The diagnosis and management of severe and complicated falciparum malaria

Part I Learner’s Guide

Training Unit
Division of Control of Tropical Diseases
World Health Organization
Geneva
The diagnosis and management of severe and complicated falciparum malaria

Part I
Learner’s Guide
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The diagnosis and management of severe falciparum malaria: Learner’s Guide
This training module on the diagnosis and management of severe *P. falciparum* malaria is intended primarily for the training of physicians, nurses, medical students and other health personnel both in malarious areas of the world and non-endemic countries.

The module consists of Part I a Learner’s Guide, and Part II a Tutor’s Guide. Within the Learner’s Guide are learning units which together provide essential information on clinical features of severe and complicated malaria and guidance on how to proceed in a logical way with diagnosis and management of the disease. The picture quiz in Learning Unit 5 helps the learner to visualize the most striking clinical manifestations of the disease and to distinguish them from similar manifestations of other infectious diseases. Learning Unit 8 is based upon a problem-solving approach to learning and allows the learners to acquire the knowledge required through guided examination of several malaria patients presenting distinct features in the manifestation of the disease.

Part II, the Tutor’s Guide provides the opportunity to check step by step the learners reasoning in the interpretation of the results of the clinical examination and laboratory investigations with the most authoritative publications. These are provided in the list of references at the end of Learning Unit 5. Answers are also provided for the picture quiz which could be used to promote a discussion on the signs of severe and complicated malaria. Solutions to the problems posed in Learning Unit 8 of the Learner’s Guide are suggested in the Tutor’s Guide.

This module is part of a series of publications in English and French prepared by the World Health Organization on the subject of severe and complicated malaria that review the latest knowledge and experience on the subject. The other publications include: Management of Severe and Complicated Malaria, A Practical Handbook (H.M. Gilles 1991), and Severe and Complicated Malaria, second edition (D.A. Warrell et al. 1990). While the Handbook could be used as an aide mémoire for practising physicians, the second document will be helpful for those involved in clinical work and research on malaria to up-date and broaden their knowledge of the subject.
Acknowledgements

The technical content of this module was prepared by Professor M.E. Molyneux, Liverpool School of Tropical Medicine. The module was then developed by Dr P.F. Beales and Dr R.L. Kouznetsov, Training Unit, Division of Control of Tropical Diseases, WHO, Geneva. Further contributions were made by Professor H.M. Gilles, Dr J.E. Touze and Dr F.A. Rio.

This is a trial edition intended to be used in the field for one or two years before final publication. Comments on experience with the use of this module would be most welcome and should be addressed to Chief, Training, Division of Control of Tropical Diseases, World Health Organization, 1211 Geneva 27, Switzerland.

The development of this training module was supported by a financial contribution from the Government of the Netherlands.
Introduction

This Learner's Guide, Part I of the module on the Diagnosis and Management of Severe Falciparum Malaria, is made up of teaching materials, problems and a picture quiz covering all the activities involved in diagnosing and managing severe and complicated malaria at the hospital level. This guide is based upon the problem solving approach to education, and working through the study cases presented, you will develop the competence to manage correctly cases of severe and complicated malaria. Together with Part II, the Tutor's Guide, it forms a training module which is designed to be used throughout a formal period of training and provides information, poses practical problems and suggested solutions in a simple, easily understandable form, so as to facilitate local adaptation and translation into local languages. It may also be used as a reference after training together with the practical handbook. (H.G. Gilles, Management of Severe and Complicated Malaria, A practical handbook, WHO, 1991).

The Guide is designed for medical tutors, physicians, medical undergraduates and other health personnel who are, or will be responsible for the diagnosis and management of cases of severe and complicated malaria.

Objectives

At the end of the training programme based on this Learner's Guide you should have acquired the skill and competence that will enable you to:

- define what is severe malaria, predict those at high risk and recognize it when it occurs
- take a history relevant to severe malaria, conduct an appropriate physical examination and request the most urgent tests necessary for diagnosis and proper management
- assess severity of the disease in adults and children
- determine what malaria specific treatment to provide, by which route and in which doses
- provide urgent and maintenance treatment to the severely ill patient, monitor progress and modify management as necessary
- assess recovery and detect residual sequelae
- arrange for follow-up as appropriate
- write a summary of events and outcome.
How this subject will be taught

The tutor and the facilitators

The tutor has extensive experience in the management of severe and complicated malaria and is able to help you to solve a wide range of problems. Facilitators who work with the tutor will collaborate with you to achieve the objectives outlined above. Facilitators will lead discussions and provide general help to individuals and to small groups of learners.

Presentations

Formal presentations (e.g. lectures) will usually be kept to a minimum and each session will be as short as possible. Most information that will be given in such sessions is already contained in this Guide, so there will be very little need for you to take notes. A lecture presentation will usually be combined with a demonstration.

Demonstrations

Demonstrations will either be used to illustrate some aspects of diagnosis and management of disease that you will later carry out yourself, or consist of looking at specimens and equipment that you need to know about and be able to use.

Practical sessions

There will be as many practical sessions as possible. They are intended to help you to gain as much practical experience as you can in all aspects of the diagnosis and management of severe and complicated malaria. In some, each facilitator will work with a small group of four or five learners. Because there are only a few learners in each group, the facilitator will be able to give a great deal of attention to each individual: this increases your opportunities to practise and to learn.

Small group discussions

In these exercises, a facilitator will lead discussions on particular subjects. These sessions provide good opportunities for you and the
other learners to give your opinions, develop your ideas and learn from one another.

Clinical work and visits to the wards

Whenever possible, sessions will take place at the patient's bedside. This will give practical experience of real-life situations and allow you to learn about the problems you may meet in the course of your daily work.

Evaluation

Evaluation of the learner

Your progress and achievement will be evaluated by the tutor, the facilitators and yourself. This will be done through multiple-choice quizzes.

In multiple-choice quizzes, each question is provided with a list of possible answers from which you must select the one you think is correct. At the end of these sessions you will not necessarily be given the correct answer to each question, but the tutor will analyse the results to identify topics that were not clearly understood. The tutor may also tell you where you made mistakes and point out areas where you need to improve.

This part of the evaluation is designed to help you and the tutor to assess how well you understand the non-practical aspects of the course. Multiple-choice tests will be given at the beginning and at the end of this training.

Evaluation of the training by the learner

By means of a questionnaire, the tutor will ask you, the learner, how you think the training has helped you and how it might be improved. This evaluation will take place at the end of the training period in order to provide as much feedback from you as possible. You may sign the questionnaire or not, as you wish, but you should feel completely free to make suggestions for improvement on the part of the tutor and facilitators as well as in the content of the course and the training facilities.
Use of the Learner's Guide

This Learner's Guide consists of instructional materials designed to enable you to achieve the objectives stated earlier. The Guide is divided into chapters called Learning Units. You must acquire the skills and knowledge contained in one Unit before progressing to the next, otherwise you may have difficulty in achieving the objectives of subsequent Learning Units. It is a progressive step ladder learning process commencing with Learning Unit 1 and ending with Learning Unit 8.
LEARNING UNIT 1

What you know about the diagnosis and management of severe falciparum malaria in your country or place of work?

Learning objectives

By the end of this Unit you should be able to:

- understand more clearly the situation of severe and complicated falciparum malaria in your country or place of work, and how it is managed.

In the following pages of this Learning Unit you will find a series of questions which you should answer the best you can. This is not an examination but is designed to make you think about the mechanism believed to be responsible for the main complications of malaria and about how to determine appropriate treatments. You should answer the questions in the sequence in which they are written. Your answers should be in respect of your country (or the country in which you are, or will be working). If you cannot answer the question relative to the whole country but can for a part of it, then please do so stating clearly to what part of the country your answers apply.

