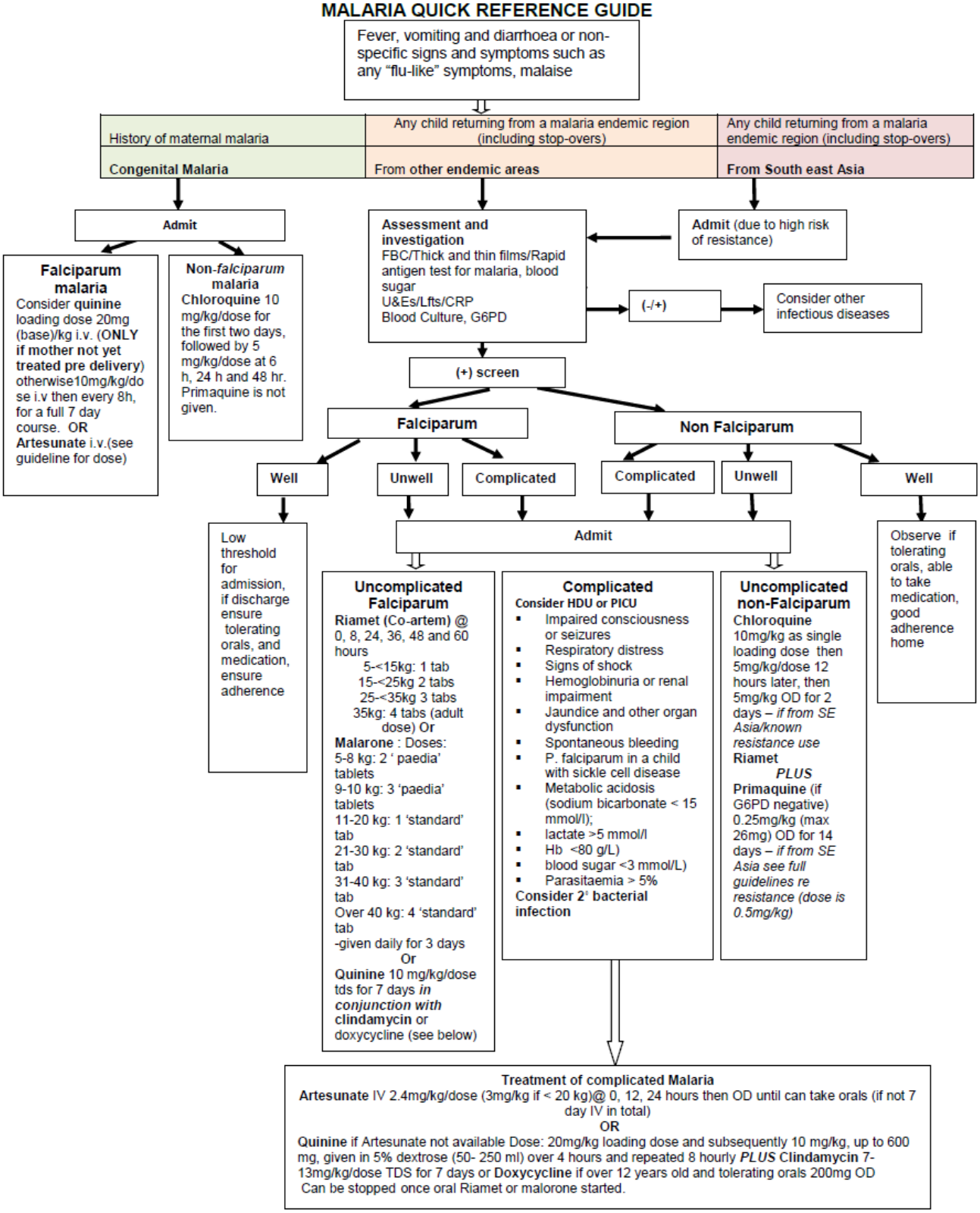
MALARIA QUICK REFERENCE GUIDE



Management of Malaria in Children

Malaria is a febrile illness caused by *Plasmodium falciparum, vivax, malariae, ovale* and *knowlesi.*Delayed diagnosis can be fatal and hence a high index of suspicion is crucial in the recognition and management of malaria. *Plasmodium falciparum* accounts for 75% of imported malaria cases in the UK. The incubation period is between a minimum of 6 days and 6-8 months, most cases present within three months of return from an endemic region. Time to presentation varies significantly between P *falciparum* and non-falciparum malaria, with 85% and 25% respectively presenting in the first month after returning from abroad. Globally there is ongoing progressive spread of drug resistance to antimalarials particularly over the Thai-Cambodian border.

Introduction:

Fever is the main symptom of malaria. It can be present all the time or go away and return at regular intervals. Other signs of falciparum malaria are shivering, sweating and vomiting. A child with malaria may have chronic anaemia (with no fever) as the only sign of illness.
Signs of malaria can overlap with signs of other illnesses like gastroenteritis, pneumonia, meningitis etc. It is important to assess and treat for other serious tropical and non-tropical infections at the same time.
In areas with very high malaria transmission, malaria is a major cause of death in children. A case of uncomplicated malaria can develop into severe malaria as soon as 24 hours after the fever first appears. **Severe malaria** is malaria with complications such as cerebral malaria or severe anaemia and is potentially fatal.

New treatments are now available and better tolerated: Artemisinin and its derivatives (artesunate, artemether, etc) lead to rapid clearance of parasitaemia and resolution of symptoms and are superior to older drugs (quinine). Only one combination is licensed for use in the UK: artemether-lumefantrine (Riamet). Malarone is a non-artemisinin combination highly effective and better tolerated than quinine however, it may cause GI upset and vomiting.

Diagnosis -

