

# **Malaria**

## **Diagnosis and Treatment Guidelines for Health Workers in Ethiopia**

**2nd Edition**



**Federal Democratic Republic of Ethiopia  
Ministry of Health**

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## **Acknowledgements**

This guideline is a revised version of the 1998 malaria diagnosis and treatment guidelines developed by the Federal Ministry of Health. The revisions and amendments incorporated in to this version are based on the nationwide therapeutic efficacy study result on anti-malarial drugs and recommendations of the national workshop on anti-malarial treatment policy in Ethiopia conducted 25 – 26 May 2004 in Addis Ababa.

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## 1. Introduction

Malaria is a major public health problem in Ethiopia. It has been consistently reported as one of the three leading causes of morbidity and mortality in the past years. The magnitude of the problem in 2002/03 has even worsened and the disease has been reported as the first cause of morbidity and mortality accounting for 15.5% out-patient consultations, 20.4% admissions and 27.0% in-patient deaths (FMOH 2004).

In a non-epidemic year, 5 - 6 million clinical malaria cases and over 600,000 confirmed cases are reported from health facilities. However, as the potential health service coverage is accessible to about 61% of the population and due to the low service utilization rate (27%, FMOH 2004); the number of malaria cases reported by health facilities is only a portion of the actual magnitude.

*P. falciparum* and *P. vivax* are the two dominant parasite species with relative frequency of 60% and 40%, respectively. This proportion varies from place to place and from season to season. In malaria epidemic situations, *P. falciparum* is the dominant parasite species that causes severe manifestations and almost all malaria deaths happen due to infection by this parasite. Moreover, the biological diversity of *P. falciparum* and its ability to develop resistance to a number of anti-malarial drugs has been a major challenge in malaria chemotherapy.

The high treatment failure rates of chloroquine for the treatment of uncomplicated falciparum malaria as documented through a nationwide study conducted in 1997/98, led to a treatment policy change that recommends the use of Sulfadoxine-Pyrimethamine as first line drug for the treatment of uncomplicated falciparum malaria and chloroquine for the treatment of vivax malaria.

At the time of introduction of sulfadoxine-pyrimethamine as first line drug, the level of treatment failure observed was about 5%. In

subsequent years, however, unpublished reports from isolated studies indicated higher treatment failure rates and the ever growing consumer and service provider complaints on the conceived poor performance of the drug and the lack of representative studies after the 1998 survey, necessitated for a nationwide representative study.

Accordingly, a nationwide study on the therapeutic efficacy of Sulfadoxine-Pyrimethamine for the treatment of uncomplicated falciparum malaria was conducted in 11 sentinel sites from October – December 2003. Results obtained from the study showed a mean treatment failure rate of 35.9% (range 21.7-53.4%) on the 14-days follow-up and 71.8% (range 53.8 – 85.7, not PCR corrected) on the 28-days follow-up. This level of treatment failure rate is much higher than the cut-off point recommended by WHO for a treatment policy change. *In-vivo* therapeutic efficacy and safety baseline study on artemether-lumefantrine was also conducted in 4 sites by enrolling 213 subjects and after a follow-up period of 14 days, no treatment failure cases and drug side effects were reported.

Cognizant of the high treatment failure rates of Sulfadoxine-Pyrimethamine and the need to discuss on the findings and to recommend on the ways forward, a national workshop on anti-malarial treatment policy in Ethiopia was convened 25 – 26 May 2004. Participants of the workshop included, Regional Health Bureaus, Research and Academic Institutions, specialized hospitals, including army and police hospitals, private companies, civil societies, WHO, UNICEF and other partners and NGOs involved in malaria prevention and control in Ethiopia.

After two days of workshop deliberations, consensus was reached to review the existing treatment policy and specific recommendations on the changes that should be incorporated were identified. Based on the workshop recommendations, therefore, the 1998 guidelines on malaria diagnosis and treatment for health workers in Ethiopia has been revised and presented in this edition.

## **2. The Health Care delivery system & Implementation of the Malaria Diagnosis & Treatment Guideline**

The health service delivery system in Ethiopia is organized in a four tier system. The most peripheral level is the health post staffed by frontline health workers. The next level of health facilities in the tier are health center, district hospital and regional/referral hospital. Laboratory based diagnostic facility is available at all levels of the health care delivery system except at health posts. At the health post level, therefore, malaria diagnosis and treatment is based on clinical signs and symptoms.

However, malaria diagnosis based on clinical sign and symptoms alone is not specific and usually leads to excessive use of anti-malarial drugs. For the improvement of diagnosis and management of malaria cases in areas where laboratory based diagnostic service is not available, therefore, diagnosis based on clinical sign and symptom and use of rapid diagnostic tests (RDTs) is the alternative approach that should be adopted until a time when microscopic diagnostic services expand.

This guideline is intended to provide adequate information to health workers on the specific details of malaria diagnosis and disease management at different levels of the health care system. The first part describes the management of uncomplicated malaria while the second part deals with management of severe malaria.

For the successful implementation of the new diagnosis and treatment guidelines, a familiarization session for all stakeholders in malaria prevention and control and training of all health workers in public and private health institutions, NGOs, private medical practitioners, private pharmacies and drug vendors and other medical professionals, is critical. On follow-up, regular, timely and well organized in-service training sessions should be given to update health workers on the malaria diagnosis and treatment

approaches. Information on the new malaria diagnosis and treatment policy should also be given to the general public through appropriately designed IEC methods to improve early diagnosis and treatment seeking practices and compliance to prescribed drug dose regimens.

Moreover, for each health care level including community based services through the Health Extension Package (HEP), relevant part of this guideline should be developed in the form of wall charts and pocket size booklets in local languages, for easy reference. The implementation of the guideline should be also ensured through continuous monitoring and technical supervision to all health facilities and community based service. Regular supply of laboratory materials, anti-malarial and other supportive treatments should be made available on regular basis and in good amount at all levels of the health system.

As the trend of malaria changes over time, the efficacy and effectiveness, tolerance and safety including mild side effects, as well as severe and life -threatening adverse effects of the recommended treatments shall be monitored. Emphasis should particularly be given to monitoring the emergence of resistance to the anti-malarial drugs in use.



### **3. Malaria Diagnosis and Treatment Approaches**

The main objective of the malaria prevention and control program in Ethiopia is to reduce morbidity and prevent mortality by applying intervention strategies that are suited to the local epidemiological situation of the disease. Early diagnosis and prompt treatment is one of the main strategies in malaria prevention and control.

In the prevention and control of malaria, prompt and accurate diagnosis is the key to effective disease management. Based on the level of the health facility, different diagnostic methods can be used. The most commonly used methods are clinical diagnosis based on signs and symptoms only and the use of microscopy and rapid diagnostic tests.

The most frequently used diagnostic method in all peripheral areas where a majority of the malaria patients are expected to present is based on clinical signs and symptoms. In the clinical diagnosis of malaria, fever or history of fever in the last 48 hours is the key diagnostic feature. However, clinical diagnosis is unreliable as the sign and symptoms used to verify malaria are non-specific and overlapping with signs and symptoms caused by other febrile illness.

