Texas Preventable Disease NEWS

Vol. 47, No. 15
April 18, 1987

contents:

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INTERNATIONAL TRAVEL
PART I: MALARIA PREVENTION

This article is the first in a three-part series on health recommendations for international travel. Parts II and III will address travelers' diarrhea and immunizations for international travel.

Malaria in humans is caused by one of four protozoan species of the genus *Plasmodium: P. falciparum, P. malariae, P. ovale,* and *P. vivax.* It is transmitted through the bite of an infected female *Anopheles* mosquito; it also occurs by blood transfusion and congenital transmission. Symptoms of malaria usually include fever and flu-like symptoms such as chills, headache, muscle aches, and malaise, which may recur at regular or irregular intervals. Severity of malarial infections ranges from asymptomatic to rapidly fatal, with *P. falciparum* infections presenting the greatest potential for serious consequences.

Malaria is present, and transmission occurs, in most tropical and many temperate areas of the world. However, the actual risk of acquiring malaria in any particular location depends upon many inter-related factors, including but not limited to: local weather conditions, vector mosquito densities, prevalence of malarial infections, accessibility of mosquitoes to humans, and human behavior. These factors can, and do, change, complicating efforts to define an individual traveler's risk of acquiring malaria. Since female anopheline mosquitoes are nighttime biters, interplay of the above factors is most important during nighttime hours.

The prevention of malaria in travelers requires three separate, but interdependent, components: information, personal protection measures, and chemoprophylaxis. While work on a malaria vaccine(s) is progressing on many fronts, travelers must still take an active role in protecting themselves from malaria.

INFORMATION

The 1986 edition of *Health Information for International Travel (HHS Publication No. (CDC) 86-8280)*, identifies 201 separate nations/territories; the CDC recommends malaria prophylaxis under at least some circumstances for travelers to 95 (47%) of them. Even then, depending upon travel activities, the actual risk of acquiring malaria will vary within a country.

For example, the typical Texan visiting Mexico generally is at minimal, if any, risk of acquiring malaria. However, a risk of malaria does exist in rural areas of 30 of Mexico's 32 states, and in 1985 ten Texans vacationing in Acapulco returned to Texas with *P. vivax* infections.

PERSONAL PROTECTION MEASURES

The ideal way to prevent malaria is to avoid being bitten by an infected mosquito. *Anopheles* mosquitoes feed primarily between dusk and dawn. Important measures to prevent/reduce contact with them include: remaining in well-screened areas, sleeping under mosquito netting or in screened rooms, and wearing clothing that covers most of the body. Additionally, the use of personal insect repellents and pyrethrum-based area insecticide sprays in living and sleeping quarters during evening and nighttime hours is strongly encouraged.

Effective insect repellents contain N,N diethylmetatoluamide (deet) in concentrations up to 100%. The higher the concentration, the longer the repellent's activity lasts. Adverse reactions associated with insect repellents have been reported (PDN, Vol. 46, No. 11, March 15, 1986).

These personal protection measures are also effective in reducing exposure to biting insects that transmit other arthropod-borne diseases including: yellow fever, dengue fever, Rift Valley fever, and Japanese encephalitis, all transmitted by mosquitoes; trypanosomiasis from reduviid bugs (American) and tsetse flies (African); and flea- and tick-borne diseases such as tick-borne encephalitis, murine typhus, and plague.

CHEMOPROPHYLAXIS

Malaria chemoprophylaxis is the use of drugs to prevent the development of malarial illness (Table 1). Malaria chemoprophylaxis, taken once weekly, should begin one to two weeks prior to arrival in a malarious area and be continued for six weeks after leaving the area. The specific agents used for chemoprophylaxis depend upon the traveler's age, health status, and itinerary, as chloroquine-resistant *P. falciparum* (CRPF) malaria is being seen increasingly in previously uninfested areas. Malaria chemoprophylaxis is not 100% effective in preventing malaria. With *P. ovale* and *P. vivax* infections, symptoms can occur up to several years after exposure, even when routine chemoprophylaxis is employed. Health care providers should consider the possibility of malaria in any traveler who develops a febrile illness even several years after travel in malarious areas.

