A. Early detection

Early detection and correct treatment and nursing care of malaria patients will result in lower mortality and morbidity rates. The mortality rate for cerebral malaria varies from 5-20% depending on concomitant major organ complications. Early detection should be accomplished by careful evaluation of the history and correct examination of the patient. Thick and thin blood films should be examined. Antigen detection / strip tests [blood for *P. falciparum* Histidine-Rich Protein-2 (Pf HRP2) or *P. falciparum* Lactate Dehydrogenase (Pf LDH)] are valuable for the rapid diagnosis of falciparum malaria (WHO, 2006).

1. History

Ask the relatives or responsible persons whether the patient has traveled to a malarious area, has a history of malaria infection, chronic malaria, or has taken any anti-malarial drugs prior to admission/consultation. If so, check the blood film more frequently (if the patient has recently taken medication, the blood film may be false-negative). At least three negative blood films are needed to rule out a diagnosis of malaria. Ask if the patient has received a blood transfusion. Even if the patient has never traveled to a malaria-endemic area, but has received a blood transfusion or has worked in a laboratory with malaria infected blood, they are at risk. It has been reported that those who live near an airport, even though there is no malaria in their community, can get malaria from mosquitoes carried by airplanes. Those who work in an insectiary with mosquitoes may also be at risk of malaria if infected mosquitoes bite them.
2. Physical examination

The level of consciousness should be graded using either the Modified Glasgow Coma Scale for adults or Blantyre Coma Scale for children. Monitor vital signs and urine output, and look for evidence of shock. Look for evidence of an enlarged spleen, which could indicate a previous malaria infection. Look for signs of anemia and bleeding, and prepare for blood transfusion, if necessary. Patients who have received quinine or are jaundiced, and women in late pregnancy, are at risk of hypoglycemia. Monitoring blood glucose in these patients is essential. In patients who remain severely ill, the dose of quinine should be reduced on day 3 by one third. Frequently evaluate the nervous system for level of consciousness (hourly) (Training Unit-WHO, 1995; Harinasuta and Bunnag, 1988).
Evaluation of level of consciousness with cerebral malaria based on the Modified Glasgow Coma Scale

(Adapted from: Regional Guidelines for the Management of Severe Falciparum Malaria in Small Hospitals, WHO, New Delhi, 2006)

Modified Glasgow Coma Scale for adults

| Eyes open       | Spontaneously 4 |
|                | To speech 3     |
|                | To pain 2       |
|                | No response 1   |

| Best verbal response (Nonintubated) | Oriented and talks 5 |
|                                     | Disoriented and talks 4 |
|                                     | Inappropriate words 3 |
|                                     | Incomprehensible sounds 2 |
|                                     | No response 1 |

| (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 ranges from 3 to 15; unrousable coma reflected in a score of <9.

This scale can be used repeatedly to assess improvement or deterioration.
### Blantyre Coma Scale for children

(“Blantyre Coma Scale”)

<table>
<thead>
<tr>
<th>Category</th>
<th>Response</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye movements</td>
<td>Directed (e.g. towards mother’s face)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Not directed</td>
<td>0</td>
</tr>
<tr>
<td>Verbal response</td>
<td>Appropriate cry</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Inappropriate cry or moan</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>None</td>
<td>0</td>
</tr>
<tr>
<td>Best motor response</td>
<td>Localises to painful stimuli</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Withdraws limb from pain</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Non-specific or absent response</td>
<td>0</td>
</tr>
<tr>
<td>Total score</td>
<td></td>
<td>0–5</td>
</tr>
</tbody>
</table>

Total score can range from 0-5; 2 or less indicates unrousable coma.
This scale can be used repeatedly to assess improvement or deterioration.
3. Differential diagnosis

Those who have altered consciousness must be evaluated for hypoglycemia, renal failure, electrolyte imbalance, and post-ictal state. Examine the blood sugar, BUN, creatinine, electrolytes, liver function tests and urine analysis. A blood culture should be taken.

