Malaria

Diagnosis

- Prompt parasitological confirmation by microscopy or alternatively by Rapid
- Diagnostic Test (RDT)is recommended in all patients suspected of malaria before treatment is started
- Treatment solely on the basis of clinical suspicion should only be considered when a parasitological diagnosis is not accessible. (WHO 2010 guideline)
- Parasite nucleic acid detection using polymerase chain reaction (PCR) is more sensitive, and very useful tool for confirmation of species and detecting of drug resistant mutations

Clinical diagnosis

- Febrile illness (continuous or remittent in endemic area without any other focal infection for several days before classically intermittent)
- Febrile convulsions commonly complicate in young children
- Non-specific symptoms (similar to acute viral illness)
- Liver and spleen are enlarged
- May progress from minor symptoms to severe disease within few hours
- ***Danger signs***
    - Not able to drink or breast feed
    - Vomits everything
    - Lethargic or unconscious
    - Unable to sit or stand up

Definite diagnosis-Requires Identification of parasite or antigen

- Parasitological diagnosis
    - Microscopy-Identification of malaria parasite from thick and thin blood film using Giemsa stain

Rapid Diagnostic Test (RDT)- The immunological methods can detect both malaria antibodies and antigens within 10-30 minute.

RDT	Positive	Acute malaria infection
MP	Positive	Partially treated infection
RDT	Positive	Treated infection within 7 days
MP.	Negative	Untreated malaria infection with very low parasitemia
RDT	Negative	No malaria infection
MP	Negative	Treated infection after 7 days
RDT	Negative	Non-HRP2* strain
MP	Positive	Improper testing method Expired or poor storage condition of RDT kit

*HRP2-Histadine rich protein 2

Treatment should be guided by three main factors:

- The infecting Plasmodium species
- The clinical status of the patient
- The drug susceptibility of the infecting parasites as determined by the geographic area where the infection was acquired and the previous use of antimalarial medicines

P. falciparum and P, knowlesi infections can cause rapidly progressive severe illness or death while the other species, p. vivax, P, ovale, or P, malaria, are less likely to cause severe manifestations.

Uncomplicated Malaria

Defined as:

- Symptomatic malaria without signs of severity or evidence of vital organ dysfunction
- Parasitemia <2% and no schizonts

Antimalarial combination therapy

Simultaneous use of two or more blood schizontocidal medicines with independent modes of action and, thus, different biochemical targets in the parasite

Treatment of confrmed uncomplicated falciparum malaria in children and infants

- Artemisinin-based combination therapies should be used in preference to Sulfadoxine -pyrimethamine (SP) plus Amodiaquine (AQ) due to high level of drug resistance to these medicines in many countries for falciparum malaria
- Reduce transmissibility of treated P, falciparum infections (Primaquine as a gametocidal drug for P, falciparum malaria)
- All P, falciparum positive cases (either by microscopy or RDT should be treated with ACT+ Primaquine (stat dose) on 2n day of treatment as gametocidal drug
- Single dose of 0.2 mg/kg body wt of Primaquine except infant age <6 months and women breast feeding infant <6 months to reduce transmission
- G6PD testing not required

Treat for 3 days with one of the following regimens (recommended by WHO)

- Artemether plus Lumefantrine
- Artesunate plus Amodiaquine
- Artesunate plus Mefloquine
- Dihydroartemisinin plus piperaquine
    - 1s/ine-Artemether-Lumefantrine0)
    - 2nd line
        - Quinine plus Doxycycline (option 1)
        - Quinine plus Clindamycin (Option 2)
    - 3-d line-Atovaquone/Proguanil (Malar one)

Duration of therapy

ACT regimens should be provided 3 days treatment with artemisinin derivative

Artemether plus lumefantrine

The first two doses should be 8 hours apart.

Table 9.6 Combined tablets containing 20mg of Artemether and 120mg of Lumefantrine

Body Weight	**Dose**	**Duration**
5-14 kg	1 tablet bd	3 days
15-24 K8	2 tablets bd	
25-34 kg	3 tablets bd	
>34Kg	4 tablets bd	

Artesunate plus Mefloquine

- A target dose of
    - 4 mg/kg/day Artesunate given once a day for 3 days AND
    - 25 mg/kg of Mefloquine either.
        - Split over 2 days as 15 mg/kg and 10 mg/kg OR
        - Over 3 days as 8.3 mg/kg/day once a day for 3 days.
        - The therapeutic dose range is between 2-10 mg/kg/day of Artesunate and7-11 mg/kg/day of Mefloquine

Table 9.7 Separate tablets of 50 mg Artesunate and 250 mg base of Mefloquine

Body Weight	Artesunate 50 mg tablet	Mefloquine 250 mg tablet
3-10 k8	½ tablet od x 3 days	½ ablet on day 2
>10 kg	1 tablet od x 3 days	1 tablet on day 2

Artesunate plus Amodiaquine

Target dose of 4 mg/kg/day Artesunate and 10 mg/kg/day Amodiaquine once a day for 3 days, with a therapeutic dose range between 2-10 mg/kg/day Artesunate and 7.5-15 mg/kg/dose Amodiaquine.