The CDC has developed three anti-malarial regimens (A,B,C) intended to provide travelers with protection according to varying needs.

Regimen A: For travel to areas of risk where CRPF malaria has NOT been reported or where only low-level or focal chloroquine resistance has been reported, once-weekly use of chloroquine alone is recommended. In some cases, hydroxychloroquine may be tolerated better than chloroquine.

Regimen B: For short-term travel (three weeks or less) to areas of risk where CRPF malaria is endemic, once-weekly use of chloroquine alone is recommended. Travelers (except those with a history of sulfonamide intolerance) should also carry a treatment dose of pyrimethamine/sulfadoxine (Fansidar), to be taken promptly in the event of a febrile illness during travel, when professional medical attention is not available. The presumptive self-treatment of possible malaria is a temporary measure and medical attention is required. Weekly use of chloroquine should continue.

Doxycycline alone, taken daily, is an alternative during short-term travel to areas where there is a risk of acquiring CRPF malaria. It may be particularly useful for travelers with a history of sulfonamide intolerance; however, precautions and side effects should be considered.

Regimen C: For prolonged travel (greater than three weeks) in areas where CRPF malaria is endemic, once-weekly use of both chloroquine and Fansidar may be indicated. Potential candidates for this regimen are travelers to areas of intense CRPF malaria transmission; travelers to areas with limited access to medical care; and travelers who are elderly, immunocompromised, or who have significant underlying medical conditions.

Primaquine is used to prevent relapses of malaria due to *P. ovale* and *P. vivax* infections. These species have stages that persist in the liver and cannot be reached by chloroquine. Primaquine is generally used during the last two weeks of chloroquine prophylaxis in travelers who have spent extended periods in malaria endemic areas. Primaquine is contraindicated in individuals who are glucose-6-phosphate dehydrogenase (G6PD) deficient.

ADVERSE REACTIONS TO ANTI-MALARIAL DRUGS

Only rarely have serious adverse reactions occurred with the use of chloroquine and hydroxychloroquine for malaria prophylaxis. Minor side effects such as gastrointestinal symptoms, headache, dizziness, blurred vision, and pruritus may occur, but generally do not require discontinuence of the drugs. Persons using chloroquine for extended periods (weekly for more than six years) should have periodic eye examinations. Chloroquine may cause acute exacerbations of psoriasis.

Fansidar has been associated with severe adverse cutaneous reactions, seven of which have been fatal. These severe reactions have primarily been associated with weekly use of Fansidar. **If once-weekly use of Fansidar is prescribed, travelers should be advised to discontinue it immediately if they develop any adverse reactions, especially if there are any skin or mucous membrane signs or symptoms (eg, itching, redness, rash, mouth or genital lesions, or sore throat).** Fansidar has also been associated with serum-sickness type reactions, urticaria, exfoliative dermatitis, and hepatitis. **Fansidar should NOT be used by persons with histories of sulfonamide intolerance or given to infants less than two months of age.**

Doxycycline is a tetracycline and has side effects similar to other drugs in that group, including the possibility of photosensitivity in persons in tropical areas. **Tetracyclines should not be used during pregnancy or in children under 8 years of age.**

MALARIA DURING PREGNANCY AND IN CHILDREN

Malaria has serious implications for both a pregnant woman and her fetus. Chloroquine and hydroxychloroquine have not been associated with adverse effects in pregnancy and are not contraindicated for malaria chemoprophylaxis. Fansidar does not appear to be contraindicated in pregnancy, but its absolute safety has not been established. Ideally, pregnant women should not travel in areas with CRPF malaria. However, some experts feel that malaria presents a greater risk than does the chemoprophylaxis. Pregnant women should be aware of possible risks before taking Fansidar. Doxycycline is generally contraindicated in pregnancy. **Primaquine should not be used by pregnant women.** If its use is indicated, chloroquine should be given weekly until delivery, after which primaquine may be used as necessary.

