghana. The efficacy of AS+AQ in Ghana requires, therefore, continuous monitoring and evaluation.



Open access | The usefulness of a new rapid diagnostic test, the First Response® Malaria Combo (pLDH/HRP2) card test, for malaria diagnosis in the forested belt of central India

Praveen K Bharti, Nipun Silawat, Pushpendra P Singh, Mrigendra P Singh, Manmohan Shukla, Gyan Chand, Aditya P Dash, Neeru Singh

Malaria Journal 2008, 7:126 (11 July 2008)

The RDTs are easy to use, reliable and simple to interpret. RDTs are more suited to health workers in situations where health services are deficient or absent. Therefore, the test can be used as an epidemiological tool for the rapid screening of malaria.

Open access | Reduction of transmission from malaria patients by artemisinin combination therapies: a pooled analysis of six randomized trials

Lucy C Okell, Chris J Drakeley, Azra C Ghani, Teun Bousema, Colin J Sutherland

Malaria Journal 2008, 7:125 (9 July 2008)

Treatment with ACT significantly reduces infectiousness of individual patients with uncomplicated falciparum malaria compared to previous first line treatments. Rapid treatment of cases before gametocytaemia is well developed may enhance the impact of ACT on transmission.

Open access | Correspondence: Artesunate for Malaria

Paul M. Arguin, Peter J. Weina, M.D. & Cindy P. Dougherty

NEJM, Volume 359:313-315 July 17, 2008 Number 3

To the Editor: Rosenthal (April 24 issue)¹ presents a hypothetical case of malaria and states that there is "major concern" about the timeliness of artesunate availability because it is available rapidly only for hospitals that are near the 20 Centers for Disease Control and Prevention (CDC) quarantine stations.

Open access | Genetic Immunisation by Liver Stage Antigen 3 Protects Chimpanzees against Malaria despite Low Immune Responses

Daubersies P, Ollomo B, Sauzet J-P, Brahimi K, Perlaza B-L, et al.

PLoS ONE 3(7): e2659

Using malaria Liver Stage Antigen-3 (LSA-3), we report that genetic immunization induces in chimpanzees, the closest relative of humans, immune responses which are as scarce as those reported using other DNA vaccines in humans, but which nonetheless confer strong, sterile and reproducible protection. The pattern was consistent in 3/4 immunized apes against two high dose sporozoite challenges performed as late as 98 and 238 days post-immunization and by a heterologous strain.

Open access | Modelling the Epidemiological Impact of Intermittent Preventive Treatment against Malaria in Infants

Ross A, Penny M, Maire N, Studer A, Carneiro I, et al.

PLoS ONE 3(7): e2661

The pattern of trial results can be accounted for by differences between the trial sites together with known features of malaria epidemiology and the action of SP. Predictions suggest that IPTi would have a beneficial impact across a variety of epidemiological settings.

Open access | Genistein-Supplemented Diet Decreases Malaria Liver Infection in Mice and Constitutes a Potential Prophylactic Strategy

Cunha-Rodrigues M, Portugal S, Prudêncio M, Gonçalves LA, Casalou C, et al.

PLoS ONE 3(7): e2732

Indeed the emergence of resistance to chloroquine and other drugs in use in these areas reinforces the need to implement alternative prophylactic strategies. Genistein is a naturally occurring compound that is widely used as a food supplement and is thought to



be effective in countering several pathologies. Results presented here show that genistein inhibits liver infection by the Plasmodium parasite, the causative agent of malaria.

Open access | Both Functional LT β Receptor and TNF Receptor 2 Are Required for the Development of Experimental Cerebral Malaria

Togbe D, Loureiro de Sousa P, Fauconnier M, Boissay V, Fick L, et al.

PLoS ONE 3(7): e2608

LT β R expressed on radioresistant resident stromal, probably endothelial cells, rather than hematopoietic cells, are essential for the development of ECM, as assessed by hematopoietic reconstitution experiment. Therefore, the data suggest that both functional LT β R and TNFR2 signaling are required and non-redundant for the development of microvascular pathology resulting in fatal ECM.

Open access | Phase 1 Trial of Malaria Transmission Blocking Vaccine Candidates Pfs25 and Pvs25 Formulated with Montanide ISA 51

Wu Y, Ellis RD, Shaffer D, Fontes E, Malkin EM, et al.

PLoS ONE 3(7): e2636

It is feasible to induce transmission blocking immunity in humans using the Pfs25/ISA 51 vaccine, but these vaccines are unexpectedly reactogenic for further development. This is the first report that the formulation is associated with systemic adverse events including erythema nodosum.