Those with cerebral malaria will have a reduced level of consciousness. Prior to altered consciousness, the patients may have been high fever, body aches, headache, nausea, vomiting or abdominal pain. After that, the consciousness level can deteriorate, resulting in confusion, decreased responsiveness, no communication or incontinence. There may be generalized or focal seizures, disconjugate gaze or muscle twitches. The clinical signs and symptoms may be similar to encephalitis or meningitis. A lumbar puncture should be performed to differentiate between cerebral malaria and other central nervous system (CNS) diseases after a normal eye ground examination (Warrell, 1997).

4. The diagnosis of malaria

Perform thick and thin blood films for malaria. The thick film is more likely to detect a smaller numbers of parasites than the thin film, because the thick film uses more blood. The thin film is useful in detecting the species of malaria, % infected red blood cells, stage of parasite development, and presence of neutrophil pigment (> 5% of neutrophils containing pigment indicates a poor prognosis)

Usually, the higher the percentage of infected red blood cells, the more serious the case is. However, some severe patients may not have hyperparasitemia, probably due to peripheral sequestration of the parasite in the brain or other vital organs. Ideally, the number of parasitized red cells per 1,000 RBCs (thin film) or the number of parasites per 200 white cells (thick film) should be reported.
**Malaria Rapid Diagnostic Test (RDT)**

The RDT is a rapid test to evaluate the presence of malaria antigens in the blood of a patient suspected of having malaria. Some RDT check for *P. falciparum* only, while others check for other malarials. The test may be a strip, card, or cassette. The tests are sensitive and as accurate as microscopy. They are good for people who do not have a microscope available, have no electricity, or where no one is trained to use a microscope. However, the World Health Organization (WHO, 2004) recommends that after starting treatment, management decisions should not be based on the RDT alone. A confirmatory test should be performed with microscopy.

**B. Early treatment**

The treatment of malaria is separated into 2 groups: uncomplicated and complicated malaria.

1. **Uncomplicated malaria.** The patient has no signs of complications. The treatment consists of:

   A. Early and appropriate antimalarial medication. The choice of medicine should be based on the drug sensitivities of the malaria parasites in that area. Artemisinin-based combination treatments are now recommended as first-line treatment for falciparum malaria by the World Health Organization (2006). Quinine combined with doxycycline, for non-pregnant adults and children > 8 years old, or clindamycin for pregnant women and children < 8 years old given for 7 days are second-line treatments. The first treatment dose should be observed. If the dose is vomited within one hour, it should be given again.
B. Symptomatic treatment. Treat symptoms, such as fever, body aches, nausea, vomiting or headaches, with appropriate medicine. Paracetamol (acetaminophen) (15 mg/kg 4 – 6 hourly) may be used to reduce fever.

C. Nursing care. Give supportive care and symptomatic treatment, such as tepid sponging for fever. Give health education regarding personal protection, prevention of malaria and compliance with treatment. The patient should be told to return if there is fever, especially in the 2 months after treatment or with *P. vivax* or *P. ovale* infection. The patient should be advised to take the full course of medication to prevent a return of malaria. If there is vomiting of the antimalarial drug, take an antiemetic medicine ½ to 1 hour before taking the antimalarial drug. If there is fever, take an antipyretic 1 hour before taking the antimalarial medicine. The patient should rest for 1–2 hours after taking the medicine, due to the risk of dizziness, vomiting, and hypotension. The patient should be given psychosocial support by encouraging the patient and giving comfort. All cases of malaria should be recorded and reported to the appropriate health authorities to help in the control of malaria. The patient should follow up with the doctor to evaluate for compliance, the therapeutic response to the drug and to evaluate for evidence of drug resistance.
2. Complicated (severe) malaria: The WHO (2006) criteria for severe malaria are as follows:

Clinical manifestations:
- Prostration
- Impaired consciousness
- Respiratory distress (acidotic breathing)
- Multiple convulsions
- Circulatory collapse
- Pulmonary edema (radiological)
- Abnormal bleeding
- Jaundice
- Hemoglobinuria

Laboratory tests:
- Severe anemia
- Hypoglycemia
- Acidosis
- Renal impairment
- Hyperlactatemia
- Hyperparasitemia

