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Prophylaxis



7. Special Categories

7.1 Children

Children are at particular risk of severe and fatal malaria; therefore, parents are advised against taking infants and young children to malarious areas.

If travel is unavoidable, infants and children should be well protected against mosquito bites and receive appropriate malaria chemoprophylaxis.

It is important that the child's carers understand the importance of trying to ensure that the child properly completes the full course of prophylactic medication.

Parents should supervise children's chemoprophylaxis, as some regimens can be difficult even for adults to follow.

Parents must be cautious not to exceed maximum recommended doses, since antimalarials can be particularly toxic to children.

Paediatric doses of antimalarials for prophylaxis are shown in tables 4-6 in chapter 4:

- Chloroquine: Take care to ensure that tablets are actually swallowed, as they have a bitter taste. Sweetened chloroquine syrup is available. Store safely away from children since an overdose can be fatal.
- Proguanil: as for adults more effective when taken with chloroquine although chloroquine resistance is present in many areas. Difficult to use for children since proguanil is only available in adult formulations and, dependent on the weight of the child, the adult-dose tablets must be broken and powdered into food.
- Chloroquine plus proguanil: see individual agents above.
- Mefloquine: Problem in administering correct dosage because there is currently no suspension available and adult-dose tablets must be broken.
- Doxycycline: Only licensed in the UK for children over the age of 12 years due to the bone damaging effects of the drug. This age limit varies between countries; tablets should be swallowed whole and must not be crushed.
- Atovaquone/proguanil: Paediatric tablets are available in the UK for malaria prophylaxis in children from 11 kg upwards. The tablets are a quarter of the strength of adult tablets and can be crushed if necessary for ease of administration.

Whilst it is preferable to avoid breaking and crushing tablets, the appropriate dose of proguanil or mefloquine or atovaquone/proguanil may be crushed if necessary and mixed with jam, honey, chocolate spread or similar food to aid administration to young children. Tablet-cutters can be purchased from some pharmacies or travel shops.

Children with malaria may deteriorate very rapidly to become critically ill. Those looking after children on their return from malarious areas -family members, friends, professional carers, or school nursing and medical staff - should be made aware that such children need medical attention and a blood test for malaria without delay if they become unwell within a year of leaving a malarious area.

Healthcare professionals should strive to improve access to advice on malaria prevention for families with children, especially travellers “Visiting Friends and Relatives”.

7.2 Elderly travellers

The elderly are at particular risk from malaria⁵¹. No reduction in antimalarial dosage is required on the basis of advanced age. However, elderly travellers are more likely to have underlying disorders, for example renal impairment, which may necessitate antimalarial dose reduction. Furthermore, the increased likelihood of elderly travellers taking additional medication, for example for cardiac conditions, will influence the choice of chemoprophylactic agent in their particular case.

7.3 Multi-trip travel

Some travellers, for example business persons or expatriate contract employees, may make several short visits to malarious areas in the same year. For instance someone working in the tropics four weeks on, four weeks off, might be taking chemoprophylaxis for most or all of the year when including the periods before and after travel that prophylaxis is required. The strategy for chemoprophylaxis will then be mainly influenced by the level of malaria risk in the area(s) to be visited. For example, in the highly malarious regions of West Africa, the risk-benefit assessment is strongly in favour of taking chemoprophylaxis, even if it means year-round administration. For less frequent trips, the regions visited should determine the chemoprophylactic agents from which to choose. When the choice lies between mefloquine or doxycycline or atovaquone/proguanil and the traveller wishes tablet-free periods between visits, the shorter period of 7 days post exposure for atovaquone/proguanil prophylaxis versus the alternatives may be helpful.

7.4 Cruises

All travellers on cruises should use insect bite avoidance measures.

Cruises are a growing part of the holiday market. Most travellers on cruises are only ashore during daylight hours when *Anopheles* bites rarely occur, and therefore do not require malaria chemoprophylaxis. However, the cruise itinerary must be reviewed carefully to determine the risk of exposure to malaria.