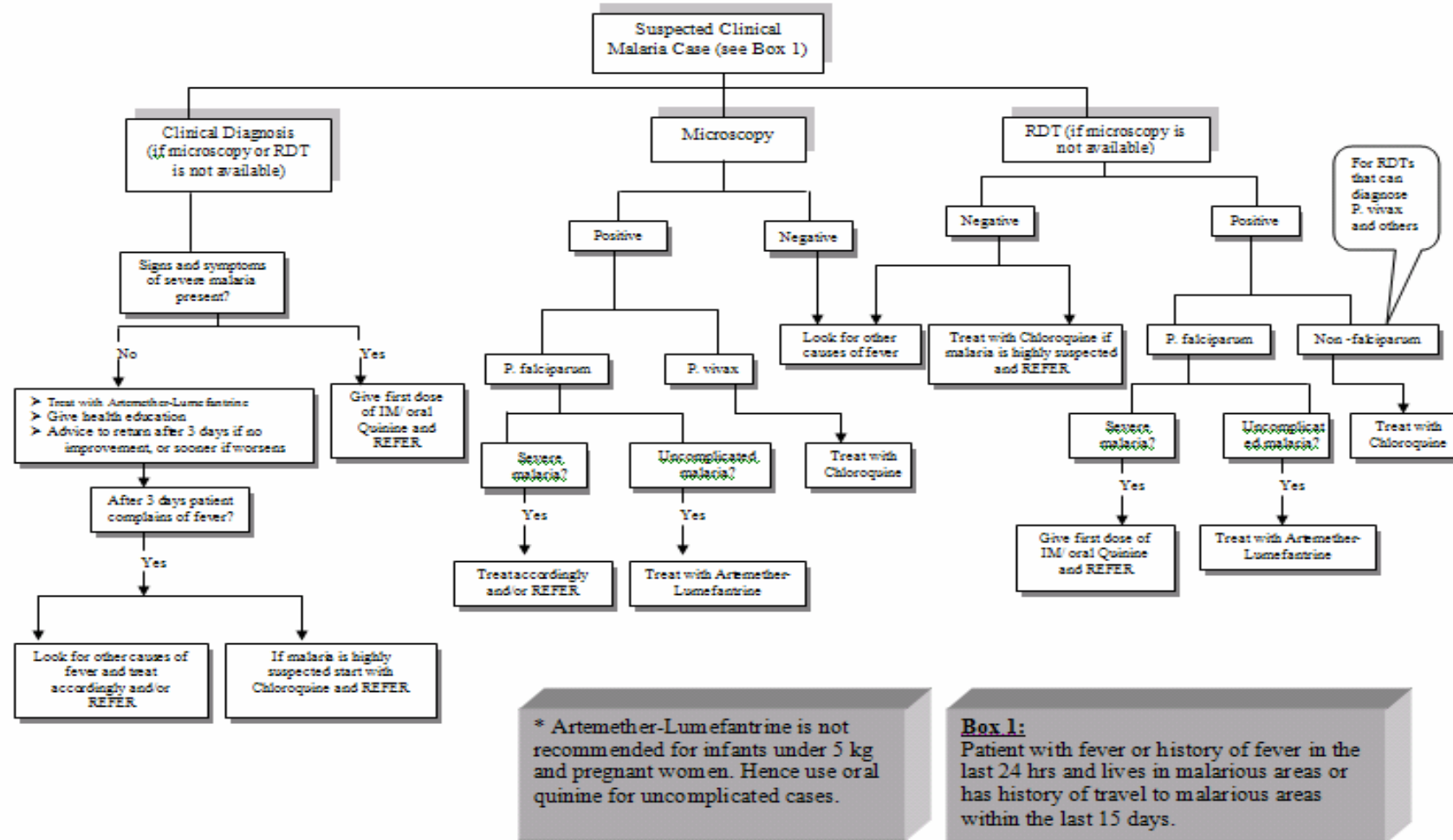
In areas where laboratory based diagnosis is not available, especially at health posts, the use of rapid diagnostic tests (RDTs), when ever possible, is great importance in making reliable diagnosis to guide treatment decision and rational use of anti-malarial drugs. Rapid Diagnostic Tests (RDTs) sometimes called “dipsticks” use immuno-chromatographic techniques to detect plasmodium-specific antigens in a finger prick blood sample. Unlike microscopic examination of blood films where the parasite is demonstrated on a properly stained blood film, RDTs detect parasite antigens that may also persist in the blood for sometime even when the parasites are cleared by chemotherapy. Therefore,

the use of RDTs in some circumstances may give false positive results. There are different RDTs that can be used to diagnose only *P. falciparum* or *P. falciparum* and other non falciparum parasite species.

Microscopic diagnosis of malaria based on examination of blood films stained with Giemsa is the gold standard method of diagnosis. This method of diagnosis also gives quantitative results that can be used in the evaluation of the degree and rate of clearance of parasitaemia. The use of microscopy for the diagnosis of malaria has also an added advantage for the diagnosis of other haemo-parasites like, rickettsia, the causative agent of relapsing fever.

Generally, the treatment of malaria should be guided based on confirmed diagnosis when ever the situation permits. To ensure appropriate intake of prescribed drugs, direct observation of treatment is also important. However, as the patient load could be beyond the capacity of the health facility, there will be a need to give drugs to patients/guardians on hand. In such circumstances, therefore, patients/guardians should be well informed on the treatment schedule to ensure intake of the complete dose. To support this effort, improving the role of community based health workers should also be strengthened.

**Fig. 1 Flow Chart for Diagnosis and Treatment of Malaria**



## **PART I**

### **1. Management of Uncomplicated Malaria**

Uncomplicated malaria is mainly characterized by clinical symptoms such as fever, chills, shivering, headache, joint pains and generalized ache in the presence of asexual forms of malaria parasites in blood sample, without any of the complications described under section 1.1.4. Patients with uncomplicated malaria may also have symptoms such as nausea, vomiting, abdominal pain, diarrhea, thirst and poor appetite. The diagnosis and management of malaria at different levels of the health system is described below.

#### **1.1 Health Post**

##### **1.1.1 Diagnosis**

Malaria diagnosis at health post level should be based on clinical assessment and/or results of Rapid Diagnostic Test (RDT). For suspected clinical malaria cases with negative RDT results, other causes of fever should be suspected.

At this level, diagnosis is mainly based on the patient's clinical signs and symptoms. In a malarious area, a patient with fever or history of fever within the past two days (48 hours) is assumed to have clinical malaria. In a non-malarious area, a patient with fever or history of fever within the past two days and a history of travel to malarious area within the last two weeks is assumed to have clinical malaria. However, other common causes of acute febrile illness (e.g., Relapsing fever, pneumonia, meningitis etc...) should be also looked for.

NB: The malaria diagnosis and treatment approach used at health post level is also applicable in currently functional health stations where there is no microscopy.
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## 1.1.2 Treatment

### 1.1.2.1 Drug therapy

At this level, artemether-lumefantrine (administered 2 times a day for 3 days) is the first-line drug for the treatment of all clinical malaria cases and for RDT confirmed *falciparum* malaria cases. For all RDT negative case with clear clinical signs and symptoms of malaria, it could be convincing to consider vivax malaria for which treatment with chloroquine at a dosage of 25mg/kg administered over three days should be started promptly and the patient referred to the next higher level of health facility. For patients with RDT negative results other causes of fever should be looked for and treated and/or referred accordingly.

(See annex II a for Artemether-Lumefantrine and annex II b for Chloroquine dosage).

In addition, advice/educate the patient that:

- He/she has got malaria;
- malaria is transmitted by mosquitoes;
- malaria can be prevented by eliminating mosquito breeding places, protecting spayed houses from re-plastering and by using insecticide treated mosquito nets;
- early treatment is important to prevent severe illness and death due to malaria;
- To take/give enough food and fluid (especially, fatty meal, to enhance drug absorption and to avoid risk of hypoglycemia).
- To return to the health post if fever persists or he/she is still sick after 72 hours after or anytime before 72 hours if conditions worsen.

For the treatment of malaria in pregnant women and children less than five kg body weight the first line treatment is oral quinine. Oral quinine is administered 3 times a day for 7 days.

### **1.1.2.2 Supportive treatment**

A patient with uncomplicated malaria may require additional treatment for other conditions that may manifest, such as dehydration, high fever.

- To reduce high fever (rectal temperature of above 39°C in children), give paracetamol and advise patient to receive tepid sponging and fanning.
- For patients with moderate dehydration, give oral re-hydration salt (ORS) and advise to take increased amount of clean water or other fluids. In the case of infants, encourage mothers to provide extra breast-feeding,

### **1.1.3 Follow-up:**

In a patient who started treatment with artemether-lumefantrine, if fever and other causes of illness persist, the patient should be advised to come back within 72 hours (3 days). However, patients should also be advised to come anytime before 72 hours if conditions worsen or unable to take oral medication. For all patients who come back to the health facility, full assessment should be done and appropriate action taken.

- Assess the overall condition of the patient,
- If patient has not taken the full course of treatment, administer the remaining dose of treatment,
- If patient has taken full course of artemether-lumefantrine and still has clinical sign and symptom of malaria, start the first dose of chloroquine and refer,
- If other causes of fever are suspected treat accordingly and/or refer patient to the nearest higher level health facility.

### **1.1.4 Referral**

A patient with one or more of the following conditions should be referred immediately to the nearest health center or hospital:

- Altered consciousness (e.g. confusion, sleepy, drowsy, comma)
- Not able to drink or feed
- Severe dehydration,
- Persistent fever,
- Frequent vomiting
- Convulsion or recent history of convulsion
- Unable to sit or stand up
- pallor (Anemia)
- No urine output in the last 24 hours
- Bleeding
- Jaundice (yellowish coloration)
- Difficult breathing
- Other conditions that cannot be managed at this level

If the patient is able to take oral treatment, give first dose of oral quinine before referral. Indicate all the findings and drugs given on the referral paper.