Open access | Antibodies Targeting the PfRH1 Binding Domain Inhibit Invasion of Plasmodium falciparum Merozoites

Gao X, Yeo KP, Aw SS, Kuss C, Iyer JK, et al.

PLoS Pathog 4(7): e1000104

Here, we identify the erythrocyte binding region of the P. falciparum reticulocyte binding protein homologue 1 (PfRH1) and show that antibodies raised against the functional binding region efficiently inhibit invasion. In addition, we directly demonstrate that changes in the expression of RBLs can constitute an immune evasion mechanism of the malaria merozoite.

Natural infectivity of Anopheles species from the Pacific and Atlantic Regions of Colombia

Lina A. Gutiérrez, Nelson Naranjo, Luz Marina Jaramillo, Carlos Muskus, Shirley Luckhart, Jan E. Conn, Margarita M. Correa

Acta Tropica, Volume 107, Issue 2, August 2008, Pages 99-105

We examined the occurrence of An. albimanus in four localities of the Pacific and three of the Atlantic Coast. Our data support the continued predominance of An. albimanus in the Pacific Coast, and demonstrate that this species is the most abundant in the Atlantic Coast as well.

A dried blood sample on filter paper is suitable for detecting Plasmodium falciparum gametocytes by reverse transcription polymerase chain reaction

Yoshimasa Maeno, Shusuke Nakazawa, Le Duc Dao, Naoki Yamamoto, Nguyen Duc Giang, Truong Van Hanh, Le Khanh Thuan, Koki Taniguchi

Acta Tropica, Volume 107, Issue 2, August 2008, Pages 121-127

The detection of gametocytes in human peripheral blood is one of the most important measures in a malaria survey. We attempted to detect gametocytes of Plasmodium falciparum by reverse transcription polymerase chain reaction (RT-PCR) of dried blood on filter paper. These results suggest that dried blood on filter paper is a useful for a molecular epidemiologic study of malaria transmission and gametocyte-targeted control.



The influence of food on the pharmacokinetics of piperazine in healthy Vietnamese volunteers

Trinh Ngoc Hai, Sofia Friberg Hietala, Nguyen Van Huong, Michael Ashton

Acta Tropica, Volume 107, Issue 2, August 2008, Pages 145-149

The combination piperazine and dihydroartemisinin is emerging as first line treatment of uncomplicated falciparum malaria in Southeast Asia. The aim of this study was to determine the influence of a standard Vietnamese meal on the single-dose pharmacokinetics of piperazine when administered in combination with dihydroartemisinin, and to gain extended data on the terminal half-life of piperazine in healthy Vietnamese volunteers.

Building small dams can decrease malaria: A comparative study from Sundargarh District, Orissa, India

Surya K. Sharma, Prajesh K. Tyagi, Ashok K. Upadhyay, Mohammed A. Haque, Tridibes Adak, Aditya P. Dash

Acta Tropica, Volume 107, Issue 2, August 2008, Pages 174-178

The adverse health effect of environmental changes brought about with the construction of large and small dams has often been reported. Here, we present results of a 5-year (2001–2005) study documenting the positive effect of such developmental projects in reducing malaria in an area where malaria transmission is mainly due to the highly efficient anthropophilic vector *Anopheles fluviatilis* with some contribution from *Anopheles culicifacies*.

Natural Plasmodium infections in Brazilian wild monkeys: Reservoirs for human infections?

Ana Maria Ribeiro de Castro Duarte et al.

Acta Tropica, Volume 107, Issue 2, August 2008, Pages 179-185

Four hundred and forty-eight samples of total blood from wild monkeys living in areas where human autochthonous malaria cases have been reported were screened for the presence of *Plasmodium* using microscopy and PCR analysis. The parasitological prevalence of *P. vivax* and *P. malariae* in wild monkeys from Atlantic forest and semideciduous Atlantic forest and the finding of a positive result for *P. falciparum* in *Alouatta* from both types of forest support the hypothesis that monkeys belonging to this genus could be a potential reservoir. Furthermore, these findings raise the question of the relationship between simian and autochthonous human malaria in extra-Amazonian regions.

In Vitro Activity of Ferroquine Is Independent of Polymorphisms in Transport Protein Genes Implicated in Quinoline Resistance in Plasmodium falciparum

Maud Henry, Sebastien Briolant, Albin Fontaine, Joel Mosnier, Eric Baret, Remy Amalvict, Thierry Fusai, Laurent Fraisse, Christophe Rogier, and Bruno Pradines

Antimicrob. Agents Chemother. 2008;52 2755-2759

The in vitro activity of ferroquine (FQ) (SR97193), a 4-aminoquinoline antimalarial compound that contains a ferrocenic nucleus, against 15 *Plasmodium falciparum* strains was assessed and compared with those of chloroquine (CQ), quinine (QN), monodesethylamodiaquine (MDAQ), and mefloquine (MQ). These data suggest the FQ may not interact with transport proteins in quinoline-resistant parasites. The present results justify further clinical trials of FQ in multidrug resistance areas.

