Malaria Case Management Training Manual for Health Professionals in Ethiopia

Participants Manual

Federal Democratic Republic of Ethiopia

Ministry of Health

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Foreword

Malaria is a major public health problem in Ethiopia. About 75% of the total area of the country is considered malarious and about 60% of the population living in these areas is at risk of malaria. According to the World Malaria Report of 2015 (WMR 2015), the country reported an estimated 2.1 million malaria cases and 213 deaths in 2013.

The National Malaria Prevention, Control and Elimination Program (NMCP) strategy (NSP 2014-2020) aims to achieve the goals of near zero malaria deaths (no more than 1 confirmed malaria death per 100,000 population at risk); reduction of malaria cases by 75% from baseline of 2013; and elimination of malaria in selected low transmission areas. To achieve the goals and objectives set out, the National Malaria Prevention, Control and Elimination program needs to have appropriately planned and targeted delivery of essential malaria interventions, including: early diagnostic testing of suspected malaria and prompt treatment of confirmed cases with effective artemisinin-based combination therapy (ACT); and application of appropriate vector control interventions, particularly the use of insecticide-treated nets (LLINs) and indoor residual spraying (IRS). To implement these interventions, the availability and readiness of trained and skilled health workforce is critical.

This training manual on malaria case management has been developed to support the staff involved in malaria prevention, control and elimination program in Ethiopia in the effective organization and execution of malaria diagnosis and case management services. The manual incorporates basics on vector control, epidemics detection and response, supply chain management, and monitoring and evaluation. Thus, it is believed this training material is comprehensive as well as timely. Therefore, all partners working in the area are advised to strictly use this manual whenever they organize training for clinicians. This avoids use of different training materials for similar competence and provides basic understanding on malaria prevention, control and elimination interventions.

Lastly, as the country is planning to go for a subnational malaria elimination program, there is a critical need for having well trained health personnel at all levels. Thus, it is my firm belief that our program partners would redouble their efforts in supporting the Ministry in its ambitious goal of ensuring availability of well-trained clinicians who could accurately diagnose and manage malaria cases at all tier of the health system. I can assure that the Ministry would maximize its efforts in the fight against malaria until the disease is wiped out from the country.

Dr. Kebede Worku
State Minister for Health

Abbreviations

Abt/PHSP	Abt Associates Private Health Sector Program
ACIPH	Addis Continental Institute of Public Health
ACT	Artemisinin-based Combination Therapy
API	Annual Parasite Incidence
EPHI	Ethiopian Public Health Institute
FMOH	Federal Ministry of Health
G_6PD	Glucose-6- Phosphate Dehydrogenase
HEW	Health Extension Worker
HMIS	Health Management Information System
HRP-2	Histidine Rich Protein II
IFHP	Integrated Family Health Program
IMNCI	Integrated Management of Newborn and Childhood Illness
IPD	Inpatient Department
IPLS	Integrated Pharmaceuticals Logistics System
IPTp	Intermittent Preventive Treatment in Pregnancy
IRS	Indoor Residual Spraying
LLIN	Long Lasting Insecticide Treated dal Nets
LMIS	Logistics Management Information System
M&E	Monitoring and Evaluation
MACEPA	Malaria Control and Elimination Partnership in Africa
MFTT	Mass Fever Testing and Treatment
MIS	Malaria Indicator Survey
MPFT	Mass Presumptive Fever Treatment
NMCP	National Malaria Control Program
OPD	Outpatient Department
PATH	Program for Appropriate Technology in Health
PCR	Polymerase Chain Reaction
PFSA	Pharmaceuticals Fund and Supply Agency
PHCU	Primary Health Care Unit
PHEM	Public Health Emergency Management
pLDH	Plasmodium Lactate Dehydrogenase
PLMP	Pharmaceuticals Logistics Master Plan

PMI	President’s Malaria Initiative
RBC	Red Blood Cell
RDT	Rapid Diagnostic Test
RRF	Report and Requisition Form
SBCC	Social Behavioral Change Communication
SCM	Supply Chain Management
SOP	Standard Operating Procedure
SPR	Slide positivity rate
TAC	Technical Advisory Committee
TET	Therapeutic Efficacy Testing
TOR	Terms of Reference
TWG	Technical Working Group
UNICEF	United Nations Children’s Fund
USAID	United States Agency for International Development
WBC	White Blood Cell
WHO	World Health Organization

Acknowledgements

This training manual was reviewed and prepared by the Federal Ministry of Health (FMOH) of Ethiopia with participation of numerous in-country partners. FMOH gratefully acknowledges the technical expert group who guided the review and preparation of this training manual. The agencies and partner organizations that have actively and directly participated through their experts who contributed to the review and preparation of this document include: USAID/PMI, WHO, UNICEF, Columbia University-ICAP in Ethiopia, IFHP, Addis Continental Institute of Public Health, Abt Associates, MACEPA/PATH- Ethiopia office, Addis Ababa University, College of Health Sciences, Faculty of Medicine and PFSA.

Most of the contents of this training manual have been adopted from the WHO training manual on malaria control: case management, guide for participants. Also, training materials from the FMOH and partner organizations have been used.

The review and preparation process for this training manual was coordinated by the National Malaria Control Program (NMCP). Dr. Kebede Etana, NMCP/FMOH has played a pivotal role in overall coordination of the process. Financial support for the workshop to develop the training material was provided by Abt Associates/PHSP.

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Methodology

The content of the training manual has been prepared based mainly on *WHO training module on malaria control: case management, guide for participants* and on *WHO's 3rd edition, guidelines for the treatment of malaria, the national malaria guideline* and on other technical documents and existing FMOH training materials. The manual was prepared through a process involving a Technical Expert Committee representing malaria experts from key partners, training and academic institutions, malaria researchers, and FMOH malaria experts.

The need for a simplified and standardized training manual for clinical health workers on malaria case management that would serve for all on-the job training, both for public and private sectors, all over the country was felt during field missions to regions and during observations made in training sessions on malaria case management. In addition to this, there were recommendations from researchers and trainers at various health training institutions on the need to have a standardized training manual. These observations and recommendations were taken up by FMOH that requested the malaria technical advisory committee (TAC) to prepare the manual. The TAC delegated the malaria case management technical working group (TWG) to develop the manual. Accordingly the TWG took the responsibility to review the existing manual and prepare an updated one. The following steps were followed to prepare the guide:

- Several TWG consultations were held at FMOH level
- The initial draft and outline was prepared by FMOH experts
- A 4-day retreat was held from 19 - 22 September 2016 for in-depth technical consultation on the draft document and to review and finalize the initial draft
- Further updated draft circulated to the TWG member for final inputs
- The TWG met again on 3 October 2016 to review the updated draft document for its content and completeness
- The draft document was reviewed and finalized by the TWG and submitted to FMOH for comments /or endorsement.
- It was submitted for Human Resources Directorate of FMOH for approval and registration
- Based on feedback from consultations and FMOH's endorsements, the manual text was finalized for publication.

INTRODUCTION

In 2015, a total of 214 million malaria cases and 438,000 malaria deaths reported globally and 90% of deaths occur in Sub-Saharan Africa and 70% deaths are children under five. The incidence rate of malaria is estimated to have decreased by 37% globally between 2000 and 2015. Malaria death rates have decreased by 60% over the same period (WHO, 2015).

The trends of malaria have showed a consistently decline in Ethiopia. It has successful achieved the Millennium Development Goals. According the FMOH (2015) Health Management Information System (HMIS) report shows the number of reported malaria cases declines form 3.8 to 1.9 million cases in the year 2012 and 2015, respectively.

Cognizant of the importance of prevention, control and elimination of malaria as a major public health interventions and providing standardized quality assured prompt malaria diagnosis and treatment in all health tier system, which a globally recommended best practice. Hence, the FMOH developed three series of national malaria guidelines in 1998, 2004, and 2012.The last malaria guidelines (2015) has additional supplementary revision as of July 2016 based on the third editions of WHO on guidelines for the treatment of malaria (WHO 2015). The main recommendation consists of adding single dose of Premaquine for Pf and mixed malaria infections, increasing the dose of Artesunate for children < 20kg body weight, form 2.4 mg/kg to 3.0 mg/kg; AL is indicated for under five kg infants etc.

The use of updated and standardized malaria guidelines and training materials is strongly recommended in order to ensure the availability of prompt diagnosis and effective treatment at all level of health of services. It also simplifies and facilitates training and supervision of health care providers, delay the development of anti-microbial resistance, improve surveillance, and assists in more rational drug procurement for the treatment of malaria.

To this effect, the Federal Ministry of Health has developed this updated training material for the proper malaria case management in the country.

The contents for each Learning Unit are summarized as follows:

Learning Unit, I: Introduction to epidemiology of malaria in Ethiopia and specific regional state. It deals with the trend of malaria and the eco-epidemiological stratification for Ethiopia. Finally, it introduces the national strategic plan for malaria prevention, control and elimination (2014- 2020).

Learning Unit II: it describes the malaria vector biology, behavior, similarities and differences of adult mosquito and larvae. This learning unit introduce the life cycle of mosquitos and factors affecting the development cycle. Finally, it deals with vector control strategies and their importance.

Learning Unit III: this learning unit deals with the etiologic agents of malaria. It describes the mode of transmission and the life cycle of the parasites. In addition, the clinical and laboratory evidences for uncomplicated malaria, its treatment at different levels of health facilities will be discussed.

Learning Unit IV: This learning unit introduces training participants with the approach in fever among children using assess, classify, identify and treat principles of integrated management of newborn and childhood illnesses (IMNCI). Furthermore, the unit explores the assessment of fever in a child with measles.

Learning Unit V: it deals with the approach to an adult patient with fever and identify possible causes of fever in adults. Trainees are expected to be capable of taking a comprehensive medical history and performing physical examination. In addition, they will also be able to order and interpret laboratory investigations and reach to relevant diagnosis

Learning Unit VI: it covers the definition of severe malaria and explains its pathophysiology. In addition, it identifies factors that expose patients for the development of severe malaria and covers the chemotherapeutic regimens, emergency and supportive measures.

Learning Unit VII: explore the effect of malaria in pregnancy, HIV, malnutrition and tuberculosis. It also deals with the management of uncomplicated and severe malaria in these special groups.

Learning Unit VIII: deals with the different methods of parasitological confirmation of malaria parasites and explain the components of quality assurance. It also explains the advantages and limitations of thin & thick blood films and RDTs.

Learning Unit IX: Covers the national Integrated Pharmaceutical Logistics Management System (IPLS). It introduce with the tools of supply chain management system (bin card, stock cards, RRF, IRRF etc.)

Learning Unit X: Introduce malaria outbreak and epidemics to trainees. It also describes the scientific methods of forecasting, early warning, detection and responses. It demonstrates the filling and interpretation of epidemic monitoring chart

Learning Unit XI: Introduce the national malaria monitoring and evaluation framework. It covers the advantage of gathering health facility data, and demonstrate utilization of information for evidence based decision making.

Learning Unit XII: Participants will visit a health facility to have practical experience on the theoretical explanations. It also gives opportunities for trainees to develop their skill in history taking, physical examination, ordering and interpreting laboratory results, appreciate clinical findings in patients with uncomplicated and severe febrile diseases, malaria logistics management system and malaria Health Management Information System.

The Learning Units

The module is designed for health professionals who diagnose and treat patients with malaria in the course of their work. It can be used alone as a standalone course on case management or as one element of comprehensive malariology course.

The principal objectives of the training are listed in the Introduction to the training manual for participants, which facilitators are asked to read before proceeding. This module is intended to stimulate active learning by working through a series of exercises. The exercises will be carried out on the basis of the training manual for participants, preferably in small groups.

Participants are taught the salient clinical manifestations of malaria. Common errors in malaria case management are highlighted. The participants acquire step by step all the knowledge and skills they need to suspect, diagnose and manage severe malaria. This type of training is performance-based and is highly effective. Each Learning Unit of the training manual for participants begins with a list of learning objectives which summarize the knowledge, skills and attitudes that each trainee should have acquired by the end of the unit.

Facilitators and their colleagues should be satisfied that everyone has achieved the stated objectives before proceeding to the next Learning Unit It is convenient to arrange the work of the participants in small group sessions; some discussion work can be done in plenary sessions.

Core Competencies for trainees

After completing this course the following core competencies are expected to attain by all trainees:

- Identify the larvae and adult forms of anopheles mosquito
- Perform a comprehensive clinical evaluation that is history taking, and performing physical examination order and interpret laboratory tests for patients with fever
- Assess, classify and select appropriate treatment for a child with fever using the IMNCI approach.
- Diagnose, treat and conduct follow up care for uncomplicated malaria cases as per the national malaria guideline.
- Identify cases with treatment failure and provide the appropriate management.
- Diagnose, treat and conduct follow up for patients with severe and complicated malaria cases as per the national guidelines
- Identify patients who need urgent referral and give the appropriate pre referral treatment.
- Diagnose and treat malaria in special groups like patients with HIV, malnutrition and pregnancy
- Request and report malaria commodities and maintain adequate stock status
- Fill and interpret malaria epidemic monitoring chart
- Record and report timely all malaria cases using HMIS and PHEM requirements.
- Use data for informed decision making.

Course syllabus for five days basic malaria case management training for health professionals

Course goal

To equip health professionals with the basic knowledge, skills, attitudes and practices needed to manage malaria cases in line with the national recommendations.

Course objectives:

- Describe global and national burden of malaria
- Identify principles of approach to fever in children and adult patients
- Able to take a comprehensive history, perform physical examination, order and interpret laboratory tests.
- Describe the basis of malaria diagnosis and treatment according to the national guideline

- Identify larva and adult forms of anopheles mosquito
- Explain malaria microscopy and rapid diagnostic test.
- Explain malaria commodities supply chain system
- Able to fill and interpret malaria epidemic monitoring chart
- Able to record and report malaria data

Training/Learning Methods

Different method will be used to deliver this training:

- Presentation and discussion
- Group Exercises./work
- Case studies
- Demonstration
- Video show
- Practical attachment

Learning equipment

- Participant manual
- LCD projector
- Computer (Laptop)
- Screen for slide projection (a white sheet is an adequate substitute)
- Colored markers
- PowerPoint Presentation (LCD & Laptop)
- Flip chart/white board
- Video shows
- Malaria Rapid Diagnostic Test kits (RDTs kits)
- Check lists for the practical clinical session
- Sheets of paper for the exercises during the working groups
- IMNCI recording forms
- Malaria Epidemic monitoring chart
- IPLS tools (bin Card, Stock Card, RRF and IRRF)
- Notebook
- Ballpoint pens

Trainers' Qualification and requirement

Trainers should be clinical certified with Malaria Case Management TOT (with the current Malaria Case Management manual for Health Professionals)

Target audience

The trainees should be practicing clinicians (physicians, health officers or nurses) or those involved in teaching clinical students

Evaluation of training

Evaluation of the training is achieved by collecting feedback from learners and trainers at the end of each day of the training and at the end of the course. When trainers review feedbacks from learners daily, they can often make immediate changes to improve the course. Daily evaluation and end of course evaluation forms are included in this manual. Pretest questionnaires are included in this trainers guide to assess participants' knowledge and experience before the training so as to reorient the course content and approach after reviewing the test results. Moreover, the pretest results will be used to assess the knowledge and competence gained after the training by comparing against the post test results.

Criteria for certificate

- 100% of attendance
- Post test score greater than 70% for basic training and 80% for TOT.

Adaptation of course content

This training manual is prepared for a standalone, learner centered course for a group of 25-30 trainees. Adaptation may be needed to address learners' need, the number of learners attending and the time or logistical constraints.

Table.1 Malaria Case Management Training Schedule.

Day	Time	Topic
1	8:30-9:00	Registration
	9:00-10:30	Opening remark Introduction to the training Objectives and expected outcomes Introduction of facilitators and participants Setting ground rules Expectations of participants Admin issues Pretest
	10:30-11:00	Tea break
	11:00-12:30	Malaria program overview
	12:30-2:00	Lunch
	2:00-3:30	Malaria vector control
	3:00-4:00	Uncomplicated malaria
	4:00-4:30	Tea break
	4:30-5:30	Uncomplicated malaria
2	8:30-9:00	Recap
	9:00-10:00	Approach to fever in children (1)
	10:00-10:30	Tea break
	10:30-12:30	Approach to fever in children including exercises (2)
	12:30-2:00	Lunch
	2:00-3:30	Approach to fever in adults (1)
	3:30-4:00	Tea break
	4:00-5:30	Exercises on approach to fever in adults (2)
3	8:30-9:00	Recap
	9:00-10:00	Severe malaria (1)
	10:00-10:30	Tea break
	10:30-11:30	Severe malaria (2)
	11:30-12:30	Severe malaria exercises (1)
	12:30-2:00	Lunch

Day	Time	Topic
	2:00-3:00	Severe malaria exercises (2)
	3:00-4:00	Malaria in special groups
	4:00-4:30	Tea break
	4:30-5:30	Malaria laboratory diagnosis (1)
4	8:30-9:00	Recap
	9:00-10:00	Malaria laboratory diagnosis (2)
	10:00-10:30	Tea break
	10:30-12:30	Malaria epidemic including exercise on EMC
	12:30-2:00	Lunch
	2:00-3:30	Supply chain management including introducing IPLS tools
	4:00-4:30	Tea break
	4:30-5:30	Malaria monitoring and evaluation including introducing M&E tools
5	8:30-12:30	Health facility visit • OPD (fever in children and adults) • IPD (severe febrile disease preferably severe malaria) • Recording and reporting • Supply chain management (malaria commodities)
	12:30-2:00	Lunch
	2:00-4:00	Feedback from health facility visit
	4:00-4:30	Tea break
	4:30-5:30	• Post test • Course evaluation • Closing

LEARNING UNIT ONE
Malaria Program Overview

Learning objectives
At the end of this training, participants will be able to:

- Describe the epidemiology of malaria in Ethiopia
- Describe the malaria trend in Ethiopia
- Describe the eco-epidemiological strata of malaria in Ethiopia

Epidemiology of Malaria in Ethiopia
In 2015, a total of 214 million malaria cases and 438,000 malaria deaths reported globally and 90% of deaths occur in Sub-Saharan Africa and 70% deaths are children under five. The incidence rate of malaria is estimated to have decreased by 37% globally between 2000 and 2015. Malaria death rates have decreased by 60% over the same period (WHO, 2015).

Malaria is a leading health problem in Ethiopia. Three quarters (75%) of the country's landmass is malarious and about 60% of the total population is at risk of malaria infection. Malaria transmission in Ethiopia mainly occurs up to the 2000 meter (m) elevation but can also occasionally affect areas up to 2300m elevation. The levels of malaria risk and transmission intensity within these geographical ranges, however, show marked seasonal, inter-annual and spatial variability because of large differences in climate (temperature, rainfall and relative humidity), topography (altitude, surface hydrology, land vegetation cover and land use, etc.) and human settlement and population movement patterns.

Classification of malaria transmission (stable and unstable)

Stable (endemic): Transmission is generally high, could be seasonal but not subject to annual fluctuations, and the resulting population immunity is high. Under endemic conditions, children under the age of five years, and pregnant mothers, are most likely to be infected as they have weaker immunity.

Unstable (epidemic): Malaria transmission is variable, being subject to marked annual fluctuations. Consequently, the collective population immunity is low. Malaria epidemics generally occur when the population in an area has weak immunity to the disease, because so many people in the population

will be vulnerable to malaria. However, it is important to remember that children and pregnant women are always at most risk, so they need particular attention.

- ***Trend of malaria in Ethiopia***

The annual number of malaria cases varies from year to year. The 2015 HMIS report indicated that total malaria cases reported across all health facilities was 1.9 million cases with over 95% completeness report. There has been a consistent decline in the number of malaria cases in the past four years despite an alarming increase in health facilities with increased access to diagnosis and case management (Figure below). On the other hand, there has also been a dramatic reduction in number of cases, admissions and deaths in some facilities (ii).

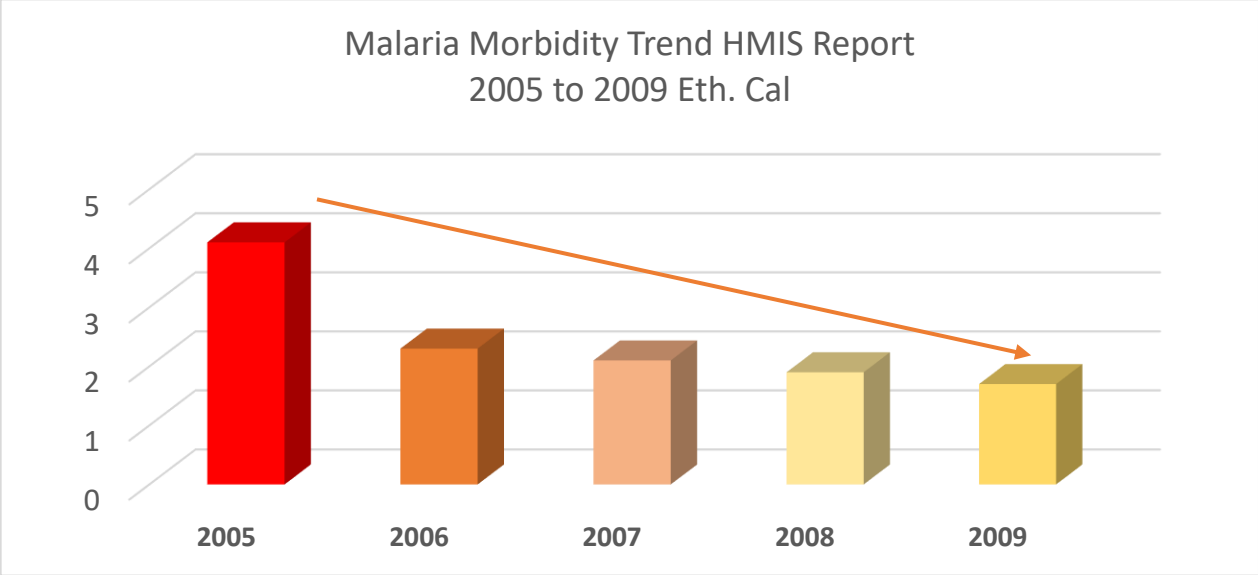


Figure 1 Annual Malaria Morbidity in millions, HMIS 2005-2009)

A survey conducted by FMOH and WHO in 39 hospitals, located below 2000-meter altitude, showed significant reduction in malaria cases, admission and deaths. The proportion of population potentially protected by an ITN increased to 62% in 2011. The proportion of facilities with ACT in-stock remained >87% during 2006–2011. In all ages, confirmed malaria cases in 2011 declined by 66%; and slide positivity rate (SPR) by 37%. In children under 5, malaria admissions and deaths fell by 81% and 73% respectively. Monthly trends of malaria indicators were lower and less variable during the post-intervention. During the same time, non-malaria cases and deaths either increased or remained unchanged while rainfall remained at levels supportive of malaria transmission. The survey indicates that malaria cases and deaths in Ethiopian hospitals decreased substantially during 2006–2011 following the scale-up of malaria interventions.

Since 2004, there was no large scale epidemic reported in Ethiopia which has been coinciding with the scaling up of major malaria interventions such as vector control and diagnosis and treatment.

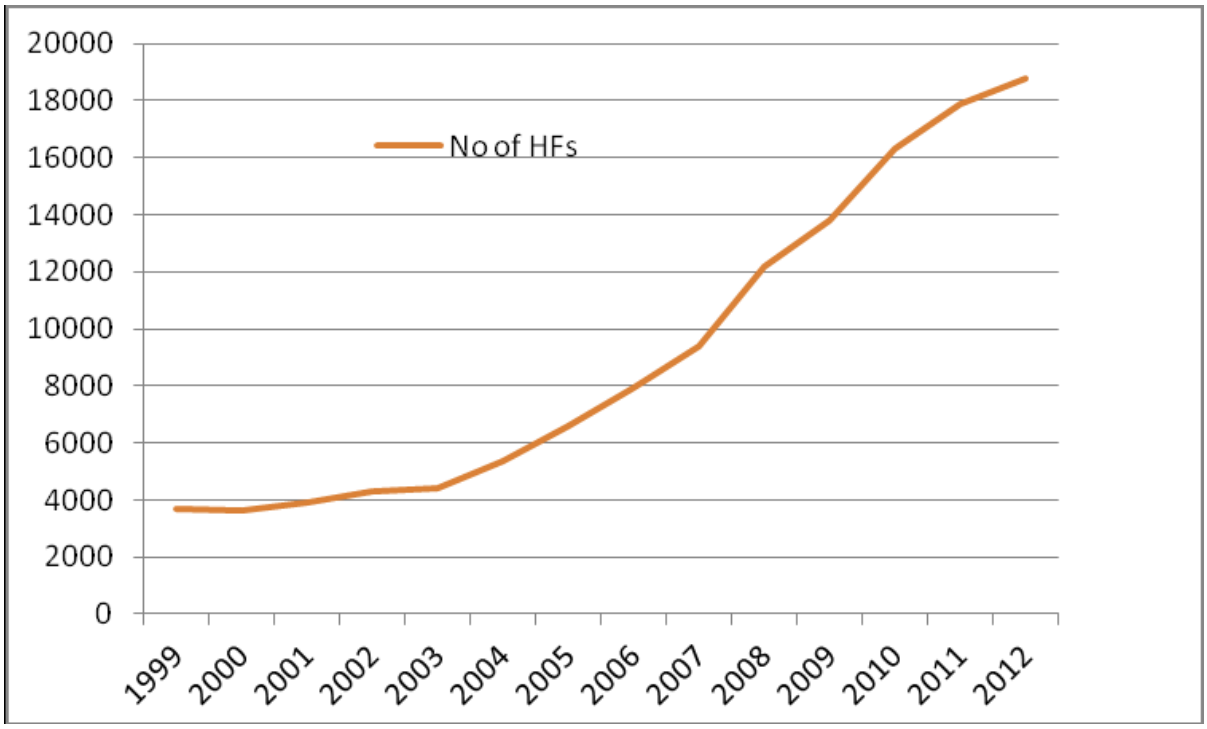
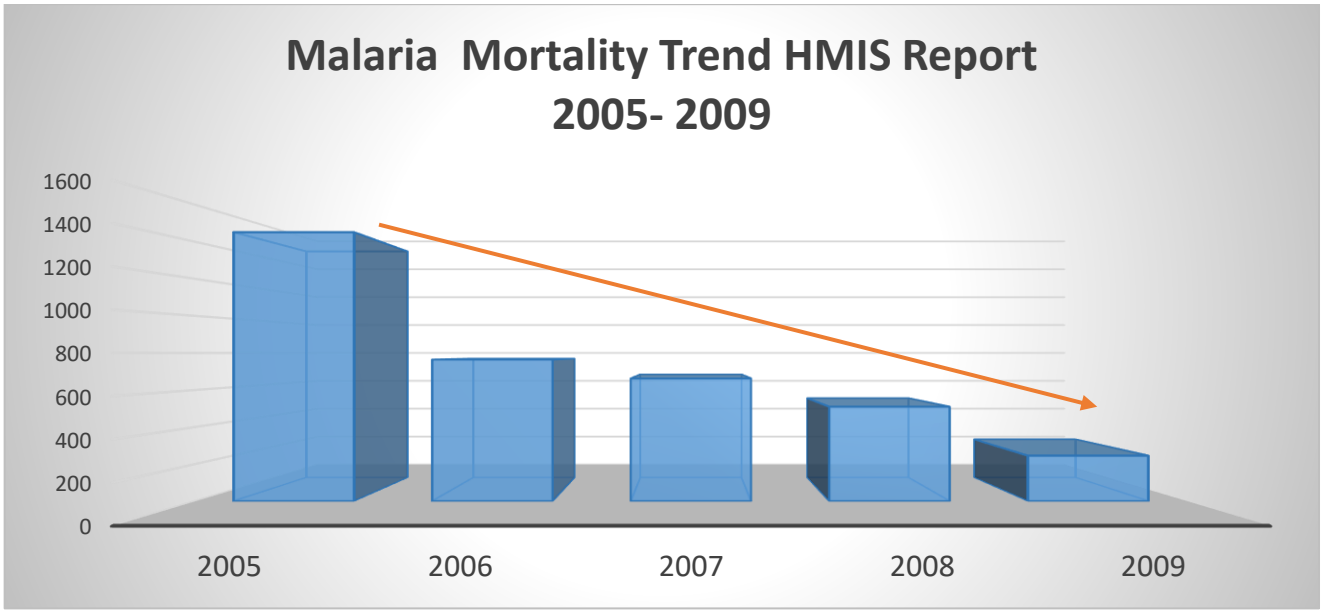


Figure 2 Number of Health Facilities



Malaria Morbidity Trend , five Years

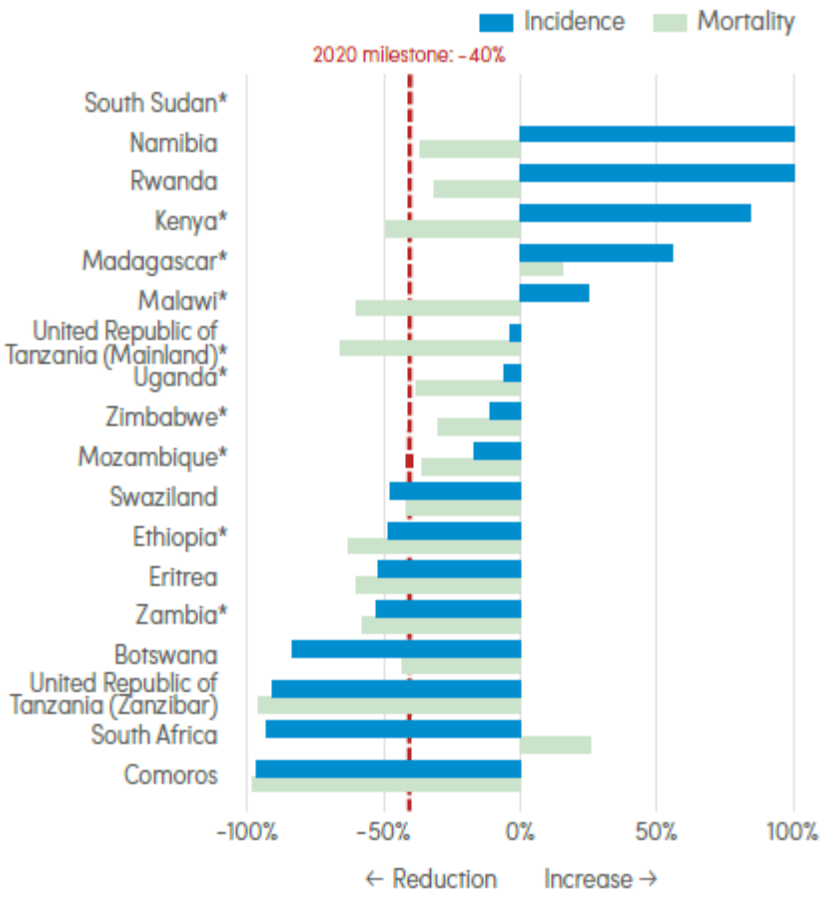


Figure 3: Reduction of malaria cases and deaths in Ethiopia (WHO 2016)

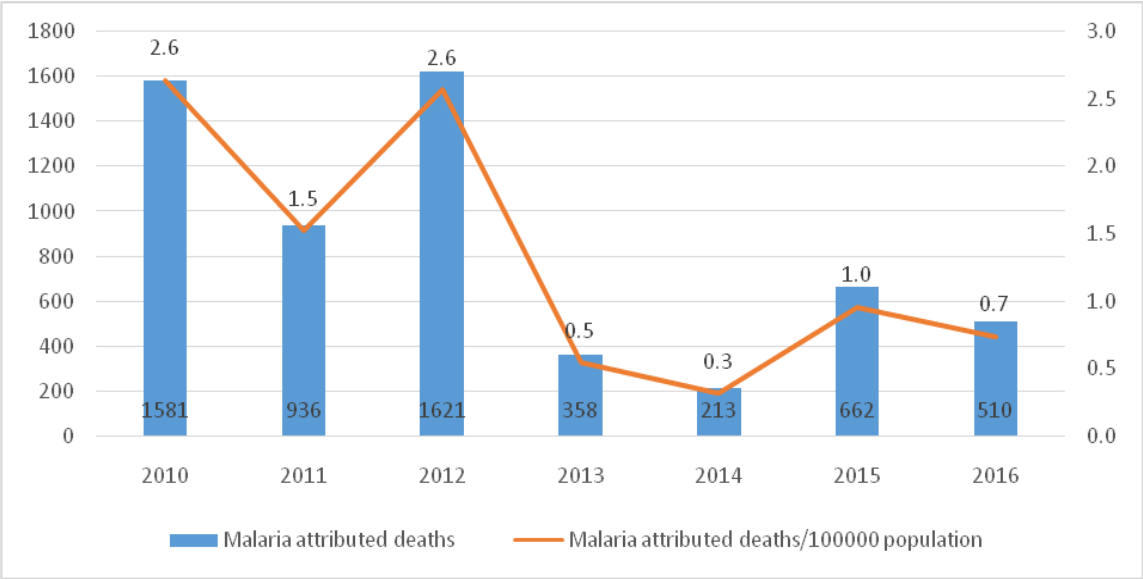


Figure 4: Malaria deaths in Ethiopia (WHO 2016)

Factors affecting malaria transmission

Altitude and climate (rainfall, temperature and relative humidity) are the most important determinants of malaria transmission in the country. Transmission is seasonal and largely unstable in character. The major transmission of malaria follows the June – September rains and occurs between September - December while the minor transmission season occurs between April – May following the February – March rains. Areas with bimodal pattern of transmission are limited and restricted to a few areas that receive the small/Belg rains.

