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Lesson of the week

Malaria at Christmas: risks of prophylaxis versus risks of malaria

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Health professionals need to educate travellers about the dangers of malaria and the importance of prophylaxis

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There was a large increase in the number of cases of falciparum malaria imported into the United Kingdom and reported to the malaria reference laboratory in the first quarter of 1998.[1] The two factors cited to explain this increase were unusually heavy rains in east Africa and a reduction in the use of the most effective antimalaria drug, mefloquine.[1] At the same time there was an increase in the number of cases of severe malaria in the United Kingdom.[1] During December 1997 and January 1998 this hospital treated five patients for severe malaria and gave advice on a further 20 patients with malaria who had been admitted to intensive care units throughout England. Of the 25 patients, 13 were male (median adult age 50; range 23 to 85) and two were children. Twenty two of those treated were of European origin. Altogether 20 patients had travelled to east Africa (16 to Kenya and at least six of these to Mombasa); five had travelled to west Africa. Median parasitaemia was 16% (range 1.1% to 60%). Ten patients (40%) had taken no prophylaxis; one of these was a Kenyan man of Asian origin who was on holiday in the United Kingdom. Prophylactic drugs had been prescribed for 15 patients: 11 had been prescribed proguanil and chloroquine, two had been prescribed mefloquine, and two had been prescribed other drugs. Nine of the 15 had not taken the drugs as prescribed. Thus 19 of the 25 (76%) had taken either inadequate doses or no prophylactic drugs. The cost to the NHS for intensive care for these patients exceeded £160 000 ($256 000). We report on four cases of severe malaria seen at our hospital.

Case reports

Case 1—A 50 year old woman who thought she had influenza was admitted to an intensive care unit with a parasitaemia of 37%, renal failure, and pulmonary haemorrhage. She had been told by a practice nurse that antimalaria drugs had too many side effects; she had sought alternative prophylaxis from homoeopathy.

Case 2—A 54 year old woman was discouraged by a friend, a community psychiatric nurse, from taking mefloquine. The patient took no prophylaxis because she thought that nothing else was available. She was subsequently admitted to the intensive therapy unit with a parasitaemia of 35% and cerebral, renal, and pulmonary involvement.

Case 3—A 55 year old man working in Nigeria had tolerated mefloquine well but his doctor was concerned about possible long term side effects and stopped the drug after six months. The patient could not tolerate chloroquine and proguanil and so took no prophylaxis. He was admitted to an intensive therapy unit on Christmas Eve with a parasitaemia of 18% and renal failure.

Case 4—A 37 year old Sudanese woman who lived in the United Kingdom was prescribed mefloquine for travel to Sudan but decided not to take it, probably thinking incorrectly that she was immune to malaria. She was admitted on Christmas Day with a fever and perianal abscess. The abscess was drained but the fever did not settle. She was readmitted eight days later with jaundice, shock, and a reduced level of consciousness.

She had a parasitaemia of 25%. She developed the adult respiratory distress syndrome and renal failure.

Discussion

Risk of malaria

In three of these four cases incorrect, misleading, or inadequate advice was given by healthcare professionals. Media coverage of the adverse effects of antimalaria drugs, such as the BBC programme *Watchdog* (November 1995), has contributed to confusion about prophylactic regimens among healthcare professionals and the public. Malaria is a common and potentially fatal disease; there are 300 to 500 million cases each year and 1.5 to 2.7 million deaths each year.[2] In the United Kingdom 11 people died of falciparum malaria in 1997 (DJ Bradley, personal communication); this figure would have been higher but for the efficient, though costly, intensive care that patients received. Mortality from treated malaria in non-immune travellers ranges from 0.4% to 10%.[3] Cerebral malaria has a mortality of 15% to 20% even if treated.[4] The incidence of falciparum malaria in travellers who do not take prophylactic drugs is high, about 0.6% in east Africa[5] and 3.5% in west Africa[6] over a two week period.

Benefits of prophylaxis

Since no prophylactic regimen is 100% effective, travellers need to take precautions to avoid being bitten by mosquitoes[8] and should be educated to seek medical help promptly if they develop a fever while abroad or after they return. Adherence to any one of the recommended prophylactic regimens is better than non-adherence to a potent regimen or no prophylactic treatment at all. If malaria is contracted while prophylactic treatment is being taken, its severity may be attenuated.[9] Mefloquine is the most effective prophylactic against malaria in sub-Saharan Africa, being 90% protective.[5] In 1987 the efficacy of proguanil and chloroquine was about 70% for west Africa and 50% for east Africa. It is likely to be lower today.[10]

Side effects of antimalaria drugs

There are discrepancies among published reports of rates of side effects. Randomised controlled trials have failed to confirm the incidence of adverse events that have been reported in observational studies as associated with the use of mefloquine.[11] This might be because controlled trials have studied male military staff rather than general travellers or because the rating of the severity of adverse events has differed between studies; it is not always clear how much an adverse event has affected a traveller. The published incidence of serious events (fatal, life threatening, or resulting in hospital admission or severe disability) associated with the use of proguanil and chloroquine or with mefloquine are of the same order of magnitude (1:13 000 and 1:10 000 respectively).[5] The incidence of trivial side effects was similar for both regimens, although there was an excess of gastrointestinal side effects with proguanil and chloroquine.[5]