The Antimalarial Trioxaquine DU1301 Alkylates Heme in Malaria-Infected Mice

Fatima Bousejra-El Garah, Catherine Claparols, Françoise Benoit-Vical, Bernard Meunier, and Anne Robert

Antimicrob. Agents Chemother. 2008;52 2966-2969



The in vivo alkylation of heme by the antimalarial trioxaquine DU1301 afforded covalent heme-drug adducts that were detected in the spleens of Plasmodium sp.-infected mice. This result indicates that the alkylation capacities of trioxaquinines in mammals infected with Plasmodium strains are similar to that of artemisinin, a natural antimalarial trioxane-containing drug.

2-N-Methyl modifications and SAR studies of manzamine A

Mohamed A. Ibrahim, Abbas G. Shilabin, Sivaprakasam Prasanna, Melissa Jacob, Shabana I. Khan, Robert J. Doerksen, Mark T. Hamann

Bioorganic & Medicinal Chemistry, Volume 16, Issue 14, 15 July 2008, Pages 6702-6706

In this study, mono- and di-methylated quaternary carbolinium cations of manzamine A were synthesized and evaluated for their in vitro antimalarial and antimicrobial activity, cytotoxicity, and also their potential for glycogen synthase kinase (GSK-3 β) inhibition using molecular docking studies. Among the analogs, 2-N-methylmanzamine A (2) exhibited antimalarial activity (IC₅₀ 0.7–1.0 μ M) but was less potent than manzamine A. However the compound was significantly less cytotoxic to mammalian kidney fibroblasts and the selectivity index was in the same range as manzamine A.

Novel amodiaquine congeners as potent antimalarial agents

Manolo Casagrande, Nicoletta Basilico, Silvia Parapini, Sergio Romeo, Donatella Taramelli, Anna Sparatore

Bioorganic & Medicinal Chemistry, Volume 16, Issue 14, 15 July 2008, Pages 6813-6823

To develop new classes of antimalarial agents, the possibility of replacing the phenolic ring of amodiaquine, tebuquine, and isoquine with other aromatic nuclei was investigated.

Mixed tetraoxanes containing the acetone subunit as antimalarials

Dejan M. Opsenica, Nataša Terzić, Philip L. Smith, Youngsun Yang, Lalaine Anova, Kirsten S. Smith, Bogdan A. Šolaja

Bioorganic & Medicinal Chemistry, Volume 16, Issue 14, 15 July 2008, Pages 7039-7045

Eleven new tetraoxanes possessing cholic acid-derived carrier and isopropylidene moiety were synthesized and were tested in vitro and in vivo.

Imidazolidin-4-one peptidomimetic derivatives of primaquine: Synthesis and antimalarial activity

Nuno Vale, Joana Matos, Jiri Gut, Fátima Nogueira, Virgílio do Rosário, Philip J. Rosenthal, Rui Moreira, Paula Gomes

Bioorganic & Medicinal Chemistry Letters, Volume 18, Issue 14, 15 July 2008, Pages 4150-4153

The synthesis of imidazolidin-4-one derivatives of primaquine containing the five-membered ring at the C-terminus of a dipeptide backbone coupled to the parent drug is described.

Design and synthesis of novel 2-pyridone peptidomimetic falcipain 2/3 inhibitors

Edite Verissimo, Neil Berry, Peter Gibbons, M. Lurdes S. Cristiano, Philip J. Rosenthal, Jiri Gut, Stephen A. Ward, Paul M. O'Neill

Bioorganic & Medicinal Chemistry Letters, Volume 18, Issue 14, 15 July 2008, Pages 4210-4214

The structure-based design, chemical synthesis and in vitro activity evaluation of various falcipain inhibitors derived from 2-pyridone are reported. These compounds contain a peptidomimetic binding determinant and a Michael acceptor terminal moiety capable of deactivating the cysteine protease active site.



Preview: Deconstructing Export of Malaria Proteins

Serge Bonnefoy, Robert Ménard

Cell, Volume 134, Issue 1, 11 July 2008, Pages 20-22

The virulence of the malaria parasite *Plasmodium falciparum* is mediated by parasite proteins exported to the surface of infected erythrocytes. In this issue, Maier et al. (2008) report a screen of malaria parasite genes predicted to be involved in parasite protein export and trafficking within the host erythrocyte and discover that many more than expected are essential for parasite survival in vitro.

