Malaria – Full Clinical Guideline

Reference no.:CG-ANTI/1316/23

A. INTRODUCTION

About 2000 cases of malaria are notified in the UK each year, of which about three quarters are the potentially fatal falciparum type. Two to eleven deaths per year occur in the UK from falciparum malaria. Malaria chemoprophylaxis does not provide 100% protection and any immunity acquired from previous exposure to malaria is short lived. Thus people brought up in endemic areas with histories of recurrent previous malaria are still at risk on return to their native homelands. This guideline covers the assessment, diagnosis and management of malaria.

B. ASSESSMENT AND DIAGNOSIS

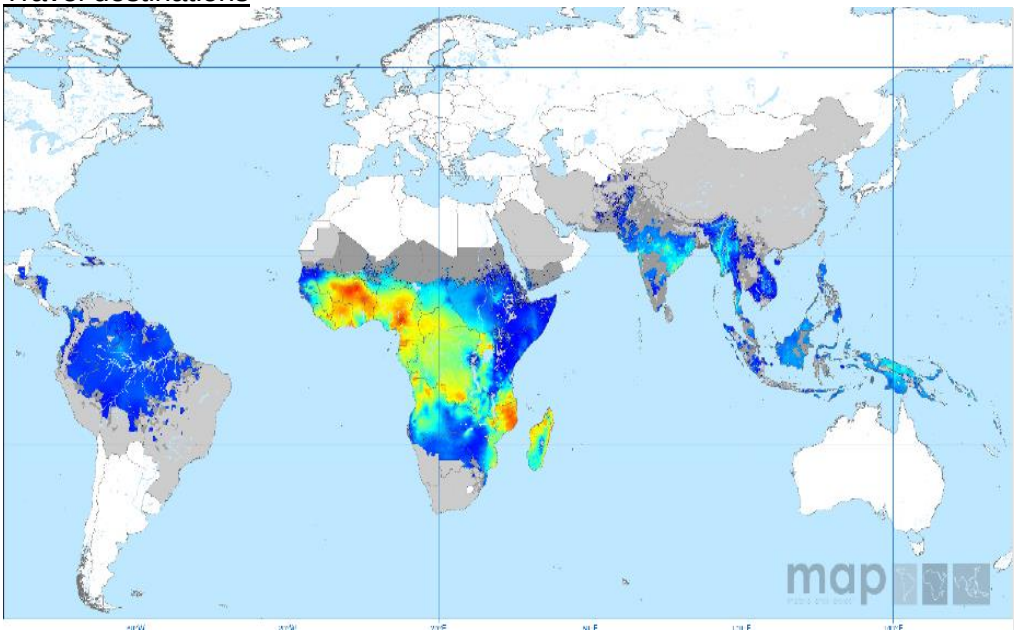
ANY PATIENT WITH SUSPECTED MALARIA SHOULD BE DISCUSSED WITH THE ON-CALL INFECTIOUS DISEASES REGISTRAR/CONSULTANT AT NOTTINGHAM CITY HOSPITAL.
Patients with malaria can deteriorate very quickly within hours!

1. Clinical suspicion of malaria

Clinical features, travel destinations and timing of travel may raise suspicion of malaria.

Clinical features – One cannot diagnose malaria purely from clinical features. Features of fever, rigors, headache and malaise are non-specific. In some series diarrhoea has been the dominant presenting symptom.

Travel destinations –



Benign or non-falciparum forms of malaria may be acquired throughout the shaded areas on the world map.

Equally, malignant falciparum malaria may be acquired throughout the world, but there are some regions with higher risk for this form of malaria:

- Sub-Saharan Africa
- Chittagong Hill Tracts of Bangladesh
- Laos, Cambodia, Myanmar and rural parts of Thailand bordering on these countries
- parts of Vietnam, Yunnan and Hainan provinces of China
- Sabah, Irian Jaya, Papua New Guinea, Solomon Islands, Vanuatu
- Amazon basin in Brazil and contiguous parts of Colombia, French Guiana, Guyana, Surinam, Bolivia and Venezuela

Timing of travel – The shortest incubation period of malaria is 6 days for falciparum. Malaria due to *Plasmodium vivax* or *P.ovale* can have a 'sleeping phase' with presentations 18 months or longer after leaving a malarious area. *P.falciparum* does not have a 'sleeping phase' and usually presents within 2 months of return (or 3 months in those who took mefloquine prophylaxis or who are pregnant).

