MALARIA GUIDELINE

20th Edition

June 2017

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INTRODUCTION

This is the 20th Edition of the Malaria guideline. It has been prepared for NGOs and other groups along the Thai-Myanmar border who encounter malaria. It is a simple, evidence based document aimed at providing a practical guide to malaria treatment.

Since the situation of artemisinin resistance in this region is so swift that the treatment options for malaria tends to be intricate and need frequent revisions depending upon the end results of the clinical trials implemented in this area. The treatment guidelines can also be downloaded in SMRU website. To help us keep this document useful, please send your comments and queries to:

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1. Glossary

A/AS:	Artesunate	AFB:	acid fast bacilli
ATN:	acute tubular necrosis	BCS:	Blantyre Coma Score
BD:	twice daily	BP:	Blood pressure
C:	Clindamycin	cc:	cubic centimetre =millilitres
CSF:	cerebrospinal fluid	D:	day
D:	Doxycycline	DP:	dihydroartemisinin-piperaquine
D5W:	dextrose 5% in water	FCR:	fever clearance rate
G6PD:	glucose 6 phosphate deficiency	GCS:	Glasgow coma score
H:	hour	Hb:	haemoglobin
Hct:	haematocrit	IM:	Intramuscular
IV:	Intravenous	IRBC:	Infected RBC
kg:	kilogram	M:	Mefloquine
MAS:	Mefloquine and Artesunate	mg:	milligrams
NSS:	normal saline solution	OD:	once daily
PCR:	Polymerase Chain Reaction	PF:	Plasmodium falciparum
PCT:	parasite clearance time	PFG:	Plasmodium falciparum gametocytes
PFS:	Plasmodium falciparum schizonts	pg:	page – as in page numbers
PM:	Plasmodium malariae	PO:	Plasmodium ovale
PR:	pulse rate	PV:	Plasmodium vivax
Q:	Quinine	QID:	four times daily
RBC:	red blood cell	RR:	respiratory rate
SaO2:	Saturated Oxygen	T:	Tetracycline
TID:	three times daily	WHO:	World Health Organisation

2. SMRU Malaria treatment guidelines summary

Artemisinin resistance is spreading along the Thai-Myanmar border so treatment failures are likely to become more common [1,13,14].

Uncomplicated *P. falciparum* malaria (PFT <4% IRBC or RDT diagnosis)

Definition: Uncomplicated *P. falciparum* is defined as presence of asexual parasitaemia (<4% IRBC; can sit, eat or drink alone without signs of severity or evidence (clinical or laboratory) of vital organ dysfunction.

1st line ACT: MAS3 or COA or DP (+single low dose primaquine)

2nd line ACT: different to 1st - A7D7, A7C7, MAS3, COA, DP (+single low dose primaquine)

Do not repeat MFQ ≤63 days; no Doxycycline in children <8 years and in pregnant women

Recent SMRU studies[14,15] show efficacy of MAS3 is decreasing on the Thai-Myanmar border*

Single dose primaquine

Primaquine 0.25 mg/kg x 1 dose on the first day of treatment without G6PD testing see Appendix 17.

Uncomplicated falciparum malaria with hyperparasitaemia (PFT ≥4% IRBC)

Definition: Patients without any signs or symptoms of severe malaria, i.e. no signs of vital organ dysfunction and parasitaemia for *P. falciparum* ≥4% IRBC

Artesunate high dose 4 mg/kg on day 0, then 2 mg/kg day 1-6 (total 7 days) PLUS

doxycycline OD (A7D7) or clindamycin 5mg/kg TID (A7C7) or MFQ 25 mg/kg split for 2-3 days (if none in the last 63 days)

OR

Artesunate high dose 4 mg/kg on day 0-3 with an ACT (3-day course) added to make total 7 days course.

All with single low dose primaquine on day 0. (Page 48-49)

Severe Malaria

Definition: Patients with *P. falciparum* and signs or symptoms of severe malaria

Artesunate IV 2.4 mg/kg at hour 0, 12 and 24 then every 24 hours until the patient can eat and drink followed by an ACT (DP, COA, A7D7, A7C7) where total duration of treatment should be 5-7 days) (+single dose primaquine on first day of feeding). Do not give mefloquine to severe malaria patients.

Severe malaria with hyperparasitaemia

If artemisinin resistance suspected start treatment of severe hyperparasitaemia malaria with intravenous artesunate and intravenous quinine.

Treatment of falciparum malaria in pregnant women

Uncomplicated malaria in **2nd** and **3rd** trimester – same as for non-pregnant (See Page 11)

Uncomplicated malaria in **1st** trimester - *the WHO Malaria Treatment Guidelines have not changed yet (Jun-2017*) but there is evidence [16,17] to support the use of ACT in the first trimester (DP, COA*). Consider …

Supervised ACT in 1st trimester if compliance to quinine is likely to be poor **OR**

Supervised Quinine (See Page 45 **45**) 10 mg/kg/dose, TID, 7days **AND**

Clindamycin (See Page 47) 5 mg/kg/dose, TID 7 days **(Q7C7)**

Note: **Coartem® at the usual adult dose had a 20% PCR confirmed failure rate in pregnant women on the Thai-Burmese border [18].*

Treatment for pregnant women with hyperparasitaemia or severe malaria is the same as non-pregnant patients.

Do not give primaquine to pregnant women

***P. vivax* malaria (or *P. malariae* or *P. ovale*)**

1st line Chloroquine 10 mg base/kg once daily on day 0 and 1, 5 mg base/kg once daily on day 2

2nd line ≥28 days repeat chloroquine; < 28 days consider possible resistance and treat with an ACT.

Primaquine for radical cure of *P. vivax*

1. If G6PD status unknown or cannot test for G6PD deficiency, consider giving primaquine 0.75 mg/kg weekly x 8 wk if you think there is a benefit. Otherwise do not give primaquine
2. If G6PD normal, give primaquine 0.5 mg/kg/d x 14d
3. Do not give primaquine to pregnant or lactating women with infants <6months
4. Primaquine doses should be supervised in all patients for adherence and in G6PD deficient or unknown patients for symptoms of haemolysis.

Confirmed positive result : malaria smear or rapid test:

☐ Pf ☐ other type of malaria ☐ Neg

Pregnancy status: urine pregnancy test if any doubt

☐ Not Pregnant ☐ Pregnant (Page 256)

Severity of malaria:

uncomplicated malaria: <4% IRBC; Sit, eat or drink alone:
☐ No ☐ Yes (if Yes Page 11)

uncomplicated hyper: >= 4% IRBC; able to sit, eat & drink alone
☐ No ☐ Yes (if Yes Page 13)

Severe: cannot sit, eat& drink by themselves
☐ No ☐ Yes (if Yes Page 1)

Signs of severity ☐ No ☐ Yes (if Yes Page 1)

Last Malaria history

Date diagnosis:|__|__||__|__||__|__| species_____& place_____
Drug treatment. _____

Mefloquine use in the last two months? ☐ No ☐ Yes

Any history of allergy to antimalarials? ☐ No ☐ Yes

Patient already treated for fever? ☐ No ☐ Yes

If you intend to treat with mefloquine, check if the patient has a history of

neuropsychiatric disorders ☐ No ☐ Yes
epilepsy ☐ No ☐ Yes
other mefloquine reactions ☐ No ☐ Yes
recent Yabba (amphetamine) use ☐ No ☐ Yes

Patient weighed correctly: Weight:|_____|kg

Patient febrile? Temperature: |_____|°C

Proceed to the treatment guidelines when you know the answer to all of the above

3. Treatment of uncomplicated P. falciparum malaria

Please check Page 10 first.

Do not use this chapter for pregnant women.

3.1 Definition of uncomplicated P. falciparum malaria:

Uncomplicated *P. falciparum* is defined as presence of asexual parasitaemia *(<4% IRBC; can sit, eat or drink alone without signs* of severity or evidence (clinical or laboratory) or vital organ dysfunction.

3.2 First line treatment

Give **artemisinin combination based treatment (ACT)**

Mefloquine -artesunate (MAS) or artemether-lumefantrine (Coartem®) or dihydroartemisinin - piperaquine (DP)

Mefloquine-artesunate (MAS3)

Treatment is once daily, Treatment-schedule: dosage table (See Page 377 and 388)

D0 - Artesunate 4 mg/kg

D1 - Artesunate 4 mg/kg + Mefloquine 15 mg/kg

D2 - Artesunate 4 mg/kg + Mefloquine 10 mg/kg

Mefloquine can also be given in split doses of 8 mg/kg per day over 3 days

Dihydroartemisinin and piperaquine (DP)

Each tablet contains 40mg of dihydroartemisinin and 320 mg piperaquine

Treatment is once daily for 3 days,

Treatment-schedule: dosage table (See Page 39)

Artemether-lumefantrine (COA), Coartem®

Each tablet contains 20mg artemether and 120 mg lumefantrine

Treatment is twice a day for 3 days,

Treatment-schedule: dosage table (See Page 39)

The absorption of oral lumefantrine is significantly enhanced with co-administration of fat so we recommend each dose is taken with some fried or oily food or a carton of milk.
Amount of fat required to obtain 90% of maximum effect of Coartem® is 1.2g [2].

Combination with primaquine single dose

Single dose 0.25mg/kg, (First day of ACT)

Treatment-schedule: dosage table (See Page 48-49)

A single dose of primaquine (0.25 mg/kg) following an ACT can reduce *P. falciparum* gametocyte carriage substantially (reduce transmission) [19] [20] *and safe even if G6PD status is unknown* [10].

NO single dose primaquine if

Pregnancy
Children<6months
Lactating women: *(if infant is < 6 months age)*

3.3 2nd line treatment

Treatment options are to either use any ACT (MAS3, Coartem®, DP, AS7D7 or A7C7). But it not advisable to use the same ACT as for the last episode.

Note: In patients with a 2nd episode of *P. falciparum* within 2 months of treatment with MAS3, don't give mefloquine again because of increased risk of neurological side effects.