SnapShot: var Gene Expression in the Malaria Parasite

Artur Scherf, Loïc Rivière, Jose Juan Lopez-Rubio

Cell, Volume 134, Issue 1, 11 July 2008, Pages 190-190.e1

No abstract available

Rapid Communication: Thymic alterations in Plasmodium berghei-infected mice

C.F. Andrade, J. Gameiro, P.R.A. Nagib, B.O. Carvalho, R.L. Talaisys, F.T.M. Costa, L. Verinaud

Cellular Immunology, Article in Press, Corrected Proof

We propose that the presence of parasites in the thymus induces histological modifications that alter the microenvironment, impairing by consequence the successful T cell development. Additional studies are currently being developed in our laboratory to verify if such thymic alterations can influence the systemic immune response to the parasite.

Malaria Chemoprophylaxis: Strategies for Risk Groups

Patricia Schlagenhauf and Eskild Petersen

Clinical Microbiology Reviews, July 2008, p. 466-472, Vol. 21, No. 3

We propose here that the best approximation of the risk to the traveler to a specific area is to use the risk to the indigenous population as a guideline for the risk to the traveler, and we provide examples on how risk in the indigenous population can be used for the estimation of risk of malarial infection for travelers. Special groups are long-term visitors and residents, who often perceive risk differently, cease using chemoprophylaxis, and rely on self-diagnosis and treatment.

Levels of soluble CD163 and malaria severity in Ghanaian children

Kwadwo A. Kusi, Ben A. Gyan*, Bamenla Q. Goka, Daniel Dodoo, George Obeng-Adjei, Marita Troye-Blomberg, Bartholomew D. Akanmori, and Jonathan P. Adjimani

CVI Accepts, published online ahead of print on 16 July 2008

The study showed that sCD163 levels are elevated during acute malaria. High sCD163 levels in UM patients may be due to the induction of higher anti-inflammatory responses enabling them to avoid disease complications, or that UM patients simply lost their CD163 receptors from macrophages in inflammatory sites while complicated malaria groups still had their receptors attached to activated macrophages, reflecting on-going and higher inflammation associated with complicated malaria.

IL12B polymorphisms are linked but not associated with Plasmodium falciparum parasitemia: a familial study in Burkina Faso

M Barbier, A Atkinson, F Fumoux & P Rihet

Genes Immun 2008 9: 405-411; advance online publication, May 1, 2008

Chromosome 5q31-q33 has been linked to *Plasmodium falciparum* parasitemia in several independent studies. This chromosomal region contains numerous immunoregulatory genes. Among these, IL12B that encodes the p40 subunit of interleukin-12 (IL-12) appeared to be a promising functional candidate gene, and IL12Bpro, a promoter polymorphism, was associated with mortality from severe malaria in children. In this



study, we characterized genetic variation in IL12B in 215 individuals belonging to 34 families and evaluated linkage and association of parasitemia with IL12B polymorphisms and haplotypes.

Variation in the ICAM1 gene is not associated with severe malaria phenotypes

A E Fry et al.

Genes Immun 2008 9: 462-469; advance online publication, June 5, 2008

Evidence from autopsy and in vitro binding studies suggests that adhesion of erythrocytes infected with *Plasmodium falciparum* to the human host intercellular adhesion molecule (ICAM)-1 receptor is important in the pathogenesis of severe malaria. Previous association studies between polymorphisms in the ICAM1 gene and susceptibility to severe malarial phenotypes have been inconclusive and often contradictory. We performed genetic association studies with 15 single nucleotide polymorphisms (SNPs) around the ICAM1 locus.

Corrigendum: Interferon regulatory factor-1 polymorphisms are associated with the control of Plasmodium falciparum infection

V D Mangano, G Luoni, K A Rockett, B S Sirima, A Konaté, J Forton, T G Clark, G Bancone, E Sadighi Akha, D P Kwiatkowski & D Modiano

Genes Immun 2008 9: 482

No abstract available

Effector CD8+ T Lymphocytes against Liver Stages of Plasmodium yoelii Do Not Require Gamma Interferon for Antiparasite Activity

Sumana Chakravarty, G. Christian Baldeviano, Michael G. Overstreet, and Fidel Zavala

Infect. Immun. 2008;76 3628-3631

We show that despite a marginal reduction in the expansion of naive IFN- γ -deficient CS-specific transgenic T cells, their antiparasite activity remains intact. Further, adoptively transferred IFN- γ -deficient CD8+ T cells were as efficient as their wild-type counterparts in limiting parasite growth in naive mice. Taken together, these studies demonstrate that IFN- γ secretion by CS-specific CD8+ T cells is not essential to protect mice against live sporozoite challenge.