## **1.2. Health Center**

### **1.2.1 Diagnosis**

At this level, diagnosis should be based on clinical assessment and microscopic examination of blood films. Patients referred from health posts and other sites and those with symptoms of severity or danger signs should get priority for microscopic diagnosis. As different drugs are used to treat malaria caused by different species, a microscopic examination of blood films should guide treatment. However, it should be noted that in some cases a blood slide may be negative even when the patient has malaria. Therefore, the health worker's judgment should dictate the decision to treat or not to treat the patient for malaria under such condition. On the other hand, malaria parasitaemia may not be the only cause of the presenting illness. Thus, the health worker has to treat the patient for malaria and then look for other causes of illness.

### **1.2.2 Treatment**

#### **a) First-line treatment**

The first-line treatment of *P. falciparum* malaria is artemether-lumefantrine administered 2 times a day for 3 days. For infants less than five kg of body weight and pregnant women, oral quinine administered 3 times a day for 7 days is the first line treatment. For the treatment of malaria caused due to *P.vivax*, *P.malariae* or *P. ovale*, the first-line drug of choice is chloroquine.

In malaria-free areas and where compliance can be insured, in order to eliminate hypnozoite forms (relapsing stages) of *P.vivax* from the liver and to bring about radical cure, primaquine may be administered daily for 14 days starting after chloroquine treatment is completed.



However, in malarious areas where there is a high risk of re-infection, and where the main purpose of treatment should be to bring about clinical cure rather than radical cure, administration of primaquine is not recommended.

See Annex IIe for primaquine dosage according to age and body weight.

## **b) Second-line treatment**

If a *P. falciparum* positive patient returns back to facility with fever or history of fever between the 4<sup>th</sup> day and 14<sup>th</sup> day after treatment with Artemether-Lumefantrine, do blood examination for malaria parasites. In addition, ask the patient if he/she has vomited the drug or had diarrhea after treatment. Check also whether the drug taken is of reliable brand and is not expired. If the blood film is positive for asexual malaria parasites and other conditions are excluded, administer oral quinine if condition of the patient permits.

In health centers where intravenous (IV) or intramuscular (IM) administration of quinine is possible, patients with severe malaria cases should be treated accordingly (see Annex II d). However, if other manifestations that are beyond the capacity of the health facility are observed, patients must be referred promptly to the next higher level of health facility.

### **1.2.3. Referral**

Patients with the following conditions should be referred to hospital if the condition can't be managed at this level:

- Altered consciousness (e.g. confusion, sleepy, drowsy, comma)
- Not able to drink or feed
- Severe dehydration,
- Persistent fever,

- Frequent vomiting
- Convulsion or recent history of convulsion
- Unable to sit or stand up
- No urine output in the last 24 hours
- Jaundice (yellowish coloration)
- Difficult breathing
- Pulmonary edema
- Bleeding tendency
- Severe anemia (if blood transfusion is required)
- Lung complications (respiratory distress syndrome)
- Other conditions that cannot be managed at this level

#### **1.2.4. Supportive treatment**

See Section 1.1.2.2 for details.

## **1.3 Hospital**

### **1.3.1 Diagnosis**

At this level, full clinical assessment should be made. Other medical conditions resembling malaria could be better diagnosed both clinically and with laboratory investigations. For suspected malaria cases, in order to guide species-specific treatment, microscopic diagnosis should be always done.

### **1.3.2 Treatment**

See Section 1.2.2 for details.

## **2. Management of Malaria in Pregnancy and in Infants Less than 5 Kg of Body Weight**

There is no fully documented evidence on the safety of the use Artemether-Lumefantrine for the treatment of malaria in infants less than five kg of body weight and pregnant women.

Hence, the drug Artemether-Lumefantrine is not recommended for the treatment of malaria in infants less than five kg of body weight and pregnant women.

Therefore, for the treatment of uncomplicated falciparum malaria in infants less than five kg of body weight and pregnant women, the first line treatment is oral quinine 8 mg/kg administered 3 times a day for seven days. For the treatment of severe falciparum malaria, intramuscular or intravenous quinine should be administered (see annex II d).

### **3. Chemoprophylaxis**

There is no safe, effective and affordable anti-malarial drug than can be used for chemoprophylaxis at large scale. Therefore, the use personal protective measures such as the use of ITNs, insect repellents and protective clothing is recommended.

However, for personal use by non-immune travelers visiting malarious areas for a period of 2 – 3 months, weekly Mefloquine administered at 5 mg/kg is the recommended drug for chemoprophylaxis. Chemoprophylaxis should be started 2 weeks before departure and four weeks after return from the malarious area.

Alcohol consumption during prophylaxis aggravates side effects. Therefore, subjects should be advised not to take alcohol while on mefloquine prophylaxis. Mefloquine prophylaxis is not recommended for pregnant women during the first trimester and infant under 3 months of age. (See Annex III for dose regimen of chemoprophylactic Mefloquine).

It should be well understood that no drug can guarantee absolute and complete protection against malaria. Therefore, in addition to taking regular prophylaxis as per the recommended instruction, the use of the above mentioned preventive measures should be used.

#### **4. Use of Antimalarial Drugs in Epidemic Control**

For the management of malaria during epidemics, mass fever treatment with Artemether-Lumefantrine and chloroquine should be used.

In areas where malaria epidemics occur, it is likely to encounter more cases with severe manifestations of malaria. If such epidemics happen in peripheral areas where patient admission and administration of IM or IV quinine is not possible, the use of IM artemether is recommended as a pre-referral treatment to prevent further progression of severity of illness (see annex II d and II f for dosage).

For detailed explanation on malaria epidemics investigation, prevention and control refer to the FMOH guideline of malaria epidemics prevention and control.

## **PART II**

### **1. Management of Severe Malaria**

Severe malaria is defined as the presence of one or more signs and symptoms of severe illness and a demonstrable asexual *P. falciparum* parasitaemia in peripheral blood sample. Severe malaria is a medical emergency that is sufficiently serious to be an immediate threat to life. Usually it is a result of delay in prompt diagnosis and adequate treatment of uncomplicated malaria. All age groups that encounter malaria are at risk of developing severe malaria. However, the problem is worse in the most vulnerable group that comprises children less than five years of age and pregnant women.

#### **1.1 Management at peripheral health service level**

At health post the health worker can identify some important signs and symptoms of severe malaria, although he/she can not manage such cases. Therefore, such levels can only judge the severity of the illness and refer cases to the next appropriate level with out delay. When ever appropriate, patients should be given pre-referral treatment.

##### **1.1.1 Diagnosis**

Generally, a patient living in a malarious area or has recently been in a malarious area should be considered as having severe malaria if one or more of the following signs and symptoms are observed.

- Altered or decreased consciousness (e.g. confusion, coma, etc.)
- Patient sleepy, confused, unable to walk or sit-up
- Not able to drink or eat (in case of children not able to breast feed)
- Convulsion, or recent history of convulsion

- Persistent vomiting
- Dark urine, "Coca-Cola urine"
- Failure to respond to treatment within three days
- Spontaneous bleeding; gum bleeding, epistaxis
- Failure to pass urine in the last 24 hours
- Difficult breathing
- Yellow eyes (Jaundice)
- High temperature (Rectal temperature >39°C)
- Extremely pale mucosa
- Systolic blood pressure of < 80 mmHg.

In field laboratories, all patients with blood film positive for *P.falciparum* malaria and with one or more of the above signs and symptoms should be regarded as having severe malaria and referred accordingly.

### **1.1.2 Treatment**

Patients diagnosed in peripheral health facilities with one or more of the above signs and symptoms should be referred to the nearby health centre or hospital. However, as a routine measure the following should be done before referral of the patient,

- Patients in coma should be nursed always in lateral position to avoid aspiration,
- Give 40% or 50% glucose to all patients with severe manifestations,
- If the patient is conscious and able to take oral medication, give start oral quinine or other pre-referral treatment (IM quinine or IM Artemether).
- Use tepid sponging, and if the patient can swallow give paracetamol to reduce fever.
- If the patient can swallow, give fluids such as ORS.
- Record all your findings and drugs given in a referral slip and refer the patient to the nearest health centre or hospital,



## **1.2 Management at Health Centre or hospital level**

Many cases of severe malaria can be managed properly at health centre level provided there is facility for in-patient care. Only very few cases who develop serious complications need referral to a hospital.