Age and immunity are host factors affecting risk of morbidity. Individuals who are exposed to repeated malaria infection, over a period of several years, become semi-immune. This means that although they are still at risk of infection when bitten by an infected mosquito, they either do not have symptoms (are asymptomatic), or their symptoms are not severe. This kind of partial immunity is not common in Ethiopia because of the unstable nature of the disease. Partial immunity will be lost with few years' absence from malaria endemic area

Historically, the unstable nature of malaria transmission has been characterized by frequent focal and cyclical epidemics which reach national scale at irregular intervals of 5–8 years.

The malaria parasites and vectors

Plasmodium falciparum and *P. vivax* are the two most dominant malaria parasites in Ethiopia. They are prevalent in all malaria endemic areas in the country with *P. falciparum* representing about 66% (HMIS 2015) of the total reported malaria cases. Relative frequency varies in time and space within a given geographical range. *P. malariae* and *P. ovale* are rare and account for <1% of all confirmed malaria cases. The major malaria vector incriminated in Ethiopia is *Anopheles arabiensis;* in some areas *A. pharoensis*, *A. funestus* and *A. nili* also play minor role in transmission of malaria.

Eco-epidemiologic strata

The current malaria National Strategic Plan (NSP 2017–2020) has stratified the country's malaria situation on the basis of annual parasite incidence [API] per 1000 population based on data from HMIS and complemented by PHEM data. API-based classification was supported by information on altitude—which is a proxy measure of temperature and rainfall—and experts' opinion (local knowledge). Accordingly, four broad strata have been identified. They are: malaria-free, low-, moderate-, and high-transmission strata (Table 1).

Table 2: Malaria strata with target antimalarial interventions, February 2017

Malaria Strata	API	Elevation (m)	Population (2016)	% Population	No. of Woreda	% Woreda	Interventions					
							LLIN	IRS	Larval Control	Case Mx	Surveillance	IEC/ BCC
FREE	0	>= 2000 asl	37,083,083	40.3%	280	33.1%	-	-	-	X	X	X
LOW	>0 & <5	< 2000 asl	17,115,269	18.6%	146	17.3%	X	X*	WA	X	X	X
MODERATE	>=5 & <100		34,782,644	37.8%	365	43.2%	X	X**	WA	X	X	X
HIGH	>=100		3036,,580	3.3%	54	6,4%	X	X	WA	X	X	X
Total			**92,017,576**	**100%**	**845**	**100%**						

*Only 32% of at risk population in highland fringe/epidemic-prone areas will be covered by IRS
**Only 14.8% of at risk population from moderate stratum will be covered by IRS
WA: where applicable; asl: above sea level

Based on the most latest epidemiological data of Table 1, the country's malaria stratification map has been updated (see Figure 2).

Districts/*woredas* below 5 cases per 1000 people per year are designated as low-transmission and are primarily targeted for pre-elimination and elimination. For the expansion of malaria-free areas starting with the low transmission stratum, malaria elimination will be driven by epidemiological stratification aimed at regular identification of districts that are eligible to embark on elimination. Given that the impact of the control programme is ongoing, the number of districts leaving moderate stratum to low and high to moderate will keep increasing. Thus, based on regular epidemiological stratification, districts will be regularly included and transitioned into the elimination phase.

National Malaria Control Strategies

Ethiopia adopted the global malaria strategies, which was developed in 1992. The core strategies include diagnosis and prompt treatment; selective vector control; epidemic prevention and control. Cognizant of the importance of community empowerment and active participation, the Ethiopian government has given due attention to behavioral change communication. Hence, IEC/BCC is considered as one of the priority interventions for malaria control.

Since 2005, a massive scale-up of anti-malaria interventions put in place which resulted in a sharp decline in reported malaria cases. The national malaria control program in collaboration with programme partners develops national malaria strategy every five years to sustain the gains achieved and incorporate new tools and strategies as deemed necessary. Accordingly, the 2014-2020 National Strategic Plan was developed in 2014. Thus, the 2014-2020 National Strategic Plan will build on the achievements of the previous strategies and, through sustaining control interventions, will move

towards malaria pre-elimination/elimination. The goals and specific strategic intervention are summarized as follows.

The goals of the national strategic plan are:

- By 2020, to achieve *near zero malaria deaths* (no more than 1 confirmed malaria death per 100,000 population at risk) in Ethiopia.
- By 2020, to reduce malaria cases by 75% from baseline of 2013.
- By 2020, to eliminate malaria in selected low transmission areas.

The priority interventions that will be targeted in the NSP are summarized as follows:

Community empowerment and mobilization

- Carry out targeted advocacy, communication and social mobilization activities.
- Empower and mobilize communities in order to own anti-malaria interventions and actively participate in planning and implementation of interventions in their respective areas.
- Build capacity on advocacy, communication and social mobilization.
- Conduct assessment to identify gaps in knowledge, attitude and practices in relation to anti-malaria interventions. This will be incorporated with malaria indicator survey.

Diagnosis and treatment

- Diagnose all suspected malaria cases;
- Sustain universal coverage of effective and efficacious treatment as per the national guidelines;
- Establish quality assurance system for malaria diagnosis.
- Monitor efficacy of anti-malaria drugs.
- Support malaria related integrated community case management activities

Prevention/vector control

- Achieve universal coverage, sustain; and improve utilization of long lasting insecticidal nets.
- Build capacity on planning, implementation and monitoring of indoor residual spraying.
- Monitor susceptibility of insecticides and distribution and behavior of vectors.
- Monitor durability and longevity of long lasting insecticidal nets in the field setting.

Elimination of malaria

- Improve immediate notification, case and foci investigation and classification.

- Reduce number of active foci and locally acquired cases to zero, and halt and sustain zero local transmission in selected areas;

Surveillance, monitoring and evaluation

- Strengthen capacity of surveillance, and M&E activities; and undertake routine and periodic data collection and analysis.
- Ensure timeliness, completeness and quality of data.
- Generate strategic information to update malaria epidemiological profile and facilitate appropriate decision making.

In addition to the above mentioned strategic areas much emphasis will be given to improvement of the overall malaria programme management and pharmaceuticals supply chain management.

As discussed above, diagnosis and case management being one of the core interventions, the following sections mainly deliberate on it.

LEARNING UNIT TWO
Malaria Vector Control

Learning objectives
At the end of the training, participants will be able to:

- Describe the malaria vector biology, behavior, and differentiate the different mosquito types and their larvae,
- Describe the life cycle of mosquitoes and factors that affecting the life cycle,
- Describe the types of vector control strategies,
- Describe the importance of implementing vector control strategies for malaria control.

Malaria Vectors' Biology and Behavior
Anopheline mosquitoes are responsible for transmitting malaria. Anophines comprise approximately 490 species including sibling species, of which only about 60-70 species worldwide can transmit malaria and of these, about 30 are vectors of major importance. With the exception of the Antarctica, there are malaria vectors in all continents of the world. The mosquito picks up the *Plasmodium* parasite when it sucks the blood of an infected person. Once inside the mosquito, the parasite multiplies as it moves from the stomach of the mosquito to the salivary glands, from where it is passed on the next time the infected mosquito bites another person.

Malaria vector biology

Vector is a carrier, especially animal (usually an arthropod) which transfers an infective agent from one host to another. There are two types of vector: biological and mechanical.

Biological vector: an arthropod vector in whose body the infecting organism develops or multiplies before becoming infective to the recipient individual.

Mechanical vector: an arthropod vector which transmits an infective organism from one host to another but which is not essential to the life cycle of the parasite.

Anopheles Mosquito Life Cycle

The life cycle of the *Anopheles* mosquito has four main stages: egg, larva, pupa and adult. Water is necessary for the egg, larval and pupal stages of the life-cycle. Understanding the life cycle, the timings and the factors influencing the life cycle is important to fully understand the epidemiology of malaria transmission and for considerations about disease control.

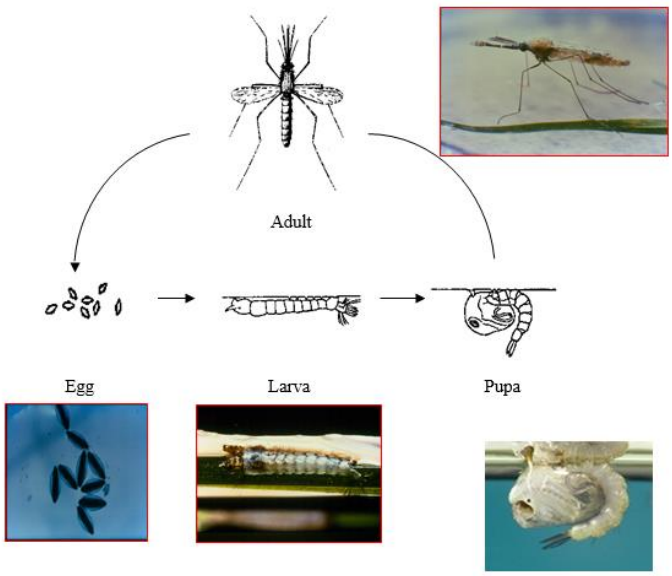


Figure 5: The life cycle of the Anopheles mosquito

Eggs:

- Each adult female will lay between 70 – 200 eggs per oviposition.
- Eggs are laid singly on water, they are about 0.5mm long and have floats on each side.
- Unlike Aedes eggs, Anopheles eggs are not resistant to drying.
- The female will lay a batch of eggs every 2-3 days.

Larvae:

- An active stage that feeds and grows rapidly moving through four instars (different sizes of larvae).
- Larvae feed on nutrients in the water using the brushes around their well-developed mouth to move the nutrients into their mouth.
- Larvae must breathe oxygen. Unlike Culicine larvae, Anopheline larvae do not have a siphon to breathe through, instead they breathe through small spiracles on the surface of their abdomen. This means that larvae must lie parallel to the water surface to keep the spiracles in contact with the air above.
- Larvae can descend into the water when startled and then return to the surface when they need oxygen.
- After the 4th instar has been reached the next phase of development is metamorphosis into a pupa.

- Larvae can dry out and must be in pools of water with some nutrients to survive.
- Anopheline larvae most times prefer clean water in temporary habitats such as pools, puddles, hoof prints, borrow pits, and rice fields.
- Anopheles mosquitoes rest parallel to the surface of the water, whereas the latter two species larvae rest at an angle to the surface.

Pupae:

- An inactive stage. The mosquito develops inside the pupa into an adult, no feeding takes place during this stage.
- Pupae are small and comma shaped and can move up and down through the water, descending from the water surface to avoid perceived threats, such as if a shadow falls over the water surface.
- The pupa also requires oxygen, they breathe whilst at the water surface through a pair of respiratory trumpets.
- After a few days as a pupa splits and an adult mosquito emerges.

Adults:

- The same or the following evening after emergence the female mosquitoes will mate with a male mosquito. She will usually mate only once in her life and stores the sperm in her body to be used for each batch of eggs she lays.
- Anopheline and culicine mosquitoes both have piercing and biting mouth parts. Male mosquitoes only feed on water and nectar; female mosquitoes also feed on water and nectar for energy but also use these mouth parts to feed on blood.
- Blood meals are taken every 2-3 days, the female rests after the blood meal to digest it and use the protein from the blood meal to develop her eggs. Mosquitoes will lay a batch of eggs every 2-3 days.

The most feasible ways of telling the difference in the field for adult mosquitoes are:

- **Resting position of the adult**: angled in Anopheles, flat – with the proboscis and body at angles to one another in Culex and Aedes.
- **Palps of the adult:** long in Anopheles female, short in Culex and Aedes females; long with swollen ends (club shaped) in anopheles male, along with non-swollen ends (tapered) in Culex and Aedes male.

Table 3 Distinguishing Anopheline and Culicine Mosquitoes

	Anophelines	**Culicines**
Eggs	Float separately and have "floaters"	Clump together in a raft (Culex) or float separately (Aedes)
Larvae	No siphon	Has siphon
	Rests parallel to water surface	Hangs down from the water surface
Pupae	Trumpet is short and has wide opening	Trumpet is long and slender with a narrow opening
Female Adults	Palps as long as proboscis	Palps very much shorter than proboscis
Male Adults	Palps as long as proboscis, club-shaped at tips	Palps longer than proboscis, with tapered tips

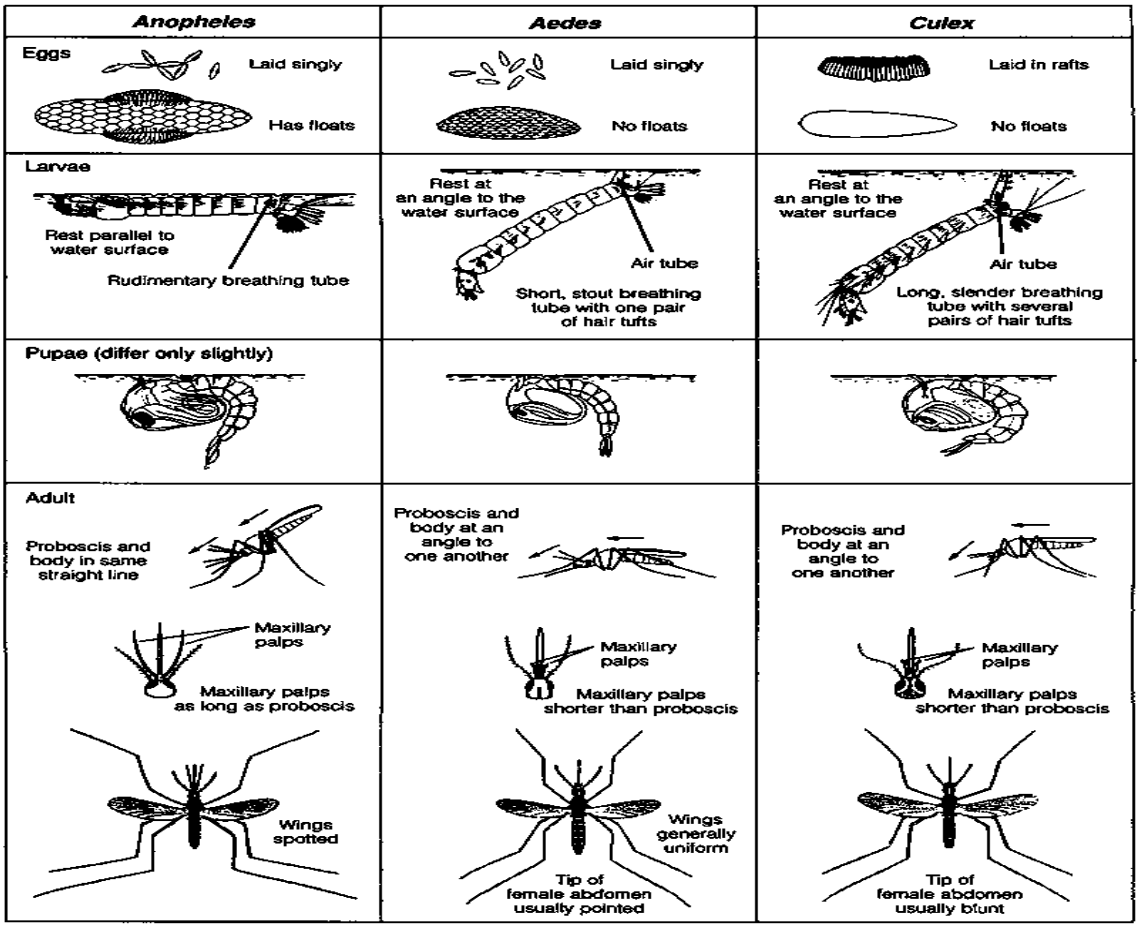


Figure 6: Differentiation of Anopheles, Aedes and Culex mosquitoes at various stages of development.

Factors affecting the life cycle

Water, temperature and humidity are the main environmental factors affecting the life cycle. At each stage different conditions are required for the mosquito to survive, and a range of suitable conditions can result in big differences in the timing of the life cycle.

Water

- Different mosquito species require different types of water in which to lay their eggs,
    - some preferring more shaded sites, other sunnier sites;
    - some preferring deeper more permanent water bodies, others shallower temporary water bodies;
- Anopheles species can only survive in fairly clean water (unlike some culicines which can breed in water rich with organic pollutants such as pit latrines).

Temperature

- Temperature affects whether the mosquitoes can survive at all as well as the timing of the life cycle
- Above 35°C the adult mosquito will die much sooner
- Temperature affects the length of time each life stage takes
    - whilst eggs may hatch 2-3 days in ideal conditions, they may take as long as several weeks at the lower temperature limits
    - larvae can progress through their four instars in about seven days at 31°C but this can take up to 20 days at 20°C.

Humidity

- Below 50% humidity the adult mosquito will die much sooner
- Ideal humidity is around 65% - 75%

Malaria Vector Behavior

There are a few specific behaviors that vary between mosquito species and these can have an important impact on levels of transmission.

Host preference

Female anopheles mosquitoes must all take a blood meal to be able to develop eggs, however the source of that blood can vary considerably. Mosquito's species that are important human malaria vectors must feed sometimes on humans, otherwise they would not be important in transmission of the disease. *An. Gambiae* species complex is an extremely efficient malaria vector that is responsible for much of the heavy malaria burden in Africa south of the Sahara. This species complex includes the most important vectors in Africa and consists of seven species. Each of these subspecies has different habitats, the most important two are *Anopheles gambiae* and *Anopheles arabiensis*. Members of the *Anopheles gambiae* complex feed almost exclusively on humans. Likewise, *An. funestus* which is found in Ethiopia also feeds mostly on humans.

In Ethiopia the main malaria vector is *An. arabiensis* which feeds both on humans and cattle. It is important to know about the vector species feeding preferences for control measures. In countries where *An. gambiae* and *An. funestus* are the main vectors, IRS would focus on spraying human dwellings only as this will ensure almost all mosquitoes trying to take a blood meal rest on the insecticide-treated surface. Where vectors such as *An. arabiensis* are important an effective IRS

strategy will need to spray both human dwellings and animal sheds, to ensure that even those mosquitoes taking a blood meal on the animals are likely to rest on the insecticide-treated surface. This is important for the overall effectiveness of the control strategy.

Biting times

Whilst some mosquitoes, e.g. *Aedes* the dengue vector, bite in the daytime, *Anopheles* mosquitoes bite in the evening and night time. Some species bite in the early evening and some late at night. The biting time is important in that it can impact on how effective some different control measures may be. For example sleeping under insecticide-treated nets (ITNs) will be particularly effective if the malaria vectors feed only later at night when most people are asleep.

Indoor or outdoor biting

Different mosquitoes prefer to take their blood meals in different locations. Some prefer to find their hosts outdoors, others come inside to find the blood meal. The terms for this are:

- Endophagic – feeds indoors
- Exophagic – feeds outdoors

In Ethiopia the main vector, *An. arabiensis* likes to both indoors and outdoors, whilst *An. funestus*, feeds mostly indoors.

Resting location

After a mosquito has taken a blood meal it must rest somewhere to digest the blood and produce eggs. Some mosquitoes prefer to rest indoors and some prefer to rest outdoors. The terms for this are:

- Endophilic – rests indoors
- Exophilic – rests outdoors

In Ethiopia the main vector, *An. arabiensis* rests both indoors and outdoors, whilst *An. funestus*, rests mostly indoors. It is important to understand that *resting* preference is not necessarily linked to feeding preference, for example some mosquitoe species that prefer to feed outdoors may come indoors to rest and digest the meal. Knowing about resting behaviour is very important for the selection of control measure. IRS where the mosquito must rest on the walls where the insecticide has been sprayed in order for the strategy to work.

Flight range

Most *Anopheles* mosquitoes can fly up to 2-3 km from their larval habitat. However, where food sources and breeding sites are readily available mosquitoes may actually move very little from where they have emerged as adults. In some urban areas where this is the case, this can result in some very focal areas of transmission. Occasionally mosquitoes travel much further than 2-3 km, but this dispersal is usually wind assisted – or relies on transport in vehicles. Understanding dispersal patterns can be important for planning environmental control measures where the breeding sites are targeted.

Malaria Vector Control Methods

The role of vector control is to augment the impact of early diagnosis and prompt treatment of malaria cases and to reduce levels of transmission, thus reducing malaria morbidity and mortality.

Vector control should be implemented to prevent epidemics; to reduce malaria incidence where urgent malaria problems exist such as situations where previously malaria-free individuals, populations or communities are at high malaria risk; and to curtail the spread of malaria in areas where the parasite is resistance to anti-malarial drugs

Interventions using vector control methods are related to three major control measures

- Larval control
    - Environmental management or source reduction: This includes habitat modification or habitat manipulation.
    - Larviciding

      Temephos (Abate) 50% EC Chemical: The application of the anti-larval chemical, temephos, must be carried out on larvae positive sites through the guidance of health extension workers, or other members of the community in areas where breeding sites are easily identifiable. Abate use is highly useful in areas of development activities such as water harvesting ponds, dams, irrigation canals, road construction and other land development activities. Considering the high cost of temephos, the need for spray equipment and human resources, it should be applied only for small breeding sites.

      Biological control: Biological control is the introduction of natural enemies into larval habitats, including predatory fish, predatory invertebrates and parasites or other disease-causing organisms. While there are a large variety of available biological control agents, only larvivorous fish have been widely used.

- Reducing man-vector contact
  - Long lasting insecticidal nets (LLINs)
  - Improved housing
  - Repellents
- Adult mosquito control: LLINs and IRS
  - LLINs: LLINs have the following main functions:
  - when mosquitoes are in contact with the net, it has a knock down as well as mass killing effect
  - It has a repellent effect
  - It reduces man-vector contact as a physical barrier.
  - LLIN has also an effect on other pests such as, head lice, ticks, housefly, bedbug and cockroaches.

Most *Anopheles* species bite late in the evening or during the night. Sleeping under LLINs provides a physical barrier against mosquitoes. Not only does a LLIN offer personal protection, because of the repellent effects it can also offer protection to others sleeping in the same room, even if they are not under LLINs.

National policy is to provide all malaria affected households with an average of 2 LLINs per household. All *Kebeles* identified as malaria affected, including epidemic affected *Kebeles* will be targeted.

The aim of LLIN distribution is to cover all sleeping spaces in households in malaria-endemic areas so that universal coverage can be ensured. The number of LLINs provided to each household will be equal to the number of sleeping spaces. This ensures the distribution of LLINs to achieve universal coverage of a population living in malaria-endemic areas.

Table 4 General guide to determine the number of nets per household based on family size

Family size	Number of LLINs to be supplied
1 to 2	1
3 to 5	2
6 to 7	3
More than or equal to 8	4

Considering field visits and experiences of the wear and tear, the average life span of an LLIN and duration of replacement in our country is 3 years.

- **IRS:** IRS is the application of long-acting chemical insecticides (insecticides with a residual effect) on the walls and roofs of all houses and domestic animal shelters in a given area, in order to kill the adult vector mosquitoes that land and rest on these surfaces.

The primary effects of IRS towards curtailing malaria transmission are:

- to reduce the life span of vector mosquitoes so that they can no longer transmit malaria parasites from one person to another, and
- To reduce the density of the vector mosquitoes. IRS does not directly prevent people from being bitten by mosquitoes. Rather, it usually kills mosquitoes after they have fed, if they come to rest on the sprayed surface. IRS thus prevents transmission of infection to other persons in contrast with ITNs which provide personal protection.

Some insecticides also repel mosquitoes and by so doing reduce the number of mosquitoes entering the sprayed room, and thus human-vector contact. To be effective as a community control measure IRS requires coverage of at least 85% of houses so that the majority of mosquitoes are exposed to the insecticide. This must be achieved before the expected peak transmission season. Delayed IRS is a waste of resources and may have little impact on malaria transmission or on a malaria epidemic.

It is to be noted that the main malaria vector control activities implemented in the country are LLINs and IRS but as a supplementary strategy environmental management is considered when it is feasible. Accordingly, Ethiopia will maintain universal coverage of LLINs targeting all malarious localities (lying below the altitude of 2000 m). IRS is targeted in epidemic-prone areas.

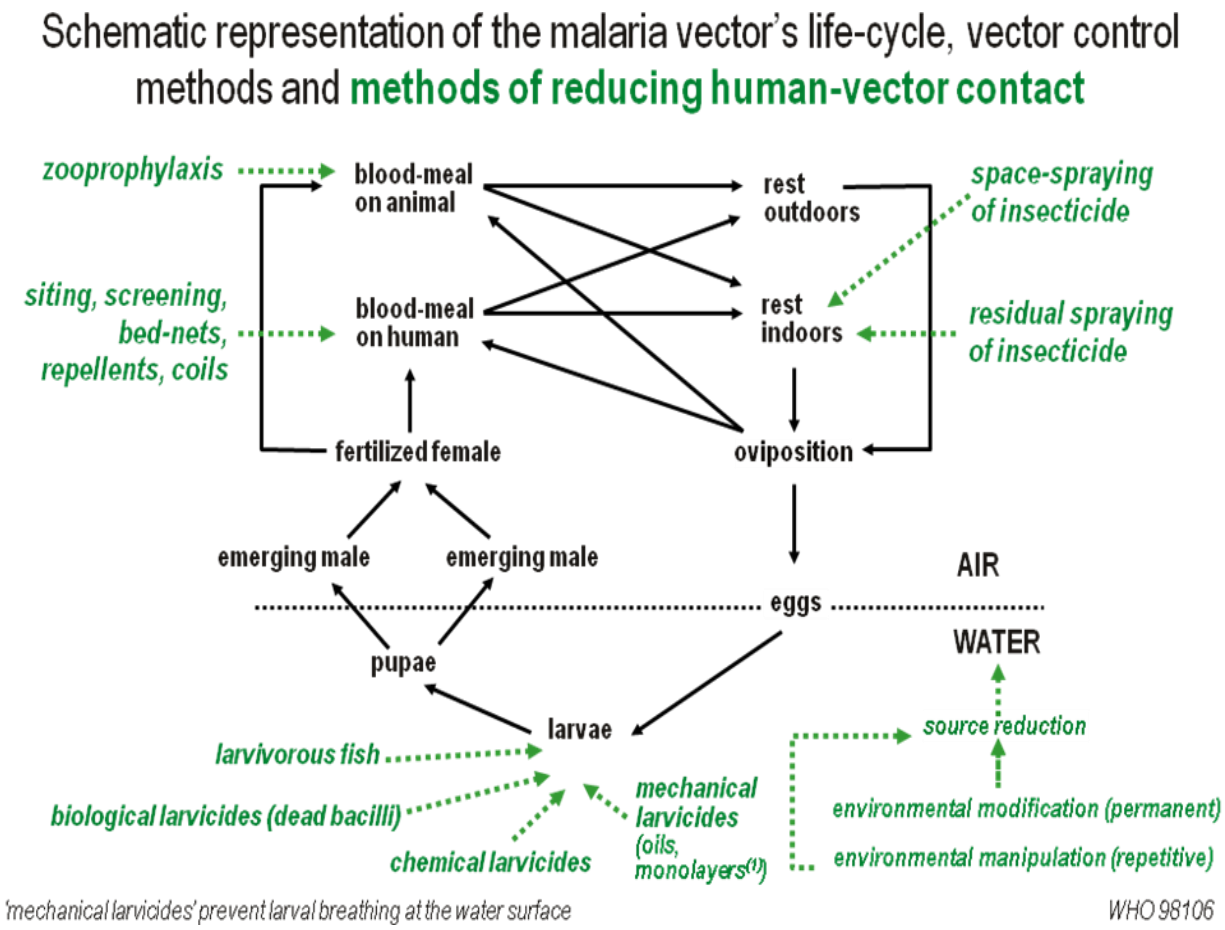


Figure 7: Schematic representation of malaria vector lifecycle and vector control methods

LEARNING UNIT FIVE

Uncomplicated Malaria

Learning Objectives

At end of this training, participants will be able to:

- Identify the etiologic agents of malaria
- Describe modes of transmission and life cycle of malaria parasites
- Explain clinical presentation of non-complicated malaria
- Diagnose and treat non complicated malaria
- Manage malaria at different levels of the health facility in Ethiopia

Definition and Etiologic Agents

Malaria is a parasitic infectious disease caused by protozoan parasites of the genus *Plasmodium* and is transmitted by mosquitoes. It is characterized by recurrent symptoms of chills, fever and generalized body pain.