As examples, cruises in the Caribbean may include several days travelling along the Amazon in Brazil, or Orinoco River in Venezuela. Cruises along the East African coast may include a stop for a night or more in the port of Mombasa, Kenya and passengers may be ashore or on deck after dusk. These itineraries will require malaria chemoprophylaxis.

In addition cruises that have an overnight stay in any other malaria endemic region of the world require malaria chemoprophylaxis.

7.5 Oil rigs

There is a large number of staff employed in the oil industry predominantly based around West Africa. Employees commonly travel to these areas every 4-6 weeks, followed by a similar period of leave back in the UK. Oil rigs may be based in river estuaries or many miles offshore. Thus, the level of risk may be difficult to assess until one period of work has been completed and therefore antimalarial chemoprophylaxis should be taken for the whole of this first trip, by when the situation will be known.

Antimalarial chemoprophylaxis is advised for those workers on oil rigs based in river estuaries.

Offshore rigs pose little risk and antimalarial chemoprophylaxis may only be needed if staying overnight onshore during transit.

7.6 Visits to national parks

Travellers visiting countries where malaria is restricted in distribution may plan to make day trips to national parks in malarious regions of the country. They should be advised on awareness of risk, bite precautions and the need for prompt attention in the event of fever during the succeeding year. If they plan to stay overnight in the malarious area, e.g. in a safari lodge, they should also take chemoprophylaxis.

7.7 Stopovers

Many stopovers are in urban or tourist areas (particularly in Asia) and have minimal malaria risk. They are often situated in countries which may have malaria transmission in parts. Therefore, in order to assess risk it is essential to establish where overnight accommodation will be.

Stopovers in most of Sub-Saharan Africa, including main cities, present a risk of malaria and antimalarial prophylaxis should be recommended.

7.8 Last minute travellers

Last minute visits to malarious regions, whether for vacation, business or family reasons, are now commonplace. This may leave the traveller little time to seek and act on travel advice.

Retail pharmacy outlets can supply over-the-counter antimalarials (chloroquine and/or proguanil) and antimosquito products, but mefloquine, doxycycline and atovaquone/proguanil are currently prescription only medicines (POMs).

If the traveller cannot obtain a GP appointment at short notice, some commercial travel clinics cater for walk-in attendees.

Doxycycline or atovaquone/proguanil should be started 2 days before travel to a malarious area. Chloroquine or proguanil or chloroquine plus proguanil one week before, and mefloquine 2-3 weeks before (to ensure tolerance). *Nevertheless, it is better to start chemoprophylaxis late than not to take it at all, as suppressive prophylactics will begin to work by the end of the incubation period.*

Where the recommended choice for the region to be visited is mefloquine or doxycycline or atovaquone/proguanil, it would be sensible to avoid mefloquine for last-minute prophylaxis if the traveller has not taken and tolerated mefloquine in the past.

ACMP does not recommend loading doses of any prophylactic antimalarial. The dosages recommended in these guidelines should be followed.

7.9 Visiting friends and relatives

(Adapted from the HPA Travel and Migrant Health Report 2006⁶⁷)

In the UK, malaria predominantly affects the non UK born population and their families, particularly those from Africa and south Asia, largely due to their high rates of travel to malarious areas.

Data suggest that people visiting friends and relatives are significantly less likely to take antimalarial prophylaxis than other travellers to Africa. Reasons for this may

be that those visiting friends and relatives in Africa substantially underestimate the risk of acquiring malaria, and overestimate the amount of protection that having been brought up in Africa may give them.

Awareness needs to be raised that malaria is not a trivial disease. Those born in malarious countries need to be aware that any immunity they may have acquired is rapidly lost after migration to the UK. The view that this group is relatively protected is a dangerous myth. Migrants from malarious areas also need to be made aware that second-generation members of their families have no clinically relevant immunity of any kind to malaria, and that their children are particularly vulnerable.

Effective chemoprophylaxis taken correctly should reduce the risk of malaria by around 90%, especially if combined with sleeping under insecticide-treated nets.