Children can be infected with malaria and are also candidates for chemoprophylaxis. Fansidar and doxycycline have age restrictions on their use. Chloroquine in the US comes in adult-dose tablets only and must be prepared for pediatric use by a pharmacist. **Overdose of anti-malarial drugs can be fatal, and the drugs should be stored in childproof containers out of the reach of children.**

The malaria situation in the world changes continuously and travelers and their health care providers must be aware of the changes. CRPF malaria has spread across Africa from east to west in just a few years, with cases having been reported recently in Nigeria and Benin. Until such time as a safe, inexpensive vaccine is available, travelers to many parts of the world will be at risk of malaria and will need accurate, timely advice to reduce that risk.

The information in this report was abstracted from the CDC publication *Health Information for International Travel*, 1986 edition. This volume, published annually, is an invaluable resource for health care providers and others who advise international travelers, providing country-specific immunization requirements, malaria risk information, and general health recommendations. It can be purchased ($4.75) from the Superintendent of Documents, US Government Printing Office, Washington, DC 20402, or through US Government Bookstores.

For further information, contact the Bureau of Epidemiology, TDH, at (512) 458-7328 or STS 824-9328.

Table 1.
Drugs used in the prophylaxis and presumptive treatment of malaria

Drug	Routine prophylaxis		Presumptive treatment for travelers to areas of chloroquine-resistance	
	Adult dose	Pediatric dose	Adult dose	Pediatric dose
Chloroquine phosphate (Aralen)	300 mg base (500 mg salt) orally, once/week	5 mg/kg base (8.3 mg/kg salt) orally, once/week, up to maximum adult dose of 300 mg base	Chloroquine is not recommended for the presumptive treatment of malaria acquired in areas of known chloroquine resistance.	
Hydroxychloroquine sulfate (Plaquenil)	310 mg base (400 mg salt) orally, once/week	5 mg/kg base (6.5 mg/kg salt) orally, once/week, up to maximum adult dose of 310 mg base	Hydroxychloroquine is not recommended for the presumptive treatment of malaria acquired in areas of known chloroquine-resistance.	
Pyrimethamine-sulfadoxine (Fansidar)	1 tablet (25 mg pyrimethamine and 500 mg sulfadoxine) orally, once/week	2-11 mos:1/8 tab/wk 1-3 yrs: 1/4 tab/wk 4-8 yrs: 1/2 tab/wk 9-14 yrs: 3/4 tab/wk >14 yrs: 1 tab/wk	3 tablets (75 mg pyrimethamine and 1500 mg sulfadoxine), orally, as a single dose	2-11 mos: 1/4 tab 1-3 yrs: 1/2 tab 4-8 yrs: 1 tab 9-14 yrs: 2 tabs >14 yrs: 3 tabs as a single dose
Doxycycline	100 mg orally, once/day	>8 years of age: 2 mg/kg of body weight orally/day up to adult dose of 100 mg/day	Tetracyclines are not recommended for the presumptive treatment of malaria.	
Primaquine	15 mg base (26.3 mg salt) orally, once/day for 14 days or 45 mg base (79 mg salt) orally, once/week for 8 weeks	0.3 mg/kg base (0.5 mg/kg salt) orally, once/day for 14 days or 0.9 mg/kg base (1.5 mg/kg salt) orally, once/week for 8 weeks	Primaquine is only recommended for use after leaving an endemic area to prevent relapses of P. vivax and P. ovale.	

TEXAS PREVENTABLE DISEASE NEWS (ISSN 8750-9474) is a free, weekly publication of the Texas Department of Health, 1100 West 49th Street, Austin, TX 78756-3180. Second-class postage paid at Austin, TX. POSTMASTER: Send address changes to TEXAS PREVENTABLE DISEASE NEWS, 1100 West 49th Street, Austin, TX 78756-3180.

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