The five *Plasmodium* species of human malaria are: *P. falciparum, P. vivax, P. ovale, P. malariae* and *P. knowlesi*.

Plasmodium falciparum and vivax are the two most common etiologies in Ethiopia

▸ ***Plasmodium falciparum*** is found worldwide, mainly in tropical and subtropical areas. It is the main species that causes severe, potentially fatal malaria.

▸ ***Plasmodium vivax*** is found mainly in Asia, Latin America, and in some parts of Africa (e.g. Ethiopia and Madagascar). Recent evidence shows that *P. vivax* can cause severe illness. *P. vivax* and *P. ovale*) have dormant liver stages, the hypnozoites, which can become activated and invade the blood to cause clinical relapse several months or years after the infecting mosquito bite. *P.vivax* does not infect individuals who are negative for the Duffy blood group, as are many residents of sub-Saharan Africa.

▸ ***Plasmodium ovale*** is found mostly in the countries of west Africa and the islands of the western Pacific. It is biologically and morphologically very similar to *P. vivax*. It is rarely reported in Ethiopia.

▸***Plasmodium malariae*** is found worldwide. *P. malariae* causes a persistant chronic infection which may be lifelong. A small number of patients develop serious complications such as the nephrotic syndrome.

▸***Plasmodium knowlesi*** is found in Malaysia, Thailand and other South East Asian countries. It is mainly transmitted in forests and along forest fringes. Under the microscope, it is indistinguishable from *P. malariae*. It can cause severe disease and death in some individuals.

Biological and clinical characteristics of different malaria species

The parasite incubation period, known as the intrinsic incubation period, differs for each parasite species. The incubation period of *P. falciparum* is 9–14 days, *P. vivax* 12–17 days, *P. ovale* 16–18 days and *P. malariae* 18–37 days. The erythrocytic cycle, which is responsible for clinical paroxysms, takes about 48 hours in *P. falciparum, P. vivax,* and *P. ovale* infections (tertian cycle), but lasts about 72 hours with *P. malariae* infection (quartan cycle).

The malaria parasite species also differ in the number of merozoites they produce in the exoerythrocytic and erythrocytic phases and the type of the red blood cells they invade. *P. falciparum* produces the greatest number of merozoites in both phases followed by *P. vivax. P. falciparum,* which is responsible for the severe forms of malaria, infects red blood cells of all ages, unlike *P. malariae* which infects older red blood cells, and *P. vivax* and *P. ovale* which infect young red cells.

Mode of transmission and life cycle of parasites

There are three modes of malaria transmission:

- the bite of an infected female anopheline mosquito (the main method of transmission);
- accidental transmission via blood transfusion or needle stick injury; and
- Congenital transmission from mother to child during pregnancy or parturition.

Malaria transmission by mosquitoes

The parasite incubation period in the vector mosquito, known as extrinsic incubation, is temperature-dependent. *P. falciparum* takes 8–11 days to complete the mosquito phase at an optimal ambient temperature of 28°C and 22 days at 20°C. The temperature of the mosquito gut equals that of its surroundings; a low environmental temperature therefore results in a longer development time for the parasite in the mosquito. *P. falciparum* is unable to develop below 19 °C while *P. vivax* can develop in the mosquito at temperatures as low as 16°C; consequently *P. vivax* transmission is found in some areas where the average temperature is too low for *P. falciparum* transmission. Due to this difference in temperature sensitivity, *P. falciparum* is common in tropical regions while *P. vivax* prevails in both tropical and temperate cold regions

Other modes of transmission

Transmission via blood transfusion, accidental needle stick, or needle sharing, leads to transfer of asexual stages of the parasite. The incubation period of the disease is therefore much shorter than it is after transmission of sporozoites by mosquito bite. Transfusion of blood infected with *P. vivax* and *P. ovale* parasites does not lead to clinical relapse because pre-erythrocytic schizogony does not occur and hence the dormant hepatic forms are not produced.

Transmission of malaria across the placenta from mother to fetus is diagnosed when parasitaemia is found in the neonate within seven days of birth, or later if there has not been any other possibility of transmission to the neonate (by blood or mosquito bite). Despite the high prevalence of placental infection, congenital transmission of malaria is rare.

Life Cycle of Malaria Parasite

Humans acquire malaria from sporozoites transmitted by the bite of an infected female anopheline mosquito. The sporozoites then travel through the bloodstream to the liver within about 30 minutes, where they invade hepatocytes and mature to become tissue schizonts (pre-erythrocytic schizogony). Tissue schizonts are a central feature of all plasmodium species that infect humans. They amplify the infection by producing large numbers of merozoites (10 000 – 30 000) from each sporozoite-infected hepatocyte.

Each merozoite released from the liver is capable of infecting a human red blood cell (RBC) and establishing the asexual cycle of replication in the red blood cells. The asexual cycle starts with

merozoite invasion and continues to schizont rupture (merozoite → ring stage → mature trophozoite → schizont → merozoites), leading to invasion of more red blood cells. Some intraerythrocytic parasites develop into the sexual forms, the gametocytes, which are necessary for the sexual reproductive cycle that takes place in the vectors.

When potent gametocytes are ingested by a female anopheline mosquito during a blood meal, micro- and macrogametocytes mature to become male and female gametes. Fertilization of the female gametes produces diploid zygotes which mature to become ookinetes. Ookinetes then undergo a meiotic reduction division to produce haploid sporozoites, which migrate to the salivary glands of the mosquito and subsequently reinfect humans. In the *P. vivax* and *P. ovale* life cycles, some sporozoites can lie dormant in the liver cells for months or years after the initial bloodstream infection and do not cause symptoms during this time. The dormant forms, called hypnozoites, eventually mature to become tissue schizonts which release infectious merozoites, resulting in a clinical relapse.

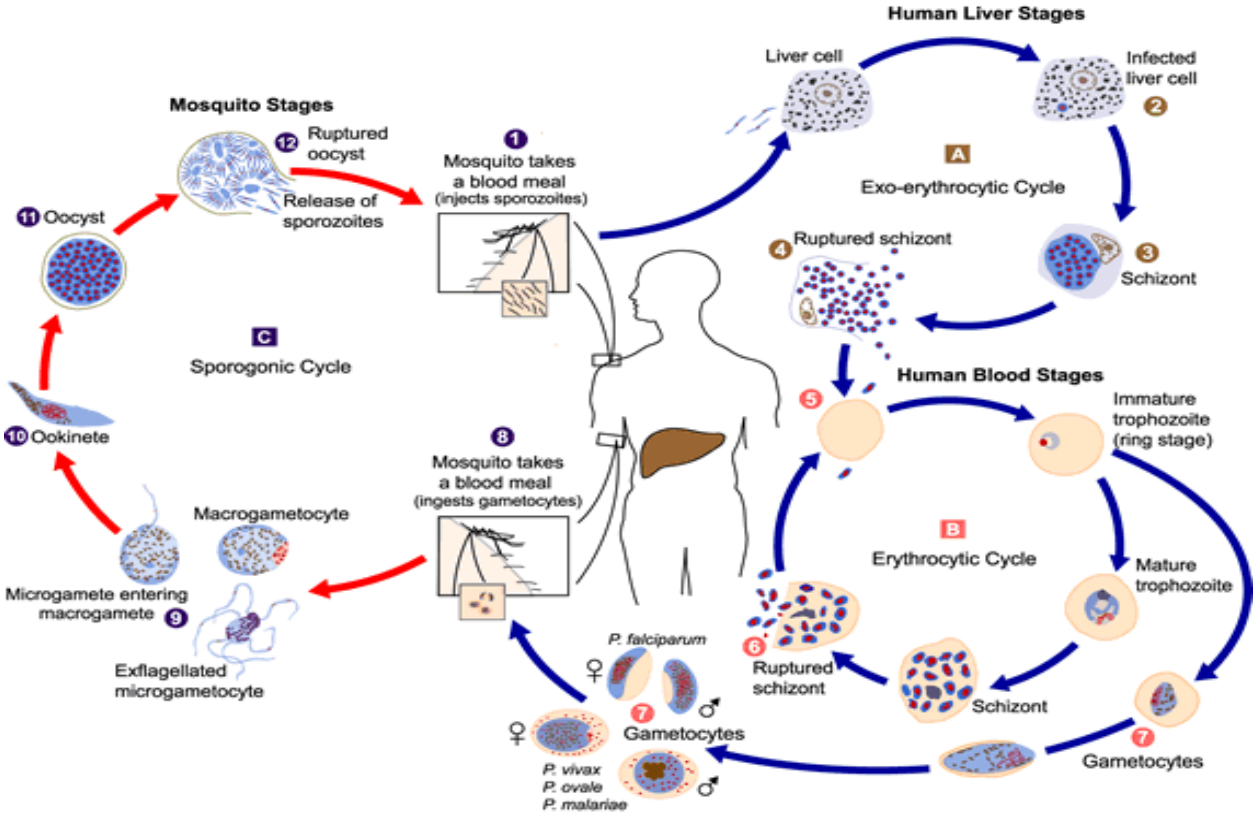


Figure 8: Life cycle of malaria parasite

Clinical presentation and Diagnosis

Non-complicated malaria is symptomatic malaria with parasitaemia without signs of severity or evidence of vital organ dysfunction. The main manifestation of uncomplicated malaria is fever. Other symptoms are chills, rigors, headaches, and body pains, malaise, nausea, vomiting, and joint weakness. Physical examination may reveal pallor and hepatosplenomegaly.

Malaria diagnosis is made by

- Proper history taking
- Physical examination and
- Laboratory method (parasitologic diagnosis)

Clinical diagnosis

A clinical diagnosis entails making a clinical assessment by taking an accurate history of the illness and performing a physical examination. Clinical diagnosis of malaria is made in a patient who has fever or history of fever in the last 48 hours and lives in malaria-endemic areas or has a history of travel within the last 30 days to malaria-endemic areas.

Basing the diagnosis on clinical features alone is not recommended, as this often has low specificity and increases the chances of the patient being misdiagnosed. Malaria treatment based on clinical diagnosis must be the last option when there is no availability of RDTs or microscopy. The health worker examining a suspected malaria case should look for other causes of fever (e.g. pneumonia, pyelonephritis, meningitis, tonsillitis, typhoid fever, relapsing fever, visceral leishmaniasis) and manage the case accordingly. Malaria should still be considered, even if the individual has another obvious cause for the fever. The national algorithm of the Integrated Management of Neonatal and Childhood Illness (IMNCI) and integrated Community-based Case Management (iCCM) should also be employed for the management of the sick child presenting with fever.

Parasitological diagnosis

Parasitological diagnosis is required for confirmation of the diagnosis of malaria. It is recommended for all suspected malaria cases in all transmission settings. The advantages of parasitological diagnosis are:

- improved care of parasite-positive patients owing to greater certainty that the cause of the present illness is malaria;
- identification of parasite-negative patients for whom another diagnosis must be sought;

- prevention of unnecessary use of antimalarials, thereby reducing the risk of adverse side effects and drug interactions;
- confirmation of treatment failures; and
- Improved malaria case detection and reporting.

N.B. Patients who test negative by malaria RDT or microscopy do not need anti-malarial medications.

The two main methods in routine use for parasitological confirmation of malaria are light microscopy and rapid diagnostic tests (RDTs). For the management of a new fever episode, quality-assured microscopy and RDTs are equivalent in terms of performance for the diagnosis of uncomplicated malaria. In addition, molecular diagnosis (e.g. polymerase chain reaction / PCR) is usually applied in research settings, and in surveillance in areas where elimination of malaria is in progress. Serological tests for malaria have no place in the management of febrile patients.

Treatment at Different Levels of Health Facility

Health post level: diagnosis of malaria is based on rapid diagnostic test result. Health extension workers may treat using clinical criteria only if RDT is not available

First line of treatment of uncomplicated malaria

***P. falciparum* positive by multi–species RDT:** Artemether-Lumefantrine (AL) plus single dose primaquine (0.25mg/kg) is the recommended first-line drug for the treatment of uncomplicated *P. falciparum* malaria. AL tablets are given according to body weight in six doses over three days as indicated in the table below

Table 5Tablet containing 20 mg artemether plus 120 mg lumefantrine in a fixed dose.

Weight (KG)	Age	Day 1		Day 2		Day 3		Color code
		Immediate	After 8hrs	Morning	Evening	Morning	Evening	
<5kg	< 4 months	1Tablet	1Tablet	1Tablet	1Tablet	1Tablet	1Tablet	Yellow*
5-14 kg	4mns-2 years	1Tablet	1Tablet	1Tablet	1Tablet	1Tablet	1Tablet	
15-24 kg	3 to 7 years	2 Tablets	2 Tablets	2 Tablets	2 Tablets	2 Tablets	2 Tablets	Blue*
25-34 kg	8 to 10 years	3 Tablets	3 Tablets	3 Tablets	3 Tablets	3 Tablets	3 Tablets	Brown
>35	=>10 years	4 Tablets	4 Tablets	4 Tablets	4 Tablets	4 Tablets	4 Tablets	Green

*Yellow and blue flavored pediatric dispersible tablets of AL is available for enhancing its use in young children.

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.

Contraindications:

- AL should not be used as malaria prophylaxis either alone or in combination;
- Persons with a previous history of reaction after using the drug;
- Pregnant women in the first trimester;
- Persons with severe and complicated malaria should not be treated with oral medications.

Note: AL has a shelf life of only two years. The drug should be stored at temperatures of below 30^{o}C and should not be removed from the blister if it is not going to be used immediately.

The first dose should be given under direct supervision of the health worker to make sure that the patient can take the medicine without any problem. AL should preferably be taken with food or fluids. A fatty meal or milk improves absorption of the drug.

If vomiting occurs within half an hour of the patient swallowing the drug, the dose should be repeated and the health worker/pharmacist should provide the patient with a replacement dose to ensure completion of treatment.

AL is available in co-formulated tablets containing artemether 20 mg and lumefantrine 120 mg per tablet. The dose ranges from 1-4 tablets (depending on the patient's body weight) taken every 12 hours for 3 days.

***P. vivax*, and malaria species positive other than *P. falciparum* by RDT:** The first line drug of choice is chloroquine at a total dose of 25 mg base/kg.

Tablets of chloroquine 150 mg base or syrup 50 mg base per 5 ml (Note, one 250 mg chloroquine phosphate salt tablet contains 150 mg chloroquine base). Never take more than four 250 mg chloroquine phosphate tablets in one day.

Table 6 Chloroquine dose

Weight (kg)	Age	Day 1	Day 2	Day 3
5 – 6	< 4 months	½ tablet *OR* 5 ml syrup	¼ tablet *OR* 5 ml syrup	¼ tablet *OR* 2.5 ml syrup
7 – 10	4 – 11 months	½ tablet *OR* 7.5 ml syrup	½ tablet *OR* 7.5 ml syrup	½ tablet *OR* 5 ml syrup
11 – 14	1 – 2 years	1 tablet *OR* 12.5 ml syrup	0.5 tablet *OR* 12.5 ml syrup	0.5 tablet *OR* 7.5 ml syrup
15 – 18	3 – 4 years	1 tablet *OR* 15 ml syrup	1 tablet *OR* 15 ml syrup	1 tablet *OR* 15 ml syrup
19 – 24	5 – 7 years	1 ½ tablets *OR* 20 ml syrup	1 ½ tablets *OR* 20 ml syrup	1 tablet *OR* 15 ml syrup
25-35	8-11 years	2 ½ tablets	2 tablets	1 tablet
36-50	12-14 years	3 tablets	2 tablets	2 tablets
51+	15 years + adult	4 tablets	4 tablets	2 tablets

Side effects:

Dizziness, skeletal muscle weakness, mild gastrointestinal disturbances (nausea, vomiting, abdominal discomfort and diarrhea) and pruritus. Pruritus may be severe but usually passes within 48-72 hours.

Contraindications:

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

In malaria elimination targeted districts, primaquine will be given for radical cure with close clinical follow up at a dose of 0.25mg/kg orally for 14 days.

Table 7 PRIMAQUINE TREATMENT SCHEDULE

Primaquine phosphate dose:

1. **For radical cure, 0.25 mg base/ kg daily for 14 days**
2. **For reducing transmission of *P. falciparum*, 0.25 mg base/ kg single dose**

Age/Month	Wt/kg	Dose (tab of 7.5 mg)
7 months - 2 years	6 to 10 kg	1/4 tab
3 to 5 years	11-15 kg	1/2 tabs
6 to 10 years	16-24 kg	3/4 tab (1 tab is tolerable)
11 – 13	25 – 50 kg	1 1/2 tab
14+	50+ kg	2 tabs

NOTE: if the tablet is 15 mg the dose should be reduced by half (1/2) of the 7.5 mg tab.

Contraindications:

- Pregnancy
- In breast feeding mothers less than six months infants
- Infants under six months
- Any condition that predisposes to granulocytopenia, such as active rheumatoid arthritis & systemic lupus erythematosus.

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.

It can induce hemolysis especially in G6PD deficient patients

Multi-species RDT is positive for P. *falciparum or* mixed infection: The recommended first-line treatment for mixed infection is AL. and single dose of primaquine.

Note: *do not treat a patient with confirmed mixed infection with both AL and chloroquine.*

Multi-species RDT negative for malaria: If the result of the multi-species RDT is negative for all malaria species, malaria is unlikely. Other causes of fever should be investigated. Treat or refer to health center or hospital as per the CCM algorithm.

No parasitological test available: Where multi-species RDT is not available, and the patient fulfills clinical criteria of malaria, AL should be given.

Supportive treatment

If patients, especially children are present with axillary temperature ≥37.5^{o}C, treat with antipyretics and, if necessary, fanning and tepid sponging. Paracetamol (acetaminophen) 15 mg/kg every 4 hours is widely used; it is safe and well-tolerated, given orally or as a suppository. Pain should be treated and the patient should be encouraged to take food and fluids.

Patient advice

Health workers should clearly explain malaria diagnosis and treatment, e.g. making patients understanding drug labels and instructions. SBCC messages should include the following:

- Malaria is a killer disease if treatment is not sought early and treatment is taken properly.
- Whenever a family member has a fever, take them to the nearest health facility, immediately or at least within 24 hours.
- Do not interrupt taking medication. Take all (full course) of the anti-malarial drugs, prescribed by health personnel.
- Do not share drugs with others, including family members.
- Come back to the health facility after three days if no improvement in symptoms after malaria treatment or any time if there is worsening of symptoms.
- All family members, especially women and children should sleep under LLINs every night.

Referral

It is important that all patients be assessed for the presence of danger signs (see **Box 3**). If a patient presents at a health post with danger signs or is found to have any of the following danger signs, they require **URGENT** medical attention and should be referred to a higher-level facility as soon as possible.

Box Danger signs of severe malaria

- Altered consciousness (e.g. sleepiness, confusion, drowsiness, coma)
- Prostration, i.e. generalized weakness so that the patient is unable to walk or sit up without assistance
- Unable to eat or drink
- Repeated vomiting, resulting in inability to retain oral medication, inability to eat or drink
- Severe dehydration
- Convulsion or recent history of convulsions
- Difficult breathing
- Jaundice (yellowish discoloration of the eyes)
- Anemia (paleness of palms is most reliable symptom in children)
- Hemoglobinuria (cola colored urine)
- Abnormal spontaneous bleeding
- No urine output in the last 24 hours

Any patient presenting with any of the above-mentioned danger signs, **regardless of whether the RDT result is negative or positive**, should be referred to the next higher-level health facility as soon as possible. However, if patients are children <6 years of age, they should be given pre-referral treatment

REMEMBER: A delay in referral could cause the unnecessary death of the patient.

20.1. Pre-referral treatment at the health post level

The conscious patient: At the health post level, treat children under six years of age with a single dose of rectal artesunate (10mg/bw) and refer immediately to an appropriate facility for further care. Do not use rectal artesunate in older children and adults.

Patients older than six years should be referred immediately to higher health facility for further investigation and management.

- If high fever is present, give paracetamol (**Annex N**);
- Encourage fluid intake during the transfer; continue breastfeeding in young infants;
- Ensure that the referral form is completed with detailed information including:
    - Clinical presentation/patient's medical history;
    - Suspected diagnosis;
    - Any tests performed and results (i.e. RDTs);
    - List of all drugs/medication given, route, dose and time of administration;
    - Reason for transfer.

The unconscious patient: The unconscious patient requires special attention prior to transfer:

- Ensure the airway is not blocked
- Show family members how to position the patient on side (**Figure 9**) to ensure a clear airway is maintained;
- Give rectal artesunate as a pre-referral treatment for children under six years of age.
- Do tepid sponging and give paracetamol suppositories for high fever if possible. This will prevent vomiting and convulsions;
- Nurse the unconscious patient on alternate sides to protect the airway, prevent aspiration and avoid pressure sores.

Rectal artesunate treatment for emergency pre-referral therapy for severe malaria dosed at 10mg/kg body weight

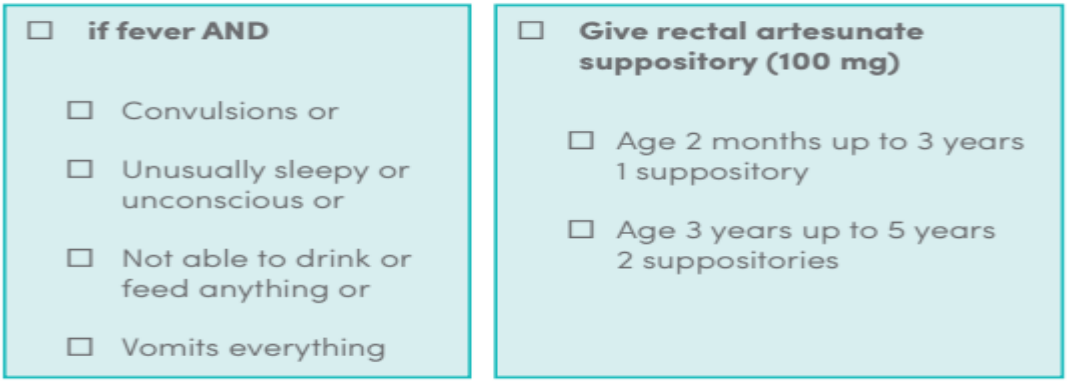
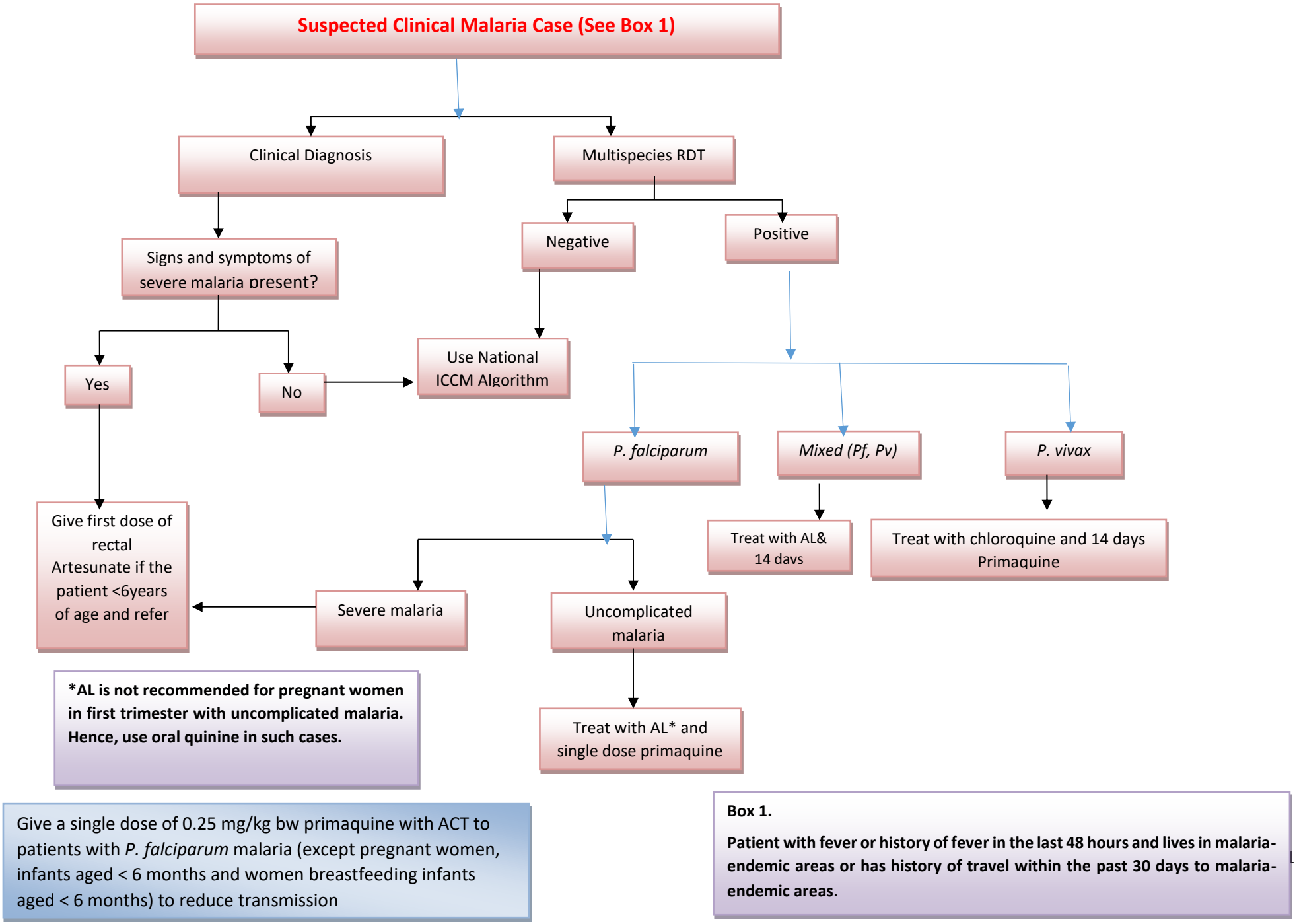


Figure 2. Diagnosis and treatment of malaria at Health post level

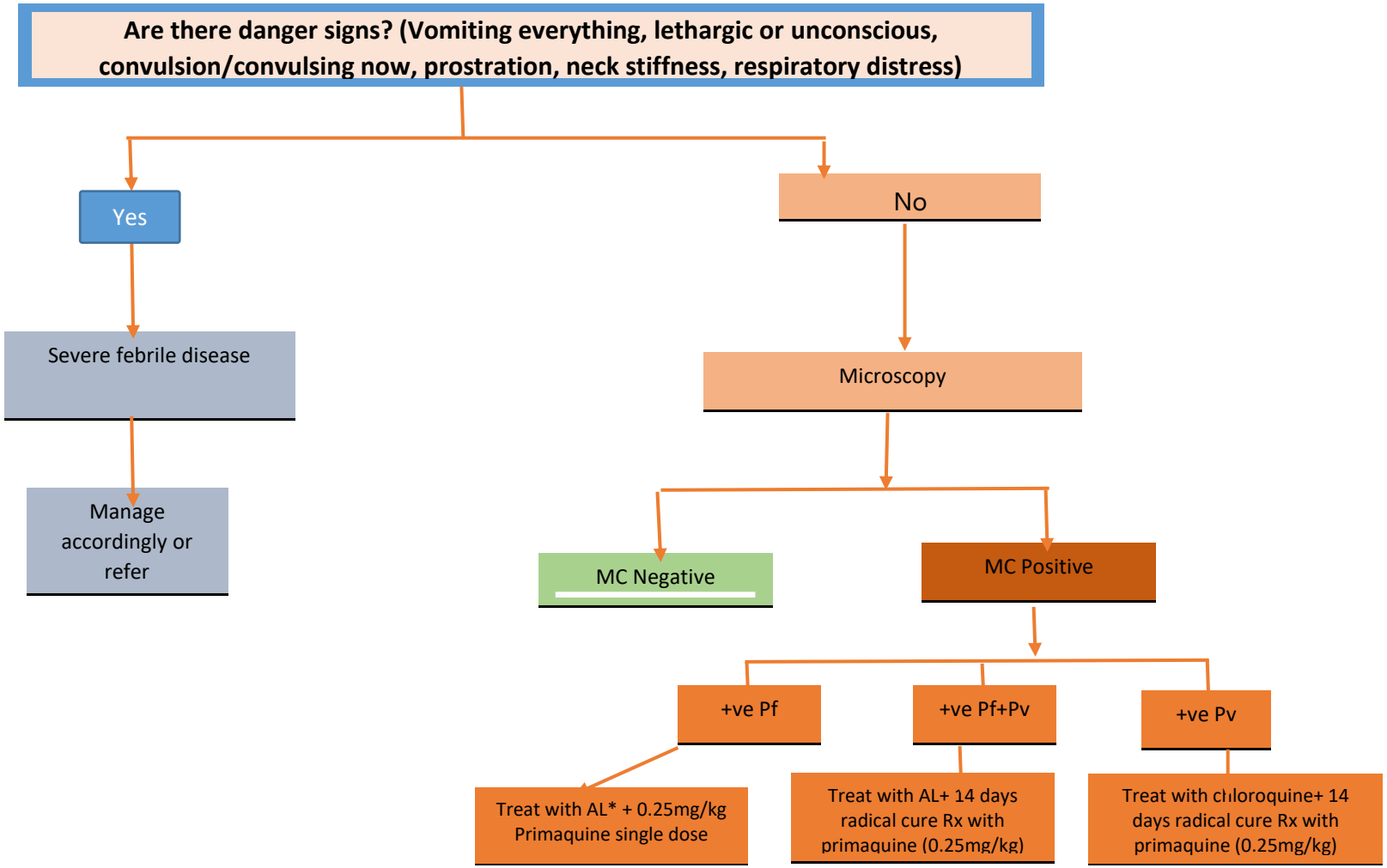


***AL is not recommended for pregnant women in first trimester with uncomplicated malaria. Hence, use oral quinine in such cases.**

Give a single dose of 0.25 mg/kg bw primaquine with ACT to patients with *P. falciparum* malaria (except pregnant women, infants aged < 6 months and women breastfeeding infants aged < 6 months) to reduce transmission

Box 1.

