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UK malaria treatment guidelines

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Summary

Malaria is the tropical disease most commonly imported into the UK, with 1500–2000 cases reported each year, and 10–20 deaths. Approximately three-quarters of reported malaria cases in the UK are caused by *Plasmodium falciparum*, which is capable of invading a high proportion of red blood cells and rapidly leading to severe or life-threatening multi-organ disease. Most non-falciparum malaria cases are caused by *Plasmodium vivax*; a few cases are caused by the other two species of *Plasmodium*: *Plasmodium ovale* or *Plasmodium malariae*. Mixed infections with more than 1 species of parasite can occur; they commonly involve *P. falciparum* with the attendant risks of severe malaria.

Management of malaria depends on awareness of the diagnosis and on performing the correct diagnostic tests: the diagnosis cannot be excluded until 3 blood specimens have been examined by an experienced microscopist. There are no typical clinical features of malaria, even fever is not invariably present. The optimum diagnostic procedure is examination of thick and thin blood films by an expert to detect and speciate the malarial parasites; *P. falciparum* malaria can be diagnosed almost as accurately using rapid diagnostic tests (RDTs) which detect plasmodial antigens or enzymes, although RDTs for other *Plasmodium* species are not as reliable.

The treatment of choice for non-falciparum malaria is a 3-day course of oral chloroquine, to which only a limited proportion of *P. vivax* strains have gained resistance. Dormant parasites (hypnozoites) persist in the liver after treatment of *P. vivax* or *P. ovale* infection: the only currently effective drug for eradication of hypnozoites is primaquine. This must be avoided or given with caution under expert supervision in patients with glucose-6-phosphate dehydrogenase deficiency (G6PD), in whom it may cause severe haemolysis. Uncomplicated *P. falciparum* malaria can be treated orally with quinine, atovaquone plus proguanil (Malarone®) or co-artemether (Riamet®); quinine is highly effective but poorly tolerated in prolonged dosage and is always supplemented by additional treatment, usually with oral doxycycline. ALL patients treated for *P. falciparum* malaria should be admitted to hospital for at least 24 h, since patients can deteriorate suddenly, especially early in the course of treatment.

Severe falciparum malaria, or infections complicated by a relatively high parasite count (more than 2% of red blood cells parasitized), should be treated with intravenous therapy until the patient is well enough to continue with oral treatment. In the UK, the treatment of choice for severe or complicated malaria is currently an infusion of intravenous quinine. This may exacerbate hypoglycaemia that can occur in malaria; patients treated with intravenous quinine therefore require careful monitoring. Intravenous artesunate reduces high parasite loads more rapidly than quinine and is more effective in treating severe malaria in selected situations. It can also be used in patients with contra-indications to quinine. Intravenous artesunate is unlicensed in the EU. Assistance in obtaining artesunate may be sought from specialist tropical medicine centres, on consultation, for named patients. Patients with severe or complicated malaria should be managed in a high dependency or intensive care environment. They may require haemodynamic support and management of acute respiratory distress syndrome, disseminated intravascular coagulation, renal impairment/failure, seizures, and severe intercurrent infections including gram-negative bacteraemia/septicaemia.

Falciparum malaria in pregnancy is more likely to be severe and complicated: the placenta contains high levels of parasites. Stillbirth or early delivery may occur and diagnosis can be difficult if parasites are concentrated in the placenta and scanty in the blood. The treatment of choice for falciparum malaria in pregnancy is quinine; doxycycline is contraindicated in pregnancy but clindamycin can be substituted for it, and is equally effective. Primaquine (for eradication of *P. vivax* or *P. ovale* hypnozoites) is contraindicated in pregnancy; after treatment for these infections a pregnant woman

should take weekly chloroquine prophylaxis until after delivery when hypnozoite eradication can be considered.

Children are over-represented in the incidence of malaria in the UK, probably because completely susceptible UK-born children accompany their overseas-born parents on visits to family and friends in endemic areas. Malaria in children (and sometimes in adults) may present with misleading symptoms such as gastrointestinal features, sore throat or lower respiratory complaints; the diagnosis must always be sought in a feverish or very sick child who has visited malaria-endemic areas. Children can be treated with most of the antimalarial regimens which are effective in adults, with appropriate dosage adjustment. Doxycycline plus quinine should not be given to children under 12 years as doxycycline is contraindicated in this age group, but clindamycin can be substituted for doxycycline, and pyrimethamine–sulfadoxine (Fansidar®) may also be an effective substitute. An acute attack of malaria does not confer protection from future attacks: individuals who have had malaria should take effective anti-mosquito precautions and chemoprophylaxis during future visits to endemic areas.

Keywords: Malaria; Symptoms; Treatment; *Plasmodium falciparum*; Rapid diagnostic tests; Hypnozoites; Uncomplicated malaria; Severe malaria; Primaquine; Chloroquine; Atovaquone–proguanil; Artesunate; Quinine; Doxycycline; Clindamycin; Pyrimethamine–sulfadoxine; Co-artem; Exchange transfusion; G6PD deficiency; Pregnancy; Children; Chemprophylaxis