Answer clearly and briefly those questions on which you have a definite opinion.

Questions

Write down your answers to these questions. This exercise may help you to get the best out of the course that follows.
1. What do you mean by "severe" malaria? (What forms may malarial illness take which make it "severe")

2. Severe malaria can present with many complications. In your place of work:

   (i) Which complications are the most common:

   (ii) Which complications are the most serious:

   (iii) How many cases (roughly) are seen at your place of work per month?
(iv) Which people in the population are most troubled by severe malaria in your area?

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

(v) How many deaths are due to malaria each month (roughly)?

________________________________________________________________________

(vi) Do you believe that most of the cases of severe malaria (among the population you serve) are brought to a health unit (clinic or hospital)? If not state why.

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

(vii) Do many deaths occur at home without reaching medical care? If yes state why.

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________
3. What are some possible reasons why some attacks of malaria are "mild" (fever, headache, etc.) while others become "severe" or even fatal?

4. How do you rank malaria as a cause of severe illness compared to other causes of severe illness?

5. What are the antimalarial drugs used to treat severe malaria in your country or place of work?

Do you think they are effective? If not state why.
6. What other drugs are being used for the treatment of severe malaria?

7. What do you think are the major constraints in your country, or place of work, to a satisfactory treatment of severe malaria?

8. How do you expect this training to be useful in your future career?

You should read carefully the next Unit of this module before the session to which it relates.
The diagnosis and management of severe falciparum malaria: Learner's Guide
LEARNING UNIT 2

Severe malaria

Learning objectives

By the end of this Unit you should be able to:

- define what is severe malaria
- identify the high risk groups likely to get severe malaria
- diagnose severe malaria
- appreciate the importance of early treatment.

What is severe malaria?

Severe malaria is falciparum malaria that is sufficiently serious to be an immediate threat to life, i.e. it is a medical emergency. You should regard a patient as having severe malaria if there are asexual forms of *Plasmodium falciparum* on a blood film and the patient has any of the following:

- a change of behaviour, confusion or drowsiness
- altered consciousness or coma
- convulsions
- hypoglycaemia
- acidosis
- difficulty in breathing or pulmonary oedema
- oliguria or acute renal failure
- severe anaemia (haematocrit < 20%, Hb < 6g/dl)
- circulatory collapse or shock
- haemoglobinuria
- jaundice
- a bleeding tendency
- prostration, i.e. generalised weakness so that the patient cannot walk or sit up without assistance.
Note:  

i) Other possible diagnoses will also have to be considered and looked for in such a patient.

ii) An individual patient may have any one or any combination of complications listed above.

iii) A patient with one or some features may go on to develop others.

Who gets severe malaria?

Any infection with *P. falciparum* can become severe if treatment is delayed or inadequate. However, people who have been repeatedly exposed to malaria develop partial immunity and are less likely to experience severe malaria. Those people who are most at risk are:

- children in areas of high endemicity - especially those aged from six months to six years
- people of all ages in areas of low endemicity
- travellers from areas where there is little or no malaria when they go into a malarious area: this may involve travel within a single country or between countries
- people returning to highly endemic areas after a few years’ absence
- indigenous pregnant women, especially those in their first pregnancy.

Why does severe malaria need special attention?

Because:

- severe malaria is a common cause of avoidable death.
- correct early treatment and careful nursing can greatly improve the outlook.
- antimalarial drugs should, if possible, be given parenterally under close supervision.
- treatment should therefore be in hospital, if possible.
- many methods of treatment which are still being used are dangerous or ineffective and should be abandoned.
How is severe malaria diagnosed?

Consider the possibility of severe malaria in patients with any of the clinical features and/or syndromes listed on page 19, even if the illness did not start with typical malaria symptoms.

A common reason for death in severe malaria is that the diagnosis is not thought of immediately in a patient presenting with one of the complications.

Most patients will also have fever, but this is not invariable.

A correct diagnosis should be based upon a complete history of the condition, a physical examination, and laboratory investigations.

Ideally a blood film should be done to demonstrate the presence of *P. falciparum* asexual parasites. But remember:

- getting a blood film done must not be allowed to delay the start of treatment unduly.
- occasionally blood films may be negative even though the patient is suffering from severe malaria. Blood films should be repeated (e.g. every 6 hours): if clinical features strongly suggest severe malaria, treatment may be started even if films are negative.
- a24 positive blood film does not prove that malaria is the cause of the severe illness. Consider and look for other possibilities as well.

You should read carefully the next Unit of this module before the session to which it relates.
Pathophysiology of severe falciparum malaria

**Learning objective**

By the end of this Unit you should be able to:

- describe the mechanism believed to be responsible for the main complications of malaria
- show how an understanding of the mechanism of the disease can help to determine appropriate treatment.

Working as a small group, read carefully the following Unit. Remember that while some of the factors and theories are established, others remain speculative.

Discuss with your colleagues first, then in plenary, what you have read. Consider the relevance of the pathophysiology in determining the appropriate treatments.

**Mechanism of malarial disease**

The possible effects of malarial infection cover an enormous range, from completely asymptomatic infection to fatal severe disease. Many factors are believed to influence the clinical manifestations of infection: some of these factors are known beyond doubt, while others remain speculative. They include:

Factors known to influence the severity of disease in a malaria infection

- The species of parasite. Only *P. falciparum* causes severe and complicated malaria, but it also (more commonly) causes mild or asymptomatic disease.
- The immunity of the individual. Adults who have lived all their
life in an endemic area are less susceptible to severe disease than:

(i) adults who visit an endemic area for the first time
(ii) young children living in the same endemic area. Pregnant women are more susceptible, perhaps because of diminished immunity.

- Therefore, the degree of parasite drug-resistance that prevails locally.
- Some genetically inherited conditions in the human host - e.g. sickle cell trait, which reduce the risk of a *P. falciparum* infection leading to severe disease.

Factors that may affect the severity of illness (but we do not yet know for certain)

- The particular strain of *P. falciparum*. Are some strains more virulent than others? There is evidence to suggest that this is so, but no proof.

- The age at which first infection takes place. Perhaps very early infections - in the first 3 months of life, when maternal antibodies still convey some protection against parasite multiplication or disease - cause gradual immunization with less risk of severe disease.

- Therefore, the intensity of transmission. If transmission is very intense, first infections in infants will tend to occur very early in life. There is evidence that the pattern and severity of disease in children differs according to the local transmission pattern.

- Other differences between people - some abnormal haemoglobins in their heterozygote state (e.g. HbS) and red cell abnormalities (α and β thalassemia, G6PD, ovalocytosis) as well as some tissue (HLA) types in some areas seem to make individuals less susceptible to severe disease.

- Other infections or circumstances that might impair immunity.
• The extent of the individuals' response to an infection - e.g. the rate and degree of production of cytokines such as tumour necrosis factor (TNF).

• The number of sporozoites injected by the mosquito (or by several mosquitoes).

Mechanism of mild (uncomplicated) illness

All species of malaria parasite can cause fever, with its associated symptoms (shivering, headache, myalgia, rigors). There is now little doubt that fever is caused not directly by the parasite, but by host substances known as cytokines. These are secreted by host cells (macrophages, endothelial and other cells) in response to parasite or red cell material released when the schizont ruptures.

Possible mechanisms of severe disease

Cytokines

It is possible, but still not proven, that cytokines if produced to excess may cause severe disease in addition to fever. One cytokine known to be secreted by the individual in response to malaria is tumour necrosis factor (TNF). Large quantities of TNF circulate in severe malaria, especially in fatal cases, and we know that TNF is capable of causing many of the symptoms, signs and complications that are typical of severe malaria - e.g. coma, hypoglycaemia, acidosis, anaemia and respiratory distress syndrome. However it is still not certain whether TNF (or other cytokines) cause malaria complications or only result from severe infection.

