Guidelines for Establishing

Sentinel Surveillance Hospitals and

Management of Severe Malaria Cases

(2009)

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CONTENTS

Chapter 1. Background

Malaria is a major cause of mortality and morbidity in the tropical and subtropical regions of the world. An estimated 3.3 billion people were living in areas at risk of malaria in 2006. The 1.2 billion people living at high risk areas (≥ 1 case per 1000 population) were mostly in the WHO African (49%) and South-East Asia regions (37%). There were an estimated 247 million episodes of malaria in the world in 2006. Eighty six percent or 212 million cases were in the African Region. Among the cases that occurred outside the African Region, 80% were in India, Sudan, Myanmar, Bangladesh, Indonesia, Papua New Guinea and Pakistan. There were an estimated 881,000 malaria deaths in 2006, of which 91% were in Africa and 85% were of children under 5 years of age.

Estimates of malaria incidence are based, in part, on the numbers of cases reported by national malaria control programmes (NMCPs). These case reports are far from complete in most countries. A total of 94 million malaria cases were reported by national malaria control programmes of all countries in 2006, i.e. only 37% of the estimated global case incidence. The NMCPs of these countries reported 301,000 malaria deaths, i.e. only 34% of estimated deaths worldwide in 2006.

In India, screening of fever cases for malaria is presently done under the National Vector Borne Diseases Control Programme (NVBDCP) covering about 10% of the population annually, of which about 1.5 million are positive for the malarial parasite; around 45 - 50% of these cases are due to *Plasmodium falciparum*. Though the Annual Parasite Incidence (API) has come down in the country, it varies greatly from one state to another. The malaria situation remains a major problem in certain states and geographical pockets. The majority of malaria cases and deaths in India are being reported from Orissa, the seven North Eastern states, Jharkhand, Chattisgarh, Madhya Pradesh and Rajasthan, with Orissa alone contributing more than 20% of the cases in the country.

Plasmodium falciparum causes the most serious form of the disease. Infections with this parasite may be become severe and fatal without early diagnosis and prompt and appropriate case management. Prompt action is especially important for high-risk groups such as young children and pregnant women. The situation is getting complicated by the increasing occurrence of chloroquine resistance in the parasite in many areas.

Malaria surveillance in India conducted through routine surveillance to obtain epidemiological data which provide trends of cases and deaths reported in the public health care system. These data, however, do not give very crucial information on severe malaria cases and deaths due to malaria. Moreover, a large number of patients seek health care from the private sector and are not included in the programme statistics.

The NVBDCP has formulated the policy for developing hospitals in high malaria endemic districts into sentinel surveillance hospitals for obtaining information on details of severe malaria cases and their pattern. The aim of this policy is not only improving the quality of care to these patients and prevents deaths but also to improve the existing referral system.

Chapter 2. Pathogenesis and Pathology of Malaria

2.1 Pathogenesis

The pathological changes in malaria are related to the development of asexual stages of the malarial parasites in blood. The sporozoites injected by the mosquito travel to the liver in about 30-40 minutes by brisk motility conferred by the Circum Sporozoite Protein (CSP). Within the hepatocyte, each sporozoite divides into 10,000-30,000 merozoites during *pre-erythrocytic schizogony.* This phase takes about 10 - 15 days in *P. vivax* malaria and about 7-10 days in *P. falciparum* malaria.

At the completion of the pre-erythrocytic schizogony, the mature *schizonts* rupture the liver cells and merozoites escape into the blood, wherein they infect the red blood cells. The merozoites grow in stages into rings - trophozoites and then divide in a schizont to form more merozoites. At the end of this cycle, the RBCs rupture and release the new merozoites into the blood, which in turn infect more RBCs. The cycle within the RBCs (e*rythrocytic schizogony*) takes about 48 hours for one cycle.

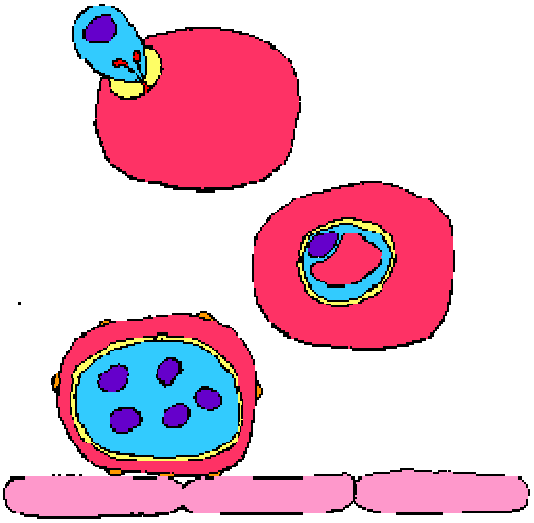
In the initial stages of the illness, this classical pattern of 48 hours may not be seen because there could be multiple broods of the parasite developing at different times. As the disease progresses, these broods join and the synchronous development cycle results in the classical pattern of alternate day fever.

It has been observed that in primary attack of malaria, the symptoms may appear with lesser degree of parasitemia or even with submicroscopic parasitemia. However, in subsequent attacks and relapses, a much higher degree of parasitemia is needed for onset of symptoms.

In *P. vivax* malaria, the young red blood cells are predominantly infected, while in *P. falciparum* malaria, red blood cells of all ages are affected. Thus the infective load and severity of infection are more in case of *P. falciparum* malaria.

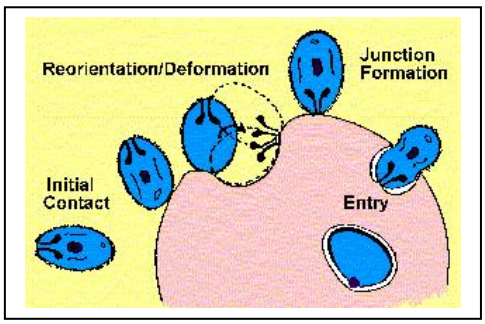
Some of the merozoites in the blood transform into sexual forms, called as *gametocytes*. These appear in the peripheral blood after 7-10 days of the infection in *P. vivax* and 10-20 days in *P. falciparum* infection. When anopheles mosquito bites an infected individual, these gametocytes enter the mosquito and continue their sexual phase of development within the gut wall of the mosquito.

In *P. falciparum* infections, the interactions between the parasite, erythrocyte and the host immune system are central to the pathogenesis of severe malaria. The release of malaria antigens, pigments and toxins gives rise to a cascade of pathological events. The production of cytokines, particularly Tumour Necrosis Factor (TNF) induced by release of parasite products during schizont rupture, appears to play a central role, complemented by the effects of other “endogenous pyrogens” such as interleukin-1 and interleukin-6. TNF and cachexin have been implicated as the cause of malarial fever. Mechanical changes also occur in the infected RBCs.



2.1.1 Host cell invasion

The malarial parasite has a close relationship with its host erythrocyte which may be described at the cellular and molecular levels. The apical organelles of the parasite are implicated in the process of host cell invasion. Merozoites rapidly (in approximately 20 seconds) enter into the erythrocyes. There are four distinct steps in the invasion process, namely, (a) merozoite binding, (b) reorientation and erythrocyte deformation, (c) junction formation and (d) entry of parasite into the erythrocyte.



The initial interaction between the merozoite and the erythrocyte is a random collision and involves interactions between proteins on the merozoite surface and the erythrocyte. Merozoite Surface Protein-1 (MSP-1) is implicated in erythrocyte invasion. After binding to the erythrocyte, the merozoite reorients itself so that the 'apical end' of the parasite is placed adjacent to the erythrocyte membrane. Apical Membrane Antigen-1 (AMA-1) localized at the apical end of the merozoite binds with the erythrocytes. A Parasitophorous Vacuolar Membrane (PVM) forms in the junction which expands as the parasite enters the erythrocyte.

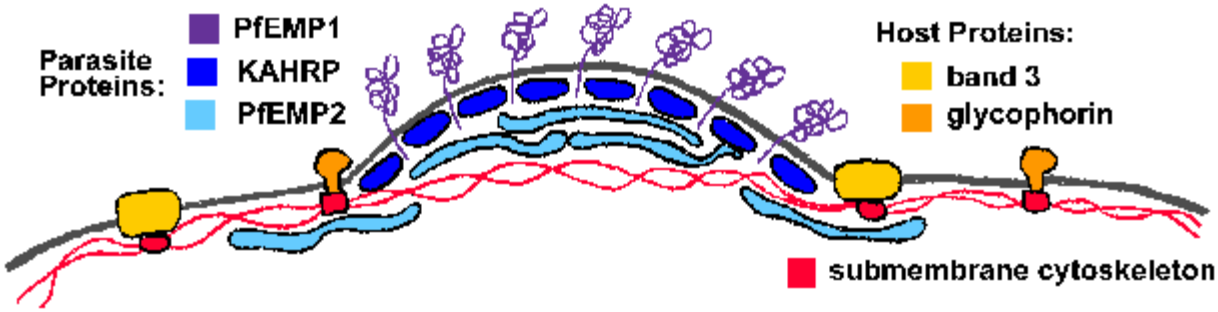
After the parasite enters the RBC, dense granules are released by it which is implicated in the modification of host cell.

2.1.2 Host Erythrocyte Modification

Once inside the erythrocyte, the parasite modifies the host cell to make it a more suitable environment by making the erythrocyte membrane more permeable to small molecular weight metabolites which are the needs of an actively growing parasite.

Another modification of the host cell is the cytoadherence of *P. falciparum*-infected erythrocytes to endothelial cells. This results in sequestration of mature parasites in the capillaries and post-capillary venules. The cytoadherence to endothelial cells confers two advantages for the parasite: 1) a microaerophilic environment which is better suited for parasite metabolism, and 2) avoidance of the spleen and subsequent destruction.

A major alteration of the erythrocyte is development of knobs on the erythrocyte membrane of *P. falciparum*-infected cells. Two proteins which participate in knob formation are the Knob-Associated Histidine Rich Protein (KAHRP) and Erythrocyte Membrane Protein-2 (*Pf*EMP2).



The knobs are believed to play a role in the sequestration of infected erythrocytes. Parasite species which express knobs exhibit the highest levels of sequestration. A polymorphic protein, called *Pf*EMP1 probably binds to receptors on host endothelial cells.

2.1.3 Endothelial Cell Receptors

Infected erythrocytes bind to CD 36, a protein found on endothelial cells, monocytes and platelets. Chondroitin sulfate A (CSA) has been implicated in the cytoadherence in the placenta and may contribute to the adverse affects of *P. falciparum* during pregnancy.

Rosetting is another adhesive phenomenon exhibited by the infected erythrocytes in which they bind with uninfected erythrocytes. *Pf*EMP1 appears to have a role in the rosetting. Rosetting causes higher microvascular obstruction than cytoadherence and is associated with cerebral malaria. Rosetting reduces blood flow, encourages cytoadherence to endothelium, enhances anerobic glycolysis and reduces the pH.

2.2 Pathology of the individual organs

Parasitization is greatest in descending order in the following organs: brain, heart, liver, lung, kidney and blood.

2.2.1 Brain

The major feature of cerebral malaria is cytoadherence of parasitized RBCs to the endothelium of cerebral capillaries and venules, resulting in sequestration and tight packing of infected cells

in these vessels. Ring hemorrhages consisting of a central 'blocked' vessel surrounded by brain tissue, and further by a ring of extravasated RBCs, is a striking feature. Death can occur with only a few parasites in cerebral vessels, but with many parasitized RBCs seen in central vessels and ring hemorrhages.

2.2.2 Cardiovascular system

The usual picture is of vessels congested with parasitized RBCs, pigment-laden macrophages, lymphocytes and plasma cells. Small subendocardial hemorrhages may occur.

2.2.3 Liver

The liver is enlarged and tense. In the acute stage there is gross congestion of sinusoids and centrilobular veins. The Kupffer cells are hypertrophied and contain parasitized and unparasitized red blood cells, remnants of parasites and masses of haemozoin.

