ABC of Healthy Travel

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MALARIA PROPHYLAXIS

Malaria is widespread in tropical and subtropical areas of the world and is spread by the bite of a female anopheline mosquito that has been infected by the malaria parasite.

During the 1960s control measures in many areas appeared to be bringing malaria under control. A resurgence has occurred, however, particularly in the Indian subcontinent, parts of South America, and Turkey. Reasons for this include the cost of maintaining control programmes, lack of enthusiasm for preventive measures when the disease is becoming uncommon, the developing resistance of mosquitos to insecticides, and drug resistance of the parasites themselves.

The increasing mobility of the population, especially through air travel, brings a further hazard since travellers may be bitten by mosquitos at airports en route as well as in the countries where they stay. The speed of travel means that first symptoms may occur in a country and in a context where the disease will not be immediately considered. Mosquitos may even be brought in aeroplanes to non-endemic areas and infect, for example, airport staff or travellers' relatives. Spread also occurs through blood transfusion (cold storage does not destroy the parasites) and the sharing of needles by drug addicts.

The most immediately life-threatening form of malaria is caused by *Plasmodium falciparum*. Because of the travelling habits of those living in Britain this form of malaria is usually imported from Africa and sometimes from south-east Asia. Prevention is primarily aimed at this parasite. Nevertheless, the same advice is given to those likely to be exposed to the less dangerous *P vivax*, *P malariae*, and *P ovale*, partly to prevent an unpleasant illness but also because *P falciparum* infection can never be presumed to be absent in any malarious area.

There is no immediate prospect of an effective vaccine, so regular ingestion of prophylactic tablets is necessary. This requires habits which some find difficult or even distasteful, but if appropriate tablets are taken falciparum malaria can largely be prevented. *P vivax* and *P ovale* have a persistent liver phase, and illness may result after prophylaxis is discontinued. If this occurs additional treatment with an 8-aminoquinoline drug not normally used for prophylaxis may be required.

Personal precautions

(1) Avoid mosquito bites, especially after sunset, when the anopheline mosquitos responsible for transmitting malaria are most active. Long trousers, sleeves, and dresses, netting on windows, and mosquito nets over beds all help to prevent mosquito bites.

(2) Insect repellents may be used on exposed skin and insecticides inside buildings or on breeding sites.

(3) Mosquitos should not be encouraged to breed by leaving stagnant water—for example, in blocked drains or around plant pots.

(4) Prophylactic tablets are necessary because the above measures, although valuable, are unlikely to be fully effective.

(a) Start tablets (see table) a day or two before departure to confirm tolerance and obtain adequate blood concentrations before exposure.

(b) Take the tablets absolutely regularly. Prophylactic doses of drugs are not normally curative once the infection is established.

Doses of antimalarials for children. (When weight and age are both available, weight gives a better guide.) Syrups are available

Weight (kg)	Age (years)	Proportion of adult dose
< 5	< 1	$\frac{1}{4}$
5-20	1-5	$\frac{1}{2}$
21-40	6-12	$\frac{3}{4}$
> 40	> 12	Adult dose

This may be applied to all antimalarials for prophylaxis.

Centres specialising in medical advice for travellers include:

Communicable Diseases (Scotland) Unit,
Ruchill Hospital,
Glasgow G20 9NB Tel: 041-946 7120

Department of Communicable and Tropical Diseases,
East Birmingham Hospital,
Bordesley Green Road,
Birmingham B9 5ST Tel: 021-772 4311

Department of Health and Social Security,
Alexander Fleming House,
Elephant and Castle,
London SE1 6BY Tel: 01-407 5522

Hospital for Tropical Diseases,
4 St Pancras Way,
London NW1 0PE Tel: 01-387 4411

Liverpool School of Tropical Medicine,
Pembroke Place,
Liverpool L3 5QA Tel: 051-708 9393

Ross Institute of Tropical Hygiene,
London School of Hygiene and Tropical Medicine,
Keppel Street (Gower Street),
London WC1E 7HT Tel: 01-636 8636

(c) Continue prophylaxis for at least four weeks after leaving an endemic area: all forms of the parasite develop first in the liver and only later re-enter the blood, where most prophylactic drugs take effect.

Determining the most appropriate drug for a particular traveller is not straightforward. The choice may have to be made from incomplete data in parts of the world where the prevalence of the disease and resistance patterns are changing. In Britain general practitioners and the public may obtain advice from specialist centres.

The conclusions of a recent meeting on appropriate antimalarial drugs are shown in the following tables.

Recommended antimalarials (adapted from report of meetings on malaria convened by Ross Institute, BMJ 1981;283:214-8)

Name	Formulation of tablet	Adult prophylactic dose
<i>In areas of chloroquine-resistant P falciparum</i>		
Fansidar	Pyrimethamine 25 mg	One tablet weekly
or	Sulphadoxine 500 mg	
Maloprim	Pyrimethamine 12.5 mg	Usually one tablet weekly
	Dapsone 100 mg	
<i>In areas without chloroquine resistance</i>		
Chloroquine	100 mg, 150 mg,	300 mg base weekly
or	or 300 mg of base	
Proguanil	100 mg	100-200 mg/day
or		
Pyrimethamine	25 mg	25 mg/week

Note: Any drugs to be used outside the United Kingdom should be prescribed privately. Pyrimethamine, proguanil, and chloroquine may be bought without prescription.