In practice, malaria should be considered in anyone presenting to hospital with a relevant travel history, whatever their symptoms, and whenever they travelled, regardless of whether they have taken prophylaxis.

2. Complicated falciparum malaria[1] [2]

Particular features characterise what is known as complicated falciparum malaria and these should be sought on assessment of the patient. These develop 3-7 days after first symptoms, but rarely may occur within 24 hours. They include:

- Impaired consciousness (GCS <11) or seizures (more than 2 seizures in 24 hours).
- Prostration: Generalised weakness so that the person is unable to sit, stand or walk without assistance
- Renal impairment (oliguria <0.4 ml/kg bodyweight per hour or creatinine >265 micromole/l).
- Acidosis (pH < 7.3).
- Jaundice
- Hypoglycemia (<2.2 mmol/l).
- Pulmonary oedema or acute respiratory distress syndrome (ARDS).
- Haemoglobin ≤80 g/L.
- Spontaneous bleeding/disseminated intravascular coagulation.
- Shock (algid malaria e BP < 90/60 mmHg).
- Haemoglobinuria (without G6PD deficiency).
- Parasitaemia >10%. (lower counts do not exclude severe malaria)

3. Investigations

General investigations in an unwell returning traveler should include:

- FBC + malaria blood films/malaria antigen card tests
- If the first malaria blood film is negative and there is a strong suspicion of malaria the film should be repeated after 12 – 24 hours.
- U&Es, LFTs, Glucose
- MSU
- Blood cultures
- CXR (because of the possibility of an atypical pneumonia)
- Further serological tests should be guided by initial findings

Any sick patients (who might turn out to have complicated falciparum malaria) should also have a clotting screen and their lactate measured and blood gases performed.

Malaria blood films

EDTA blood samples (FBC bottle) should be sent to Haematology for a blood film (ask for "Malaria Parasites"). After initial screening for parasite antigens, 'thick' and 'thin' films are then examined and sent to Liverpool for confirmation. Samples sent to Liverpool first thing in the morning will be processed and results sent on the same day. Samples sent out of hours will be processed at point of arrival but only examined the next morning – unless the initial screening shows positive results.

A single negative film does not exclude malaria. Failure to find parasites on careful examination of **three** films taken over 24-48 hours makes the diagnosis unlikely. Conversely the presence of parasites in a semi-immune individual does not mean that malaria is the explanation for the presenting illness.

If it is unclear what type of malaria is present, the default should be to initially treat for falciparum malaria, as treatment for this will cover benign species. A senior decision can then be made on further treatment.

If falciparum malaria is diagnosed, daily blood films, FBC and platelets should be performed. The parasitaemia may rise in the first 24 hours before falling in response to treatment. Parasitaemia should disappear before the end of treatment, although gametocytes may persist for longer.

Additional investigations

For *P.vivax* and *P.ovale* an EDTA blood sample (FBC bottle) should be sent for G6PDH levels prior to treatment with primaquine.

C. MANAGEMENT [1 2 3 6](Evidence grade – 1a / 2a / 4)

ANY PATIENT WITH SUSPECTED MALARIA SHOULD BE DISCUSSED WITH THE ON-CALL INFECTIOUS DISEASES REGISTRAR/CONSULTANT AT NOTTINGHAM CITY HOSPITAL.
Patients with malaria can deteriorate very quickly within hours!

If it is unclear what type of malaria is present, the default should be to initially treat for falciparum malaria, as treatment for this will cover non-falciparum species. A senior decision can then be made on further treatment.

1. Non-falciparum malaria

Non-falciparum malarias due to *P.vivax, P.ovale* , *P.malariae, or P. knowlesi* are treated with

- Chloroquine base 620mg stat (written up as **four x 250 mg chloroquine phosphate tablets**, containing 620 mg of base)

  then 310mg (written up as **two x 250 mg chloroquine phosphate tablets**, containing 310 mg of base) 6-8 hours later,

  then 310mg od (**two x 250 mg chloroquine phosphate tablets**) for 2 days.

For *P.vivax* and *P.ovale*, **provided** the G6PDH level is normal and the patient is not pregnant, chloroquine is followed by treatment with (Primaquine should be started as soon as G6PDH status is known).