Sequestration

In falciparum malaria, a consistent pathological feature is the sequestration of red blood cells containing maturing parasites (schizonts; large trophozoites) in deep capillaries and venules. This phenomenon is observed in many different organs and tissues, including the brain, lung, heart, bone marrow and gut. It seems likely (but is not proven) that sequestration is in some way responsible for certain complications such as altered consciousness and acidosis. We
know that sequestration is not invariably harmful, because it occurs in mild as well as in severe falciparum malaria.

If sequestration is important in causing severe disease, how does it do so? It is unlikely that sequestration actually blocks blood vessels so that blood-flow is reduced or stopped. If sequestration had this effect, we would expect most people who recover from malarial coma to have persisting brain damage, but this is not so. Most survivors recover fully. A few (5-10%) do have neurological sequela (focal brain damage), with abnormalities on CATscan pictures, so it may be that sequestration sometimes leads to obstruction of blood flow.

Alternatively, sequestered parasites, which we know to be highly metabolically active, may use up vital substances, such as glucose and oxygen, so that these are not available to host cells (e.g. brain cells). The parasites may also produce waste matter (e.g. lactate) or toxins (e.g. free iron, toxic oxygen radicals) that are directly injurious to local host tissues.

Another attractive theory is that sequestration serves to concentrate schizonts in vital tissues. Rupture of schizonts may then stimulate the release of large quantities of cytokines locally which could then have a powerful local effect even if cytokine levels in the general circulation are not particular high.

In vitro, a parasitised cell may attract unparasitised red cells, which adhere to the surface of the parasitised cell forming a "rosette". There is not yet any convincing evidence that rosettes play an important part in pathogenesis in vivo.

Raised intracranial pressure

Children with cerebral malaria commonly have a high opening-pressure of the cerebrospinal fluid, indicating raised pressure in the brain and spinal column. This is not always present, and may vary over time. In some adults this phenomenon has also been observed. The cause of raised intracranial pressure is not clear. It is not due to cerebral oedema, although this may occasionally develop as a terminal event. Intracranial pressure may sometimes be high because of the increased mass of red cells sequestred in the brain, or because of dilatation of vessels in the brain in response to locally generated cytokines.

Raised intracranial pressure is not the cause of coma or of death in the majority of cases. It may, however, play a part in pathogenesis or affect the course of the disease in ways that are not yet understood.
Other mechanisms of some specific complications

Anaemia

Anaemia is partly due to the destruction of all red cells that contain parasites. Several other mechanisms may accelerate the development of anaemia: non-parasitised red cells are destroyed more quickly than normal during malarial illness, and bone marrow does not function adequately. Anaemia is worsened if there is abnormal bleeding, intravascular haemolysis or renal failure.

Pulmonary oedema

Pulmonary oedema may result from excessive fluid replacement by intravenous infusion, especially if there is renal failure. Respiratory distress syndrome appears to be due to a direct effect of parasites sequestered in the lungs, possibly through release of cytokines.

Renal failure

Renal failure is acute tubular necrosis. It is therefore fully reversible if the patient is kept alive (e.g. by peritoneal dialysis) for long enough - usually 2-3 weeks. Renal failure is most likely to develop if there has been a period of low blood pressure or shock.

Hypoglycaemia

Hypoglycaemia may be due to impaired gluconeogenesis in the liver, or may result from the fact that maturing parasites consume large quantities of glucose from the plasma. In children hypoglycaemia may develop during any period of fasting, and it therefore complicates many childhood illnesses in addition to malaria.

Another mechanism of hypoglycaemia, most commonly (but not only) seen in pregnant women, may develop during the course of treatment with quinine or quinidine. These drugs stimulate the pancreas to secrete insulin, which may lead to hypoglycaemia.
Acidosis

Acidosis is probably due to a relative shortage of oxygen in tissues occupied by sequestered parasites. This lack of oxygen forces tissues to get their energy by other biochemical pathways not dependent on oxygen; a result of this is the release of lactic acid, leading to metabolic acidosis.

You should read carefully the next Unit of this module before the session to which it relates.
Guidelines for diagnosis and assessment of severe malaria

Learning objectives

By the end of this Unit you should be able to:

• record a complete history from the patient

• conduct a physical examination of the patient looking for significant signs

• request the most urgent tests necessary for the diagnosis and management of severe disease.

The history

Malaria may be confused with a whole variety of disease syndromes; a careful history may provide a firm basis of differentiation.

The patient’s relatives should be carefully questioned in order to gain information that is of great value in establishing a diagnosis.

A complete history has two important aims:

• to look for clues to possible diagnoses other than malaria

• to assess the severity of malaria and of any of its complications.

In the course of taking a complete history, pay special attention to:
<table>
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<th>Table 1</th>
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<tr>
<td><strong>Geographical history</strong></td>
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<td><strong>Drugs taken</strong></td>
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<td>- for this illness</td>
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<td><strong>Symptoms: their duration and time course</strong></td>
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<td><strong>Previous illnesses and treatment</strong></td>
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<td><strong>Previous blood transfusions</strong></td>
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<td><strong>Is the patient pregnant?</strong></td>
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<td><strong>Other illnesses in the family</strong></td>
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There may be other clues in the history - e.g. a dog bite in a patient with rabies, head injury in a patient developing a subdural haematoma, drug overdose, chronic alcoholism.

This outline suggests some common points requiring emphasis. Much other useful information may come from a complete history.

The physical examination

Like the history, the complete examination aims at:

(i) identifying other possible diagnoses; and
(ii) assessing the severity of malaria and any of its complications.

Pointers to an alternative diagnosis

These examples are quoted because they are commonly neglected:

Table 2

<table>
<thead>
<tr>
<th>In all patients</th>
<th>In children</th>
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</thead>
<tbody>
<tr>
<td>• <strong>Rash:</strong> rare in malaria, may suggest typhus, typhoid, measles, an arbovirus infection, relapsing fever, chicken-pox, leptospirosis or meningococcaemia.</td>
<td>• <strong>Eardrums:</strong> acute or chronic otitis media.</td>
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<tr>
<td>• <strong>Neck stiffness:</strong> note that absence of this does not exclude meningitis, and some children with severe malaria have neck stiffness (as part of generalized hypertonicity in some patients with cerebral malaria).</td>
<td>• <strong>Buccal mucosa:</strong> Koplik spots of prodromal measles.</td>
</tr>
<tr>
<td>• <strong>Sepsis:</strong> look for signs of sepsis in any limb or organ.</td>
<td>• <strong>Pharynx:</strong> tonsillitis, diphtheria.</td>
</tr>
<tr>
<td>• <strong>Enlarged lymph nodes:</strong> trypanosomiasis, tuberculosis, AIDS related infections and many other possibilities.</td>
<td>• <strong>Bulging fontanelle:</strong> suggests meningitis (in small children).</td>
</tr>
<tr>
<td></td>
<td>• <strong>Shallow, rapid breathing with nasal flare:</strong> may suggest acute respiratory infection (ARI) or pneumonia (but remember that some patients with severe malaria have abnormalities of breathing).</td>
</tr>
</tbody>
</table>
Clinical features indicating severe malaria

Each of the clinical features and/or syndromes listed on page 19 that define malaria as severe or complicated may be suspected on the basis of clinical assessment (history and physical signs):

Behavioural changes

May include confusion, delirium, agitation, somnolence, hallucinations, psychosis.

Differential diagnosis: typhoid, heat stroke, drug or alcohol intoxication, hypoglycaemia of any cause, encephalitis (including rabies), metabolic failure (e.g. hepatic failure, renal failure).

