MALARIA

Introduction

- It is a communicable diseases caused by sporozoan of the genus *Plasmodium*
- *There are four species;*
  - *Plasmodium falciparum; self limited, last about 1 yr if untreated but has high mortality rate; its fever recurs after every 2 days*
  - *Plasmodium vivax; fever lasts for three yrs if untreated*
  - *Plasmodium malariae*
  - *Plasmodium ovale*

Life history of the parasite; two cycles

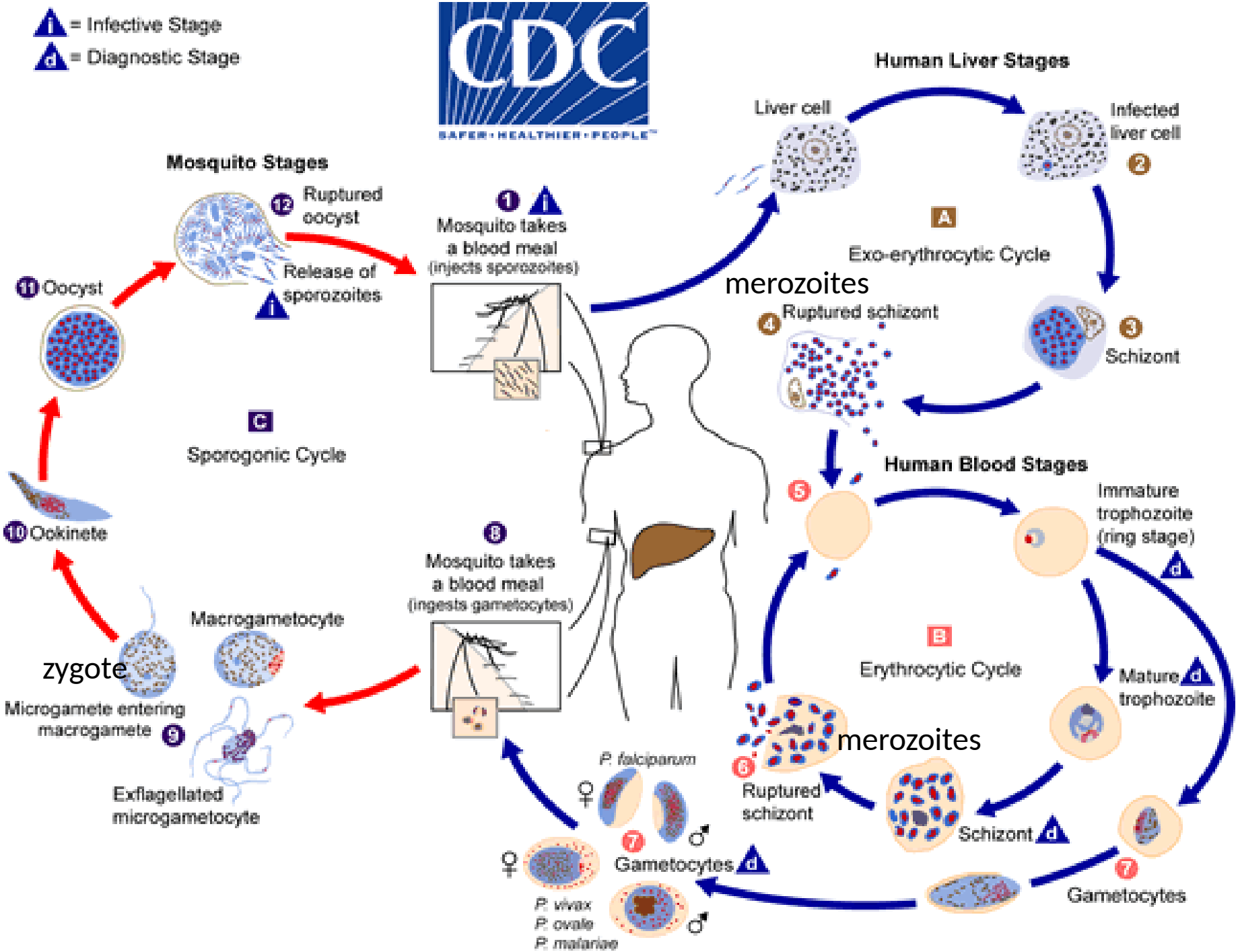
Sexual cycle

Takes place in mosquito

- Some **merozoites** instead of repeating the cycle, **grow into male and female gametocytes**
- The gametocytes are **ingested by mosquitoe** during sucking of blood into stomach
- Male gametes **impregnate female gamete forming zygote** which is motionless
- Zygote **begin to move after 12 to 18 hrs hence called ookinete**. It penetrates the mosquito stomach wall forming oocyst on its outer surface
- It grows rapidly and ruptures releasing sporozoites which migrate into salivary glangs of the mosquito and become infective to human

Asexual cycle; in the human blood stream

- Infected mosquito bites human and injects sporozoites
- Some are are destroyed but others reach the liver
- After 1 to 2 weeks, they become hepatic schizonts which bursts releasing merozoites that enter blood stream (extra erythrocytic phase). This phase is delayed in P. vivax and when taking antimalarials
- Most merozoites are destroyed but afew penetrate RBCs and pass through the stage of trophozoites and schizonts (erythrocytic phase)
- The schizonts release merozoites that either infect new RBCs completing erythrocytic stage or grow into male and female gametocytes


i = Infective Stage
d = Diagnostic Stage
CDC
SAFER·HEALTHIER·PEOPLE™
Human Liver Stages
Liver cell
Infected liver cell
2
A
Exo-erythrocytic Cycle