Treatment-schedule of AS7D7: dosage table (See Page 377 and 47)

Day 0 - Day 6 Artesunate (AS) 2 mg/kg + Doxycycline (D) 4 mg/kg/day

Do not give doxycycline to pregnant women and children younger than 8 years

Treatment-schedule of AS7C7: dosage table (See Page 37**37** and 47)

Day 0 - Day 6 Artesunate (AS) 2 mg/kg + Clindamycin (C) 5 mg/kg/TID for 7days

There is some evidence to suggest infections which are truly recrudescent (failure of the drug treatment and not a new infection) will have higher cure rates with a 7 day treatment [18].

3.4 Treatment of anaemia

Treatment-schedule of ferrous sulphate and folic acid: (See Page 50). Anaemia is a common complication of malaria but tends to resolve quickly with treatment (2 weeks). Start ferrous only when the patient is trophozoite negative. Review the patient in 2 weeks. If still anaemic give an additional 2 weeks treatment. Think of other causes of anaemia: worms, thalassaemia, or G6PD deficiency. Take the opportunity to make a stool test and deworm if necessary.

4. Treatment of uncomplicated hyperparasitaemia

Please see the check list first (See Page 10)

4.1 Definition of uncomplicated hyperparasitaemia:

Patients without any signs or symptoms of severe malaria, i.e. no signs of vital organ dysfunction and high parasitaemia for P. falciparum (≥4% IRBC).

Note: Although WHO has put hyperparasitaemia as one criterion of severe malaria since 1990 [21], there is no enough evidence on hyperparasitaemia to recommend a cut-off. WHO initially set >5% parasitaemia for low-transmission settings and >10% for high and later revised the thresholds to >2% or 100 000/µL in low and >5% or 250 000/µL in areas of high stable malaria transmission intensity [22]. The cut-off of ≥4% has been followed consistently in this context since SMRU had shown that the overall mortality of hyperparasitaemia was 3% whilst that of uncomplicated falciparum malaria was 0.1%, [3] and that longer treatment courses were required [4] because of high recrudescence rates [3,23].

4.2 Treatment of uncomplicated hyperparasitaemia

Artesunate high dose 4 mg/kg on day 0 to day 3 with an ACT added (3-day course) with single dose primaquine on Day 0 and **total 7 days** of treatment.

Options for ACT:

-With Mefloquine split in3 days (Day 4, 5 6). (Total MFQ 25 mg/kg)

-With DP: day 4, 5, 6

(Recommended regimen; more efficacious than mefloquine and better compliance than Coartem)

-With Coartem: day 2,3,4,5,6

If these patients develop signs or symptoms of severe malaria during treatment switch to the severe malaria protocol using IV artesunate AND IV quinine (See page 42 and 46).

A single dose of primaquine (0.25 mg/kg) with an ACT can reduce *P. falciparum* gametocyte carriage substantially and hence reduce the transmission [10,19].

Treatment-schedule: dosage table (See Page 48 and 49)

NO single dose primaquine if
Pregnancy
Children<6months
Lactating women: *(if infant is < 6 months age)*

4.3 Routine observations

On admission, check temperature (Temp), respiratory rate (RR), pulse (PR), blood pressure (BP), consciousness using the Glasgow or Blantyre coma score (See Page 52), glucose, haematocrit (haemoglobin), quantity and colour of urine.

Then every 4-6 hours, check Temp, RR, PR, BP, consciousness/ coma score, quantity and colour of urine, and glucose, depending on the condition of the patient (awake, eating, drinking).

4.4 Hyperparasitaemia in children <1 year:

It is often difficult to administer the oral dose of artesunate accurately and absorption may be less reliable. Very young patients deteriorate faster. It is safer to treat them initially with IV or IM artesunate (Dose: 2.4 mg/kg)

4.5 Parasite clearance in hyperparasitaemia with oral artesunate

Check parasite count every 4-6 hours. By using the graph (See Page Error! Bookmark not defined.), plot the parasitaemia as % of the baseline against time. If the dotted line is reached, the patient should be watched closely. If the upper line is reached, give the patient a rescue dose of IV or IM artesunate (1.2 mg/kg) (Page 43) or IM artemether (3.2 mg/kg). (See Page 44).

Make sure the parasitaemia is decreasing on the 4-6 hourly malaria smears. If not, consider changing treatment to artesunate IV or IM. (Dose: 2.4 mg/kg). (See Page 42)

Notes:

The parasite clearance time after treatment with artesunate in getting longer in patients on the Thai-Burmese Border [1]. We recommend vigilant monitoring of parasite clearance in all patients with uncomplicated hyperparasitaemia.

4.6 Patients with schizonts

If schizont is reported on the baseline smear of patients with hyperparasitaemia the patient is likely to have a sharp rise in parasitaemia. If you cannot monitor the parasitaemia every 6 h consider giving at least the first dose of artesunate IV or IM. (See Page 42)

4.7 Very high parasitaemia >20%

At any age, very high parasitaemia is more safely treated with artesunate IV or IM at least for the first dose. (See Page 42)

Points for hyperparasitaemia

* Hyperparasitaemia as the important reservoir of drug resistance.

* Hyperparasitaemia (though regarded by WHO as one of the criteria for severe malaria) without any signs of severe malaria are usually treated with oral regimen [1,3,4] but admitted for close supervision since the risk of death is higher.

* Again, the patients with hyperparasitaemia have greater risk of recrudescence as there are more parasites to eliminate and anti-malarial drug levels may fall below the minimum inhibitory concentration before all the parasites are gone from the body [5-8].

* This guideline follows the WHO suggestion that all the patients with hyperparasitaemia should be monitored closely and treated conservatively with seven days of an artemisinin derivative, plus a full course of partner drug [10,12].

5. Treatment of severe falciparum malaria

It is a medical emergency. Most of the deaths are due to delay in treatment or inappropriate therapy. Along the Thai-Burmese border and in much of Asia, severe malaria is seen in all age groups. The two groups most at risk are children under five years and pregnant women.

5.1 Definition of severe P. falciparum malaria

"In a patient with *P. falciparum* asexual parasitaemia and no other obvious cause of symptoms, the presence of one or more of the following clinical or laboratory features classifies the patient as suffering from severe malaria" [10]

Clinical features

– Impaired consciousness or coma

– Prostration (generalized weakness; the patient is unable to sit, stand or walk without assistance)

– Multiple convulsions – more than two episodes in 24 hours

– Deep breathing, respiratory distress (acidotic breathing)

– Shock (systolic blood pressure < 80 (adults) or < 70 mmHg (children) or capillary refill time ≥ 3 seconds)

– Jaundice (serum/plasma bilirubin > 50 μmol/l with hyperparasitaemia)

– Abnormal spontaneous bleeding, prolong bleeding time, haematemesis or malena

– Pulmonary oedema (radiological or oxygen saturation < 92% in room air with signs of respiratory distress and crepitations in lungs)

Laboratory findings:

– Hypoglycaemia (blood glucose < 2.2 mmol/l or < 40 mg/dl)

– Acidosis (plasma bicarbonate < 15 mmol/l or venous plasma lactate ≥ 5 mmol/l)

– Severe normocytic anaemia (Hb < 7 g/dl, HCT 20%)

– Hyperparasitaemia with other signs of severity

– Renal impairment (serum creatinine > 265 μmol/l or blood urea > 20 mmol/l)

5.2 1st line treatment –severe malaria

WHO recommends IV artesunate [24]:

5.2.1.1 Intravenous (IV) Artesunate

Hour 0	Artesunate 2.4 mg/kg.
Hour 12	Artesunate 2.4 mg/kg.
Hour 24	Artesunate 2.4 mg/kg.
Then every 24 hours:	Artesunate 2.4 mg/kg until the patient can tolerate oral medication

Artesunate can be given intra muscularly in the same dose as intravenous.

If injectable artesunate is not available, give injectable artemether or quinine.

5.2.1.2 Intramuscular (IM) Artemether

H0 Artemether 3.2mg/kg

H24 Artemether 1.6mg/kg (every 24 hours until oral medication is tolerated)

OR

5.2.1.3 Intravenous (IV) Quinine

H0 to H4 20 mg/kg given over four hours
(Preferably in a Metroset / burette)

H8 10 mg/kg given over 2 hours and this is repeated every 8 hours

(H16, H24 etc…total **daily** dose 30 mg/kg)

OR

5.2.1.4 Intra muscular (IM) Quinine

H0 Loading dose of quinine according to table (See Page 46) instead of putting into burette, dilute with same volume of sterile water and give 2 injections in the 2 antero-lateral thighs.

Maintenance dose of quinine according to table (See Page 46) instead of putting into burette, dilute with same volume of sterile water and give 2 injections in the 2 antero-lateral thighs.

5.2.1.5 Severe malaria with hyperparasitaemia

(In an area of established artemisinin resistance OR uncomplicated hyperparasitaemic malaria becoming severe after artesunate treatment)

Should be treated with Artesunate IV 2.4 mg/kg at hour 0, 12 and 24 then every 24 hours **AND IV Quinine** until the patient can eat and drink then follow treatment of **Uncomplicated Hyperparasitaemia** total duration of treatment should be 7 days plus single dose primaquine.

This is based on the evidence of increasingly slow parasite clearance rates in hyperparasitaemic patients.

5.2.1.6 Treatment after coma recovery

Oral treatment will replace parenteral therapy as soon as the patient can sit, eat and drink. The regimen of choice will be Artesunate (See Page 37) and Doxycycline (See Page 47); or an ACT given on the last 3 days of the 7-day treatment: Replace artesunate on day 4, 5, 6 with Coartem® or DP at the usual dose (see Page 39).

Mefloquine should not be used. It is contra-indicated because it increases the risk of post malaria neurological syndrome

5.2.1.7 In pregnant women

Treatment is the same as non-pregnant (See page 16) but avoid doxycycline.
If only A7C7 is available, it can be used.

5.2.1.8 Combination with primaquine single dose(except pregnant woman)

Single dose, (First day of ACT or when patient can eat)
Treatment-schedule: dosage table (See Page 48-49)

A single dose of primaquine (0.25 mg/kg) following an ACT can reduce *P. falciparum* gametocyte carriage substantially (reduce transmission potential)

5.2.1.9 Guideline for the treatment of complications related to severe malaria

Management depends on the level of health care that is available.

