

- Urgent treatment of severe malaria is essential if the patient has any of the following:
 1. any degree of altered consciousness,
 2. jaundice,
 3. oliguria,
 4. severe anaemia or
 5. hypoglycaemia
 6. a parasite count above 100 000/mm³ (>2% of red blood cells parasitised)
 7. the patient is vomiting or clinically acidotic.
- Chloroquine-resistant *Plasmodium falciparum* must be assumed to be the infective agent.
- Once mandatory IV therapy has been started, seek expert advice.

- A recent large multicentre randomised controlled trial has shown mortality in severe *P. falciparum* malaria is lower when IV artesunate is used rather than IV quinine.
- Artesunate should be used in preference to IV quinine if it is immediately available.

Use:
 artesunate 2.4 mg/kg IV, on admission and repeat at 12 hours and 24 hours, then once daily until oral therapy is possible. When patient is able to tolerate oral therapy, give a full course of artemether+lumefantrine, as for uncomplicated *Plasmodium falciparum* malaria OR (if parenteral artesunate is not immediately available)
 quinine dihydrochloride IV, as outline below
 - An initial loading dose of quinine should be given unless the patient has received 3 or more doses of quinine or quinidine in the previous 48 hours, or mefloquine prophylaxis in the previous 24 hours, or a mefloquine treatment dose within the previous 3 days.
 - Frequent measurements of blood pressure and blood glucose are required as quinine stimulates insulin secretion and can cause hypoglycaemia. Cardiac monitoring is advised if there is pre-existing heart disease.
 - For loading dose, use:
 quinine dihydrochloride 20 mg/kg IV, over 4 hours
 OR
 quinine dihydrochloride 7 mg/kg IV, over 30 minutes, followed immediately by 10 mg/kg IV, over 4 hours.
 - For maintenance dose, use:
 quinine dihydrochloride 10 mg/kg IV, over 4 hours, 8-hourly, commencing 4 hours after loading regimen is completed and continuing until the patient is able to begin oral treatment.
 - If IV quinine is required for longer than 48 hours, seek expert advice, as a dose adjustment may be necessary especially in patients with renal impairment. When the patient has clinically improved, continue treatment with oral quinine combined with doxycycline or clindamycin as for uncomplicated *P. falciparum* malaria, to complete a total of 7 days of treatment with quinine.

- For *Plasmodium vivax*, *Plasmodium malariae* and *Plasmodium ovale*, use: chloroquine 620 mg base (= 4 tablets) (child: 10 mg base/kg up to 620 mg base) orally, initially, then 310 mg (= 2 tablets) (child: 5 mg base/kg up to 310 mg base) 6 hours later and on days 2 and 3, making a total adult dose of 10 tablets.

- To eliminate liver forms of *P. vivax* infections, add or follow within a few days with: primaquine 30 mg (child: 0.5 mg/kg up to 30 mg) orally, daily with food, or if nausea occurs 15 mg (child: 0.25 mg/kg up to 15 mg) orally, 12-hourly with food for 14 days.
- To eliminate liver forms of *P. ovale* infections, add or follow within a few days with: primaquine 15 mg (child: 0.25 mg/kg up to 15 mg) orally, daily with food for 14 days.

- Reports of chloroquine-resistant *P. vivax* have come from areas in Papua New Guinea, Indonesia and South-East Asia and this should be considered if a patient with *P. vivax* fails to respond to standard doses of chloroquine. Mefloquine or artemether+lumefantrine or quinine are potential alternative therapies in these cases, but it is advisable to obtain specialist advice.

- If the patient relapses after the primaquine treatment, seek expert advice.
- Exclude glucose-6-phosphate dehydrogenase (G6PD) deficiency prior to the use of primaquine, as severe haemolysis may occur in these patients. If the patient is G6PD deficient, seek expert advice.
- If the patient is unable to tolerate oral therapy, which is best taken with food, treat as severe malaria as above and consult an experienced specialist.

treatment of severe falciparum malaria

general

- Malaria must be considered in any patient who has visited a malarious area and presents with a febrile illness.
- A blood sample collected into an EDTA tube should be sent to an appropriate laboratory for examination, including thick and thin films. A single negative blood film or negative antigen test does not exclude the diagnosis of malaria, particularly if antimalarials or antibiotics have been taken recently.
- Of the 4 species that infect humans, *Plasmodium falciparum* is the most pathogenic and most resistant to standard antimalarials.
- Certain antibiotics that are commonly used by travellers, such as trimethoprim+sulfamethoxazole, tetracyclines and the fluoroquinolones, have some antimalarial activity and may modify or suppress malaria symptoms and make diagnosis by blood film more difficult.

pathogenesis

- *Plasmodium* spp (*P. vivax*, *P. malariae*, *P. ovale*, *P. falciparum*) are the cause of malaria
- transmission occurs from bites from female *Anopheles* mosquitoes as sporozoites which multiply in human bloodstream as merozoites, enter red blood cells and multiple as trophozoites which are released with haemolysis
- *Plasmodium vivax* & *Plasmodium malariae* have dormant hypnozoites in the liver
- *P. falciparum* is the cause of cerebral malaria and multiple organ failure
- severe haemolysis with haemoglobinuria is called blackwater fever

treatment of uncomplicated falciparum malaria

- Artemether+lumefantrine is now the drug of first choice for the treatment of uncomplicated *Plasmodium falciparum* malaria.
- Initial treatment in hospital is recommended. Use:
 artemether+lumefantrine 20+120 mg
 adult and child >34 kg: 4 tablets (child 5 to 14 kg: 1 tablet; 15 to 24 kg: 2 tablets; 25 to 34 kg: 3 tablets) orally with fatty food, at 0, 8, 24, 36, 48 and 60 hours, making a total adult dose of 24 tablets in 6 doses
 OR
 quinine sulfate 600 mg (adult <50 kg: 450 mg) (child: 10 mg/kg up to 600 mg) orally, 8-hourly for 7 days
 PLUS EITHER
 doxycycline 100 mg (child >8 years: 2.5 mg/kg up to 100 mg) orally, 12-hourly for 7 days
 OR (for pregnant females or children)
 clindamycin 300 mg (child: 5 mg/kg up to 300 mg) orally, 8-hourly for 7 days
 OR
 atovaquone+proguanil 250+100 mg adult formulation
 adult: 4 tablets (child 11 to 20 kg: 1 tablet; 21 to 30 kg: 2 tablets; 31 to 40 kg: 3 tablets) orally with fatty food, daily for 3 days
 OR (if no nausea or vomiting)
 mefloquine 750 mg (child: 15 mg/kg up to 750 mg) orally, initially, then 500 mg (child: 10 mg/kg up to 500 mg) 6 to 8 hours later.
 NOTE: Atovaquone+proguanil and mefloquine should not be used for treatment of malaria in patients who took these drugs as prophylaxis.

treatment of other forms of malaria