

## EXPERIENCES WITH MALARIA CHEMOPROPHYLAXIS IN DUTCH TROOPS

A. HOPPERUS BUMA, P. VAN THIEL

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**ABSTRACT** • This article describes the situation for malaria chemoprophylaxis among Dutch military personnel. Any malaria chemoprophylaxis advice given to Dutch troops is based on a close co-operation between national military and civilian experts. Most studies, related to a deployment in Cambodia, describe the experiences with mefloquine. Overall it has been well tolerated. From an African deployment, it has been learned that anticircumsporozoite antibodies could be demonstrated in 11% of the personnel. Future options for Dutch troops will concentrate on atovaquone/proguanil and tafenoquine. Furthermore some kind of individualisation will be accepted. In conclusion malaria in Dutch troops has remained a manageable problem but vigilance remains necessary.

**KEY WORDS** • Malaria - Army - Chemoprophylaxis.

### L'EXPERIENCE DE L'ARMEE NEERLANDAISE EN MATIERE DE CHIMIOPROPHYLAXIE ANTIPALUDIQUE

**RESUME** • Cet article fait le point sur les moyens de chimioprophylaxie antipaludique utilisés dans l'armée néerlandaise. En matière de chimioprophylaxie antipaludique, toute recommandation repose sur une étroite coopération entre les experts militaires et civils. La plupart des études, liées à un déploiement des troupes au Cambodge, présentent l'expérience acquise avec la méfloquine dont la tolérance était globalement bonne. Une opération en Afrique a enseigné que la présence d'anticorps anticircumsporozoitaires peut être mise en évidence chez 11 % des militaires. Les options futures pour les troupes néerlandaises se concentrent sur l'association atovaquone-proguanil et sur la tafénoquine. Cependant, un certain degré d'individualisation sera accepté. En conclusion, le paludisme est resté un problème bien contrôlé parmi les troupes néerlandaises, mais la vigilance reste de mise.

**MOTS-CLES** • Paludisme - Armée - Chimioprophylaxie.

Following several deployments in malarious areas, the Dutch military have gained considerable experience with malaria chemoprophylaxis. Over the last few years, deployments were performed in Cambodia, Haiti, Rwanda/Zaire, Angola, Mozambique, Belize, Honduras, and most recently Eritrea and Ethiopia. This article will discuss the organisation and the present state of advice, experiences with malaria chemoprophylaxis during recent missions, and our considerations for future missions.

### ORGANISATION OF MALARIA CHEMOPROPHYLAXIS ADVICE

Concerning the organisation of advice, it should be mentioned that there is no specific military institute for tropical medicine in Holland. Instead, the Dutch Forces have created a strong alliance with the Department of Infectious Diseases and Tropical Medicine of the Academic Medical Center in Amsterdam. Before every mission, an overall infectious risk-assessment is made, which then leads to the consequent malaria chemoprophylaxis. The guidelines as given by

the National Co-ordination Centre for Travellers Health Advice are followed, unless specific military conditions dictate otherwise. The national policy is based on the current WHO guidelines. Recent malaria chemoprophylaxis advice contained mefloquine for Africa, Southeast Asia, and South America (Amazon area), with doxycycline as an individual alternative option. Furthermore, Dutch troops have been on chloroquine in Central America and Haiti. In addition, the personal protection measures comprise permethrin-impregnated bednets, insect repellent (DEET up to 50%), and a long sleeves and trousers policy between dusk and dawn. Due to national legislation, so far uniforms have not been permethrin impregnated. However for the coming deployment to Eritrea and Ethiopia, special permission has been granted for the impregnation of the uniforms with permethrin. It is unclear yet if this is going to be a standard procedure for the future.