Appropriately tailored health information should be targeted to migrant communities, especially of African descent, to stress the importance of chemoprophylaxis. Health advisers for this group, including primary care practitioners working in areas with large numbers of migrants, can have a major role to play.

Those who feel unwell following any trip to tropical areas should be encouraged to present to their doctors early, and to inform the doctors that they are at risk of malaria. Patients of African origin, and occasionally even doctors, can underestimate the severity of malaria in this group.

7.10 Students and children at boarding school

Many people from malaria-endemic areas come to the UK for secondary or higher education.

Those who stay in Britain for a year or more will lose a significant degree of any malarial immunity they had acquired and become more susceptible to clinical malaria. When they return home they should be advised as for the section on long term visitors to the UK returning to live in malarious parts of the world

Those who are making short visits home (e.g. in school or college vacations) should be considered as VFR travellers and should be advised to use chemoprophylaxis in addition to personal protective measures against mosquito bites.

Students may become infected during their school or college vacations but the first symptoms of clinical malaria may actually occur in term time whilst they are in the UK. Therefore, it is essential that school/college nursing and medical staff consider malaria from the outset in any pupil from, or with a history of travel to, a malarious region and arrange a blood test for malaria without delay.

7.11 The long-term traveller

7.11.1 Risk assessment

The long term traveller is defined here as those travelling through, or visiting malaria-endemic countries for over six months.

One major problem for the long-term traveller is the variable access to and quality of medical care available overseas⁶⁸. The provision of details of healthcare facilities or points of information could be crucial.

The main issues influencing the choice of malaria chemoprophylaxis on a long-term basis are the same as for short-term use, i.e. malaria risk, adverse events profile, compliance and efficacy. However, the licensing criteria for antimalarial drugs often restrict the recommended periods of administration (usually due to a lack of formal trials of long-term administration, rather than from evidence of adverse effects). This leads to uncertainty about the safety of long-term prescribing.

A decision on whether chemoprophylaxis is continued on a long-term basis may be influenced by the overall length of stay, seasonal risk in the area, and access to medical facilities. Travellers living or backpacking in rural areas may be far from appropriate medical attention and the need for standby emergency medication should also be considered. The continued use of chemoprophylaxis will also depend on current personal health, current medication, previous medical history, pregnancy, and relevant family medical history. However, long-term travellers are at high risk from malaria, and should not neglect necessary prophylaxis.

Health risks for the long-term traveller will vary considerably, depending in part on the reasons for travel including:

Visiting friends and relatives (VFR)

Individuals who originate from countries where malaria is transmitted, but who have settled in the UK. They may later visit their country of origin and remain there for long periods of time while working or visiting friends and relatives. They may perceive little risk from malaria infection or believe they are immune. This is not true (see section on VFR in this chapter).

Expatriates

Usually based at a single location where the risk of malaria is known, they often have access to medical care, a good standard of accommodation and are usually more aware of the malaria risks. However, up to 30% of some expatriates develop malaria within two years and many cases can be attributed to poor compliance with prophylaxis⁶⁹.

Backpackers

Often younger than expatriates, they may be less careful of their personal safety and less adherent to medical advice, in addition to having less experience of overseas travel in general. They have less control over their environment as they are constantly moving on.

7.11.2 Chemoprophylaxis for long-term travellers

Adverse events

The cumulative risk of contracting malaria is roughly proportional to the

length of stay in a malarious area over the first few months. A three-month visit carries a risk around six times greater than a visit of two weeks.

Whilst the risk of new adverse events falls off over time, the risk of contracting malaria continues to increase roughly linearly as exposure to malaria continues (see figure 8). Thus, chemoprophylaxis in highly malarious areas is even more important for long-term visitors than it is for short-term travellers. Indeed, long-term travellers may wish to consider using malaria prophylaxis, or have standby medication, when short-term travellers might not, because of their sustained exposure to a small risk of infection.

