

# CHILDHOOD MALARIA — PREVENTION AND EMERGENCY SELF-TREATMENT

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*Family travel to holiday destinations where malaria is endemic has become increasingly popular in recent years. Additionally, many British people or United Kingdom residents make regular trips to such areas in order to visit relatives abroad, making the UK one of the highest importers of malaria in the world. In both situations children may accompany their parents. This article examines the particular risks and issues concerning prevention and emergency self-treatment of malaria contracted by children*



In 2001 around 115,000 children under the age of 15 years from the United Kingdom visited areas where malaria is endemic: 16 per cent to sub-Saharan Africa, 61 per cent to the Indian subcontinent, 15 per cent to South East Asia and 7 per cent to South America.<sup>1</sup> In that year, of the 2,050 people contracting malaria, 14 per cent were under 15.<sup>2</sup> The case fatality rate in the late 1990s was around 1 per cent of individuals contracting malaria, although this has fallen to half that in recent years.

## EPIDEMIOLOGY OF TRAVEL MALARIA IN CHILDREN TRAVELLING FROM THE UK

Undoubtedly sub-Saharan Africa possesses the greatest risk to the UK travelling public, since of the 100 deaths attributed to malaria among UK travellers recorded over the past 10 years, 94 were contracted in that part of the world. This is reflected by the numbers of recorded cases of malaria in 2001. Out of the 2,050 cases, 1,483 were contracted in sub-Saharan Africa, 1,017 from areas of West Africa alone. Furthermore most of these cases occurred in people who were African or of African descent, identifying travellers visiting their families as a particular risk group. Among children under the age of 15 there were 278 recorded cases of malaria, again the majority (182) were African, or of African descent. A retrospective study<sup>3</sup> of childhood malaria treated in St George's Hospital, south-west London, during the period 1975 to 1999, found that the incidence had increased over this period, with only 22 per cent accounted for by immigrants arriving in the UK. In only 41 per cent of the cases were children taking malaria prophylaxis and the numbers not

taking such prophylaxis seemed to be increasing. There have so far been 10 deaths among those under 15 contracting malaria while overseas.

In endemic countries, by far the largest proportion of deaths due to malaria among the local population is in childhood; 70 per cent of the one million deaths worldwide occur in children under five years of age. This is because after continued exposure to the most dangerous type of malaria, *Plasmodium falciparum*, semi-immunity will develop. Thus those who survive childhood will have some protection from the disease through adult life. However, if not continually exposed such immunity does wane over a few years. Those who are travelling to such areas are therefore in a position of having no immunity to this form of malaria and are at risk. It is likely that many of the cases among Africans returning to visit relatives in their country of origin is due to a mistaken belief that they still possess immunity and as a result fail to take prophylaxis. The other forms of malaria, of which *P. vivax* is the most common, is rarely fatal in adult or child travellers, but immunity does not develop.

## SIGNS AND SYMPTOMS OF MALARIA IN TRAVELLERS

The particular complications associated with *P. falciparum* infection are related to the changes caused to red blood cells (RBCs) invaded by the organism as part of the

malaria life cycle. Unlike other forms of malaria, affected RBCs tend to adhere to blood vessels causing damage and local ischaemia. If this occurs in the central nervous system then cerebral malaria can ensue, carrying a high mortality.

The particular issue for travellers is that the time between developing initial non-specific symptoms to life threatening complications can be short, sometimes as little as 24 hours. Initial presentation may be a fever accompanied by a variety of other symptoms including lethargy, gastrointestinal disturbance and headaches. Onset of such symptoms may be from one week to three months after being bitten by a mosquito, and up to a year with some other forms of malaria, so it is not surprising that diagnosis can be initially missed in the returned traveller. This may be quite quickly followed by coma and death.

The issue for the child contracting malaria is that progress of the disease can be even faster than seen in the adult, with symptoms of a greater severity and increased risk of fatality, sometimes within a few hours of onset.<sup>4</sup> There are two reasons for this difference. First, the small body mass and blood volume means that parasitaemia will be proportionally higher than in an adult. Secondly, an underdeveloped immune system would result in the child being overwhelmed by such an infection. Fever will be present in the majority of cases and often does not follow the pattern of regular fever seen for *P. vivax* in adults. Diagnosis based on symptoms can be difficult due to the possibility of the occurrence of other common childhood infection such as otitis media. A range of symptoms may present which are also attributable to other

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causes in children, eg, nausea and vomiting, abdominal pain, coughing and irritability. For these reasons the World Health Organization has issued a general recommendation that children do not travel to areas where malaria is endemic if this can be avoided.

If parents or guardians do choose to take children to areas where malaria is endemic the following advice should be followed.

#### BITE AVOIDANCE

It is essential that measures are taken to avoid mosquito bites even if malaria chemoprophylaxis is being taken. Young babies should be protected from bites when resting or sleeping by using well screened rooms that have been cleared of mosquitoes using a knockdown spray. In addition a mosquito net, treated with an insecticide, should be used to cover a cot. Nets specifically designed for this purpose can be purchased or those used for an adult adapted. Taking a baby out of doors after dusk should be avoided.