2.2.4 Lungs

The smaller vessels in lungs are packed with parasitized RBCs and haemorrhages may be present. The alveoli are congested with pigment-laden macrophages, plasma cells, neutrophils and parasitized RBCs. The basic lesion in pulmonary oedema cases is injury to capillaries of lungs with congestion and leakage of oedema fluid.

2.2.5 Kidneys

In *falciparum* malaria an acute and transient self-limiting glomerulonephritis is common. In blackwater fever, large amounts of haemoglobin are cleared by the kidney following intravascular haemolysis. This may lead to oliguric or anuric renal failure. The histological changes are those of acute tubular necrosis. Pigment is commonly seen in vessels and interstitial tissue of glomeruli. Hyaline, epithelial, and granular casts may be present in the tubules. Scattered small haemorrhages may be seen in the cortex and medulla.

2.2.6 Blood

The mechanism of causation of anaemia in malaria is multifactorial and may include the following:

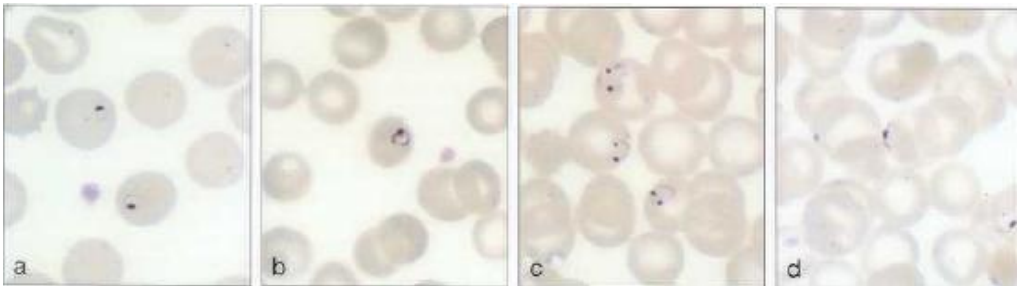
- Both parasitized and unparasitized cells are phagocytosed and destroyed
- Anaemia is not necessarily related to the degree of parasitaemia
- Erythropoiesis in bone marrow is depressed.
- Transfused cells in malarial patients may be destroyed more rapidly than in non-malaria recipients

TNF is considered to be an important aggravating factor in the pathogenesis of anaemia by stimulating erythrophagocytosis and causing bone marrow depression. The anaemia is haemolytic and is usually normocytic and normochromic, or hypochromic and macrocytic. In an acute attack there may be a sudden fall in haemoglobin values.

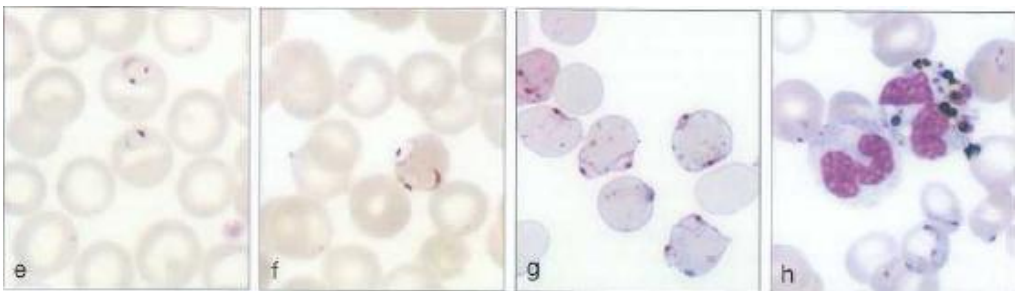
The peripheral blood film shows many parasites, polychromasia, anisocytosis, poikilocytosis, target cells, basophilic stippling and, in severe cases, Cabot's rings, Howel Jolly bodies, and nucleated red cells. Reticulocytosis may be present. Thrombocytopaenia is common due to reduced platelet survival and enhanced splenic uptake. Mild leucopenia is usual in uncomplicated malaria but leucocytosis is an important abnormality in severe malaria associated with a poor prognosis.

The various stages of P. falciparum in the peripheral smear are given in the following pictures.

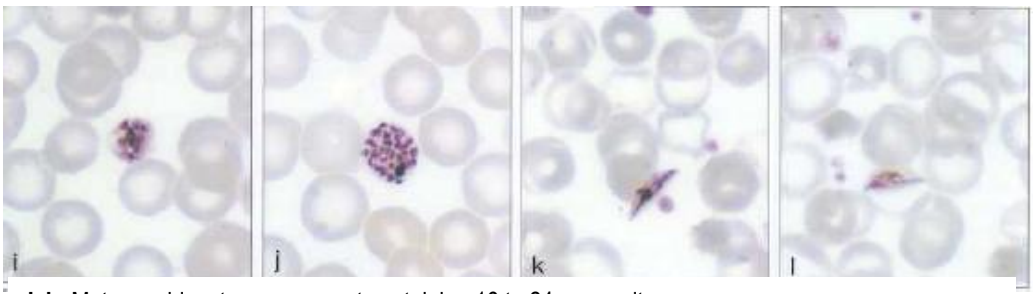
Plasmodium falciparum **– Microscopic features**



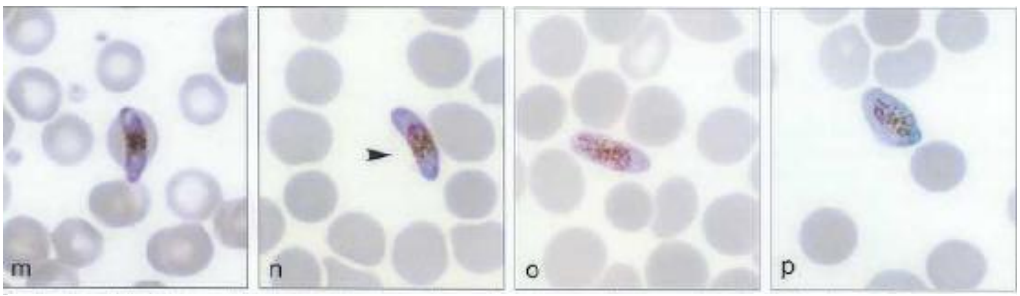
a, b: Trophozoites are small, with thin ring of cytoplasm, a vacuole and prominent chromatin dot
c: Red cells with double chromatin dots is a frequent feature.
d: Parasites at margin of red cells referred to as accole or appliqué forms



f, h: Multiple invasion of erythrocytes is a frequent feature
f, g: Sometimes marginal forms displaced markedly with parasite extending beyond cell margin



I, j: Mature schizonts are compact containing 16 to 24 merozoites
K, l: Gametocytes, initially spindle-shaped



m-o: Develop into banana- or sausage-shaped bodies with rounded ends.
m-n: chromatin concentrated as a mass
o: pigment tends to be more scattered
p: occasionally, gametocytes assume bizarre shapes
Gametocytes are only usually seen in peripheral blood smear in P. falciparum infections.
Trophozoites and schizonts are seen only when infection is severe with high parasitaemia.

In the majority of cases, examination of thick and thin films of the peripheral blood will reveal malaria parasites. Thick films are more useful than thin films in the detection of a low-density malaria parasitaemia.

In general, the greater the parasite density in the peripheral blood, the greater the likelihood that severe disease is present or will develop. However, some individuals may develop severe and even fatal malaria with a very low peripheral parasitaemia. Very rarely the blood film may actually be negative in a patient who is then proved at autopsy to have intense tissue sequestration of parasites.

Frequent monitoring of parasitaemia (every 4–6 hours) is very important in the first 2 – 3 days of treatment. The prognosis is worse if there is a predominance of mature parasite stages. The presence of malaria pigment in polymorphonuclear leukocytes (neutrophils) is a useful indication of the diagnosis of malaria in patients with severe malaria associated with absent or low parasitaemia.

Haemozoin is commonly present in the monocytes and may occur in the polymorphonuclear leukocytes as well. Haemosiderin, a dark yellow pigment formed in the reticulo-endothelial system, is deposited mainly in the spleen, liver and marrow.

2.2.7 Gastro-intestinal tract

Sequestration and cytoadherence have been seen, both in the small and large bowel, especially in the capillaries of lamina propria. Malabsorption of amino-acids, sugars and fats have been described.

2.2.8 Placenta

It is black or slaty grey and the sinusoids are packed with infected RBCs. It appears that the 'stickier' parastized cell tends to 'sludge' in eddies of the slow-moving placental stream. This most probably favours fibrin deposition on the villi and hastening the degenerative processes interfering with the nutriment of the fetus and causing stillbirths and premature labour. The maternal blood in the intervillous spaces is high in glucose content favouring the development of the parasite.

2.2.9 Spleen

In the acute attack the spleen is enlarged and tense. Rupture of the spleen is a not an uncommon complication of malaria and usually occurs through the hilar region. With increasing immunity, the spleen diminishes in size the capsule becomes fibrotic and wrinkled, with some evidence of perisplentitis and some fibrosis in the pulp.

2.3 Biochemical findings

In severe malaria, the levels of serum creatinine, bilirubin and enzymes aminotransferases and 5'-nucleotidase, may be raised. The levels of liver enzymes are much lower than in acute viral hepatitis. Severely ill patients are commonly acidotic, with low capillary plasma pH and bicarbonate concentrations. Fluid and electrolyte disturbances are variable. Concentrations of lactic acid in the blood and cerebrospinal fluid are often high both in adults and children, in proportion to the severity of the disease.

Chapter 3. Clinical features of severe malaria and management of complications

A case of uncomplicated malaria usually presents with fever, rigors, headache, bodyaches, fatigue, anorexia and nausea. In a young child there may be irritability, refusal to eat and vomiting. On physical examination fever may be the only sign. In some patients the liver and spleen are palpable. Serious complications can arise in *P.falciparum* infection. Unless the condition is diagnosed and treated promptly the clinical picture may deteriorate at an alarming rate and often with catastrophic consequences. Complications sometimes develop suddenly over a span of time as short as 12 -24 hours and may lead to death, if not treated promptly and adequately. Severe malaria has recently been described even in some vivax malaria cases in South and South-East Asia including India.

3.1 Severe malaria

A patient with severe falciparum malaria may present with confusion or drowsiness with extreme weakness (prostration). The following manifestations can occur singly or more commonly in combination in severe malaria cases.

- Cerebral malaria, defined as unrousable coma not attributable to any other cause in a patient with falciparum malaria
- Generalized convulsions
- Severe normocytic anaemia
- Hypoglycaemia
- Metabolic acidosis with respiratory distress
- Fluid and electrolyte disturbances
- Acute renal failure
- Acute pulmonary oedema and adult respiratory distress syndrome (ARDS)
- Circulatory collapse, shock, septicaemia ("algid malaria")
- Abnormal bleeding
- Jaundice
- Haemoglobinuria
- High fever
- Hyperparasitaemia

3.1.1 Diagnosis

All attempts should be made to confirm the diagnosis using microscopy or RDTs. If microscopy results can be obtained without any delay, a blood smear should be taken for immediate examination. If there is a possibility of delay and RDT is available, it should be used to diagnose *Pf* malaria. RDTs should be used in hospitals only in emergency hours when the laborotary technician/microscopist is not available. If microscopy result is not immediately available and RDT is also not available, a blood smear is made and treatment started on the basis of the clinical suspicion of severe malaria.

Wherever possible, the treatment should be guided by microscopy. High degree of parasitaemia and presence of stages of the parasite other than ring and gametocyte indicate poor prognosis. Severe malaria in the absence of microscopic evidence of asexual Plasmodium falciparum is exceedingly rare. In such cases, all efforts should be done to

identify an alternative cause. If microscopy is negative and RDT is positive for *P.falciparum*, it is possible that antigen is persisting from an earlier infection. However, if the symptoms clearly point to severe malaria and there is no other explanation, such a case should be managed as a case of severe malaria. Such occurrences are more common in patients, who have started an ACT treatment a few days earlier. Severe malaria with negative microscopy and negative RDT is is extremely rare. Such a patient should not be recorded as severe malaria, but may be treated as such, if the treating physician deems it absolutely necessary.