Table 9.8 Separate tablets of 50 mg Artesunate and 153 mg base of Amodiaquine

Body Weight	Artesunate 50 mg tablet	Mefloquine 153 mg tablet
3-10 k8	½ tablet od x 3 days	½ ablet on day 2
>10 kg	1 tablet od x 3 days	1 tablet on day 2

Dihydroartemisinin plus Piperaquine

Pediatric tablet contains 160 mg Dihydro-artemisinine and 20 mg Piperaquine (once a day dose for 3 days)

Table 9.9 Separate tablets of 160 mg Dihydro-artemisinin and 20 mg Piperaquine

Body Weight	**Dihydro-artemismine**	**Piperaquine**
<25 kg	2.5 mg/kg	
>25 kg	4 mg/kg (2.5-10 mg/kg)	24 mg/kg (20-32 mg/kg) x 3 days

Infant <5 kg- ACT same mg/kg body wt target dose as for children weighing 5 kg

Second Line Quinine Sulphate Combination

- Quinine sulfate plus Doxycycline, Tetracycline, or Clindamycin is the next

treatment option.

- For the Quinine sulfate combination options, Quinine sulfate plus either

Doxycycline or Tetracycline is generally preferred to Quinine sulfate plus

Clindamycin because there are more data on the efficacy of Quinine plus

Doxycycline or Tetracycline.

- Quinine treatment should continue for 7 days for infections acquired in Southeast Asia

Treatment Failure

Early treatment failure

- Development of danger signs or severe malaria during the first three days in presence of parasitemia
- Axillary temperature >37.5'C on day 2 with parasite count greater than that of day 0
- Axillary temperature >37.5'C on day 3 in the presence of parasitemia
- Irrespective of axillary temperature on day 3 with parasite count >25% of that of day 0

Late treatment failure

- Development of danger signs or severe malaria on any day between day 4and day 14 in the presence of parasitemia
- Axillary temperature >37.5°C in the presence of parasitemia on any day from day 4 to day 14

Management

- Artesunate (2 mg/kg once a day) Plus
    - Tetracycline (4 mg/kg four times a day) OR
    - Doxycycline (3.5 mg/kg once a day) OR
    - Clindamycin (10 mg/kg twice a day)
- Any of these combinations should be given for 7 days
- Tetracycline & doxycycline are not recommended in children <8 years

Treatment of Vivax, Ovale and Malariae Malaria

- Chloroquine
    - 10 mg/kg on day 1
    - 10 mg/kg on day 2
    - 5 mg/kg on day 3
- Radical curative treatment with Primaquine (0.25mg base/kg/day for 14 days
- Primaquine is contraindicated in severe G6PD deficiency, pregnancy and infancy
- In areas with chloroquine resistant P. vivax:

- Artemisinin-based combination OR
- Quinine sulfate plus Doxycycline OR Tetracycline OR Atovaquone-proguanil OR Mefloquine
- These treatment options are equally recommended

Treatment of Plasmodium malariae and Plasmodium knowlesi

- There has been no widespread evidence of chloroquine resistance in p malariae and P. knowlesi species
- Chloroquine (or hydroxychloroquine) may still be used for both of these infections.
- In addition, any of the regimens listed above for the treatment of chloroquine resistant malaria may be used for the treatment of p, malariae and p Knowlesi infections

Treatment of Mixed Infections (Plasmodium vivax + Plasmodium falciparum)

- All mixed infections should be treated with full course of ACT and Primaquine0.25 mg/ kg body weight daily for 14 days.
- In people with G6PD deficiency-Primaquine 0.75 mg/kg once per week for8 weeks

Severe Complicated Malaria in Children

- Parasitemia >2% or Parasitemia <2% with schizonts reported on blood film or
- Parasitemia<2% with complications
- Severe life threatening malaria is nearly always due to P, falciparum
- Treat as a medical emergency
- Presumptive treatment may be started before confirmation after collecting blood for examination
- Presence of one or more of the following clinical or laboratory features classifies severe malaria

Clinical features

- Hyperpyrexia (axillary temperature >39.5°C)
- Impaired consciousness or unrousable coma
- Prostration i.e. generalized weakness so that the patient is unable walk or sit up without assistance

- Failure to feed
- Multiple convulsions-More than two episodes in 24 hours
- Acidotic breathing
- Circulatory collapse or shock
- Clinical jaundice plus evidence of other vital organ dysfunction
- Haemoglobinuria
- Abnormal spontaneous bleeding
- Pulmonary edema