- ***Thick and thin films*** allow specification and quantification of malaria parasitaemia (prepared from EDTA blood). If the initial test is negative but the diagnosis is suspected, the film needs to be repeated up to 3 times.

- ***Rapid antigen tests*** are sensitive, and should be requested on the blood form, but can remain positive for 4 months after treatment.

Other essential investigations:

- FBC
- Blood glucose rapid test and laboratory sample
- U+Es and LFTs
- CRP
- Blood cultures
- G6PD if primaquine is required

Also consider (depending on severity and differential diagnosis)

- Blood gas
- Clotting
- Sickle status
- Group and save or crossmatch
- Urine – dipstick and M+C+S
- LP - M+C+S, proteins, glucose, virology
- Stool - M+C+S, virology
- Throat swab – M+C+S, virology
- NPA – virology
- CXR

Initial Assessment

The initial assessment should be based on clinical and laboratory parameters.

Clinical examination may reveal anaemia, jaundice, splenomegaly, respiratory distress, convulsions and reduced GCS.

Neurological signs suggest cerebral malaria (potentially fatal).

Other complications are blackwater fever (haemolytic anaemia,

haemoglobinuria, renal failure), DIC and pulmonary oedema.

It is important to separate uncomplicated and severe malaria:

1. Severe Malaria
Severe or complicated malaria is defined by one or more of the following: (for more details see WHO malaria guidelines)

- Impaired consciousness or seizures
- Prostration
- Respiratory distress (careful fluid balance, fluid overload may induce pulmonary oedema)
- Signs of shock
- Hemoglobinuria or renal impairment
- Jaundice and other organ dysfunction
- Abnormal spontaneous bleeding
- P. falciparum in a child with sickle cell disease
- Parasitaemia > 5% red blood cells parasitized
- Metabolic acidosis (sodium bicarbonate < 15 mmol/l)
- Raised lactate (lactate >5 mmol/l)
- Severe anaemia (<8 g/dL)
- Hypoglycaemia (blood sugar <3 mmol/L)

2. Uncomplicated malaria
Positive blood film for malaria and none of the above in a clinically stable child.

During day time please discuss with either Dr Bandi or Dr Radcliffe. For out of hours' advice please contact the on-call microbiologist.