3.2 Management of severe malaria and its complications

Treatment of severe and complicated malaria calls for close supervision between the clinician and the nursing staff. The medication should also be given strictly on schedule and at correct doses.

3.2.1 General management

The following measures should be applied to all patients with clinically diagnosed or suspected severe malaria:

- A rapid clinical assessment of the patient should be made with special attention to the level of consciousness, blood pressure, rate and depth of respiration and pallor.
- The patient should be admitted to an intensive care unit, if it is available.
- Antimalarial chemotherapy should be started intravenously. If intravenous infusion is not immediately possible, an appropriate drug may be given intramuscularly. Once the condition of the patient improves and he/she can swallow and retain tablets, parenteral treatment should be substituted with oral treatment.
- The core temperature (preferably rectal temperature), respiratory rate and depth, blood pressure, level of consciousness and other vital signs should be monitored regularly.
- Careful attention should be paid to fluid balance, if fluids are being given intravenously, in order to avoid over- and under-hydration.
- Urine output should be recorded and the appearance of black urine (haemoglobinuria) or oliguria should be looked for, which may indicate acute renal failure.
- The optic fundi should be examined by ophthalmoscope for papilloedema, which is a contraindication to performing a lumbar puncture. Meningitis is excluded by lumbar puncture or covered by treatment.
- Regular checks should be done on packed cell volume (haematocrit), haemoglobin concentration, blood glucose, urea or creatinine and electrolytes.
- If the patient goes into shock, blood cultures should be taken and antibiotics started without waiting for blood culture results.
- The therapeutic response, both clinical and parasitological, should be monitored by regular observations and examination of blood films.
- Drugs that increase the risk of gastrointestinal bleeding (aspirin, corticosteroids) should be avoided.

Table - 1 . Immediate management of manifestations of severe malaria

Complication	Recognition	Immediate management
Coma (cerebral malaria)	Assessment by Glasgow scale (10 or less) in adults and children above the age of 12 years; and Blantyre scale (3 or less) in children below the age of 12 years	Maintain airway, place patient on his or her side, exclude other treatable causes of coma (e.g. hypoglycaemia, bacterial meningitis); avoid harmful ancillary treatment such as corticosteroids, heparin and adrenaline; intubate if necessary.
Hyperpyrexia	Monitor core temperature (preferably rectal)	Administer tepid sponging, fanning and antipyretic drugs.
Convulsions	Fits comprising of tonic or clonic convulsions followed by loss of consciousness or abnormal behavior	Maintain airways; treat promptly with intravenous diazepam 0.3 mg/kg bw (or 10 mg in adults) or intramuscular paraldehyde.
Hypoglycaemia (blood glucose concentration of < 2.2 mmol/l: <40 mg/100ml)	Anxiety, sweating, palpitation, dilatation of pupils, breathlessness or oliguria	Check blood glucose, correct hypoglycaemia with a bolus of 50% dextrose and maintain with glucose-containing infusion.
Severe anaemia (haemoglobin < 5 g/100 ml or packed cell volume < 15%)	Pale conjunctiva, tongue, lips, palms	Transfuse with screened fresh whole blood/packed cells
Acute pulmonary oedema *	Tachypnoea, dyspnoea and bilateral basal rales	Prop patient up at an angle of 45^{o}, give oxygen' give a diuretic; stop intravenous fluids; intubate and add positive end-expiratory pressure / continuous positive airway pressure in life-threatening hypoxaemia.
Acute renal failure	Urine output < 400 ml / 24 hours in adults and <0.5 ml / kg / hour in children	Exclude pre-renal causes, check fluid balance and urinary sodium. If in established renal failure, treat with haemofiltration or haemodialysis, or if unavailable, peritoneal dialysis. The benefits of diuretics/dopamine in acute renal failure are not proven.
Spontaneous bleeding and coagulopathy	Significant bleeding from gums, nose, venipuncture sites, gastrointestinal tract	Transfuse with screened fresh whole blood (cryoprecipitate, fresh frozen plasma and platelets if available); give vitamin K injection.
Metabolic acidosis	Labored deep hyperventilation with increased respiratory effort and a clear chest on auscultation	Exclude or treat hypoglycaemia, hypovolaemia and septicaemia. If severe, treat with haemofiltration or haemodialysis.
Shock	Cold, clammy and cyanotic skin and extremities, weak peripheral pulse and hypotension (systolic BP < 80 mm Hg in adults and children over 10 years; < 70 mm Hg in children aged 1 month to 10 years and < 60 mm Hg in neonates).	Suspect septicaemia, take blood for cultures; give parenteral antimicrobials, correct haemodynamic disturbances.

* Prevent by avoiding excess hydration.

3.2.2 Nursing care

Good nursing care of the patient with severe malaria is of vital importance.

- Meticulous nursing care can be life-saving, especially for the unconscious patient. Maintain a clear airway. Nurse the patient in the lateral or semi-prone position to avoid aspiration of fluid. Insert a nasogastric tube and suck out the stomach contents to minimize the risk of aspiration pneumonia. Turn the patient every 2 hours. Do not allow the patient to lie in a wet bed. Pay particular attention to pressure points.
- Keep a careful record of fluid intake and output.
- Note any appearance of black urine (haemoglobinuria).
- Check the speed of infusion of fluids frequently. Too fast or too slow an infusion can be dangerous.
- Monitor the temperature, pulse, respiration, blood pressure and level of consciousness (use Glasgow coma scale for adults and Blantyre Scale for children). These observations should be made at least every 4 hours until the patient is out of danger.
- Report changes in level of consciousness, occurrence of convulsions or changes in behaviour of the patient immediately.
- Clean insertion sites for intravenous lines at least twice daily with iodine and alcohol.
- If the rectal temperature rises above 39 ºC, start tepid sponging and fanning. Give paracetamol.

3.2.2 Coma

The level of coma is assessed in adult patients and children over 12 years as per guidelines in the following table.

Table - 2 . Modified Glasgow Coma Scale for adults and children over 12yrs)*

Eye opening	Spontaneously	4
	To speech	3
	To pain	2
	No response	1
Best verbal response (Non-intubated)	Oriented and talks	5
	Disoriented and talks	4
	Inappropriate words	3
	Incomprehensible sounds	2
	No response	1
Verbal response (Intubated)	Seems able to talk	5
	Questionable ability to talk	3
	Generally unresponsive	1
Best Motor response	Verbal commands	6
	Localizes to pain	5
	Withdraws to pain	4
	Decorticate	3
	Decerebrate	2
	None	1
Total score		**3 – 15***

Total score = Eye opening score + Verbal (intubated or nonintubated) score + Motor score.
* Total score may vary from 3-15. Unrousable coma reflected in a score of <9.
This scale should be used repeatedly to assess improvement or deterioration.

3.2.2.1 ABC of Coma Management

A. Airway

- Maintain the airway by keeping it clean, i.e., free from saliva, vomitus, etc.
- Oral or oropharyngeal airway should be used to prevent the tongue from falling back and to keep the airway clean.
- Unconscious patients should be nursed on side, preferably left lateral position, on a flat surface without a pillow. This reduces chances of aspiration of gastric contents.
- Insert a nasogastric tube to prevent aspiration pneumonia and aspirate stomach contents.
- If facilities exist, endotracheal intubation should be done in a coma patient if needed.
- Keep changing the side every two hours.

B. Breathing

- If tachypnoea, laboured respiration or acidotic breathing is present or develops in the course of the management, patient may need oxygen inhalation and ventilatory support. Hence, such patients should be transferred to centres with facilities for intensive care.

C. Circulation

- Check for dehydration by examining the pulse rate, blood pressure, skin elasticity, jugular venous pressure, moisture of the tongue, urinary volume and colour.
- If dehydration is present, infuse intravenous fluids.
- Frequently check the rate of infusion to prevent overhydration. If patient has overhydration, stop or restrict IV fluids and give intravenous diuretics. Keep an accurate record of fluid intake and output. Strict intake and output chart should be maintained. Normal urine output is approximately 1 ml/min.
- Suspected infections must be treated with antibiotics.

Specific antimalarial treatment for severe malaria cases

In severe malaria cases, a parenteral artemisinin derivative or quinine is the drug of choice. Severe malaria should always be treated with parenteral antimalarials because gastrointestinal absorption of oral drugs may be unpredictable.

Artesunate is given by intravenous (preferably) or intramuscular route. Artesunate is available as artesunic acid powder. 60 mg of the drug is dissolved in 0.6 ml of 5% sodium bicarbonate which is further diluted to 3-5 ml with 5% dextrose and administered immediately by intravenous bolus injection. A dose of 2.4 mg/kg bw is given on admission (time=0), followed by 2.4 mg/kg at 12 and 24 hours, and then once daily for at least 3 days. The solution should be prepared freshly for each administration and should not be stored. The intramuscular injections should be administered in the anterior thigh.

As an alternative to artesunate injections, one of the following parenteral artemisinin derivatives may be used for a minimum of 3 days following which the complete course of oral ACT is given:

- Artemether 3.2 mg/kg bw on the first day, followed by 1.6 mg/kg bw daily for 3 days
- Arteether (in adults only), at a dose of 150 mg i.m. daily for 3 days

Once the patient can tolerate oral therapy, parenteral treatment should be switched to a complete course of an oral Artemisinin based Combination Therapy (ACT) as recommended in the national treatment guidelines for uncomplicated malaria as given below.

These cases are treated with ACT as follows with ACT Combination {Artesunate (50 mg) tablets + sulfadoxine-pyrimethamine (500 + 25 mg) tablets combination}. The dosage is Artesunate 4 mg/kg body weight daily for 3 days plus Sulfadoxine-pyrimethamine (25mg/kg + 1.25 mg/kg) as a single dose on the first day as given in the following table. Primaquine will be given on day 1 as in above table.

Age (in years)	Drug	Day - 1 (No. of tablets)	Day - 2 (No. of tablets)	Day - 3 (No. of tablets)
<1	AS	½	½	½
	SP	¼	Nil	Nil
1-4	AS	1	1	1
	SP	1	Nil	Nil
5-8	AS	2	2	2
	SP	1 ½	Nil	Nil
9-14	AS	3	3	3
	SP	2	Nil	Nil
15 & above	AS	4	4	4
	SP	3	Nil	Nil

Parenteral quinine is preferably given by the intravenous route. Quinine hydrochloride is given in a loading dose of 20 mg/kg bw diluted in 5% dextrose or dextrose saline and given by intravenous infusion over four hours, followed by maintenance dose of 10 mg/kg bw over four hours and repeated every eight hours in adults until the patient can swallow. The infusion rate should not exceed 5 mg salt/kg per hour. Loading dose should not be given if the patient has already received quinine or if the clinician feels inappropriate. As soon as the patient is able to take medicines orally, parenteral treatment should be substituted with oral quinine treatment. The total duration of treatment should be 7 days including parenteral dose. In children, the maintenance dose is infused over a period of two hours and repeated every eight hours.

Patients on IV treatment require monitoring of pulse, blood pressure, and blood glucose. Patients should be kept flat on a bed while on IV quinine treatment. If intravenous injection is not possible, quinine is given IM and the dose should be split and injections given in the anterior part of the thigh. The IM injection carries the risk of necrosis at the injection site and the injection is very painful. Injectable solutions of quinine hydrochloride, quinine dihydrochloride or quinine sulphate containing 82%; 82% and 82.6% quinine base, respectively. Under the NVBDCP, Quinine dihydrochloride 2 ml ampoules (300 mg per ml) are generally supplied. The dosage of IM quinine injection is a loading dose of 20mg/kg and maintenance of 10mg/kg body weight.

For administration of quinine by intramuscular route, the patient should be weighed first. Use a 10 ml sterile syringe. Draw up 5 ml of sterile water for injection. Then into the same syringe, draw up 300 mg (1 ml) from an ampoule of quinine. Mix the drug by shaking the syringe before injection. The syringe now contains 50 mg quinine per ml. A maximum of 3ml only should be

injected into one injection site. If the amount to be injected exceeds 3 ml, half the amount should be injected into each injection site. An example of body weights and dose (ml) of injection is given in the table below.

