

Malaria: the issues and advice

Using case studies, Sarah Marshall takes a practical look at the role pharmacists in the UK can play in malaria prevention

Malaria is caused by infection with one of four different species of parasite: *Plasmodium falciparum*, *P vivax*, *P malariae* and *P ovale*. Although it is thought of primarily as a tropical disease, in the UK some 1,500–2,000 people develop malaria each year and between five and 16 deaths occur.¹ Most cases are in settled immigrants who contract malaria while visiting their native country because they failed to take prophylaxis, took the wrong prophylactic drugs or did not take prophylactics as instructed.

P falciparum is responsible for most of the deaths from malaria. The other three parasites cause “benign” malarias, which are rarely fatal, although symptoms can be severe. Pharmacists can play a vital role in the A, B, C, D of malaria advice. They can:

- Raise **awareness** of the risk of malaria in areas to be visited
- Communicate the importance of mosquito **bite** prevention
- Advise on **chemoprophylaxis**
- Assist prompt **diagnosis**

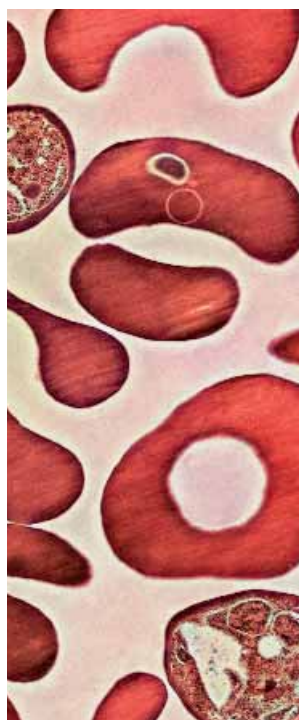
Bite prevention

The first step in preventing malaria is to protect exposed skin from infective mosquito bites, for example, by using mosquito repellents and insecticides.

The most effective repellent for travel to malarious areas is considered to be DEET (diethyltoluamide), which is available in various forms (eg, sprays, creams) and concentrations. Stronger concentrations last longer on the skin and require fewer daily applications. A strength of 50 per cent provides protection for up to 12 hours² but higher concentrations do not appear to be of additional benefit.³ DEET preparations are contraindicated in babies aged two months or less, but up to 50 per cent concentrations can be used in children above this age, pregnancy and in breastfeeding.² However, pharmacists are advised to check individual product labelling. A recent study suggests that DEET might work by interfering with the way that mosquitoes detect their prey, by blocking mosquito sensory neuron responses to the attractants exuded, such as carbon dioxide and lactic acid.⁴

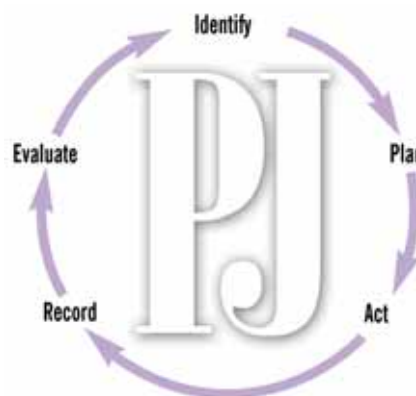
According to Clinical Knowledge Summaries,⁵ other repellents are not recommended unless DEET is contraindicated, in which case lemon eucalyptus, picaridin (hydroxyethyl isobutyl piperidine carboxylate) or 3-ethylaminopropionate may be appropriate. These alternatives may give less protection than higher concentrations of DEET.⁵

Although mosquitoes that carry malaria only bite between dusk and dawn, if a person wishes to use a repellent and sunscreen, the latter should be applied first. Pharmacy staff should warn customers that DEET can damage some fabrics and plastics.



Dr Gary Gaugler/Science Photo Library

Malaria is caused by infection with one of four different species of parasite



Identify knowledge gaps

1. What advice would you give to a pregnant woman about malaria prevention?
2. How long does immunity to malaria last?
3. What are the alternatives to DEET?

Before reading on, think about how this article may help you to do your job better. The Royal Pharmaceutical Society's areas of competence for pharmacists are listed in “Plan and record”, (available at: www.uptodate.org.uk). This article relates to “common disease states” (see appendix 4 of “Plan and record”).