Some experts define the laboratory tests as follows: severe anemia is a Hb < 5g/dl, especially with > 100,000 parasites/µl; hypoglycemia is a serum glucose < 2.2 mmol/l or < 40 mg/dl; acidosis is a HCO₃⁻ < 15 mmol/l; renal impairment is a serum creatinine > 3 mg/dl or 250 µmol/l; hyperlactatemia is a serum lactate > 5 mmol/l; and hyperparasitemia is ≥ 5%.
### Antimalarial drugs in severe malaria (WHO, 2006)

<table>
<thead>
<tr>
<th>Antimalarial drug</th>
<th>Dosage and administration</th>
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</thead>
</table>
| Artemisinin derivatives | **Artesunate:** 2.4 mg/kg body weight (bw) intravenous (IV) or intramuscular (IM) on admission (time=0), followed by 2.4 mg/kg at 12 and 24 hours, followed by once daily for 7 days. Once the patient can tolerate oral therapy, treatment should be switched to a complete dosage of artemisinin-based combination therapy (ACT) for 3 days, as recommended in the national treatment guidelines for uncomplicated malaria.  
**Artemether:** 3.2 mg/kg bw IM on the first day followed by 1.6 mg/kg bw daily for 7 days. Once the patient can tolerate oral therapy, treatment should be switched to a complete dosage of an ACT.  
**Arteether:** 3.2 mg/kg bw IM on the first day, followed by 1.6 mg/kg bw for the next 4 days. Once the patient can tolerate oral therapy, switch to a complete dosage of an ACT. |
| Quinine | **Loading dose:** Quinine dihydrochloride 20 mg salt/kg bw diluted in 10 ml/kg bw of 5% dextrose or dextrose saline administered by IV infusion over a period of 4 hours. **Maintenance dose:** Quinine dihydrochloride 10 mg salt/kg bw diluted in 10 ml/kg bw of 5% dextrose or dextrose saline administered by IV infusion. In adults, the maintenance dose is infused over a period of 4 hours and repeated every 8 hours. In children, it is infused over a period of |
2 hours and repeated every 8 hours (calculated from the beginning of the previous infusion) until the patient is in a position to swallow. An oral medication can be given following this, to complete the 7-day treatment. The amount of fluid for infusion of quinine should be considered keeping in mind the hydration status of the patient. For instance, if the patient has volume overload or pulmonary edema, quinine in 10 ml/kg IV fluid may be harmful. Therefore, the calculation of fluid for quinine infusion should be made accordingly.

For choice of oral drugs for follow-on treatment, it is recommended to prescribe a combination therapy: 3 days of ACT according to the national treatment guidelines. If ACT is not in use in the country, quinine should be administered in combination with tetracycline or doxycycline or clindamycin, to complete the 7-day treatment, except for pregnant women and children <8 years of age, for whom tetracycline/doxycycline is contraindicated.
Refer patient to a hospital with better facilities to care for severe malaria

Indication to refer severe malaria patients. The decision to refer a patient with severe malaria is based on the ability of the facility to give appropriate management for severe malaria. This includes medications, hemofiltration or hemodialysis, artificial ventilation, multiple transfusions, treating pregnant women, postpartum patients, multi-organ failure, active bleeding, and cerebral malaria not responding to appropriate treatment within 48 hours.

• Pre-referral. Provide information to the family, guardian and patient about the diagnosis and treatment plan. Explain that the disease can be lethal if not treated early and properly in the hospital. Know where to refer the patient and how to transfer the patient safely. Make sure the referral facility has the ability to perform dialysis and has a ventilator for the management of respiratory failure. Check blood glucose before transfer.

When referring to another hospital, if possible, communicate directly with the hospital personnel about the patient’s diagnosis and condition. Send all information, laboratory results, malaria smear slides and other studies of the patient with them to the referral hospital. If possible, send the patient by ambulance with oxygen, medicine to control blood pressure, convulsions, and hypoglycemia. A doctor or nurse should accompany the patient to manage problems during transport.

Give antimalarial drugs before transport. They should be given by IV injection (artesunate), or rectal artesunate if possible. If quinine is given, it must be given by rate-controlled infusion or IM injection, since gastrointestinal absorption in severe malaria is poor and the patient may aspirate (Winstanley, 2001). If the patient has reduced consciousness or respiratory problems, intubate before transport. If the patient has anuric renal failure, then hemofiltration or dialysis may be required.
• **During transfer.** Maintain continuous close observation. Give life support based on the condition of the patient. For example, if the oxygen level is low or there is dyspnea, give oxygen. Monitor intake and output precisely in milliliters per hour, by placing a Foley catheter to monitor urine output. Provide psychosocial support for the family and patient by explaining what is happening and that if the patient receives correct and early treatment they will recover.