Absolute indications for referral to well equipped hospital

- Acute renal failure (needs dialysis),
- Respiratory insufficiency
  (Needs intubation and mechanical ventilation)
- Shock not responding to fluid resuscitation

Coma Management (Steps A-K)

The arrival of the comatose/unconscious patient requires medical staff to be skilled in basic life support (BLS) and to operate quickly to reduce morbidity and mortality.
(See coma drill page 54)

Hypoglycaemia

Blood glucose must be confirmed with a glucometer or glucose sticks.

Treatment for hypoglycaemia: 5ml/kg of 10% dextrose*** (D10W) over 10 minutes. It is important to follow this bolus with an infusion of 10% dextrose (the rate being adjusted according to blood sugar and it can be run alongside normal maintenance fluids).

***10% dextrose can be made by removing 50ml from a 500ml bag of 5% dextrose (D5W) and adding 50ml of 50% dextrose. Rate and volume detail: (See Page 51) and for the management of infants less than 4 weeks (for more detail-see SMRU Paediatric Guidelines)

Notes:

The chance of hypoglycaemia is higher in children, pregnant women and treatment with quinine.
Always check blood glucose if there is deterioration in the level of consciousness.
Check plasma glucose every 4 hours in the unconscious patient.
Make sure that hypoglycaemia, shock or a different disease like meningitis is not the cause of altered consciousness.

Evaluate for meningitis

If not sure about the diagnosis of cerebral malaria, a lumbar puncture should be performed to rule out bacterial meningitis (if there are no contraindications). The following symptoms are uncommon in cerebral malaria. Meningitis should be considered if:

- Signs of meningeal involvement like a stiff neck
- Slide is negative for asexual forms of *P. falciparum*
- Patient is in shock
- Leucocytosis and/or a left shift in the white cell count
- Cloudy cerebrospinal fluid (CSF)

Treatment for meningitis: ideally with a 3rd generation cephalosporin

Ceftriaxone: Adults 2gm IV BD: Children 50mg/kg IV BD

If possible, the CSF should be sent for cell count, glucose and protein level, Gram and AFB stain, and culture. The Gram stain and cultures (CSF and blood) are the most valuable.

Contraindications for Lumbar puncture

Do not perform a lumbar puncture if there are signs of raised intracranial pressure such as unequal pupil size, non-reactive pupils, a very slow heart rate (<50 bpm in adults), focal neurological sign or irregular breathing.

Convulsions

Observe for convulsions, these may be very subtle. Convulsions should be treated.

Acute treatment:

Diazepam: Adults 10 mg IV over 5 minutes (maximum 30 mg)

Children 0.4 mg/kg IV over 5 minutes (maximum 10 mg)

Rectal administration (use IV formulation) 0.4 mg/kg

May repeat dose every 5 - 10 minutes for total of 3 doses or to maximum dose

Check the blood glucose level.

Phenobarbital is not recommended for prophylaxis of recurrent convulsion as it was related to increased mortality in cerebral malaria [25,26].

Notes:

IV diazepam will stick to PVC so don't inject it in the giving set.

Seizures are more common in children than adults with severe malaria. Prophylaxis for convulsions is not recommended by WHO [10,11].

Shock

Shock (systolic blood pressure below 70 mm Hg in adults, Capillary refill time > 2 seconds in children) is an uncommon finding in severe malaria and if present concomitant sepsis should be suspected. If the patient has severe hypotension:

Do blood cultures before antibiotics, if available.

Run fluid bolus: Adults 1 L NSS, Children 20 ml/kg NSS

If the blood pressure does not improve, refer to the hospital. Colloids (albumin) are expensive and do not give more benefit.

Always use NSS bolus for shock or dehydration NOT D5W

Start empirical antibiotic therapy to cover Gram negative organisms;

Ceftriaxone: Adults 2 gm IV BD, Children 50 mg/kg IV OD

Cefotaxime: Adults 1 gm IV TID, Children 50 mg/kg IV QID

Gentamicin: 7 mg/kg IV single dose can be given if there is no improvement while on Ceftriaxone or Cefotaxime in suspected septic shock.

Continue fluid resuscitation until mean blood pressure is > 60-70 mmHg.

Mean BP = diastolic BP + 1/3*(systolic BP-diastolic BP)

Normally, blood transfusion is given if Hct< 20% (HB<6 g/dL). If the Hct is ≥ 20% (HB≥6 g/dL) and the patient is very sick, **DO NOT WAIT** until Hct drops below 20% (HB<6 g/dL), blood transfusions can be given early especially in patients with high parasite counts.

Notes: Be careful with fluid

Volume overload (pulmonary oedema) can be dangerous and can kill. Symptoms include: dyspnoea, orthopnoea and lung crepitations.

Between boluses, check respiratory rate and lungs.

Fluid management and renal failure

This remains one of the most difficult parts of caring for an unconscious malaria patient.

Notes:

Insert urinary catheter

Monitoring fluid input and output

Fluid bolus if (+) sign of dehydration or urine output< 0.5 ml/kg/hr

Observe for signs of pulmonary oedema

Fluid bolus for pre-renal failure

Adults: 1 L Normal Saline given at 200 ml/hour (maximum 2 Liters)

Children: 20 ml/kg (maximum 40 ml/kg)

Treat with furosemide 1 mg/kg. Repeat dose 2 mg/kg in 30 minutes if necessary (maximum for each dose 200 mg)

Points to check pulmonary oedema:

Dyspnoea, Orthopnoea, and

Crepitations in the basal lung fields

Check respiratory rate and lung exam

Management:

The patient should be in sitting position.

Oxygen therapy (nasal catheter or face mask)

Treat with furosemide 1mg/kg and can repeat dose 2 mg/kg in 30 mins (*maximum for each dose 200 mg*)

The dose of furosemide for acute pulmonary oedema is different than for renal failure that does not respond to fluid bolus. Higher doses are used in renal failure. If there are no symptoms of pulmonary oedema after the fluid bolus, start maintenance fluid:

Maintenance fluid calculation

Adults:

100 ml/hr alternating D5W and NSS

The rate of infusion may be slower or faster depending on the patient

Children aged over 5 years:

First 10 kg body weight, give 4 ml/kg/h, next 10 kg bodyweight, give 2ml/kg/h, and for each additional kg body weight, give 1 ml/kg/h. (4,2,1 formula)

Example 27 kg = 4 + 2 + 7 = 13 ml/kg/h

Children ages 4 weeks old to ≤ 5 years old:

Should use 0.81% saline and 5% dextrose

How to make: Takeout 50ml from 500ml of normal saline then put in 50ml of 50% dextrose. For more detail, see SMRU Paediatric guideline.

Monitor closely during maintenance IV fluids:

Close monitoring of the fluid balance is important in severe malaria, since dehydration will lead to renal failure and volume overload will lead to pulmonary oedema

Urine output should be > 0.5 ml/kg/hr. Example: Weight 40kg, urine volume 120 ml in last 3 hours: 120 ÷ 3 ÷ 40 = 1 ml/kg/hr. Urine output is OK.

If urine output is less than 0.5 ml/kg/hr give furosemide

Start with 40 mg IV. If no response in 30 minutes, repeat dose 100 mg IV → 200 mg IV → Acute Tubular Necrosis (ATN) refer to hospital

Points to check hydration

Skin turgor
Dry lips and mouth
Tears
Jugular venous pressure

Management for respiratory Failure

Pulmonary oedema with Acute Respiratory Distress Syndrome (ARDS) is mainly a complication in adults and pregnancy, and can still develop in the days after admission. It is caused by capillary leakage due to malaria, but fluid overload is an important risk factor.

Differential diagnosis:

Metabolic acidosis (deep breathing called Kussmaul breathing)

Severe anaemia (pallor)

Pneumonia (one sided lung crepitations)

Investigations:

Peripheral white blood cell count (WBC) (if available):

A high WBC may be a sign of infection other than malaria

Chest X-ray:

It may show diffuse shadowing of the lung fields in ARDS. It may be normal or show an infiltrate in pneumonia

When to refer to the hospital

Severe dyspnoea (high RR, increased work of breathing)

Cyanosis (if pulse oximetry not available)

Pulse oximetry (SaO2<90%) if available

Check for parasitaemia

Severe malaria patients should be monitored with regular malaria smear (4-6 hourly) until negative.

Management for severe anaemia:

Check the haemoglobin or haematocrit on admission and every 24 hours.

Give blood transfusion for all patients with Hct< 20% (Hb ≤ 6 g/dL) or in shock.

Beware that dehydration can also cause high haematocrit masking the underlying anaemia.

If an anaemic patient is symptomatic, the benefits of blood transfusion should outweigh the risks (e.g. HIV, Hepatitis B, transfusion reaction).

Monitor during blood transfusion

(Every 15-30 minutes)

Temp, HR, RR, BP

Check for rash or itching

Check for lung crepitations

(Volume overload)

Check for lung wheezing

(Anaphylaxis)

If an allergic reaction develops

Stop transfusion. Give Adrenaline, chlorpheniramine STAT, hydrocortisone or other IV steroid should be given for the next 24-48 hours.

Both whole blood and packed red cells can be given.

Adults: generally require 2 units

Children: give 20 ml/kg. Give 1 unit (or 20ml/kg in children) over 4 hours.

Screen donor blood: blood group, cross-match, HIV and Hepatitis B, (Hepatitis C and syphilis if available), malaria smear and Hct (or Hb).

Jaundice

Patients with severe malaria can be severely jaundiced, due to intravascular haemolysis of parasitized (and unparasitized) red cells and hepatic dysfunction. It is a prognostic sign, but there is no specific therapy.

Blackwater fever

Haemoglobinuria due to massive intravascular haemolysis is associated with quinine therapy and G6PD deficiency. Transfusion of fresh blood should aim to maintain a haematocrit above 20% (haemoglobin 6g/dL). There is no specific therapy. Antimalarial therapy must not be stopped.