Table – 3. Dosage of intramuscular injections of Quinine after dilution

Body weight (Kg)	Volume of diluted Quinine injection to be administered	Dosage of Quinine being administered	Number of injection sites at anterior aspect of thighs
Under 5	1.0 ml	50 mg	One
5.1 – 7.5	1.5 ml	75 mg	One
7.6 – 10	2.0 ml	100 mg	One
10.1 – 12.5	2.5 ml	125 mg	One
12.6 – 15	3.0 ml	150 mg	One
15.1 – 17.5	3.5 ml	175 mg	Two
17.6 – 20	4.0 ml	200 mg	Two
20.1 – 22.5	4.5 ml	225 mg	Two
22.6 – 25	5.0 ml	250 mg	Two
25.1 – 27.5	5.5 ml	275 mg	Two
27.6 – 30	6.0 ml	300 mg	Two
30.1 – 32.5	6.5 ml	325 mg	Three
32.6 – 35	7.0 ml	350 mg	Three
35.1 – 37.5	7.5 ml	375 mg	Three
37.6 – 40	8.0 ml	400 mg	Three
40.1 – 42.5	8.5 ml	425 mg	Three
42.6 – 45	9.0 ml	450 mg	Three
45.1 – 47.5	9.5 ml	475 mg	Four
47.6 – 50	10.0 ml	500 mg	Four
50.1 – 52.5	10.5 ml	525 mg	Four
52.6 – 55	11.0 ml	550 mg	Four
55.1 – 57.5	11.5 ml	575 mg	Four
57.6 – 60	12.0 ml	600 mg	Four
60.1 – 62.5	12.5 ml	625 mg	Four
62.6 – 65	13.0 ml	650 mg	Four
65.1 – 67.5	13.5 ml	675 mg	Four
67.6 – 70.0	14.0 ml	700 mg	Four
70.1 – 72.5	14.5 ml	725 mg	Four

Parenteral treatment is followed by oral treatment with Quinine tablets 10 mg quinine salt/kg bw every eight hours in combination with doxycycline 3 mg/kg bw daily (except children below 8 years of age and pregnant women) or clindamycin 10 mg/kg bw twice daily to complete 7 days treatment or a full course of the ACT recommended in the national treatment guidelines for uncomplicated malaria is given. Quinine Sulphate 300 mg tablets are made available through the NVBDCP.

The number of tablets to be given per dose is given below:

Table – 4. Dosage of Quinine tablets

Weight (in Kg)	Number of tablets per dose
6-11	¼
12-17	½
18-23	¾
24-35	1
36-47	1 ½
48 & above	2

Quinine is not contraindicated during pregnancy and in children. The features of quinine toxicity include cinchonism, hypoglycemia and hypotension. Cinchonism is characterized by tinnitus, high tone deafness, visual disturbances, headache, dysphoria, nausea, vomiting and postural hypotension all of which disappear on withdrawal of the drug. Hypotension is often associated with excessively rapid intravenous infusion. Hypoglycemia is common in pregnancy and prolonged in severe infection. Other side effects include nausea, vomiting, diarrhea, blurred vision, distorted colour perception, photophobia, diplopia and night blindness, cutaneous flushing, pruritus, rashes, and dyspnoea.

The DVBDCO/ DMO should list all facilities in the district where emergency care for severe malaria is available and this list should be available in PHCs and with all Community Workers like ASHA. MO-PHC should develop links with these institutions. For timely referral of severe cases, transportation should be provided from untied funds available under NRHM.

Treatment of severe vivax malaria

Although *P. vivax* malaria is considered to be benign malaria, it can also very occasionally result in a severe disease as in falciparum malaria. Severe vivax malaria manifestations that have been reported are cerebral malaria, severe anaemia, severe thrombocytopenia and pancytopenia, jaundice, splenic rupture, acute renal failure and acute respiratory distress syndrome. In such cases, prompt and effective case management should be instituted just like that for severe and complicated falciparum malaria.

3.3 Special clinical features of severe malaria and management of common complications in children

3.3.1 Clinical features

In children, febrile convulsions, repeated vomiting and dehydration are common if the temperature is high from any cause. Therefore, these symptoms are not necessarily indicative of severe malaria in children. However in routine program situations, children with such symptoms should be referred to a health facility equipped to manage severe malaria and a diagnosis of malaria should be confirmed at the earliest.

Many of the clinical features of severe malaria described above in adults also occur in children. The commonest and most important complications of *P. falciparum* infection in children are:

- Cerebral malaria

- Severe anaemia
- Respiratory distress (acidosis)
- Hypoglycaemia

The differences between severe malaria in adults and in children are given in table below.

Table - 5. Differences between severe malaria in adults and in children

Sign or symptom	Adults	Children
History of cough	Uncommon	Common
Convulsions	Common	Very common
Duration of illness	5-7 days	1-2 days
Resolution of coma	2-4 days	1.2 days
Neurological sequelae	< 5%	> 10%
Jaundice	Common	Uncommon
Pre-treatment hypoglycaemia	Uncommon	Common
Pulmonary oedema	Uncommon	Rare
Renal failure	Common	Uncommon
CSF opening pressure	Usually normal	Usually raised
Respiratory distress (acidosis)	Sometimes	Common
Bleeding/clotting disturbances	Up to 10%	Rare
Abnormality of brainstem reflexes (e.g. oculovestibular, oculocervical)	Rare	More common

3.3.2 Management

The management of severe malaria in children is generally similar to that in adults. Some specific aspects are re-emphasized.

- The parents or other relatives should be questioned about: (i) History of residence or travel; (ii) Previous treatment with antimalarials or other drugs; (iii) Recent fluid intake and urine output and (iv) Recent or past history of convulsions.
- If the child is unconscious, insert a nasogastric tube to minimize the risk of aspiration pneumonia. Evacuate the stomach contents.
- If parasitological confirmation is likely to be delayed, treatment should be started even before the diagnosis is confirmed.
- Treat convulsions with intravenous diazepam, 0.3 mg/kg of body weight as a slow bolus ("push") over 2 minutes. In an emergency it is easier and quicker to give it rectally than intravenously, unless an intravenous line is already running. The dose is 0.5mg/kg (0.1 ml/kg) rectally. Reassess the child after 10 minutes. If still convulsing, give a second dose of diazepam, rectally, (or diazepam intravenously slowly over 1 minute if an IV infusion is running). If convulsions do not stop after 10 minutes of second dose of diazepam, Inj Phenytoin can be given intravenously if access has been achieved. 15 - 20 mg/kg Phenytoin is diluted in about 20 ml of saline and given slowly (not more than 1 mg/kg Phenytoin per minute). Alternatively phenobarbitone can be used in a dose of 15-20mg/kg IV (in 20 ml 5% dextrose or saline) or IM. At this stage, seek help of a senior or more experienced person, if available. Diazepam can affect the child's breathing, so it is important to reassess the airway and breathing regularly.

- In general, children with metabolic acidosis who have not previously received parenteral fluids are dehydrated and should be managed accordingly.
- In any child with convulsions, hyperpyrexia and hypoglycaemia should be excluded.
- Use tepid sponging and fanning in an effort to keep the rectal temperature below 39 °C. Paracetamol, 15 mg/kg of body weight 4-hourly, should also be given as an antipyretic.

3.3.2.1 Initial assessment

Key aspects of the initial assessment of children with severe malaria are:

- Level of consciousness (coma scale for children, given in table below)
- Rate and depth of respiration
- Presence of anaemia
- Pulse rate and blood pressure
- State of hydration
- Temperature

Table - 6. Blantyre Coma scale for children below 12 years

Eye movements	Directed (e.g. towards mother's face)	1
	Not directed	0
Verbal response	Appropriate cry	2
	Inappropriate cry or moan	1
	None	0
Best motor response***	Localizes painful stimulus	2
	Withdraws limb from pain	1
	Non-specific or absent response	0
Total score		**0 – 5**

Total score can range from 0 - 5; A score of 2 or less indicates unrousable coma.
This scale should be used repeatedly to assess improvement or deterioration.
*** - Best motor response elicited by one of the following three methods:

- Press knuckles firmly on the patients sternum
- Press firmly on the thumbnail bed with side of a horizontal pencil
- Press firmly on the supra-orbital groove with the thumb

Immediate tests must include:

- Thick and thin blood films
- Packed cell volume (haematocrit)
- Finger-prick blood glucose
- Lumbar puncture (If it is decided to delay lumbar puncture, antibiotics must be given to cover the possibility of bacterial meningitis)

3.3.2.2 Nursing care

Nursing must include all the well-established principles of the care of the unconscious child including frequent turning (every 2 hours) and careful attention to airway, eyes, mucosae, skin and fluid requirements. The child should be nursed in the lateral or semi-prone position.

3.3.2.3 Emergency measures

- Insert nasogastric tube to minimize risk of aspiration pneumonia.
- Correct hypoglycaemia.
- Restore circulating volume.
- Treat anaemia.

3.3.3 Cerebral malaria

3.3.3.1 Clinical features

- The earliest symptom of cerebral malaria in children is usually fever, followed by failure to eat or drink. Vomiting and cough are common.
- A child who loses consciousness after a febrile convulsion should not be classified as having cerebral malaria unless coma persists for more than 1 hour after the convulsion. However, antimalaria treatment must not be delayed.
- The depth of coma may be assessed according to the coma scale for children by observing the response to standard vocal or painful stimuli (rub knuckles on child's sternum; if there is no response, apply firm pressure on thumbnail bed with horizontal pencil).
- Always check blood sugar and treat hypoglycemia if present.
- Convulsions are common before or after the onset of coma.
- Deep breathing with a clear chest is a sensitive and specific sign for the presence of metabolic acidosis.
- A few children may have cold and clammy skin in a state of shock with a systolic blood pressure below 50 mmHg. However, measurement of blood pressure is not required for identifying shock because low blood pressure is a late sign in children and may not help identify treatable cases, and the correct size BP cuff necessary for children of different age groups may not be available.
- In some children, extreme opisthotonos is seen, which may lead to a mistaken diagnosis of tetanus or meningitis.
- CSF opening pressure is usually raised.
- Leukocytosis is not unusual in severe disease and does not necessarily imply an associated bacterial infection.
- About 10% of children who survive cerebral malaria have neurological sequelae which persist into the convalescent period. Sequelae may take the form of cerebellar ataxia, hemiparesis, speech disorders, cortical blindness, behavioural disturbances, hypotonia or generalized spasticity.

3.3.3.2 Management

The management of severe malaria in children is the same as in adults, including careful nursing and monitoring of the unconscious patient. The child with cerebral malaria may also

have anaemia, respiratory distress (acidosis) and hypoglycaemia and has to be managed accordingly.

3.3.4 Anaemia

3.3.4.1 Clinical features

The rate of development and degree of anaemia depend on the severity and duration of parasitaemia. Children with hyperparasitaemia may develop severe anaemia rapidly. Children with severe anaemia may present with tachycardia and dyspnoea. Anaemia may contribute to cerebral signs – confusion, restlessness, coma and retinal haemorrhages; signs of acidosis – deep, laboured breathing and rarely, cardiopulmonary signs – gallop rhythm, cardiac failure, hepatomegaly and pulmonary oedema.

3.3.4.2 Management

- The need for blood transfusion must be assessed with great care in each individual child. Not only packed cell volume (PCV) or haemoglobin concentration, but also the density of parasitaemia and the clinical condition of the patient must be taken into account.
- In general, a PCV of 12% or less, or a haemoglobin concentration of 4 g/dl or less, is an indication for blood transfusion.
- In children with less severe anaemia (i.e. PCV of 13–18% or Hb 4–6 g/dl), transfusion should be considered for high-risk patients with any one of the following clinical features: (i) respiratory distress (acidosis); (ii) impaired consciousness; (iii) hyperparasitaemia (>20%). (iv) shock, and (v) heart failure.
- Use blood that has been screened and found negative for transfusion-transmissible infections. Do not use blood that has passed its expiry date or has been out of the refrigerator for more than 2 hours. Large volume rapid transfusion at a rate >15 ml/kg/hour of blood stored at 4° C may cause hypothermia, especially in small babies. Preferably give packed cells if available in place of whole blood.
- The common reason for respiratory distress in anaemic children with malaria is acidosis, resulting from tissue hypoxia. A diuretic is usually not indicated as many of these children are hypovolaemic. However, if there is fluid overload, frusemide, 1–2 mg/kg of body weight up to a maximum of 20 mg, may be given intravenously.