Make sure the airway is secure. If no ventilator is available, give oxygen by mask. Position the patient so the airway is clear. Suction to clear the airway, as necessary. Use an oral airway as necessary, especially with bag and mask.

Monitor the blood pressure, pulse, intake and output frequently. If too much IV fluid is given, fluid overload (positive fluid balance), and eventually pulmonary edema, may result. If too little IV fluid is given (negative fluid balance), renal insufficiency or failure (pre-renal azotemia) may occur. Maintain a Foley catheter to monitor urine output.

Monitor for hypoglycemia, particularly in severe malaria patients, when using quinine or in treating pregnant women and children by following blood sugar levels regularly. Insert a nasogastric tube (NG) and give glucose via NG tube. Stopping IV dextrose suddenly may result in hypoglycemia, especially in malnourished patients. Giving glucose by mouth or by NG tube is less likely to result in sudden hypoglycemia.

If referral is not possible, maintain the above advice. Treatment with early and correct antimalarial drugs is the most important factor to improve survival.

Treat fever with tepid sponging and antipyretic drugs. In children < 5 years old, this may prevent febrile seizures. Prevent falls from, and injuries in, bed.

The hematocrit level should be followed. There is a risk of severe anemia with complicated malaria and hyperparasitemia. When
hyperparasitemia and a low hematocrit are present, if possible, crossmatch and prepare for a blood transfusion. Blood is usually given if hematocrit < 20%. If there is a concomitant low serum albumin level, give packed red cells with serum albumin or whole blood.

If there is severe anemia and the patient is volume overloaded, give packed red cells and a diuretic.

Give dextrose 10% by IV if blood sugar is low.

If there are seizures, give diazepam as needed to control them. Consider phenobarbital or phenytoin only if facilities for ventilation are available. Hypoglycemia can cause seizures. Check the glucose level to rule this out if there are seizures, and if present, treat as mentioned above.

If the patient is short of breath, look for other evidence of pulmonary edema, such as crackles in the lungs. Check the intake and output record for a positive fluid balance. If pulmonary edema is present, give a diuretic and consider using a colloid, especially for those with low serum albumin.

- **Post-referral care.** After the patient returns from treatment, they need to follow up for periodic blood malaria checks. If they have fever after leaving hospital, check and evaluate a blood film for malaria for relapse or recrudescence. Encourage the patient to complete the course of drugs.

- **Prevention.** Educate the patient and family about preventive measures. Use a mosquito net, repellent, mosquito coil, or fire, to decrease bites. Stay indoors at night during the malaria season. If going out, cover the arms and legs. Residual mosquito spraying the inside walls of the house can help to reduce bites.

- **Advice for travelers.** Besides the prevention advice already mentioned, travelers may choose to use malaria-chemoprophylactic
drugs. Commonly used drugs for prophylaxis include: mefloquine (Lariam®), doxycycline, atovaquone-proguanil (Malarone®). Chloroquine, in most parts of the world, does not protect against falciparum malaria. Primaquine is used after an infection with *P. vivax* or *P. ovale*, to prevent relapse (Wilairatana *et al.*, 1997).

Malarial chemoprophylactic drugs are not 100% effective, and they may alter the history and mask symptoms of malaria patients. Incubation periods may be prolonged and the drugs may induce resistance (Wilairatana *et al.*, 2002). They may also cause a false negative blood smear for malaria.

If there is a history of travel to a malaria-endemic area, even if malaria chemoprophylaxis was taken, there should be a high index of suspicion for malaria, even with a negative blood film.

- **No malaria.** If no malaria is found, other causes of illness should be investigated and treated according to the etiology. If there is no clinical confirmation of another disease and there is a high risk of malaria, the patient may be treated as having malaria. If they still have fever and have been suspected of malaria, a blood film for malaria should be repeated frequently.