A patient with severe malaria may present with one or more of the following complications:

- Cerebral malaria defined as unarousable coma not attributable to any other cause in a patient with falciparum malaria.
- Generalised convulsions.
- Normocytic anaemia.
- Renal failure.
- Hypoglycaemia.
- Fluid, electrolyte and acid-base disturbances.
- Pulmonary oedema.
- Circulatory collapse and shock (“algid malaria”).
- Spontaneous bleeding (disseminated intravascular coagulation).
- Hyperpyrexia.
- Hyper-parasitaemia.
- Malarial haemoglobinuria.

In addition, a patient with severe malaria may present with impaired consciousness, extreme weakness, and jaundice.

### **1.2.1 General management**

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

- Anti-malarial chemotherapy must be given parenterally (intravenously). Oral treatment should be substituted as soon as possible,

- Doses must be calculated on a mg/kg of body weight basis. It is therefore important whenever possible to weigh the patient. This is particularly important for children,
- If an intensive care unit is available, patients should be admitted to it,
- If fluids are being given intravenously, careful attention to fluid balance is important in order to avoid over-hydration or under-hydration,
- A rapid initial check of blood glucose level and frequent monitoring for hypoglycaemia are important, when possible; otherwise glucose should be given,
- Laboratory measurements should include regular checks on erythrocyte volume fraction (haematocrit), glucose, urea or creatinine, and electrolytes.
- Monitor urine output constantly and In dwelling urinary catheters should be removed as soon as they are no longer necessary,
- Other causes of coma such as meningitis should be excluded by the examination CSF obtained by lumbar puncture,
- Frequent monitoring of the therapeutic response, both clinical and parasitological should be evaluated,
- Look for and manage any complicating or associated infections. Blood cultures should be taken if the patient goes into shock while undergoing treatment to rule out other infection. Insertion sites for intravenous lines should be cleaned at least twice daily with iodine and alcohol,
- Regular monitoring of the core temperature, respiration rate, blood pressure, level of consciousness and other vital signs is mandatory,
- Reduce high body temperatures (>39°C) by vigorous tepid sponging and fanning. Antipyretics may also be given.
- Initial ophthalmoscopic examination of the fundus is important, since the presence of retinal haemorrhages has diagnostic and prognostic significance,
- Administer a prophylactic anticonvulsant, e.g. Phenobarbital sodium, a single dose of 200 mg for adults only by

intramuscular injection (This chemoprophylactic regimen is not RECOMMENDED for CHILDREN).

- Drugs that increase the risk of gastrointestinal bleeding (aspirin, corticosteroids) should be avoided as far as possible.

More sophisticated monitoring may be useful if complications develop, and will depend on the local availability of equipment, experience and skills.

### **1.2.2 Nursing care**

The management of the patient with severe malaria is as important as chemotherapy and here the nurse has a crucial role to play.

- Meticulous nursing care should be given to unconscious patients. Maintain a clear airway. Turn the patient every two hours. Do not allow the patient to lie in a wet bed. Particular attention should be paid to pressure points and the patient should be nursed on his or her side to avoid aspiration of fluid. Aspiration pneumonia is a potentially fatal complication, and must be dealt with immediately.
- A careful record of fluid intake and output must be kept the appearance of black urine noted and specific gravity measured.
- The speed of infusion of fluids should be checked frequently.
- Temperature, Pulse, respiration and blood pressure must be monitored regularly every 4-6 hours for at least the first 48 hours.
- Changes in the level of consciousness, occurrence of convulsions or changes in behaviour of the patient must be reported immediately.
- If rectal temperature rises above 39 °C, vigorous tepid sponging and fanning must be applied, and paracetamol may be given.

### 1.2.3 Anti-malarial drug

Quinine should be given with an initial loading dose of 20 mg/kg by intravenous infusion; this should be replaced by oral administration of as soon as possible.

#### ***Important points in the administration of quinine***

- For all patients with severe malaria, intra-venous quinine should be given at least for the first 48 hours.
- In patients requiring more than 48 hours of parenteral therapy, reduce the quinine maintenance dose by one-third to one-half (i.e. 5-7 mg salt/kg of body weight every 8 hours).
- It is unusual to have to continue intravenous infusions of quinine for more than 4-5 days. If it is more convenient, quinine may be given by continuous infusion (Infusion rates should not exceed 5 mg per kg of body weight per hour).
- A loading dose should not be used if the patient received quinine within the preceding 24 hours or mefloquine within the preceding 7 days.
- Quinine is not given by subcutaneous injection.
- Do not attempt to give oral medication to unconscious children; if parenteral injection is not possible and referral is likely to be delayed, anti-malarials may be given by nasogastric tube. However, nasogastric administration may cause vomiting and produce inadequate drug levels in the blood.

## **1.2.4 Salient clinical features and management of complications**

In all cases of severe malaria, parenteral anti-malarial chemotherapy should be started immediately any complications can then be dealt with as described below.

### **1.2.4.1 Cerebral malaria**

#### ***a) Clinical features in adults***

The patient with cerebral malaria is comatose, the depth of consciousness being variable (for assessment of coma, see Glasgow coma scale in Annex IV). If in doubt as to cause, test for other locally prevalent encephalopathies, e.g. bacterial and fungal meningoencephalitis and viral encephalitis. Asexual malaria parasites are usually demonstrable on a peripheral blood smear. Convulsions are common in both adults and children. Retinal haemorrhages are associated with a poor prognosis in adults; papilloedema is rare. A variety of transient abnormalities of eye movement, especially disconjugate gaze, have been noted. Fixed jaw closure and tooth grinding (bruxism) are common. Pouting may occur or a pout reflex may be elicited (by stroking the sides of the mouth). Mild neck stiffness occurs but neck rigidity and photophobia are absent. The commonest neurological picture in adults is one of a symmetrical upper motor neurone lesion. The duration of coma varies from about 6 to 96 hours in adults.

Motor abnormalities such as decerebrate rigidity decorticate rigidity (arms flexed and legs stretched), and opisthotonos occur. The opening pressure at lumbar puncture is usually normal in adults, but may be elevated; the cerebrospinal fluid (CSF) is clear, with fewer than 10 white cells per  $\mu\text{l}$ ; the protein is raised, as is the CSF lactic acid concentration. A variety of non-specific electroencephalogram (EEG) abnormalities have been described. Hepatosplenomegaly is common. The abdominal reflexes are invariably absent; this is a useful sign for

distinguishing hysterical adult patients with fevers of other causes, in whom these reflexes are usually brisk.

### **b) Clinical features in children**

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

- The earliest symptom of cerebral malaria in children is usually fever (37.5-41 °C), followed by failure to eat or drink. Vomiting and cough are common; diarrhoea is unusual.
- The history of symptoms preceding coma may be very brief, commonly one or two days.
- A child who loses consciousness after a febrile convulsion should not be considered to have cerebral malaria unless coma persists for more than half an hour after the convulsion.
- The depth of coma may be assessed according to the Blantyre coma scale (Annex V), by observing the response to standard vocal or painful stimuli (rub knuckles on child's sternum; if no response, apply firm pressure on thumbnail bed with horizontal pencil).
- Always exclude or treat hypoglycaemia
- Convulsions are common before or after the onset of coma. They are significantly associated with morbidity and sequelae.
- In some children the breathing is laboured and noisy; in others, deep breathing with a clear chest suggests acidosis.
- In patients with profound coma, corneal reflexes and "doll's eye" movements may be absent.
- In some children, extreme opisthotonos is which may lead to a mistaken diagnosis of tetanus or meningitis.
- CSF opening pressure is variable; it is raised more frequently than in adults, and is sometimes very high.

- Leukocytosis is not unusual in severe disease and does not necessarily imply an associated bacterial infection. (This is also true in adults.)
- A proportion of children (about 10%) who survive cerebral malaria have neurological sequelae which persist into the convalescent period. Sequelae may take the form of hemiparesis, cerebellar ataxia, cortical blindness, severe hypotonia, mental retardation, generalised spasticity, or aphasia.