Disseminated Intravascular Coagulation (DIC)

DIC can be suspected if there is spontaneous bleeding and oozing from venepuncture sites. It is relatively rare in severe malaria (5%), but much more common in septicaemia. If you suspect DIC, septicaemia should be considered.

Diagnosis:

High suspicion as stated above (To test clotting time at the local hospital blood needs to be put into a citrate tube. This is not important in the field situation.)

Management:

Vitamin-K 10 mg IV (slowly) every 24 hours for 3 days

Nursing care and feeding

A recent study provides evidence that early nasogastric tube feeding is detrimental in patients with cerebral malaria treated in resource poor settings where endotracheal intubation is not generally available. Early enteral feeding increases the risk of aspiration pneumonia and conveys no clear benefits. Surviving patients with cerebral malaria frequently recover consciousness over the first 24–72 hours [27].

Notes

Risk of aspiration in unconscious patient (Keep upright as close as possible to 45 degrees and insert a nasogastric tube to empty the stomach)

Risk for bedsores (change position every 2 hours)

Risk for corneal ulceration (irrigate eyes with saline or artificial tears)

Eye lids kept closed with eye pads

Risk for malnutrition

Avoid these mistakes in severe malaria

- Fail to diagnose severe signs
- Missing hypoglycaemia
- Inappropriate fluid management

(may lead to pulmonary oedema OR renal failure)

- Delay in blood transfusion

6. Treatment of malaria in pregnancy

6.1 Treatment of uncomplicated P. falciparum malaria in pregnancy

Uncomplicated malaria in **2nd** and **3rd** trimester – same as for non-pregnant (See Page 11)

Uncomplicated malaria in **1st** trimester - *the WHO Malaria Treatment Guidelines have not changed yet (Jun-2017*) but there is evidence [16,17] to support the use of ACT in the first trimester (DP, COA*).

Consider …

Supervised ACT in 1st trimester if compliance to quinine is likely to be poor **OR**

Supervised Quinine (See Page 45) 10 mg/kg/dose, TID, 7days **AND**

Clindamycin (See Page 47) 5 mg/kg/dose, TID 7 days **(Q7C7)**

Note: **Coartem® at the usual adult dose had a 20% PCR confirmed failure rate in pregnant women on the Thai-Burmese border[4].*

Do not give primaquine to pregnant women

6.2 Treatment of uncomplicated hyperparasitaemia in pregnancy

In all trimester treatment is the same as in non-pregnant patients (See Page 13)

If schizonts are present on the malaria smear:
Pregnant women with uncomplicated hyperparasitaemia and *Pfs* (schizonts) at baseline need to be treated with the severe malaria protocol (See Page 17).
Continue IV until the parasitaemia has decreased to approximately 10% of the baseline count e.g. *PFT* 50/1000 RBC (5.0%) to *PFT* 5/1000 RBC (0.5%).

Severe Hyperparasitaemia
Pregnant women with hyperparasitaemia who deteriorate to severe malaria after artesunate should be treated with artesunate IV + Quinine IV.

6.3 Treatment of severe malaria in pregnancy

In all trimesters treatment is the same as in non-pregnant patients (See Page 16).

* When IV Artesunate is not available: give IM Artemether **OR** IV Quinine

6.4 Severe malaria with hyperparasitaemia

In an area of artemisinin resistance consider artesunate IV + Quinine IV.

6.5 Pregnancy related complications of severe malaria

Hypoglycaemia:

Hypoglycaemia is a common problem in pregnant women with severe malaria. When IV quinine is used for treatment 50% of pregnant women will develop hypoglycaemia. Quinine treated women in the 2nd and 3rd trimesters of pregnancy are at high risk of hypoglycaemia even if they are not severe.

Pulmonary oedema:

This may present on admission or develop suddenly, commonly develops immediately after delivery and may occur at any time in the 1st week post-partum.

Gram negative sepsis is common and should be treated appropriately. Look for a source of infection and if found treat appropriately. If no source is identified, follow the recommendations for severe malaria shock.

General treatment points for malaria in pregnancy

1) In pregnancy morbidity and mortality from malaria is increased.
    - *Supervise treatment in pregnancy until the malaria smear is negative*
2) The failure rate of quinine alone is unacceptably high.
    - *(Quinine (Q) should always be used in combination with clindamycin (C))*
3) Careful confirmation of gestation is needed (ultrasound, LMP or fundal height Page 53).
    - *Before prescribing antimalarials (or any medication!) to women of childbearing age ask if they could be pregnant.* Do urine pregnancy testing when in doubt.
4) Always treat anaemia.
5) Find a stand-by blood donor at the time of delivery in case of PPH.
6) Premature labour: Treat fever quickly and use dexamethasone and nifedipine (if BP is stable) as part of the normal management of confirmed preterm labour (<35 weeks gestation).
7) Monitor for foetal distress including bradycardia which is a *common* complication of malaria or its treatment with quinine.

6.6 Special measures when the mother is positive at the time of delivery

Malaria can be transmitted while the infant is *in utero;* when we treat the mother the fetus will be treated by transfer of drug across the placenta.

Infection in the mother in the days before or at the time of delivery is a high risk time for congenital malaria. Infant risk for malaria is high if the cord and placenta blood are positive.

How to collect cord specimens

-Obtain cord specimens before delivery of the placenta.
-Wipe the cord clean
-Puncture the cord with a syringe and needle (small gauge)
-Withdraw blood from the vessel (2.0 ml is plenty)
-Re-clamp the cord above the puncture site.
-The blood obtained needs to go directly onto the glass slide before it clots.

How to collect placenta blood

-Place the delivered placenta maternal surface (red colour) upward.
-Choose a site midway between the edge of the placenta and the cord
-Wipe it clean with gauze
-Make an incision about 1 cm deep and 3-4 cm in length with a scalpel blade (do not pierce the fetal surface (white colour))
-Use a syringe and needle (or haematocrit tube) to withdraw blood that pools in the incised area.
-Place this blood onto the glass slide before it clots.
-Take a smear from the baby as well.

6.7 Congenital malaria and treatment of malaria in very young infants

Definition:

Positive malaria slide in the neonate within 7 days of birth

***P. falciparum* congenital malaria can cause death.**

Clinical features:

If the infection has been detected and treated early there may be no symptoms.

- Fever ≥ 38 °C on one occasion or > 37.5 °C on two occasions separated by at least one hour
- Poor perfusion – shock: Cold hands and feet, CRT > 2s, Mottled, Tachycardia
- Respiratory distress: Fast RR > 60/min and/or chest in-drawing
- Anaemia
- Hypothermia (not responding to treatment)
- Apnoeas or slow respiratory rate
- Seizures/ Sleepy/Unconscious
- Hepatosplenomegaly • Jaundice
- Abdominal distension
- Bile from the NGT

Differential Diagnosis: Sepsis, CMV, herpes simplex, rubella, toxoplasmosis, syphilis

Management

ABC- (these infants can be very sick: stabilize first)
Make the diagnosis
Take the investigations (Malaria smear/ Blood glucose/ Hct/Hb)

P. falciparum

IM/IV artesunate 2.4.mg/kg at least for the first dose

(The clinical condition can decrease rapidly and the absorption in neonates is unknown).

If there is a reduction in parasite count, the clinical condition of the infant is good and the infant can tolerate oral medication- give oral artesunate 2 mg/kg/day OD for 7 days.

P. vivax

If the infant is unwell, give IM/IV artesunate for the first dose: as for *P. falciparum*.

If the infant is well, give standard doses of chloroquine once daily for 3 days (See Page 41)

Do not give primaquine for congenital malaria because there are no hypnozites.

Follow-up: All these infants should be follow up weekly to day 63

If P. vivax infection is detected again:

If ≥ 28 days, repeat chloroquine treatment

If < 28 days, use ACT.

Supportive treatment for neonates with congenital malaria
M – **M**ilk
A – **A**ntibiotics
C – **C**ord care
H – **H**eat
O – **O**xygen

Quinine, chloroquine, mefloquine and primaquine are excreted in the breast milk, but the sucking neonate would receive only a few mg/day.

7. Treatment of non *P. falciparum* malaria

7.1 Standard treatment

Chloroquine 10 mg base/kg once daily: Day 0 and Day 1

Chloroquine 5 mg base/kg once daily: Day 2 (See Page 40)

P. vivax recurring > 28 days — Can be treated with standard treatment and must be supervised.

P. vivax recurring ≤ 28 days — Maybe due to resistance (exclude non-compliance). An alternative treatment with ACT should be given and must be supervised.
Do not use sulfadoxine-pyrimethamine.
It is not effective against *P. vivax*.

7.2 Alternative treatment [28,29]

(Doses are the same for Pf and Pv. For treatment schedule (See Page 37-39)

Mefloquine – Artesunate(MAS) (3 days)

Effective against *P. vivax*, but is not listed as a recommended treatment [30,31]

Dihydroartemisin – Piperaquine(DP)(3 days)

Effective against *P. vivax* in areas of Asia where there is chloroquine resistance [28,32]

Artemether-Lumefantrine(COA)(3 days)

Effective against *P. vivax* but day 42 recurrence is high due to shorter half-life of lumefantrine compared to piperaquine and mefloquine.[33,34]

7.3 Treatment of liver stage (P. vivax and P. ovale)

Primaquine (PMQ) is the only available drug to treat the liver stage. WHO currently recommends that primaquine should be given with chloroquine (or ACT) for patients who meet the criteria below.

When to give primaquine:

In all patients with *P. vivax* who are:
Known G6PD normal
Known G6PD deficient

NO primaquine

Pregnancy
Children <6 months old
Lactating women *(if infant is < 6 months age)*
G6PD status unknown – you may consider using primaquine if there is a clear benefit of radical cure:
Anaemia from recurrent episodes
Recurrent episodes are affecting work or daily life
(e.g. missing work or school 2 to 3 days every month).
If patient is will leave the malaria endemic area

Primaquine dosing (See Page 41) Children and Adults

If G6PD normal	0.5 mg base/kg/day for 14 days
If G6PD deficient	0.75 mg base/kg given once a week for 8 weeks. Supervise and monitor for acute haemolytic anaemia (clinical and laboratory if available)

Side-effects

It is very important to supervise primaquine when possible because of the side effects.
The side effects of primaquine (abdominal pain or gastritis) can be reduced by asking the patient to take the primaquine directly after food (preferably a full meal).