  Details of blood transfusion and transfusion reaction are given in annexure 'E'

3.3.5 Respiratory distress (acidosis)

3.3.5.1 Clinical features

Deep breathing, with indrawing of the lower chest wall, in the absence of localizing chest signs suggests metabolic acidosis. Respiratory distress (acidosis) commonly accompanies cerebral malaria or anaemia. It is associated with an increased risk of death.

3.3.5.2 Management

- Correct any reversible cause of acidosis, in particular dehydration and severe anaemia. Intravenous infusion is best, using the most accessible site, including the

femoral vein. If this is impossible, give an intraosseous infusion. Take care not to give excessive fluid, as this may precipitate pulmonary oedema.

- If the PCV is more than 15% or the Hb is more than 5 g/dl, give 20 ml/kg of body weight of isotonic saline, by intravenous infusion over 30 minutes.
- If the PCV is less than 15% or the Hb is less than 5 g/dl in a child with signs of metabolic acidosis, give whole blood, 10 ml/kg of body weight over 30 minutes and a further 10 ml/kg of body weight over 1–2 hours.

Monitor response by continuous clinical observation supported by repeated measurement of acid–base status, haematocrit or haemoglobin concentration, and glucose, urea and electrolyte levels.

3.3.6 Hypoglycaemia

3.3.6.1 Clinical features

Hypoglycaemia (blood glucose < 54 mg/dl) is particularly common in children under 3 years and in those with convulsions or hyperparasitaemia or in a profound coma. Unconscious children should be given dextrose regularly to prevent starvation hypoglycaemia. It may be provided as 5% dextrose in saline infusion. If there is a possibility of this causing fluid overload, smaller volumes of concentrated dextrose may be given at regular intervals.

3.3.6.2 Management

- If hypoglycaemia occurs, give intravenous 10% dextrose in a dose of 5.0 ml/kg of body weight (0.5 g/kg) diluted in approximately the same volume of IV fluid slowly over several minutes. This should be followed by a slow intravenous infusion of 5% or 10% dextrose to prevent recurrence of hypoglycaemia. If the intravenous route is impossible, intra-osseous access should be tried. If this fails, 50% dextrose – or of any sugary solution – may be given through a nasogastric tube.
- The duration and amount of dextrose infusion will be dictated by the results of blood glucose monitoring. Monitoring of blood glucose levels should continue even after successful correction as hypoglycaemia may recur.

3.3.7 Dehydration and Shock

3.3.7.1 Clinical features

The best evidence of mild to moderate dehydration in children is decreased peripheral perfusion, decreased skin turgor evidenced by slow return of skin pinch, < 2 seconds, irritability and restlessnes and increased thirst. Severely dehydrated children have 2 of the following signs;(i) Sunken eyes, (ii) Lethargy (iii) very slow skin pinch, longer than two seconds, and (iv) inability to drink.
Presence of cold extremities with capillary refill (longer than 3 seconds) and weak and fast pulse suggests presence of shock. Capillary refill is a simple test that assesses how quickly blood returns to the skin after pressure is applied. It is carried out by applying pressure to the pink part of the nail bed of the thumb or big toe in a child and over the sternum or forehead in a young infant for 3 seconds. The capillary refill time is the time from release of pressure to complete return of the pink color. It should be less than 3 seconds. If it is more than 3 seconds the child may be in shock. Lift the limb slightly above heart level to assess arteriolar capillary

refill and not venous stasis. This sign is reliable except when the room temperature is low, as cold environment can cause a delayed capillary refill. In such a situation check the pulses and decide about shock.

Evaluation of pulses is critical to the assessment of systemic perfusion. The radial pulse should be felt. If it is strong and not obviously fast (Rate > 160/min in an infant and > 140/min in children above 1 year), the pulse is adequate; no further assessment is needed. In an infant (less than one year of age) the brachial pulse may be palpated in the middle of upper arm. In a child with weak peripheral pulses, if central pulses (femoral or carotid) are also weak it is an ominous sign.

3.3.7.2 Management

Treatment of shock requires teamwork. The following actions need to be started simultaneously

• Give oxygen
- Make sure the child is warm

• Select an appropriate site for administration of fluids
• Establish IV or intraosseous access
• Take blood samples for emergency laboratory tests
• Begin giving fluids for shock.
• Assessment of shock in severe acute malnutrition (SAM) is difficult and the fluid therapy is also different. The recommended volumes of fluids to treat shock depending on the age/weight of child are shown in Annexure 'F' . If the child has severe malnutrition, you must use a different fluid and a different rate of administration and monitor the child very closely. Therefore a different regime is used for these children.

- Children having signs of severe dehydration but not in shock should also be rehydrated quickly with isotonic saline. Frequently examine the jugular venous pressure, blood pressure, chest, heart and liver size, to make sure the patient is not being given too much fluid. Following table gives the guidelines for fluid therapy for severe dehydration:

Age	First give 30 ml/ kg in	Then give 70 ml/ Kg in
Infants (Age less than 12 months	I hour*	5 hours
Children (12 mo- 5 years)	30 minutes*	2 ½ hours

* Repeat once if radial pulse is still very weak or not detectable.

- Where facilities for monitoring and maintenance of adequate sterility exist, fluid balance may be adjusted in accordance with direct measurement of the central venous pressure through a central venous catheter.

If, after careful rehydration, urine output in the first 8 hours is less than 4 ml/kg of body weight, furosemide (frusemide) can be given intravenously, initially at 2 mg/ kg of body weight, then doubled at hourly intervals to a maximum of 8 mg/kg of body weight (given over 15 minutes).

3.4 Special clinical features and management of severe malaria in pregnancy

3.4.1 Clinical features

The clinical manifestations of malaria in pregnancy may vary greatly according to their level of immunity. In pregnancy, malaria, especially *P.falciparum*, is a serious disease because with each bout of malaria, there is a reduction in haemoglobin and profound anaemia may develop rapidly. Later in pregnancy, sequestration of parasites in placenta may restrict oxygen and nutrient flow to the fetus, causing intrauterine growth retardation. Falciparum malaria commonly induces uterine contractions and gives rise to premature labour. The frequency and intensity of contractions appear to be related to the height of the fever. Fetal distress is common, but frequently not diagnosed. The prognosis for the fetus is poor in severe disease. The risk of abortion and low infant birth weight is increased, especially in first pregnancies.

Non-immune pregnant women are susceptible to all the complications seen in severe malaria described above. They have also an increased risk of abortion, stillbirth, premature delivery and low birth weight. They are more likely to develop cerebral and other forms of severe malaria, and to suffer a higher mortality. They are particularly susceptible to hypoglycaemia and acute pulmonary oedema.

Partially immune pregnant women, especially primigravidae, are susceptible to severe anaemia. They are particularly at risk because their malarial infection is often asymptomatic and may be overlooked because peripheral blood films may be negative.

3.4.2 Management

Pregnant women with malaria must be treated promptly because the disease is more severe, is associated with high parasitaemia and is dangerous for mother and fetus.

- Pregnant women with severe malaria should be transferred to intensive care whenever possible.
- Malaria may lead to threatened premature labour or may result in established labour, despite prompt antimalarial treatment.
- Once labour has started, fetal or maternal distress may indicate the need to intervene, and the second stage may need to be shortened by the use of forceps, vacuum extraction or caesarean section.

Women with severe anaemia in endemic areas, especially primigravidae, should be given full antimalarial treatment even if peripheral blood films are negative and there are no other features to suggest malaria. ACT is not advised in pregnancy, as per National Drug Policy for Malaria – 2008. However, according to current WHO guidelines, ACT is safe for use in the second and third trimester of pregnancy and in severe malaria it is considered that the benefits of artemisinin derivatives outweigh the possible side-effects. Quinine, in the doses advocated for the treatment of life-threatening malaria, is also safe in pregnancy. Its major adverse effect is hypoglycaemia for which particular attention must be given.

3.4.3 Hypoglycaemia

3.4.3.1 Clinical features

Hypoglycaemia may be present in pregnant women on admission, or may occur after quinine infusion. In patients who have been given quinine, abnormal behaviour, sweating and sudden

loss of consciousness are the usual manifestations. Hypoglycemia may be asymptomatic or associated with fetal bradycardia and other signs of fetal distress. In the most severely ill patients, it is associated with lactic acidosis and high mortality.

3.4.3.2 Management

If the diagnosis is in doubt, a therapeutic trial with 50% dextrose (20–50 ml intravenously) given over 5–10 minutes should be used. If injectable dextrose is not available, dextrose or sugary solution can be given to an unconscious patient through a nasogastric tube.

3.4.4 Pulmonary oedema

3.4.4.1 Clinical features

Pulmonary oedema may develop in pregnant women suddenly and unexpectedly or may occur immediately after childbirth.

3.4.4.2 Management

Treatment is to be given as for pulmonary oedema in adults, given above.

3.4.5 Anaemia

3.4.5.1 Clinical features

Maternal anaemia is associated with maternal and perinatal morbidity and mortality and an increased risk of fatal postpartum haemorrhage. The malarial anaemia may be complicated by iron and/or folic acid deficiency anaemia. Women who go into labour when severely anaemic or fluid-overloaded may develop pulmonary oedema after separation of the placenta.

3.4.5.2 Management

Women with a PCV lower than 20% or Hb concentration less than 7 g/dl should receive a slow transfusion of screened packed cells over 6 hours with precautions and frusemide 20 mg intravenously. Folic acid and iron supplements may be required.

The DVBDCO/ DMO should list all sentinel surveillance hospitals and other facilities in the district where emergency care for severe malaria is available and make it available at all PHCs and with all health workers and health volunteers. The MO-PHC should develop links with these institutions. For timely referral of severe cases, transportation can be provided from untied funds available under NRHM from Rogi Kalyan samity (RKS).

Prognostic indicators

The major indicators of a poor prognosis in children and adults with severe malaria are listed below.

Clinical indicators

- Age under 3 years
- Deep coma
- Witnessed or reported convulsions
- Absent corneal reflexes
- Decerebrate/decorticate rigidity or opisthotonos
- Clinical signs of organ dysfunction (e.g. renal failure, pulmonary oedema)
- Respiratory distress (acidosis)
- Circulatory collapse
- Papilloedema and/or retinal oedema

Laboratory indicators

- Hyperparasitaemia (>250 000/µl or >5%)
- Peripheral schizontaemia
- Peripheral blood polymorphonuclear leukocytosis (>12 000/µl)
- Mature pigmented parasites (>20% of parasites)
- Peripheral blood polymorphonuclear leukocytes with visible malaria pigment (>5%)
- Packed cell volume less than 15%
- Haemoglobin concentration less than 5 g/dl
- Blood glucose less than 2.2 mmol/l (<40 mg/dl)
- Blood urea more than 60 mg/dl
- Serum creatinine more than 265 µmol/l (>3.0 mg/dl)
- High CSF lactic acid (>6 mmol/l) and low CSF glucose
- Raised venous lactic acid (>5 mmol/l)
- More than 3-fold elevation of serum enzymes (aminotransferases)

Chapter 4. Sentinel surveillance hospitals

Surveillance is defined as the ongoing and systematic collection, analysis, interpretation, and dissemination of data about cases of a disease and is used as a basis for planning, implementing, and evaluating disease prevention and control activities.