Two recent updates (*WHO Weekly Epidemiological Record* 1982;57: 381-4, and PHLS Malaria Reference Laboratory, see p 787) reflect the evolution of thought about prophylaxis. Both emphasise the importance of preventing mosquito bites and that no ideal prophylactic drug exists. Neither recommends the use of pyrimethamine alone, and the WHO does not recommend proguanil. The main difference is that the WHO would like to restrict Fansidar solely to *therapeutic* use in Africa, as the distribution of chloroquine resistance is patchy and the resistance is low compared with that in South America and south-east Asia. Such infections usually present in travellers when chloroquine prophylaxis is stopped. The WHO recommends that non-immune travellers should take chloroquine prophylaxis and carry a treatment course of Fansidar to use if fever develops and diagnostic facilities are not readily available. The reports illustrate the differing opinions and continuing need to seek advice from specialist centres.

Notes on drugs

Areas with chloroquine resistant *P falciparum* (1982)

Central and South American

Bolivia, Brazil, Colombia,
Ecuador, French Guiana, Guyana,
Panama, Surinam, Venezuela

Asia

Bangladesh (north and east),
Burma, China (Hainan Island
and southern provinces), India
(north east—Orissa, Assam, and
Uttar, Andhra, and Madhya Pradesh),
Indonesia (Kalimantan, Irian, Jaya,
Java, Sumatra), Kampuchea, Laos,
Malaysia (Peninsular and Sabah
and Sarawak), Nepal, Nicobar and
Andaman Islands, Philippines,
Thailand, Vietnam

Oceania

Papua New Guinea, Solomon Islands
(west), Vanuata

Africa

Kenya, Sudan, Tanzania, Uganda,
Zambia, Comoro Islands, Madagascar,
Zanzibar

Of the two drugs used in chloroquine-resistant areas—Fansidar and Maloprim—there is already some evidence of resistance developing to Fansidar, and Maloprim may need to be taken twice weekly if future surveillance shows that one tablet is giving unsatisfactory protection. Both these drugs are less effective against the benign forms of malaria than against malignant falciparum infection, and if it is essential while abroad to prevent symptoms from all types chloroquine at usual doses may be taken as well.

Resistance to proguanil and pyrimethamine is widespread even in chloroquine-sensitive areas but is not well documented. Two new drugs, mefloquine and ginghamosu, which are likely soon to have a place in the treatment of chloroquine-resistant malaria, may also have a role, still to be determined, in prophylaxis.

Fansidar	— avoid in first few weeks of life — avoid in 3rd trimester — contains sulphonamide
Maloprim	— optimal dose in future may be more than one tablet weekly
Chloroquine	— corneal and retinal changes change after 2-3 years
Proguanil	— very safe
Pyrimethamine	— tasteless

} resistance occurs

Side effects—Fansidar, Maloprim, chloroquine, proguanil, and pyrimethamine rarely cause side effects. Any nausea may be eased by taking tablets after a meal. The rashes due to sulphonamides can result from Fansidar, and the manufacturers recommend that sulphonamide sensitivity is a contraindication to Maloprim, which contains a sulphone (dapson).

Prolonged use of chloroquine can result in corneal and retinal changes, and the drug should be changed after two or three years' use. Proguanil and pyrimethamine are antifolate drugs but rarely give haemopoietic problems in the doses listed. Supplements of folic acid can be given in pregnancy.

Pregnancy and infancy—The risks from malaria during pregnancy outweigh risks from all these drugs except Fansidar, which should be avoided during the third trimester and during the first few weeks of life because it can induce jaundice in the newborn. Otherwise all drugs should be given from birth.

Declining immunity

Prevention is especially important in those without immunity, which for practical purposes includes those who have never lived in malarious areas and those who have not recently been exposed. This includes, for example, students from Africa who have been in Britain for as little as a year. Having grown up in malarious areas and survived to develop immunity they may not want to start a habit of regular prophylaxis on visits home if they eventually intend to return permanently. Nevertheless, their immunity will be waning and urgent treatment of attacks will be necessary. This may require them to carry a course of treatment when travelling to areas remote from medical services.

Those who have immigrated to Britain also require special advice. When they left their country of origin, as well as incorrectly believing they had lifelong immunity to malaria, they may have been in a malaria-free area to which the disease has now spread. At present this is a problem for those paying return visits to the Indian subcontinent.

Failed prophylaxis

Compliance ?

P vivax, *P malariae*, *P ovale* ?

Vomiting ?

Always consider malaria if fever occurs

Patients, particularly those who have been in malarious areas for many years, sometimes complain of contracting malaria despite prophylaxis. Consequently they may lose confidence in prophylaxis and stop taking precautions, with possibly fatal results.

There are various reasons for "failure." Prophylaxis against *P falciparum* is less effective against *P vivax* and *P ovale* because these parasites may persist in the liver and produce illness after prophylaxis has been stopped.

If falciparum malaria occurs while travellers are taking prophylaxis it must be established whether they have been taking tablets regularly and in the correct dose. Sometimes a gastrointestinal upset may have resulted in tablets being vomited back or not absorbed properly. Some people confuse prophylaxis with treatment and do not realise that prophylactic doses are not normally curative if the disease has become established. If there is no doubt about compliance or the accuracy of the diagnosis drug resistance must be considered and adjustments made in the recommended tablets.

Finally, the best prophylaxis is not always effective and malaria should be considered whenever fever occurs in someone who has been exposed to infection or even apparently successfully treated, since partially resistant infections may recrudescence during a period of up to six weeks.

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The photograph of the mosquito was reproduced by permission of WHO and the world map of malarious areas from *Communicable Disease Report* 1983;83/01.