Laboratory features

- Hypoglycaemia (blood glucose <2.2 mmol/l or <40 mg/dl)
- Metabolic acidosis (plasma bicarbonate <15 mmol/l)
- Severe normocytic anaemia (Hb <5 g/dl, packed cell volume <15%)
- Haemoglobinuria
- Hyperparasitaemia (>5% RBC infected
- Hyperlactataemia (lactate >5 mmol/l)
- Renal impairment (serum creatinine >265 µmol/l)
- Jaundice (total serum bilirubin >3 mg/dL)

Most common complications

- Cerebral malaria
- Severe anaemia
- Respiratory distress (acidosis)

Hypoglycemia

Table 9.10 Treatment of severe malaria

Artesunate 2.4 mg/kg body weight IV or IM given on admission (time=0), then at 12 hours and 24 hours, then once a day OR
Quinine 20 mg salt/kg body weight on admission (IV infusion or divided IM injection), then 10 mg/kg body weight every 8 hours, infusion rate should not exceed 5 mg salt/kg body weight per hour OR
Artemether 3.2 mg/kg body weight IM given on admission then 1.6 mg/kg body weight per day should only be used if none of the alternatives are available

**<20 kg children should receive larger Artesunate dose 3 mg/kg than adult and children >20 kg*

**Patients do not need both IV Quinine and IV Artesunate. When the Artesunate arrives you should discontinue the Quinine once the patient has received the first dose of Artesunate*

Following oral medications for 3 day course (with same drug) should replace parenteral treatment in all three regimens, when patient can tolerate orally:

- Artemether plus lumefantrine
- Artesunate plus amodiaquine
- Artesunate plus clindamycin or doxycycline
- Quinine plus clindamycin or doxycycline

Complications	Immediate treatment
Convulsion or coma (cerebral malaria) convulsion are common before or after onset of coma.	Exclude hyperpyrexia and hypoglycaemia Refer to management of active seizures
Hypoglycaemia (BGL: <2.2 mmol/ or <40 mg/dl) Particularly common in children under 3 years old	Give IV 5 ml/kg of 10% glucose (dextrose) rapidly Recheck BGL in 30 minutes, and repeat dextrose (5 ml/kg) if the level is low Prevent further hypoglycaemia in an unconscious child by dextrose infusion Add 10 ml of 50% glucose to 90 ml of a 5%glucose solution, or 10 ml of 50% glucose to40 ml of sterile water If the child develops signs of fluid overload, stop the infusion repeat dextrose (5 ml/kg) at regular intervals
Severe anaemia More common in children than adults. HCT S12% or Hb of s4 g/dl Less severely anaemic (HCT 12-15%, Hb 4-5 g/dl) with any of the following: Dehydration Shock Impaired consciousness Heart failure Very high parasitemia (>10% of red cells parasitized	Packed cells (10 ml/kg), over 3-4 hours If not available, give fresh whole blood (20 ml/kg) over 3-4 hours Diuretics is not usually indicated because many have low blood volume Check respiratory and pulse rate every 15 minutes and transfuse more slowly if one of them rises If there is any evidence of fluid overload due to the blood transfusion, give IV furosemide (1-2 mg/kg body weight) After transfusion, if the Hb remains low repeat transfusion In severely malnourished children, give whole blood (10 ml/kg rather than 20 ml/kg) once only and do not repeat the transfusion
Acute pulmonary edema	Stop IV fluids Prop patient up at an angle of 45° Give oxygen and diuretic Intubate and ventilate in life threatening hypoxaemia

Acute renal failure • Oliguric or non-oliguric renal failure • Suspected when urine output <0.5 ml/kg/hour • Confirmed when serum creatinine >1.5 gm/dl (130umol/l)	• Check fluid balance and urinary sodium • Established renal failure ○ Peritoneal dialysis or ○ If available, haemofiltration or haemodialysis (Refer Page-241 Management of acute kidney injury)
Spontaneous bleeding and coagulopathy Usually seen in non-immune children	• Transfuse with screened fresh whole blood (cryoprecipitate, fresh frozen plasma and platelets, if available) • Give vitamin K injection
Metabolic acidosis Exclude or treat hypoglycaemia, hypovolaemia and septicaemia	• Correct reversible causes of acidosis, especially dehydration and severe anaemia • If severe, add haemofiltration or haemodialysis
Shock Associated with • Severe dehydration • Gram (-) septicemia • Massive GI haemorrhage	• Correct hypovolaemia with appropriate fluid e.g. Normal saline or 5% Dextrose saline (10.20 ml/kg) • Look for the possible site of infection • Take blood culture and start broard spectrum antibiotics e.g.3rd generation cephalosporin • If not respond to fluid therapy, consider inotropic Dopamine/ Dobutamine infusion5-20 ug/kg/min