The Oligomerization Domain of C4-Binding Protein (C4bp) Acts as an Adjuvant, and the Fusion Protein Comprised of the 19-Kilodalton Merozoite Surface Protein 1 Fused with the Murine C4bp Domain Protects Mice against Malaria

Solabomi A. Ogun, Laurence Dumon-Seignovert, Jean-Baptiste Marchand, Anthony A. Holder, and Fergal Hill

Infect. Immun. 2008;76 3817-3823

Highly purified protein antigens are usually poor immunogens; in practice, adjuvants are needed to obtain satisfactory immune responses. *Plasmodium yoelii* 19-kDa merozoite surface protein 1 (MSP119) is a weak antigen, but mice vaccinated with this antigen in strong adjuvants can survive an otherwise lethal parasite challenge. Fusion proteins comprising this antigen fused to the oligomerization domain of the murine complement inhibitor C4-binding protein (C4bp) and a series of homologues have been produced.

The Making of a Tropical Disease—A Short History of Malaria

Markley H. Boyer

JAMA. 2008;300(3):336-337

Now that The Gates Foundation, Ted Turner, and the Bush administration have all decided to eliminate malaria from the world, many health workers (especially those at the recent Gates-sponsored "Eradicate Malaria" convocation in Seattle, Washington) should read and reflect on the lessons presented in this excellent monograph, *The Making of a Tropical Disease—A Short History of Malaria*.



Identification of Residues in the C_μ4 Domain of Polymeric IgM Essential for Interaction with Plasmodium falciparum Erythrocyte Membrane Protein 1 (PfEMP1)

Ashfaq Ghumra et al.

J Immunol 2008;181 1988-2000

The binding of nonspecific human IgM to the surface of infected erythrocytes is important in rosetting, a major virulence factor in the pathogenesis of severe malaria due to *Plasmodium falciparum*, and IgM binding has also been implicated in placental malaria. Herein we have identified the IgM-binding parasite ligand from a virulent *P. falciparum* strain as PfEMP1 (TM284var1 variant), and localized the region within this PfEMP1 variant that binds IgM (DBL4β domain). We have used this parasite IgM-binding protein to investigate the interaction with human IgM.

Efficacy of Intermittent Preventive Treatment versus Chloroquine Prophylaxis to Prevent Malaria during Pregnancy in Benin

Valérie Briand, Lise Denoeud, Achille Massougbodji, and Michel Cot

The Journal of Infectious Diseases 15 August 2008, Vol. 198, No. 4: 594-601

In West Africa, treatment for the prevention of malaria during pregnancy has recently changed from chloroquine (CQ) prophylaxis to intermittent preventive treatment (IPTp). We assessed the benefits of IPTp with respect to those of CQ, using a before-after study. We clearly evidenced that IPTp is substantially more beneficial than CQ for the prevention of malaria during pregnancy.

Recovery of Endothelial Function in Severe Falciparum Malaria: Relationship with Improvement in Plasma L-Arginine and Blood Lactate Concentrations

Tsin W. Yeo et al.

The Journal of Infectious Diseases 15 August 2008, Vol. 198, No. 4: 602-608

Recovery of endothelial function in severe malaria is associated with recovery from hypoargininemia and lactic acidosis. Agents that can improve endothelial NO production and endothelial function, such as L-arginine, may have potential as adjunctive therapy early during the course of severe malaria.

Factors Determining the Heterogeneity of Malaria Incidence in Children in Kampala, Uganda

Tamara D. Clark et al.

The Journal of Infectious Diseases 1 August 2008, Vol. 198, No. 3: 393-400

Malaria risk may be heterogeneous in urban areas of Africa. Identifying those at highest risk for malaria may lead to more targeted approaches to malaria control. Malaria incidence was highly heterogeneous in this urban cohort of children. Malaria control interventions in urban areas should target populations living in pockets of high malaria risk.

α+-Thalassemia Protects against Anemia Associated with Asymptomatic Malaria: Evidence from Community-Based Surveys in Tanzania and Kenya

Jacobien Veenemans et al.

The Journal of Infectious Diseases 1 August 2008, Vol. 198, No. 3: 401-408

We assessed to what extent α+-thalassemia influences the association between mild, asymptomatic *Plasmodium falciparum* infection and hemoglobin concentration. α+-Thalassemia limits the decline in hemoglobin concentration that is associated with afebrile infections, particularly those that are accompanied by inflammation.