Patient with fever or history of fever in the last 48 hours and lives in malaria-endemic areas or has history of travel within the past 30 days to malaria-endemic areas.



*AL is currently recommended for infants under 5 kg at the same dose above 5 kg and but not recommended for pregnant women in first trimester with uncomplicated malaria.

* Urine color follow up as per the prepared Rx protocol

Box 2.
Patient with fever or history of fever in the last 48 hours and lives in malaria-endemic areas or has history of travel within the past 30 days to malaria-endemic areas & spending at least one night.

Figure Diagnosis and treatment of malaria at Health Center and Hospital level

Health center and hospital level:

First line treatment of uncomplicated malaria: First-line treatment of uncomplicated *P. falciparum* malaria at the health center or hospital level is nearly the same as that outlined above (HP level) including the advice and supportive treatment. For *P. vivax*, radical cure with primaquine is recommended for patients with limited risk of malaria infection in the future, i.e. who are not living in malaria-endemic areas. It is also recommended in selected elimination targeted areas. Mixed infections diagnosed with microscopy are treated with AL and single dose primaquine. Radical cure with primaquine is given for those patients who are living in non malarious areas and those living in the selected elimination targeted districts. The standard protocol for provision of radical cure primaquine should be followed during administration of the drug. Health workers should be vigilant to detect hemolysis which is the most feared complication of primaquine. Regarding supportive treatment, the difference from health posts is that health workers at health center and hospital level can assess and manage mild and moderate anemia.

Second line treatment of uncomplicated malaria: Second-line treatment is used when the first-line treatment is not available, or during failure or non-response to first-line treatment. The second-line treatment for both *P. falciparum* and *P. vivax* is oral quinine.

Treatment failure:

Treatment failure is defined as failure of anti-malarial drug to resolve fever and/or parasitemia. For clinical purpose, consider treatment failure in a patient with malaria who was treated for malaria in the past 28 days. Treatment failures may result from drug resistance, poor adherence or inadequate drug exposure (i.e. from under-dosing, vomiting or unusual pharmacokinetic properties in that individual), drug interaction, misdiagnosis or substandard medicines. Anti-malarial drug resistance refers to the ability of a parasite strain to survive and/or multiply despite the administration and absorption of a medicine given in doses equal to or higher than those usually recommended, but within tolerance of the subject, and the drug must gain access to the parasite or the infected red blood cell for the duration of the time necessary for its normal action and anti-malarial drug resistance can cause treatment failure but not all treatment failure is due to parasite resistance to the drugs. It is important to determine from the patient's history whether the antimalarial was vomited or whether the full course was not completed Monitoring treatment failure is very important because it can signal the appearance of anti-malarial drug resistance.

Treatment failure within first 28 days:

Owing to the potency of AL, treatment failure within 28 days of receiving an AL is very unusual. Recurrence of *P. falciparum* malaria may be the result of a reinfection, or a recrudescence (i.e. treatment failure). In an individual patient, it may not be possible to distinguish between recrudescence and reinfection, although if fever and parasitemia fail to resolve, or recur within 4 weeks of treatment, then treatment is considered to have failed. Wherever possible, treatment failure should be confirmed parastiologically, preferably, a blood smear should be obtained and labelled properly to verify–amongst others– *Plasmodium* species and parasite count, and to rule out other diseases (e.g. relapsing fever). RDTs may remain positive for weeks after the initial infection even without recrudescence so this requires referring a patient from health post to health center where microscopy is available; referral may also be necessary to obtain second-line treatment. .

Treatment failure after 28 days:

The majority of treatment failures occur after two weeks of initial treatment. Such failures can result from either recrudescence or a new infection. This distinction can only be made through parasite genotyping by PCR, which is not used in patient management in Ethiopia. Thus, to simplify operational management and medicine deployment, all presumed treatment failures after four weeks of initial treatment should be considered as new infections and be treated with the first-line antimalarial drug, which is AL for P. falciparum and CQ for *P. vivax*. Primaquine should be given as appropriate.

Management of treatment failure:

The following recommendations should be followed after a full history, clinical assessment and laboratory examination:

- If a cause for treatment failure is identified (e.g. anti-malarial drug is vomited), such cause must be addressed and treatment reinstituted with the first-line anti-malarial drug;
- If a *P. falciparum* or *P. vivax*-infected patient returns to the health facility with fever or history of fever between days 4 to 28 of treatment, a microscopic blood examination should be made (**Note:** do not use RDTs). If parasites are detected, the treatment should be changed to the second-line drug, i.e. quinine tablets;
- In patients who are suspected to have treatment failure after 28 days, the first-line anti-malarial drug should be used;
- If the blood smear is negative and no other obvious causes are found, the patient should be reevaluated, or referred to the next level of health care for proper management.

Appropriate management of treatment failure, is important because the patient may progress to severe malaria, and resistant parasites may be present and transmitted to others.

NB: All malaria patients should be asked for history of malaria treatment in the past 28 days. If they have such history they should be diagnosed at least at health center level with microscopy, health extension workers should refer such patients

Chemoprophylaxis

Persons who travel to malaria-endemic areas are at risk of acquiring malaria. Health workers should advise all persons traveling to such areas to avoid mosquito bites, specifically by using mosquito repellent and sleeping under LLINs at night. Chemoprophylaxis is an option and mefloquine and atovaquone-proguanil 2weeks before departure and 4 weeks after return can be used as anti-malarial chemoprophylaxis in Ethiopia.

NB: *If the person develops fever while on chemoprophylaxis he/she should seek medical advice.*

Chemoprophylaxis

Table 8 Mefloquine: 5 mg /kg mefloquine salt once weekly

Weight (Kg)	Age (approx.)	Number of tablets per week
<9	< 3 months	Not Recommended
9 – 19	3 – 23 months	¼
20 – 30	2 – 7 year	½
31 – 45	8 – 10 year	¾
36 – 50+	11 – 14+	1

Table 9 Atovaquone-proguanil

Weight (kg)	Atovaquone/ Proguanil HCl	Dosage Regimen
11-20	62.5 mg/25 mg	1 Pediatric Tablet daily
21-30	125 mg/50 mg	2 Pediatric Tablets as a single dose daily
31-40	187.5 mg/75 mg	3 Pediatric Tablets as a single dose daily
>40	250 mg/100 mg	1 Tablet (adult strength) as a single dose daily

PHARMACOVIGILANCE

Pharmacovigilance is the science and activity of the detecting, assessing, understanding and preventing the adverse effects or any other possible drug-related problems, such as substandard medicines, medication errors, lack of efficacy reports, use of medicines for indications that are not approved and for which there is inadequate scientific basis, case reports of acute and chronic poisoning, assessment of drug-related mortality, abuse and misuse of medicines and adverse interactions of medicines with chemicals, other medicines, and food. The rationale towards the importance of this activity is the limitation of drug safety information obtained during the initial premarketing phases of drug development.

In order to maintain safety and prevent the public from injury as a result of the use of medicines at large, a national adverse event monitoring system or pharmacovigilance is necessary. In Ethiopia a pharmacovigilance center was established in 2002 and is situated at the Food Medicine and Health Care Administration and Control Authority. This important activity is carried out through the active collaboration of various stakeholders and partners, including health providers, health facilities, academic institutions, drug manufacturers, professional associations, consumers and the media.

To help carry out these lifesaving activities the pharmacovigilance center has developed an adverse drug event guideline and yellow page postage prepaid reporting form to be used by all health providers in the country to report suspected drug-related injuries, including anti-malaria drugs, observed and suspected to be caused as a result of using modern drugs, traditional and complementary drugs, blood products, biological, vaccines, medical devices, medicated cosmetics and any other chemicals. It is clearly stated in the report form what and to whom to report these instances. It is also possible to report drug reactions directly by telephone (011 552 3142, 011 552 3205) and via email by downloading the reporting form that is available at http://www.fmhaca.gov.et/pharmacovigilance.html. Each individual report will be analyzed by

experts and measures will be taken based on the information obtained so that the public will be protected from further drug-related injury.

LEARNING UNIT FOUR

Approach to Fever in Children, IMNCI (Integrated Management of Newborn and Childhood Illnesses)

Learning objectives

By the end of this training, participants will be able to:

- Ask the mother about fever in children.
- Check for general danger signs.
- Assess a child with fever
- Classify a child with fever
- Select appropriate treatment for a child with fever

Assess and Classify Fever

A child with fever may have malaria, measles or another severe disease. Or, a child with fever may have a simple cough or cold or other viral infection.

P. falciparum and *P. vivax* are the two dominant parasite species causing malaria in Ethiopia, with relative frequencies of about 60% and 40%, respectively. This proportion varies from place to place and from season to season. *P. falciparum* is the dominant parasite species in malaria epidemic situations, and this species causes severe and complicated manifestations and almost all malaria deaths.

Fever is the main symptom of malaria. It can be present all the time or recur at regular intervals. Other signs of falciparum malaria are shivering, sweating and vomiting. A child with malaria may have chronic anemia (with no fever) as the only sign of illness.

Signs of malaria can overlap with signs of other illnesses. For example, a child may have malaria and cough with fast breathing, a sign of pneumonia. Studies show that cough and fast breathing are common in children who have fever and falciparum malaria confirmed by blood smear. Even expert Clinicians need laboratory tests to reliably distinguish falciparum malaria from pneumonia in a child with fever, cough and fast breathing. This child needs treatment for both falciparum malaria and pneumonia. Children with malaria may also have diarrhoea. They need an anti-malarial and treatment for the diarrhoea.

In areas with very high malaria transmission, malaria is a major cause of death in children. A case of uncomplicated malaria can develop into severe malaria within 24 hours of onset the illness. Severe malaria is malaria with complications such as cerebral malaria, severe anemia or hypoglycaemia. The child can die if he does not receive urgent treatment.

Deciding Malaria Risk: Malaria risk is defined as the presence of malaria transmission in the area where the patient lives or travel history to malarious area in the past 30 days.

MEASLES: Fever and a generalized rash are the main signs of measles. Measles is highly infectious. Maternal antibody protects young infants against measles for about 6 months. Then the protection gradually disappears. Most cases occur in children between 6 months and 2 years of age. Overcrowding and poor housing increases the risk of measles occurring early.

Measles affects the skin and the layer of cells that line the lung, gut, eye, mouth and throat. The measles virus damages the immune system for many weeks after the onset of measles. This leaves the child at risk for other infections.

Complications of measles occur in about 30% of all cases. The most important are: diarrhoea (including dysentery and persistent diarrhoea), pneumonia, stridor, mouth ulcers, ear infection and severe eye infection (which may lead to corneal ulceration and blindness).

Encephalitis occurs in about one in one thousand cases. A child with encephalitis may have a general danger sign such as convulsions or lethargic or unconscious.

Measles contributes to malnutrition because it causes diarrhoea, high fever and mouth ulcers. These problems interfere with feeding. Malnourished children are more likely to have severe complications due to measles. This is especially true for children who are deficient in vitamin A. One in ten severely malnourished children with measles may die. For this reason, it is very important to help the mother to continue to feed her child during measles.

Assess Fever

A child has the main symptom fever if:

* the child has a history of fever or
* the child feels hot or
* the child has an axillary temperature of 37.5°C or above

When the **axillary** temperature is taken: fever is 37.5°C (99.5°F), high fever is 38.5°C (101.3°F) or more.

Decide the malaria risk (High/low or no).

If the malaria risk in the area is absent, ask the mother about travel:

Has the child traveled outside this area to a malarias area during the previous 30 days?

If she has traveled to a malarious area, decide the malaria risk as low or high depending on the level of malaria risk of the visited area. If the area she had traveled is known to be malarious but not specified as low or high then decide the area as high malaria risk.

Then assess a child with fever for:

- General danger signs
- How long the child has had fever
- History of measles
- Stiff neck
- Bulging fontanels (< 1 year of age)
- Look for signs suggest any bacterial cause of fever
- Runny nose
- Signs suggesting measles -- which are generalized rash and one of these: cough, runny nose, or red eyes.
- If the child has measles now or within the last 3 months, assess for signs of measles complications. They are: mouth ulcers, pus draining from the eye and clouding of the cornea.

A general danger sign is present if the child:

- is not able to drink or breastfeed
- vomits everything
- has had convulsions
- is convulsing now
- is lethargic or unconscious

When you check for general danger signs:

ASK: Is the child able to drink or breastfeed?

- A child has the sign "not able to drink or breastfeed" if the child is not able to suck or swallow when offered a drink or breast milk.

ASK: Does the child vomit everything?

A child who vomits after each feed has the sign "vomits everything." What goes down comes back. A child who vomits everything will not be able to hold down food, fluids or oral drugs. A child who vomits several times but can hold down some fluids does not have this general danger sign.

ASK: Has the child had convulsions?

Convulsions can be generalised or localized. Focal convulsions can present with twitching of the fingers, the mouth or rolling of the eyes. Focal convulsions can easily be missed and therefore needs to be carefully assessed.

LOOK: See if the child is convulsing now.

During a convulsion, the child's arms and legs stiffen because the muscles are contracting. There may be drooling of saliva and rolling of the eyes upwards. The child may lose consciousness. If the child is convulsing in the Health facility now, treat the child by managing the airway and giving Diazepam, before completing the assessment.

LOOK: See if the child is lethargic or unconscious.

A lethargic child is abnormally sleepy and is difficult to awaken by calling and even by gentle shaking. If he wakes up he immediately relapses into sleep. He is too weak to sustain an alert state even under stimulation. Sometimes a lethargic child may stare blankly into space without noticing what is going on around him.

An unconscious child may not respond to verbal or physical stimulus or may respond inappropriately. However, ask the mother if the child seems unusually sleepy or if she cannot wake the child. Look to see if the child wakens when the mother talks or shakes the child or when you clap your hands.

If malaria risk is high/low or there is history of **travel** to a malarious area, then do a blood film or RDT if NO severe classification.

Microscopic test and RDTs are the methods employed for parasitological confirmation or malaria classification. Laboratory evidence providing confirmation of malaria (i.e., microscopy or RDT) by malaria species requires prompt treatment with the appropriate antimalarial medications. The availability of multi-species RDTs is capable of specifically detecting both P. falciparum and P. vivax and mixed infections. It also provides the opportunity to accurately identify parasite-negative patients

in whom another cause of fever (diagnosis) must be sought without delay. Patients who test negative by malaria RDT or microscopy do not need antimalarial medications.

The box below lists the steps for assessing a child for fever. There are two parts to the box. The top half of the box (above the broken line) describes how to assess the child for signs of malaria, measles, meningitis and other causes of fever. The bottom half of the box describes how to assess the child for signs of measles complications if the child has measles now or within the last 3 months.

<table>
<tr><td colspan="2">Does the child have fever? (by history or feels hot temperature 37.5ºC or above)
IF YES:
• Decide Malaria Risk: High/Low or No .
If “ no” malaria risk, then ask:
• Has the child traveled outside this area during the previous 30 days?
• If yes has he been to a malarious area?

Do blood film or RDT, if malaria risk is High/Low or history of travel to a malarious area, AND there is no Severe Classification.</td></tr>
<tr><td>THEN ASK

□ For how long has the child had fever?
□ If more than 7 days, has fever been present every day?
□ Has the child had measles within the last 3 months?</td><td>LOOK AND FEEL:
□ Look or feel for stiff neck.
□ Look or feel for bulging fontanels (< 1 year of age)
□Look for signs suggest any bacterial cause of fever
□ Look for runny nose.
□ Look for signs of MEASLES
- Generalized rash, AND one of these: cough, runny nose or red eyes.</td></tr>
<tr><td>If the child has measles now or within the last 3 months:</td><td>□ Look for mouth ulcers:
- Are they deep or extensive?
- Are they not deep or extensive?
□ Look for pus draining from the eye.
□ Look for clouding of the cornea.</td></tr>
</table>

Ask about (or measure) fever in ALL sick children.

ASK: Does the child have fever?

Check to see if the child has a history of fever, feels hot or has a temperature of 37.5°C or above.

The child has a history of fever if the child has had any fever with this illness. Use words for "fever" that the mother understands. Make sure the mother understands what fever is. For example, ask the mother if the child's body has felt hot. Feel the child's abdomen or axilla and determine if the child feels hot.

Look to see if the child's temperature was measured today and recorded on the child's chart. If the child has a temperature of 37.5°C or above, the child has fever. If the child's temperature has not been measured, and you have a thermometer, measure the child's temperature.

If the child does not have fever (by history, doesn't feel hot or temperature <37.5°C), tick (√) No on the Recording Form. Ask about the next main symptom, ear problem. Do not assess the child for signs related to fever.

If the child has fever (by history, feels hot or temperature 37.5°C or above), assess the child for additional signs related to fever. Assess the child's fever even if the child does not have a temperature of 37.5°C or above or does not feel hot now. History of fever is enough to assess the child for fever.

DECIDE Malaria Risk

Decide if there is malaria risk. In some areas, the malaria risk is always high. If the malaria risk in the local area is low or absent, ask:

Has the child traveled outside this area to a malarious area during the previous 30 days?

Reclassify the malaria risk as high/low if there has been travel to a malarious area. The child may have acquired malaria during travel.

Many mothers will know whether the area they have traveled to <u>with the child</u> has malaria transmission. If she does not know or is not sure, ask about the area and use your own knowledge of whether the area has falciparum malaria. If you are still not sure, assume the malaria risk is <u>high.</u>

Circle the malaria risk (high/low) on the Recording Form.

You will use this information when you classify the child's fever.

ASK: For how long? If more than 7 days, has fever been present every day?

Ask the mother how long the child has had fever. If the fever has been present for more than 7 days, ask if the fever has been present every day.

Most fevers due to viral illnesses go away within a few days. A fever which has been present every day for more than 7 days can mean that the child has a more severe disease such as typhoid fever. Refer this child for further assessment.

ASK: Has the child had measles within the last 3 months?

Measles damages the child's immune system and leaves the child at risk for other infections for many weeks.

A child with fever and a history of measles within the last 3 months may have an infection due to complications of measles.

LOOK or FEEL for stiff neck.

A child with fever and stiff neck may have meningitis. A child with meningitis needs urgent treatment with injectable antibiotics and referral to a hospital.

While you talk with the mother during the assessment, look to see if the child moves and bends his neck easily as he looks around. If the child is moving and bending his neck, he does not have a stiff neck.

If you did not see any movement, or if you are not sure, draw the child's attention to his umbilicus or toes. For example, you can shine a flashlight on his toes or umbilicus or tickle his toes to encourage the child to look down. Look to see if the child can bend his neck when he looks down at his umbilicus or toes.

If you still have not seen the child bend his neck himself, ask the mother to help you lay the child on his back. Lean over the child; gently support his back and shoulders with one hand. With the other hand, hold his head. Then carefully bend the head forward toward his chest. If the neck bends easily, the child does not have stiff neck. If the neck feels stiff and there is resistance to bending, the child has a stiff neck. Often a child with a stiff neck will cry when you try to bend the neck.

LOOK or FEEL for bulging fontanels (age < 12 months).

Hold the infant in an upright position. The infant must not be crying. Then look at and feel the fontanels. If the fontanel is bulging rather than flat, this may mean the young infant has meningitis.

LOOK for local tenderness; orals sores; refusal to use a limb; hot tender swelling; red tender skin or boils; lower abdominal pain or pain on passing urine in older children

LOOK for runny nose.

A runny nose in a child with fever may mean that the child has a common cold.

If the child has a runny nose, ask the mother if the child has had a runny nose only with this illness.

When malaria risk is low, a child with fever and a runny nose does not need an antimalarial. This child's fever is probably due to the common cold.

LOOK for signs suggesting MEASLES.

Assess a child with fever to see if there are signs suggesting measles. Look for a generalized rash and for one of the following signs: cough, runny nose, or red eyes.

Generalized rash

In measles, a red rash begins behind the ears and on the neck. It spreads to the face. During the next day, the rash spreads to the rest of the body, arms and legs. After 4 to 5 days, the rash starts to fade and the skin may peel. Some children with severe infection may have more rash spread over more of the body. The rash becomes more discoloured (dark brown or blackish), and there is more peeling of the skin.

Measles rash does not have vesicles (blisters) or pustules. The rash does not itch. Do not confuse measles with other common childhood rashes such as chicken pox, scabies or heat rash. (The chicken pox rash is a generalized rash with vesicles. Scabies occurs on the hands, feet, ankles, elbows, buttocks and vesicles which itch. It also itches. Heat rash can be a generalized rash with small bumps and vesicles which itch. A child with heat rash is not sick. You can recognize measles more easily during times when other cases of measles are occurring in your community.

Cough, Runny Nose, or Red Eyes

To classify a child as having measles, the child with fever must have a generalized rash AND one of the following signs: cough, runny nose or red eyes. The child has "red eyes" if there is redness in the white part of the eye in the absence of other causes.

If the child has MEASLES now or within the last 3 months:

Look to see if the child has mouth or eye complications. Other complications of measles such as stridor in a calm child, pneumonia, and diarrhoea are assessed earlier; malnutrition and ear infection are assessed later.

LOOK for mouth ulcers. Are they deep or extensive, <u>or not</u> deep or extensive?

Mouth ulcers are common complications of measles which interfere with the feeding of a sick child. Look for mouth ulcers in every child with measles and determine whether they are deep or extensive or a mouth ulcer which is not deep or extensive.

The mouth ulcers should be distinguished from Koplik spots. Koplik spots occur inside the cheek during the early stages of measles infection. They are small irregular bright spots with a white center. They do not interfere with feeding.

LOOK for pus draining from the eye.

Pus draining from the eye is a sign of conjunctivitis. If you do not see pus draining from the eye, look for pus on the conjunctiva or on the eyelids.

Often the pus forms a crust when the child is sleeping and seals the eye shut. It can be gently opened with clean hands. Wash your hands after examining the eye of any child with pus draining from the eye.

LOOK for clouding of the cornea.

Look carefully for corneal clouding in every child with measles. Corneal clouding is a dangerous complication. The corneal clouding may be due to Vitamin A deficiency which has been made worse by measles. If the corneal clouding is not treated, the cornea can ulcerate and cause blindness. A child with clouding of the cornea needs urgent referral and treatment with Vitamin A.

If there is clouding of the cornea, ask the mother how long the clouding has been present. If the mother is certain that clouding has been there for some time, ask if the clouding has already been assessed and treated at the hospital. If it has, you do not need to refer this child again for corneal clouding.

Classify Fever

If the child has fever and no signs of measles, classify the child for fever only.

If the child has signs of both fever and measles, classify the child for fever and for measles. There are two fever classification tables on the *ASSESS & CLASSIFY* chart. One is for classifying fever when the risk of malaria is high/low and the second for classifying fever when there is no malaria risk. To classify fever, you must know if the malaria risk is high/low or no. Then you select the appropriate classification table.

HIGH/LOW MALARIA RISK:

There are three possible classifications of fever when the malaria risk is high/low.

- VERY SEVERE FEBRILE DISEASE
- MALARIA
- FEVER: NO MALARIA

HIGH/LOW MALARIA RISK		
SIGNS	**CLASSIFY**	**TREATMENT (Urgent pre-referral treatments are in bold print)**
□ Any general danger sign, OR □ Stiff neck, OR □ Bulging fontanels (< 1yr)	VERY SEVERE FEBRILE DISEASE	□ Give first dose Artesunate or Quinine for severe malaria* □ Give first dose of IV/IM Ampicillin and Gentamycin □ Treat the child to prevent low blood sugar □ Give Paracetamol in health facility for high fever (≥38.5°C) □ Refer or admit URGENTLY to hospital or health center
□ Positive blood film/RDT, OR □ If blood film/RDT not available, any fever (by history, or feels hot, or temp ≥ 37.5ºC)	MALARIA	□ Treat with Artemeter-Lumefantrine** for P. Falciparum or mixed or no confirmatory test done. □ Treat with Chloroquine for confirmed P. vivax***. □ Give Paracetamol in health facility for high fever (38.5°C or above) □ Give an appropriate antibiotic for identified bacterial cause of fever □ Advise mother when to return immediately. □ Follow-up in 2 days if fever persists. □ If fever is present every day for more than 7 days, refer for assessment
□ RDT negative, OR □ Blood film negative □ Other cause of fever present	FEVER: N0 MALARIA	□ Give one dose of Paracetamol in health facility for high fever (≥38.5°C) □ Give an appropriate antibiotic for identified bacterial cause of fever □ Advise mother when to return immediately□ Follow-up in 2 days if fever persists. □ If fever is present every day for more than 7 days, refer for assessment.

* IM Artemether is also an option in the absence of Artesunate for treatment of severe malaria

**Add single dose primaquine for children more than six months of age

*** Add radical cure with primaquine in selected geographical areas

VERY SEVERE FEBRILE DISEASE *(High/Low Malaria Risk*)

If the child with fever has any general danger sign or a stiff neck or bulging fontanel in less than one year of age, classify the child as having VERY SEVERE FEBRILE DISEASE.

Fever Management/Treatment

A child with fever and any general danger sign or stiff neck or bulged fontanel (in less than one year of age) may have meningitis, severe malaria (including cerebral malaria) or sepsis. It is not possible to distinguish between these severe diseases without laboratory tests. A child classified as having VERY SEVERE FEBRILE DISEASE needs urgent treatment and referral. Before referring urgently, you will give several treatments for the possible severe diseases (Refer to Treat the Child module).

MALARIA *(High/Low Malaria Risk)*

If a general danger sign or stiff neck or bulged fontanel is not present, look at the yellow row. Because the child has a fever (by history, feels hot, or temperature 37.5°C or above) in a high malaria risk area, classify the child as having MALARIA if RDT is positive.

When the risk of malaria is high/low, the chance is also high that the child's fever is due to malaria.

Treatment

If a child has fever, cough and fast breathing, the child may have malaria in addition to pneumonia. It is not possible without laboratory tests to find out if the child has malaria. Therefore, the child should be treated for malaria and pneumonia with **Artemeter-Lumefantrine** and Amoxicillin respectively, if there is no RDT or blood film.

Most viral infections last less than a week. A fever that persists every day for more than 7 days may be a sign of typhoid fever or other severe disease. If the child's fever has persisted every day for more than 7 days, refer the child for additional assessment.

FEVER: NO MALARIA

In high/low risk malaria area and if blood film or RDT is negative for malaria, classify as having FEVER: NO MALARIA. In many areas of the country health extension workers are deployed and are treating malaria. They use RDT for malaria diagnosis.

FOR NO MALARIA RISK ONLY:

There are two possible classifications of fever in a child with No malaria risk:

- VERY SEVERE FEBRILE DISEASE
- FEVER

NO MALARIA RISK and No Travel to Malarious Area		
• Any general danger sign, OR • Stiff neck, OR	VERY SEVERE FEBRILE	□ Give first dose of IV/IM Ampicillin and Gentamycin □ Treat the child to prevent low blood sugar. □ Give Paracetamol in health facility for high fever

• Bulging fontanels (< 1 year of age)	DISEASE	(≥38.5°C) □ Refer URGENTLY to hospital
• Any fever	FEVER	□ *Give one dose of Paracetamol in health facility for high fever (≥38.5°C*) □ Give an appropriate antibiotic for identified bacterial cause of fever □ Advise mother when to return immediately □ Follow-up in 2 days if fever persists □ If fever is present every day for more than 7 days refer for assessment

VERY SEVERE FEBRILE DISEASE *(No Malaria Risk)*

If the child has any general danger sign, a stiff neck or bulging fontanel, and there is no malaria risk, classify the child as having VERY SEVERE FEBRILE DISEASE.

Treatment

The treatment for a child classified as having VERY SEVERE FEBRILE DISEASE when there is no malaria risk, is not the same as VERY SEVERE FEBRILE DISEASE in high/low malaria risk area (see Section 5.2).

FEVER

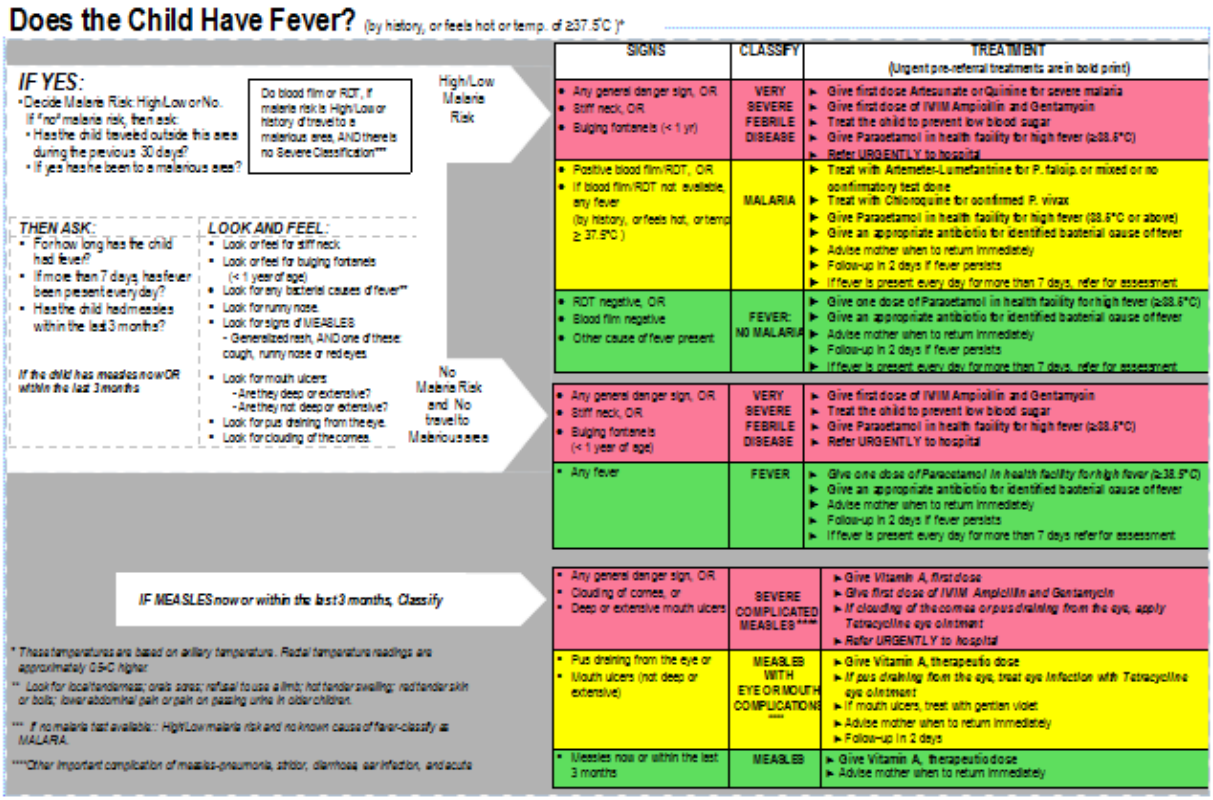
If the child does not have any signs of VERY SEVERE FEBRILE DISEASE, look at the next row. When there is NO MALARIA RISK, a child with fever and who has not traveled to a malarious area should be classified as FEVER. The fever may be due to a problem included in another classification – such as a cold, pneumonia, dysentery or ear infection. Or the fever may be due to another obvious cause such as cellulitis or an abscess.

