**MALARIA QUICK REFERENCE**

Fever, vomiting and diarrhoea or non-specific signs and symptoms such as any “flu-like” symptoms, malaise

**Admit**

**Falciparum malaria** Consider IV **quinine** (in 10% Dextrose); loading dose 20mg (base)/kg. (**ONLY if mother not yet treated pre delivery**) otherwise 10mg/kg/dose i.v then every 8h, for a full 7 day course. **OR 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.

**Well**

|  |  |  |
| --- | --- | --- |
| History of maternal malaria | Any child returning from a malaria endemic region (including stop-overs) | Any child returning from a malaria endemic region (including stop-overs) |
| **Congenital Malaria (+) screen** | From **other endemic areas** | **From South east Asia** |



**Assessment and investigation** FBC/Thick and thin films/Rapid antigen test for malaria U&Es/LFTs/CRP

Blood Culture G6PD

Blood Glucose

**Assessment and investigation** FBC/Thick and thin films/Rapid antigen test for malaria U&Es/LFTs/CRP

Blood Culture G6PD

Blood Glucose

**(+) screen**

**Admit** (due to high resistance in these areas)



Consider other imported infectious diseases

**(-) screen**

**Non Falciparum**

**Unwell**

**Well**

Observe if tolerating orals, able to take medication, good adherence home with Pinckney Ward f/u the following day (*d/w PID SpR*)

**(+) screen**

**Falciparum**

**Unwell**

**Complicated**

**Complicated**

Low threshold for admission.

If discharge ensure tolerating oral medications, ensure adherence. Arrange ward review the following day.

**Admit**

**Admit**

**Uncomplicated Falciparum**

**Riamet (Co-artem)** @ 0, 8, 24,

36, 48 and 60 hours

5-<15kg: 1 tab

15-<25kg 2 tabs

25-<35kg 3 tabs 35kg: 4 tabs (adult dose)

**Or Malarone** : Doses:

Over 40 kg: 4 „standard‟ tab

-given daily for 3 days

**Or**

**Quinine** (*less preferable*)10 mg/kg/dose tds for 7 days ***in conjunction with* clindamycin** (7-13 mg/kg/dose 8 hourly for 7 days) or doxycyline (if >8 years old) 200 mg once daily for 7 days.

**Complicated**

**Consider HDU or PICU**

* Impaired consciousness or coma
* Seizures
* Respiratory distress (pulmonary oedema)
* Signs of shock
* Hemoglobinuria or renal impairment
* Jaundice and other organ dysfunction
* Spontaneous bleeding
* P. falciparum in a child with sickle cell disease
* Metabolic acidosis (plasma bicarbonate < 15 mmol/l);
* Hyperlactataemia (lactate

>5 mmol/l)

* Severe anaemia (<8 g/dL)
* Hypoglycaemia (blood sugar

<3 mmol/L)

* Parasitaemia > 5%

**Consider 2˚ bacterial infections**

**Uncomplicated non- Falciparum**

**Chloroquine** 10mg/kg as single loading dose orally, then 5mg/kg/dose 12 hours later, then 10mg/kg OD for 2 days

*– if from SE Asia/known resistance use* **Riamet**

***PLUS***

**Primaquine** (if G6PD negative) 0.25mg/kg (max 26mg) OD for 14 days *– if from SE Asia see full guidelines re resistance (dose is 0.5mg/kg)*

**Treatment of complicated Malaria**

**Artesunate** IV 2.4mg/kg/dose @ 0, 12, 24 hours then OD until can take orals (if not 7 day IV in total)

***PLUS***

**Clindamycin** 7-13mg/kg/dose TDS for 7 days or **Doxycycline** if over 8 years old and tolerating orals 200mg OD

**OR**

**Quinine** if Artesunate not available 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***

**Clindamycin** 7-13mg/kg/dose TDS for 7 days or **Doxycycline** if over 8 years old and tolerating orals 200mg OD for 7 days only while on IV monotherapy. Can be stopped once oral Riamet or malarone started.

**Discuss with PID consultant, SGH if mixed infection**



**Malaria**

Kiang KM, Bryant PA, Shingadia D, Ladhani S, Steer AC, Burgner D *The treatment of imported malaria in children: an update* Arch Dis Child Educ Pract Ed. 2013 Feb;98(1):7-15

WHO malaria guidelines: <http://whqlibdoc.who.int/publications/2010/9789241547925_eng.pdf>

### Introduction:

Malaria is transmitted by Anopheles mosquitoes and is caused by *Plasmodium falciparum, vivax, malariae, ovale* and *knowlesi. P. falciparum* almost exclusively causes severe disease. The incubation period is between a minimum of 6 days to 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 amtimalarials particularly over the Thai-Cambodian border.