Malaria surveillance in India was traditionally a system mainly based on slide results, which has been refined over many years. It relied on surveillance of fever cases in the community by means of active fortnightly case detection conducted mainly by the Multi Purpose Worker – Male {MPW-M}. Active case detection (ACD) implies that the MPW (M) would visit all villages within the subcentre area fortnightly and look for fever cases which occurred between the current and previous visit. Due to shortages of MPW-M in the health care delivery system, the case yield from active case detection had been very low. As a result, the strategy has been revised recently with more focus on passive case detection at the community level by community health volunteers (ASHAs) deployed under the NRHM. Passive case detection (PCD) implies the detection of malaria in fever cases reporting to health facilities and health workers/volunteers. The volunteers are trained and deployed for providing early diagnosis (RDT and blood slide preparation) and effective treatment including use of ACT. ACD and case management will continue to be done by the MPWs in villages where the community level volunteers are not available.

The following forms have recently been introduced for routine case management and surveillance of malaria in the country:

M – 1. Fortnightly surveillance report of fever cases by ASHA/ MPW/ Health facility.
M – 2. Laboratory request form for slide examination.
M – 3. Record of slide examination in PHC laboratory.
M – 4. Fortnightly report of cases – Subcentre/ PHC/ district / state.

Timely referral of cases to hospitals is necessary for proper management of severe malaria cases and limit mortality associated with malaria. Patients with symptoms and signs of severe disease suggesting malaria and associated pregnancy as well as those, who do not improve quickly on antimalarial treatment or whose symptoms return within 14 days, will be referred to higher levels of care, where their problems can be competently managed. Though malaria morbidity is common, 0.5 - 2 % of falciparum malaria cases may develop complications. Cases of severe malaria will receive in-patient care and parenteral treatment with artesunate. artemether, arte-ether or quinine. For timely referral of severe cases, transportation should be provided from untied funds available under NRHM from Rogi Kalyan Samity (RKS).

A death can be medically certified as due to malaria only if blood smear and/or RDT have been positive for *P.falciparum*. All deaths due to malaria should be investigated in detail by the DMO/AMO/DVBDCO after consultating the medical officer. The proforma prescribed for the detailed investigation of malaria death and important epidemiological considerations are given in Annexure D. Recent literature points to the possibility of severe malaria in patients with Plasmodium vivax. Although this is very rare, it should be recognized, so cases with only *P.vivax* may also be recorded as severe, if they fulfill the clinical criteria. If the slide is positive for *P.vivax* only, death can only be certified as due to malaria by a tertiary level or higher facility, and a case report must be submitted to the State VBDCP for detailed death investigation.

The purpose of sentinel surveillance is to manage and report severe cases of malaria in an effective and efficient manner. There is at present insufficient data available on severe cases of malaria and malaria deaths in India. Sentinel surveillance is necessary for documenting events which are not being captured by the regular system of reporting viz. severe cases of malaria, their management, malaria deaths and effectiveness of the antimalarial drugs used. Monitoring of these events is also important for assessing impact of the malaria control programme. It is expected that with the introduction of RDTs and ACT for falciparum malaria in the programme, there will be a steady reduction in the number of severe cases and deaths. Thus, monitoring of trend of these events will indicate the availability, accessibility and efficiency of primary level services. High or increasing numbers of in-patients from a specific geographical area will serve as a warning sign of poor peripheral level services or impending outbreaks.

To obtain reliable, representative information on severe cases of malaria, hospitals in high endemic districts will be developed into sentinel sites. The overall objective of the sentinel surveillance hospital for severe malaria is to improve the management of such cases in order to reduce case fatality. The specific objectives are:

- To assess the magnitude of severe cases of malaria
- To know the patterns of severe cases of malaria
- To analyze the reasons / situations which lead to complications of malaria
- To improve referral from primary health care facilities to sentinel surveillance hospitals
- To improve the capacity of medical and paramedical staff in management of severe cases of malaria
- To improve the infrastructure in identified hospitals for management of severe cases of malaria.

Establishing Sentinel Sites/Hospitals

It is planned to establish a minimum of two sentinel surveillance hospitals in each district which has high malaria endemicity. The numbers of these hospitals may be increased subsequently. Private hospitals which provide regular, authentic data may also be designated as sentinel surveillance hospitals. The sentinel sites will be adequately staffed and the medical officers and LTs will be trained. A Sentinel Surveillance Medical Officer (SSMO) will be in charge of all activities regarding malaria in the sentinel surveillance hospitals. The laboratory will have a qualified Sentinel Surveillance Laboratory Technician (SSLT), and the malaria microscopy will be quality controlled.

These hospitals will be equipped with laboratory and all the facilities required to manage complications of severe malaria and other vector borne diseases. The minimum requirements of manpower, drugs and commodities at a sentinel surveillance hospital are given below.

Staff

- Trained medical officers including specialists
- Trained nursing staff

Drugs and equipment

- IV sets
- Disposable syringes and needles
- Inj. Arteether/Artesunate/Artemether

- Inj. Quinine
- Inj. Diazepam
- Inj. Sodium bicarbonate
- ACT blister packs
- Tab. Quinine
- Tab. Primaquine
- Tab. Paracetamol
- Antibiotics
- Oxygen
- Thermometer
- Sphygmomanometer
- Ophthalmoscope
- Nasogastric tube
- Endotracheal tube
- Indwelling catheter
- Tongue depressor and airway

Laboratory facility for

- Smear for malarial parasites including their density
- Routine blood examination (Hb, TLC, DLC)
- Urine – Albumin, sugar and microscopic examination
- Blood sugar
- Blood urea and serum creatinine
- Serum electrolytes
- Examination of CSF to exclude meningitis
- Blood culture to exclude bacterial infections and septicaemia
- RDTs for malaria for use in emergency when the laboratory technician may not be present

In addition to high quality case management services, there will be regular recording and reporting system which will provide data for use of the programme managers for disease control action. Timely referral of cases to sentinel surveillance hospitals and their proper management in these hospitals will limit mortality associated with malaria.

Selected medical college hospitals and other tertiary care hospitals will be identified as training establishments for personnel of the sentinel surveillance hospitals. It is proposed to have a two-day training course for the personnel.

At each sentinel site, the LT (SSLT) working under the supervision of the SSMO will be responsible for the quality of the malaria laboratory results and for data compilation. Each day the SSLT will record information of all fever cases tested for malaria from the lab register into the sentinel surveillance site malaria register (SSMR). The format of the register is attached as appendix B. The information of all fever cases from different OPDs and on in-patients is entered on the same form to avoid double-counting and difficulties in patient identification. The record of inpatients is completed from the case sheets and the final outcome cured and discharged / died/ referred / left without discharge is carefully recorded. Every SSMR, which has not been completed with in-patient information, is taken to the relevant in-patient department weekly until it has been completed. The paper based SSMR are filed in the health

facility, where they have been generated. At the end of each fortnight the sentinel site report is generated from the SSMR by the SSLT. The sentinel site report is attached as appendix C.

The data from sentinel sites will give information on age-specific morbidity and mortality due to malaria, especially under-5 morbidity and proportional mortality rate due to malaria. The following indicators will be derived from the data obtained from every fortnight from the sentinel sites.

Table – 6. Indicators

S. No.	Indicator (age-specific)	Description
1.	% OPD cases attributed to malaria	Total No. of outdoor cases of malaria cases / Total No. of all-cause outdoor cases x 100
2.	% in-patient cases attributed to malaria	Total No. of indoor cases of malaria cases / Total No. of all-cause indoor cases x 100
3.	Proportional mortality due to malaria	Total No. of deaths due to malaria in admitted cases / Total no of all-cause deaths in admitted cases x 100
4.	Case fatality rate of confirmed severe malaria	Total No. of confirmed malaria deaths / Total No. of confirmed severe malaria cases X100

Higher case fatality rate indicates delayed referrals, inadequate services at the health facility, entry of new infection in previously non-immune community, recent development project area. If there is a sudden increase in severe malaria cases reported from a specific block or PHC that will indicate an outbreak situation, which should normally be detected in routine surveillance.

Chapter - 5. Case studies

Guidelines for trainers

1. The trainees will then be divided into 3 groups. Each group will discuss 1 case study and come to consensus on the answers to the questions (20 minutes for group discussion).

2. Each group should present its findings of each case study in ten minutes, to be followed by a discussion of each case study for 20 minutes. This process is extremely important because of the problem solving approach on which this module is based.

3. As a trainer, it should be ensured that all participants understand the reasoning behind the answers to each question before proceeding to the next case study.

4. Active participation of trainees will be ensured by way of revision of the subjects. This gives the trainees the opportunity to make a clear synthesis of the subject as a whole.

5. The suggested answers to the case studies (given at the end) will help the trainer in the discussion session following the presentation of the group work. They can be photocopied and used as handouts after the case studies have been completed.

CASE STUDY - 1

A woman from Punjab, aged 25 years, wife of an officer in Assam Rifles is brought to a central hospital at Dimapur (Nagaland). She is in the seventh month of her first pregnancy.

The patient became ill five days ago, with chills, sweating and headache. An antibiotic was prescribed and her condition seemed to improve, but yesterday she developed rigors and persistent vomiting. A blood film at the local clinical revealed malaria parasites, and oral quinine (600 mg every 8 hours) was prescribed. She took two doses.

Today she has been referred to a central hospital because of restlessness and increasing mental confusion. Examination reveals a semiconscious woman, who is unable to converse. She withdrew her hand from a painful stimulus. There is no neck stiffness, jaundice, pallor or rash. Axillary temperature is 39° C, pulse 90 beats/min. and blood pressure 110/70 mm Hg. The uterine fundus is palpable (26-28 weeks), and the foetal heartbeats can be heard.

Question 1. What tests are urgently required?

Answer 1:

Blood glucose. Pregnant women are susceptible to hypoglycaemia with any stress or infection. They are particularly likely to develop hypogycaemia during treatment with quinine. This patient is pregnant, has already received quinine and has altered consciousness. Hypoglycemia is therefore, a strong possibility and must be urgently checked for.

Haematocrit. Because she is pregnant she may already be anaemic due to iron or folate deficiency. Malaria may rapidly exacerbate anemia. The risk of developing pulmonary oedema is increased in patients with severe anaemia.

Parasite density.

Lumber puncture (where possible). Meningitis may coexist with malaria and can be impossible to identify without examination of the cerebrospinal fluid.

Blood culture (where possible). Septicemia may complicate severe malaria. In pregnancy there is increased susceptibility to bacterial infections – e.g. pneumococcal infection.

Question 2. If the whole-blood glucose is 1.2 mmol/L, what treatment will you give?

Answer: 50% dextrose, 20 ml by intravenous injection. As hypoglycaemia may recur and can be severe in pregnancy, monitor the blood glucose level frequently.

Question 3. If the blood film shows *P.falciparum* rings '++++', and the cerebrospinal fluid is normal except for low glucose, in that case:

a) What animalarial drugs will you administer and by which route?

Answer: Quinine by intravenous infusion. An alternative route for quinine is intramuscular, but the intravenous route is preferable in a centre where a drip can be set up.

b) Is there an alternative to quinine in the pregnant woman?

Answer: As per WHO Treatment Guidelines 2006, parenteral artesunate preparations may safely be used in 2nd and 3rd trimesters of pregnancy.

c) Would you give a loading dose of quinine?

Answer:A loading dose of quinine should not be given, because the patient has received quinine within the last 24 hours, and a loading dose may therefore, lead to dangerously high blood levels of the drug.

d) What nursing procedures are important during this treatment?

Answer: An important nursing responsibility is the control of the rate of infusion. If quinine is allowed to run too rapidly, hypotension and hypoglycemia may develop. On the other hand, if the infusion is too slow, inadequate blood levels of the drug may be achieved. Meanwhile, care of the semiconscious patient is essential. As she is restless she must be protected from falling and from pulling out drip lines.

Question 4. After six hours, the patient becomes increasingly restless. The respiratory rate increases to 40/ minute. The blood glucose level is normal. Under these conditions, what special observations would you make?

Answer: Look for evidence of pulmonary oedema, which may complicate falciparum malaria, especially in pregnancy. Review the urinary volumes passed, the volumes of intravenous fluid given and the fluid balance.
Assess the central venous pressure (clinically or, if possible, with the help of a central venous pressure line).
Examine carefully for gallop rhythm, basal crepitations and hepatic enlargement.

Question 5. What other observations are particularly important in this patient?