merozoites
4 Ruptured schizont
3 Schizont
Human Blood Stages
5
Immature trophozoite (ring stage)
d
Mature trophozoite
B
Erythrocytic Cycle
6 Ruptured schizont
merozoites
Schizont
7 Gametocytes
Gametocytes
P. falciparum
P. vivax
P. ovale
P. malariae
8 Mosquito takes a blood meal (ingests gametocytes)
Macrogametocyte
zygote
Microgamete entering macrogamete
9
Exflagellated microgametocyte
10 Ookinete
11 Oocyst
C
Sporogonic Cycle
12 Ruptured oocyst
Release of sporozoites
Mosquito Stages
1 i Mosquito takes a blood meal (injects sporozoites)

Malaria cont’

- **Communicability;**
  - P. vivax; 4 to 5 days after appearance of sexual forms
  - P. falciparum; 10 to 12 days
- **Vector;**
  - Female anopheles mosquitoe
- **Mode of transmission**
  - Bite of female Anopheles mosquitoe
  - Direct transmission during transfusion of blood/plasma
  - Congenital malaria
- **Incubation ; btn bite and first attack of fever**
  - P. falciparum; 12 days
  - P. vivax; 13 to 15 days
  - P. malariae; 1 month

Host factors

- Men are exposed than females
- People with sickle cell traits usually have milder illness
- More common in less developed countries and movement population
- Man has no natural immunity
- It common during or immediately after rainy seasons, in temp 20 to 30 degrees, humidity of 60%

Attack of malaria occurs in three stages;

- **Cold stage**; sudden onset of fever and chills which lasts for 15 minute an hour
- **Hot stage**; temperature rises up to 41 degrees with headache which lasts for 2 to 6 hours
- **Sweating stage**; fever comes down by profuse sweating

Malaria cont’

- Severe malaria is most commonly caused by infection, with *Plasmodium falciparum*
- Recognizing and promptly treating uncomplicated malaria prevents complicated malaria

Who is at risk of Malaria?