**Management of cerebral malaria in adults:**

- The comatose patient should be given meticulous nursing care
- Insert a urethral catheter using a sterile technique,
- Keep an accurate record of fluid intake and output (See Annex VI),
- Monitor and record the level of consciousness (using the Glasgow coma scale, Annex IV), temperature, respiratory rate, blood pressure, and vital signs,
- Give a single intramuscular injection of Phenobarbital sodium 200 mg, to prevent convulsions,
- Treat convulsions if and when they arise with diazepam. A slow intravenous injection of diazepam (0.15 mg/kg of body weight, maximum 10 mg for adults) will usually control convulsions. Diazepam can also be given intra-rectally (0.5-1.0 mg/kg of body weight) if injection is not possible,

### **Management of cerebral malaria in children**

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

- The parents or other relatives should be questioned about: (i) history of residence or travel; (ii) previous treatment with anti-malarials or other drugs; (iii) recent fluid intake and urine output; and (iv) recent or past history of convulsions,
- A rapid initial examination should be carried out to assess: (i) hydration; (ii) anaemia; (iii) pulmonary oedema; (iv) level of consciousness; and (v) hyperpyrexia,
- Immediate tests must include: (i) thick and thin blood films; (ii) haematocrit; (iii) finger-prick blood glucose; and (iv) lumbar puncture,
- If parasitological confirmation is likely to take more than one hour, treatment should be started before the diagnosis is confirmed,
- If the child has a convulsion, this should be treated with diazepam 0.15 mg/kg of body weight intravenously can be used,
- Any child with convulsions should be examined for hyperpyrexia and hypoglycaemia and given appropriate treatment,
- Simple practical manoeuvres, such as tepid sponging and fanning, should be employed to try to keep the rectal temperature below 39 °C. Relatives are usually happy to do this when instructed,
- Paracetamol, 15 mg/kg of body weight, may also be given as an antipyretic.



***Avoid the following in the treatment of cerebral malaria:***

- corticosteroids,
- other anti-inflammatory agents,
- other agents given for cerebral oedema (urea, invert sugar),
- low molecular weight dextran,
- epinephrine (adrenaline),
- heparin,
- epoprostenol (prostacyclin),
- pentoxifylline (oxpentifylline),
- hyperbaric oxygen,
- Cuckisoirub (cyclosporin A.)

**1.2.4.2 Anaemia**

***Clinical features***

The rate of development and degree of anaemia depend on the severity and duration of parasitaemia. In some children, repeated untreated episodes of otherwise uncomplicated malaria may lead to normochromic anaemia in which dyserythropoietic changes in the bone marrow are prominent. Parasitaemia is often scanty, although numerous pigmented monocytes can be seen in the peripheral blood.

In other children, severe anaemia may develop rapidly in association with hyperparasitaemia. In these cases, acute destruction of parasitized red cells is responsible.

Children with severe anaemia may present with tachycardia and dyspnoea. Anaemia may contribute both to *cerebral signs*, confusion, restlessness, coma and retinal haemorrhages- and to *cardiopulmonary signs* - gallop rhythm, cardiac failure, hepatomegaly and pulmonary oedema.

Anaemia is often associated with secondary bacterial infection, retinal haemorrhage and pregnancy in adults.

### **Management of Anaemia in adults**

- If the haematocrit falls below 15%, give a transfusion of pathogen-free compatible fresh blood or packed cells. (Stored bank blood may be used if fresh blood is not available.) In areas where facilities for screening blood for viral and other infections are inadequate, the general condition of the patient (e.g. shock, cardiac failure) and the response to oxygen and colloid infusion should be the guiding principles rather than the haematocrit alone,
- Give small intravenous doses of furosamide 20 mg during the blood transfusion as necessary to avoid circulatory overload,
- Remember to include the volume of transfused cells or blood in calculations of fluid balance.

### **Management of Anaemia in children**

- The need for blood transfusion must be assessed with great care in each individual child. Not only the level of the haematocrit, but the density of parasitaemia and the clinical condition of the patient must be taken into account,
- In general and with the proviso mentioned above, a haematocrit of less than 15% in a normally hydrated child is an indication for blood transfusion. In some children, an initial transfusion is required with the utmost urgency (10 ml of packed cells or 20 ml of whole blood per kg of body weight),
- Furosamide, 1-2 mg/kg of body weight up to a maximum of 20 mg, may be given intravenously to avoid fluid overload.

### **1.2.4.3 Renal failure**

#### **Clinical features**

Renal failure as a complication of malaria is virtually confined to adults. There is a rise in serum creatinine and urea, oliguria and eventually anuria due to acute tubular necrosis. Renal failure is usually oliguric but may occasionally be polyuric. The mechanism of acute tubular necrosis in malaria is not fully understood. Studies of renal blood flow have shown cortical ischaemia and medullary congestion as in other forms of acute tubular necrosis. Acute renal failure is usually reversible.

### **Management of Renal Failure**

- Exclude dehydration (hypovolaemia) by clinical examination, including measurement of jugular or central venous pressure, and blood pressure drop between the patient lying supine and when propped up to 45°,

- Peritoneal dialysis or haemodialysis is indicated if the patient remains oliguric after adequate rehydration and the blood urea and creatinine rise progressively,
- Peritoneal dialysis should not be undertaken lightly. If possible, refer the patient to a dialysis unit or centre.

#### **1.2.4.4 Hypoglycaemia**

##### ***a) Clinical features in adults***

Hypoglycaemia is increasingly being recognised as an important manifestation of falciparum malaria. It occurs in three different groups of patients, which may overlap:

- Patients with severe disease, especially young children;
- Patients treated with quinine as a result of a quinine-induced hyperinsulinaemia;
- Pregnant women, either on admission or following quinine treatment.

In conscious patients, hypoglycaemia may present with classic symptoms of anxiety, sweating, dilatation of the pupils, breathlessness, laboured and noisy breathing, oliguria, a feeling of coldness, tachycardia and light-headedness. This clinical picture may develop into deteriorating consciousness, generalised convulsions, extensor posturing, shock and coma.

The diagnosis is easily overlooked because all these clinical features also occur in severe malaria itself. Deterioration in the level of consciousness may be the only sign. If possible, groups mentioned above.

***b) Clinical features in children***

Hypoglycaemia is particularly common in young children (under 3 years), in those with convulsions or hyperparasitaemia, and in patients with profound coma. It is easily overlooked clinically because the manifestations may be similar to those of cerebral malaria.

**Management of Hypoglycaemia in adults**

- If hypoglycaemia is detected by blood testing or suspected on clinical grounds, give 40% or 50% glucose, 50 ml (1.0 ml/kg for children) by intravenous bolus injection,
- Follow with an intravenous infusion of 5% or 10% glucose,
- Continue to monitor blood glucose levels (using a “stix” method if available, or clinically and biochemically if not) in order to regulate the glucose infusion. Remember that hypoglycaemia may recur even after an intravenous bolus of 50% glucose,
- Encourage feeding.

### **Management of Hypoglycaemia in children**

- Unconscious children should be given glucose regularly to prevent starvation hypoglycaemia. It is most conveniently provided as 5% dextrose in water infusion, but if this would be likely to lead to fluid overload, smaller volumes of more concentrated glucose may be given at regular intervals,
- If hypoglycaemia occurs, it should be treated with an intravenous bolus injection of 50% glucose ( up to 1.0 ml/kg) of body weight) followed by a slow intravenous infusion of 10% glucose to prevent recurrence of hypoglycaemia. The duration and amount of glucose monitoring (which should be done in blood taken from arm opposite to that receiving the infusion), using a “stix” method,
- Monitoring of blood glucose level should continue even after apparent recovery, since hypoglycaemia may recur.

### **1.2.4.5 Fluid, electrolyte and acid-base disturbances**

#### ***a) Clinical features in adults***

Patients with severe falciparum malaria often show the following on admission: clinical evidence of *hypovolaemia* (low jugular venous pressure, postural hypotension, and oliguria with high urine specific gravity) and clinical signs of *dehydration* (reduced ocular tension and decreased skin turgor).

Acidotic breathing-hyperventilation may develop in severely ill patients who are shocked, hypoglycaemic, hyperparasitaemic, or in renal failure. Lactic acidosis is a common complication and both blood and CSF lactic acid concentrations are raised. Perfusion is improved by correcting hypovolaemia.

#### ***b) Clinical features in children***

The best clinical indications of mild to moderate dehydration in children are decreased peripheral perfusion, deep (Acidotic) breathing, decreased skin turgor, raised blood urea (>6.5 mmol/l), increased thirst, loss of about 3-4% of total body weight and evidence of metabolic acidosis.

In children presenting with oliguria and dehydration, examination of urine usually reveals a high specific gravity, low urinary sodium, and normal urinary sediment, indicating simple dehydration rather than renal failure, which is rare in children.