Answer: Foetal heart rate. Foetal distress is common in malaria, especially if there is high fever. Assisted vaginal delivery or even Caesarian section must be considered if foetal distress is severe.

Question 6. What is the first question that you would ask this patient's relatives?

Answer: Ask about travel history – when had she visited parts of the country where transmission of malaria occurs? Had she received a blood transfusion in the recent part (an alternative source of malarial infection).

CASE STUDY – 2

In PHC Borda, District Kalahandi, Orissa, various antimalarial drugs are available, but intravenous infusions cannot be given.

A child aged 20 months became feverish two days ago and has vomited several times today. One hour ago the child had a convulsion, described by the mother as a repetitive twitching of limbs and mouth, followed by unresponsiveness for a few minutes. The child is now febrile, fully conscious, and able to localize and respond to a painful stimulus. A thick blood film shows *P. falciparum* rings '++++'. The child repeatedly vomits any antimalarial drug given by mouth

Question 1. Does the child have cerebral malaria?

Answer:The fact that the child is now fully conscious suggests that the convulsion was a 'febrile convulsion' rather than a component of cerebral malaria. Convulsions occur in cerebral malaria but they are not followed by rapid recovery of consciousness.

a) What should you do about the convulsions?

Answer:Make sure that the risk of further convulsions is minimized by reducing the child's temperature by pararcetamol, tepid sponging, fanning, etc.

Question 2. The district hospital is 30 km away and the journey will probably take several hours by bus.

a) Should the patient be referred to hospital?

Answer:The decision to refer the patient will depend on facilities available at the health centre. This child needs antimalarial drugs and fluids, and should receive them at a centre where they are available, secondly observe the child's progress carefully.

b) What treatment would you give in the meanwhile?

Answer:Because the child is persistently vomiting, the first dose of antimalarial drug should be given parenterally. Ideally, this should be by slow intravenous infusion, but since this is not

possible in this facility in this case, if may be given by intramuscular injection: quinine (10 mg salt / kg).
A loading dose of quinine (20 mg salt / kg) can safely be given by the intramuscular route, as long as the patient has not received quinine or quinidine in the preceding 24 hours. A reasonable approach is to give quinine 10/mg/kg intramuscularly immediately, followed by 10 mg/kg intramuscular (i. e. the remainder of the loading dose) after 4 hours.
Because of the history of a febrile convulsion, make sure that the mother continues to give her child tepid sponging and fanning to reduce the risk of further convulsions. The child may cease to vomit soon after the injection, especially if the temperature has been successfully lowered. It may then be possible to continue treatment by mouth, without referral to a larger centre.

Question 3. The child successfully took the second and third doses of quinine by mouth and was brought back to the clinic the next day; there had been little change; the child was still febrile and the parasitaemia was similar to the previous day. Does this suggest that the child has drug-resistant malaria?

Answer: Fever commonly persists, and degree of parasitaemia may remain same for up to 24 hours after the start of treatment, even if the parasite is fully sensitive to the drug being given. By 48 hours, however, the density of parasitaemia should be greatly reduced and the condition of the patient improves.

CASE STUDY - 3

The patient, a 28 year old male from Chandrapur District of Maharashtra was posted in Ladakh for five year. He returned home last month.

One week ago he developed fever. He decided this could not be malaria because he had grown up in a malarious area and believed he was therefore immune. Two days ago he became confused, especially at night. He stayed in bed and was attended by a servant who today called the doctor because the patient was increasingly confused. The last urine he had passed was a small volume of very dark fluid 24 hours ago.

On examination, the patient was a well nourished adult man. He was afebrile (rectal temperature 36.5^0 C). He was restless but could make brief appropriate answers to questions, and localize the site of painful stimuli. He was jaundiced and his mucous membrane was pale. There was bleeding from the gums and there were a few retinal haemorrhages in the eyes.

Question 1. What is the differential diagnosis?

Answer:Consider all diseases that may lead to encephalopathy with jaundice: i.e. fulminant hepatitis. Yellow fever, viral fevers, relapsing fever, septicaemia, leptospirosis, alcoholism, sickle cell crisis, etc. Nevertheless, under the circumstances if the patient is not able to pass urine, severe falciparum malaria may be the most likely diagnosis. Retinal haemorrhages are common in severe malaria, and do not on their own indicate the presence of abnormal bleeding tendency.

a) Was the patient right to think he was immune to malaria?

Answer: No. Immunity to malaria is partial, and may be almost completely lost if the patient doesn't stay in endemic area for a few years.

Question 2. The thick blood film shows *P.falciparum* '++++' and the thin blood film shows that 26% of red cells are parasitized.

a) What else would you look for in the thin blood film?

Answer: Platelets. Thrombocytopaenia is usual in falciparum malaria but may be particularly severe in this patient who has signs of bleeding tendency. Severe thrombocytopaenia may be evident on a thin blood film.

b) What other tests would you carry out to investigate the bleeding tendency?

Answer: Platelet count and prothrombin time. If possible it would be useful to know the plasma fibrinogen and fibrin degradation products. If the platelet count and plasma fibrinogen are very low in a patient with spontaneous bleeding the bleeding can be attributed to disseminated intravascular coagulation (DIC). However, if only the thin blood film can be done, the scantiness of platelets in the presence of bleeding in a patient with malaria suggests DIC. The best bedside test for the presence of abnormal bleeding due to DIC is the bleeding time. In this patient, this is likely to be prolonged, since there is abnormal bleeding spontaneously from the gums. A record of bleeding time would be useful in order to monitor progress in response to treatment.

c) What treatment is needed for the bleeding?

Answer: Fresh blood transfusion and alternatively, platelet-rich plasma. Vitamin K is not hel*pf*ul since the bleeding is not due to vitamin K deficiency. This patient may need blood transfusion for malarial anaemia also.

Question 3. The patient has not passed urine for 24 hours. What investigations and actions are appropriate?

Answer: Palpate the abdomen to see if the bladder is distended. Try to get the patient to pass urine; if he cannot, catheterize with full sterile precautions and record urine volumes. Do routine examination of urine and if possible, for sodium concentration and specific gravity also. Correct any under-hydration by careful saline infusion (urine specific gravity > 1. 015 and sodium < 20 mmol/L suggests dehydration), and if necessary, use drugs such as furosemide and dopamine for proper flow of urine. Measure plasma urea, creatinine and electrolytes if possible; and electrocardiograph helps to demonstrate hyperkalaemia. If acute tubular necrosis gets established, intensive care is required, with peritoneal dialysis or haemodialysis.

Question 4. 15 ml of dark brown urine was obtained by catheter. The urine examination revealed albumin '++', blood '+++', conjugated bilirubin '++' and urobilinogen '++'. Microscopy of the urine showed no cells and a few casts. How do you interpret the results of the urine test?

Answer:The presence of 'blood in the urine (i.e. haemoglobin) in the absence of red blood cells indicates that there is free haemoglobin in the urine, as a result of intravascular haemolysis, a

complication of severe falciparum malaria. Bilirubinuria indicates that there is some increase in the conjugated hyperbilirubinaemia, as in haemolysis. Proteinuria is usual in the presence of acute tabular necrosis, which is the commonest of renal failure to complicate falciparum malaria.

Question 5. Acute renal failure is confirmed. Is it possible that the kidneys may recover?

Answer:Yes, in acute tubular necrosis, recovery commonly takes place within a period of few weeks, It is therefore important to keep the patient alive, if possible, by dialysis (usually peritoneal dialysis) – because full recovery is then likely, without the need for continued long – term dialysis.

How should quinine therapy be given to this patient with acute renal failure?

Answer:If acute renal failure is confirmed, the first dose of quinine should be the same as in any other patient with severe malaria, but if acute renal failure is established, the dose should be reduced by 50% from the third day onwards.
Note: Peritoneal dialysis can be life-saving and the results are achieved without the use of costly equipment. However it requires experience and competence. Guidelines for indications and methods of peritoneal dialysis are available and should be taught and demonstrated to hospital staff who may be responsible for management of patients with severe malaria. Fortunately, acute renal failure is very rare in African children with severe malaria.

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Annexure 'A'

Patient Referral Form

Name …….. Age …… Sex ……
Address ……..
Contact person(s) ……..
Date and time of admission …….. Date and time of referral ……..
Chief complaint …… Pregnancy status …….
Present illness ……
Past history ……...

Physical examination

Vital signs	BP (mm Hg)	Pulse rate per minute	Respiratory rate per minute	Temperature (°C)	Glasgow Coma/ Blantyre score
At admission (date & time)……					

Events in health centre

Events	Observations	Events	Observations
Convulsions		Hypoglycaemia	
Bleeding		Blood transfusion	
Oliguria		Others(s)	
Respiratory distress			
Shock			

Antimalarials

Drug	Dosage	Start		Last dose	
		Date	Time	Date	Time
1. ……..					
2. ……..					

Other medications

Drug	Dosage	Start		Last dose	
		Date	Time	Date	Time
1. ……..					
2. ……..					

Fluid chart

Date					
Intake					
Output					

Parasite density

Date					
Parasite density					

Other investigations

Investigation	Date and time	Result
Chest X-ray		
12 Lead ECG		
Others		

Reasons for referral …….....
Signature of referring doctor ……. Name ……..
Telephone/Mobile ……Fax …….. e-mail …….....
Name and address of referring hospital ……

Annexure 'B'

NATIONAL VECTOR BORNE DISEASE CONTROL PROGRAMME

Sentinel Surveillance Hospital - Malaria Register

Period From …… To ……

Sentinel site: District/Sub-district/ CHC/PHC/ Medical College/ Public Sector/ Private sector……

Name of district: ……

S. No.	Date	Name of patient (Father's/ spouse's name)	Address - Subcentre	Village (with landmark)	Age (Yrs)	Sex (M/ F)	Pregnant (Y/ N)	Date of onset of fever	Date of first contact with Govt health system	Investigations for malaria			Date of reporting to Sentinel Hospital	Date of initation of treatment	Whether Admitted (Yes/ No)	If admitted				
										Place of Investigation	Result of Blood slide (*Pv*/ *Pf*)	Result of *Pf* RDT (Pos/ Neg)				Date of Admission	Final Diagnosis	discharged/ referred/ Left without discharge/	Treatment given	Outcome*

* Coding for outcomes: CD – Cured and discharged; RF – Referred; DD – Died; LD – Left without discharge

Annexure 'C'

NATIONAL VECTOR BORNE DISEASE CONTROL PROGRAMME

Sentinel Hospital Report

Name of Sentinel Hospital: ……

Month/Year…… Fortnight……

A.

Total New OPD Cases	Suspected Malaria Cases	Malaria Cases Confirmed			Pregnant women with malaria	Malaria Cases								Total
						less than 1 year		1-4 years		5-14 years		more than 15 years		
		Pv	*Pf*	Total		M	F	M	F	M	F	M	F	
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15

B.