Insecticides, such as the pyrethroid permethrin, are available in spray form, as vapourising mats or as coils. However, there is no evidence that these reduce the risk of contracting malaria, and there is concern about the safety profile of coil and mats when burnt indoors.⁶ Pyrethroids are also used to treat mosquito nets, reducing the risk of mosquitoes biting through the net. This has been shown to reduce the incidence of malaria.⁷

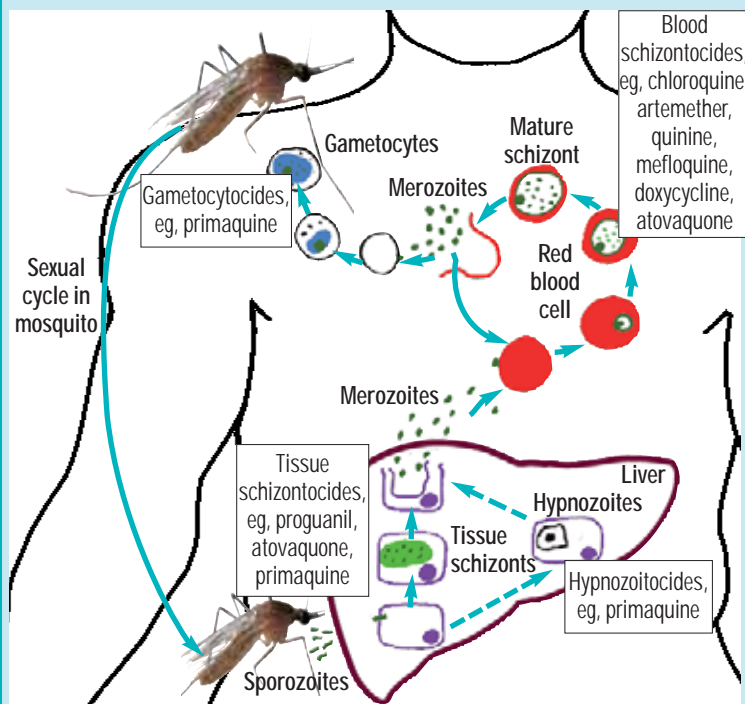
Herbal or homoeopathic remedies should not be used to prevent malaria.⁸ Wrist bands impregnated with DEET, citronella products and electronic buzzers for repelling mosquitoes are not effective.^{3,9} Vitamin B₁, garlic, yeast spreads (eg, Marmite), tea tree oil and bath oils also provide no protection.^{2,3,6}

Chemoprophylaxis

Antimalarial drugs act at various stages of the parasite lifecycle (see Panel 1, p604). UK recommendations are to use chloroquine or proguanil, or both, for prophylaxis. However, for areas where chloroquine resistant *P falciparum* is present, mefloquine, doxycycline or atovaquone with proguanil are used. In areas of mefloquine resistance doxycycline or atovaquone with proguanil are appropriate. The British National Formulary and MIMS give brief advice on prophylactic drugs by region but detailed maps showing which drugs should be taken in which area, are available (see Resources). It is essential to use the most

Sarah Marshall, PhD, MRPharmS, is a freelance pharmaceutical writer from Aberdeenshire

Panel 1: Lifecycle of malaria parasites and sites of action of antimalarials



The malaria life cycle requires two hosts: human and mosquito. An infected mosquito bites a human, injecting malarial parasites through the skin. These sporozoites migrate to the liver where they reproduce to form tissue schizonts. (*Plasmodium vivax* and *P. ovale* also have dormant forms [hypnozoites], which are formed and lodge in the liver so they can cause relapses). The tissue schizonts rupture to liberate merozoites into the circulation. These invade red blood cells, growing and reproducing in them to form erythrocytic schizonts, which burst to release more merozoites into the circulation. This erythrocytic phase causes symptoms, such as fever. The merozoites either generate more merozoites or gametocytes. The latter are ingested by a biting mosquito, allowing a sexual cycle to take place producing more sporozoites to infect the next human host.

up-to-date information on malaria prevention because advice can change.