Coma

May be moderate or profound, gradual or sudden in onset. Coma is a usual sequel of a convulsion of any cause, but if due only to convulsion, consciousness is usually restored within a few minutes to a few hours.

Differential diagnosis - all conditions listed under behavioural changes, above.

Convulsions

Relatives may describe what they believe were convulsions, occurring before the patient came to the clinic/hospital. Ask a person who witnessed the event, and request details including movements of hands and face, biting of tongue, incontinence. Sometimes any loss of consciousness, or even drowsiness, is described by the same words used for convulsions.

Hypoglycaemia

May manifest as altered behaviour, loss of consciousness, convulsions or simply vague symptoms or none. Sweating and cold, clammy skin may be present but are not invariable.
Acidosis

Deep (not necessarily rapid) breathing is a good indication of acidosis. However this may not be a dependable sign, as the breathing pattern may be obscured by other influences - e.g. depression or excitation of the breathing centre in the brain, pulmonary oedema or chest infection. It may be possible to detect acidotic fetor (sweet smell).

Other breathing difficulties

The breathing pattern in severe malaria is influenced by many factors.

- Central effects, resulting from diseases in the brain. These include irregular breathing, Cheyne-Stokes breathing, and noisy or stertorous breathing.
- Acidaemia - causing deep respiration.
- Infection - e.g. aspiration pneumonia, causing laboured breathing.
- High fever - causes rapid breathing.
- Pulmonary oedema - causes rapid breathing with crackles heard on auscultation and, in severe cases, pink frothy sputum and central cyanosis (tongue).
- Heart failure, which may complicate severe malarial anaemia, giving hepatomegaly, gallop rhythm and pulmonary oedema.
- Respiratory distress syndrome - indistinguishable from pulmonary oedema, but in the absence of fluid overload.

Acute renal failure

This is detected by monitoring urine output. If there is persistent oliguria (volume of urine produced is less than 17 ml/hour in an adult or less than 0.3 ml/kg/hour in a child, despite adequate correction of dehydration or hypotension), then renal failure is present or imminent. Hiccup is an indicator of advanced failure.

Severe anaemia

Properly diagnosed only by measuring haematocrit or haemoglobin level. Suggestive sign is severe pallor of mucosae (especially tongue). Severe anaemia may cause heart failure (breathlessness, enlarging liver, gallop rhythm, pulmonary oedema) or altered consciousness.
The diagnosis and management of severe falciparum malaria: Learner’s Guide

Shock

There is low blood pressure, a feeble pulse, and impaired tissue perfusion with cold, clammy skin and peripheral cyanosis (nail beds, lips).

Haemoglobinuria

The urine is dark, tests strongly positive for blood (haemoglobin) but contains no red blood cells on microscopy. Plasma may also be dark, due to haemoglobin freed from red cells.

Jaundice

Best detected on sclerae of eyes. This is quite commonly seen in severe malaria, but signs of hepatic failure are rare. Jaundice in malaria occurs concomitantly with fever (unlike jaundice due to hepatitis).

Bleeding tendency

There may be spontaneous bleeding from gums or in the skin, or prolonged bleeding at venepuncture sites. Best tested for by measuring the bleeding time (pierce earlobe with lancet, mop every 15 seconds with filter-paper; in normal circumstances bleeding will stop within 2 minutes).

Extreme weakness

The patient cannot sit or stand without help from others. There may be many contributing causes.

Assessing the coma score

A score is based on the patient’s ability to move and speak in response to commands and painful stimuli. In infants who have not yet acquired speech, you can assess the cry and the child’s ability to watch its mother’s face, and also the response to pain. You may grade coma according to one of the following scales (Tables 3 and 4).
The Glasgow coma scale (Table 3) is suitable for adults and for older children.

For children aged about 9 months to 12 years, the Blantyre score, Table 4, may be used.

Measurement of coma in younger infants is difficult. It is best to describe how the child responds to a standard painful stimulus.

Table 3.
The Glasgow coma scale

<table>
<thead>
<tr>
<th></th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Eyes open:</strong></td>
<td></td>
</tr>
<tr>
<td>spontaneously</td>
<td>4</td>
</tr>
<tr>
<td>to speech</td>
<td>3</td>
</tr>
<tr>
<td>to pain</td>
<td>2</td>
</tr>
<tr>
<td>never</td>
<td>1</td>
</tr>
<tr>
<td><strong>Best verbal response:</strong></td>
<td></td>
</tr>
<tr>
<td>oriented</td>
<td>5</td>
</tr>
<tr>
<td>confused</td>
<td>4</td>
</tr>
<tr>
<td>inappropriate words</td>
<td>3</td>
</tr>
<tr>
<td>incomprehensible sounds</td>
<td>2</td>
</tr>
<tr>
<td>none</td>
<td>1</td>
</tr>
<tr>
<td><strong>Best motor response:</strong></td>
<td></td>
</tr>
<tr>
<td>obeys commands</td>
<td>6</td>
</tr>
<tr>
<td>localizes pain</td>
<td>5</td>
</tr>
<tr>
<td>flexion to pain:</td>
<td></td>
</tr>
<tr>
<td>withdrawal</td>
<td>4</td>
</tr>
<tr>
<td>abnormal</td>
<td>3</td>
</tr>
<tr>
<td>extension to pain</td>
<td>2</td>
</tr>
<tr>
<td>none</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>3-15</td>
</tr>
</tbody>
</table>

To obtain the Glasgow coma score, obtain the score for each section, then add the three figures to obtain a total.
Table 4.
The modified Glasgow coma scale (The Blantyre coma scale)

<table>
<thead>
<tr>
<th></th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Eyes movements:</strong></td>
<td></td>
</tr>
<tr>
<td>directed (e.g. follows mother’s face)</td>
<td>1</td>
</tr>
<tr>
<td>not directed</td>
<td>0</td>
</tr>
<tr>
<td><strong>Verbal response:</strong></td>
<td></td>
</tr>
<tr>
<td>appropriate cry</td>
<td>2</td>
</tr>
<tr>
<td>moan or inappropriate cry</td>
<td>1</td>
</tr>
<tr>
<td>none</td>
<td>0</td>
</tr>
<tr>
<td><strong>Best motor response:</strong></td>
<td></td>
</tr>
<tr>
<td>localizes painful stimulus a</td>
<td>2</td>
</tr>
<tr>
<td>withdraws limb from pain b</td>
<td>1</td>
</tr>
<tr>
<td>nonspecific or absent response</td>
<td>0</td>
</tr>
</tbody>
</table>

Total 0-5

a) press your knuckles firmly on the patient’s sternum
b) press firmly on patient’s thumbnail bed with the side of a horizontal pencil.

These scales can be used repeatedly to assess improvement or deterioration.

**Laboratory investigations**

- Thick and thin blood films for malaria parasites.¹

- Blood glucose in any patient with altered consciousness, confusion or convulsions. This is best done using a "stix" method. The test requires one drop of finger-prick blood and the

---

result can be read within 1-2 minutes, either by eye or more accurately by reflectance meter.

- Haematocrit.

- Lumbar puncture to exclude meningitis. Meningitis cannot be diagnosed without a lumbar puncture. Neck stiffness may be absent in meningitis, especially in children and after a convulsion; some patients with malaria have neck retraction or opisthotonos, without meningitis. A clear cerebrospinal fluid should be examined microscopically for cells, since a fluid may look clear with up to 300 cells/mm³. Do not wait for the cell count result if this will take more than a few minutes.

With these results you should initiate immediate treatment without waiting for other test results.

**Other laboratory investigations if possible**

These are not essential to management, but if available may be helpful or of prognostic usefulness.

