Cystscint ES - ICN vs 8 ml of Universol Cocktail), and to resuse scintillation vials, thus decreasing the logistical difficulties involved in transporting scintillation fluid and vials to endemic areas.

528 EFFECT OF FIRST LINE MALARIA THERAPY STRATEGY CHANGE IN DIELMO (SENEGAL) ON *IN VITRO* SUSCEPTIBILITY OF *PLASMODIUM FALCIPARUM* AGAINST ANTIMALARIALS. Pradines B*, Tall A, Parzy D, Rogier C, Spiegel A, Fusai T, Hienne R, Trape JF, and Doury JC. Unite de Parasitologie, Institut de Medecine Tropicale du Service de Sante des Armees, Marseille, France; Service d'Epidemiologie, Institut Pasteur, Dakar, Senegal; and Laboratoire de Paludologie, ORSTOM, Dakar, Senegal.

An indirect approach to evaluate the efficacity of antimalarial drugs is the determination of their *in vitro* activity against fresh isolates. The *in vitro* activities of chloroquine, quinine, cycloguanil (biologically active metabolite of proguanil) and pyrimethamine were evaluated against isolates from Dielmo and Ndiop (Senegal), obtained between Oct. 1995 and Jan. 1996 then between Oct. and Dec. 1996, using an isotopic, micro, drug susceptibility test. Cutoff values for resistance to chloroquine, quinine, cycloguanil and pyrimethamine were 100 nM, 500 nM, 500 nM and 2,000 nM, respectively. In 1995, *in vitro* resistance to chloroquine, quinine, cycloguanil and pyrimethamine was observed in 59%, 2%, 13%, 13% in Dielmo and in 43%, 0%, 15% and 20% in Ndiop. In 1996, *in vitro* resistance to chloroquine, quinine, cycloguanil and pyrimethamine was observed in 37%, 6%, 31%, 40% in Dielmo and in 42%, 0%, 21% and 26% in Ndiop. Besides, 5% (Dielmo) and 7% (Ndiop) of isolates were resistant to chloroquine and to cycloguanil in 1995 versus 17% and 11% in 1996. So, resistance increase to cycloguanil, pyrimethamine and cycloguanil-chloroquine was found in Dielmo. In 1995, patients from Dielmo were treated by quinine. Since the beginning of 1996, sulfadoxine-pyrimethamine has became the first line drug for the treatment of uncomplicated *Plasmodium falciparum* malaria in Dielmo. This use may explain *in vitro* resistance increase to pyrimethamine and cycloguanil. A significant positive correlation, suggesting *in vitro* cross-resistance among pyrimethamine and cycloguanil was found ($r2 = 0.72$, $p < 0.001$). This study showed the repercussion of malaria therapy policy on *P. falciparum* resistant strains circulation.

529 TRANSFORMATION OF *PLASMODIUM FALCIPARUM* WITH HUMAN DIHYDROFOLATE REDUCTASE RENDERS THEM INSENSITIVE TO WR99210 THOUGH DOES NOT AFFECT PROGUANIL. Fidock DA* and Wellems TE. Malaria Genetics Section, LPD, NIAID, NIH, Bethesda MD; Biomedical Parasitology, Pasteur Institute, Paris cedex, France.

Extensive use of synthetic antimalarial drugs has led to the genesis and rapid spread of drug-resistant *Plasmodium falciparum* strains. Among the most serious losses are chloroquine and the dihydrofolate reductase (DHFR) inhibitors pyrimethamine and cycloguanil (an active metabolite of proguanil), necessitating investigation and development of alternative compounds. WR99210 is among the most potent antimalarials ever synthesized and is effective across a broad spectrum of drug-resistant malaria parasites, as well as being active on *Pneumocystis carinii* and *Mycobacterium avium* complex. Several observations have raised doubts as to whether this drug is acting upon DHFR or has an alternative target. A related question has also emerged in studies of the new drug Malarone, a combination of proguanil and the mitochondrial inhibitor atovaquone. To address these questions, we have transformed *P. falciparum* with human methotrexate-resistant DHFR. The high level of WR99210 resistance observed in transformed parasites indicates that DHFR is the essential target of this compound. While these parasites also show increased resistance to the antifol cycloguanil, no change was found in levels of susceptibility to proguanil, suggesting that this drug has a separate target, the identification of which may provide insights on new drug targets.

530 THREAT OF MALARIA TO MILITARY OPERATIONS IN THAILAND; EPIDEMIOLOGY AND RESULTS OF A PILOT ARTESUNATE CHEMOPROPHYLAXIS STUDY. Eamsila C, Kaowsathien P, Pradutpongpet P, Supakalin P*, Walsh DS, and Heppner DG. Royal Thai Army Component, AFRIMS, Bangkok, Thailand; Medical Battalion, 4th Infantry Division, Third Army, Phitsanulok, Thailand; and Department of Immunology and Medicine, AFRIMS, Bangkok, Thailand.

Malaria is the leading operational disease threat for Thai soldiers deployed along international borders, despite the successful Thai National Malaria Control Program reduction of mortality from 351 to 1.4/100,000/yr and morbidity from 286 to 1.5/1,000/yr between 1947 and 1995. Malaria is also underestimated as an operational threat because joint Thai-U.S. military exercises (Cobra Gold, Balanced Torch) take place in central areas with a low malaria risk. In contrast, the 5 provinces with >10 cases/1000/yr form international borders. Soldiers deployed along these borders suffer attack rates some 100 fold greater than local provincial civilian rates, a military occupational hazard due to the proximity of infected populations, and military duties, such as night patrol. In 1995, some unit attack rates were 28%/month. Chemoprophylaxis is difficult, since resistance to mefloquine is widespread, and daily doxycycline is poorly tolerated for extended periods. Preventive medicine efforts have concentrated on personal protective

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