### MILITARY EXPERIENCES

Most published studies relate to the Cambodia deployment in the early nineties: some 2,500 Dutch troops participated in 6 months tours in Northwest Cambodia as part of the UNTAC-operation. The malaria chemoprophylaxis was mefloquine (250 mg weekly). Full compliance to the chemoprophylaxis regimen was reported by 86%. Possible mefloquine related adverse events were reported by 30%. Most adverse events were mild, 7 persons (0.3%)

• *Travail de la Royal Netherlands Navy, (A.H.B., M.D. PhD) La Hague, et de l'Academic Medical Centre ((P.V.T., MD), Amsterdam, Pays-Bas.*

• *Correspondance : A. HOPPERUS BUMA, Deputy Director Medical Service, Royal Netherlands Navy, The Hague, The Netherlands • Fax : +31 70 316 25 00 • e-mail : scgz.post@dpkm.navy.dist.mindef.nl •*

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consulted the medical service for serious problems. However overall 64 malaria infections were diagnosed in 59 marines, the majority (n=43) from one location (Sok San). During deployment 31 *Plasmodium falciparum* and no *Plasmodium vivax* infections occurred; after return to The Netherlands, 11 persons were diagnosed with *Plasmodium falciparum* and 22 with *Plasmodium vivax* malaria. Mefloquine resistance was demonstrated in 4 Dutch patients. We concluded that long term mefloquine chemoprophylaxis was well tolerated but that the effectiveness in this area was incomplete (1). Another study monitored possible mefloquine related side effects with special emphasis on QT-prolongation on the ECG in 73 volunteers (2). After 3 months, the heart rate at rest and the total white blood cell count were both lower ( $p < 0.05$ ). The mean QTc-interval was longer and the liver transaminases had increased ( $p < 0.05$ ), although both within the normal range. There was no need to stop the chemoprophylaxis in any of the participants. No accumulation of mefloquine in serum occurred and no relation was observed between the incidence of possible adverse events and serum mefloquine concentrations.

It should be mentioned that we have experienced several problems with military personnel suffering from *post-deployment complaints* which we related to the long term use of mefloquine. Despite several independent studies, a causal relation between the long term use of mefloquine and the complaints could not be confirmed nor excluded (3). However it caused serious concerns among our troops, which still has practical implications for the acceptance of mefloquine as chemoprophylaxis.

From the Africa deployments, it is worth while mentioning the study on anti-circumsporozoite antibodies among 125 Dutch military personnel after their duties in Goma, Zaire. All were on mefloquine as chemoprophylaxis. Although no clinical malaria was diagnosed, anti-circumsporozoite antibodies could be demonstrated in 14 (11 %) of the participants (4). Experiences with mefloquine malaria chemoprophylaxis (250 mg weekly) from South-America, where Dutch troops regularly undertake jungle training in the Guyana's, are unfortunately not well documented. So far we have not noticed any major concerns about the effectiveness or acceptance. Finally chloroquine has been

used as malaria chemoprophylaxis for troops serving in Haiti and Belize. This proved to be well tolerated and effective (unpublished data).

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### FUTURE OPTIONS

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Concerning the future options, the Dutch attention concentrates on atovaquone/proguanil and tafenoquine. Atovaquone/proguanil for chemoprophylaxis seems to be well tolerated but expensive. In The Netherlands however it has not been registered yet for malaria chemoprophylaxis. Tafenoquine looks to be very promising because of the easy dosing regimen and good effectiveness. A clear policy for G6PD deficiency seems to be well feasible for the Dutch forces, where risk groups are easy to be determined. For the coming deployment to Eritrea and Ethiopia the policy will be mefloquine (weekly 250 mg) as first choice with doxycycline (100 mg daily) as an easy available second option. Therefore we accept the introduction of some kind of individualisation in malaria chemoprophylaxis among our troops.

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### CONCLUSION

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In conclusion, considering the gained experience with malaria chemoprophylaxis, malaria in Dutch troops has remained a manageable problem considering the important risk. However vigilance remains necessary to secure that «risk» does not become «reality».

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