Doxycycline Information Paper

Licensed antimalarial drug developed by DoD and its partners

UNITED STATES ARMY MEDICAL RESEARCH AND MATERIEL COMMAND

Product Name: Doxycycline
Commercial name: Vibramycin
Application: Anti-malarial drug for prophylaxis
Date of U.S. licensure: New indication approved December 1992
Type of product: long-acting tetracycline
Company of manufacture: Pfizer

Reasons for development: Doxycycline -- originally developed as an antibacterial agent -- was found to have slow-acting antimalarial action against tissue malaria parasite forms relating to binding of doxycycline to malaria ribosomes, thereby inhibiting malaria protein synthesis. (Erythromycin and azithromycin --a modern erythromycin analog -- also inhibit malarial mitochondrial protein synthesis.)

Doxycycline was developed as an antimalarial agent because of (1) resistance to the effective action of mefloquine (initially effective against all chloroquine-resistant *P. falciparum* strains) especially noted in Southeast Asia; (2) adverse effects associated with the use of mefloquine.

Role of DoD:
The Walter Reed Army Institute of Research (WRAIR) conducted Phase 2 challenge and clinical trials for doxycycline in Thailand, and obtained FDA approval for doxycycline as prophylaxis for both *Plasmodium falciparum* and *P. vivax* malaria.

From June 1992 to November 1993, three Dutch military units served in western Cambodia under the United Nations Transitional Authority. Air Force physicians advised doxycycline for malaria prophylaxis because of concerns that mefloquine had neurological effects that interfered with piloting skills. Of more than 2,000 personnel treated with doxycycline, only 59 developed malaria.

Although doxycycline is a valuable preventative antimalarial agent, the drug requires daily adminstration and may cause phototoxicity, gut discomfort and diarrhea, all of which impact negatively on compliance. Further, the drug cannot be given to pregnant women and children because it can cause tooth discoloration in developing teeth. Quinine and doxycycline have an additive effect when combined and this combination is used for treatment of *P. falciparum*. Clindamycin is frequently used in place of doxycycline and combined with quinine to treat *P. falciparum* malaria in pregnant women and children.

Doxycycline references:

Pang L, Limsomwong N, Singharaj P: Prophylactic treatment of vivax and falciparum malaria with low-dose doxycycline. J Infect Dis 1988;158:1124-7.

Pang LW, Limsomwong N, Boudreau EF: Doxycycline prophylaxis for falciparum malaria. Lancet 1987; 1:1161-4.