Important Notes

Check *Haematocrit (or haemoglobin)* before giving primaquine if there is concern about hemolysis or anaemia.
Counsel the patient to complete the treatment course [9]. If he/she develops *pallor, dizziness, difficulty breathing* or *other signs of anemia* they should return to the clinic.
Refer to the hospital if a patient develops haematuria or severe anaemia
(Should be admitted to the hospital for transfusion and treatment)

7.4 P. knowlesi and treatment

Recently *P. knowlesi* had been observed to occur in forested regions of SE Asia. *P. knowlesi* is human infection with the monkey malaria parasite and reported mostly in people living close to the natural monkey hosts [35].

Microscopically the young ring stages of *P. knowlesi* resemble *P. falciparum*, but older forms are similar to the band forms of *P. malariae*.

PCR genotyping assays are able to differentiate between these 2 species correctly. Similar to *P. falciparum, P. knowlesi* can reach high parasitaemias rapidly which can be fatal.

Recommended treatment is same as for *P. falciparum* –

for uncomplicated cases ACT (See Page 11)

for severe cases IV artesunate (See Page 16)

7.5 Vomiting

Observe the patient for 1 hour after taking antimalarials, for vomiting. Patients who vomit have a higher risk of drug treatment failure. The best way to give the medicines is to give them as separate doses (e.g. artesunate first and mefloquine second).

Occurs **within 30 minutes**: Repeat the whole dose.
Occurs **between 30 minutes and one hour**: Repeat half the dose

7.6 Allergy

If the documented history of allergy was severe never give the drug again.

QUININE AND CHLOROQUINE:

Try to give alternative drugs e.g. artesunate or artemether. If not available, pre-medicate the patient with dexamethasone (adults 12 mg; children 0.25 mg/kg) or hydrocortisone sodium succinate (adult 2g; children 2 mg/kg) IM/IV, and oral chlorpheniramine (adult 4 mg; children 0.1mg/kg) before starting.

ARTESUNATE:

Artesunate allergy can be severe: use quinine (plus doxycycline or clindamycin) or mefloquine.

7.7 Common serious side effects

MEFLOQUINE:

Neuropsychiatric side-effects remain the most common side-effect. Treat the patient with diazepam if symptoms are severe. Do not repeat mefloquine in these patients.

CLINDAMYCIN:

Antibiotic associated colitis is the most toxic side effect and can be fatal. Explain the risk of developing diarrhoea to the patient before giving the drug. Explain if diarrhoea develops stop the drug immediately. Treat the diarrhoea according to the severity. Severe cases will need IV fluids and metronidazole.

PRIMAQUINE:

Primaquine has 2 common serious side effects: Haemolysis & Methaemoglobinaemia (oxidized form of hemoglobin). Higher risk of haemolysis can be seen in people with G6PD deficiency. Higher risk of methaemoglobinaemia can be seen in some metabolic disorders. If a patient appears cyanotic, has difficulty breathing or headache, this could be due to increased methaemoglobin levels. In this case, stop primaquine dosing and observe the patient daily. If symptoms are severe, refer to a hospital. Symptoms should resolve in approximately 1 week. If a patient has symptoms of haemolysis, refer the patient to a clinic where haemotocrit can be measured. Depending on the severity of symptoms and degree of haemolysis, clinical judgment should be used to make the decision to stop primaquine.

Cautions in prescribing primaquine

The daily primaquine dose of 0.5 mg/kg/day for 14 days for radical cure of *P. vivax* should not be given to persons with G6PD deficient or unknown status.

7.8 Supervision of treatment

All treatment doses should be supervised (if possible).

When 3 days of supervision of treatment is not possible, (e.g. mobile teams) the recommended regimen for confirmed *P. falciparum* malaria is artesunate 4 mg/kg stat followed by MFQ 25 mg/kg stat. The rest of the artesunate is given to the patient with explanation of the importance of completing the full treatment course.

7.9 Treatment of P. falciparum malaria in very young children

Mefloquine and artesunate have been given to very young children (starting 3 months old; 4-5kg). Mefloquine gives less late side-effects in children than in adults. The incidence of vomiting during the first hour after mefloquine intake is very high. Artesunate is very well tolerated. For children less than 3 months of age (or less than 5 kg), or when mefloquine is not tolerated due to vomiting, we recommend 7 days of artesunate (2 mg/kg/daily) + clindamycin (5 mg/kg/TID) for treatment, or to use parenteral treatment for first dose.

Recommendations to give mefloquine to children:

1) Reduce the fever.

2) Wait until the child is calm. Explain to the mother the importance of her help.

3) Crush 1 tablet of mefloquine in 5cc of water and take in a syringe the exact dose.

4) Give the medicine to the child with the syringe.

Do not fight with the child or pinch the nose.

5) Give sugar or breast milk.

6) Supervise 1 hour.

Some children do not tolerate mefloquine.

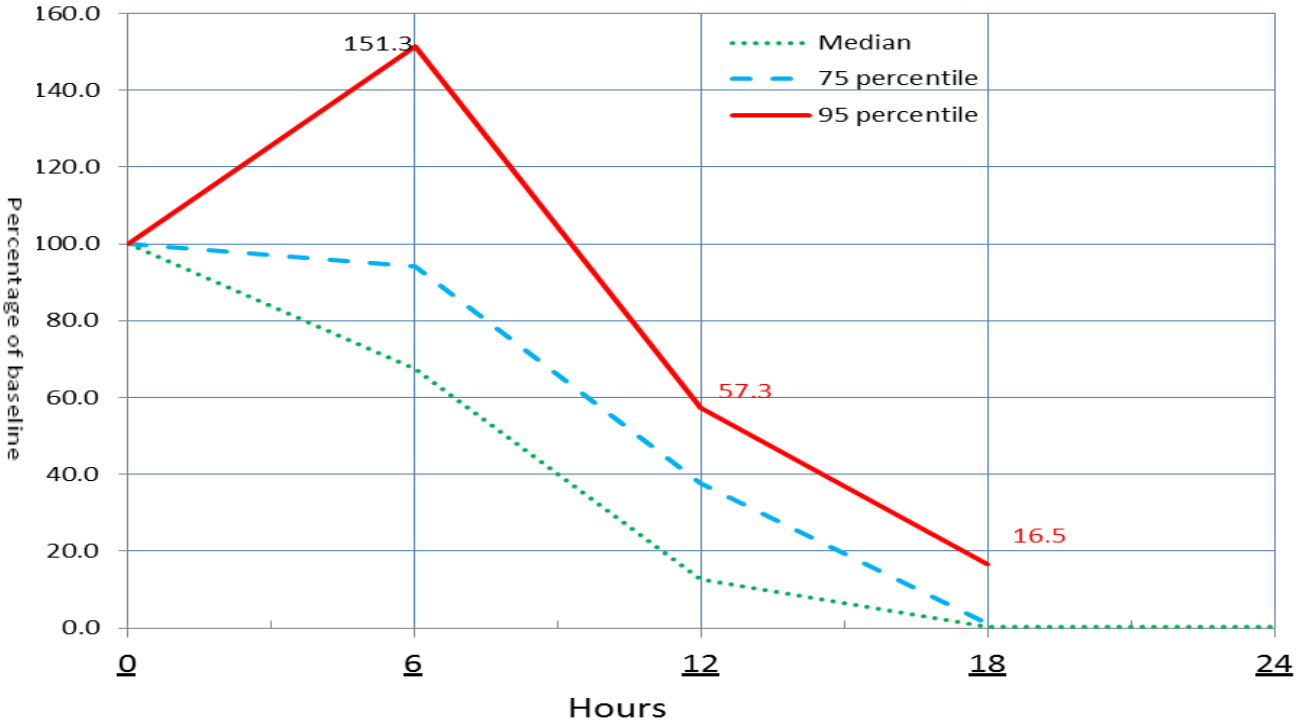
Do not repeat more than twice.

Continue artesunate for a total of 7 days in such cases (4-2-2-2-2-2-2 mg/kg).