### **Management in Adults**

- Look for evidence of dehydration and hypovolaemia:
  - reduced ocular tension,
  - reduced skin turgor,
  - relatively cool extremities,
  - postural drop in blood pressure (as the patient is propped up from the lying-down position to 45°)
  - reduced peripheral venous filling,
  - low jugular venous pressure,
  - reduced urine output,
  - high urine specific gravity,
  - urine sodium concentration less than 20 mmol/l.
- If there is evidence of dehydration give modest volumes of isotonic fluids (0.9% saline or 5% dextrose) by intravenous infusion, but avoid fluid overload.
- Monitor blood pressure, urine volume (every hour),
- Improve oxygenation
  - clearing airway,
  - increasing concentration of inspired oxygen, and
  - supporting ventilation artificially, if necessary.



**Management in children**

- Careful rehydration with isotonic saline is mandatory, with frequent examination of the jugular venous pressure, blood pressure and chest,
- Where facilities for monitoring and maintenance of adequate sterility exists, 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 over 24 hours is less than 4 ml/kg of body weight, furosamide 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).

**1.2.4.6 Pulmonary oedema*****Clinical features***

Pulmonary oedema is a grave complication of severe malaria, with a high mortality (over 50%). It may appear several days after chemotherapy has been started and at a time when the patient's general condition is improving and the peripheral parasitaemia is diminishing. It must be differentiated from iatrogenically produced pulmonary oedema resulting from fluid overload. Hyperparasitaemia, renal failure and pregnancy are often associated, as well as hypoglycaemia and metabolic acidosis. The first indication of impending pulmonary oedema is an increase in the respiratory rate, which precedes the development of other chest signs.

Hypoxia may cause convulsions and deterioration in the level of consciousness and the patient may die within a few hours.

### **Management**

- Keep patient upright; raise the head of the bed or lower the foot of the bed,
- Give a high concentration of oxygen by any convenient method available, including mechanical ventilation,
- Give the patient a diuretic, such as furosemide 40 mg, by intravenous injection. If there is no response, increase the dose progressively to a maximum of 200 mg,
- In well-equipped intensive care units, mechanical ventilation with positive end expiratory pressure (PEEP), a wide range of vasoactive drugs and haemodynamic monitoring will be available,

If there is overhydration/fluid over load:

- Stop all intravenous fluids.
- Use haemofiltration immediately, if available.
- If there is no improvement, withdraw 250 ml of blood initially by venesection into a blood transfusion donor bag so that it can be given back to the patient later.

#### **1.2.4.7 Circulatory collapse (“algid malaria”)**

##### ***Clinical features***

Some patients are admitted in a state of collapse, with a systolic blood pressure less than 80 mmHg in the supine position (less than 50 mmHg in children); a cold, clammy, cyanotic skin; constricted peripheral veins; rapid feeble pulse.

Circulatory collapse is also seen in patients with pulmonary oedema or metabolic acidosis, and following massive gastrointestinal haemorrhage. Dehydration with hypovolaemia may also contribute to hypotension.

Possible sites of associated infection should be sought, e.g. lung, urinary tract (especially if there is an indwelling catheter), meningitis, intravenous injection sites, intravenous lines.

**Management**

- Correct hypovolaemia with and appropriate plasma expander (fresh blood, plasma, polygeline or dextran 70) or chrisaloids,
- Take a blood culture and start patient on broad-spectrum antibiotics immediately, e.g. combined treatment with benzympenicillin and gentamicin,
- Once the results of blood culture and sensitivity testing are available, give the appropriate antibiotic,

**1.2.4.8 Spontaneous bleeding and disseminated intravascular coagulation**

***Clinical features***

Bleeding gums, epistaxis, petechiae, and subconjunctival haemorrhages may occur. Disseminated intravascular coagulation, complicated by clinically significant bleeding e.g. haematemesis or melaena, occurs in fewer than 10% of patients; it seems to occur more often in non-immune patients. It is relatively common in non-immune patients with imported malaria in the Temperate Zone. Thrombocytopenia is common, and is not related to other measures of coagulation or to plasma fibrinogen concentrations; in most cases it is unaccompanied by bleeding. The platelet count usually returns to normal after successful treatment of the malaria.

**Management**

- Transfuse fresh blood, clotting factors or platelets as required.

### 1.2.4.9 Hyperpyrexia

#### *Clinical features*

Hyperpyrexia is more common in children and is associated with convulsions, delirium, and coma. In unacclimatized visitors to the tropics, it must be differentiated from heat stroke.

High body temperatures (42 °C and above) may cause permanent severe neurological sequelae. There is evidence that high body temperature in pregnant women contributes to foetal distress.

#### **Management**

- Monitor temperature frequently.

#### ***In children***

- If rectal temperature is above 39°C, apply vigorous tepid sponging and fanning, and give paracetamol, 15 mg/kg of body weight by mouth, suppository or nasogastric tube.

#### ***In adults***

- If the temperature is above 39°C, give 1 gm of paracetamol orally in addition, to fanning and tepid sponging.

### 1.2.4.10 Hyperparasitaemia

#### *Clinical features*

In general, and especially in non-immune subjects, high parasite densities (above 5% or +++) and peripheral schizontaemia are associated with severe disease. parasitaemia is particularly dangerous in children as it can easily lead to severe anaemia.

**Management**

- An initial loading dose of parenteral antimalarial therapy is prudent, even if the patient can take medication by mouth.

**1.2.4.11 Malarial haemoglobinuria**

***Clinical features***

Patients with glucose-6-phosphate dehydrogenase deficiency and some other erythrocyte enzyme deficiencies may develop vascular haemolysis and haemoglobinuria when treated with oxidant drugs such as primaquine, even in the absence of malaria. “Blackwater fever” which typically occurred in nonimmune Caucasian patients taking quinine irregularly for prophylaxis or presumptive treatment, was accompanied by mild or absent fever, scanty or absent parasitaemia, and carried a poor prognosis-is now very rare.

**Management**

- Continue appropriate antimalarial treatment if parasitaemia is present.
- Transfuse fresh blood to maintain haematocrit above 15%.
- Monitor jugular or central venous pressure to avoid fluid overload and hypovolaemia.
- If oliguria develops and blood urea and serum creatinine levels rise, peritoneal dialysis or haemodialysis may be required.

### **1.3 Special clinical features and management of severe malaria in Pregnancy**

#### ***Clinical features***

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 foetus.

Pregnant women are susceptible to all the manifestations described. Moreover they have an increased risk of abortion, stillbirth, premature delivery and low birth weight of their infant. They are more likely to develop cerebral and other forms of severe malaria, and to suffer a high mortality 2 to 10 times higher than non-pregnant patients are. They are particularly susceptible to hypoglycaemia and acute pulmonary oedema.

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. Foetal distress is common, but frequently not diagnosed. The prognosis for the foetus is poor in severe disease.

Hypoglycaemia may be present in pregnant women on admission, or may occur after quinine infusion. It is commonly asymptomatic, although it may be associated with foetal bradycardia and other signs of foetal distress. In the most severely ill patients, it is associated with lactic acidosis and high mortality. For treatment refer the section 1.2.4.4, for the management of hypoglycaemia. If the diagnosis is in doubt, a therapeutic test with 50% glucose (25-50 ml intravenously) should be used. Recurrent severe hypoglycaemia may be a problem in some cases. If indictable glucose is not available, glucose solutions can be given to unconscious patients through a nasogastric tube.

Pulmonary oedema may be present in pregnant women on admission, may develop suddenly and unexpectedly several days after admission, or may develop immediately after childbirth.

Maternal anaemia is associated with prenatal mortality, maternal morbidity and an increased risk of fatal maternal postpartum haemorrhage. Women who go into labour when severely anaemic or with fluid-overloaded may develop pulmonary oedema after separation of the placenta (See section 1.2.4.6 for management of pulmonary oedema).

In patients who have been given quinine, abnormal behaviour, sweating and sudden loss of consciousness are the usual manifestations.

Associated infections occur; pneumonia and urinary tract infections are common.

#### **Management**

- Pregnant women with severe malaria should be transferred to intensive care if possible.
- Monitoring of uterine contractions and foetal heart rate may reveal asymptomatic labour and foetal tachycardia, bradycardia, or late deceleration in relation to uterine contractions, indicating foetal distress.
- Once labour has started, foetal or maternal distress may indicate the need to shorten the second stage by forceps or vacuum extraction, or caesarean section.

Quinine, in the doses advocated for the treatment of life-threatening malaria, is safe. It has been shown that the initial intravenous infusion of quinine in women who are more than 30 weeks pregnant is not associated with uterine stimulation or foetal distress. Its major adverse effect is hypoglycaemia.

