Malaria Prophylaxis in Travelers

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Each year increasing numbers of Americans travel to countries where the risk of acquiring malaria is considerable. Appropriate advice from family physicians about malaria prophylaxis is important to prevent malaria in American travelers. All travelers to malarious areas should receive chloroquine prophylaxis. Physicians should consider the diagnosis of malaria when fever develops in travelers returning from malarious areas.

In 1979 more than four million Americans visited developing countries.[1] In many of these countries American travelers are at considerable risk for acquiring malaria (Figure 1). In spite of the attention given to this disease by the Center for Disease Control, which publishes *Health Information for International Travel*,[3] a large number of Americans are traveling in areas of high risk for malaria without adequate prophylaxis.[4,5] Although malaria attack rates for travel are low (15.3/100,000),[6] failure to prevent malaria may have devastating consequences. Between 1973 and 1978, 25 American travelers died of malaria after returning home.[2]

All information available suggests that the agencies with the capacity to advise travelers about malaria risk and prophylaxis, such as airlines and travel bureaus, have failed to take responsibility in this matter. Advice from the family physician has become extremely important in preventing malaria in travelers. Family physicians should be able to advise their patients about the appropriate chemoprophylactic agent to take during their trip and after their return.

Malaria Risk

The Center for Disease Control publishes information about malaria risk yearly in *Health Information for International Travel* and updates this information regularly in the *Morbidity and Mortality Weekly Reports*.[7] Some of the information provided by the Center for Disease Control attempts to estimate the relative risk of acquiring malaria in individual countries and even within different geographic areas in a single country. It is impractical for the physician to attempt to estimate malaria risks for individual travelers on the basis of itinerary, lifestyle, and occupation. As a general rule all travelers to malarious areas should receive malaria prophylaxis with chloroquine.

Chloroquine

Although there has been great argument among British and American experts about the most useful prophylactic drug, chloroquine, a 4-aminoquiniline, is preferred for prophylaxis of all malaria. It should be taken once a week; on the same day, at the same time, preferably after a meal (Table 1).

Chloroquine reaches adequate levels in the blood very soon after ingestion. Nevertheless, it should be started two weeks prior to departure to help the traveler establish his pill taking routine. Pre-travel dosage also provides the physician the opportunity to dispel any qualms his patient might have about adverse effects of the medication. Minor gastrointestinal disturbances and headaches are rare complaints and usually will resolve after several days. Retinopathy has been reported with

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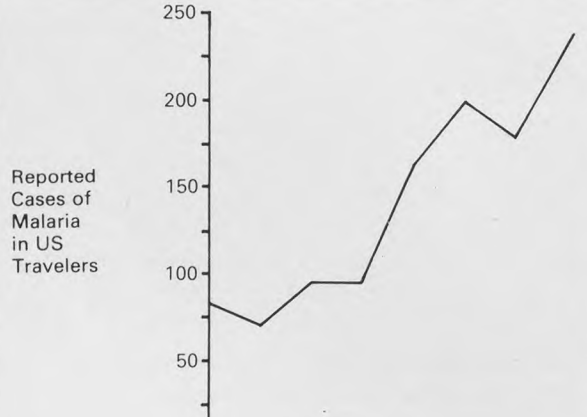
Table 1. Drugs for Malaria Prophylaxis

Generic Drug	Adult Dose	Pediatric Dose	Side Effects	Comments
Chloroquine phosphate	500 mg (300 mg base) orally once a week. Begin 2 weeks before arrival. Continue 6 weeks after return	5 mg (base)/kg body weight. Children greater than 50 kg can receive adult dose.	Minor GI disturbances, headache, blurred vision	The drug of choice for all malarious areas. Safe for pregnant women
Pyrimethamine-sulfadoxine	50 mg pyrimethamine, 1000 mg sulfadoxine orally every other week. Continue 6 weeks after return	In terms of sulfadoxine 6-11 mos: 125 mg 1-3 years: 250 mg 4-8 years: 500 mg 9-14 years: 750 mg greater than 14 years: adult dose	Stevens-Johnson syndrome	Not recommended except under special circumstances. Pyrimethamine-resistant strains of P vivax may cause clinical attack of malaria while on prophylaxis. Contraindicated in pregnancy. Not licensed in USA but available overseas
Amodiaquine	400 mg (base) orally once a week	To 1 yr: 50 mg (base) 1-4 yrs: 50-100 mg 5-8 years: 150-200 mg 9-12 yrs: 200-300 mg once per week orally	Like chloroquine	Available in pediatric syrup. Can be used as a substitute for chloroquine



Adapted from Center for Disease Control: Malaria Surveillance Reports, Annual Summaries 1970-1977. Excludes US military personnel

Figure 1. Cases of imported malaria in US travelers[2]

accidental ingestion of chloroquine and with prolonged high dose treatment, but has never been observed following routine prophylactic use. The World Health Organization does not consider risk of retinopathy to begin until over 100 gm of chloroquine have been ingested.[8]

Chloroquine should be continued for six weeks after leaving a malarious area. This is usually sufficient time to achieve a suppressive cure of most malarias. If fever should develop in travelers who have had six weeks of post-exposure prophylaxis, the physician must be prepared to examine blood films for evidence of infection with Plasmodium vivax or P ovale, or more rarely for chloroquine-resistant P falciparum. Because P vivax and P ovale persist in the liver and can cause delayed attacks of malaria as many as four years after chloroquine suppression is discontinued, travelers must be strongly advised to report exposure to malaria to their physicians for up to five years after a return from malarious areas.