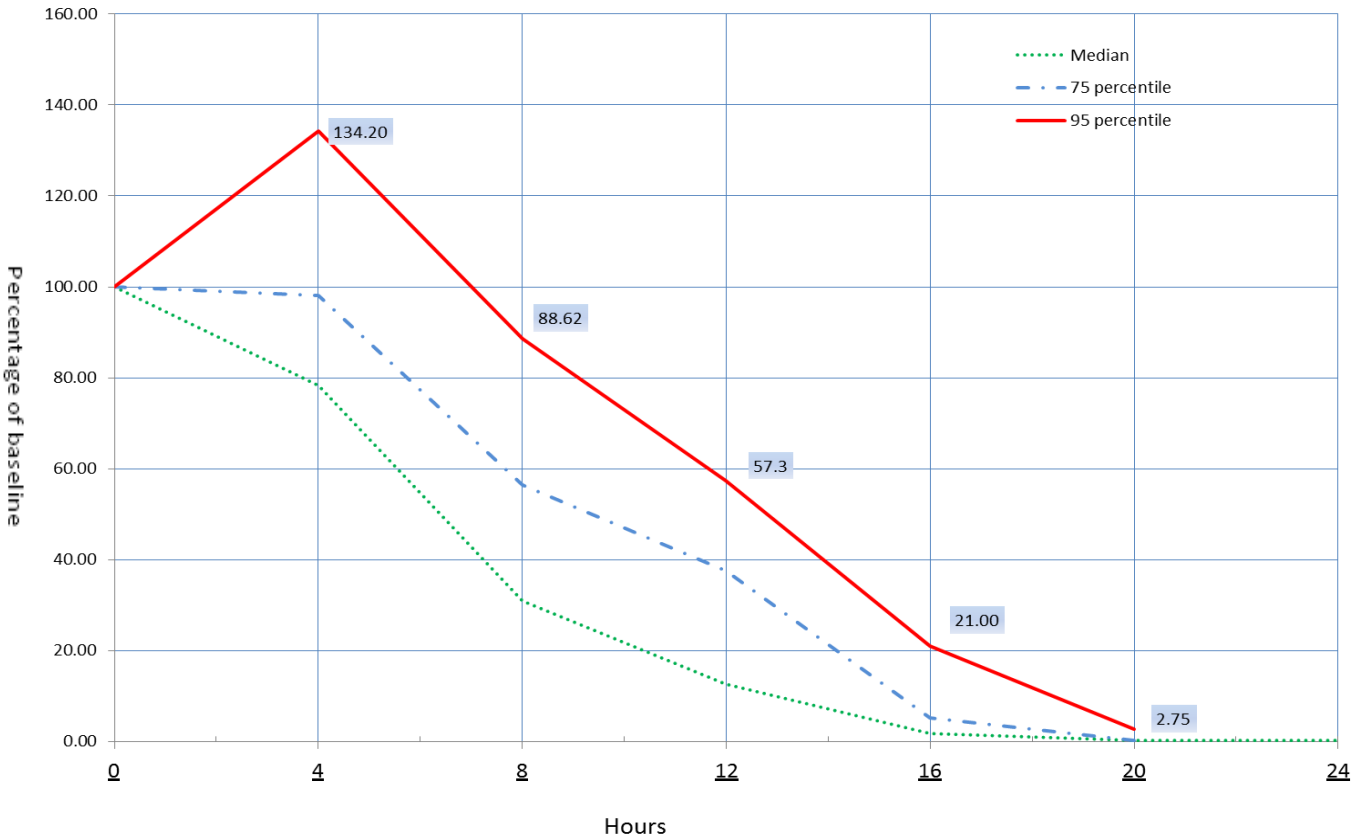
8. Appendix

Appendix .1. Parasite clearance graph to be use in uncomplicated hyperparasitaemia

Monitoring the parasite clearance with 6 hourly malaria smear



Monitoring the parasite clearance with 4 hourly malaria smear



Give parenteral artesunate 1.2 mg/kg if the parasite count crosses the 95 percentile (Red) line.

Appendix .2. Oral artesunate dosing table

1 tablet contains 50 mg

Weight (kg)	4 mg/kg (OD)		2 mg/kg (OD)	
	tab	ml	tab	ml
2		0.8		0.4
3		1.2		0.6
4		1.6		0.8
5		2.0		1.0
6	½	2.4	¼	1.2
7	½	2.8	¼	1.4
8	¾	3.2	¼	1.6
9	¾	3.6	¼	1. 6
10	¾	4.0	½	2.0
11	1		½	
12	1		½	
13 - 14	1		½	
15 - 16	1 ¼		½	
17 - 20	1 ½		¾	
21	1 ¾		¾	
22 - 23	1 ¾		1	
24 - 26	2		1	
27 - 28	2 ¼		1	
29	2 ¼		1 ¼	
30 - 32	2 ½		1 ¼	
33 - 34	2 ¾		1 ¼	
35	2 ¾		1 ½	
36 - 39	3		1 ½	
40	3 ¼		1 ½	
41 - 42	3 ¼		1 ¾	
43 - 45	3 ½		1 ¾	
46	3 ¾		1 ¾	
47 - 48	3 ¾		2	
49 - 51	4		2	
52 - 53	4 ¼		2	
54	4 ¼		2 ¼	
55 - 57	4 ½		2 ¼	
58 - 59	4 ¾		2 ¼	
60	4 ¾		2 ½	
61 - 64	5		2 ½	
65	5 ¼		2 ½	
66 - 67	5 ¼		2 ¾	
68 - 70	5 ½		2 ¾	

A suspension is made by allowing 1 tablet to dissolve in 5ml clean water (1ml=10mg)

Appendix .3. Oral mefloquine dosing table

	Single STAT dose		Split dose in 2 days				Split dose in 3 days	
Weight	25 mg/kg(STAT)		15 mg/kg		10 mg/kg		8 mg/kg(OD)	
(kg)	tab	(ml)	Tab	(or ml)	Tab	(ml)	tab	(ml)
5	½	2.5	¼	1.5	¼	1	½	0.8
6	½	3	¼	1.8	¼	1.2	½	1.0
7	¾	3.5	½	2.1	¼	1.4	¾	1.2
8	¾	4	½	2.4	¼	1.6	¾	1.3
9	1	4.5	½	2.7	½	1.8	1.0	1.5
10	1	5	½	3	½	2	1.0	1.7
11	1	5.5	½	3.3	½	2.2	1.0	1.8
12-14	1 ¼		¾		½		½	
15-16	1 ½		1		½		½	
17-18	1 ¾		1 ¼		½		¾	
19-21	2		1 ¼		¾		¾	
22-23	2 ¼		1 ½		¾		¾	
24-26	2 ½		1 ½		1		1	
27-28	2 ¾		1 ¾		1		1	
29-31	3		1 ¾		1 ¼		1	
32-33	3 ¼		2		1 ¼		1	
34-36	3 ½		2		1 ½		1 ¼	
37-38	3 ¾		2 ¼		1 ½		1 ¼	
39-41	4		2 ½		1 ½		1 ¼	
42-43	4 ¼		2 ½		1 ¾		1 ¼	
44-46	4 ½		2 ¾		1 ¾		1 ½	
47-48	4 ¾		2 ¾		2		1 ½	
49-51	5		3		2		1 ¾	
52-53	5 ¼		3 ¼		2		1 ¾	
54-56	5 ½		3 ¼		2 ¼		2	
57-58	5 ¾		3 ½		2 ¼		2	
59-61	6		3 ½		2 ½		2	
62-63	6 ¼		3 ¾		2 ½		2	
64-66	6 ½		4		2 ½		2 ¼	
67-68	6 ¾		4		2 ¾		2 ¼	
69-71	7		4		3		2 ¼	
72	7 ¼		4 ¼		3		2 ½	
73-77	7 ½		4 ½		3		2 ½	
78	7 ¾		4 ¾		3		2 ¾	
79-81	8		4 ¾		3 ¼		2 ¾	

For the young children, mefloquine can be given by dissolving in sugar water/sweet juices and a suspension is made by allowing 1 tablet to dissolve in 5ml (1ml=50mg), or tablet can be cut and a fraction of tablet is given depending on the compliance.

Appendix .4. DP dosing table

1 adult tablet contains 40mg of dihydroartemisinin and 320 mg piperaquine OR
1 paediatric tablet contains 20 mg of dihydroartemisinin and 160 mg of piperaquine

Weight(kg)	Tab (40 mg DHA)	ml (40 mg DHA)	Tab (20 mg DHA)	ml (20 mg DHA)
5		1.3 ml		2.6 ml
6		1.6 ml		3.2 ml
7		2 ml		4 ml
8-12	0.5		1	
13-20	1.0		2	
21-30	1.5		3	
31-40	2.0			
41-50	2 .5			
51-60	3.0			
61-70	3 .5			
71-84	4.0			
85-100	5.0			

A suspension is made by allowing 1 adult tablet to dissolve in 5ml clean water.

Appendix .5. Artemether-lumefantrine dosing table

1 tablet contains 20mg artemether and 120 mg lumefantrine.

Twice a day

Weight (kg)	tab
≤15	1 per dose
16-25	2 per dose
26-35	3 per dose
>35	4 per dose

Need to take with some fried or oily food or a carton of flavored milk.

Appendix .6. Chloroquine dosing table

1 tablet contains 250 mg chloroquine phosphate (approx. 150 mg base)
Chloroquine phosphate 161mg salt = 100mg base
D0 & D1 10mg/kg D25 mg/kg

Weight (kg)	D0 &D1	D2
3-5	¼	¼
6-9	½	¼
10-11	¾	¼
12	¾	½
13-17	1	½
18-19	1 ¼	½
20	1 ¼	¾
21-25	1 ½	¾
26-27	1 ¾	¾
28	1 ¾	1
29-33	2	1
34-35	2 ¼	1
36	2 ¼	1 ¼
37-41	2 ½	1 ¼
42	2 ¾	1 ¼
43-44	2 ¾	1 ½
45-48	3	1 ½
49-50	3 ¼	1 ½
51-52	3 ¼	1 ¾
53-56	3 ½	1 ¾
57	3 ¾	1 ¾
58-60	3 ¾	2
61-64	4	2
65-66	4 ¼	2
67	4 ¼	2 ¼
68-72	4 ½	2 ¼
73	4 ¾	2 ¼
74-75	4 ¾	2 ½
76-79	5	2 ½
80-82	5 ¼	2 ½

Appendix .7. Primaquine dosing table for *Plasmodium vivax*

0.5 mg/kg/day daily for 14 days

Be careful if the tablet is different than 15 mg. You will need to adjust the dose accordingly!

Give food before dose to prevent abdominal pain and nausea

Suspension

Use this table for **persons <= 17 kg** or if cannot take tablets

1 tablet contains 15 mg. A suspension is made with sugar water and/or Vit C

If you have 7.5 mg tablets, mix one tablet with 2.5 ml sugar water. The daily dose (ml) will be the same

Weight (kg)	# of **15 mg** tablets to mix	Sugar water (ml)	Daily dose (ml)
4	½	5	1.3
5	½	5	1.7
6	½	5	2
7	½	5	2.3
8	½	5	2.7
9	½	5	3
10	½	5	3.3
11	½	5	3.7
12	½	5	4
13	½	5	4.3
14	½	5	4.7
15	1	5	2.5
16	1	5	2.7
17	1	5	2.8

Tablets

Use this table for all **persons ≥ 18 kg** or patients that can take tablets

1 tablet contains either 7.5mg or 15 mg

Use tablet cutter to cut tablets

Weight (kg)	# **7.5 mg** tablets	# **15 mg** tablets
11 -12	¾	Use suspension
13 - 14	¾	½
15 - 17	1	½
18 - 20	1 ¼	¾
21 - 25	1 ½	¾
26 - 33	2	1
34- 40	2 ½	1 ¼
41 - 48	3	1 ½
49 - 56	3 ½	1 ¾
57 - 65	4	2
66 - 80	5	2 ½
81 - 100	6	3

Appendix .8. IV artesunate dosing table

For severe malaria (2.4 mg/kg) 1 vial contains 60 mg artesunate (60 mg/ml)
H0, H12 & h24 2.4 mg/kg and then 2.4 mg/kg every 24 hourly until the patient can tolerate oral medication.