Molecular Markers of In Vivo Plasmodium vivax Resistance to Amodiaquine Plus Sulfadoxine-Pyrimethamine: Mutations in pvdhfr and pvmdr1



Jutta Marfurt, Frédérique de Monbrison, Sara Brega, Laetitia Barbolat, Ivo Müller, Albert Sie, Mary Goroti, John C. Reeder, Hans-Peter Beck, Stéphane Picot, and Blaise Genton
The Journal of Infectious Diseases 1 August 2008, Vol. 198, No. 3: 409-417

The present study identified a new molecular marker in *pvm-dr1* that is associated with the *in vivo* response to AQ+SP. We suggest suitable marker sets with which to monitor *P. vivax* resistance against AQ+SP in countries where these drugs are used.

Assessment of Alternative Mating Strategies in *Anopheles gambiae*: Does Mating Occur Indoors?

Dao, Adama; Adamou, Abdoulaye; Yaro, Alpha Seydou; Maïga, Hamidou Moussa; Kassogue, Yaya; Traoré, Sékou Fantamady; Lehmann, Tovi

Journal of Medical Entomology, Volume 45, Number 4, July 2008, pp. 643-652(10)

Altogether, these results suggest that indoor mating is an alternative mating strategy of the M molecular form of *An. gambiae*. Because naturally occurring mating couples have not yet been observed indoors, this conclusion awaits validation.

Mating Competitiveness of Male *Anopheles arabiensis* Mosquitoes Irradiated with a Partially or Fully Sterilizing Dose in Small and Large Laboratory Cages

Helinski, M. E. H.; Knols, B. G. J.

Journal of Medical Entomology, Volume 45, Number 4, July 2008, pp. 698-705(8)

Male mating competitiveness is a crucial parameter in many genetic control programs including the sterile insect technique (SIT). We evaluated competitiveness of male *Anopheles arabiensis* Patton as a function of three experimental variables: (1) small or large cages for mating, (2) the effects of either a partially sterilizing (70 Gy) or fully sterilizing (120 Gy) dose, and (3) pupal or adult irradiation.

Active transcription is required for maintenance of epigenetic memory in the malaria parasite *Plasmodium falciparum*

Ron Dzikowski, Kirk W. Deitsch

Journal of Molecular Biology, Article in Press, Accepted Manuscript

No abstract available

Commentary: Minocycline in cerebral malaria

Richard E. Kast

Journal of Neuroscience Research, Published Online: 14 Jul 2008

No abstract available

Editorial: Preventing malaria in infants: a strategy that works

The Lancet, Volume 372, Issue 9635, 26 July 2008-1 August 2008, Page 264

No abstract available

Effect of intermittent preventive treatment of malaria on health and education in schoolchildren: a cluster-randomised, double-blind, placebo-controlled trial

Siân E Clarke, Matthew CH Jukes, J Kiambo Njagi, Lincoln Khasakhala, Bonnie Cundill, Julius Otodo, Christopher Crudder, Benson BA Estambale, Simon Brooker

The Lancet 2008; 372:127-138

IPT of malaria improves the health and cognitive ability of semi-immune schoolchildren. Effective malaria interventions could be a valuable addition to school health programmes.

Laboratory evaluation of traditional insect/mosquito repellent plants against *Anopheles arabiensis*, the predominant malaria vector in Ethiopia

Kaliyaperumal Karunamoorthi, Adane Mulelam, Fentahun Wassie

Parasitology Research, Volume 103, Number 3 / August, 2008 : 529-534



The present study identified these four traditional indigenous insect/mosquito repellent plant materials are very promising and can be used as safer alternative to modern synthetic chemical repellents against mosquito vectors of disease. Since people have been using these plants for some medicinal purposes, no side effects have been found.

Diagnosis of vivax malaria using an IgM capture ELISA is a sensitive method, even for low levels of parasitemia

Jae-Won Park, Seung Bum Yoo, Jae Hoon Oh, Joon-Sup Yeom, Young-Ha Lee, Young Yil Bahk, Yu Sam Kim, Kook Jin Lim

Parasitology Research, Volume 103, Number 3 / August, 2008 : 625-631

Although diagnosis of *Plasmodium vivax* malaria has been difficult when it is present at a low parasite density, it was recently revealed that an antibody assay was a good method of screening for malaria in blood banks. However, the use of this method for the diagnosis of malaria is limited due to the persistence of specific immunoglobulin (Ig) G. Therefore, we evaluated specific IgM antibody responses against the C-terminal region of the merozoite surface protein 1 of *P. vivax* (PvMSP1c) in sera obtained from patients with vivax malaria using various assays.