- In high-transmission areas, the risk for severe falciparum malaria is greatest among **young children** and **visitors (of any age) from non endemic areas**.
- In other areas, severe malaria is more evenly distributed across all age groups.
- Risk is **increased in the second and third trimesters of pregnancy**, in patients with **HIV/AIDS** and in people who have undergone **splenectomy**

Presentation of uncomplicated malaria in children

- **Fever** is common – irregular, may be absent
- **Chills**
- **Headache**, body aches and pains elsewhere
- **Abdominal pain and diarrhoea**
- **Irritability,** refusal to eat and vomiting.
- On physical examination, the **liver and spleen** are palpable.

Presentation of Severe /complicated malaria

Severe malaria is defined by clinical or laboratory evidence of vital organ dysfunction.

- **Impaired consciousness** – Un rousable coma (GCS)
- **Prostration** – generalized weakness such that child is unable to sit, walk, stand, feed without assistance
- **Multiple convulsions** – more than 2 in 24 hrs
- Deep breathing and **respiratory distress**, **pulmonary edema**
- Circulatory collapse – **shock** – systolic BP below 50
- **Acute kidney injury**
- **Clinical jaundice**

Lab Findings

- Hypoglycemia – Below 2.0mmol/l
- Severe normocytic anemia – Hb below 5g/dl and PCV below 15%
- Hemoglobinuria
- Hyperlactatemia
- Impaired renal functions – creatinine elevated(acute kidney injury)
- Radiology – Pulmonary edema

Parasitological diagnosis of severe falciparum malaria

- Microscopy is the gold standard and preferred option for diagnosing malaria.
  - Thick a blood films will reveal malaria parasites. the greater the parasite density, the higher the likelihood that severe disease is present.
    - Nevertheless, parasites in severe falciparum malaria are usually sequestered in capillaries and venules (and therefore not seen on a peripheral blood slide), patients may present with severe malaria with very low peripheral parasitaemia.

Parasitology cont’

- Where microscopy is unavailable , **a rapid diagnostic test (RDT)** should be used.
  - RDTs detects *HRP2* antigen
  - Can be useful for diagnosing malaria in patients who have recently received antimalarial treatment and in whom blood films are transiently negative for malaria .
  - It does not provide information on parasite density or the stage of malaria parasites,

Management of Complicated/ severe malaria

The commonest, most important complications of *P. falciparum* infection in children are;

1. Cerebral malaria,
2. Severe anaemia,
3. Respiratory distress (acidosis) and
4. Hypoglycaemia.
5. Shock

In all cases of severe malaria**, parenteral antimalarial chemotherapy should be started immediately**.

History

- The parents or other relatives should be questioned about:
  - Residence and history of travel;
  - Previous treatment with antimalarial or other drugs;
  - Recent fluid intake and urine output; and
  - Recent or history of convulsions.

Initial assessment of severe malaria

- Level of consciousness (coma scale for children)
- Evidence of seizures
- Posturing (decorticate, decerebrate or opisthotonic), which is distinct from seizures
- Rate and depth of respiration;
- Presence of anaemia
- Pulse rate and blood pressure - low
- State of hydration - dehydration
- Capillary refill time - prolonged
- Temperature – fever(can be absent)

Immediate laboratory tests

- Thick and thin blood films or RDT if microscopy is not immediately possible or feasible
- PCV (haematocrit)
- Blood glucose level
- Analysis of cerebrospinal fluid (CSF; lumbar puncture).
- Blood culture where feasible

Only the results of a lumbar puncture can rule out bacterial meningitis in a child with suspected cerebral malaria. If lumbar puncture is delayed, antibiotics must be given to cover the possibility of bacterial meningitis.

Emergency measures

- Check that the airway is patent; if necessary, insert an oropharyngeal airway
- Provide oxygen for children with proven or suspected hypoxia (oxygen saturations < 90%). E.g those with seizures, severe anaemia and those with impaired perfusion (delayed capillary refilling time, weak pulse or cool extremities).
- Nursing :
  - Lay the child in the lateral or semi-prone position, turn them frequently (every 2h) to prevent pressure sores, and provide prospective catheterization to avoid urinary retention and wet bedding.