Treatment

If the child's fever is high, give Paracetamol. Advise the mother to return for follow-up in 2 days if fever persists. If the fever has been present every day for more than 7 days, refer for assessment

Classify Measles

A child who has the main symptom "fever" and measles now or within the last 3 months is classified both for fever and for measles. First you must classify the child's fever. Next you classify measles.



If the child has no signs suggesting measles, or has not had measles within the last three months, do not classify measles. Ask about the next main symptom, ear problem.

There are three possible classifications of measles:

- SEVERE COMPLICATED MEASLES
- MEASLES WITH EYE OR MOUTH COMPLICATIONS
- MEASLES

The table for classifying measles if present now or within the last 3 months is shown below.

□ Any general danger sign, OR □ Clouding of cornea, or □ Deep or extensive mouth ulcers	SEVERE COMPLICATED MEASLES ***	□ Give *Vitamin A, first dose* □ *Give first dose of IV/IM Ampicillin and Gentamycin* □ *If clouding of the cornea or pus draining from the eye, apply Tetracycline eye ointment* □ *Refer URGENTLY to hospital*
□ Pus draining from the eye or □ Mouth ulcers (not deep or extensive)	MEASLES WITH EYE OR MOUTH COMPLICATIONS ***	□ Give Vitamin A, therapeutic dose □ *If pus draining from the eye, treat eye infection with Tetracycline eye ointment*□ If mouth ulcers, treat with gentian violet □ Advise mother when to return immediately □ Follow–up in 2 days
□ Measles now or within the last 3 months	MEASLES	□ Give Vitamin A, therapeutic dose □ Advise mother when to return immediately

SEVERE COMPLICATED MEASLES

If the child has any general danger sign, clouding of cornea or deep or extensive mouth ulcers, classify the child as having SEVERE COMPLICATED MEASLES. This child needs urgent treatment and referral to hospital.

Children with measles may have other serious complications of measles. These include stridor in a calm child, severe pneumonia, severe dehydration, or severe malnutrition. You assess and classify these signs in other parts of the assessment. Their treatments are appropriate for the child with measles.

Treatment

Some complications are due to bacterial infections. Others are due to the measles virus which causes damage to the respiratory and intestinal tracts. Vitamin A deficiency contributes to some of the complications such as corneal ulcer. Any Vitamin A deficiency is made worse by the measles infection. Measles complications can lead to severe disease and death.

All children with SEVERE COMPLICATED MEASLES should receive urgent treatment. Also give the first dose of Vitamin A and an appropriate antibiotic and refer

If there is clouding of the cornea, or pus draining from the eye, apply eye ointment. If it is not treated, corneal clouding can result in blindness. Ask the mother if the clouding has been present for some time. Find out if it was assessed and treated at the hospital. If it was, you do not need to refer the child again for this eye sign.

MEASLES WITH EYE OR MOUTH COMPLICATIONS

If the child has pus draining from the eye or mouth ulcers which are not deep or extensive, classify the child as having MEASLES WITH EYE OR MOUTH COMPLICATIONS. A child with this classification does not need referral.

You assess and classify the child for other complications of measles (pneumonia, diarrhoea, ear infection and malnutrition) in other parts of this assessment. Their treatments are appropriate for the child with measles.

Treatment

Identifying and treating measles complications early in the infection can prevent many deaths. These children should be treated with Vitamin A. It will help correct any Vitamin A deficiency and decrease the severity of the complications. The mother should be taught how to treat the child's eye infection or mouth ulcers at home. Treating mouth ulcers helps the child to more quickly resume normal feeding.

MEASLES

A child with measles now or within the last 3 months and with none of the complications listed in the pink or yellow rows is classified as having MEASLES. Give the child therapeutic dose of Vitamin A to help prevent measles complications. <u>All</u> children with measles should receive therapeutic dose of Vitamin A.

Exercises

In this exercise, you will classify illness in children with signs of fever and, if present, signs suggesting measles. First, you will study an example. Then you will begin the exercise.

Read the example case study that begins on this page. Also study how the health worker classified this child's illness. When all the participants are ready, there will be a group discussion about this example.

* * *

EXAMPLE: Pawlos is 10 months old male infant. He weighs 8.2 kg. His length is 71 cm. His temperature is 37.5°C. His mother says he has a rash and cough.

The health worker checked Pawlos for general danger signs. Pawlos was able to drink, was not vomiting, did not have convulsions and was not convulsing, lethargic or unconscious.

The health worker next asked about Pawlos's cough. The mother said Pawlos has been coughing for 5 days. He counted 43 breaths per minute. He did not see chest in drawing. He did not hear stridor when Pawlos was calm.

Pawlos did not have diarrhoea.

Next the health worker asked about Pawlos's fever. The malaria risk is high. The mother said Pawlos has felt hot for 2 days. Pawlos did not have a stiff neck. He has had a runny nose with this illness, his mother said.

Pawlos has a rash covering his whole body. Pawlos's eyes were red. The health worker checked the child for complications of measles. There were no mouth ulcers. There was no pus draining from the eye and no clouding of the cornea. Blood film or RDT is not available in the health facility.

Here is how the health worker recorded Pawlos's case information and signs of illness.

MANAGEMENT OF THE SICK CHILD AGE **2 MONTHS UP TO 5 YEARS**

Child's Name: Pawlos Age 10 months Sex M Weight: 8.2kg Lt/Ht 71 cm Temp 37.5ºC

ASK: What are the child's problems? Rash and Cough Initial visit? ✓ Follow-up visit? ____

ASSESS (Circle all signs present, tick or fill dashes/spaces)

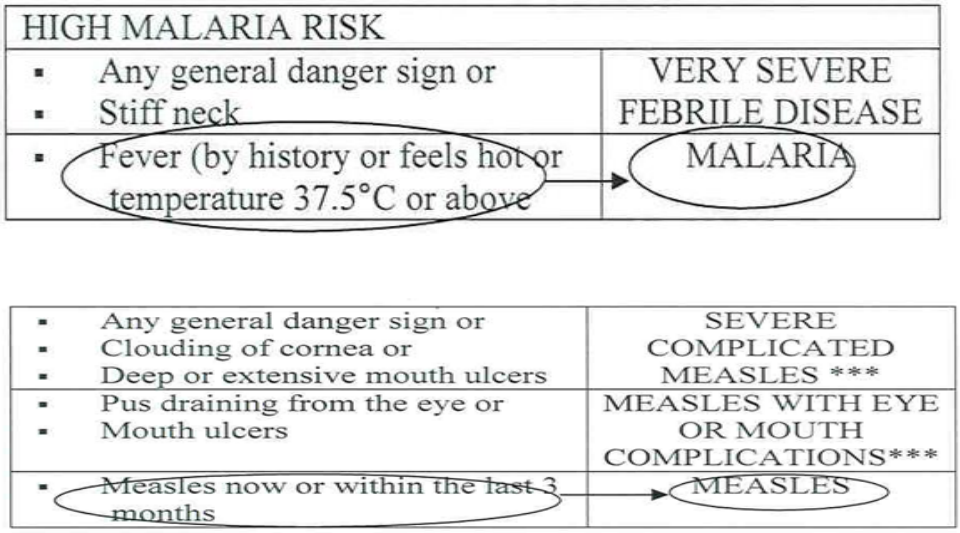
	CLASSIFY
CHECK FOR GENERAL DANGER SIGNS NOT ABLE TO DRINK OR BREASTFEED CONVULSING NOW VOMITS EVERYTHING LETHARGIC OR UNCONSCIOUS History of CONVULSIONS	
DOES THE CHILD HAVE COUGH OR DIFFICULT BREATHING? Yes ✓ No_____	Cough/cold
For how long? 5 Days □ Count the breaths in 1 minute. 43 breaths/minute. Fast breathing? □ Look for chest indrawing. □ Look and listen for stridor.	
DOES THE CHILD HAVE DIARRHOEA? Yes ____ No ✓	
For how long? _____ Days Is there blood in the stool? □ Look at the child's general condition. Is the child: Lethargic or unconscious? Restless & irritable? □ Look for sunken eyes. □ Offer the child fluid. Is the child: Not able to drink or drinking poorly? Drinking eagerly, thirsty? □ Pinch the skin of the abdomen. Does it go back: Very slowly (> 2 seconds)? Slowly?	
DOES THE CHILD HAVE FEVER? (by history/feels hot/temperature ≥37.5^{0}C) Yes ✓ No____	

- Decide MALARIA risk: High/low No, - If no" malaria risk, Has child traveled to malarious area in the last 30 days? - For how long has the child had fever? 2 Days - If >7 days, has fever been present every day? - Has child had measles within the last 3 months?	□ Look or feel for stiff neck. □ Look for bulging fontanel □ Look for any other cause of fever □ Look for runny nose □ Look for signs of MEASLES NOW : Generalized rash, And one of these: Cough, Runny nose or Red eyes. □ Blood Film or RDT: Positive____ Negative____ Not Done ✓	Malaria
If the child has measles now or within the last 3 months:	□ Look for mouth ulcers: If Yes, are they deep and extensive? □ Look for pus draining from the eye. □ Look for clouding of the cornea.	Measles

2. To classify Pawlos's fever, the health worker looked at the table for classifying fever when there is a High Malaria Risk.
   a. He checked to see if Pawlos had any of the signs in the pink row. He thought, "Does Pawlos have any general danger signs? No, he does not. Does Pawlos have a stiff neck? No, he does not. Pawlos does not have any signs of VERY SEVERE FEBRILE DISEASE."
   b. Next, the health worker looked at the yellow row. He thought, "Pawlos has a fever. His temperature measures 37.5^{o}C. He also has a history of fever because his mother says Pawlos felt hot for 2 days. He classified Pawlos as having MALARIA."
   c. Because Pawlos had a generalized rash and red eyes, Pawlos has signs suggesting measles. To classify Pawlos's measles, the health worker looked at the classification table for classifying measles.
   d. He checked to see if Pawlos had any of the signs in the pink row. He thought, "Pawlos does not have any general danger signs. The child does not have clouding of the cornea. There are no deep or extensive mouth ulcers. Pawlos does not have SEVERE COMPLICATED MEASLES."

e. Next the health worker looked at the yellow row. He thought, "Does Pawlos have any signs in the yellow row? He does not have pus draining from the eye. There are no mouth ulcers. Pawlos does not have MEASLES WITH EYE OR MOUTH COMPLICATIONS."

f. Finally the health worker looked at the green row. Pawlos has measles, but he has no signs in the pink or yellow row. The health worker classified Pawlos as having MEASLES.



HIGH MALARIA RISK	
▪ Any general danger sign or ▪ Stiff neck	VERY SEVERE FEBRILE DISEASE
▪ Fever (by history or feels hot or temperature 37.5°C or above	MALARIA
▪ Any general danger sign or ▪ Clouding of cornea or ▪ Deep or extensive mouth ulcers	SEVERE COMPLICATED MEASLES ***
▪ Pus draining from the eye or ▪ Mouth ulcers	MEASLES WITH EYE OR MOUTH COMPLICATIONS***
▪ Measles now or within the last 3 months	MEASLES

Now read the following case studies. Record each child's signs and their classifications on the Recording Form. Remember to look at the chart to classify the signs.

Case 1: Abdi

Abdi is 3 years old male child. He weighs 9.4 kg. His height is 92 cm His temperature is 37°C. His mother says he feels hot. He also has a cough, she says. The health worker checked for general danger signs. Abdi was able to drink, had not vomited, did not have convulsions, and was not convulsing, lethargic or unconscious. The mother said Abdi had been coughing for 3 days. The health worker counted 51 breaths a minute. He did not see chest in drawing. There was no stridor when Abdi was calm. Abdi does not have diarrhoea.

The health worker also thought that Abdi felt hot. He assessed the child further for signs of fever. The risk of malaria is high. He has felt hot for 5 days, the mother said. He has not had measles within the last 3 months. He did not have a stiff neck; there was no runny nose, and no generalized rash. RDT is found to be positive. Record the child's signs and classify them on the Recording Form below.

MANAGEMENT OF THE SICK CHILD AGE **2 MONTHS UP TO 5 YEARS**

Child's Name: _____ Age_____ months Sex _____ Weight: _____kg Lt/Ht _____ cm Temp _____^{0}C

ASK: What are the child's problems? _____ Initial visit? _____ Follow-up visit? ____

ASSESS (Circle all signs present, tick or fill dashes/spaces)

CLASSIFY

CHECK FOR GENERAL DANGER SIGNS

NOT ABLE TO DRINK OR BREASTFEED
CONVULSING NOW
VOMITS EVERYTHING
LETHARGIC OR UNCONSCIOUS
History of CONVULSIONS

DOES THE CHILD HAVE COUGH OR DIFFICULT BREATHING?

Yes _____ No_____

For how long? _____ Days

- Count the breaths in 1 minute. _____ breaths/minute. Fast breathing?
- Look for chest indrawing.
- Look and listen for stridor.

DOES THE CHILD HAVE DIARRHOEA? Yes _____ No____

For how long? _____ Days

Is there blood in the stool?

- Look at the child's general condition. Is the child: Lethargic or unconscious? Restless and irritable?
- Look for sunken eyes.
- Offer the child fluid. Is the child: Not able to drink or drinking poorly? Drinking eagerly, thirsty?
- Pinch the skin of the abdomen. Does it go back: Very slowly (> 2 seconds)? Slowly?

DOES THE CHILD HAVE FEVER? (by history/feels hot/temperature ≥37.5^{0}C)

Yes___ No____

- Decide MALARIA risk: High/Low No,
- If "low or no" malaria risk, Has child traveled to malarious area in the last 30 days?
- For how long has the child had fever? _ Days
- If >7 days, has fever been present

- Look or feel for stiff neck.
- Look for bulging fontanel
- Look for runny nose
- Look for signs of MEASLES NOW : Generalized rash,

And one of these: Cough, Runny nose or Red eyes.

- Blood Film or RDT: Positive √

every day? - Has child had measles within the last 3 months?	Negative___ Not Done ____	
If the child has measles now or within the last 3 months:	□ Look for mouth ulcers: If Yes, are they deep and extensive? □ Look for pus draining from the eye. □ Look for clouding of the cornea.	

Case 2: Leya

Leya is 5 months old female infant. She weighs 5 kg. Her length is 55 cm. Her temperature is 36.5°C. Her family brought her to the Health facility because she feels hot and has had cough for 2 days. She is able to drink. She has not vomited or had convulsions, and is not convulsing, lethargic or unconscious.

The health worker said, "I am going to check her cough now." The health worker counted 43 breaths per minute. There was no chest indrawing and no stridor when Leya was calm. Leya did not have diarrhoea. "Now, I will check her fever," said the health worker. Leya lives in an area where many cases of malaria occur all year long (high malaria risk). Her mother said, "Leya has felt hot on and off for 2 days." She has not had measles within the last 3 months. She does not have stiff neck or runny nose. Leya has a generalized rash. Her eyes are red. She has mouth ulcers. They are not deep and extensive. She does not have pus draining from the eye. She does not have clouding of the cornea. Neither blood film nor RDT is available at the health facility. Record the child's signs and classify them on the Recording Form below.

MANAGEMENT OF THE SICK CHILD AGE **2 MONTHS UP TO 5 YEARS**

Child's Name: _____ Age____ months Sex ____Weight: _____kg Lt/Ht _____ cm Temp _____^{0}C

ASK: What are the child's problems? _____ Initial visit? _____ Follow-up visit? ____

ASSESS (Circle all signs present, tick or fill dashes/spaces)

CLASSIFY

CHECK FOR GENERAL DANGER SIGNS NOT ABLE TO DRINK OR BREASTFEED CONVULSING NOW VOMITS EVERYTHING LETHARGIC OR UNCONSCIOUS History of CONVULSIONS		
DOES THE CHILD HAVE COUGH OR DIFFICULT BREATHING? Yes _____ No_____		
For how long? _____ Days	□ Count the breaths in 1 minute. _____ breaths/minute. Fast breathing? □ Look for chest indrawing. □ Look and listen for stridor.	
DOES THE CHILD HAVE DIARRHOEA? Yes _____ No____		
For how long? _____Days Is there blood in the stool?	□ Look at the child's general condition. Is the child: Lethargic or unconscious? Restless and irritable? □ Look for sunken eyes. □ Offer the child fluid. Is the child: Not able to drink or drinking poorly? Drinking eagerly, thirsty? □ Pinch the skin of the abdomen. Does it go back: Very slowly (> 2 seconds)? Slowly?	
DOES THE CHILD HAVE FEVER? (by history/feels hot/temperature ≥37.5^{0}C) Yes___ No____		
- Decide MALARIA risk: High/Low No, - If "low or no" malaria risk, Has child traveled to malarious area in the last 30 days? - For how long has the child	□ Look or feel for stiff neck. □ Look for bulging fontanel □ Look for runny nose □ Look for signs of MEASLES NOW : Generalized rash, And one of these: Cough, Runny nose or Red eyes. □ Blood Film or RDT: Positive____	

had fever? _____ Days - If >7 days, has fever been present every day? - Has child had measles within the last 3 months?	Negative____ Not Done ____	
If the child has measles now or within the last 3 months:	□ Look for mouth ulcers: If Yes, are they deep and extensive? □ Look for pus draining from the eye. □ Look for clouding of the cornea.	

Case 3: Sitti

Sitti is 12 months old female infant. She weighs 7.2 kg. Her length is 73 cm and her axillary temperature is 36.5°C. Her mother brought Sitti to the health centre today because she feels hot. Sitti has no general danger signs. She does not have cough or difficult breathing. When asked about diarrhoea, the mother said, "Yes, Sitti has had diarrhoea for 2 to 3 days." She has not seen any blood in the stool. Sitti has not been lethargic or unconscious. Her eyes are not sunken. She drinks normally. Her skin pinch returns immediately. The health worker said, "You brought Sitti today because she feels hot. I will check her for fever." The risk of malaria is low. She has no recent travel history. Her mother said that Sitti has felt hot for 2 days. She has not had measles within the last 3 months. There is no stiff neck, no runny nose, and no generalized rash. She has no other cause of fever. RDT is negative.

Record the child's signs and classify them on the Recording Form below.

MANAGEMENT OF THE SICK CHILD AGE **2 MONTHS UP TO 5 YEARS**

Child's Name: _____Age_____ months Sex _____ Weight: _____kg

Lt/Ht _____ cm Temp _____^{0}C

ASK: What are the child's problems? _____Initial visit? _____ Follow-up visit? ____

ASSESS (Circle all signs present, tick or fill dashes/spaces)

CLASSIFY

CHECK FOR GENERAL DANGER SIGNS

NOT ABLE TO DRINK OR BREASTFEED

CONVULSING NOW

VOMITS EVERYTHING LETHARGIC OR UNCONSCIOUS History of CONVULSIONS

DOES THE CHILD HAVE COUGH OR DIFFICULT BREATHING?

Yes _____ No_____

For how long? _____ Days

□ Count the breaths in 1 minute. _____ breaths/minute. Fast breathing?

□ Look for chest indrawing.

□ Look and listen for stridor.

DOES THE CHILD HAVE DIARRHOEA? Yes _____ No____

For how long? _____ Days

Is there blood in the stool?

□ Look at the child's general condition. Is the child:
Lethargic or unconscious? Restless and irritable?

□ Look for sunken eyes.

□ Offer the child fluid. Is the child:
Not able to drink or drinking poorly?
Drinking eagerly, thirsty?

□ Pinch the skin of the abdomen. Does it go back:
Very slowly (> 2 seconds)?
Slowly?

DOES THE CHILD HAVE FEVER? (by history/feels hot/temperature ≥37.5^{0}C) Yes___ No____

- Decide MALARIA risk: High/Low No,
- If "low or no" malaria risk, Has child traveled to malarious area in the last 30 days?
- For how long has the child had fever? _____ Days

□ Look or feel for stiff neck.

□ Look for bulging fontanel

□ Look for runny nose

□ Look for signs of MEASLES NOW :
Generalized rash,
And one of these: Cough, Runny nose or Red eyes.

□ Blood Film or RDT: Positive____

- If >7 days, has fever been present every day? - Has child had measles within the last 3 months?	Negative____ Not Done ____	
If the child has measles now or within the last 3 months:	□ Look for mouth ulcers: If Yes, are they deep and extensive? □ Look for pus draining from the eye. □ Look for clouding of the cornea.	

Case 4: Lemlem

Lemlem is 3 years old female child. She weighs 10 kg. Her height is 91 cm. Her axillary temperature is 38°C. Her mother brought her to the health centre because she has a cough. She also has a rash. The health worker checked for general danger signs. She was able to drink, she had not been vomiting everything, and she did not have convulsions. She was not convulsing, lethargic or unconscious. The health worker assessed Lemlem's cough. The mother told the health worker Lemlem had been coughing for 2 days. The health worker counted 42 breaths per minute. The health worker did not see chest indrawing. He did not hear stridor when Lemlem was calm. When the health worker asked if Lemlem had diarrhoea, the mother said, "No." Blood film was negative. Next the health worker assessed Lemlem's fever. It is the dry season and the risk of malaria is low. She has no recent travel history. She has felt hot for 3 days, the mother said. She does not have stiff neck. Health worker identified a hot tender swelling on the right arm. She does not have a runny nose. Lemlem has a generalized rash. Her eyes are red. She does not have mouth ulcers. Pus is not draining from the eye. There is no clouding of the cornea. Record the child's signs and classify them on the Recording Form below.

MANAGEMENT OF THE SICK CHILD AGE **2 MONTHS UP TO 5 YEARS**

Child's Name: _____Age___ months Sex ___Weight: ___kg Lt/Ht __ cm Temp ___^{0}C

ASK: What are the child's problems? _____Initial visit? _____ Follow-up visit? ____

ASSESS (Circle all signs present, tick or fill dashes/spaces)

CLASSIFY

CHECK FOR GENERAL DANGER SIGNS NOT ABLE TO DRINK OR BREASTFEED CONVULSING NOW VOMITS EVERYTHING LETHARGIC OR UNCONSCIOUS History of CONVULSIONS		
DOES THE CHILD HAVE COUGH OR DIFFICULT BREATHING? Yes _____ No_____		
For how long? _____ Days	□ Count the breaths in 1 minute. _____ breaths/minute. Fast breathing? □ Look for chest indrawing. □ Look and listen for stridor.	
DOES THE CHILD HAVE DIARRHOEA? Yes _____ No____		
For how long? _____ Days Is there blood in the stool?	□ Look at the child's general condition. Is the child: Lethargic or unconscious? Restless & irritable? □ Look for sunken eyes. □ Offer the child fluid. Is the child: Not able to drink or drinking poorly? Drinking eagerly, thirsty? □ Pinch the skin of the abdomen. Does it go back: Very slowly (> 2 seconds)? Slowly?	
DOES THE CHILD HAVE FEVER? (by history/feels hot/temperature ≥37.5^{0}C) Yes___ No____		
- Decide MALARIA risk: High/Low No, - If "low or no" malaria risk, Has child traveled to malarious area in the last 30 days? - For how long has the child had fever? ____ Days - If >7 days, has fever been present every day? - Has child had measles within the last 3 months?	□ Look or feel for stiff neck. □ Look for bulging fontanel □ Look for runny nose □ Look for signs of MEASLES NOW: Generalized rash, And one of these: Cough, Runny nose or Red eyes. □ Blood Film or RDT Positive____ Negative____ Not Done ____	
If the child has measles now or within the last 3 months:	□ Look for mouth ulcers: If Yes, are they deep and extensive? □ Look for pus draining from the eye. □ Look for clouding of the cornea.	

Classify all Sick Young Infants for Very Severe Disease

Classify all sick young infants for bacterial infection. Compare the infant's signs to signs listed and choose the appropriate classification. If the infant has any sign in the top row, select VERY SEVERE DISEASE.

Here is the classification table for very severe disease.

SIGNS	CLASSIFY AS	TREATMENT* (Urgent pre-referral treatments are in bold print)
□ **Not feeding well, OR** □□□ **History of Convulsions/convulsing now, OR** □ **Fast breathing (≥60 breaths per minute), OR** □ **Severe chest indrawing, OR** □□□ **Fever (≥37.5°C* or feels hot), OR** □ **Low body temperature (< 35.5°C* or feels cold), OR** □ **Movement only when stimulated or no movement even when stimulated.**	VERY SEVERE DISEASE	• Give first dose of intramuscular Ampicillin and Gentamycin • Treat to prevent low blood sugar • Warm the young infant by skin-to-skin contact if temperature is less than 36.5°C (or feels cold to touch) while arranging referral • Advise mother how to keep the young infant warm on the way to the hospital • Refer URGENTLY to hospital

* consider malaria if the neonate lives in malaria risk area

LEARNING UNIT FIVE

Fever in Adults

Learning objectives

At the end of this training, participants will be able:

- Define acute fever
- List possible causes of fever
- List common reported caused of fever in Ethiopia
- Describe clinical approach (History, physical examination and investigation) to a patient with acute febrile illness
- List differential diagnosis of acute febrile illnesses
- Outline management principles of acute febrile illnesses

Definition

Acute fever is defined as a report of recent fever ($\leq$2 weeks) of elevated axillary temperature ($\geq$37.5°C). Acute fever can have different patterns although it may not strongly correlate with specific diagnosis. The pattern may not also be observed due to treatment with antipyretics. Pattern of acute fever can be

- Acute: for a short time (less than 2 weeks)
- Chronic: fever persisting for more than two weeks
- Intermittent: falls to normal in regular periodical intervals.
- Remittent: temperature always elevated but swings may be large
- Relapsing: short febrile periods between one or several days of normal temperature

When the result of a malaria test (RDT or microscopy) is positive for a patient with fever, the episode is considered to be malaria. When the result is negative, the fever is considered not to be due to malaria and is sometimes referred to as ‘non-malaria febrile illnesses’.

These definitions are suitable for the clinical management of patients and hence decisions on treatment. The national malaria guideline recommends that all patients with a positive malaria test result should be treated with an antimalarial medicine, while those with a negative result do not require such treatment. From the clinical point of view, all patients should be fully assessed, as they

may have more than one disease (e.g. malaria and pneumonia) and would require more than one treatment.

Health workers face the challenge to manage non malaria acute febrile illnesses when parasitological diagnosis is negative. To improve the compliance of health workers with malaria test results, guidance is needed on managing non-malaria febrile illness, especially in peripheral health care facilities. Improving the management of fever not only reduces unnecessary use of antimalarial drugs, but also ensures appropriate treatment and referral of patients with non-malaria febrile illness, thus reducing morbidity and mortality.

Causes of fever

The causes of fever can vary according to geography, season, the age and immunity of the patient and the level of care (outpatient, inpatient, ICU…). There is a wide spectrum of diseases that can cause fever which can be minor like upper respiratory tract infection or serious and life threatening like pyogenic meningitis. Priority should be given to identify the cause of the fever before instituting specific treatment.

The most common cause of fever is infection. Infection may be due to organisms such as viruses, bacteria, fungi or parasites. Fever may also be due to inflammatory processes in the body. Common and important conditions that are associated with fever, and their causative agents, include the following.

- Infections
    - Viral infections
- Main clinical manifestations: tonsillitis, laryngitis, pharyngitis, tracheitis, laryngotracheobronchitis (LTB or croup), bronchitis, bronchiolitis, pneumonia.
- Main viral agents: measles, mumps, chicken pox, varicella-zoster virus, hemorrhagic fevers (e.g. Ebola, Dengue, yellow fever), rhinovirus, influenza virus, HIV, hepatitis virus (HAV, HBV, HCV).
    - Bacterial infections
- Main clinical manifestations: tonsillitis, otitis media, sinusitis, dental abscess, pneumonia, urinary tract infection, pelvic inflammatory disease (PID), cellulitis, septic arthritis, osteomyelitis, meningitis, secondary syphilis, typhoid (enteric fever), relapsing fever
- Main bacterial agents: group A β-hemolytic streptococci, *Streptococcus pneumoniae*, *Mycobacterium tuberculosis*, *Haemophilus influenzae*, *Staphylococcus aureus*, *Mycoplasma pneumoniae*, *Klebsiella pneumoniae*, *Escherichia coli*, *Neisseria meningitidis*, *Treponema pallidum*, *Salmonella typhi*, *Salmonella paratyphi*, *Shigella* spp., *Borrelia recurrentis*.

- Rickettsial infections

- Louse borne typhus fever
  - Fungal infections
- Cryptococcal meningitis
  - Protozoan infections
- Malaria, leishmaniasis, amebic liver abcess
  - Helminthic infections
- Schistosomiasis,
- Noninfectious causes of fever: consider these after ruling out common infectious causes in the appropriate clinical situation
  - Inflammatory diseases: rheumatoid arthritis, auto-immune diseases.
  - Malignancy: lymphoma, acute leukemia.
  - Injury: crushing injury.
  - Thrombosis: pulmonary embolus, myocardial infarction (heart attack).
  - Drug reactions.
  - Allergic reaction.