- Primaquine for 14 days
  - 30 mg od for *P.vivax*
  - 15 mg od for *P.ovale*

In cases of pregnancy, G6PDH deficiency and when the non-falciparum malaria has been acquired in Oceania the Consultant in Microbiology or Infectious Diseases will advise on variations on primaquine treatment.

2. Uncomplicated falciparum malaria

Uncomplicated falciparum malaria consists of symptomatic *Plasmodium falciparum* infection with a positive parasitological test and parasitemia <2 percent, in the absence of symptoms consistent with severe malaria.

This is treated with:

First choice

Riamet (Artemether-lumefantrine) – only if weight >35kg
- 4 tablets stat followed by 4 tablets at 8h, 24h, 36h, 48h and 60h. Contra-indicated in patients with LVF, arrhythmias, QT prolongation or familial hx of QT prolongation or sudden death, or acute porphyria. See BNF for further information and for drug interactions
- Riamet is available in the pharmacy out of hours cupboard

Other options

Malarone (Atovaquone 250mg plus Proguanil 100mg per tablet)
4 tablets OD for 3 days. For patients weighing < 40kg discuss dosing with a pharmacist.
Contact the pharmacist on call for supply if needed out of hours.

or

Oral quinine sulphate 600 mg TDS for 5-7 days

- plus a second agent chosen on specialist advice from
    - Doxycycline 200 mg /day for 7 days for adults (not if it has been used as prophylaxis)
    - Or if pregnant: Clindamycin 450 mg TDS for 7 days

The dose of any anti-malarial tablet should be repeated if the patient vomits within one hour or consider changing to IV treatment. Parenteral therapy should be considered in pregnant women following specialist advice. Parenteral treatment is also indicated in all patients with severe or complicated malaria, if parasitemia is greater than 2% (at high risk of developing severe disease).

The Consultant in Microbiology at UHDB or Infectious Diseases at NCH will advise on:

- Any alterations in quinine dosage after commencement of above
- The choice of treatment in patients from certain parts of South East Asia, where quinine resistance is prevalent.

3. Complicated falciparum malaria or severe malaria

ANY PATIENT WITH COMPLICATED FALCIPARUM MALARIA SHOULD BE DISCUSSED WITH THE ON-CALL INFECTIOUS DISEASES REGISTRAR/CONSULTANT AT NOTTINGHAM CITY HOSPITAL

(NOTE - BOTH IV QUININE AND ARTESUNATE ARE UNLICENSED)
If there are any features of complicated malaria, as listed above, treatment is with:

Intravenous Artesunate (first line)

- 2.4mg/kg given at 0, 12h, 24h then once daily thereafter
- After completion of minimum of 24h therapy (maximum 5 days), commence full course of oral Riamet (see previous section for dosing)
- Patients should be warned of symptoms of anaemia (haemolysis may occur due to treatment 7-21 days post treatment, often self-limiting)
- Haemoglobin level (Hb) should be routinely measured 14 days after completing treatment
- Artesunate will be stored in the pharmacy out of hours cupboards at RDH and QHB.

OR

Intravenous quinine dihydrochloride (only if Artesunate not available)

- Loading dose of 20 mg / kg (max 1.4g) in 5% Dextrose, or Dextrose/saline over 4 hours (loading dose is not required if quinine or mefloquine have been taken orally in the previous 12 hours). Note dextrose preferred to sodium chloride due to the risk of hypoglycaemia.
- Followed after 8 hours by maintenance doses of 10mg / kg IV (max 700mg) in 5% Dextrose, or Dextrose/saline over 4 hours every 8 hours for first 48h (or until patient can swallow). Reduce dosing frequency to 12hrly if IV quinine continues for > 48hrs. Once the patient is stable & able to swallow, switch to oral quinine sulphate 600mg tds to complete 7 days of quinine in total**.**
- Caution should be exercised for patients with a history of cardiac disease or the elderly owing to the potential risk of quinine induced arrhythmias. ECG monitoring recommended during infusion
- In patients with renal impairment or severe hepatic impairment the IV maintenance dose should be reduced to 5-7 mg/kg (discuss renal dosing with a pharmacist). Discuss with ID consultant/registrar at Nottingham.
- Quinine infusion stimulates insulin secretion and blood glucose must be checked hourly during infusions for hypoglycaemia, but this is not necessary for oral treatment
- Quinine treatment should always be accompanied by a second drug: doxycycline 200mg daily (or clindamycin 450mg 8 hourly for pregnant women) given orally for a total of seven days from when the patient can swallow