Cerebral malaria

Clinical features

- The earliest symptom fever (37.5–41℃) and failure to eat or drink
- Headache, confusion, irritable
- Convulsions followed by a coma that persists for more than 30min after the convulsion. (peds GCS)
  - Convulsions can be obvious and others may present in a less noticeable way - nystagmus, salivation, minor twitching of a single digit or a corner of the mouth, an irregular breathing and sluggish pupillary light reflexes.
  - Rule out other possible causes of convulsions – febrile seizures, treat hypoglycaemia

- Prostration (inability to sit unsupported in children ≥ 8 months or inability to breastfeed if younger

- **Abnormal motor posturing** is often observed in children with cerebral malaria, it may be associated with raised intracranial pressure and recurrence of seizures e.g opisthotonus is seen which may lead to a mistaken diagnosis of tetanus or meningitis.
- **Papilledema and retinal hemorrhage**
- **CSF opening pressure is usually raised** (mean, 160mm) in children with cerebral malaria.

- **Deep breathing (increased work of breathing, without s pulmonary infection -** sign of metabolic acidosis.
- **Signs of impaired perfusion** (delayed capillary refilling > 2s, cool hands and/or feet or weak pulse)are common. Moderate hypotension (systolic BP 70–80mm Hg
- **Leukocytosis -** not always due to bacterial infection.

NB - Between 5% and 30% of children who survive cerebral malaria have some **neurological issues -** ataxia, hemiparesis, speech disorders, behavioural disturbances, hypotonia or epilepsy. This develops several weeks or months after the initial illness.

Management of Cerebral Malaria

- Emergency measures, (ABC approach)
- **MX of convulsions-** Always set up a IV line. The most commonly available drug is diazepam; newer-generations(e.g. midazolam, lorazepam) are associated with a lower f respiratory depression. –– Wait 10min after giving diazepam. If the convulsions persist, give a second dose. Do not give more than two doses in 12hrs.
- Diazepam is poorly absorbed intramuscularly and should be given intravenously or rectally. –– If the convulsions persist after two doses of diazepam, give a loading dose of phenytoin or phenobarbitone if it is the only available option

- Check for respiratory depression and if present, provide ventilatory/ breathing support.
- Check and treat for hypoxia ($PaO_2 < 90\%$). If a pulse oximeter is not available, oxygen should still be given, especially for prolonged convulsions.
- Children with cerebral malaria may also have anaemia, respiratory distress (acidosis) and hypoglycaemia and should be managed accordingly.

Anaemia

Severe anaemia is the leading cause of death in children with malaria.

In chronic anaemia, physiological adaptation occurs

Severe anaemia develops rapidly after infections with high parasite densities, acute destruction of RBCs s is responsible for the anaemia

SIGNS INCLUDE;

- Pallor
- Tachycardia and dyspnoea.
- Confusion and restlessness;
- Signs of acidosis (deep breathing)
- Cardiopulmonary signs (cardiac failure), and pulmonary oedema
- Hepatospleenomegaly
- Jaundice
- Hemoglobinuria – dark urine

Management of Anemia

- Assess the need for blood transfusion -PCV(haematocrit), Hb, density of parasitaemia and the clinical condition of the patient must be taken into account.

Indication for blood transfusion include;

- In High-transmission settings,
  - Haematocrit of ≤ 12% or a
  - Haemoglobin concentration **of ≤ 4g/dl** is an,
- In low-transmission settings
  - A threshold of 20% haematocrit or
  - Hb of 7g/dl, i s recommended for transfusion
- In children with less severe anaemia (Hb of 4–6g/dl),
  - Transfusion should be considered for those with respiratory distress (acidosis), impaired consciousness, hyperparasitaemia , shock or heart failure