Studies on effect of *Acalypha indica* L. (Euphorbiaceae) leaf extracts on the malarial vector, *Anopheles stephensi* Liston (Diptera: Culicidae)

M. Govindarajan, A. Jebanesan, T. Pushpanathan, K. Samidurai

Parasitology Research, Volume 103, Number 3 / August, 2008 : 625-631

The leaf extract of *Acalypha indica* with different solvents viz, benzene, chloroform, ethyl acetate and methanol were tested for larvicidal, ovicidal activity and oviposition attractancy against *Anopheles stephensi*. The results that the leaf extract of *A. indica* is promising as larvicidal and ovicidal activity and oviposition attractancy against malaria vector *A. stephensi*.

Investigations of the effects of the antimalarial drug dihydroartemisinin (DHA) using the Frog Embryo Teratogenesis Assay-Xenopus (FETAX)

Monica Longo, Sara Zanoncelli, Paola Della Torre, Francesco Rosa, AnnaMaria Giusti, Paolo Colombo, Marco Brughera, Guy Mazué, Piero Olliaro

Reproductive Toxicology, Volume 25, Issue 4, August 2008, Pages 433-441

In order to further investigate the susceptibility of primitive RBCs to artemisinins and to establish whether this susceptibility is species-specific or inherent to the compound, we studied dihydroartemisinin (DHA), both a drug in its own right and the main metabolite of current artemisinin derivatives in use, in the Frog Embryo Teratogenesis Assay-Xenopus (FETAX). These results implicate artemisinin-induced embryotoxicity through perturbation of metabolically active RBCs; whereas this mode of action does not appear to be species-specific, the stages of susceptibility varied between different species. The window of susceptibility and duration of exposure must be considered to evaluate the clinical relevance of these findings.

'He is now like a brother, I can even give him some blood' – Relational ethics and material exchanges in a malaria vaccine 'trial community' in The Gambia

P. Wenzel Geissler, Ann Kelly, Babatunde Imoukhuede, Robert Pool

Social Science & Medicine, Volume 67, Issue 5, September 2008, Pages 696-707

This paper explores social relations within the 'trial community' (staff and volunteers) of a Malaria Vaccine Trial (MVT), implemented by the Medical Research Council (MRC) in The Gambia between 2001 and 2004. It situates ethical concerns with medical research within the everyday life of scientific fieldwork.

Taking social relationships seriously: Lessons learned from the informed consent practices of a vaccine trial on the Kenyan Coast



Caroline Gikonyo, Philip Bejon, Vicki Marsh, Sassy Molyneux

Social Science & Medicine, Volume 67, Issue 5, September 2008, Pages 708-720

Individual informed consent is a key ethical obligation for clinical studies, but empirical studies show that key requirements are often not met. Common recommendations to strengthen consent in low income settings include seeking permission from community members through existing structures before approaching individuals, considering informed consent as a process rather than a single event, and assessing participant understanding using questionnaires. In this paper, we report on a qualitative study exploring community understanding and perceptions of a malaria vaccine trial (MVT) conducted in a rural setting on the Kenyan Coast.

Promoting the social value of research in Kenya: Examining the practical aspects of collaborative partnerships using an ethical framework

Geoffrey Mbaabu Lairumbi, Sassy Molyneux, Robert W. Snow, Kevin Marsh, Norbert Peshu, Mike English

Social Science & Medicine, Volume 67, Issue 5, September 2008, Pages 734-747

The findings point to significant gaps in the 'research to policy to practice' pathway, particularly for national research institutions with a focus on clinical/biomedical research. These gaps reflect poorly effective partnerships among stakeholders and limit the potential social value of much research. While more investment is needed to establish strong structures for promoting and directing collaboration and partnership, how to target this investment is not entirely clear, especially in the context of the considerable power of the global health agenda and the research financing tied to it.

The persistent problem of malaria: Addressing the fundamental causes of a global killer

Leeanne Stratton, Marie S. O'Neill, Margaret E. Kruk, Michelle L. Bell

Social Science & Medicine, Volume 67, Issue 5, September 2008, Pages 854-862

We explore the more distal determinants of malaria burden that create underlying vulnerabilities, evaluating malaria risk as a function of socioeconomic context, environmental conditions, global inequality, systems of health care provision, and research. We recommend that future action to combat malaria be directed by a broad-spectrum approach that meaningfully addresses both the proximal and fundamental causes of this disease.