Weight (Kg)	Rescue ml	Severe ml	Weight (Kg)	Rescue ml	Severe ml
2-3	0.1	0.1	42-43	0.9	1.7
4-6	0.1	0.2	44-46	0.9	1.8
7-8	0.2	0.3	47-48	1.0	1.9
9-11	0.2	0.4	49-51	1.0	2.0
12-13	0.3	0.5	52-53	1.1	2.1
14-16	0.3	0.6	54-56	1.1	2.2
17-18	0.4	0.7	57-58	1.2	2.3
19-21	0.4	0.8	59-61	1.2	2.4
22-23	0.5	0.9	62-63	1.3	2.5
24-26	0.5	1.0	64-66	1.3	2.6
27-28	0.6	1.1	67-68	1.4	2.7
29-31	0.6	1.2	69-71	1.4	2.8
32-33	0.7	1.3	72-73	1.5	2.9
34-36	0.7	1.4	74-76	1.5	3.0
37-38	0.8	1.5	77-78	1.6	3.1
39-41	0.8	1.6	79-80	1.6	3.2

For rescue treatment, 1.2 mg/kg STAT dose
A suspension is made by dissolving 1 vial in 1 ml 5% sodium bicarbonate

The solution is light sensitive, prepare directly before injection.
Throw away the excess solution.

Appendix .9. Paracetamol dosing table (tab)

1 tablet contains 500 mg Do not use more than 4 doses a day

Weight (kg)	tab
13-18	½
19-26	¾
27-33	1
34-41	1 ¼
42-48	1 ½
49-56	1 ¾
57 and above	2

Appendix .10. Paracetamol dosing table (suspension)

5ml of paracetamol suspension contain 120 mg First dose 20 mg/kg and then 15 mg/kg

Weight (kg)	First dose (ml)	Following dose (ml)
1.5	1.3	1
2	1.5	1.3
2.5	2	1.5
3	2.5	2
3.5	3	2
4	3.5	2.5
4.5	4	3
5	4	3
5.5	4.5	3.5
6	5	3.5
6.5	5.5	4
7	6	4.5
7.5	6	4.5
8	6.5	5
8.5	7	5.5
9	7.5	5.5
9.5	8	6
10	8.5	6
10.5	9	6.5
11	9	7
11.5	10	7
12	10	7.5

Appendix .11. IM Artemether dosing table (for severe malaria management)

Artemether I.M. (1 ml=80 mg) For doses of =3.2 mg/kg

Weight (Kg)	ml (cc)	Weight (Kg)	ml (cc)
2-3	0.1	44-46	1.8
4-8	0.2	47-48	1.9
9-11	0.4	49-51	2.0
12-13	0.5	52-53	2.1
14-16	0.6	54-56	2.2
17-18	0.7	57-58	2.3
19-21	0.8	59-61	2.4
22-23	0.9	62-63	2.5
24-26	1.0	64-66	2.6
27-28	1.1	67-68	2.7
29-31	1.2	69-71	2.8
32-33	1.3	72-73	2.9
34-36	1.4	74-76	3.0
37-38	1.5	77-78	3.1
39-41	1.6	79-80	3.2
42-43	1.7		

IM Artemether dosing table For doses of 1.6 mg/kg

Weight (Kg)	ml (cc)	Weight (Kg)	ml (cc)
2-3	0.05	43-47	0.9
4-7	0.1	48-52	1.0
8-12	0.2	53-57	1.1
13-17	0.3	58-62	1.2
18-22	0.4	63-67	1.3
23-27	0.5	68-72	1.4
28-32	0.6	73-77	1.5
33-37	0.7	78-80	1.6
38-42	0.8		

Appendix .12. Oral quinine dosing table (tablet)

1 tablet contains 300 mg quinine sulphate (salt)
10 mg salt/kg TID (30 mg salt/kg/d) x 7 days

Weight (Kg)	Tab	Frequency
15-18	½	TID
19-26	¾	TID
27-33	1	TID
34-41	1 ¼	TID
42-48	1 ½	TID
49-56	1 ¾	TID
57-63	2	TID
64-71	2 ¼	TID
72-78	2 ½	TID
79-86	2 ¾	TID

Appendix .13. Oral quinine dosing table (for young children)

1 ml suspension contains 60 mg quinine sulphate (salt)

Weight (Kg)	Suspension (ml)	Frequency
4	0.7	TID
5	0.8	TID
6	1.0	TID
7	1.2	TID
8	1.3	TID
9	1.5	TID
10	1.7	TID
11	1.8	TID
12	2.0	TID
13	2.2	TID
14	2.3	TID

A suspension is made by allowing 1 tablet to dissolve in 5ml clean water

Appendix .14. Quinine infusion table

1 vial of Quinine 2ml = 600 mg

IV fluid using metroset or burette: 1ml = 60 drops

Use D10W for pregnant women and children

Loading dose = 20mg/kg Maintenance dose = 10 mg/kg

Weight Kg	From H0 until H4 Quinine Loading dose Check dextrose hourly		H8 until H10 Quinine Maintenance dose		H16 to H18 Quinine Maintenance dose Continue IV Quinine 8 hourly if cannot take oral	
	Amount of Quinine in IV fluid	drop/min	Amount of Quinine in IV fluid	drop/min	Amount of Quinine in IV fluid	drop/min
4 - 5	0.3 ml in 10 ml	3 d/min or Use syringe driver	0.15 ml in 10 ml	3 d/min or Use syringe driver	0.15 ml in 10 ml	3 d/min or Use syringe driver
6	0.4 ml in 20 ml	5 d/min or Use syringe driver	0.2 ml in 10 ml	5 d/min or Use syringe driver	0.2 ml in 10 ml	5 d/min or Use syringe driver
7-9	0.6 ml in 50 ml	12 d/min	0.3 ml in 25 ml	12 d/min	0.3 ml in 25 ml	12 d/min
10-12	0.8 ml in 75 ml	18 d/min	0.4 ml in 40 ml	20 d/min	0.4 ml in 40 ml	20 d/min
13-15	1 ml in 100 ml	25 d/min	0.5 ml in 50 ml	25 d/min	0.5 ml in 50 ml	25 d/min
16-18	1.2 ml in 125 ml	31 d/min	0.6 ml in 65 ml	32 d/min	0.6 ml in 65 ml	32 d/min
19-21	1.4 ml in 150 ml	37 d/min	0.7 ml in 75 ml	37 d/min	0.7 ml in 75 ml	37 d/min
22-24	1.6 ml in 200 ml	50 d/min	0.8 ml in 100 ml	50 d/min	0.8 ml in 100 ml	50 d/min
25-27	1.8 ml in 250 ml	62 d/min	0.9 ml in 125 ml	62 d/min	0.9 ml in 125 ml	62 d/min
28-31	2 ml in 250 ml		1 ml in 125 ml		1 ml in 125 ml	
32-34	2.2 ml in 250 ml		1.1 ml in 125 ml		1.1 ml in 125 ml	
35-37	2.4 ml in 250 ml		1.2 ml in 125 ml		1.2 ml in 125 ml	
38-40	2.6 ml in 250 ml		1.3 ml in 125 ml		1.3 ml in 125 ml	
41-43	2.8 ml in 250 ml		1.4 ml in 125 ml		1.4 ml in 125 ml	
44-46	3 ml in 250 ml		1.5 ml in 125 ml		1.5 ml in 125 ml	
47-49	3.2 ml in 250 ml		1.6 ml in 125 ml		1.6 ml in 125 ml	
50-52	3.4 ml in 250 ml		1.7 ml in 125 ml		1.7 ml in 125 ml	
53-55	3.6 ml in 250 ml		1.8 ml in 125 ml		1.8 ml in 125 ml	
56-59	3.8 ml in 250 ml		1.9 ml in 125 ml		1.9 ml in 125 ml	
>59	4 ml in 250 ml		2 ml in 125 ml		2 ml in 125 ml	

Appendix .15. Clindamycin dosing table

Clindamycin cap (150 mg) 5 mg/kg TID for 7 days

Weight(Kg)	Capsule (for 150 mg)	Frequency
< 35	1	TID
35 - 69	2	TID
> 69	3	TID

Appendix .16. Doxycycline dosing table

One capsule (cap) is 100mg; capsules cannot be split or broken
Contraindication: <8 years old and pregnant woman
Dose given once a day for 7 days (4 mg/kg/day)

Weight (Kg)	Nearest cap	Frequency
15 - 37	1	OD
38 - 62	2	OD
> 62	3	OD

Appendix .17. Primaquine dosing table for Plasmodium falciparum

Single dose

Be careful if the tablet is different than 15 mg. You need to adjust the dose accordingly!

Give food before dose to prevent abdominal pain and nausea

Low dose (0.25 mg/kg stat dose)

Use this table for all persons ≤ 17 kg or if cannot take tablets.

If you have 7.5 mg tablets, use the same # tablets in the chart. Mix with 1.25 ml sugar water. The single dose (ml) will be the same.

A suspension is made by allowing 1 tablet to dissolve in 5 ml sugar water and/or Vit C.

Weight (kg)	# of 15 mg tablets to mix with sugar water	mix with ml (sugar water)	Dose (ml)
5	½	2.5	0.5
6	½	2.5	0.5
7	½	2.5	0.6
8	½	2.5	0.7
9	½	2.5	0.8
10	1	2.5	0.5
11 - 12	1	2.5	0.5
13 - 14	1	2.5	0.6
15 - 17	1	2.5	0.7

*Give food before dose to prevent abdominal pain and nausea.

Single dose

Use this table for all persons ≥ 18 years or patients that can take tablets
1 tablet contains either 7.5mg or 15 mg.
Use tablet cutter to cut tablets.