4. Management of complications [1 2 3]

Issues include:

- transfer to HDU / ITU for central line insertion ± ventilation for ARDS
- in cerebral malaria a lumbar puncture may be considered to ensure that there is not a concomitant bacterial meningitis
- in cerebral malaria the occurrence of seizures warrants the use of anti-convulsants, but these should not be used prophylactically as this has been associated with a poorer outcome.
- In cerebral malaria corticosteroids are contra-indicated (evidence grade 1b)
- strict attention to fluid balance is required so that the patient is neither too dry nor too wet. In trials the ideal CVP is 5cm, and this should be kept < 10 cm H_2O.
- in shock there may be secondary bacterial sepsis and in any complicated falciparum patient the addition of a broad spectrum anti-microbial should be considered as per the sepsis antibiotic guideline, after blood cultures
- hypoglycaemia may require 10% dextrose infusions or boluses of more concentrated glucose
- hyperpyrexia should be treated with tepid sponging and paracetamol
- supportive treatment is required for anaemia and DIC, and transfusion is advised if the haemoglobin falls <70 g/L.

5.Prophylaxis[4]

Even if patients have developed and been treated for malaria, they should complete their course of malaria prophylaxis for the remainder of the four weeks following their return from an endemic area. In particular, patients with falciparum malaria should be warned to be vigilant for the return of any symptoms for two months after treatment.

6.Notification

Malaria is a notifiable disease.

7. Follow up

Patients with non-falciparum malarias, and no other problems do not require routine follow up. All patients with falciparum malaria should be given a follow up appointment for 2–4 weeks.

E. NURSING ISSUES

1) Patients with suspected malaria do not have to be isolated in a side room

2) Observations include:

   - standard temperature, pulse, BP at 4-6 hourly intervals, unless otherwise indicated by NEWS or the presence of complications/treatment when more frequent observations are required
   - oxygen saturations should be monitored closely for falciparum patients even if they are not initially short of breath
   - fluid balance

3) Please ensure the patient has been weighed as dose calculations may be based on weight

4) Blood precautions should be followed

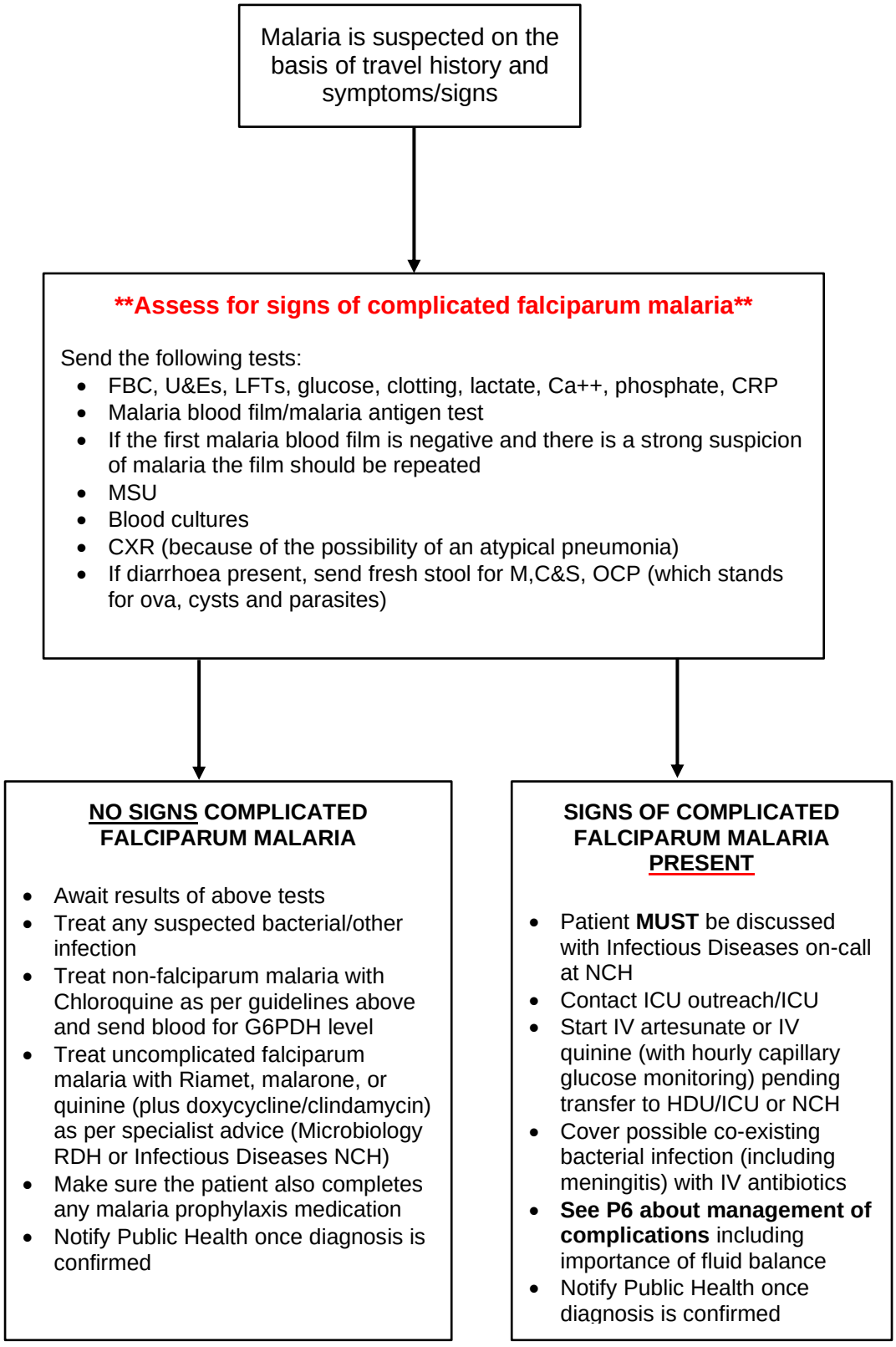
5) Patients with hyperpyrexia may require tepid sponging as well as paracetamol