Adherence to chemoprophylaxis

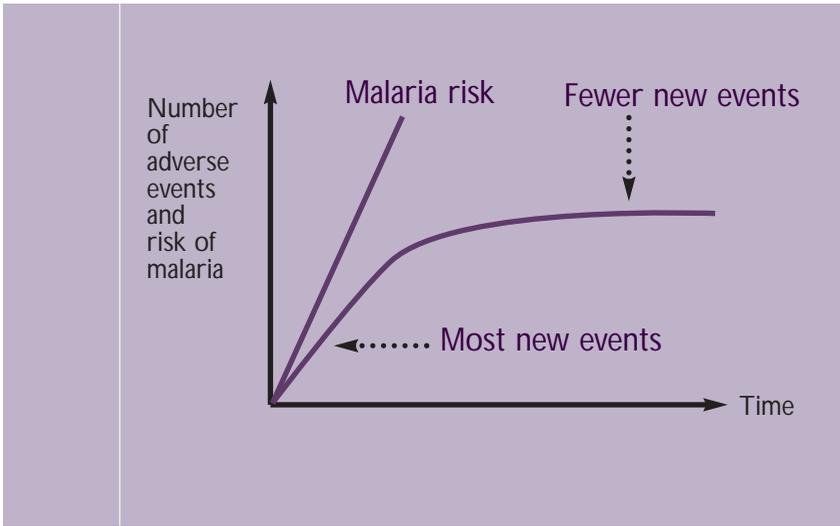
Compliance has been shown to decrease with the duration of travel⁷⁰, except where military-style discipline tends to support compliance. There is also evidence of weekly regimens having increased compliance over daily regimens⁷⁰.

Possible reasons for reduced compliance in long-term travellers may include:

- Fear of long-term side effects.
- Actual adverse events on one or more regimens.
- Conflicting advice.
- Complex regimen/daily tablets.
- Reduced confidence if intercurrent fever misdiagnosed as malaria.
- Perception from anecdotal evidence that chemoprophylaxis is unnecessary⁷¹.

In addition, long-term travellers may overlook personal protective measures against mosquitoes⁷².

FIGURE 8 CUMULATIVE RISK OF ADVERSE EVENTS AND OF MALARIA



Efficacy of regimens

It is important to stress that no chemoprophylactic regimen is 100% effective and that anti-mosquito measures should also be used. Travellers should be encouraged to continue chemoprophylaxis despite suffering what they believe to be a malarial illness. Many febrile episodes in long-term travellers or expatriates are incorrectly diagnosed as malaria.

Licensing restrictions

The specific problem relating to prophylaxis advice for long-term travellers is that long-term use of many of the currently advised malaria drugs falls outside the terms of their current Marketing Authorisation (Licence).

There have been a number of approaches in response to this time limit:

- Switching from one chemoprophylactic regimen to another as the time limit is reached.
- Using chloroquine and proguanil, the only regimen licensed for long-term use but considered to give suboptimal protection in areas of markedly chloroquine-resistant falciparum malaria.
- Discontinuing prophylaxis in favour of access to local advice and standby or physician-guided treatment
- Continuing with one prophylactic regimen beyond its licensed length of use.

General advice for all regimens

- Once an individual is compliant on one prophylactic regimen and is tolerating it well, transfer to another regimen increases the likelihood of the development of side effects due to the introduction of a different drug.
- There is no evidence of new side effects emerging during long-term use of any currently available prophylactics, though it is often thought that there may be risks associated with long-term use of chloroquine, see below.
- Evidence for safety in long-term use comes more from an accumulating lack of evidence of harm than from scientific evidence of safety.
- Individual risk assessments are important when deciding what advice should be given. In particular advice on prophylaxis may be influenced by other measures that might be used by those staying in areas where the risk is seasonally variable.
- Simplicity in regimen can, as always, be expected to improve compliance. The safest option is compliance with one of the most effective regimens.
- Minimising exposure to infection is important, especially taking precautions against being bitten whilst asleep.
- It is essential to seek medical advice promptly if symptoms develop.

ACMP advice on long-term use of specific antimalarials is summarised in table 16.

7.11.3 Specific considerations for women

See section on pregnancy and breastfeeding in chapter 6 which

includes advice on chemprophylaxis prior to conception.

7.11.4 Specific considerations for infants and older children

Refer to section on children above.