According to the Health and health related indicators, 2007 E.C, acute febrile illnesses (AFI) are the leading causes of outpatient morbidity. Based on observations from the field most AFI patients are treated with ciprofloxacin and doxycycline considering typhoid and typhus fever. These are mostly patients with non-reactive widal and Weil felix tests; and negative blood film results. The other diseases among the top ten that have fever as main manifestation are acute upper respiratory infections (2^{nd}), pneumonia (3^{rd}), urinary tract infection (7^{th}), and falciparum malaria (10^{th}). There seems to be over diagnosis of typhoid and typhus due to the poor specificity of widal and weil felix tests that are used at most public and private institutions. A rational approach to fever diagnosis may reveal other pattern of ten top causes of morbidity.

Recently there is a report of dengue fever in Somali, Dire Dawa and Afar regions. There is evidence of Chikungunya virus presence in Ethiopia.

Table 10 The integrated disease surveillance report of 2007 EC

Disease	**Cases**	**Deaths**	**Case fatality rate (%)**
Typhoid fever	790,304	17	0.002
Typhus fever	183, 375	28	0.02
Relapsing fever	2958	33	1.1
Rabies	2684 (dog bite?)	53	

Dengue fever	190		
Yellow fever	0		

Globally there are very few studies that describe the pattern of diseases that cause fever in adults. In studies in northern United Republic of Tanzania (inpatients), Cambodia and the Lao People's Democratic Republic (outpatients) of non-malaria causes of fever (patients with ARI or other clinically documented local infections included), *Leptospira* was found in 10%, 13% and 12% of patients, dengue in 0%, 7% and 25%, typhus group rickettsioses in 1%, < 1% and 25%, spotted fever rickettsioses in 9%, 0% and 0%, and scrub typhus in 0%, 4% and 26%, respectively. In the United Republic of Tanzania, 8% of patients had Q fever, 5% brucellosis and 6% chikungunya

Principles of evaluation of a patient with fever

The following principles are important while examining a patient with fever.

- Observe the general condition of the patient, take vital signs and ask targeted questions to determine if there is any life threatening condition. Respiratory distress (use of accessory muscles, grunting, nasal flaring), very weak/unable to stand, lethargy, decreased level of consciousness, convulsions, severe abdominal pain and deranged vital signs (hypotension, rapid pulse or respiratory rate) indicate possibility of severe disease like severe malaria, severe pneumonia, pyogenic meningitis or sepsis. Such patients will require urgent lifesaving treatments.
- After ruling out the possibility of severe life threatening conditions (or initiating lifesaving managements for patients with severe disease), the next step is to determine if the patient has focus of infection by thorough history and targeted physical examination. Focus of infection is the organ or system which is affected by the infection and is believed to be the source/cause of the fever. For example, the lungs are the focus of infection in a patient with pneumonia.
- In addition, consider causes of acute febrile illnesses based on the epidemiology. Consider to test for malaria if the patient has malaria risk (lives in malarious area or has travel history to malarious area in the previous one month); typhus or relapsing fever if the patient has poor hygiene and visible body lice; typhoid fever if there is possible oro-fecal contamination; dengue or yellow fever or chikungunya or leishmaniasis if there is a risk (living in at risk areas or travel history). It is also good to consider possible exposure to certain pathogens e.g. contact to patients in meningitis, measles, chicken pox and dog or animal bite in rabies.

- Give attention to underlying conditions like HIV, diabetes, chronic respiratory or cardiac diseases, malignancies and malnutrition
- Unless the patient is in critical condition demanding emergency and empirical treatment, it is good to take the time to confirm the underlying cause of fever before initiating specific treatment.
- Patients should be followed to document response or detect complications after initiating treatment.
- Consider reporting to health program managers as most conditions causing acute febrile illnesses are reportable.

Clinical evaluation

History: the purpose of history taking is to

- Obtain a professional rapport with the patient and gain his confidence.
- Obtain all relevant information which allows assessment of the illness, and provisional diagnoses.
- Obtain general information regarding the patient, his background, social situation and problems. In particular it is necessary to find out how the illness has affected him, his family, friends, colleagues and his life.
- Understand the patient's own ideas about his problems, his major concerns and what he expects from the hospital admission, outpatient or general practice consultation.

Good communication skills are important to enable patients tell their stories with confidence, without fear or lie. Patients will most probably accept the recommendations of the health worker with regard to laboratory tests (e.g. if they don't require widal or weil felix tests), treatments (e.g. if they don't require antimalarial for negative malaria test; antibiotics for common cold) or behavior change advices (e.g. adherence to treatment). The following points highlight some good practices with regard to good communication

- Sit so that your head is in level with your client
- Maintain eye contact and pay attention
- Don't take note while talking to your client
- Don't act hurried
- Use open and closed ended questions, don't use leading questions
    - How are you feeling today? (open ended question)

- Do you have fever? (closed ended question)
- Are you taking your medicine properly? You are better today, aren't you? (leading questions)

- Show gestures that show interest like nodding
- Reflect back what the client says
- Avoid using judging (blaming) words
- Empathize, show that you understand how the client feels
- Listen carefully the patient, don't interrupt frequently

Identifying data (age, sex, occupation, and marital status) may help to consider some clinical conditions. For example malaria tends to be severe in children under five and pregnant women; a health worker may acquire relapsing fever from his/her patient.

Describe the chief and associated complaints of the patient according to onset, course, severity, timing, relation with meals, effect on sleep and normal daily activities and body location of the symptom.

There are group of symptoms that point to dysfunction to a certain system. For example cough, chest pain, shortness of breathing may indicate disease of respiratory or cardiovascular system. Urgency, frequency, dysuria and flank pain indicate disease of urinary system. Seizure, altered consciousness, paralysis, numbness or loss of sensation indicates disease of nervous system. The presence of symptoms that point to dysfunction of a certain system may suggest focus of infection.

Important features of the history

- duration of fever (less than or more than 7 days)
- exposure to locally endemic diseases
    - consider the local geographical distribution of diseases, e.g. malaria, dengue, leishmaniasis
    - consider outbreaks of specific infections, e.g. malaria, meningitis
    - consider seasonal variation of diseases
- recent exposure history
    - ask about recent travel – consider diseases that are common in the area that was visited
    - contact with animals and birds (brucellosis, rabies, Q fever)
    - known TB contact
    - recent unprotected sex (acute HIV syndrome, syphilis)
    - intravenous drug use

- co-morbidities
    - consider infections that a patient may be predisposed to as a result of comorbidities such as diabetes, HIV, chronic respiratory, cardiac or kidney diseases, cancer, malnutrition
    - medical history of recent illness and the possibility of incompletely treated disease or drug resistance, e.g. malaria, typhoid, TB;
    - current medications;
    - consider drug reactions if the patient has recently initiated a new medication known to commonly cause drug reactions, e.g. cotrimoxazole, ART (especially nevirapine or abacavir), TB medication.

Physical examination

All patients with fever should be examined, even if they don't report symptoms of local infection. Examine the patient thoroughly paying attention to sites of possible infection:

- general examination
    - monitor temperature (might be normal at that particular moment)
    - assess for confusion or decreased level of consciousness
    - assess hydration, count heart rate and respiratory rate
    - look for pallor, jaundice, lymphadenopathy, nail abnormalities (splinter hemorrhages)
    - skin lesions, including rash
    - insect or animal bites
    - nutritional status (wasting)
- head and neck
    - neck pain or stiffness
    - throat, tonsils, ears for inflammation and discharge
    - sinus tenderness
    - mouth (ulcers or lesions)
- chest and precordium
    - difficult breathing, fast breathing
    - crackles, bronchial breathing, absent breath sounds
    - new heart murmur, change in old murmur
- abdominal or genitourinary:

- enlarged liver or spleen
- abdominal tenderness or mass
- pain over kidneys (flank pain)
- pelvic tenderness or mass
- rectal and vaginal examination for pain, discharge, ulcers, mass

- muscles and joints
  - red, hot, swollen, painful joint(s) with reduced mobility
  - Swollen, painful limb (deep venous thrombosis, cellulitis).
- Nervous system
  - Level of consciousness
  - Meningeal signs,
  - Paralysis

If there is evidence of focal infection like pneumonia or UTI treat the patient as per the national standard treatment guideline.

Laboratory investigations

Laboratory tests are complementary to history and physical investigation to make appropriate diagnosis. They should be interpreted in line with the clinical presentation; e.g. reactive widal test does not indicate typhoid if the patient does not have fever.

For all patients, consider

- Malaria test (if the patient fulfils clinical criteria)
- Urinalysis
- Hemoglobin and WBC count

Additional tests, as indicated (see Differential Diagnosis tables in next Section):

- full blood count with differential white cell count
- blood smear for louse-borne relapsing fever (Borrellia recurrentis), in endemic areas
- liver function tests
- chest X-ray
- sputum for microscopy, acid fast bacilli, and sometimes culture
- urine culture
- lumbar puncture
- bone marrow, lymph node, or splenic aspirate for microscopy (leishmaniasis)

- serum or whole blood for rapid test
- stool microscopy (antibiotics should not be given for the mere presence of “many bacteria”)
- stool culture
- ultrasound
- Blood cultures.

Widal and weil felix tests are not recommended as per the existing scientific literature due to their lack of sensitivity and specificity. However these tests are still widely used in Ethiopia. These tests may be relevant under the following conditions

- The patient should have clinical features of typhus or typhoid (almost all patients with typhoid or typhus have fever)
- Tube titration (not slide agglutination) should be done
- Interpretation should be based on demonstration of four fold increase in antibody level after 7-10 days of first test; or single test which is above local cut-off value for that particular location. The limitation of using cut-off values is; usually these values are not available, and they vary with time in the same place and from place to place
- At the moment there is no good laboratory test for typhus and blood culture where available should be considered for typhoid

Consider likely differential diagnosis using Differential Diagnosis tables

Classify the fever according to its duration and symptoms or signs found on examination and laboratory investigations:

- fever with obvious focus of infection – treat accordingly as per the national standard treatment guidelines
- fever 7 days or less without clinically obvious focus (use the first Differential Diagnosis table below)
- fever more than 7 days (use the second Differential Diagnosis table below)
- For the severely ill patient – refer to severe malaria section.

Table 11 Differential Diagnosis: Fever 7 days or less without clinically obvious focus or site

Condition	In favor
Malaria	Living in, or travelled to malaria endemic area Positive malaria test (RDT or microscopy)
Typhoid fever	Remittent fever Malaria ruled out No focus of infection Risk factor for typhoid (poor hygiene)
Louse borne typhus fever	High grade intermittent fever Poor hygiene, may have visible body lice Malaria and relapsing fever ruled out Usually occur as epidemic
Bacterial sepsis	Seriously ill with no obvious apparent cause Hypotension Complete blood count (CBC) – leucocytosis, leucopoenia, or thrombocytopenia Risk factors – HIV, immunocompromised Blood cultures – positive Any sign of organ dysfunction – confusion, low urine output, respiratory depression Blood chemistry if available – acidosis, elevated creatinine
Meningococcal septicemia	Maculopapular hemorrhagic petechial rash Shock, hypotension
Dengue fever	History of travel to endemic area or local outbreak (e.g. Somali, Dire Dawa or Afar regions) Positive dengue RDT for non-structural protein 1 (NS1) or IgM Headache, pain behind the eyes Backache, arthralgia, myalgia Fine macular rash, petechiae CBC – leukopenia, thrombocytopenia In severe cases: • signs of plasma leakage, shock • severe bleeding, e.g. from GI or orifices, dark urine

Condition	In favor
	• organ failure
Chikungunya	Resembles non-severe dengue fever Severe joint pains with fever and rash No simple test available to confirm the diagnosis (PCR available at EPHI)
Influenza	Sudden onset of fever and cough Sometimes rhinitis or sore throat Frequent systemic symptoms (headache, arthralgia, or myalgia) Local epidemics, or history of travel to epidemic areas Close contact with a person with a similar illness, or contact with person from epidemic area with influenza
Yellow fever	History of travel to endemic area or local outbreak (Gambella, South Omo) Sudden onset of acute fever and rigors Headache, backache, bone pains Followed by jaundice within 2 weeks
Primary HIV	Lymphadenopathy Rash, pharyngitis History of unprotected sexual contact in the last 3 months HIV rapid test may be negative
Drug induced fever	New drug initiated days or weeks prior Associated rash Patient on drugs – ART (NVP, ABC, EFV) , cotrimoxazole, dapsone, B-lactams, INH, anticonvulsants
Measles in adolescents and adults	Conjunctivitis, coryza, and cough Koplik's spots on buccal mucosa ("grains of salt on a red background") Maculopapular, blanching rash Lymphadenopathy Complications include:

Condition	In favor
	• respiratory tract infection (pneumonia, tracheobronchitis, bronchiolitis) • encephalitis (acute and chronic) • keratitis
Relapsing fever	Recurrent fever Spread from person-to-person among louse-infested populations (e.g. prisons, refugee camps, street children, war, or famines with overcrowded populations with poor personal hygiene) Rash, often petechial Jaundice, impaired liver function Spirochetes on Giemsa-stained thick or thin blood fi lm, Jarisch-Herxheimer reaction (fever, rigors, hypotension within 2 hours of antibiotic administration)
Acute schistosomiasis (Katayama fever)	Exposure to fresh water in an endemic area (with sometimes skin itch just after exposure) Between 2 and 12 weeks after infection CBC – eosinophilia

Table 12 Differential Diagnosis: Fever more than 7 days without clinically obvious focus or site

Condition	In favor
Malaria	Living in, or travelled to malaria endemic area Positive malaria test (RDT or microscopy)
Typhoid fever	Remittent fever Malaria ruled out No focus of infection Risk factor for typhoid (poor hygiene)
Tuberculosis	Loss of weight, night sweats, fever, malaise Cough >2 weeks Signs of extrapulmonary disease – e.g. lymphadenopathy, pallor, abdominal pain Common complication of HIV

Condition	**In favor**
Osteomyelitis	Limb pain, tenderness and swelling Contiguous skin infection or chronic ulcer X-ray showing periosteal reaction or bone destruction (after 2 to 4 weeks)
Endocarditis	Low grade fever, night sweats New heart murmur (or change in old heart murmur) Signs of embolic disease (stroke, petechiae, splinter hemorrhage) Splenomegaly Risk factors: known cardiac valvular disease
Liver abscess	Right upper quadrant pain or tenderness Liver focal lesion at ultrasound
Yellow fever	History of travel to endemic area or local outbreak (Gambella, South omo) Sudden onset of acute fever and rigors Headache, backache, bone pains Followed by jaundice within 2 weeks
Lymphoma	Weight loss, night sweats Enlarged lymph nodes, hepatosplenomegaly
Visceral leishmaniasis	Endemic area Fever, wasting syndrome, pallor of mucous membranes Generalized lymphadenopathy Splenomegaly, darkening of skin

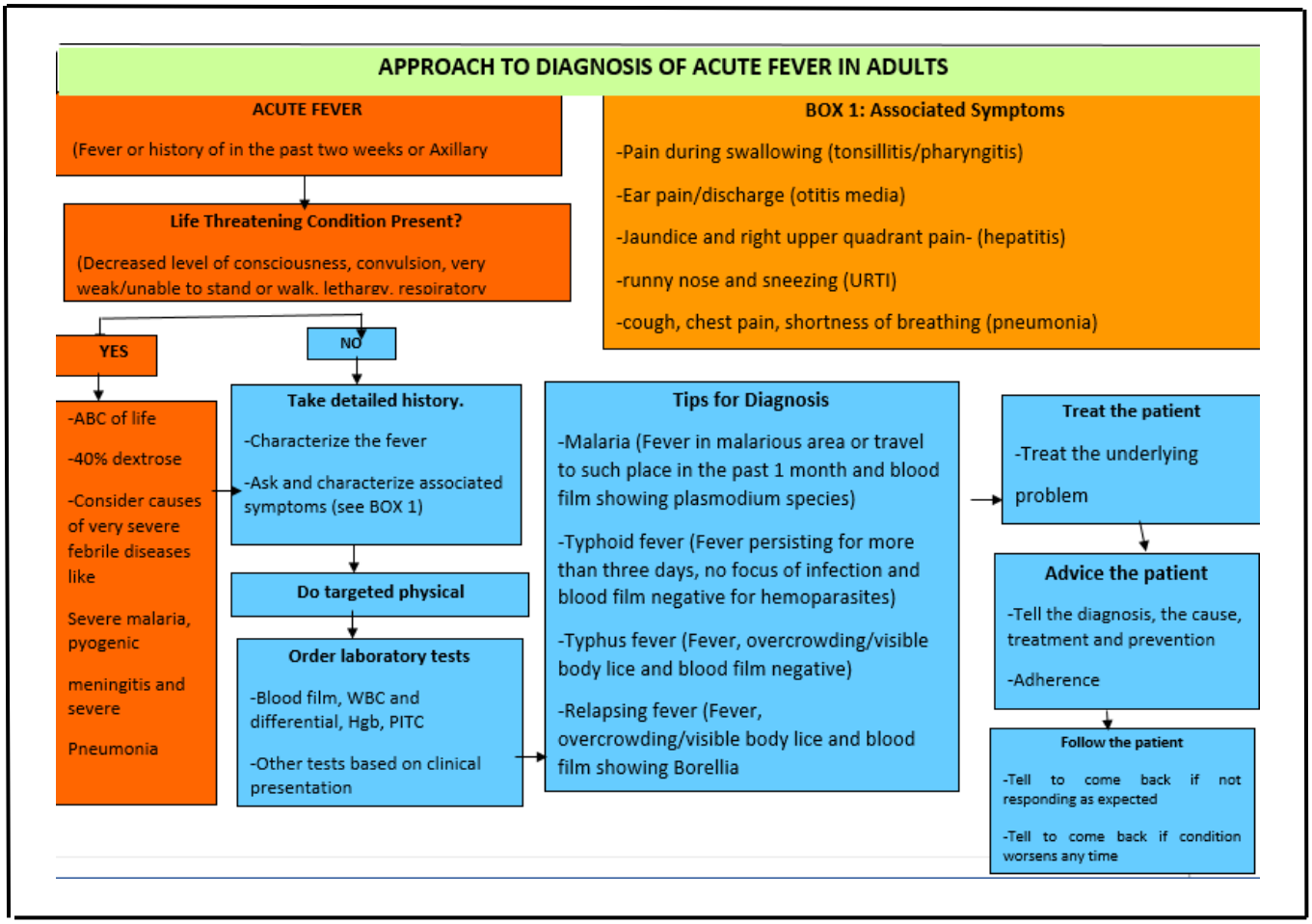


Figure 9: Approach to Diagnosis of Acute Fever in Adults

Management of fever Principles

1. As much as possible try to make specific diagnosis (with initial and subsequent evaluations if the patient doesn't have life threatening condition)
2. Definitive treatment (the underlying disease with specific treatment)
3. Symptomatic treatment of fever pain and dehydration
4. Educate the patient about the diagnosis, adherence to treatment, expected side effects, when to return (if fever does not improve or comes back after treatment; if the fever is accompanied by a cough, diarrhea, severe pain, confusion, stiff neck or change in consciousness)
5. Ensure adequate follow up

Some often-missed sites that may cause fever include:

- dental abscesses
- sinusitis – percuss face and forehead
- endocarditis – auscultate for murmur, if possible perform blood cultures

- urinary tract infection
- prostatitis and pelvic inflammatory disease
- intra-abdominal, retroperitoneal, or paraspinal abscess
- cholangitis, liver abscess
- deep venous thrombosis – examine for lower limb swelling
- malignancy – check for breast lumps, cervical nodes, splenomegaly, hepatomegaly, prostate abnormalities
- connective tissue diseases (e.g. lupus, rheumatoid arthritis)
- fever due to medications
- pus that cannot drain (after trauma)

Exercises: Group Work

- A 28 year old female Bank manager living in malaria endemic area came to you with fever of two days duration. She has arthralgia and myalgia. She had two episodes of vomiting.
    - What additional information will you ask her?
    - Physical examination showed, acutely sick looking woman, T^{o}=39.3^{o}C, left side costo vertebral angle tenderness. No other abnormal finding
- What is your differential diagnosis
- What laboratory test will you order? And what do you expect?
- What is the treatment for your most likely diagnosis?
- A 20-year-old man living in a malaria endemic area presents with a 1-week history of fever, headache, abdominal pain and constipation. He has a high temperature (39°C) and his spleen is palpable. He says the fever is worsening over time.
    - What additional information will you ask him?
    - What causes do you think of?
    - What laboratory tests will you order?
    - Write the complications for your first differential diagnosis
- A thirty year old man visited a health center because he had fever for three days. He lives in Addis Ababa. He gives history of travel to malaria endemic area three weeks back.
    - What additional history and physical examination will you check?
    - What laboratory tests will you order?
    - If blood film shows *P.falciparum* ring stage, outline the steps in the management of this patient
- A 22 year old male patient presented with high grade fever, head ache and vomiting of four days. On physical examination he is restless and talks irrelevant words. You find that he has stiff neck. History is obtained from his father.
    - What additional history will you ask?
    - What laboratory tests will you order?
    - How do you treat him?

LEARNING UNIT SIX

Severe Malaria

Learning objectives
By the end of this training, participants should be able to:

- Define severe malaria
- Discuss the host-parasite interaction that contributes to the pathogenesis of severe malaria
- List the determinants of severe malaria and identify groups at high risk
- Make a diagnosis of severe falciparum malaria
- Describe the recommended antimalarial chemotherapeutic regimens for severe malaria
- Specify the emergency and supportive measures and follow-up guidance for malaria patients with different types of complications

Diagnosis of Severe Malaria
Characteristics of severe falciparum malaria

Severe falciparum malaria is characterized by evidence of vital organ dysfunction. Severe falciparum malaria should be diagnosed if there are asexual forms of *P. falciparum* in a blood film from a patient showing any of the following clinical features or laboratory findings.

Clinical signs:

Impaired consciousness or unarousable coma (Glasgow coma scale < 11 for adults or Blantyre coma scale < 3 for children). Retinal hemorrhages are common in falciparum malaria comatose patients;

Prostration, i.e. generalized weakness so that the patient is unable walk or sit up without assistance (affected children are unable to feed);

Multiple convulsions – more than two in 24 hours;

Deep breathing, respiratory distress (acidotic breathing);

Circulatory collapse or shock, systolic blood pressure < 70mmHg in adults and < 50mmHg in children;

Jaundice with evidence of other vital organ dysfunction;

Abnormal spontaneous bleeding;

Pulmonary edema (presence of rapid breathing (>30 /min) with bilateral basal crackles in the lungs or radiological confirmed or oxygen saturation less than 90 % at room air).

Severe anemia (paleness of palms is most reliable symptom in children)

No urine output in the last 24 hours

Table 13 Glasgow Coma Scale

Parameter	**Response**	**Score**
Eye opens	Spontaneously	4
	To speech	3
	To pain	2
	Never	1
Best verbal response	Oriented	5
	Confused	4
	Inappropriate words	3
	Incomprehensible sounds	2
	None	1
Best motor response	Obeys command	6
	Localizes pain	5
	Withdrawal from pain	4
	Flexion to pain	3
	Extension to pain	2
	None	1
	Total score	3-15

A state of unarousable coma is reached at a score of <11. This scale can be used repeatedly to assess improvement or deterioration.

Table 14 The Blantayers Coma Scale (for children)

Parameter	Response	Score
Eye movements	Directed (e.g. follows mother's face)	1
	Not directed	0
Best verbal response	Appropriate cry	2
	Moan or inappropriate cry	1
	None	0
Best motor response	Localizes painful stimulus (rub knuckles on patient's sternum or firm pressure on thumbnail bed with horizontal pencil)	2
	Withdraws limb from pain	1
	Nonspecific or absent response	0
	Total score	0 - 5

A state of unarousable coma is reached at a score of <3. This scale can be used repeatedly to assess improvement or deterioration.

Laboratory findings:

Hypoglycaemia (blood glucose < 40mg/dl);

Metabolic acidosis (plasma bicarbonate < 15mmol/liter);

Severe normocytic anemia (Hb < 5g/dl, packed cell volume < 15%);

Haemoglobinuria; (Dark color of urine/ Cola color urine in the absence of haematuria)

Hyperparasitaemia (>2% of red blood cells parasitized or >100,000 parasites per microliter);

Hyperlactataemia (lactate > 5mmol/liter);

Acute kidney injury (serum creatinine 3 mg/dl or greater).

Note that:

- Each of the individual clinical features is important for the diagnosis of severe malaria;
- An individual patient may have any single complication or any combination of the complications listed above;

- A patient with one or more of the complications may go on to develop others;
- Other possible diagnoses in such a patient must be carefully considered.

Risk groups for severe falciparum malaria

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

Those most at risk are:

- People of all ages in areas of low endemicity (like most malaria endemic places in Ethiopia)
- Residents of areas where there is little or no falciparum malaria who travel to a high transmission area: this may involve travel within a single country or between countries;
- Non-immune pregnant women (at risk of some specific complications);
- Internally-displaced persons moving from an area of low transmission to an area of high transmission;
- Children in areas of high endemicity – especially those aged from 6 months to 5 years;
- People returning to highly endemic areas after a few years' residence in area with little or no falciparum malaria;
- Patients who have had a splenectomy.

Diagnosis of severe falciparum malaria

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

Both thick and thin blood films should be examined at health center or hospital level to demonstrate the presence of P. falciparum asexual parasites.

However, it is important to note that:

- Waiting for a blood smear result must not be allowed to delay the start of treatment unduly: if clinical features strongly suggest severe falciparum malaria, treatment may be started before the results are available.

- Occasionally blood films may be negative even though the patient is suffering from severe falciparum malaria. Following a negative result, blood films should be repeated, e.g. every 6 hours. Parenteral Artesunate may be initiated in such patients.
- A positive blood film does not prove that severe falciparum malaria is the only cause of the severe illness. Other possible causes should also be considered.

Pathophysiology of severe falciparum malaria

Mechanism of malaria disease

The possible effects of malarial infection cover an enormous range, from completely asymptomatic infection to severe fatal disease.

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

- The species of parasite. P. falciparum causes almost all cases of severe malaria. However, P. vivax is being increasingly recognized as a cause of severe malaria;
- The immunity of the individual. Adults who have lived all their life in an endemic area are less susceptible to severe disease than:
- Adults who visit an endemic area for the first time
- Young children living in the same endemic area
- Pregnancy
- The availability and efficacy of antimalarial medicines;
- The degree of parasite drug-resistance that prevails locally;
- HIV/AIDS, especially in pregnant women and those with advanced immune deficiency;
- **Some genetically inherited conditions in the human host, e.g. sickle-cell trait, s-thalassemia, and probably G6PD deficiency have a protective effect;**

How parasites cause severe disease

Microvascular obstruction of vital organs

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, lungs, heart, bone

marrow and gut. It seems likely that sequestration is involved in complications such as altered consciousness and acidosis, through pathophysiological mechanisms that are not fully understood.

Sequestration contributes to microvascular obstruction and mechanical obstruction causes hypoxia. In addition, sequestered parasites, which are known to be highly active metabolically, may use up vital substances such as glucose, so that these are not available to host cells, such as brain cells. The parasites may also release substances, e.g. lactate or toxins, free iron, and toxic oxygen radicals that are directly injurious to local host tissues.

It is thought that sequestration may also serve to concentrate schizonts in vital tissues. Rupture of schizonts may then stimulate the release of large quantities of cytokines locally with a powerful local effect even if cytokine levels in the general circulation are not particularly high.

Sequestration is due to

- Cytoadherence: is attachment of parasitized red blood cells to endothelial wall. Sequestration appears to be confined to P. falciparum and does not occur in P. vivax infection. At approximately 12–14 hours of development, P. falciparum parasites begin to exhibit a high molecular weight protein strain-specific to this variant – Plasmodium falciparum Erythrocytic Membrane Protein1 (pfEMP1) – on the surface of infected red blood cells which mediate attachment to vascular endothelium. This is associated with knob-like projections from the erythrocyte membrane. The red cells progressively adhere to the walls of venules and capillaries (cytoadherence) in vital organs, producing sequestration.
- Rosetting: There is also formation of ‘rosettes’ by un parasitized red blood cells within microvasculature. In vitro, a parasitized cell may attract unparasitized red cells which adhere to its surface to form a rosette.
- Agglutination: is the attachment of parasitized red blood cells with each other

Cytokines

It is possible, but still not proven, that excessive production of pro-inflammatory cytokines may cause severe disease in addition to fever. The cytokine TNF is known to be secreted by the individual in response to malaria. Large quantities of TNF circulate in severe falciparum malaria, especially in fatal cases, and TNF is known to be 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. The ratio of pro-inflammatory to anti-inflammatory cytokines has been observed to be high in fatal cases of malaria.

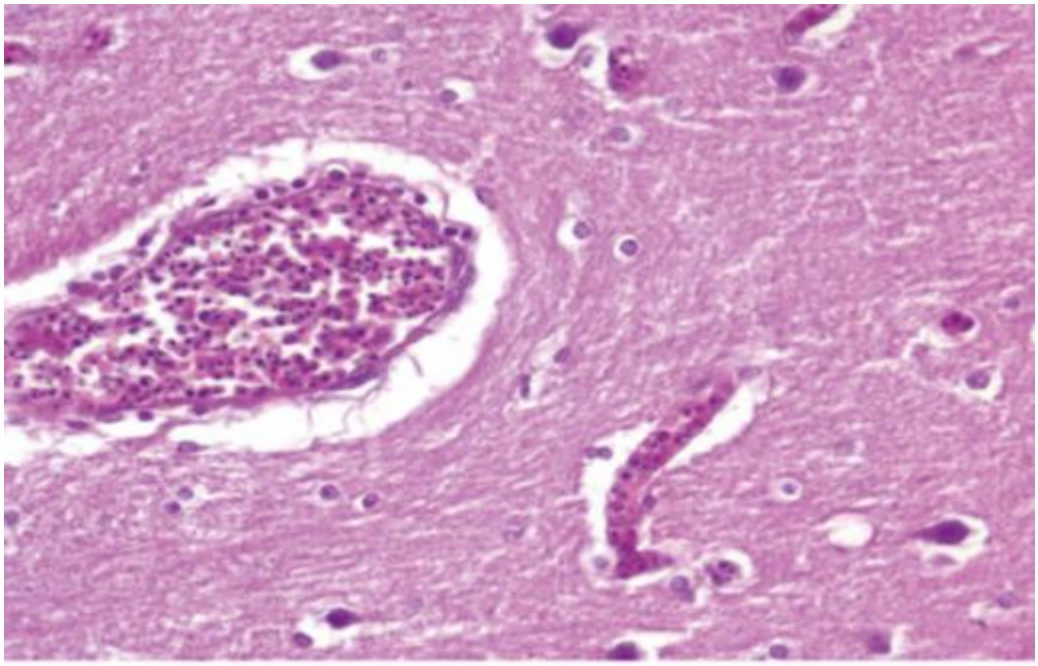


Figure 10: Brain tissue from a patient who died of cerebral malaria, showing microvascular sequestration of parasitized red blood cells in both capillaries and small venules, with mild perivascular edema around the larger vessels

Processes contributing to specific complications

Altered consciousness or coma

It is believed that altered consciousness or coma (cerebral malaria) is caused by sequestration of parasites in the brain. However, complete obstruction to blood flow is unlikely, since the survivors rarely have any permanent neurological deficit. Other processes like hypoglycemia, convulsion and concomitant CNS infections may cause or contribute to altered consciousness or coma.