- The sicker the child, the more rapidly the transfusion must be given.
- A diuretic is **usually not indicated**, due to hypovolaemia. But if there is clinical evidence of fluid overload (signs are an enlarged liver; gallop rhythm, fine crackles at lung bases and/or fullness of neck veins when upright)- GIVE furosemide IV
- Follow-up of haemoglobin (haematocrit) levels after blood transfusion is essential. Many children require a further transfusion within the next few hours, days

Respiratory distress (acidosis)

Clinical features

- Deep breathing, with chest indrawing, suggests metabolic acidosis.
  - Acidosis commonly accompanies cerebral malaria, severe anaemia, hypoglycaemia and features of impaired tissue perfusion.
- Anaemic child with respiratory distress is due to acidosis, resulting from tissue hypoxia, often associated with hypovolaemia.

In many of these cases, respiratory distress is associated with an increased risk for death.

Management of Respiratory distress

- If the facilities are available, measure blood gases and arterial pH and continue to monitor oxygenation by oximetry (SPO2)
- Correct any reversible cause of acidosis, in particular dehydration and severe anaemia.
  - Intravenous infusion is best, at the most accessible peripheral site. If this is impossible, give an intra-osseous infusion . Take care not to give excessive fluid, as this may precipitate pulmonary oedema
- Monitor the response by continuous clinical observation supported by repeated measurement of acid–base status, haematocrit or Hb and glucose, urea and electrolyte levels.

Hypoglycaemia

Clinical features

- Owing to increased metabolic demands and limited glycogen stores(poor feeding), **hypoglycaemia (blood glucose < 2.2mmol/l**) is particularly common in children under 3 years especially those with under-nutrition and in those with coma, metabolic acidosis (respiratory distress) or impaired perfusion.
- Hypoglycaemia should also be considered in children with convulsions or hyperparasitaemia.
- Hypoglycaemia is easily overlooked clinically because the manifestations may be similar to those of cerebral malaria
- Children who are receiving a blood transfusion or who are not able to take oral fluids are at higher risk for hypoglycaemia and should be carefully monitored

Management

- Hypoglycaemia (below 3mmol/l) should be corrected Using parenteral dextrose, immediately give **5ml/kg of 10% dextrose through a peripheral line, followed by a slow intravenous infusion of 10% or 5%**
  - If only 50% dextrose is available, dilute 1 volume of 50% dextrose with 4 volumes sterile water to get 10% dextrose).
- Not recommended to directly give hypertonic glucose (20% - 50%) as it is irritant to veins.
- **If the IV route is not feasible, intra-osseous access** should be attempted.
  - **If this fails, give 1ml/kg body weight of 50% dextrose—or a sugar solution** (4 level tea spoons of sugar in 200ml of clean water) through a nasogastric tube.
  - **Alternatively sugar may be given into the sublingual space**. Check glucose levels after 30min.

Shock

Clinical features

- **Signs of impaired perfusion are common** (capillary refilling time > 2s, cool hands and/or feet). Moderate **hypotension** (systolic blood pressure < 70mm Hg)

Management

- Correct hypovolemia with maintenance fluids **at 3–4ml/kg per hour.**
- Take blood for culture, and start the patient on appropriate broad-spectrum antibiotics immediately.

Dehydration and electrolyte disturbance

Clinical features

- Severe dehydration may complicate severe malaria and may also be associated with signs of decreased peripheral perfusion, raised blood urea (> 6.5mmol/l; > 36.0mg/dl) and metabolic acidosis.
- Caused by reduced oral intake , vomiting and fever

Management

- Children with severe dehydration should be given rapid IV rehydration **with IV Ringer's lactate followed by oral rehydration therapy.**
- If Ringer's lactate is not available, normal saline solution (0.9% NaCl) can be used.
  - 5% glucose (dextrose) solution on its own is not effective and should not be used.
- **After rehydration, acute kidney injury should be suspected if the urine output remains low and signs of fluid overload (pulmonary oedema, edema, increasing hepatomegaly) - give furosemide IV**
- Monitor electrolytes and renal functions

Children unable to retain oral medication

- As a delay in effective treatment for malaria may eventually result in severe malaria, **such children should be admitted and treated with parenteral antimalarial agents** or, when not possible, given pre-referral antimalarial treatment and referred to a centre where the appropriate supportive management can be provided until the child is able to tolerate oral medication.