Children will need regular applications of repellent, particularly when going out after dusk. They will also need to wear long sleeves/trousers and sleep in the conditions described above. The use of topically applied repellents in children has been a somewhat contentious issue. Diethyltoluamide (DEET) based repellents are claimed to be more effective than other types, and are recommended as a first line in malaria endemic areas. There have been some reports of toxicity occurring in children and, in particular, a few cases of encephalopathy. However, this needs to be put into context of the extremely widespread use of DEET over the past 50 years,<sup>5</sup> and a maximum concentration of repellent of around 20 per cent is advised for children. However, with the usual application rate such a concentration may not give effective protection for more than an hour or two. Long acting preparations would therefore be preferable and these can be obtained from specialist outlets. Alternative non-DEET preparations include lemon eucalyptus (Mosiguard) and Bayrepel (Autan).

Probably the best method of personal protection is to apply a repellent to the skin and treat the clothing with an insecticide such as permethrin. Currently available UK formulations of permethrin for clothing treatment are not licensed for children under 12 years.

#### MALARIA PROPHYLAXIS IN CHILDREN

For those parts of the world where chloroquine resistant *P falciparum* malaria is not a problem or *P vivax* predominates, eg, the Indian subcontinent, then chloroquine and proguanil prophylaxis may be used. Chloroquine is available as syrup for children and is administered just once a week, but proguanil can only be given as tablet formulation daily. Dosage must be calculated according to body weight (not by age as previously) resulting in the need to break up proguanil tablets into halves or quarters and, if unable to be swallowed whole, to crush or hide them in food that the child will accept, eg, jam or peanut butter. There is little data on use for children weighing less than 5kg. Courses must be given for one week preceding entry of the malaria endemic area and then continued for four weeks after leaving. Both drugs appear to have a good safety profile in children at the recommended doses, although just 300mg of chloroquine as a single dose may be lethal for a baby.

In areas such as sub-Saharan Africa there are three potential regimens of equal efficacy: atovaquone/proguanil (Malarone), doxycycline and mefloquine (Lariam). Doxycycline is contraindicated in children under 12 years of age due to the potential to damage developing teeth and bones. Mefloquine is given once a week, but like proguanil tablets may need to be broken to obtain the correct dose. Treatment may need to be initiated up to three weeks before departure to identify potential side effects. CNS side effects such as anxiety and nightmares are reported to be less common in children than in adults,<sup>6</sup> but it should not be given to those with a psychiatric condition or epilepsy. The prophylaxis must then again be continued for four weeks on returning home to deal with parasites emerging from the liver stage of the life cycle.

Atovaquone/proguanil must be administered daily, but it can be started the day before travel and only needs to be continued for one week after leaving the endemic area because it is effective against the liver stages of the parasite. Paediatric tablets have recently become available. These are smaller than the adult formulation and taken as whole tablets, depending on the body weight of the child. As absorption is improved by taking the tablets with a fatty meal, disguising or crushing them in peanut butter or a chocolate spread may be desirable. At present atovaquone/proguanil is only licensed for those over 11kg due to lack

of data to support prophylaxis at lower body weights and for a maximum of 28 days. The side effect profile also appears favourable.

If a child on prophylaxis vomits within an hour of administration the dose should be readministered.

#### STANDBY MALARIA TREATMENT

No prophylactic medication is 100 per cent effective and it is occasionally advised that people travelling to areas where medical help is not readily available also carry emergency self-treatment. This should be of an agent that is not of the same type being used by the traveller for prophylaxis and if taken medical help should still be sought at the first opportunity. Expert opinion should be sought regarding the choice of standby treatment of which there are a number of options; oral quinine with tetracycline/fansidar, atovaquone/proguanil, mefloquine and artemether/lumefantrine (Riamet). It must be remembered that emergency self-treatment is not actually a licensed indication for these preparations, although they are licensed for the treatment of acute uncomplicated *P falciparum* malaria.

For children, side effects from oral quinine may be unacceptable for self-treatment and tetracyclines could be used, a potential alternative being clindamycin. Likewise adverse effects from higher doses of mefloquine make it less desirable as standby treatment. Atovaquone/proguanil (250mg/100mg) would be a useful agent in this respect in children over 11kg as it is generally well tolerated and needs only to be administered once a day for three days. Artemether/lumefantrine can be given as whole tablets to children over 12 years of age and weighing more than 35kg, but the regimen is rather more complicated.

*P vivax* malaria is not eradicated by these regimens and may return years later due to the development of long lived liver stages. Radical cure can be achieved by the use of primaquine, but this is contraindicated in children under four years of age.

#### SUMMARY

Malaria in childhood is an even more serious condition than for adults and parents should consider the risks of taking children to highly endemic areas. Malaria prophylaxis should be administered according to the child's body weight. For those countries where *P falciparum* is endemic either mefloquine or atovaquone/proguanil should be considered.

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