- Plasma creatinine; urea is an alternative, but there is no need to measure both, as creatine is more useful.

- Electrolytes, these may occasionally reveal a correctable abnormality such as hyponatraemia. Both creatine and electrolytes are of most value when acute renal failure threatens or develops.

- Blood culture, because septicaemia may complicate severe malaria and cause shock or unresolving fever.

- Full blood cell count and differential white cell count. Sometimes these may indicate the possibility of an additional diagnosis (e.g. gross eosinophilia) or complication (e.g. profound thrombocytopenia).

- Blood gases, pH and anion gap. The main electrolytes routinely measured in plasma are sodium ions (Na⁺), chloride ions (Cl⁻), potassium ions (K⁺), and bicarbonate ions (HCO₃⁻). The sum of the measured cations (Na⁺ and K⁺) normally exceeds that of the measured anions by about 14 mmol/l (reference range 10 to 18 mmol/l. This difference is known as "anion gap" and is
attributable largely to negatively charged proteins but also to phosphate, sulphate, and some organic acids. Calculation of the anion gap is principally of value in the differential diagnosis of metabolic acidosis and in following the progress of therapy. Acidaemia is an indicator of severe disease, in both conscious and unconscious patients.

- Chest X-ray. May identify pulmonary oedema, respiratory distress syndrome, or lobar consolidation (pneumonia).

- Plasma and cerebrospinal fluid lactate concentrations. These are raised in lactic acidosis: high levels (5 mmol/litre or above) are associated with a poor prognosis.

- Liver functions tests.

Investigations during management

Some investigations will be equally (or more) valuable if repeated during the course of treatment, according to clinical indications (e.g. blood glucose for deepening coma or convulsions, creatinine and electrolytes if renal failure is suspected, chest X-ray for possible pulmonary oedema or respiratory distress syndrome). Some tests nearly always need repeating at intervals: blood films, haematocrit or haemoglobin concentration.

You should read carefully the next Unit of this module before the session to which it relates.
LEARNING UNIT 5

Picture Quiz

Learning Objectives

By the end of this Unit you should be able to:

• interpret physical signs of severe disease in children and adults
• decide on differential diagnoses
• determine tests that need to be carried out.

Figure 1
The children seen in Figures 1, 2 and 3 were all brought to a clinic in an area where *P. falciparum* is hyperendemic. Each child is unconscious and has a heavy *P. falciparum* parasitaemia. The children were 3 to 5 years old. They were febrile (38°C - 40°C). The children had been immunized against the communicable diseases of childhood through the EPI programme.

**Question 1**

What do the pictures show?

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

**Question 2**

What is the differential diagnosis?

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

**Question 3**

What tests would you do?

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________
The children seen in Figures 4 and 5 each have a short history of fever followed by progressive loss of consciousness. Both are in deep coma and have a heavy *P. falciparum* parasitaemia. They are 3 and 4 years old. Neither of them had been immunized against the common childhood diseases.

**Question 4**

What do the pictures show?

__________________________________________________________

__________________________________________________________

__________________________________________________________

**Question 5**

What could be the explanation for this?

__________________________________________________________

__________________________________________________________

__________________________________________________________
Figure 6
The patient seen in Figure 6 has *P. falciparum* malaria. She was admitted in coma, treated with quinine and recovered consciousness. Two days later she had a convolution and collapsed into coma again.

**Question 6**

What are the possible causes of the convolution and subsequent coma?

**Question 7**

What investigation would you do to ascertain the causes?

**Question 8**

How would you manage this patient?
Figure 7
Figure 7 shows the supportive treatment given to a patient with severe malaria.

**Question 9**
What exactly does the picture show?

**Question 10**
What is the most frequent complication in severe malaria that leads the physician to perform this approach?

**Question 11**
What are the complications to be afraid of in carrying out this technique in rural hospitals?
Pictures 8 and 9 refer to the clinical and radiological presentation of a woman soon after labour.

She has severe malaria with hyperparasitaemia and the condition shown in pictures 8 and 9 was preceded by an increase in the respiratory frequency.

**Question 12**

What is the condition shown in these pictures?

**Question 13**

What is the differential diagnosis?

You should read carefully the next Unit of this module before the session to which it relates.
The diagnosis and management of severe falciparum malaria: Learner's Guide
The management of severe and complicated malaria

Learning objectives

By the end of this Unit you should be able to:

- provide urgent treatment to the severely ill patient
- provide maintenance treatment throughout the period of illness
- arrange for regular monitoring and appropriate actions as necessary.

How is severe and complicated malaria managed?

Under ideal conditions the severely ill patient, especially comatose, should be managed in an intensive care unit. This is not possible in most endemic areas. In such conditions the nurse assures the role of the intensive care unit monitoring system. Thus the nurse must be appropriately trained to a very high level to assure the essential role in patient management.

Urgent treatment

- Establish an intravenous infusion.
- Correct hypoglycaemia if present: give 50% dextrose intravenously over 1-2 minutes, 1 ml/kg in children, 20 ml in adults. Re-check the blood glucose after 30 minutes: (further monitoring of blood glucose will be necessary throughout the course of management).
- Access the fluid requirement based on body weight and set up the appropriate volume to run in the first four hours.
- Add the correct antimalarial drug, in the correct dose according to the patient’s weight, to the infusion fluid (Table 5).
• Reduce body temperature if greater than 39°C. This is best done by giving paracetamol, by mouth if possible, alternatively by suppository. In addition, wet the skin with tepid water and fan vigorously and repeatedly. Relatives can help with this task.

• Control convulsions: first, correct any detectable cause of convulsions (hypoglycaemia, hyperpyrexia). Give an anticonvulsant drug (e.g. for prevention in adults phenobarbital sodium 10-15 mg/kg/im).

• Consider the need for blood transfusion. Does the patient need blood? Is this a more important question than: "What is the haematocrit?" Blood (packed cells) is needed if anaemia is contributing to cardiac failure, or if anaemia appears to be life-threatening.

• Decide whether a urinary catheter should be passed. This is necessary if either acute renal failure or pulmonary oedema is suspected, in order to guide fluid balance.

• Decide whether a central venous pressure line is to be set up. This is of most value where pulmonary oedema is suspected, and may be useful in the patient with shock or impending renal failure. It requires the necessary facilities, expertise and a sufficient number of trained staff to use it properly. It is a difficult procedure in children.

Treatments which are not recommended

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

Continuing treatment

This calls for close cooperation between medical and nursing staff. Responsibility for various observations must be allocated according to
availability and expertise of personnel. Proper nursing care of the unconscious patient is of utmost importance in patients with cerebral malaria.

You should have a record chart on which the important complications of the patient’s illness are summarized, treatment is prescribed, and all important observations are recorded at suitable intervals.

A sample chart is provided (Table 6). Make your own modifications to this chart according to local facilities and experience.

Stipulate how frequently observations should be made: this will depend on the particular circumstances of each patient and the severity, stage and complications of the illness. For example, blood glucose should be checked hourly in a comatose pregnant woman receiving intravenous quinine, but less frequently in a man whose condition is steadily improving.