Post discharge follow-up of children with severe malaria

- Severe anaemia and neurological complications are important causes of mortality immediately after treatment for severe malaria. It is recommended that children be **followed up on days 7, 14 and 28** (1 month) after discharge to monitor haemoglobin recovery.
- Persistent neurological monitoring will require a longer follow-up.

Antimalarial drugs

- Uncomplicated malaria – **Oral drugs** (Artemether based drugs) for AL
  - Child weighing 5 – < 15 kg: one tablet twice a day for 3 days
  - Child weighing 15–24 kg: 2 tablets twice a day for 3 days
  - Child > 25 kg: 3 tablets twice a day for 3 days

Complicated malaria

- Antimalarial drugs should be given **parenterally for a minimum of 24h and replaced by oral medication as soon as it can be tolerated**. Weigh the patient, and calculate the dose of malaria
- For children, the **recommended treatment is artesunate at 2.4mg/kg body weight given intravenously or intramuscularly at admission (time = 0), then at 12h, 24h, then once a day**.

- **Artemether or quinine is an acceptable alternative if parenteral artesunate is not available**:
  - Artemether at 3.2mg/kg body weight IM given at admission, then 1.6mg/kg body weight per day
  - Quinine at 20mg salt/kg body weight at admission (intravenous infusion or diluted divided IM injection), then 10mg/kg body weight every 8h;
    - The infusion rate should not exceed 5mg salt/kg body weight per hour.
    - Intramuscular injections should be given into the anterior thigh and *not* the buttock.

Note;

- Do not attempt to give oral medication to unconscious children;
  - If parenteral injection is not possible and referral is likely to be delayed, suppositories containing artesunate or any artemisinin should be administered as pre-referral treatment, while all efforts are made to transfer the child to a centre where appropriate care can be provided.
  - If these routes are not possible, artemisinin-based combination therapy can be crushed and given by nasogastric tube. Nasogastric administration may, however, cause vomiting and result in inadequate drug levels in the blood.
  - May also give IM loading dose

Common errors in diagnosis and management

Errors in diagnosis

- failure to consider a diagnosis of malaria in a patient with either typical or atypical illness
- failure to elicit a history of exposure (travel history),including travel within a country with variable transmission
- Misjudgement of severity of malaria
- failure to do a thick blood film
- missed hypoglycaemia

- Failure to diagnose alternative or associated infections (bacterial, viral), especially in an endemic area with high transmission
- Misdiagnosis: making an alternative diagnosis in a patient who actually has malaria (e.g. influenza, encephalitis, meningitis, pneumonia)
- Failure to recognize respiratory distress (metabolic acidosis)
- Failure to conduct an ophthalmoscopic examination for the presence of papilloedema and malarial retinopathy

Errors in management

- Delay in starting antimalarial therapy this is the most serious error, as delays in starting treatment may be fatal.
- Inadequate nursing care
- Incorrectly calculated dosage of antimalarial medicines
- Inappropriate route of administration of antimalarial agents
- intramuscular injections into the buttock, particularly of quinine, which can damage the sciatic nerve
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- • Failure to switch patients from parenteral to oral therapy after 24h, or as soon as they can take and tolerate oral medication
- Failure to review antimalarial treatment for a patient whose condition is deteriorating
- Failure to re-check blood glucose concentration in a patient who develops seizure or deepening coma
- Failure to recognize and treat minor convulsions

- Failure to recognize and manage pulmonary oedema
- Failure to notice kidney injury
- Failure to give antibiotics to treat possible meningitis if a decision is made to delay lumbar puncture
- Fluid bolus resuscitation in children with severe malaria who are not severely dehydrated – leads to pulmonary edema