Areas are graded according to the risk of exposure to infective bites. For "very low risk areas" chemoprophylaxis is not used. Instead, bite prevention is recommended. For other levels of risk, chemoprophylaxis is necessary.

Pharmacists should carry out a thorough risk assessment for each traveller before advising on chemoprophylaxis,⁴ considering:

- Itinerary (including stop overs) and other travel details (eg, reason for travel, length of stay, time of year)
- Personal characteristics (eg, age, weight [if child], pregnancy or breastfeeding and, if returning to a native land, the time elapsed since leaving)
- Medical history and current medicines (choosing chemoprophylaxis for those with pre-existing conditions, such as epilepsy, psychiatric illness and psoriasis, can be challenging; several organisations [see Resources] offer advice for these people)
- History of use of antimalarials (eg, side effects)

The main features of prophylactic drugs are summarised in Panel 2.

Pharmacists should also be prepared to give advice on immunity, children, pregnancy, complex itineraries, long-term travel and emergency standby treatment, as illustrated by the case studies below.

Case 1 A woman who has been living in the UK for five years is returning to Sierra Leone tomorrow, to visit her father who is terminally ill. She asks for advice regarding chemoprophylaxis for her four-year-old son, who weighs 17kg. She used doxycycline in the past for acne, but had to stop taking it because it irritated her stomach.

People growing up in a malarious area can develop a degree of immunity as a result of repeated infections. However, this acquired immunity fades if the person moves from the transmission zone and the Health Protection Agency suggests that protection can be lost in as little as six months.⁸ People returning to their country of origin can, therefore, be as likely to contract malaria as anyone else and both the woman and her son will require chemoprophylaxis.

The antimalarials of choice for Sierra Leone are mefloquine, doxycycline or atovaquone-proguanil because chloroquine-resistant *P. falciparum* is prevalent. Choice will depend on patient factors. In this case, doxycycline should be avoided because the woman suffered gastrointestinal side effects previously, so either mefloquine or atovaquone-proguanil could be used. In first time users, mefloquine should be started two and a half weeks before departure to allow any adverse effects (eg, neuropsychiatric reactions) to be detected before travel. In travellers who have taken mefloquine previously this can be shortened to one week. In contrast, atovaquone with proguanil can be started one or two days before travel.

Parents should be strongly advised not to take infants or children to areas where malaria is prevalent unless travel is unavoidable. The choice of antimalarial will depend in part on the age and weight of the child. For example, doxycycline is contraindicated in children under 12 years old and mefloquine is only suitable for children over 5kg and atovaquone with proguanil for those over 11kg. Children may be more likely to comply with a weekly dose (ie, mefloquine) than a daily one but due to the last-minute nature of the trip, atovaquone with proguanil would be the most suitable choice.

Case 2 A woman in her first trimester of pregnancy and originally from Sri Lanka, is returning to Jaffna to go to her sister's wedding. She has lived in the UK for two years. She asks which antimalarial she can use.

If contracted during pregnancy malaria frequently leads to miscarriage or premature

Panel 2: Features of prophylactic antimalarial drugs

| Regimen | Start | Continue for | Duration | Comments |
|---|------------------------------------|-------------------------|-----------------------------------|--|
| Chloroquine and proguanil (alone or in combination) | One week before travel | Four weeks after return | Safe for long-term use (years) | Not appropriate for many areas Complex daily and weekly combined regimen can affect compliance Suitable for infants with body weight under 6kg (chloroquine is available in syrup form and proguanil in crushable tablets) |
| Mefloquine | Two and a half weeks before travel | Four weeks after return | Licensed for up to a year's use | Effective in most areas |
| Doxycycline | One or two days before travel | Four weeks after return | Licensed for up to two years' use | Can cause photosensitivity and predispose to vaginal candida Useful for last-minute travel |
| Atovaquone with proguanil | One or two days before travel | One week after return | Only licensed for 28 days' use | Useful for short trips but expensive for long trips Paediatric tablets available |