Determinants of provider choice for malaria treatment: Experiences from The Gambia

Virginia Wiseman, Anthony Scott, Lesong Conteh, Brendan McElroy, Warren Stevens

Social Science & Medicine, Volume 67, Issue 4, August 2008, Pages 487-496

This study estimates two models of demand for malaria treatment in the Farafenni region of The Gambia. Results show that older people were more likely to opt for self-care, or no treatment. The longer the time spent ill or the more severe the fever, the more likely a treatment was sought outside the home. Time of the year and availability of community infrastructure played a key role in both models. Poorer households and those from the Fula ethnic group were much more likely to visit an 'other' provider than a hospital. The policy and methodological implications of these findings are discussed.

Short Communication: Febrile illness at the emergency department of Cayenne Hospital, French Guiana

Marc de Lavaissiere, Eric D'Ortenzio, Philippe Dussart, Jean Michel Fontanella, Felix Djossou, Bernard Carme and Bruno Marchou

Transactions of the Royal Society of Tropical Medicine and Hygiene, Article in Press, Corrected Proof



Febrile illness is a common cause of attendance at emergency departments. The purpose of this study was to describe infectious aetiologies of fever in a tropical setting. We prospectively included 1443 febrile patients, all French Guiana residents, who presented at Cayenne Hospital emergency department. This report will propose an overview of aetiologies of febrile illness in French Guiana, and tropical diseases such as malaria and arbovirus infections are discussed.

Community factors affecting long-lasting impregnated mosquito net use for malaria control in Sri Lanka

S.D. Fernando, R.R. Abeyasinghe, G.N.L. Galappaththy, N. Gunawardena, L.C. Rajapakse
Transactions of the Royal Society of Tropical Medicine and Hygiene, Article in Press, Corrected Proof

The Anti Malaria Campaign distributed approximately 300 000 long-lasting impregnated nets (LLINs) to malaria-endemic areas in Sri Lanka during the years 2005 to 2007. We conducted a community-based cross-sectional survey among 2467 households distributed among the three major ethnic groups of Sri Lanka to study the perceptions and practices with regard to the use of LLINs in order to improve their use.

Fitness costs of resistance to antimalarial drugs

Ingrid Felger, Hans-Peter Beck

Trends in Parasitology, Volume 24, Issue 8, August 2008, Pages 331-333

It has been recently reported that the prevalence of mutations associated with chloroquine resistance declined during the dry season. Fitness costs of drug resistance were suggested to be responsible for reduced survival of mutant parasites, and only parasites surviving chronic infections were transmitted at the onset of the rainy season. This implies that during seasonal transmission, significant changes can occur in allele frequency over the course of months, rather than years.

Opinion: Plasmodium falciparum population dynamics: only snapshots in time?

Anna Färnert

Trends in Parasitology, Volume 24, Issue 8, August 2008, Pages 340-344

Infections caused by the malaria parasite *Plasmodium falciparum* often comprise multiple genetically distinct clones. Individuals in endemic areas can have different clones detected in their peripheral blood over a few days or even hours. This reveals interesting within-host dynamics of multiclonal infections, which seem to differ in asymptomatic and symptomatic infections.

Short Report: Hyponatraemia and hypokalaemia in adults with uncomplicated malaria in Thailand

Vipa Thanachartwet et al.

Trop Doct 2008;38 155-157

In a retrospective study of 1415 patients aged 15 and over, we determined the incidence of clinically important hyponatraemia and hypokalaemia in adults with uncomplicated malaria.

Case Series and Case Reports: Bullous erythema multiforme after treatment with Malarone(R), a combination antimalarial composed of atovaquone and proguanil hydrochloride

Shon A Remich, Walter Otieno, Mark E Polhemus, Bernhards Ogutu, and Douglas S Walsh

Trop Doct 2008;38 190-191

We report on a Kenyan woman who developed bullous erythema multiforme, in association with Malarone treatment.



Preclinical assessment of the receptor-binding domain of Plasmodium vivax Duffy-binding protein as a vaccine candidate in rhesus macaques

A. Moreno, I. Caro-Aguilar, S.S. Yazdani, A.R. Shakri, S. Lapp, E. Strobert, H. McClure, C.E. Chitnis, M.R. Galinski

Vaccine, Volume 26, Issue 34, 12 August 2008, Pages 4338-4344

The receptor-binding domain of Plasmodium vivax Duffy-binding protein, region II (PvRII), is an attractive candidate for a vaccine against P. vivax malaria. Here, we have studied the safety and immunogenicity of recombinant PvRII in Macaca mulatta (rhesus monkeys). These results provide support for further clinical development of a vaccine for P. vivax malaria based on recombinant PvRII.

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