In any child returning from a malaria endemic region (including stop-overs) with fever, vomiting and diarrhoea or on-specific signs and symptoms such as any “flu-like” symptoms, malaise, malaria has to be suspected. Even if correct malaria prophylaxis was taken with good adherence, it is not 100% effective. Children with malaria can deteriorate extremely quickly and diagnosis must be made urgently. Interestingly the majority of patients in the UK returning with malaria are the „visiting family and friends‟ category rather than the tourists.

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 anemia (with no fever) as the only sign of illness.

Signs of malaria can overlap with signs of other illness. For example, a child may have malaria and cough with fast breathing, signs of pneumonia. This child needs treatment for both falciparum malaria and pneumonia. Children with malaria may also have diarrhoea. They need an antimalarial and treatment for the diarrhoea.

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 anemia. The child can die if he does not receive urgent treatment.

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.

**Differential Diagnosis** (see previous chapter infection in children returning from abroad):

* Common viral infections eg. Influenza
* Gastroenteritis
* Typhoid and other bacterial infections
* Meningitis/encephalitis
* Pneumonia
* Dengue fever
* Rarer tropical infections eg. viral haemorrhagic fever, Japanese B encephalitis, brucella, bartonella,

Q fever, Rickettsiosis

### 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, protein, 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);
	+ Hyperlactataemia (lactate >5 mmol/l)
	+ Severe anaemia (<8 g/dL)
	+ Hypoglycaemia (blood sugar <3 mmol/L);

### Uncomplicated malaria

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

If child is diagnosed please inform the NHS HPA England (phone number: 020 8812 7850) – malaria is a notifiable disease

**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 Appropriate next day follow up needs to be arranged as a ward attendant on Rupert Bear ward, family must agree with this arrangement.

Children with uncomplicated non-falciparum malaria if clinically well, after have been observed in ED for 4 hours can be treated as outpatient providing they are able to tolerate their medications (supervised in ED). They will need to be followed up on Rupert ear Ward ward the following day to ensure there has not been an Hb drop and the parasitaemia is no longer present.

They also need G6PD test done as primaquine needs to be started once the negative result is available (not in under 4s).

**Children should be closely monitored on the ward depending on clinical state if they fulfill 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 immediately with an appropriate drug that is readily available.

**- If switching to another drug do not delay the doses. First line treatment for severe malaria:**

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

**Dose:** 2.4mg/kg/dose 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.

#### PLUS:

**Clindamycin PO or doxycycline PO**.

**Doses**: **clindamycin** (7-13 mg/kg/dose 8 hourly for 7 days); **doxycycline** in children over 8 years old who can tolerate oral medications: 200 mg once daily for 7 days. **Oral treatment needs to be started whilst the child is on iv artesunate,** and can be stopped when oral Riamet or Malarone are started**.**

### 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) (preferred option for non artemeter resistant regions) 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> 8 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.

### 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%.*

### 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.

### Co-artem (Riamet) schedule: 6 doses are necessary and it needs to be given at 0, 8, 24, 36, 48 and 60 hours: Giving it with milk or similar fatty foods increases significantly the bioavailability .

**Doses:**

5-<15kg: 1 tab

15-<25kg 2 tabs

25-<35kg 3 tabs

35kg: 4 tabs (adult dose)

### Malarone (Atovaquone + proguanil) is another effective oral alternative medication. Doses:

Over 40 kg: 4 „standard‟ tablets daily for 3 days

**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.

### Treatment of Non-falciparum malaria

Chloroquine 10mg/kg initially as single loading dose, then 5mg/kg/dose 12 hours later, then 10 mg/kg OD orally for 2 more days. In cases of *Plasmodium ovale*, resistance to chloroquine has been reported and use of an arthemeter derivative may need to be considered.

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) if over 4 years of age.

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

# Congenital and Neonatal Malaria

This is a very rare occurrence, in babies born from mothers with malaria and it is secondary to placental transmission. 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.

Being a very rare occurrence 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.

Travel information can be found at the following links <http://www.who.int/malaria/travellers/en/> <http://www.cdc.gov/malaria/map/>

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