There is dispute over the adverse effects classed as being of intermediate severity. In their retrospective study of returning travellers Barrett et al found that 9.2% of travellers taking mefloquine experienced neuropsychiatric symptoms that were severe enough to interfere with daily activities.[12] These events occurred about twice as often as side effects in travellers taking proguanil and chloroquine. In 0.7% of travellers taking mefloquine, neuropsychiatric events were temporarily disabling—that is, bad enough to prevent them carrying out the activity for which they made the journey—compared with 0.09% for proguanil and chloroquine. In contrast Croft et al's prospective randomised double blind trial, which had a less than ideal response rate, found no evidence of a difference in the incidence of gastrointestinal or neuropsychiatric side effects between soldiers assigned to take mefloquine and those taking proguanil and chloroquine.[13]

Balancing the risks

In the United States mefloquine is the prophylactic drug most likely to be recommended.[14] In contrast, the 1997 United Kingdom guidelines for the prevention of malaria in travellers have, after balancing the risks of side effects from antimalaria drugs against the risks of acquiring severe malaria, allowed proguanil and chloroquine to be used for some short visits to the east African coast.[15] The guidelines predicted that reducing the number of neuropsychiatric reactions through reducing the use of mefloquine would result in an increase in the number of cases of malaria. The guidelines thus indicate the need to inform travellers of the lesser effectiveness of proguanil and chloroquine.

Communicating the risks

The decision that travellers take with regard to antimalaria drugs is often based on folklore rather than sound advice. These cases of malaria occurring over the Christmas holidays make it clear that some travellers are not getting balanced, clearly presented information about antimalaria drugs. Those responsible for giving travel advice should be familiar with the 1997 guidelines and be able to communicate them accurately. Those who are not should be wary of giving advice. It is important that travellers know the advantages and disadvantages of the prophylactic regimens available. Advice should be given by informed professionals rather than by less well informed acquaintances or the media, whose aim may be to sensationalise rather than to provide a balanced public health message.

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Science commentary

Science commentary: Protection against malaria

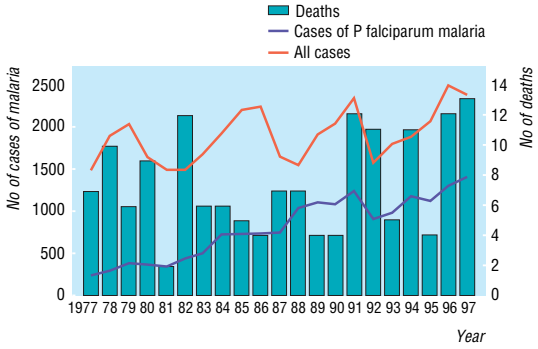
Malaria can be prevented. Unfortunately, travellers to areas where malaria is common often put themselves at risk of contracting the disease by ignoring the key steps in malaria prevention. The steps are simple but if ignored can result in unnecessary morbidity and, in some cases, death. The key steps to protect against malaria are:

A—Awareness: know about the risk of malaria
B—Bites by mosquitoes: prevent or avoid
C—Compliance: with appropriate drug regimen
D—Diagnosis: diagnose malaria swiftly and obtain treatment promptly.

Incidence of side effects from prophylactic drugs

The number of cases of malaria imported into the United Kingdom is rising (figure), and over half of them are potentially fatal (falciparum malaria). The risks from the disease must be compared sensibly with the risks associated with the drugs recommended for prophylaxis. Obtaining true figures for the incidence of side effects is difficult and in some cases controversial. This is partly because as doctors become more aware of potential side effects, more side effects are looked for and then reported. Also, it is virtually impossible to perform anything other than observational studies on side effects because sending people to malarious areas with placebo drugs only would be unethical.

Two other factors make it difficult to determine the incidence of side effects. Firstly, of the huge number of people taking antimalaria drugs some will get concurrent symptoms and diseases while abroad, and deciding whether to attribute these to the antimalaria drugs is difficult. Secondly, attributing subjective side effects to drugs is a common phenomenon, even for placebo drugs.



Number of cases of malaria, number of cases of falciparum malaria, and number of deaths from malaria in the United Kingdom, 1977-97. Data supplied by the Malaria Reference Laboratory, London School of Hygiene and Tropical Medicine (E Walker, personal communication)

With short acting drugs (for example, proguanil, which is taken daily) side effects usually occur after just one dose. With longer acting drugs (for example, mefloquine, which is taken weekly), side effects may not become apparent until after the third dose.

Two large studies have reported the incidence of side effects of mefloquine compared with chloroquine and proguanil. Barrett et al found that both regimens had similar rates of any side effect occurring (40%), although most side effects were trivial.[1] About 0.7% of travellers taking mefloquine reported severe, disabling neuropsychiatric symptoms compared with 0.09% of people taking chloroquine and proguanil. Also a significantly higher number of moderate neuropsychiatric symptoms occurred in mefloquine users compared with travellers who took chloroquine and proguanil. Steffen et al found that 18.8% of travellers taking mefloquine had experienced side effects while 30.1% of the chloroquine and proguanil group reported problems.

Abi Berger *Science editor, BMJ*

Commonly reported side effects of antimalaria drugs

Mefloquine	**Chloroquine**	**Proguanil**	**Maloprim**
Nausea	Nausea	Nausea	Agranulocytosis
Dizziness	Visual accommodation problems	Mouth ulcers	
Neuropsychiatric problems (anxiety, depression, panic, hallucinations)	Corneal or retinal changes (after prolonged use)		

1 Barrett PJ, Emmins PD, Clarke PD, Bradley DJ. Comparison of adverse events associated with the use of mefloquine and combination of chloroquine and proguanil as antimalarial prophylaxis: postal and telephone survey of travellers. *BMJ* 1996;313:525-8.
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