

and US soldiers in 1993-2003. For US soldiers, we studied morbidity reports for persons currently and previously assigned to duty in Korea. Military cases were interviewed to determine incubation periods, probable sites of exposure and compliance with the use of personal protective measures (PPM). Malaria cases peaked in 1998 (1,156 cases) in the ROK active duty military population and declined thereafter. Peaks in ROK civilian cases (1580) and discharged Korean soldiers (1273) were not seen until 2000, with subsequent declines in cases. Malaria cases in US soldiers deployed to Korea peaked in 1997 at 27 and averaged 18.3 per year during 1998-2003. Cases due to exposure in Korea and reported in US soldiers outside the ROK peaked in 1999 at 42 and declined thereafter. Interviews were conducted with 68 military cases between 2001 and 2003. Both short (1-4 months) and long (9-13 months) incubation periods were seen. The most probable sites of exposure were training areas within 25 km of the Demilitarized Zone separating North and South Korea. In 2003, one case was ascribed to exposure at a training site near Yongin, approximately 35 Km south of Seoul. Proper wear of the uniform limits exposed body surface (uniform discipline) and was the most commonly employed PPM; 57 (83.8%) patients reported practicing uniform discipline during field exercises. Only 18 (26.5%) reported having permethrin-treated uniforms. Forty-four (64.7%) patients reported using N,N-diethylmetatoluamide (DEET). Of these, only 29 (65.9%) reported using the US military extended duration formulation. Vivax malaria persists in the ROK. Transmission has occurred primarily along the highly fortified DMZ between North and South Korea. Barriers to communication and coordination with North Korea make eradication in the near future unlikely. Therefore, control measures (surveillance, environmental interventions, use of PPM and clinical awareness) must be continued and improved.

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## **SAFETY AND IMMUNOGENICITY OF RTS,S+TRAP MALARIA VACCINE, FORMULATED IN THE AS02A ADJUVANT SYSTEM, IN INFANT RHESUS MONKEYS**

**Walsh DS, Pichyangkul S, Gettayacamin M, Tongtawe P, Siegrist CA, Hansukjariya P, Kester KE, Holland CA, Voss G, Cohen J, Stewart AV, Miller RS, Ballou WR and Heppner DG Jr**

Malaria vaccine RTS,S combined with thrombospondin-related anonymous protein (TRAP) and formulated with AS02A (RTS,S+TRAP/AS02A) is safe and immunogenic in adult humans and rhesus monkeys (*Macaca mulatta*). Here, RTS,S+TRAP/AS02A was administered on a 0-, 1-, and 3-month schedule to three cohorts of infant monkeys, along with adult comparators. Cohort 1 evaluated 1/5, 1/2, and full adult doses, with the first dose administration at one month of age; cohort 2 monkeys received full adult doses, with the first dose administration at one versus three months of age; and, cohort 3 compared infants gestated in mothers with or without previous RTS,S/AS02A immunization. Immunization site reactogenicity was mild. Some infants, including the phosphate-buffered saline only recipient, developed transient iron-deficiency anemia, which is considered a result of repeated phlebotomies. All RTS,S+TRAP/AS02A

regimens induced vigorous antibody responses that persisted through 12 weeks after the last vaccine dose. Modest lympho-proliferative and ELISPOT (interferon- $\gamma$  and interleukin-5) responses, particularly to TRAP, approximated adult comparators. RTS,S+TRAP/AS02A was safe and well tolerated. Vigorous antibody production and modest, selective cell-mediated immune responses suggest that RTS,S+TRAP/AS02A may be immunogenic in human infants.

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### **VARIATION OF CIRCUMSPOROZOITE 26 AND 29 GENOTYPES OF *PLASMODIUM FALCIPARUM* INFECTING PATIENTS AND ASSOCIATION WITH HLA-DQA ALLOTYPES IN WESTERN THAILAND**

**Kollars TM, Phasuk R and Sattabongkot J**

We evaluated the proportion of variants of circumsporozoite protein (cp) gene 26 and cp29 antigenic epitopes of *Plasmodium falciparum* infecting patients among 3 provinces in western Thailand, in addition to published variants from Gambia. The proportion of patients coinfecting with cp26 and cp29 strains was significantly higher in patients reporting to malaria clinics in Tak than in Kanchanaburi and Ratchaburi and higher in Kanchanaburi than in Ratchaburi. In western Thailand, coinfection with cp26 and cp29 appears to increase with increasing latitude. There were also significant differences in proportion of these variants among Thai provinces and Gambia. An association of patient human leukocyte antigen (HLA) class II genotype was associated with *P. falciparum* strains. There were significant associations among the HLA-DQA alleles in patients, the province of origin, and cp variants of *P. falciparum*.

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### **ANTIFOLATE WR99210 EFFECTIVE AGAINST *PLASMODIUM VIVAX* ISOLATES GENETICALLY NOT SENSITIVE TO PYRIMETHAMINE**

**Kaewthamasorn M, Khuntirat B, Viseshakul N, Prachumsri J, Udomsangpeth R and Tan-Ariya P**

Vivax malaria has attracted a high attention in the last decade due to the incidence of the chloroquine resistant strain of *P. vivax* reported from several endemic areas. The objectives of this study were to assess and compare in vitro drug sensitivity of *P. vivax* to chloroquine and two antifolates ie pyrimethamine and WR99210 using the modified WHO microtest. In addition, *P. vivax* dihydrofolate reductase (*dhfr*) genes among different isolates were also amplified and analyzed by restriction fragment length polymorphism (RFLP) technique and DNA sequencing in order to clarify their polymorphisms and correlation to antifolate responses. The EC<sub>50</sub> values of chloroquine ranged between 50-191.98 nM (Mean  $\pm$  SD = 109.09  $\pm$  40.57, n = 44), while the range of pyrimethamine is 313.95-1,825.20 nM (Mean  $\pm$  SD = 1,065.93  $\pm$  396.37, n = 44)