If child is diagnosed please inform Public Health – malaria is a notifiable disease

Do not give empirical therapy

Management:

Have a low threshold for admission of children with P. falciparum malaria for observation overnight regardless of parasite load.
However in a well child, if discharge is considered on clinical ground there should be

- a period of observation with evidence of taking medication
- the child needs to demonstrate he/she can take and tolerate oral medications
- Arrange a day care review in the next 24 – 48 hours
- Open access to CAU for 48 hours

Children with uncomplicated non-falciparum malaria if clinically well, after have been observed for 4 hours can be treated as outpatient. They will need to be followed up on day care between 24 – 48 hours to ensure there has not been an Hb drop and the parasitaemia is no longer present. They also need a G6PD test as primaquine needs to be started once the negative result is available.

Children should be closely monitored on the ward/PICU depending on clinical state if they fulfil the criteria for severe malaria or cannot tolerate oral medications.

Please admit all patients returning from South East Asia (Cambodia, Thailand, Vietnam and Laos) even if they fulfill the criteria for uncomplicated malaria, given the high probability of resistance in this area.

Treatment

1. Treatment of complicated malaria (mostly due to P falciparum, but occasionally to P ovale,vivax, malariae, knowlesi).
- **Start drug immediately that is readily available.**
- If switching to another drug, no dose delay.

First line treatment for severe malaria:

1.1 Intravenous artesunate - Also can be used if the patient cannot tolerate oral treatment.

Dose: 2.4mg/kg/dose (3 mg/kg if < 20 kg) at time 0, 12, 24 and then daily until able to take medications orally. In severe malaria iv artesunate needs to be given for a minimum of 24 hours. When treatment is stopped a full course of oral treatment, as specified in uncomplicated malaria needs to be given. Alternatively artesunate can be continued IV for 7 days.

Hourly observations including neurological observations are essential in the first 12 hours as there is risk for rapid deterioration.

When the patient is able to tolerate oral medications, a full course of oral Co-artem (Riamet) OR Atovaquone + proguanil (Malarone) (see below)

OR

Quinine + clindamycin 7–13 mg/kg/dose (max. 450 mg) every 8 hours for 7 days OR quinine + doxycycline (in children>12 years of age and tolerating orals) 200 mg once daily for 7 days is required.

The decision to admit to **PICU** is guided by clinical criteria in a case by case basis by the treating clinician.

1.2 Second line treatment for severe malaria: Intravenous Quinine
Dose: 20mg/kg loading dose and subsequently 10 mg/kg, up to 600 mg, given in 5% dextrose (50- 250 ml) over 4 hours and repeated 8 hourly.

PLUS:
Clindamcyin or doxycyline as above

Major side-effects include hypoglycaemia and arrhythmias. It needs to be given as a slow infusion. The monitoring in addition to hourly neurological observations includes a cardiac monitoring. Bedside blood sugar is more likely to drop and needs to be checked 2 hourly.

Consider exchange transfusion if parasitaemia > 15%.

1.3 Adjunct Management
- IV Ceftriaxone
- Oxygen
- Urinary catheter and strict fluid balance
- Transfuse if Hb<8g/dl (watch for fluid overload)
- Support clotting if necessary

2. **Treatment of uncomplicated falciparum malaria**

Co-artem (Riamet) or Atovaquone + proguanil (Malorone) are the preferred options in children tolerating oral medication. Quinine can be given orally, but needs to be combined with clindamycin or doxycycline and given for 7 days. It is not as well tolerated as the other antimalarial and preferably avoided.

2.1 Co-artem (Riamet) schedule: 6 doses are necessary and it needs to be given at 0, 8, 24, 36, 48 and 60 hours:
Doses:
5-<15kg: 1 tab
15-<25kg 2 tabs
25-<35kg 3 tabs
35kg: 4 tabs (adult dose)

2.2 Malarone (Atovaquone + proguanil) is another effective oral alternative medication.

Doses:
5-8 kg 2 ' paediatric' tablets daily for 3 days
9-10 kg 3 'paediatric' tablets daily for 3 days
11-20 kg 1 'standard' tablet daily for 3 days
21-30 kg 2 'standard' tablets daily for 3 days
31-40 kg 3 'standard' tablets daily for 3 days
Over 40 kg: 4 'standard' tablets daily for 3 days

2.3 Oral Quinine is the least preferable drug

Dose:
10 mg/kg tds for 7 days and needs to be given in conjunction with clindamycin (7-13 mg/kg/dose 8 hourly for 7 days) or doxycycline (if >8 years old) 200 mg once daily for 7 days.