Observations should be aimed at:

- controlling the delivery of drugs and infusion fluids
- detecting the development of complications of malaria
- detecting toxic effects of drugs being given
- documenting the patient’s recovery.
### Table 5: Antimalarial chemotherapy of severe falciparum malaria in adults and children

<table>
<thead>
<tr>
<th>Chloroquine-sensitive malaria</th>
<th>Chloroquine-resistant malaria or sensitivity not known</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloroquine 5 mg base/kg of body weight in isotonic fluid by constant-rate intravenous infusion over 6 hours, calculated from the beginning of the previous infusion (continuous administration) for a total of 5 doses</td>
<td>Quinine dihydrochloride 20 mg salt/kg of body weight (loading dose) by infusion over 4 hours, in 5% dextrose saline (5-10 ml/kg of body weight depending on the patient’s overall fluid balance).</td>
</tr>
<tr>
<td>or</td>
<td>Eight to twelve hours after the start of the loading dose, given a maintenance dose of quinine 10 mg salt/kg of body weight dextrose saline diluted as above over 4 hours. This maintenance dose should be repeated every 8-12 hours, calculated from the beginning of the previous infusion, until the patient can take oral medication&lt;sup&gt;b&lt;/sup&gt; (e.g. 08h00, 16h00, 24h00).</td>
</tr>
<tr>
<td>(If intravenous infusion is not possible) chloroquine 3.5 mg base/kg of body weight every 6 hours intramuscularly or subcutaneously&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Note: Use quinine every 12 hours in areas without known quinine-resistance. Use the 8-hourly regimen where there is known or increasing quinine resistance.</td>
</tr>
</tbody>
</table>

---

<sup>a</sup> Total dose 25 mg base/kg of body weight; change to oral therapy when patient can swallow.

<sup>b</sup> The choice of oral medication will be governed by drug availability and sensitivity of the parasites. The following may be used:

- quinine tablets, 10 mg/kg of body weight, every 8 hours, to complete 7 days of treatment or a single dose of sulfadoxine/pyrimethamine (Fansidar) following a shorter course of quinine.

- sulfadoxine/pyrimethamine (Fansidar) or sulfalene/pyrimethamine (Metakelfin) as a single oral dose; sulfadoxine/sulfalene, 25 mg/kg of body weight; pyrimethamine, 1.25 mg/kg of body weight. These drug combinations preferably not be given to pregnant women.

- mefloquine, 15 mg/kg body weight up to a maximum of 1000 mg, in two doses 12 hours apart. Mefloquine should not be administered until 12 hours have elapsed after the completion of parenteral quinine administration. This drug should not be given to women in the first trimester of pregnancy.
Some important points to note in relation to Table 5.

1. In areas with a significant degree of quinine resistance (e.g. Cambodia, Thailand, Viet Nam), add an oral course of tetracycline 250 mg four times a day for 7 days, as soon as the patient can swallow. It is unnecessary and dangerous to give tetracycline intravenously. Tetracycline is contraindicated for children under 8 years and pregnant women. As an alternative, mefloquine could be given as indicated in footnote b to Table 5.

2. In patients requiring more than 48 hours of parenteral therapy, reduce the quinine or quinidine maintenance dose by one-third to one-half (i.e. 5-7 mg salt/kg of body weight every 8-12 hours).

3. Total daily doses of intravenous quinine are as follows:
   - day 0 (first day of treatment): 30-40 mg/kg of body weight
   - day 1: 20 mg/kg of body weight
   - day 2 and subsequent days: 15 mg/kg of body weight

   It is unusual to have to continue intravenous infusions of quinine for more than 4-5 days. In children the infusion can usually be stopped after 1-2 days.

4. 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.)

5. A loading dose should not be used if the patient received quinine or quinidine within the preceding 24 hours, or mefloquine within the preceding 24 hours.

6. If for some reason quinine cannot be administered by infusion, quinine dihydrochloride can be given in the same dosage by intramuscular injection in the anterior thigh. The dose of quinine should be divided between two sites - half the dose in each anterior thigh. If possible, for intramuscular use, quinine should be diluted in sterile normal saline to a concentration of 60 mg/ml.

An example of a chart for recording regular observations during treatment of severe malaria is shown on page 56. This could be modified to suite particular circumstances. Clinical notes should also be kept separately. Frequency of observations should be according to clinical need.
**Table 6: Treatment/Progress/Observation Chart.**

<table>
<thead>
<tr>
<th>Ref. ward</th>
<th>Bed no.</th>
<th>Sex</th>
<th>Indigenous</th>
<th>Pregnant?</th>
<th>Weight</th>
<th>Drugs pre-admission</th>
<th>Date &amp; time of admission</th>
</tr>
</thead>
</table>

**SUMMARY OF CONDITIONS ON ADMISSION**

(Level of consciousness)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**FREQUENCY OF OBSERVATIONS**

(2-4 hourly)

<table>
<thead>
<tr>
<th>FREQUENCY</th>
<th>OBSERVATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DRUGS (include i.v. fluids, glucose, blood)**

<table>
<thead>
<tr>
<th>DRUGS</th>
<th>dose</th>
<th>route</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DATE:**

<table>
<thead>
<tr>
<th>Date:</th>
<th>Time:</th>
<th>Hours since admission:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**TEMPERATURE °C**

(Rectal)

<table>
<thead>
<tr>
<th>Temperature °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>41°</td>
</tr>
<tr>
<td>40°</td>
</tr>
<tr>
<td>39°</td>
</tr>
<tr>
<td>38°</td>
</tr>
<tr>
<td>37°</td>
</tr>
<tr>
<td>36°</td>
</tr>
</tbody>
</table>

**Temperature ± 1°:**

<table>
<thead>
<tr>
<th>Temperature °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>42°</td>
</tr>
<tr>
<td>41°</td>
</tr>
<tr>
<td>40°</td>
</tr>
<tr>
<td>39°</td>
</tr>
</tbody>
</table>

**Infusion fluid:**

specify, and show duration and volume, e.g. 5% dextrose 500 ml

**Urine volume:** (ml)

**Input minus Output:** (± ml)

**Patient's Weight:**

<table>
<thead>
<tr>
<th>Weight</th>
<th>(kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Pulse rate/m**

<table>
<thead>
<tr>
<th>Pulse rate/m</th>
</tr>
</thead>
</table>

**BP mm Hg**

<table>
<thead>
<tr>
<th>BP mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

**Respiratory rate/m**

<table>
<thead>
<tr>
<th>Respiratory rate/m</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

**CVP (if placed) cm water**

<table>
<thead>
<tr>
<th>CVP cm water</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

**Level of consciousness:**

* using ----------- coma scale

**Blood glucose (mmol/l)**

<table>
<thead>
<tr>
<th>Blood glucose (mmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

**Haematocrit (%)**

<table>
<thead>
<tr>
<th>Haematocrit (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

**Parasitaemia (x 10^9 mm^3)**

<table>
<thead>
<tr>
<th>Parasitaemia (x 10^9 mm^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

**Able to drink**

<table>
<thead>
<tr>
<th>Able to drink</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

**Able to sit**

<table>
<thead>
<tr>
<th>Able to sit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

**Convulsion**

<table>
<thead>
<tr>
<th>Convulsion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

**Other observations (specify)**

<table>
<thead>
<tr>
<th>Other observations (specify)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

* Urine's volume hourly if catheterized, otherwise when possible.

** Blood glucose should be measured immediately with any deterioration of consciousness or convulsion, otherwise 2-6 hourly.
The following table indicates some of the important observations during treatment and their implications.