## **1.4 Common errors in diagnosis and management**

The common errors in the diagnosis and management of severe malaria are listed below.

### **a) Errors in diagnosis**

- Failure to do a malarial blood film
- Failure to take a travel history
- Misjudgement of severity
- Faulty parasitological diagnosis and laboratory management
- Failure to diagnose other associated infection
- Missed hypoglycaemia
- Failure to carry out an ophthalmoscopic examination (when available) for the presence of retinal haemorrhages,
- Misdiagnosis (e.g. influenza, viral encephalitis, hepatitis, scrub typhus, etc.)

### **b) Errors in management**

- Inadequate nursing care,
- Errors of fluid and electrolyte replacement,
- Delay in starting antimalarial therapy,
- Use of an inappropriate drug,
- Unjustified withholding of an antimalarial drug,
- Dosage not correctly calculated,
- In appropriate route of administration,
- Failure to elicit a history of recent chemotherapy,
- Unjustified cessation of treatment,
- Failure to control the rate of intravenous infusion,
- Failure to prevent cumulative effects of antimalarial drugs,,
- Failure to switch patients from parenteral to oral therapy as soon as they can take oral medication,
- Unnecessary continuation of chemotherapy beyond the recommended length of treatment,



- Unnecessary endotracheal intubations,
- Failure to prevent or control convulsions,
- Failure to recognise and treat severe anaemia,
- Use of potentially dangerous ancillary therapies,
- Delay in considering obstetrical interventions in late pregnancy,
- Failure to recognise and manage pulmonary oedema, aspiration pneumonia, and metabolic acidosis,
- Delay in starting peritoneal dialysis or haemodialysis,
- Failure to review antimalarial treatment in a patient whose condition is deteriorating,
- Lack of good record keeping,
- Inadequate or lack of information to patients and guardians.

## Annex I: Field and Laboratory Diagnostic Tools

### a) Microscopy

Microscopy is the gold standard diagnostic method for malaria. Diagnosis of malaria is based on microscopic examination of Giemsa-stained blood films. In laboratory diagnosis the following three points should be stated clearly:

- species of the parasite,
- stage of the parasite and
- level of parasitaemia (in the case of seriously ill patients and patients with high parasite density)

The following semi-quantitative method, expressed as one to four “pluses”, should be used for designation of parasite count:

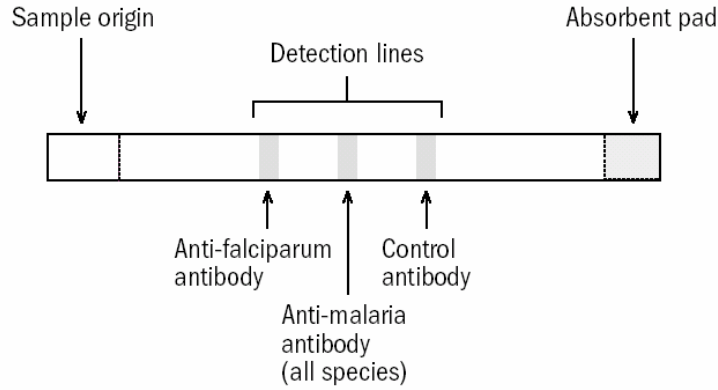
+	1 – 10 parasites per 100 fields of thick film
++	11- 100 parasites per 100 fields of thick film
+++	1 – 10 parasites per field of thick film
++++	more than 10 parasites per field of thick film

Always 100 fields of thick blood film should be examined before pronouncing the slide negative for asexual forms of malaria parasites. For blood film preparation, staining and examination details refer the WHO laboratory manual.

**b) Rapid Diagnostic Test Kits (RDTs)**

Rapid Diagnostic Tests (RDTs) use immuno-chromatographic techniques to detect plasmodium-specific antigens in a finger prick blood sample. As RDTs are produced by different companies, test should be performed following specific instruction provided by manufacturer. The general description of a typical RDT is shown in fig.1.

**Fig.2. Basic Components of an Antigen Detection System**



## Annex II: Treatment Schedules

### IIa. Artemether-Lumefantrine:

Tablet containing 20 mg Artemether plus 120 mg Lumefantrine in a fixed dose combination.

Weight (kg)	Age (Years)	Number of tablets per dose Twice daily for 3 days					
		Day1		Day2		Day3	
		Morning	Evening	Morning	Evening	Morning	Evening
5 – 14	3 months – 2 years	1	1	1	1	1	1
15 – 24	3 – 7 years	2	2	2	2	2	2
25 – 34	8 – 10 years	3	3	3	3	3	3
35+	>10 Years	4	4	4	4	4	4

### **Side effects:**

The following adverse effects have been reported; Dizziness and fatigue, anorexia, nausea, vomiting, abdominal pain, palpitations, myalgia, sleep disorders, arthralgia, headache and rash.

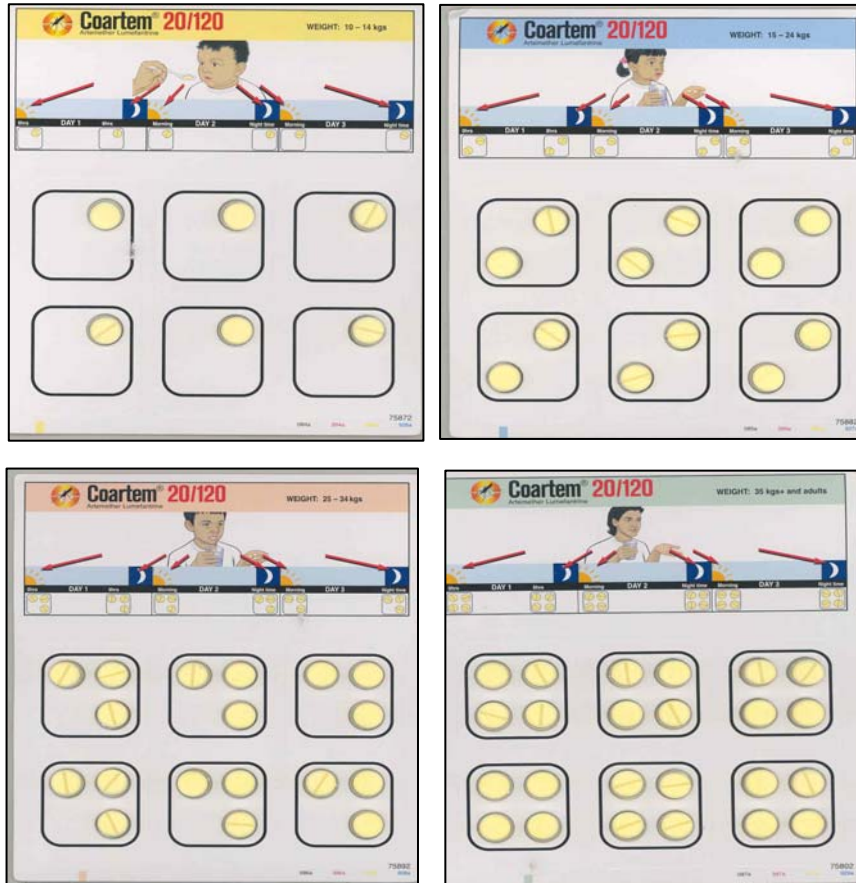
### **Contra-indications:**

- Malaria prophylaxis either alone or in combination.
- Persons with a previous history of reaction after using the rug
- Pregnant women, mothers with infants less than three months of age and Infants less than five kg
- Persons with severe malaria.

**Note: Appropriate storage and use of Artemether-Lumefantrine**

Artemether-Lumefantrine has a short shelf life of two years only. It is a highly hygroscopic chemical compound that moisture and temperature of 30 degree Celsius and above severely affects the efficacy of the drug. To prevent this, therefore, the drugs should be stored in temperatures of below 30 degree Celsius and should not be removed from the blister if it is not going to be used immediately. The form of presentation of Artemether-Lumefantrine is shown below.

**Fig 3. Form of Presentation of Artemether-Lumefantrine**



## I**ib. Chloroquine**

Tablets of 150 mg base or syrup 50 mg base per 5 ml.

Total dose of 25 mg base per kg over 3 days (10 mg base per kg on Days 1 and 2, and 5 mg base per kg on day 3).