Panel 3: Advice pharmacists can give to travellers

- Take antimalarial drugs exactly as prescribed
- Always use insect repellents on exposed skin (the concentration of DEET should be 20 per cent or more)²
- Cover up when outside in the evenings and at night
- Sleep in a screened, air conditioned room or under an insecticide treated mosquito net
- Kill any mosquitoes in the room before sleeping
- Seek medical advice if you develop side effects to prophylactic antimalarials or develop a fever seven or more days after entering an area where malaria occurs or up to one year after returning to the UK (especially within the first three months)

labour, so travel to areas of risk should be avoided unless absolutely necessary. UK guidelines recommend chloroquine plus proguanil for this part of Sri Lanka and this is a safe regimen to be used in pregnancy. However, because proguanil is a folate antagonist, pregnant women should take a daily 5mg supplement of folic acid. Doxycycline is contraindicated in pregnancy because it affects fetal bones and teeth and there is insufficient safety data to advocate the use of atovaquone with proguanil. Mefloquine can be used in the second and third trimesters. Bite prevention measures are essential.

Pharmacists should advise women who are planning a pregnancy while staying in a malarial area or in the months following return to seek specialist advice.

Case 3 A 19-year-old student asks which antimalarials he should take during his gap year. He will backpack in India for a month, then travel through Myanmar, Thailand and Indonesia for four months. He does not know exactly where he will go in each country. He plans to stay in Australia and New Zealand before returning to the UK.

The malaria risk to which the student will be exposed varies from low (in Bali and parts of India) to substantial (in Myanmar). If a person is visiting several areas and different antimalarial regimens are recommended the one for the highest risk region should be taken for the whole trip to give blanket cover. It should

The Health Protection Agency suggests that acquired immunity against malaria can be lost in as little as six months

be remembered that although mefloquine, atovaquone with proguanil and doxycycline are suitable alternatives to chloroquine plus proguanil the reverse is not true.

Chloroquine plus proguanil is relatively cheap and a suitable choice for the parts of India where malaria poses a risk and it would, theoretically, be possible for the student to take these for the first part of his trip (switching to another regimen before entering an area of increased risk). However, because the student is then travelling to areas of high risk (and not all of his destinations are known), it would be more practical for him to take atovaquone with proguanil, mefloquine or doxycycline to cover all his time in malaria endemic countries. Atovaquone with proguanil would be expensive if needed for several months. It is only licensed for 28 days' use, although the BNF comments that it can be used safely for up to a year or more. Mefloquine is licensed for use for up to a year, although it can be used safely for three years.² However, according to the BNF, mefloquine resistance is present in parasites occurring along the Myanmar-Thailand border, making the drug inappropriate in this case. Doxycycline would be suitable for all the malarious locations to be visited, and may be used for up to two years.²

The pharmacist should ensure that the student has a sufficient quantity of antimalarials for his trip or at least warn him of the risk of counterfeit antimalarials, which are common in many developing countries.

The pharmacist should also emphasise the importance of adhering to prophylactic and insect repellent measures because people tend to become less observant of these measures with time and the risk of contracting malaria increases with length of stay.² A bed net impregnated with an insecticide is recommended because backpackers' accommodation is unlikely to be screened or air-conditioned.

Standby medicine allows a traveller who develops a fever seven days or more after arriving in a malarious area (and who cannot get to a doctor within 24 hours) to begin treatment for presumed malaria. Drugs chosen for standby treatment should be different from

Panel 4: Treatment of malaria

Since the signs and symptoms of malaria are non-specific it cannot be definitively diagnosed until parasites are detected in a stained blood film or by a dipstick test (rapid diagnostic test). However, it is essential to start treatment immediately because death can occur if therapy is delayed. The drugs used will depend on the species of parasite and its level of drug resistance, the severity of the illness and patient factors. If the type of malaria is unknown, the regimen for *P falciparum* should be prescribed.

For non-falciparum malaria, a three-day course of oral chloroquine is used for *P malariae*, *P ovale* and *P vivax*. For chloroquine-resistant strains of vivax malaria, quinine; artemether with lumefantrine (co-artemether); or atovaquone with proguanil can be used. Primaquine is used to eradicate dormant forms of *P vivax* and *P ovale* infections and thus prevent relapse.