**Table 7**

<table>
<thead>
<tr>
<th>Regular observations</th>
<th>Possible abnormality</th>
<th>Appropriate actions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. Clinical</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breathing</td>
<td>Increased rate or difficulty</td>
<td>Review urine output and fluid balance. Assess lung, heart and liver size. Chest X-ray if available. If pulmonary oedema is demonstrated, or seems likely, treat.</td>
</tr>
<tr>
<td>Rectal temperature</td>
<td>&gt;39°C</td>
<td>Give paracetamol (rectal or oral) if not given within past 4 hours. Tepid sponge and fanning - get relatives to help with this. If temperature remains high or rises despite 24 hours of antimalarial therapy Reconsider your diagnosis, while continuing treatment</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>Falls: &lt;80 mm Hg systolic in an adult, and &lt;50 mm Hg in infants and children</td>
<td>Review fluid balance, urine output, quinine infusion rate and haematocrit. Give plasma or saline infusion if indicated - i.e. if hypovolaemic. Look for haemorrhage. Take blood for bacteriological culture if facilities are available. Give broad spectrum antibiotic (for possible bacteraemia).</td>
</tr>
<tr>
<td>Fluid balance (use input and output chart); weigh patients as accurately as possible. Catheterize if acute renal failure or pulmonary oedema is suspected.</td>
<td>Oliguria: &lt;17 ml/hour in an adult or &lt;0.3 ml/kg/hour in infants and children</td>
<td>Review adequacy of hydration and infusion. Correct deficit if necessary. Prevent or manage acute renal failure if suspected (see pages 37 and 52).</td>
</tr>
<tr>
<td>Coma score</td>
<td>Deterioration</td>
<td>Immediately check blood glucose. Reconsider other diagnosis. Repeat lumbar puncture.</td>
</tr>
<tr>
<td>Convulsions</td>
<td>These can recur, or develop for the first time during treatment and may be due to hyperpyrexia, abnormal blood glucose, or electrolyte imbalance.</td>
<td>Check rectal temperature if &gt;39°C, treat as above. Check blood glucose; check fluid balance; check electrolytes if possible (hyponatraemia). Correct any cause; give anticonvulsant drug.</td>
</tr>
</tbody>
</table>
The diagnosis and management of severe falciparum malaria: Learner's Guide

Prolonged bleeding from venepuncture sites or spontaneous haemorrhage | Disseminated intravascular coagulation (DIC) | Check bleeding time (see text page 34). Crossmatch blood. Give **whole fresh blood** as needed to correct blood loss and bleeding tendency.

### B. Laboratory

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Action/Consideration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood glucose</td>
<td>Falls &lt;2.2 mmol/l</td>
<td>Review infusion; a child will become hypoglycaemic if deprived of glucose for more than 12-24 hours. Give i.v. 50% glucose.</td>
</tr>
<tr>
<td>Haematocrit</td>
<td>Falls &lt;18-20%</td>
<td>Cross-match blood: consider need for transfusion, but give only if clinically indicated, using <strong>packed cells</strong>. Repeat haematocrit at regular intervals.</td>
</tr>
<tr>
<td>Parasitaemia</td>
<td>Remains high for 2-3 days, or remains positive for &gt; 5 days.</td>
<td>Review adequacy of antimalarial drug and dosage. Consider alternative or give an additional drug. Commonly remains at the initial level for 12-24 hours, even if drugs are fully effective; then falls.</td>
</tr>
</tbody>
</table>
Table 8

<table>
<thead>
<tr>
<th>Common errors in the management of severe malaria</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Delay in starting antimalarial therapy</td>
</tr>
<tr>
<td>• Dosage not correctly calculated</td>
</tr>
<tr>
<td>• Inappropriate route or schedule of drug administration, and/or</td>
</tr>
<tr>
<td>• Failure to elicit a history of recent chemotherapy, and/or</td>
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<td>• Unjustified cessation of treatment</td>
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<tr>
<td>• Failure to control the rate of intravenous infusion, and/or</td>
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<td>• Failure to prevent cumulative effect of antimalarial drugs</td>
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<tr>
<td>• Failure to recognize and treat severe anaemia</td>
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<td>• Failure to look for and correct hypoglycaemia</td>
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<tr>
<td>• Failure to recognize and manage pulmonary oedema, aspiration pneumonia, and metabolic acidosis</td>
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<tr>
<td>• Delay in starting peritoneal dialysis or haemodialysis</td>
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<tr>
<td>• Inadequate nursing care</td>
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<tr>
<td>• Error of fluid and electrolyte replacement</td>
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<tr>
<td>• Use of an inappropriate drug (e.g. chloroquine in areas of resistance)</td>
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<tr>
<td>• Unjustified withholding of an antimalarial drug</td>
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<tr>
<td>• Failure to switch patients from parenteral to oral therapy as soon as they can take oral medication</td>
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<tr>
<td>• Unnecessary continuation of chemotherapy beyond the recommended length of treatment</td>
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<tr>
<td>• Unnecessary endotracheal intubation</td>
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<tr>
<td>• Use of potentially dangerous ancillary therapies</td>
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<tr>
<td>• Failure to review antimalarial treatment in a patient whose condition is deteriorating.</td>
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You should read carefully the next Unit of this module before the session to which it relates.
LEARNING UNIT 7

Assessment of recovery

Learning objectives

By the end of this Unit you should be able to:

• assess the extent to which the patient has recovered
• record any residual sequelae
• arrange for follow-up
• write a summary of the events and outcome.

How do you assess the patient’s recovery?

This is an extension of the previous learning unit. Your records and observations will provide some indications of patient recovery - e.g. falling temperature, falling parasite count, and an improving coma score.

In addition, also record the patient’s ability to:

• drink
• eat
• talk
• sit
• stand
• walk

When a patient has recovered, assess for possible sequelae of the disease or the treatment. In particular you should:
Perform a neurological examination

It is assumed that the Glasgow coma scale follow-up is being done.

Especially assess functional capacity in holding and using objects, ability to feed, gait and posture. Try to determine whether the patient can do the things that he or she was able to do before the illness began. For a young child this requires asking parents or guardians about the child's previous activities.

Assess vision and hearing

Use the best available methods. Repeated examination of the fundus oculi may be preferred to assess retinal haemorrhages. You can use simple bedside measures, especially for infants and children (e.g. does the child turn its head towards a noise? does the child watch the mother when she moves?). Use audiometry and vision charts if these are available.

Repeat haematocrit and blood films

Ideally these should be repeated on the 7th and 14th day after recovery and again one month later. Monitor reticulocyte response. Also make sure that on the 7th day the Hb is not continuing to fall. If so there may be another cause of anaemia that needs to be looked for. By day the 14th full recovery should have occurred.

Review and synopsis

When you are discharging the patient, summarize the events of the patient’s illness. Indicate the distinguishing features of the illness and the patient’s responses to treatment. A form to enter this information could be attached to the other record sheets.

You should read carefully the next Unit of this module before the session to which it relates.
Exercises in the diagnosis and management of severe malaria

Learning objectives

By the end of this Unit you should be able to:

• assess the severity of the disease in adults
• assess the severity of the disease in children
• determine what malaria specific treatment to provide by which route and in which doses
• decide which investigations need to be carried out and when
• interpret correctly the results of special investigations
• provide appropriate management of the patient for various complications of severe malaria.
Case study: Patient A

The place: a country where *P. falciparum* malaria is transmitted in forested areas but not in the main cities.

A woman aged 25 years is brought to the outpatient department of the central hospital in the capital. She is a local resident, the wife of a business executive, and is in the seventh month of her first pregnancy.

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

Today she has been referred to your hospital because of restlessness and increasing mental confusion. Examination reveals a semiconscious woman, who is unable to converse. She withdraws her hand from a painful stimulus but cannot localize a stimulus applied to the sternum or forehead. There is no neck stiffness, jaundice, pallor or rash. Axillary temperature is 39°C, pulse 90 beats/min., blood pressure 110/70 mmHg. The uterine fundus is palpable (26-28 weeks), and the foetal heart can be heard.
The diagnosis and management of severe falciparum malaria: Learner’s Guide

Question 1

What tests are urgently required?


Question 2

If the whole-blood glucose is 1.2 mmol/l, what treatment will you give?


Question 3

If the blood film shows *P. falciparum* rings "++++", and the cerebrospinal fluid is normal except for low glucose, then:

(a) what antimalarial drug will you administer and by which route?