Hypoglycaemia

Hypoglycaemia may be due to impaired production or release of glucose in the liver, and to increased intake in the tissues. There is also increased consumption of glucose by the parasite. In children, hypoglycaemia complicates other childhood infections in addition to malaria. Hypoglycaemia can also develop during prolonged fasting.

Another mechanism leading to hypoglycaemia, most commonly but not exclusively seen in pregnant women, may develop during the course of treatment with quinine infusion. These medicines stimulate the production of insulin which contributes to hypoglycaemia.

Convulsions

In relation to a convulsion, unconsciousness occurs both during the convulsion (ictal) and for a period of up to several hours after the convulsion (post-ictal). Convulsions may be due to the direct effect of parasites in the brain, or may result from accompanying metabolic disorders, e.g. hypoglycaemia, severe acidosis, hyponatraemia or hypoxia. A very high temperature may exacerbate any of these causes of convulsion, or may itself trigger a convulsion.

Raised intracranial pressure

The majority of children with cerebral malaria have a high opening pressure of the cerebrospinal fluid, indicating raised pressure in the brain and spinal column. The presence of high pressure may vary over time. It has also been observed in some adults. The cause of raised intracranial pressure is not clear, but it is probably largely due to cerebral edema. Additional contributing factors may include the increased mass of red blood cells sequestered in the brain, and the dilatation of vessels in the brain in response to mechanisms triggered by parasite sequestration and schizont rupture. Raised intracranial pressure **is not** the cause of coma or of death in the majority of cases. Therefore it doesn't need specific treatment like steroid or mannitol.

Anemia

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

Acidosis

Acidosis is probably due to a relative shortage of oxygen in tissues occupied by sequestered parasites. This shortage of oxygen is made worse when there is hypovolemia and/or severe anemia, as both of these conditions may impair the supply of oxygen to tissues. Lack of oxygen forces tissues to obtain energy by other biochemical pathways not dependent on oxygen; one result is the release of lactic acid, leading to metabolic acidosis. There is evidence that medicines containing salicylates, which are often given to lower the fever, may exacerbate the metabolic acidosis. Concomitant gram-negative septicaemia aggravates the acidosis.

Acute renal failure

Acute renal failure – acute tubular necrosis – is a common complication in adults, but is rarely seen in children. It is fully reversible if the patient is kept alive for long enough, usually between a few days to three weeks, e.g. by peritoneal dialysis. Renal failure is most likely to develop if there has been a period of low blood pressure or shock. Sequestration is also observed in the kidneys.

Pulmonary edema and acute respiratory distress syndrome

Pulmonary edema (non-cardiogenic) may result from excessive fluid replacement by intravenous infusion, especially if there is renal failure. Acute respiratory distress syndrome (ARDS) appears to be due to a direct effect of parasites sequestered in the lungs, possibly through release of cytokines. Both of these complications are unusual in children in endemic areas.

Hemoglobinuria

Hemoglobinuria results from the rapid breakdown of red blood cells in the circulation (massive intravascular hemolysis).

Jaundice

Jaundice is more common in adults than in children and is due partly to hemolysis and partly to liver dysfunction.

Shock

Shock is due to inadequate cardiac output and poor tissue perfusion. In some patients it may occur concurrently with bacteremia.

Bleeding disorders

In falciparum malaria, the platelet count is typically low. Nevertheless, spontaneous bleeding is rare in both children and adults. When it develops it results from disseminated intravascular coagulation (DIC).

Severe non-falciparum malaria

P. vivax and more recently *P. knowlesi* have been recognized as causes of severe malaria particularly in Asia and in certain forested areas of South-East Asia respectively. Severe vivax malaria may present with pathologies similar to severe *P. falciparum* malaria and can be fatal. Severe anemia, respiratory distress, multiple organ failure and impaired consciousness (cerebral malaria) occur in all age groups but the risk is greatest among young children and pregnant women.

Treatment of severe malaria

The main objective of treatment is to prevent the patient from dying; secondary objectives are prevention of recrudescence, transmission or emergence of resistance and prevention of disabilities. Special attention is required because severe falciparum malaria is a common cause of avoidable death and because correct early treatment and careful nursing can greatly improve the outcome.

The following special measures are indicated:

- Antimalarial medicines should be given parenterally if possible, under close supervision;
- Treatment should be undertaken in hospital if possible;
- Medicines that are ineffective and potentially dangerous should not be used.

Under ideal conditions the severely ill patient, especially one who is comatose, should be managed in an intensive care unit. Where this is not possible, as in most places in Ethiopia, the health worker has to provide emergency care. Meticulous nursing care can be life-saving, especially for the unconscious patient.

Immediate supportive treatment

In severe malaria, the patient has a number of life-threatening complication(s) which can be fatal if not urgently treated. Some of the most urgent measures that will be required are to:

- Start immediate resuscitation measures, paying particular attention to the airways;
- Establish an intravenous infusion, which is necessary to administer medicines and fluids;
- Correct hypoglycemia if present by infusing dextrose over a period of 3–5 minutes. This can be done by any one of the following procedures:
  - 4ml/kg of 10% dextrose given by slow intravenous infusion over several minutes in children;
  - 40–60ml of 40% dextrose given as intravenous bolus in adults;
  - where intravenous access is impossible, give sugar solution by nasogastric tube (NGT);
  - Re-check blood glucose 2–4 hourly during the course of treatment, particularly in comatose patients.
- Control convulsions: correct hypoglycemia if it is present and give rectal paracetamol if the temperature is above 39°C. If the convulsions continue for more than 5 minutes give diazepam by slow intravenous injection (0.15ml/kg body weight, maximum 10mg for adults). In children always calculate according to weight in order to avoid dangerous respiratory depression. Diazepam can be given intra-rectally (0.5–1.0mg/kg bw) only if injection is not possible. Monitor the breathing carefully. If the first dose of diazepam fails to control convulsions, a second dose may be given after 10 minutes. If seizures continue, give

phenytoin (18mg/kg infused over 20 minutes as a loading dose, followed by 2.5mg/kg twice daily for 48 hours). If you have given two doses of diazepam and seizures continue, and if phenobarbitone is the only additional anticonvulsant drug available, you may give phenobarbitone (15mg/kg IM or iv loading dose, then 5mg/kg daily for 48 hours), but extreme vigilance is necessary because these two drugs (phenobarbitone and diazepam) in combination may cause respiratory arrest - monitor breathing continuously and be ready to give assisted ventilation, by bag-and-mask if a manual ventilator is not available.

Continued supportive treatment

- Assess the patient's fluid requirements. The rate of infusion will be determined based on the degree of dehydration. Children with severe metabolic acidosis may benefit from a resuscitation bolus of fluid, preferably a plasma expander, e.g. normal saline. The usual route for fluid infusion is intravenous; if this cannot be achieved alternatives are intraosseous or nasogastric infusions. Intra-osseous infusion may be performed when there is life threatening hypovolemia, under strict sterile procedure.
- Reduce body temperature if greater than 39.5ºC to prevent convulsion. This is best done by giving paracetamol, by mouth if possible, alternatively by suppository. In addition, remove the patient's clothes and start tepid sponging and fanning from the sides or back of the patient. Relatives can help with this task.
- Consider the need for blood transfusion. The most common indication for blood transfusion is severe anemia (Hb < 5g/dl). Assess the patient's clinical condition rather than relying on the hematocrit and/or Hb level. "Does the patient need blood?" is a more important question than "What is the PCV/Hb?" If the patient's life is threatened by anemia-associated acidosis, or by shock, or the parasitemia is so high that a critical drop is predictable, packed cells (10ml/kg in children) or whole blood transfusion should be given urgently with frusemide as follows:
    - if the patient has spontaneous bleeding give whole fresh blood if available or a platelet transfusion if possible;
    - where blood is unavailable, give pre-referral treatment and refer the patient;
    - If the patient is unconscious, insert a nasogastric tube and start the procedures for management of the comatose patient.

- Decide whether to insert a urinary catheter. This is necessary if either acute renal failure or pulmonary edema is suspected, in order to guide fluid balance. Be cautious of catheter associated urinary tract infection
- Decide whether a central venous pressure line is to be set up. This is of most value where pulmonary edema is suspected, and may be useful in the patient with shock or impending renal failure. It requires the necessary facilities, sterile procedures, expertise and a sufficient number of trained staff to use it properly.
- Consider the need for intubation and mechanical ventilation if the necessary facilities are available.
- Consider antibiotics if there is a suspicion of concomitant bacterial infections.
    - Patients diagnosed with concomitant infections like pneumonia, UTI, meningitis
    - Patients suspected to have infections (shock which is not responding to fluid management, metabolic acidosis with hypotension especially if not responding to fluid management, comatous patients when CSF analysis is not possible)

Specific antimalarial treatment

After rapid clinical assessment and confirmation of the diagnosis, appropriate and correct regimen of parenteral antimalarial medicines should be administered to patients with severe malaria without delay. Patients with severe malaria should not be treated with oral medications. The Ethiopian national malaria guidelines recommendation for first line treatment for severe malaria at the health center and hospital level in order of priority is:

- Above 20 kg,: IV is preferable/IM Artesunate (2.4 mg/kg on time 0 (admission), 12h and 24h after admission, then if the patient can take orally and is improving change to full dose oral Artemether-lumefantrine. If the patient can't take Artemether-lumefantrine for any reason, complete treatment with seven days course of quinine tablets.
- For children under 20kg: The dose of Artesunate is 3mg/kg.
    - Artesunate reduces mortality in both adults and children, has fewer side effects and is easy to administer as compared to quinine infusion.
    - It is available in ampoules, containing 60mg anhydrous artesunic acid with a separate ampoule of 5% sodium bicarbonate solution.
    - Reconstitution: the vial of artesunate powder should be mixed with 1ml of 5% sodium bicarbonate solution (provided) and shaken 2–3 minutes for better dissolution. The solution should be prepared freshly for each administration and should not be stored. Then:

    - IV administration: add 5ml of 5% glucose or normal saline to make the concentration of artesunate as 10mg/ml and administer by slow infusion;
    - IM administration: add 2ml of 5% glucose or normal saline to make the concentration of artesunate as 20mg/ml. (See video on Artesunate preparation)
- IM artesunate (2.4 mg/kg on time 0 (admission), 12h and 24h after admission, then plan to change to full dose oral Artemether-lumifantrene. If the patient can't take Artemether-lumifantrene for any reason, complete treatment with seven days course of quinine tablets. The dose of Artesunate is 3mg/kg for children under 20 kg of weight or under 3 years of age).
- IM artemether (3.2mg/kg bw IM (loading dose) followed by 1.6mg/kg daily until the patient can swallow or 24 hours of treatment. Then change to full dose oral Artemether-lumifantrene. If the patient can't take Artemether-lumifantrene for any reason, complete treatment with seven days course of quinine tablets.)
- IV quinine infusion: 20mg salt/kg bw (loading dose) diluted in 10ml isotonic fluid/kg by IV infusion over 4 hours; followed by 8 hourly maintenance dose of quinine 10mg salt/kg bw over 4 hours, calculated from the beginning of the previous infusion, until the patient can swallow.
    - Rapid administration of quinine is not safe and may cause sudden death due to arrhythmia or refractory hypotension. Each dose of parenteral quinine must be given as a slow, rate-controlled infusion (usually diluted in 5% dextrose and infused over four hours). The infusion rate should not exceed 5 mg salt/kg body weight per hour. If it is possible, continuous infusion should be given.
    - For all patients with severe malaria, IV quinine infusion should be given at least for the first 48 hours. In patients requiring more than 48 hours of parenteral therapy, the quinine maintenance dose should be reduced by one-third to one-half (i.e., 5-7 mg salt/kg of body weight every eight hours). It is unusual to have to continue IV infusions of quinine for more than 4-5 days.
    - A loading dose of quinine should not be used if the patient received quinine within the preceding 24 hours or mefloquine within the preceding seven days.
    - Quinine is not given by subcutaneous injection.
    - Quinine is safe in pregnancy and in anemic patients, if the doses are carefully calculated by body weight.
- IM quinine: this is the last option in case of no Artesunate or Artemether, and IV access can't be established, and patient can't be referred. If for any reason quinine cannot be administered

by IV infusion, quinine dihydrochloride can be given in the same dosages by IM injection in the anterior thigh (not in the buttock). The dose of quinine should be divided between two sites – half the dose in each anterior thigh. If possible, for IM use, quinine should be diluted in normal saline to a concentration of 60–100mg salt/ml.

- Parenteral antimalarials in the treatment of severe malaria should be given for a minimum of 24 hours (48 hours for quinine), once started (irrespective of the patient's ability to tolerate oral medication earlier).

Pre-referral treatment

At Health Post level

The conscious patient:

- Give rectal artesunate at a dose of 10mg/kg for children under six years of age. Artesunate suppositories are currently available in 50mg and 200mg formulations. If the suppository is expelled from the rectum within 30 minutes of insertion, re-insert another dose and, especially in young children, the buttocks should be held together for 10 minutes to ensure retention of the suppository
- If high fever is present, give paracetamol or tepid sponging;
- Encourage fluid intake during the transfer; continue breastfeeding in young infants;
- Ensure that the referral form is completed with detailed information including:
    - Clinical presentation/patient's medical history;
    - Suspected diagnosis;
    - Any tests performed and results (RDT);
    - List of all drugs/medication given, route, dose and time of administration;
    - Reason for transfer.

The unconscious patient:

a. Ensure "ABC" Airway, Breathing and Circulation;

b. Show family members how to position the patient on side to ensure a clear airway is maintained;

c. Give rectal artesunate at a dose of 10mg/kg for children under six years as pre-referral treatment;

d. Do tepid sponging and give paracetamol suppositories for high fever if possible. This will prevent vomiting and convulsions;

e. Nurse the unconscious patient on alternate sides to protect the airway, prevent aspiration and avoid pressure sores.

At Health Center and Hospital levels

Give pre-referral treatment with IV/IM Artesunate, IM Artemether or IM Quinine. Provide the necessary supportive care (ABC, Treat high fever, prevent or treat hypoglycemia, coma care). Ensure that the referral form is filled with the necessary information (history, physical findings, laboratory results, drugs and fluids administered and reason for referral)

Continuing treatment and nursing care

Continuing care calls for close cooperation between medical and nursing staff. Proper nursing care of the unconscious patient, in an intensive care unit if available, is of utmost importance in patients with cerebral malaria. The patient must be turned every two hours and not allowed to lie in a wet bed. Particular attention must be paid to pressure points and the patient should be nursed on his/her side to avoid aspiration of fluids. Sufficient nutritional support is necessary for patients who have a prolonged illness.

Following are the parameters to be monitored on a routine basis:

- Level of consciousness (see Blantyre and Glasgow coma scales in Annex 1);
- vital signs: blood pressure, temperature, pulse rate and respiratory rate;
- Fluid input and output. Examine regularly for signs of dehydration or fluid over load;
- urine volume, color and specific gravity;
- Blood glucose;
- Parasitemia;
- Hemoglobin (Hb/Ht) if anemia is suspected to be worsening;
- Occurrence of convulsions;
- Uterine contractions and fetal heart rate in pregnant women.

A record chart should be kept on which the important complications of the patient's illness are summarized; the treatment prescribed, and all important observations are recorded at suitable intervals. The record chart is useful as a checklist to observe and follow all important parameters and not to overlook important ones which may cost the life of the patient.

A decision is taken on how frequently observations should be made; this should be as often as possible with the avail-able staff (e.g. every four hours), but will also 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.

Table 15 Management of Severe Malaria: Daily observation sheet (acute phase)

Date of admission: ____/____/____ **Time (h/min):** ____/____

Name of patient: _____

Record No. ____ Age: ____ Sex: ____ M☐ F☐ Weight ____ Medicines given before admission (including OPD) ____ ____		Hours									
		1			4				8			
	Real time (h) minutes											
Investigations done on admission	Temperature (2x/day) Pulse (2x/day)											
Parasite count ____	Respiratory rate (2x/day)											
Haemotocrit/Hb ____	Blood pressure (2x/day)											
Blood sugar ____	Glasgow/Blantyre coma scale (3x/day)											
Urine analysis ____												
Cerebral spinal fluid (CSF) ____	Convulsions (Y N)											
Blood group ____	Able to drink (Y N)											
	Able to sit (Y N)											
	Parasite count											
	Haemotocrit/Hb											
	Blood sugar											
	iv artesunate or quinine in mg											
	iv fluids – dextrose saline											
	Other medicines, e.g. iv diazepam/antibiotics											
	Urine volume											
	Blood transfusion											

							Hours							
12				16				20				24			

Different abnormalities may be noted during observation which should be managed based on the following table. The above follow up form and the following table should be available at health facilities as health workers' support tool to help them manage severe malaria.

Table 16 Appropriate actions for clinical and laboratory abnormalities

Regular observations	Possible abnormality	Appropriate actions
A. CLINICAL		
Breathing	Increased rate or difficulty Deep breathing in children	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, prop the patient up, give oxygen, IV frusemide 2–4mg/kg. Treat acidosis with normal saline and bicarbonate.
Body temperature	rectal temperature: > 40°C OR axillary temperature: > 39.5°C If temperature remains high or rises despite 24 hours of antimalarial therapy	Give paracetamol (rectal or oral) if not already given within past 4 hours. Tepid sponging and fanning. Aspirin can be given to adults (instead of paracetamol) but not to children. Reconsider your diagnosis, while continuing treatment.
Blood pressure (BP)	Falls: < 80mmHg systolic in an adult, and < 50mmHg in infants and children. In children, BP is not always reliable: check for peripheral perfusion, looking at nailbed refill.	Review fluid balance, urine output, quinine infusion rate and haematocrit. Give plasma or saline infusion if hypovolaemia is present. Look for haemorrhage. Take blood for bacteriological culture if facilities are available. Give broad spectrum antibiotic for possible sepsis.
Fluid balance (use input and output chart); weigh patients as accurately as possible. Catheterize if acute renal failure or pulmonary oedema is suspected.	Oliguria: < 17ml/hour in an adult or < 0.3ml/kg/hour in infants and children	Review adequacy of hydration and infusion. Correct deficit if necessary. Prevent or manage acute renal failure if suspected. Give fluid challenge 20ml/kg of normal saline with frusemide 2–3mg/kg. Dialysis if this fails.
Coma score	Deterioration	Immediately check blood glucose. Reconsider other diagnoses. Provide appropriate nursing care for the unconscious patient.
Convulsions (subtle convulsions can be easily missed)	These can recur, or develop for the first time during treatment. They may be due to malaria, to high fever, abnormal blood glucose levels, or electrolyte imbalance. **Convulsions often precede coma.**	Check rectal temperature; if > 39°C, manage as above. Check blood glucose and fluid balance; check electrolytes if possible as there is risk of hyponatraemia. Correct any imbalance; give anticonvulsant medicine. Maintain the airway. Treat promptly with IV or rectal diazepam or IM paraldehyde.
Prolonged bleeding from vein puncture sites or spontaneous haemorrhage	Disseminated intravascular coagulation (DIC)	Check bleeding time. Cross-match blood. Give whole fresh blood or platelet infusion as needed to correct blood loss and bleeding tendency.

Regular observations	Possible abnormality	Appropriate actions
B. LABORATORY		
Blood glucose	Falls < 2.2mmol/l (40mg/dl)	Review infusion; a child will become hypoglycaemic if deprived of glucose for more than 12–24 hours. Give IV 50% dextrose (1ml/kg) diluted with an equal volume of normal saline.
Packed cell volume OR Haemoglobin	Falls < 15% OR < 5g/dl	Cross-match blood: consider need for transfusion with whole blood or packed cells (10ml/kg). Repeat Hb or haematocrit at regular intervals.
Parasitaemia	Remains high for 2–3 days, or remains positive for > 5 days. Commonly remains at the initial level for 12–24h, even when medicines are fully effective, then falls.	Review adequacy of antimalarial medicine and dosage. Consider alternative or give an additional medicine. Artemisinin derivatives are so effective that exchange transfusion is usually unnecessary.

The following boxes indicate common errors in diagnosis and treatment of severe malaria

Errors in the diagnosis of severe malaria

- Failure to think of malaria in a patient with either typical or atypical illness
- Failure to elicit a history of exposure (travel history) – including travel within a country with variable transmission
- Misjudgment of severity
- Failure to do a thick blood film in a non-immune patient
- Failure to identify *P. falciparum* in a dual infection with P. vivax (the latter may be more obvious)
- Missed hypoglycaemia
- Failure to diagnose alternative or associated infections (bacterial, viral, etc.)
- Misdiagnosis making an alternative diagnosis in a patient who is actually suffering from malaria (e.g. influenza, viral encephalitis, hepatitis, scrub typhus, etc.)
- Failure to recognize respiratory distress (metabolic acidosis)
- Failure to carry out an ophthalmoscopic examination for the presence of papilloedema, and malarial retinopathy

Errors in the management of severe malaria

- Inadequate nursing care
- Errors of fluid and electrolyte replacement
  - failure to control the rate of intravenous infusion
- Delay in starting antimalarial therapy
- Use of an inappropriate medicine
  - ineffective antimalarial medicine
  - unjustified withholding of an antimalarial treatment
  - dosage of antimalarial medicine not correctly calculated
  - inappropriate route of administration
  - unjustified cessation of antimalarial treatment
  - failure to adjust the dose to prevent cumulative effects of antimalarial medicines
  - 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
  - failure to review antimalarial treatment in a patient whose condition is deteriorating
- Failure to elicit a history of recent intake of medicines
- Failure to identify or treat metabolic acidosis
- Unnecessary endotracheal intubation
- Unduly delayed endotracheal intubation (when it is indicated and possible)
- Failure to prevent or control convulsions
- Failure to recognize minor ("subtle") convulsions
- Failure to recognize and treat severe anaemia
- Delay in considering obstetrical intervention in late pregnancy
- Failure to recognize and manage pulmonary oedema
- Undue delay in starting peritoneal dialysis or haemodialysis
- Failure to pass a nasogastric tube to prevent aspiration pneumonia
- Failure to cover with antibiotics if the decision is taken to delay lumbar puncture

How to assess the patient's recovery

The records and observations will provide some indications of patient recovery e.g. lowering temperature, decreasing parasite count, and an improving coma score. In addition, the patient's ability to drink, eat, talk, sit, stand or walk should be recorded. When a patient has recovered, an assessment should be made of possible sequelae of the disease or the treatment. In particular you should:

- Perform a neurological examination: In particular, assess the patient's functional capacity to hold and use objects, ability to feed, the gait and posture. Try to determinate 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. Simple bedside measures can be used, especially for infants and children (e.g. does the child turn his/her head towards a noise? does the child watch the mother when she moves?). Use audiometry and vision charts if these are available.

Review and synopsis

When the patient is discharged, a discharge summary should be prepared of the events of the patient's illness, indicating the distinguishing features of the illness and the patient's responses to treatment. A discharge form to enter this information should be attached to the patients chart (card).

Key points

a. Severe malaria is a medical emergency requiring nursing, medical and laboratory staff to be alert at all times. Prompt action is especially important for high-risk groups such as young children and pregnant women.

b. Artesunate IV or IM should be used in preference to quinine IV or IM for the treatment of severe malaria.

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

d. Regular monitoring of the core temperature, respiration (rate and depth), blood pressure, level of consciousness and other vital signs is essential. These observations will make it possible to identify the late onset of important complications such as hypoglycaemia, metabolic acidosis, pulmonary edema and shock. Urine output should be recorded. Use checklist to follow your patient

e. Laboratory measurements should include regular checks on Hb, glucose, urea or creatinine (also electrolytes and arterial blood gases when possible).

f. A proportion of children who survive cerebral malaria have neurological sequelae which persist into the convalescent period.

Exercises

Picture quiz

The picture plates provided below are intended to help the participants to interpret physical signs of severe disease in children and adults, decide on differential diagnoses, and determine tests that need to be carried out.

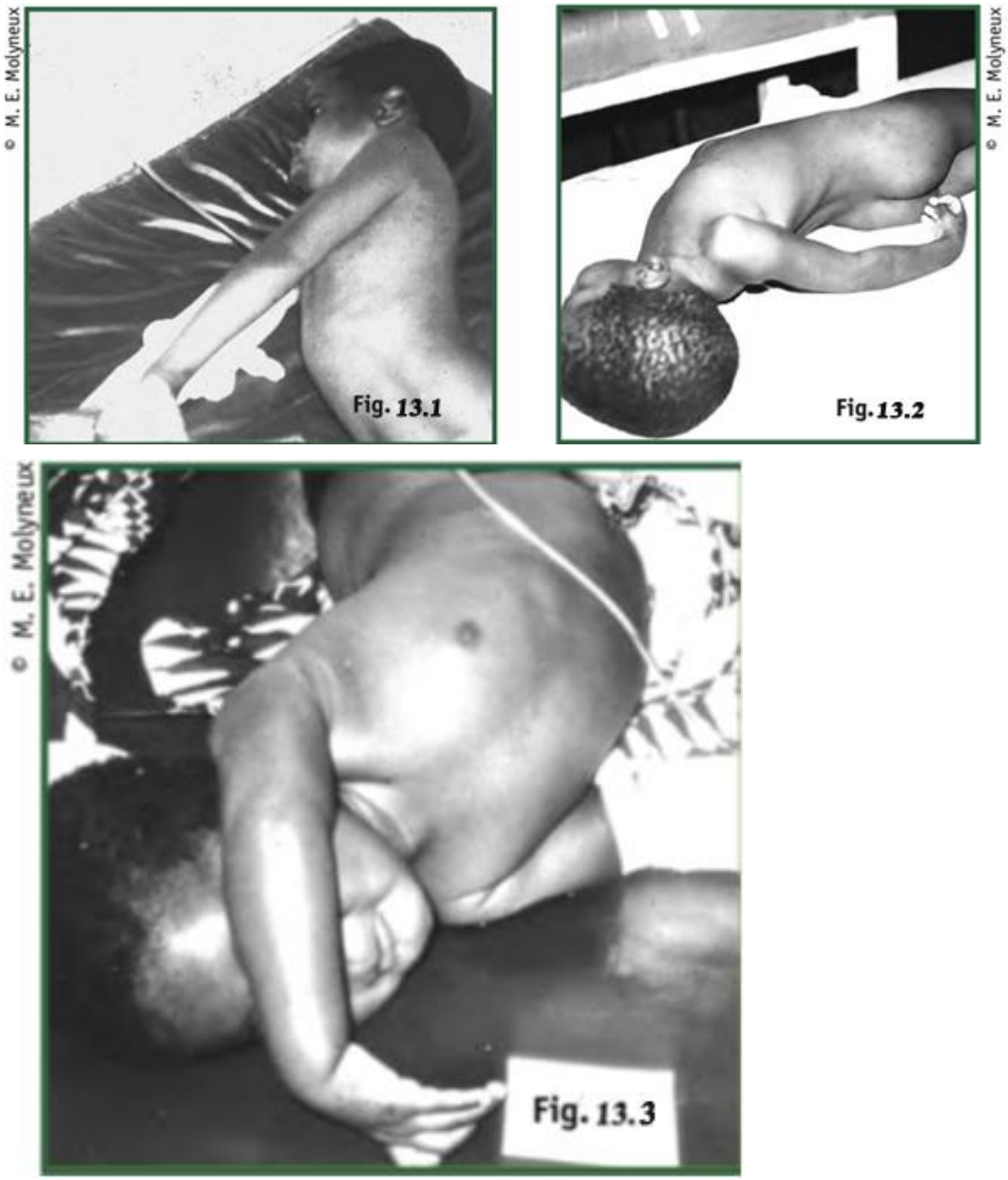


Figure 11: Pictures for questions 1-3

The children seen in Figures 13.1, 13.2 and 13.3 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 are 3 to 5 years old. They are febrile (axillary temperature: 38°*C*– 40 °*C*). They have been immunized against measles,
diphtheria, tetanus, and whooping cough through the EPI services.

Question 1: what do pictures 13.1-13.3 show?

Question 2: what is the differential diagnosis?

Question 3: what tests should be carried out?

The children seen in Figures 14.1 and 14.2 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 has been immunized against the common childhood diseases.

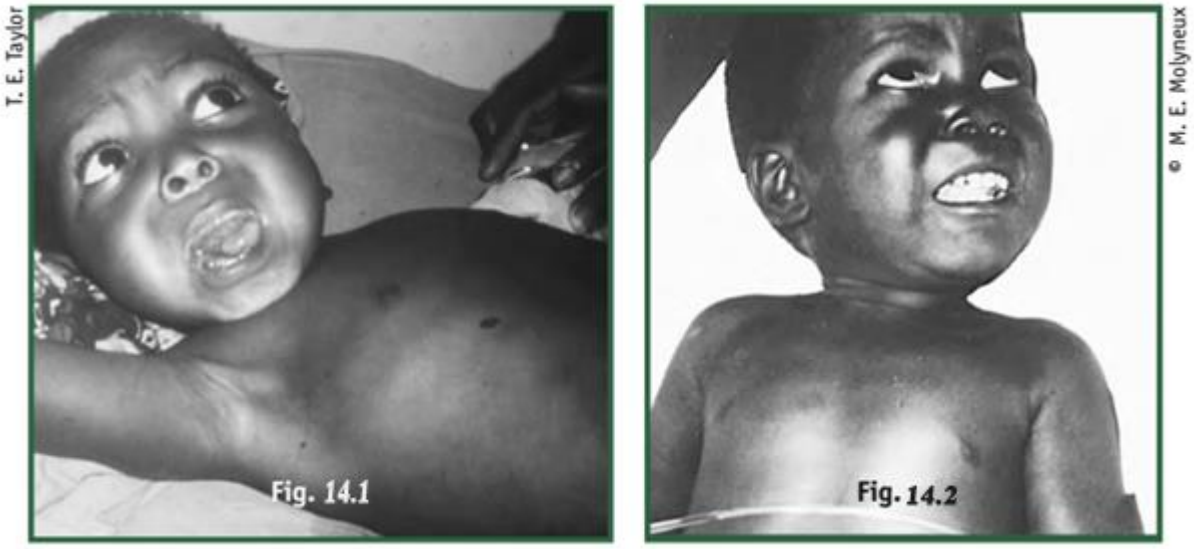


Figure 12: Pictures for questions 4 and 5

Question 4: what do the pictures seen in 14.1 and 14.2 show?