<b>Weight (kg)</b>	<b>Age (years)</b>	<b>Day 1</b>	<b>Day 2</b>	<b>Day 3</b>
5 – 6	<4 months Tablets Syrup	1/2 5 ml	1/4 5 ml	1/4 2.5 ml
7 – 10	4 – 11 months Tablets Syrup	1/2 7.5 ml	1/2 7.5 ml	1/2 5 ml
11 – 14	1 – 2 years Tablets Syrup	1 12.5 ml	1 12.5 ml	1/2 7.5 ml
15 – 18	3 – 4 years Tablets Syrup	1 15 ml	1 15 ml	1 15 ml
19 – 24	5 – 7 years Tablets Syrup	1 1/2 20 ml	1 1/2 20 ml	1 15 ml
25 – 35	8 – 10 years	2 ½	2 ½	1
36 – 50	11 – 13 years	3	3	2
50+	14+ years	4	4	2

### **Side effects:**

Dizziness, skeletal muscle weakness, mild gastrointestinal disturbances (nausea, vomiting, abdominal discomfort and diarrhoea) and pruritus. Pruritus may be severe but is usually over within 48 – 72 hours.

### **Contra-indications:**

- persons with known hypersensitivity
- persons with a history of epilepsy
- persons suffering from

**Iic. Quinine**

Quinine 8 mg base/kg 3 times daily for 7 days

Weight (kg)	Age years)	Oral (tablets) Dosage to be given daily	
		200 mg salt	300 mg salt
4 – 6	2 – 4 Months	1/4	-
6 – 10	4 – 12 months	1/3	¼
10 – 12	1 – 2 years	1/2	1/3
12 – 14	2 – 3 years	3/4	½
14 – 19	3 – 5 years	3/4	½
20 – 24	5 – 7 years	1	¾
25 – 35	8 – 10 years	1 1/2	1
36 – 50	11 – 13 years	2	1 ½
50+	14+	3	2

**Side effects:**

Dizziness, ringing in the ears, blurred vision and tremors known collectively as “Cinchonism”. At the above dosages these symptoms are not severe enough to stop treatment and subside spontaneously when administration of the drugs ends. Hypoglycemia may be caused by quinine.

**Contra- indications:**

No contraindication to the oral administration of the drug with in the above dosage.

## II d: Quinine Dosage for Severe Falciparum Malaria

### ***Wherever IV administration of quinine is not possible.***

1. Quinine dihydrochloride 20 mg salt per kg loading dose intramuscularly (divided in to two sites, anterior thigh)
2. Then quinine dihydrochloride 10 mg salt per kg IM every 8 hours until patient can swallow.
3. Then administer artemether-lumefantrine as indicated in annex IIa or oral quinine if the first drug is not available. However, if a patient has a history of intake of artemether-lumefantrine before complications developed, give quinine tablets 10 mg salt per kg every 8 hours to complete 7 days treatment.

*(If possible, for intramuscular use, quinine should be diluted in sterile normal saline to a concentration of 60 mg/ml).*

### ***Where IV administration of quinine is possible***

#### **Loading dose:**

- Quinine 20 mg salt/kg of body weight by infusion over 4 hours, in 5 % dextrose saline (5-10 ml/kg of body weight depending on the patient's overall fluid balance).

#### **Maintenance does:**

- Twelve hours after the start of the loading dose, give quinine 10 mg salt/kg of body weight in dextrose saline over 4 hours.
- Repeat the same dose of quinine (i.e. 10 mg salt/kg) every 8 hours until the patient can take oral medication.
- Then administer artemether-lumefantrine as indicated in annex IIa. Or oral quinine if the first drug is not available. However, if a patient has a history of intake of artemether-lumefantrine before complications developed, give quinine tablets 10 mg salt per kg every 8 hours to complete 7 days treatment.



**Ile. Primaquine**

0.25 mg base per kg daily for 14 days

Weight (Kg)	Age (Years)	Number of tablets	
		7 .5 mg tablet	15 mg tablet
19 – 24	5 – 7	3/4	-
25 – 35	8 – 10	1	1/2
36 – 50	11 – 13	1 1/2	3/4
50+	14+	2	1

**Side effects:**

Anorexia, nausea, vomiting, abdominal pain and cramps are dose related and relatively rare at daily doses up to 0.25 mg base/kg. They may also be accompanied by vague symptoms such as weakness and uneasiness in the chest.

**Contraindications:**

- Pregnancy
- Children under four years
- Any condition that predisposes to granulocytopenia, such as active rheumatoid arthritis & systemic lupus erythematosus.

### **IIf. Artemether Injection**

3.2 mg/kg loading dose on the first day followed by 1.6 mg/kg daily for two days.

#### **Side effects:**

- Adverse effect may include headache, nausea, vomiting, abdominal pain, itching, drug fever, abnormal bleeding and dark urine.

#### **Contraindications:**

- IM Artemether is not recommended during the first trimester of pregnancy.

**Annex III: Chemoprophylactic regimen:****Mefloquine**

5 mg base per kg weekly

<b>Weight (kg)</b>	<b>Age (years)</b>	<b>Number of tablets per week</b>
<5	<3 months	not recommended
5 – 12	3 – 23 months	1/4
13– 24	2 – 7	½
25 – 35	8 – 10	3/4
36 – 50+	11 – 14+	1

**Side effects:**

Dizziness mild to moderate gastrointestinal disturbances (nausea, vomiting, abdominal pain and diarrhoea).

**Contra-indications:**

- persons with known hypersensitivity
- persons with a history of severe neuropsychiatric disease
- pregnant women in the first trimester,
- infant less than 3 months
- persons who have received treatment with mefloquine in the previous 4 weeks
- persons performing activities requiring fine coordination and spatial discrimination

## Annex IV: The Glasgow coma scale

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<b>Eyes Open:</b>	<b>Score</b>
Spontaneously	4
To speech	3
To pain	2
Never	1
<b>Best Verbal Response:</b>	
Oriented	5
Confused	4
Inappropriate words	3
Incomprehensible words	2
None	1
<b>Best Motor Response:</b>	
Obeys command	6
Localises pain	5
Flexion to pain:	
Withdrawal	4
Abnormal	3
Extension to pain	2
None	1
<b>TOTAL</b>	<b>3 - 15</b>

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**Annex V: The Blantyre Coma Scale**

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		<b>Score</b>
<b>Eyes Movement:</b>	Directed (e.g. follows mother's face)	1
	Not directed	0
<hr/>		
<b>Verba Response:</b>	appropriate cry	2
	Moan or inappropriate cry	1
	None	0
<hr/>		
<b>Best Motor Response:</b>	Localises painful stimulus	2
	Withdraws limb from pain	1
	<u>Non-specific or absent response</u>	<u>0</u>
	<b>TOTAL</b>	<b>0 - 5</b>

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**Annex VI: Treatment/Progress/Observation Chart**

DATE \_\_\_\_\_

CARD No. _____ BED No. _____		TIME																			
NAME: _____		TIME SINCE ADMIS.																			
AGE: _____		DRUG [INCLUDING IV FLUIDS, GLUCOSE, BLOOD TRANSFUSION] DRUG DOSE ROUTE																			
SEX: _____																					
WEIGHT _____ KG		TEMP. °C 41 40 39 38 37																			
DRUGS PRIOR TO ADMISSION:			INFUSION FLUID: Specify, duration and volume, e.g. 5% D/S																		
DATE/TIME ADMISSION:				URINE VOL: _____ ml INPUT minus OUTPUT: _____ [+/-]																	
SUMMARY OF CONDITION ON ADMISSION	FREQ. OF OBSERVATION				WT: _____ KG																
GLASGOW SCALE _____ BLANTYER _____	[2-4 hourly]					PP beats per min. _____															
CONVULSION ? Y _____ N _____	[1-4 hourly]	BP: ____/____ mmHg																			
JAUNDICE? Y _____ N _____	*		RR: _____ / min																		
SHORTNESS OF BREATH? Y _____ N _____	[ 12 hourly]			LEVEL OF CONSCIOUSNESS SCALE:																	
SHOCK ? Y _____ N _____	[1-8 hourly]				Hg or Hct _____																
OLIGURIA ? Y _____ N _____	[1-8 hourly]					PARASITAEMIA IN “+”															
HEAMOGLOBINURIA? Y _____ N _____	[1-8 hourly]	ABLE TO DRINK																			
PARASITAEMIA IN “+”	[4 hourly]		ABLE TO SIT																		
Hg OR Hct _____	[8-12 hourly]			CONVULSION?																	
	[8-12 hourly]				OTHER OBSERVATIONS																

\* URINE VOLUME SHOULD BE MEASURED HOURLY IF CATHETERIZED, OTHERWISE WHEN POSSIBLE.