6) During iv quinine treatment, blood glucose should be monitored hourly.

Reference links

1. WHO guidelines for malaria treatment (2010) http://whqlibdoc.who.int/publications/2010/9789241547925_eng.pdf
2. WHO Management of Severe Malaria (2013) http://apps.who.int/iris/bitstream/10665/79317/1/9789241548526_eng.pdf
3. Lagoo DG et al. UK malaria treatment guidelines 2016. *Journal of Infection 2016;* 72:635-649. http://www.journalofinfection.com/article/S0163-4453(16)00047-5/pdf
4. UK Guidelines for malaria prevention (2015)
5. White NJ et al. Malaria. *Lancet* 2014;383:723-35.

Quick reference flow chart: management of malaria



Always follow the NEWS2 protocol. Escalate sick patients early.
Read the full guideline for full details of the management of malaria

Documentation Controls

Reference Number CG-ANTI/1316/23	**Version:** 4		**Status** Final	
Version / Amendment History	Version	Date	Author	Reason
		December 2023	Review of existing guideline: Antimicrobial Pharmacist Angelina Dyche	Minor changes to previous guidelines reviewed by Dr Chris Durojaiye -Infectious Diseases Consultant. • Added clinical features of complicated falciparum malaria. • Benign malaria changed to Non-falciparum malaria • Storage of artesunate in pharmacy out of hours cupboards added

Intended Recipients: Clinical staff in acute medicine at RDH and QHB	
Training and Dissemination: minor changes to original guideline - non needed	
Development of original Guideline: MAU (Dr Kanwaldeep Atwal) Dr Nicola Cooper (adapted from Nottingham guideline)	
Original Guideline in Consultation with: Infectious Diseases Consultant RDH (Dr Chris Durojaiye), Infection Diseases Nottingham (Dr Venkatesan), Antimicrobial Pharmacist Revision completed by: Angelina Dyche - Antimicrobial Pharmacist	
Keywords: Malaria	
Approval	**Group: Antimicrobial Stewardship Group Date: 19/12/2023**
Divisional Sign Off	**Group: Medicine Division Date: 19/12/2023**
Date of Upload	20/12/2023
Review Date	December 2026
Contact for Review	Kayleigh.lehal@nhs.net Kayleigh Lehal - Lead Antimicrobial Pharmacist