Table 2. Areas in Which Chloroquine-Resistant Strains of Plasmodium falciparum Have Been Reported*[3]

Americas
Brazil
Colombia
Ecuador
Guyana
Panama
Surinam
Venezuela

Africa
Kenya, Tanzania — Not yet confirmed by WHO

Asia
Bangladesh
Burma
Cambodia
India
Indonesia
Malaysia
Philippines
Thailand
Viet Nam
Western New Guinea

*Chloroquine resistant strains may be confined to only isolated areas in countries in which they have been reported. For more detailed geographic information consult the Center for Disease Control

Very rarely a patient cannot take chloroquine. In such cases amodiaquine can be substituted for chloroquine.

Fansidar and Chloroquine-Resistant Falciparum Malaria

Fifteen years ago there could have been little argument about the selection of chloroquine as the chemoprophylactic agent of choice for travelers to all parts of the world. However, chloroquine-resistant falciparum malaria has been appearing in new areas of the world (Table 2). Recently, there have been reports of chloroquine resistance in Kenya and Tanzania,[9] although this has not yet been confirmed by the World Health Organization. Since the majority of cases of falciparum malaria are acquired in Africa, the recent appearance of chloroquine resistance in this area is particularly disturbing. Difficulty in prophylaxis of chloroquine-resistant falciparum could lead to more malaria deaths in travelers.

There is no clear agreement on the choice of prophylactic agent for travelers going to areas where chloroquine-resistant falciparum has been reported. Many malariologists continue to recommend chloroquine on the assumption that the actual risk of acquiring chloroquine-resistant falciparum malaria is low. Chloroquine advocates point to the fact that even in areas where

chloroquine-resistant P falciparum has been documented, most strains continue to be susceptible to chloroquine. In spite of this evidence, some experts are now recommending the use of a combination of pyrimethamine and sulfadoxine (Fansidar) which, although not available in the United States, can be purchased in most areas where chloroquine-resistant malaria has occurred. If Fansidar is prescribed for prophylaxis, chloroquine should be begun two weeks before departure and the switch to Fansidar (50 mg pyrimethamine and 1,000 mg sulfadoxine given once every two weeks) should be accomplished after arrival and purchase of the drug. To achieve a suppressive cure of P falciparum and P malariae, Fansidar should be continued for six weeks after last exposure.

The use of Fansidar as a prophylactic has several drawbacks. Although it will produce a suppressive cure of P falciparum infection and suppress most infections with P vivax, P ovale, and P malariae, pyrimethamine-resistant strains of P vivax may cause an acute attack of malaria in an individual on prophylaxis. In addition, even though there is no evidence to date that Fansidar has serious toxic side effects,[10,11] experience with its use is limited. It should not be given to newborns and pregnant women.

Prophylaxis of Pregnant or Lactating Women and Newborns

Physicians must give special consideration to pregnant women, lactating mothers, and newborns. Because malaria infection in a pregnant female is associated with placental infection, a high incidence of low birthweight babies, and occasionally congenital infection, malaria prophylaxis of all pregnant women is imperative. There is no contraindication to the use of chloroquine during pregnancy. However, Fansidar should not be used as it is associated with reports of teratogenesis in animals.

One report indicated that lactating mothers can protect their nursing infants through transfer of active drug in the milk.[12] Although chloroquine is excreted in human milk, there is, however, no solid evidence that breast fed infants of mothers taking this drug for prophylaxis are protected. Therefore, all infants at risk for malaria while traveling should be given chloroquine beginning shortly after the first week of life. Chloroquine syrup is not available in the United States, but it may be purchased overseas. Chloroquine is bitter but can be made palatable by mixing the crushed tablets in chocolate syrup. Amodiaquine, an alternative drug, can be purchased in liquid form for children.

References

1. United States Bureau of Census: Statistical Abstract of the United States: National Data Book and Guide to Sources. Government Printing Office, 1979, p 224

2. Center for Disease Control: Annual Summaries, 1970-1978. From the US Public Health Service, Center for Disease Control, Atlanta. Government Printing Office, 1970-1978

3. Center for Disease Control, Bureau of Epidemiology, Quarantine Division: Health Information for International Travel. Atlanta, Center for Disease Control, 1978

4. Reilly PC: Letter. N Engl J Med 296:1536, 1977

5. Kean B, Reilly PC: Malaria: The mime. Am J Med 51:160, 1976

6. Center for Disease Control: Malaria Surveillance Annual Summary: 1977. From the US Public Health Service, Center for Disease Control, Atlanta. Government Printing Office, 1977

7. Center for Disease Control: Chemoprophylaxis of malaria. Morbid Mortal Weekly Rep 27(10)(suppl):83, 1978

8. WHO information of malaria risk for international travellers. Weekly Epidemiol Rec 51:181, 1976

9. Center for Disease Control: Chloroquine-resistant malaria acquired in Kenya and Tanzania—Denmark, Georgia, New York. Morbid Mortal Weekly Rep 27:463, 1978

10. Laing ABG: Malaria suppression with fortnightly doses of pyrimethamine with sulfadoxine in the Gambia. Bull WHO 43:513, 1970

11. Chin W, Contacos P, Coatney R, et al: The evaluation of sulfonamides alone or in combination with pyrimethamine in the treatment of multiresistant falciparum malaria. Am J Trop Med Hyg 15:823, 1966

12. Clyde DF: Prolonged malaria prophylaxis through pyrimethamine in mothers' milk. East Afr Med J 37:659, 1960