Evidence in support of long-term use of antimalarials in infants and older children is limited. Advice for long-term use in these age groups is the same as for adults.

- Chloroquine: safe for both infants and young children.
- Proguanil: safe for use by infants and young children⁷³.
- Mefloquine: well tolerated⁷⁴. Long-term use of mefloquine is reported to be safe, well tolerated and not associated with an increase in adverse effects⁷⁵⁻⁷⁷.
- Doxycycline: Not for use in those under 12 years of age. No data available on the long-term use of doxycycline; however, long-term use of other tetracyclines for other indications is generally well tolerated⁷⁸.
- Atovaquone plus proguanil: both highly effective and safe⁴².

7.12 Long term visitors to the UK returning to live in malarious parts of the world

Persons returning to their original homes in malarious regions after prolonged residence in the UK are likely to have suffered a decline in the partial immunity to malaria that develops during childhood and is maintained by repeated exposure in endemic regions. They may

TABLE 16 LONG TERM CHEMOPROPHYLAXIS FOR ADULTS UPDATED FROM THE 2003 ACMP GUIDELINES ON MALARIA PROPHYLAXIS FOR LONG-TERM TRAVELLERS⁵⁵

MALARIA CHEMOPROPHYLAXIS	ACMP ADVICE ON LONG-TERM USE
Chloroquine	Considered safe for long-term use.* Consider ophthalmic examination 6 to 12 monthly, commencing at 6 years' prophylactic usage
Proguanil	Considered safe for long-term use*
Mefloquine	No evidence of harm in long-term use if tolerated in the short term. Suggest can be used safely for up to three years in the absence of side effects.
Doxycycline	No evidence of harm in long-term use. Evidence suggests that it may be used safely for periods of at least up to two years.
Atovaquone/ Proguanil	No evidence of harm in long-term use. Suggest can be used confidently for travel up to one year and possibly longer, but only with caution until more post-licensing experience is available.

* Considered safe for long-term use but considerable concern regarding level of protective efficacy of the combination of chloroquine plus proguanil in certain geographical areas where the regimen used to be useful

TABLE 17 HALF-LIVES OF SELECTED ANTIMALARIAL DRUGS

DRUG	HALF-LIFE
Chloroquine	Can extend from 6 to 60 days
Mefloquine	2 to 3 weeks
Doxycycline	12 to 24 hours
Atovaquone	2 to 3 days
Proguanil	14 to 21 hours

therefore be at increased risk of suffering an acute attack of malaria after returning home.

Pregnant women and small children are at higher risk than others of suffering severe disease.

Risk assessment and personal counselling is essential to warn individuals of the risk of suffering from malaria, emphasising avoidance measures, and the need for immediate diagnosis and treatment of acute feverish illnesses

7.12.1 Preventive measures appropriate to an endemic setting⁷⁹

Bednets

Bed nets and other personal barrier protective measures (e.g. suitable clothing) are very low-cost, are effective long-term, have virtually no side-effects and will also help to protect from other mosquito-borne infections.

Intermittent Preventive Therapy (IPT)

If IPT is local policy in their destination country to prevent malaria in pregnancy and childhood, the returning visitor should be advised to seek medical advice on this immediately on arrival.

Case management of illness

People should be advised to seek medical attention immediately if either they or their children become feverish after repatriation in the endemic country. They should be warned that a malaria attack may be more serious because of diminished immunity.

Guidance

See the World Health Organisation/national country guidance on the appropriate measures in endemic settings which include IPT, insecticide-treated bednets and case-management of illness with therapy.

7.12.2 Prophylaxis

Intended use

The ACMP prophylaxis guidance is for temporary protection for the UK traveller. This is not appropriate for individuals who are returning to permanent residence in their country of origin.

Exception for pregnant women and young children

A limited period of prophylaxis of four to six weeks for pregnant women and young children may be appropriate in some circumstances, to allow them to settle and arrange for future healthcare after arrival in the endemic country.

Standby treatment

Offering standby treatment is inappropriate where there are likely to be health services to diagnose and manage malaria.