(b) would you prefer an alternative to quinine because the patient is pregnant?


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(c) would you give a loading dose of quinine? (Justify your answer).

(d) what nursing procedures are important during this treatment?

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?

Question 5

A chest X-ray gives the picture shown (Fig. 10). What is the diagnosis and treatment?
Question 6

What other observations are particularly important in this patient?

Question 7

What other questions would you ask this patient’s relatives?
Case study: Patient B

The place: a rural clinic in a hyperendemic *P. falciparum* area. 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 (39°C), 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.
The diagnosis and management of severe falciparum malaria: Learner's Guide

Question 1

(a) Does the child have cerebral malaria?

(b) What should you do about the convulsion?

Question 2

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

(a) Should the patient be referred to hospital?

(b) What treatment will you give meanwhile?
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?

Question 4

The child was well and aparasitaemic on the third day, and went on to complete a seven-day course of oral quinine. At the end of that time a further blood test showed gametocytes "+".

What should be done about the gametocytes present in the blood after treatment?
The diagnosis and management of severe falciparum malaria: Learner's Guide
Case study: Patient C

The place: a country where *P. falciparum* is hyperendemic.

The patient, a 28-year-old male economist, was born and brought up locally, but attended university in Northern Europe for five years. 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°C). He was restless but could make brief appropriate answers to questions, and could localize the site of a painful stimulus. He was jaundiced and his mucous membranes were pale. There was some bleeding from the gums, and there were a few retinal haemorrhages in each eye.
Question 1

(a) What is the differential diagnosis?
________________________________________________________________________________
________________________________________________________________________________
________________________________________________________________________________

(b) Was the patient right to think he was immune to malaria? (Justify your answer.)
________________________________________________________________________________
________________________________________________________________________________
________________________________________________________________________________

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?
________________________________________________________________________________
________________________________________________________________________________
________________________________________________________________________________

(b) What other tests would you do to investigate the bleeding tendency?
________________________________________________________________________________
________________________________________________________________________________
________________________________________________________________________________
(c) What treatment is needed for the bleeding?


Question 3

The patient has not passed urine for 24 hours.

What kind of investigations and actions are appropriate?


Question 4

Fifteen ml of dark brown urine was obtained by catheter. The urine 'stix' tests revealed albumin "++", blood "++++", conjugated bilirubin "++", urobilinogen "++". Microscopy of the urine showed no cells and a few casts.

How do you interpret the results of the urine test?


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Question 5

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

How should quinine therapy be given to this patient with acute renal failure?
Case study: Patient D

The place: a country with hyperendemic *P. falciparum* malaria in low-lying areas but no malaria transmission on the high central plateau.

A nineteen-year old woman was brought to a clinic in the malaria-endemic area. The medical officer recorded that the patient gave a history of fever for the past three days with rigors and vomiting. On examination she was febrile (axillary temperature 39°C) and slightly jaundiced. She was fully conscious. Because she had never been out of the country, the doctor considered it unlikely that she was suffering from *P. falciparum* malaria, but nevertheless checked a thin blood film. No malaria parasites were seen on the film so he diagnosed hepatitis and advised rest and a fat-free diet.
Question 1

Do you think the medical officer was right to decide that this patient did not have malaria? (Justify your answer.)

Could the doctor have done better with

(a) the history?

(b) the investigation?

Question 2

Two days later the patient was brought back to the clinic by anxious relatives. She had become drowsy and was not answering questions properly. On examination the patient was afebrile, slightly jaundiced and confused. She could not answer questions but could withdraw her hand from a painful stimulus. The possible diagnoses considered were fulminant hepatitis, sickle cells crisis, relapsing fever and cholecystitis. Malaria was ruled out because she was apyrexial. Treatment was started urgently with tetracycline intravenously and enemas to empty the large bowel. She remained unconscious and her temperature rose to 38°C.; a blood film now revealed scanty *P. falciparum* parasitaemia.
This was considered 'probably incidental' because low-grade parasitaemia was common among young adults in the area, but "to cover malaria", chloroquine was prescribed: 600 mg intravenously, to be followed by 300 mg intravenously every eight hours.

What errors were made:

(a) in clinical judgement?

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

(b) in patient treatment?

________________________________________________________________________

________________________________________________________________________

Question 3

The next day the patient was increasingly febrile and the parasitaemia had increased, so quinine 20 mg base/kg was given to run intravenously over one hour in normal saline, to be repeated 8-hourly. Twenty-four hours later the patient became increasingly breathless. There were no signs in the chest but pneumonia was diagnosed and treated with penicillin. After a further twelve hours the patient was still breathless and suddenly had a convulsion. Her level of consciousness deteriorated and she died ten hours later.

(a) What errors were made in administration of quinine?
(b) What errors were made in diagnosis of clinical complications?
Case study: Patient E

A four-year-old girl is brought to the outpatients department of your hospital by her mother, late in the evening.

The child was well until yesterday morning (36 hours ago), when she began to have fever. Yesterday she took meals but seemed listless; today she has refused food, but has drunk a little. The mother says the child had a "fit" this morning; she regained consciousness immediately. For the past few hours the child has been increasingly drowsy, and for the last hour has been unconscious.

At the examination the child is a well-nourished, unconscious, not dehydrated. The axillary temperature is 40.2°C; pulse 120/beats/min, regular; blood pressure 90/70 mmHg. No neck stiffness. Pupils are equal; a few retinal haemorrhages seen; no papilloedema. Some yellowish sticky fluid is seen filling the left external auditory meatus. Reflexes are symmetrical. No rash.
Question 1

If facilities are limited which laboratory tests are essential for this child as a guide for immediate action?

Question 2

(a) Why does the blood glucose test have the priority in this case?

(b) Should you wait for the result of the blood glucose test if it will take 2 hours?

(c) If not, what should you do?
Question 3

In this child a "stix" test on finger-prick capillary blood revealed a glucose level of 1.0 mmol/l (18 mg dl). 50% dextrose intravaneously was given, but the child remained unconscious.

What does this suggest?

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

Question 4

Figure 11 is the thick and thin blood film from this patient as seen under the high power microscope (magnification x700).

(a) What does the film show?

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

(b) What species of parasite is present?

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

(c) How heavy is the infection?

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________
(d) How could you quantify it more accurately?


Question 5

This child has *P. falciparum* parasitaemia "++++" with hypoglycaemia:

(a) Does this exclude a diagnosis of meningitis?


(b) Is it still necessary to do the lumbar puncture?


(c) Does clear colourless fluid exclude meningitis?


Question 6

In this patient microscopy of the cerebrospinal fluid revealed 3 wbc/mm³ and 7 rbc/mm³ (normal).

(a) Could the ear discharge be important in this patient?

(b) What should be done about it?

Question 7

What is your decision on how to proceed with antimalarial treatment?

(a) Which drug(s)?

(b) By which route?
The diagnosis and management of severe falciparum malaria: Learner's Guide

(c) What is the correct dosage schedule?

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

Question 8

Apart from antimalarial drug(s), is any other drug therapy indicated for this patient?

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

Question 9

How should fluid replacement be given?

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

Question 10

The haematocrit is 19%. What are the implications of the levels of parasitaemia and haematocrit in this patient?

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________
(a) Would you transfuse?

(b) If blood transfusion is or becomes necessary, how would you give the blood?

Question 11

What clinical observations would you make during the course of treatment in this patient?

Question 12

What laboratory tests would you repeat (and when) during treatment?
Question 13

What should be done if the patient fails to pass urine?

Question 14

What should be looked for after the child has recovered?
Figure 11

Appearance of falciparum infection in a Giemsa stain - Thin blood film
Bibliography


Selected further reading


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