Total inpatients	Total inpatients admitted with severe malaria	Severe Malaria Cases Confirmed			Pregnant women with severe malaria	Severe Malaria Cases								Time lag between onset and reporting to Sentinel Hospital			Total hospital deaths	Deaths due to confirmed malaria
						less than 1 year		1-4 years		5-14 years		more than 15 years						
		Pv	*Pf*	Total		M	F	M	F	M	F	M	F	< 3 days	3-7 days	>7 days		
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19

INVESTIGATION REPORT FOR DEATH DUE TO MALARIA

Investigation to be done by District Malaria Officer/AMO/ District VBD Consultants in consultation with a Medical Officer

Date of Investigation:_____

1. Basic information:

- Name of the deceased _____Age (in years)_____Sex _____
- In adult female, indicate status of pregnancy and its complications, if any:_____
- Date of onset of illness _____ Date of Death _____
- Date of first contact with health care provider (ASHA/MPW/SC/PHC/CHC/District Hospital/ Other (specify) _____
- Occupation of the deceased:_____
- Complete address (usual place of residence)_____
  _____
  _____
- Place where disease started_____
- History of movements (within 3 weeks preceding from the date of onset of illness)
  _____
  _____
- Source of information: Relatives/Paramedical staff/ Treating physician/ Specialist/other (specify)___

2. Major Signs and symptoms (S/S) with duration:

S/S	Duration	S/S	Duration	S/S	Duration	S/S	Duration
Fever		Anaemia		Jaundice		Rash	
Bleeding		Diarrhoea		Dyspnoea		Oliguria/anuria	
Neck rigidity		Altered Sensorium		Convulsions		Coma	

Other signs/symptoms:_____
_____

H/O of chronic illnesses (Diabetes, hypertension, asthma, HIV etc)_____
Relevant History in the past:_____
H/O of similar illness in family/neighbourhood in the past:_____

3. Parasitological Investigation:

Date	Date of RDT Testing/Colle slide	Place of test	Results (Pf/Pv/Other)	Date of Receipt of result
RDT				
Blood slide				

4. Other Biochemical/Pathological investigations done (specify): _____
_____
_____

5. Diagnosis: Clinical Diagnosis:_____
Confirmed Diagnosis: Malaria (Pf or PV specify) _____ other _____

6. Treatment before hospitalization: Date of starting treatment _____
Details of Treatment given before hospitalization:

Name of Drug	Dose	Date		Route of Administration
		From	To	

7. Treatment after admission to hospital:

Name of Drug	Dose	Date		Route of Administration
		From	To	

- Other supporting treatment_____
  _____
  _____

8. Cause of Death:

Confirmed Malaria (*Pf/Pv*/Others)	Clinically suspected Malaria	Others (Specify)

- Post-mortem diagnosis (if undertaken)_____

9. Public health follow-up preventive/control actions taken by State/District/local health authorities in affected area:

10. Remarks of the investigating officers:

Name and Signature of DMO/ Assistant DMO/VBD Consultant

Name/ Signature Medical

Blood Transfusion		
General indications for blood transfusion:	**Before transfusion, check the following:**	**During transfusion, check the following**
Acute blood loss, when 20–30% of the total blood volume has been lost and bleeding is continuing Severe anaemia if packed cells are available, give 10 ml/kg over 3-4 hours preferably. If not, give whole blood 20 ml/kg over 3-4 hours. Septic shock if IV fluids are insufficient to maintain adequate circulation and in addition to antibiotic therapy	• The blood is the correct group and the patient's name and number are on both the label and the form (in an emergency, reduce the risk of incompatibility or transfusion reactions by cross-matching group-specific blood or giving O-negative blood if available. • The blood transfusion bag has no leaks. • The blood pack has not been out of the refrigerator for more than 2 hours, the plasma is not pink or has large clots, and the red cells do not look purple or black. • Any signs of heart failure. If present, give 1mg/kg of furosemide IV at the start of the transfusion in children whose circulating blood volume is normal. Do not inject into the blood pack.· • Do a baseline recording of the child's temperature, respiratory rate and pulse rate. The volume transfused should initially be 20 ml/kg body weight of whole blood, given over 3–4 hours.	• If available, use an infusion device to control the rate of the transfusion • Check that the blood is flowing at the correct speed. • Look for signs of a transfusion reaction (see below), particularly carefully in the first 15 minutes of the transfusion. • Record the child's general appearance, temperature, pulse and respiratory rate every 30 minutes.· • Record the time the transfusion was started and ended, the volume of blood transfused, and the presence of any reactions.

Transfusion reactions

If a transfusion reaction occurs, first check the blood pack labels and patient's identity. If there is any discrepancy, stop the transfusion immediately and notify the blood bank immediately.

Type of transfusion reTatyction		
Mild reactions (Due to mild Hypersensitivity	• Itchy rash	• Slow the transfusion • Give chlorpheniraamine 0.25 mg/kg IM • Continue the transfusion at the normal rate if there is no progression of symptoms after 30 minutes • If symptoms persist, treat as

		moderate reaction
Moderately severe reactions (Due to moderate hypersensitivity, nonhemolytic reactions, pyrogens or bacterial contamination	• Severe itchy rash (urticaria) • Flushing • Fever >38 ° C or >100.4 °F (Note: fever may have been present before the transfusion) • Rigors • Restlessness • Raised heart rate	Stop the transfusion, but keep the IV line open with normal saline • Give IV hydrocortisone, or chlorpheniramine 0.25 mg/kg IM, if available • Give a bronchodilator, if wheezing • Send the following to the Blood Bank: the blood-giving set that was used, blood sample from another site, and urine samples collected over 24 hours. • If there is improvement, restart the transfusion slowly with new blood set and observe carefully • If no improvement in 15 minutes, treat as life-threatening reaction (see below), and report to doctor in charge and to the blood bank
Life-threatening reactions (Due to haemolysis, bacterial contamination and septic shock, fluid overload or anaphylaxis)	• Fever>38°Cor >100.4° F (note: fever may have been present before the transfusion) • Rigors • Restlessness • Raised heart rate • Fast breathing • Black or dark red urine (haemoglobinuria) • Unexplained bleeding • Confusion • Collapse	Stop the transfusion, but keep the IV line open with normal saline • Maintain airway and give oxygen • Give epinephrine (adrenaline) 0.01 mg/kg body weight (equal to 0.1 ml of 1 in 10000 solution • Treat shock • Give IV hydrocortisone, or chlorpheniramine IM, if available • Give a bronchodilator, if wheezing • Report to doctor in charge and to blood laboratory as soon as possible • Maintain renal blood flow with IV furosemide 1mg/kg • Give antibiotic as for septicaemia

* Note that in an unconscious child, uncontrolled bleeding or shock may be the only signs of a life-threatening reaction.

Type of transfusion
After transfusion:
Reassess the child. If more blood is needed, a similar quantity should be transfused.
Give treatment with iron (daily dose of iron/folate tablet or iron syrup) for 14 days, once acute infections have been treated.

• Ask the parent to return with the child after 14 days. Assess the child for response to iron therapy. Children become less irritable and have improved appetite. Rise in Hb can be documented by 10-14th day. If there is no response to iron therapy, assess for the cause (inadequate dose taken, diarrhoea, malabsorption, presence of infection like UTI and TB). Treatment should be given for 3-4 months, where possible. It takes upto 8 weeks to correct the anaemia and 2–3 months after the haemoglobin reverts to normal to build up iron stores
• Advise the mother about good feeding practices.

T

Annexure 'F'

Management of shock in a child without severe acute malnutrition

- Weigh the child. Estimate the weight if child cannot be weighed or weight not known
- Check that the child does not have severe acute malnutrition
- Give Oxygen
- Make sure child is warm

Insert an intravenous line and draw blood for emergency laboratory investigations

Chart 4: Management of shock in a

↓

· Give Ringer's lactate or Normal saline
· Infuse **First Bolus** -20 ml/kg as rapidly as possible in a child & over 20-30 minutes in a young infant

↓

Reassess child

↓

No improvement

↓

If improvement with fluid bolus at any stage:*
Fluid responsive shock
· Observe and continue fluids (70 ml/ kg over 5 hours in infants and over 2 ½ hours in a child)
· Give additional fluids if losses

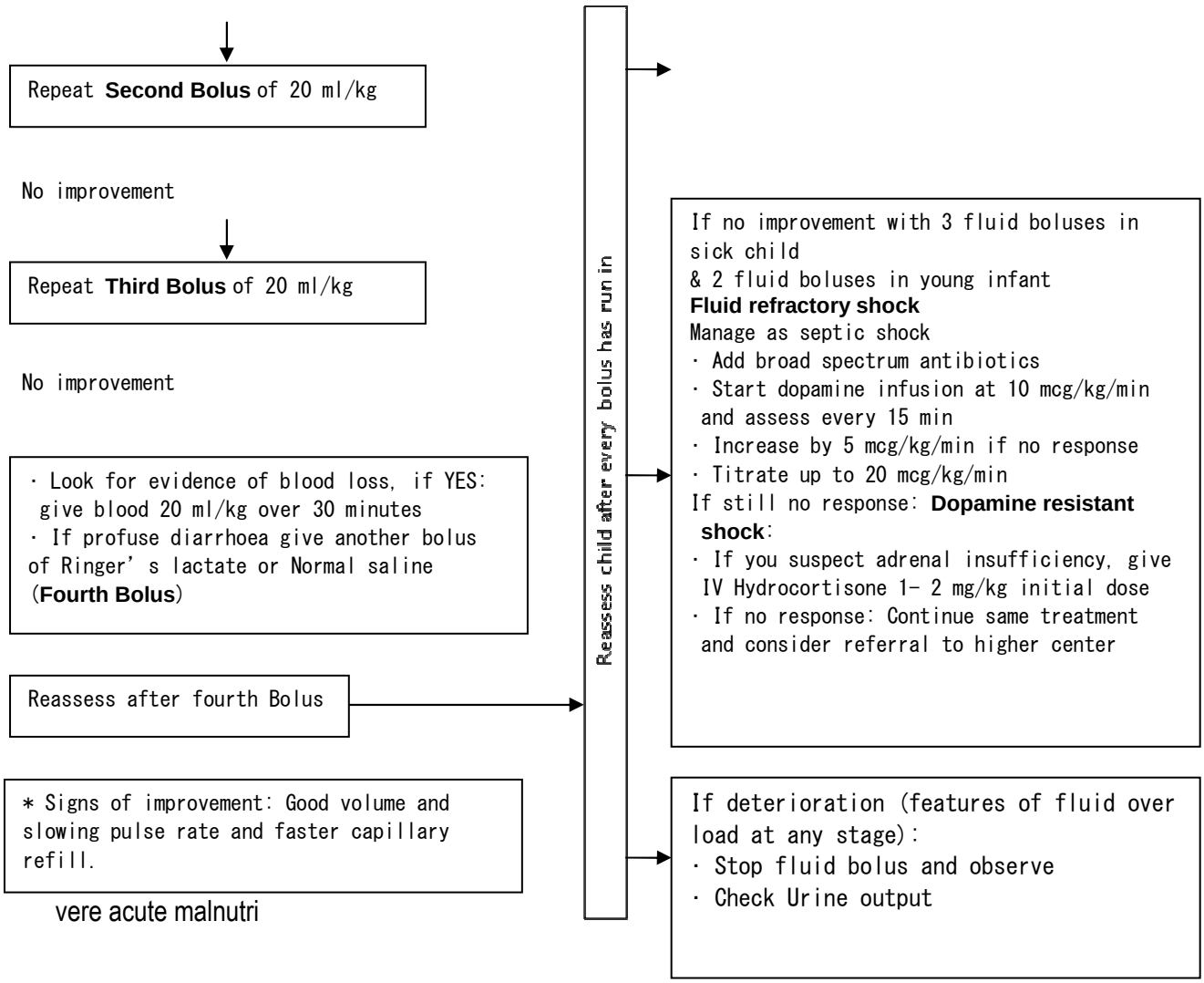
↓

↓

↓

↓

↓


Repeat **Second Bolus** of 20 ml/kg
No improvement
Repeat **Third Bolus** of 20 ml/kg
No improvement
· Look for evidence of blood loss, if YES: give blood 20 ml/kg over 30 minutes
· If profuse diarrhoea give another bolus of Ringer's lactate or Normal saline (**Fourth Bolus**)
Reassess after fourth Bolus
* Signs of improvement: Good volume and slowing pulse rate and faster capillary refill.
vere acute malnutri
Reassess child after every bolus has run in
If no improvement with 3 fluid boluses in sick child
& 2 fluid boluses in young infant
Fluid refractory shock
Manage as septic shock
· Add broad spectrum antibiotics
· Start dopamine infusion at 10 mcg/kg/min and assess every 15 min
· Increase by 5 mcg/kg/min if no response
· Titrate up to 20 mcg/kg/min
If still no response: **Dopamine resistant shock**:
· If you suspect adrenal insufficiency, give IV Hydrocortisone 1- 2 mg/kg initial dose
· If no response: Continue same treatment and consider referral to higher center
If deterioration (features of fluid over load at any stage):
· Stop fluid bolus and observe
· Check Urine output

Management of shock in a child with severe acute malnutrition