3. Treatment of Non falciparum malaria

- P.vivax, ovale, malariae
- Complications are rare
- Usually sensitive to chloroquine (chloroquine-resistant P.vivax reported in Indonesia, New Guinea and some adjacent islands)
- Does not need routine admission unless ill/complicated

Treatment:

- **Chloroquine:** 10 mg/kg initial dose then, 5 mg/kg after 6-8 hours and then once daily for 2 days

If malaria due to *P.vivax* or *P.ovale* and the child is **not** G6PD deficient this is followed by a 14 day course of Primaquine 0.25 mg/kg od (maximum 26mg/day).

In Oceania and South-East Asia the dose of primaquine should be 0.5mg/kg once daily due to increased resistance.

G6PD levels need to be checked and seen before giving Primaquine as severe haemolysis can occur if G6PD deficient. Primaquine should not be used under 6 months of age.

Congenital and Neonatal Malaria

Congenital malaria is very rare and is acquired via placental transmission from an infected mother. It is mostly caused by P falciparum, ovale and vivax. The signs are similar to neonatal sepsis (fever, poor feeding, irritability, lethargy). The baby might be born IUGR, or premature and anaemia, haepatosplenomegaly at birth has been described.

The evidence for treatment doses is scarce.

Falciparum malaria

Consider quinine (in 10% Dextrose); loading dose 20mg (base)/kg i.v. (**ONLY if mother not yet treated pre delivery**) otherwise 10mg/kg/dose i.v then every 8h, for a full 7 day course. All infusions have to be over 4 hours. Alternatively Artesunate i.v. initial dose 2.4mg/kg/dose at 0 and 12 hrs on day 1, then once daily for a full 7-day course or i.v.

Non-*falciparum* malaria

Chloroquine 10 mg/kg/dose for the first two days, followed by 5 mg/kg/dose at 6 h, 24 h and 48 hr. **Primaquine is not given.**

References:

- Lalloo D.G. et al. UK malaria treatment guidelines 2016. J inf (2016) 72, 635 – 649. http://www.journalofinfection.com/article/S0163-4453(16)00047-5/pdf
- WHO guidelines for the treatment of malaria. 2015. http://apps.who.int/iris/bitstream/10665/162441/1/9789241549127_eng.pdf
- Paediatric malaria guideline. St George's' hospital, London 2013
- Dondorp A, Nosten F, Stepniewska K, Day N, White N. Artesunate versus quinine for treatment of severe falciparum malaria: a randomised trial. Lancet 2005; 366(9487):717-725.
- Dondorp AM, Fanello CI, Hendriksen IC, Gomes E, Seni A, Chhaganlal KD et al. Artesunate versus quinine in the treatment of severe falciparum malaria in African children (AQUAMAT): an open-label, randomised trial. Lancet 2010; 376(9753):1647-1657.
- Sinclair D, Donegan S, Isba R, Lalloo DG. Artesunate versus quinine for treating severe malaria. Cochrane Database Syst Rev 2012; 6:CD005967.
- Kiang KM; Bryant PA;SHingadia D; Ladhani S; Steer AC; Burgner DThe treatment of imported malaria in children: an update; *Arch Dis Child Educ Pract Ed 2013;**98**:1 7-15 Published Online First: 20 November 2012*
- Dondorp AM, Fairhurst RM, Slutsker L, Macarthur JR, Breman JG, Guerin PJ et al. The threat of artemisinin-resistant malaria. N Engl J Med 2011; 365(12):1073-1075.