Weight (kg)	# 15 mg tablets	Range mg(total)/kg
18 - 22*	¾	(0.31-0.26)
23 - 30	1	(0.33-0.25)
31 - 37	1 ¼	(0.3-0.25)
38 - 45	1 ½	(0.3-0.25)
46 - 52	1 ¾	(0.29-0.25)
53 - 60	2	(0.28-0.25)
61 - 67	2 ¼	(0.28-0.25)
68 - 75	2 ½	(0.28-0.25)
76 -82	2 ¾	(0.27-0.25)
83 - 90	3	(0.27-0.25)

* if person is 16-17 kg and you give ½ tablet of a 15mg tablet, the dose will be approximately 0.5 mg/kg thus, consider using suspension or try to give 1/3 tablet.

Appendix .18. Ferrous sulphate suspension dosing (<10kg)

Weight (kg)	Dose (mg elemental iron)	ml TID
1	2	0.1
2	4	0.2
3	6	0.2
4	8	0.3
5	10	0.4
6	12	0.5
7	14	0.6
8	16	0.6
9	18	0.7
10	20	0.8

Appendix .19. Ferrous sulphate and folic acid dosing (for anaemia patient)

Age group	Ferrous sulphate	Folic acid
Adult	1 TID	5mg OD
>12 year	1 BID/TID	5 mg OD
5-12 Year	1 ½ OD	5 mg OD
1-5 year	1 OD	5 mg OD
<1 year	½ OD	0.5 mg/kg daily
Child under 10 kg (if suspension available) please see dosing table(above).		

Appendix .20. Table for maintenance fluid amount and rate

Weight (kg)	Drops per minute via metroset
4	17
5	21
6	25
7	29
8	33
9	38
10	40
11	42
12	44
13	46
14	48
15	50
16	52
17	54
18	56
19	58
20	60
21 – 25	65
26 - 30	70
31 – 35	75
36 – 40	80

2 litres per day = **28 drops per minute** with normal giving set
3 litres per day = **42 drops per minute** with normal giving set

If an infant or child has signs of dehydration increase the amount per hour by 10%

Appendix .21. Glasgow Coma Scale (GCS) & Blantyre Coma Scale(BCS)

The **New** Glasgow coma scale: the **new** GCS is now out of 15 – the motor is out of 6.

	1	2	3	4	5	6
Eyes	Does not open eyes	Opens eyes in response to painful stimuli	Opens eyes in response to voice	Opens eyes spontaneously	N/A	N/A
Verbal	Makes no sounds	Incomprehensible sounds	Utters inappropriate words	Confused, disoriented	Oriented, converses normally	N/A
Motor	Makes no movements	Extension to painful stimuli	Abnormal flexion to painful stimuli	Flexion / Withdrawal to painful stimuli	Localizes painful stimuli	Obeys Commands

Unrousable coma is reached at a score of <10. This scale can be used repeatedly to assess improvement or deterioration.

AVPU is also a good quick emergency assessment A = alert

V = responds to voice

P = responds to pain

U = unrousable

A coma scale for children - Blantyre coma scale

The following coma scale – the "Blantyre coma scale" – modified from the widely used Glasgow coma scale (1974), is applicable to children, including those who have not learned to speak.

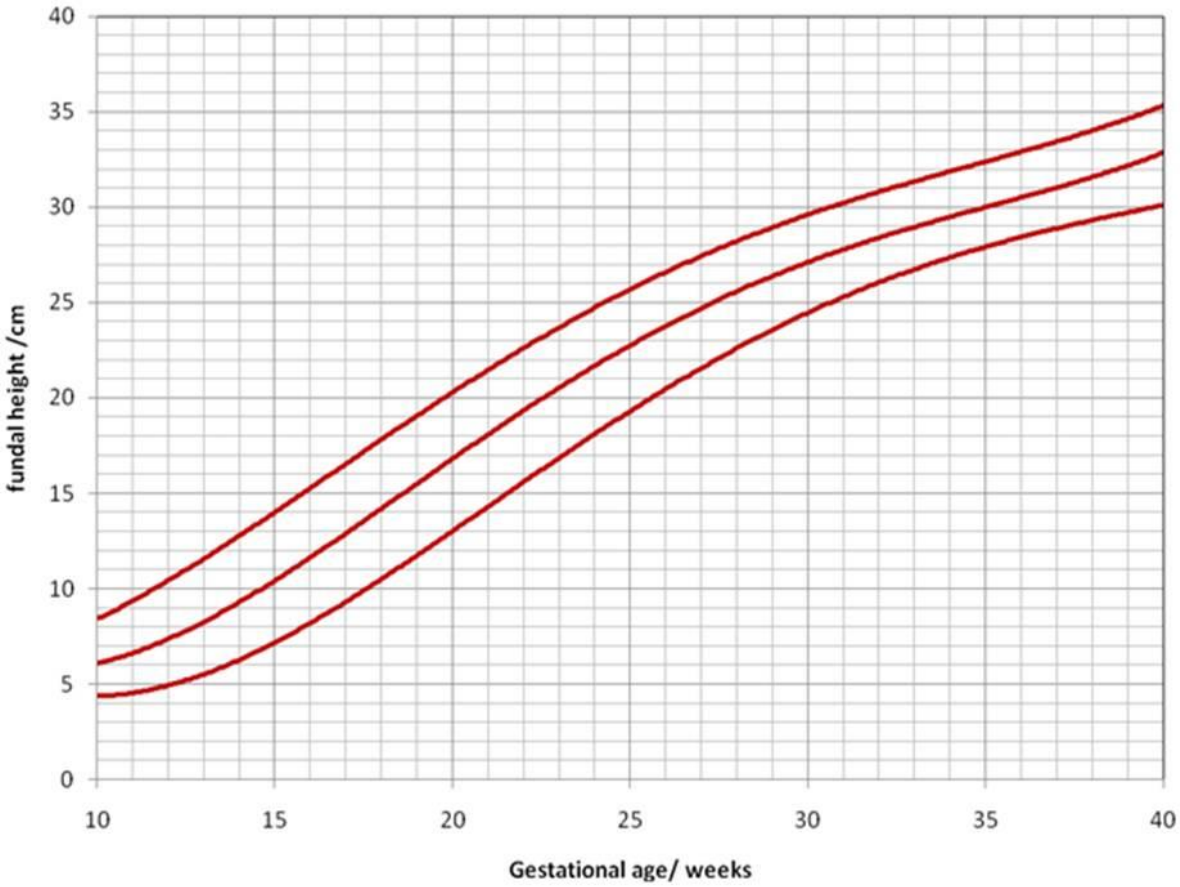
		Score
Best motor response:	Localizes painful stimulus [a] Withdraws limb from pain [b] Nonspecific or absent response	2 1 0
Verbal response:	Appropriate cry Moan or inappropriate cry None	2 1 0
Eye movements:	Directed (e.g. follows mother's face) Not directed	1 0
	Total	0–5

A state of unrousable coma is reached at a score of <3. This scale can be used repeatedly to assess improvement or deterioration.

[a] Rub knuckles on patient's sternum. [b]Firm pressure on thumbnail bed with horizontal pencil.

Appendix .22. Karen pregnant women gestation by fundal height

The 10th, 50th and 90th centiles for Karen and Burmese women [36].



FUNDAL HEIGHT in CM	EGA IN WEEKS	FUNDAL HEIGHT in CM	EGA IN WEEKS
4	8.1	19	21.6
5	9.3	20	22.5
6	10.4	21	23.4
7	11.4	22	24.4
8	12.3	23	25.4
9	13.2	24	26.4
10	14.1	25	27.5
11	15.0	26	28.6
12	15.8	27	29.9
13	16.6	28	31.2
14	17.4	29	32.6
15	18.3	30	34.2
16	19.1	31	36.0
17	19.9	32	38.0
18	20.8	33	40.4

Fundal height is measured from the top of the pubic symphysis to the top of the fundus (after the woman has emptied her bladder)

This table has been produced for refugee and migrant women on the Thai-Burmese border.
Pregnant women who had a crown-rump fetal length measured (<60 mm)
by ultrasound, and delivered within +/- 5 days of their expected date of delivery, were included.

Appendix .23. Coma Management STEPS: A to K

A – Airway? – open the airway

B – Is this patient **B**reathing? - look, listen and feel

C – Circulation - Does this patient have a pulse? Assess the pulse

D – Diagnosis of Hypoglycaemia and Malaria.

Perform an urgent: Paracheck or Malaria smear (MS) and blood glucose

– Hypoglycaemia = < 2.2 mmol/l; < 40 mg/100ml and treat if necessary;

5ml/kg of 10% dextrose (D10W) in 10 mins (repeat blood glucose in 30 mins)

- Malaria positive Paracheck or MS: IV artesunate 2.4 mg/kg stat

Evaluate for meningitis, such as stiff neck: if present consider performing a lumbar puncture and start IV antibiotics .-Do not perform a lumbar puncture if there are signs of raised intracranial pressure such as unequal pupil size, non reactive pupils, a very slow heart rate (<50 in adults) or irregular breathing. If you cannot perform a lumbar puncture but you are concerned about meningitis start antibiotics

Fitting? Observe for convulsion, these may be very subtle. Convulsions should be treated.

GCS, **G**lucose and **G**eneral Observations

Hourly observations until the patient is stable and then every four hours,

GCS or BCS – conscious level

Blood glucose

Pulse rate

Respiratory rate

Blood pressure – consider shock

Hydration: Monitor and record fluid input and output. A urinary catheter should be inserted.

If urine output is less than 0.5ml/kg/hr or there are signs of dehydration a fluid bolus should be considered. This can be repeated to a maximum of 2L in an adult and 40ml/kg in a child. Observe for signs of oedema, auscultate the chest for crepitations (pulmonary oedema), if present administering furosemide (1mg/kg)

NSS, initially 1L in adults, 20ml/kg in children

Increasing parasitaemia? Monitor parasitaemia 6-12 hourly until negative

Just confirm haemoglobin or haematocrit(haemoglobin) every 24 hours

Keep caring - Follow good nursing care (position, eyes, clean, NG, food?)

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