For uncomplicated falciparum malaria three suggested oral regimens are:

- Oral quinine sulphate (for five to seven days) plus doxycycline for seven days
- Atovaquone with proguanil for three days
- Artemether with lumefantrine for 60 hours

The quinine-containing regimen has the disadvantage of being longer and poorly tolerated. Adverse effects include nausea, deafness and tinnitus.

Uncomplicated malaria can progress to severe malaria (ie, with vital organ disturbance) or complicated malaria (ie, with potentially fatal complications such as coma, severe anaemia, renal failure, respiratory distress syndrome, hypoglycaemia, shock, spontaneous haemorrhage and convulsions).

For severe or complicated falciparum malaria intravenous quinine is the first-line treatment. Loading doses are required to achieve high blood levels to eradicate parasites. Parenteral therapy is given until the patient is well enough to take tablets. Quinine is given for five to seven days, together with or followed by doxycycline for seven days. Clindamycin can be used for children and pregnant women (unlicensed indication). Patients with severe or complicated malaria may need antipyretics, blood transfusions, dextrose infusions, broad spectrum antibiotics (to treat infections, such as septicaemia), support in respiratory failure or renal replacement therapy. Patients are usually treated in intensive care.

those used for prophylaxis and may include artemether with lumefantrine, atovaquone with proguanil, or quinine and doxycycline.² Travellers should be given written instructions for when and how to take standby treatment. Other advice pharmacists can give to travellers is listed in Panel 3 (p605).

Case 4 A man in his 50s asks for a flu remedy. He is feeling feverish and shaky and has a headache and muscle aches. You advised him earlier in the year about antimalarials for a trip to Kenya.

All four types of malaria begin with non-specific flu-like symptoms, such as fever, sweats and chills, malaise, muscle aches, headache, diarrhoea and cough. Malaria should always be suspected in anyone who develops flu-like symptoms and who has travelled to a malarious country within the past year, but especially if they have returned in the previous three months, even if they have complied fully with all antimalarial measures.

The average time between being bitten by an infective mosquito and showing symptoms of malaria is about 10 days for *P falciparum*. For benign malarias, the incubation period may be similar or prolonged because hypnozoites of *P vivax* and *P ovale* can reawaken, leading to symptoms up to a year or more later (see Panel 1, p604). *P falciparum* infection can take longer to develop in travellers who

Action: practice points

Reading is only one way to undertake CPD and the Society will expect to see various approaches in a pharmacist's CPD portfolio.

1. With your staff, review the insect repellents that you stock. Work out which you would recommend for which age groups and why.
2. Explore the electronic resources listed above.
3. Make sure your staff ask people with influenza symptoms about travel to malarious areas.

Evaluate

For your work to be presented as CPD, you need to evaluate your reading and any other activities. Answer the following questions: What have you learnt? How has it added value to your practice? (Have you applied this learning or had any feedback?) What will you do now and how will this be achieved?

have taken incomplete or partially effective antimalarial prophylaxis, or who have some immunity. These individuals may also show less severe symptoms.

In *P falciparum* infection, life-threatening malaria can develop within 24 hours of symptoms appearing. The man should be referred to his GP immediately and be advised to specifically mention exposure to malaria. Treatment is discussed in Panel 4.

It may be good practice to keep records of over-the-counter sales of antimalarial prophylactic drugs. The Royal Pharmaceutical Society suggests, in its guidance for recording interventions, that advice on malaria prophylaxis linked to prescriptions could be recorded.

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Resources

- Up to date prophylaxis recommendations are available from the National Travel Health Network and Centre (www.nathnac.org; Tel 0845 602 6712) and Travax (for registered NHS users only; www.travax.nhs.uk; Tel 0141 300 1100).
- A malaria prophylaxis resource pack is available from the National Pharmacy Association.
- Checklists for giving advice on chemoprophylaxis are available from the NPA and the Health Protection Agency.²

Signposting

- Information for the public is available from the National Travel Health Network and Centre and the Scotland NHS fit for travel website: (www.fitfortravel.nhs.uk).
- MASTA provides personalised travel health advice for £3.99 (www.masta.org).

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