Question 5: what could be the explanation for this?

The patient seen in pictures of Figure 15 has *P. falciparum* malaria. She was admitted in coma, treated with quinine and recovered consciousness. Two days later she had a convulsion and collapsed into coma again.

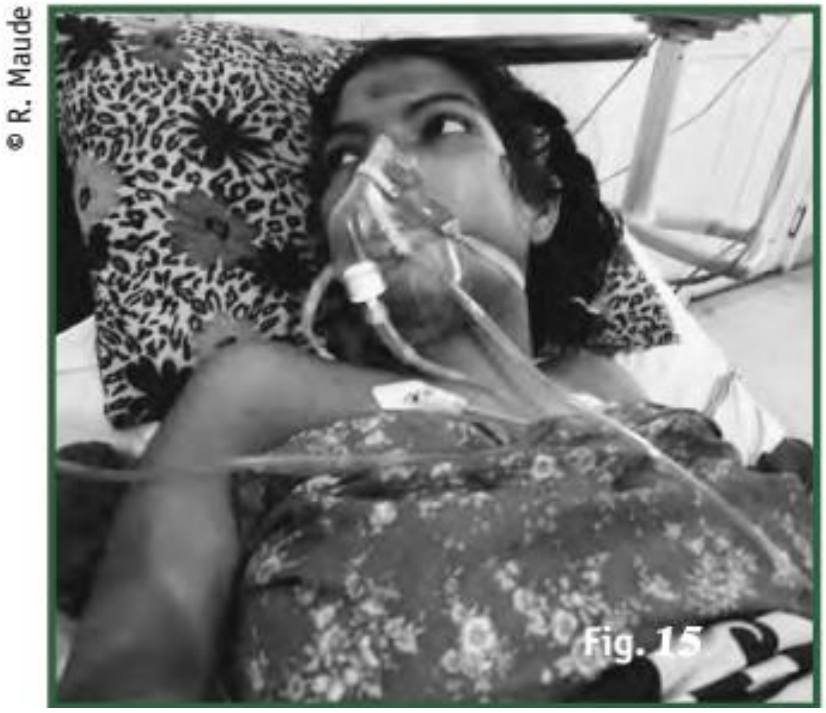


Figure 13: Picture for questions 6-8

Question 6. What are the possible causes of comma and subsequent convulsion?

Question 7. What investigations would you carry out to ascertain the causes?

Question 8. How would you manage this patient?

Figure 16. Shows the supportive treatment given to a patient with severe malaria

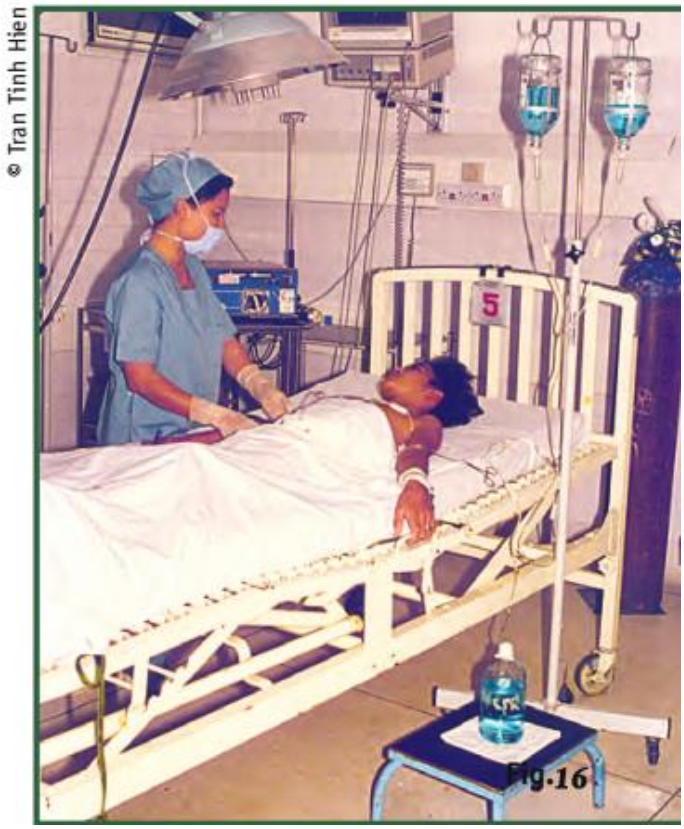


Figure 14: Picture for question 9-11

Question 9. What exactly does the picture seen in Figure 16 show?

Question 10. What is the most frequent complication in severe malaria that lead the physician to do this procedure?

Question 11. What are the complications to be feared in carrying out this procedure in rural hospitals?

Figures 17.1 and 17.2 refer to the clinical and radiological presentation of a woman soon after delivery. She has severe falciparum malaria with hyperparasitaemia and the condition shown in Figures 17.1 and 17.2 was preceded by difficulty in breathing with an increased respiratory rate.

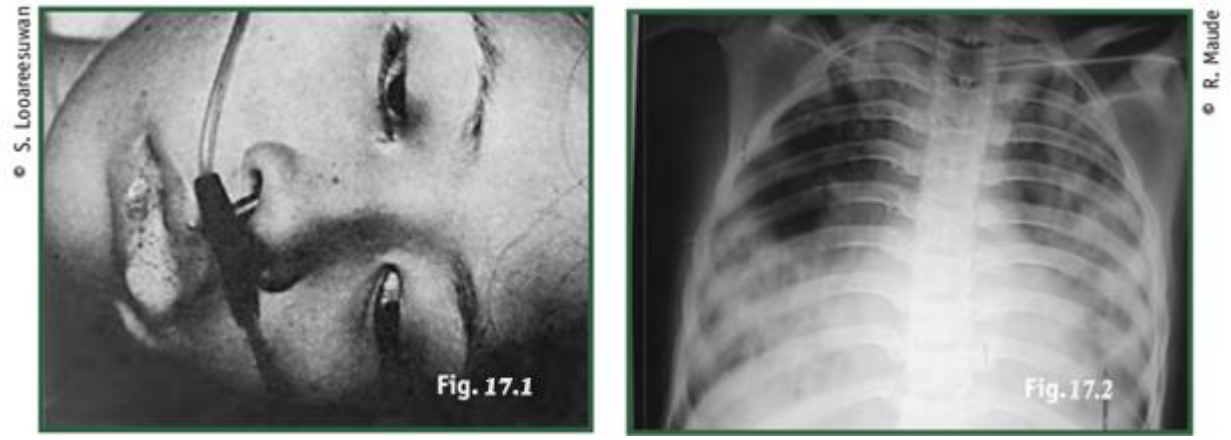


Figure 15: Picture for questions 12 and 13

Question 12. What is the condition suggested by these pictures?

Question 13. What is the differential diagnosis for this condition?

PATIENT A

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

The patient: 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 (28 weeks) 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 showed malaria parasites, and oral quinine (600mg 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 shows a semiconscious woman who is unable to speak. 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 rate 90/min, blood pressure 110/70mmHg. The uterine fundus is palpable (26–28 weeks), and the fetal heart can be heard.

Question 1

What tests are urgently required?

Question 2

If the blood glucose is 1.2mmol/l (22mg/dl) what treatment should be given?

Question 3

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

a. What antimalarial drug should be administered and by which route?

b. Should a loading dose of quinine be given? Justify your answer.

c. What nursing procedures are important during this treatment? d. In a health unit without facilities for parenteral therapy, what alternative treatment could be considered?

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 diagnostic steps should be taken?

Question 5

A chest X-ray gives the picture shown (Fig. 18). What is the diagnosis and treatment?

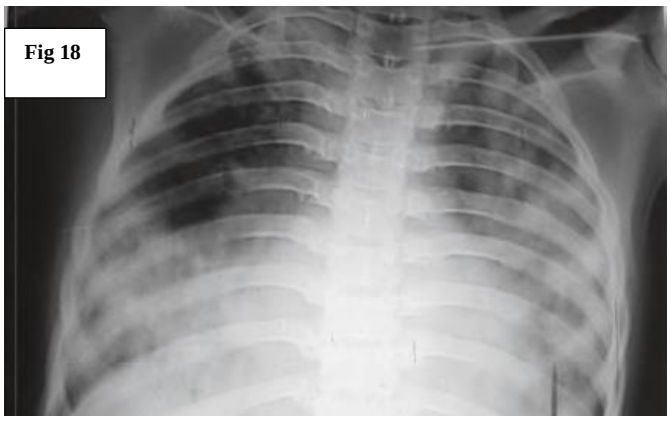


Fig 18

Figure 16: Chest X ray

Question 6

What other observations are particularly important in this patient?

Question 7

What other questions should this patient's relatives be asked?

PATIENT B

The place: A rural clinic in an area where P. falciparum is hyperendemic. Various antimalarial medicines are available, but intravenous infusions cannot be given.

The patient: 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 (39.3°C), conscious, and able to localize and respond to a painful stimulus. Malaria rapid diagnostic test shows a positive result for P. falciparum. The child repeatedly vomits any antimalarial medicine given by mouth.

Question 1

a. Does the child have cerebral malaria?

b. What should be done about the convulsions?

Question 2

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

a. Should the patient be referred to hospital?

b. What treatment should be given in the meantime?

Question 3

On arrival at the district hospital, the child was still unable to take oral medication and was admitted. A thick blood smear showed P. falciparum rings "++++" and he was given quinine IV. On the third day, there had been some improvement but the child was still febrile and the

parasitaemia reduced a little. *Does this suggest that the child has drug-resistant malaria?*

Question 4

The child was able to feed and take oral medication on the third day.

Should the parenteral treatment with quinine be continued?

Question 5

On completion of the treatment, a further blood test showed gametocytes "+". *What should be done about the gametocytes present in the blood after treatment?*

PATIENT C

The place: A country where P. falciparum is hyperendemic.

The patient: A male economist aged 28 years, 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 malaria-endemic 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 called the doctor today 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 with a rectal temperature of 36.5°C. He was restless but could give 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 both eyes.

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* rings "++++" and the thin blood film shows that 26% of red cells are parasitized.

a. What else should be looked for in the thin blood film?

b. What other tests are necessary 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

15ml of dark brown urine was obtained by catheter. The urine 'stix' tests showed albumin "++", blood "++++", conjugated bilirubin "++", urobilinogen "++". Microscopy of the urine showed no cells and a few casts.

How are the results of the urine test to be interpreted?

Question 5

Acute renal failure is confirmed.

a. Is it possible that the kidneys may recover?

b. What therapy should be given to this patient with acute renal failure?

PATIENT D

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

The patient: A woman aged 19 years 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 with an axillary temperature of 39.1°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

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

b. Could the doctor have done better with:

i. *The history?*

ii. *The investigations?*

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-cell crisis, relapsing fever and cholecystitis. Malaria was ruled out because she was not febrile. 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 showed scanty *P. falciparum* parasitaemia. Tis was considered "probably incidental" because low-grade parasitaemia was common among young adults in the area.

a. What errors were made in clinical judgment?

b. What errors were made in the treatment of the patient?

Question 3

The next day the patient was increasingly febrile and the parasitaemia had increased. The parenteral artesunate (IV or IM), the preferred antimalarial medicine for the treatment of severe malaria, was out of stock. Therefore, quinine 20mg base/kg was given intravenously to run 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. Twelve hours later 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?

LEARNING UNIT SEVEN

Malaria in Special Groups

Learning Objectives

By the end, participants should be able to:

- Describe the relationship between malaria and pregnancy and lactation
- List measures to prevent malaria during pregnancy
- State the recommended therapeutic regimens for the treatment of uncomplicated and severe malaria during pregnancy and lactation
- Describe the prevention of malaria during pregnancy
- Describe the effect of malnutrition on malaria
- Describe the effect of HIV on malaria

Malaria in Pregnancy

The symptoms and complications of malaria in pregnancy vary according to transmission intensity and the level of acquired immunity. Pregnant women living in areas of low or unstable malaria transmission (like many malarious areas in Ethiopia) have little or no immunity to malaria, and are at higher risk of developing severe malaria than are non-pregnant adults living in the same area.

In these areas, malaria is a major cause of maternal anaemia, spontaneous abortion, stillbirth, premature delivery, low birth weight (birth weight < 2.5kg), neonatal death and maternal death. In non-immune women, severe malaria symptoms (hypoglycaemia, cerebral malaria, and pulmonary oedema being particular problems) are more common in pregnancy.

In stable transmission settings, the deleterious impact of malaria is particularly apparent in first and second pregnancies. Partial clinical immunity acquired during years of exposure to the malaria parasite prior to pregnancy does not prevent infection, but does reduce the risk of severe disease. Clinical malaria is not, therefore, a prominent feature of infection during pregnancy, and the major detrimental effects of infection are low birth weight (LBW) and maternal anaemia.

HIV infection impairs pregnant women's ability to control *P. falciparum* infection. Women with HIV infection are more likely to have symptomatic malaria infections and to have an increased risk of an

adverse birth outcome due to malaria. In the presence of HIV infection, placental malaria appears to be independent of the number of pregnancies, so that the risk of placental malaria is similar in HIV-infected multigravidae and HIV-negative primagravidae.

Severe anaemia, exacerbated by malaria, is an important complication of pregnancy in many tropical countries. Especially in communities where chronic hookworm anaemia is prevalent, high output anaemic cardiac failure may develop in late pregnancy.

Asymptomatic hypoglycaemia may occur in pregnant women with malaria before antimalarial treatment, and pregnant women with uncomplicated or severe malaria are particularly vulnerable to quinine-induced hypoglycaemia.

There is an increased risk of pulmonary oedema precipitated by fluid overload or by the sudden increase in peripheral resistance, or autotransfusion of hyperparasitaemic blood from the placenta which occurs just after the delivery

Treatment of uncomplicated malaria in pregnancy

Pregnant women with symptomatic acute malaria are a high-risk group, and require effective antimalarial medication. There is insufficient information on the safety and efficacy of most antimalarial medicines in pregnancy, particularly for exposure in the first trimester, and treatment recommendations differ from those for non-pregnant adults. Therefore as a standard practice for the administration of any medicine pregnant women, all women of child-bearing age should be asked whether they are, or could possibly be, pregnant before an antimalarial medicine is prescribed. The following are the antimalarial medicines recommended for the treatment of uncomplicated falciparum malaria during pregnancy:

- In the first trimester, give a 7-day course of quinine. Artemether-lumefantrine (AL) is not recommended as routine treatment in early pregnancy because its safety has not been fully established. AL is indicated only if (i) it is the only treatment immediately available, (ii) if treatment with 7-day quinine fails, or (iii) if there is uncertainty about the patient's compliance with a 7-day course of treatment.
- In the second and third trimesters, give AL.

For the treatment of vivax malaria in pregnancy,

- chloroquine, which is the treatment of choice for *P. vivax* (chloroquine-sensitive), *P. ovale* and *P. malaria,* is safe in pregnancy.
- Primaquine is contraindicated during pregnancy

Treatment of severe malaria in pregnancy

A pregnant woman with severe malaria should be given a parenteral antimalarial medicine in full doses without delay. Parenteral artesunate is more effective than parenteral quinine in reducing the risk of death from severe malaria.

Although safety data on the use of artemisinins in the first trimester are limited, saving the mother's life is the primary objective. Therefore artesunate (IV or IM) is the preferred drug for all severe forms of malaria in all trimesters of pregnancy. IM Artemether is the second option while Quinine (IV or IM) may be considered as the last option. After 24 hours of parenteral drug administration, treatment should be completed with full dose of AL in the second and third trimesters and quinine tablets for seven days during the first trimester

The amount of antimalarial drugs passed into breast milk and consumed by the breast feeding infant is very small, so the treatment is the same as the non-pregnant adults except primaquine should be avoided.

Prevention of malaria during pregnancy

Pregnant women should be given priority in LLIN utilization. Intermittent preventive treatment of malaria during pregnancy (IPTp) is recommended in high transmission areas, however it is not recommended in Ethiopia

Malaria and Malnutrition

- Malaria and malnutrition frequently coexist.
- Malnutrition may result in in accurate dosing if we use age or weight of the child.
- Different conditions may hamper the absorption of anti-malarial drugs if given orally or parenteral, e.g. Chronic(persistent) diarrhoea, vomiting, rapid gut transit or atrophy of the small intestine villi (enteropathy)
- Diminished muscle mass may also make repeated intramuscular injection difficult.
- Hypoalbuminemia may also lead rapid clearance of the drugs as some drugs need albumin for binding.
- Although these findings are concerning, they are insufficient to warrant dose modification of any anti-malarial drugs in a patient with malnutrition, however, their response to treatment should be monitored more closely.

Malaria and HIV

- There is geographical overlap between malaria and HIV, and many people are co-infected.
- Worsening HIV related immunodeficiency may lead to manifestation of severe malaria
- In areas of stable malaria transmission patients have more frequent and higher density infection due to partial immunity while in unstable transmission area, HIV infection is associated with increased risk for severe malaria and malaria related death.
- Early studies suggested that HIV related immunosuppression was associated with decreased response to anti-malarial drugs but now there is insufficient information to change the drugs and dose of anti-malarial drugs we used for non HIV infected individuals**.**

Malaria and TB

- There are evidences that show patients taking Rifampicin with quinine, ACTs and mefloquine have a three to nine fold decrease of the anti-malarial drugs in the serum as well as higher recrudescence rate.
- However, there is insufficient evidence to change the drug and dosing in patients who are taking anti-TB drugs.
- But these patients are at higher risk of recrudescent infection, they should be monitored closely.

LEARNING UNIT EIGHT

Malaria Laboratory Diagnosis and Quality Assurance

Learning objectives

At end of this training, participants should be able to:

- Describe the different methods used for diagnosing malaria
- Explain the significance of microscopy and RDT in malaria control
- Explain the principle and general procedure of microscopy and RDT
- Describe the significance of performing microscopic thick and thin blood film slides
- Describe the principles of Quality assurance of malaria laboratory diagnosis
- Describe activities of External Quality Assessment (EQA) schemes of malaria laboratory diagnosis

Clinical Diagnosis

A clinical diagnosis entails making a clinical assessment by taking an accurate history of the illness and performing a physical examination. Clinical diagnosis of malaria is made in a patient who has fever or history of fever in the last 48 hours and lives in malaria-endemic areas or has a history of travel within the last 30 days to malaria-endemic areas. Basing the diagnosis on clinical features alone is not recommended, as this often has low specificity and increases the chances of the patient being misdiagnosed.

Parasitological Diagnosis/ Laboratory Methods

Laboratory diagnostic methods can be classified in to two:

- Routine lab diagnostic methods (Microscopy & Rapid Diagnostic Testing/RDT)
- Advanced diagnostic methods
    - Quantitative Buffy Coat /QBC/test
    - Microscopy using fluorochromes
    - Polymerase chain Reaction/PCR/
    - Serology: Ab detection
    - Flowcytometry

Microscopic diagnosis and RDTs are the routine methods employed for confirmation of malaria etiology in Ethiopia. Confirmed malaria is suspected malaria confirmed with microscopic diagnosis or RDTs for plasmodium parasites.

Benefits parasitological diagnosis:

- Rational drug use and hence cost saving
- improved patient care in parasite-positive patients owing to greater certainty that the patient has malaria;
- consideration and searching for alternative diagnoses on identification of parasite-negative patients;
- prevention of unnecessary treatment with antimalarials, thereby reducing side-effects, drug interactions and selection pressure;
- improved health information;
- Confirmation of treatment failures.

Malaria microscopy

Microscopy has a high degree of sensitivity and specificity when performed well. In addition, it allows quantification of malaria parasites and identification of the infecting species. It is inexpensive and considered to be the "Gold standard" against which the sensitivity and specificity of other methods must be assessed.

Quality of microscopy is ensured by supporting laboratories to perform internal quality control, performing external quality assessment especially using the blinded rechecking, proficiency testing methods and by continuous quality improvement. Quality microscopy will provide reliable result and will help to build the trust of clinicians on laboratory results.

Light microscopy has important advantages:

- Low direct costs, in areas of high turnover, if the infrastructure to maintain the service is available
- High sensitivity if the quality of microscopy is high
- Differentiation between plasmodia species and the stage of the parasite
- Determination of parasite densities
- Can be used to diagnose many other conditions.

Type of blood films

There are two types of blood films, thin and thick blood film. Both thin and thick blood film should be prepared on a single microscope slide. Giemsa stain is the best stain for identification of malaria parasites. It stains cells and blood parasites (e.g. malaria, Borelliae, trypanosomes etc.). Malaria parasites are identified by microscopic examination of thick and thin blood films stained with Giemsa stain. Other stains that can be used to stain blood film are Wright's stains, Fleishman's stain, and Field's stain. Thick smears are more sensitive for detecting the presence of parasites, and thin smears can provide more details for species determination. An adequate amount of time must be spent to analyze multiple forms and to determine if there is a mixed infection.

Types and characteristics of thin and thick blood film:

Thick smear

- Lysed RBCs
- Many layers
- Large volume
- Good screening test
- Low density infection can be detected
- More difficult to diagnose species

Thin smear

1. Fixed RBCs
2. Single layer
3. Smaller volume
4. Good species differentiation
5. Low density infection can be missed

Slide examination

- Giemsa stain thick blood smears are the basis for microscopic diagnosis with a standard of looking at 100 fields.
- The limit of detection is usually 5-10 parasites per µl of blood. If blood film is negative, look for other causes of fever.

Parasite density

In addition to definitive diagnosis of malaria and differential diagnosis of the species of malaria parasites, microscopic examination also enables their number in a unit volume of blood to be determined. Knowledge of the degree of parasitaemia may be of diagnostic and prognostic value in the case of severe *P. falciparum* malaria infection and also helps in following up the changes produced by treatment and also helps to measure therapeutic efficacy of antimalarial drugs.

Methods of counting malaria parasites:

- % of parasitized RBC (thin film)
- Number of parasites/µL of blood (thick film)

- Number of parasites/µL of blood (thin film)
- Semi quantitative count /Plus system (thick film)

The semi quantitative (plus) system should be used only when it is not possible to undertake the more acceptable parasite count per µl of blood.

Malaria Rapid Diagnostic Testing

Malaria RDTs detect antigens from the malaria parasites in blood using an immunochromatographic process. An antigen-antibody reaction leads to a visible colour change that indicates a positive test result.

These tests use finger-stick or venous blood, take only few minutes, and do not require a laboratory, electricity, or any special equipment.

Currently multi-species RDTs capable of specifically detecting both P. falciparum and P. vivax, are being supplied by FMOH /PFSA. Malaria RDT is recommended to be used in the health posts.

Basic Principles of RDTs

Rapid diagnostic tests are immune-chromatographic tests that detect specific parasite antigens mainly Histidine Rich Protein 2 (HRP2) or *Plasmodium* lactate dehydrogenase (*p*LDH). *Plasmodium* aldolase is another antigen that is used in some tests. Some RDTs can detect only one species (*Plasmodium falciparum)* while others detect one or more species of malaria parasites that infect humans. Antigens detected by currently used RDTs are:

1. Histidine Rich Protein II (HRP-2): is a protein produced by trophozoites and young gametocytes of *P. falciparum*. A substantial amount of HRP 2 is secreted by the parasite in to the host bloodstream and the antigen can be detected in erythrocytes, serum, plasma, cerebrospinal fluid and even urine as a secreted water-soluble protein. Tests based on HRP-2 detect only *P. falciparum.* HRP-2 has been shown to persist and may be detectable for more than a month after clinical symptoms of malaria have disappeared and parasites are cleared from the host. HRP-2 based tests are relatively more stable at high ambient temperatures and humidity, and usually less costly.

2. Plasmodium Lactic Acid (Lactate) Dehydrogenase (pLDH): is produced by both trophozoites and gametocytes of malaria parasites. The *p*LDH antigen is present in and released from parasite-infected erythrocytes. pLDH is found in all 4 human malaria species, and different isomers of pLDH

for each of the 4 species exist. Currently available *p*LDH RDTs detect *p*LDH specific to *P. falciparum*, *P. vivax* or are pan-specific detecting all *Plasmodium* species that infect humans. Some pLDH RDTs are specific for *P. vivax*. Since *p*LDH is disappeared from the circulation within five days of successful antimalarial therapy, this test has the ability to differentiate untreated from treated malaria, and may therefore be used for patient follow up, although *p*LDH is also produced by gametocytes. Tests based on *p*LDH are less stable at high ambient temperatures and humidity, and are more costly.

3. Plasmodium aldolase: is an enzyme produced in the glycolytic pathway by all species of human Plasmodium parasites (pan-specific) and has been used in a combined 'P.f/P.v' immune-chromatographic test. Tests that detect aldolase appear to be less sensitive than tests that detect the other parasite products. Aldolase behaves in much the same way as *p*LDH.

The various RDTs appear to be similar; they vary considerably in their functioning due to the intrinsic character of the critical components employed and their final result.

Mode of action malaria RDT

Lateral flow antigen-detection tests, which rely on the capture of dye-labeled antibodies to produce a visible band on a strip. The dye-labeled antibody first binds to a parasite antigen, and the resultant complex is captured on the strip by a band of bound antibody, forming a visible line (test line). A control line gives information on the integrity of the antibody-dye conjugate (See figure 1)

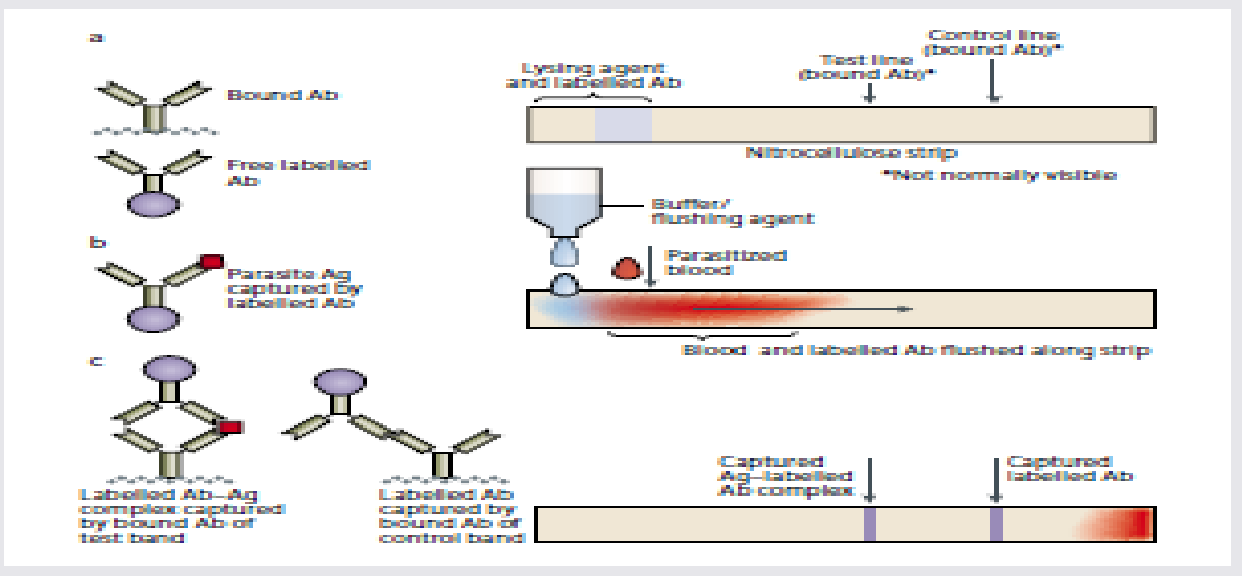


Figure 17: Mode of action malaria RDT

Procedure of RDT (e.g. Care Start test kit)

Content of test kit are:

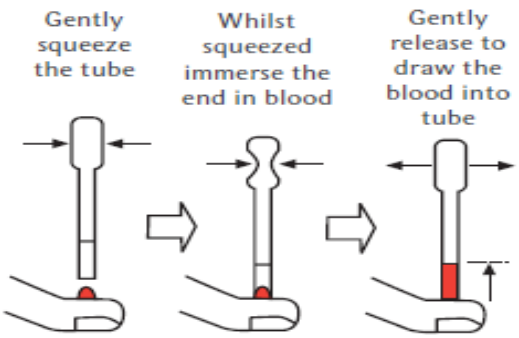
- Test device
- Assay buffer
- Pipette/dropper
- Alcohol pads
- Lancet
- Procedure card

Materials required while doing RDT

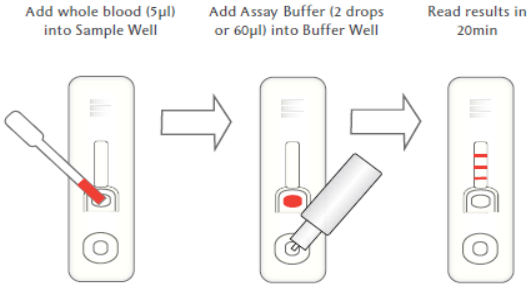
- Timer or hand watch
- Sharp disposal box
- Biohazard bag
- Lead pencil or pen for labeling

Procedure

- Open the test pouch: check all kit items are in place; if not then discard
- Prepare the RDT device and label it with name of the patient or give serial number
- Clean the finger of the patient with alcohol swab
- After the alcohol dries out prick the finger of the patient
- Wipe out the first drop of blood
- Collect sample from the finger prick using pipette provided, and while gently squeezing the tube, immerse the open end in the blood drop and then gently release the pressure to draw blood into the sample pipette up to the black line (5µl).
- Add 5µl of whole blood into the sample well



- Add two drops (60 µl) of assay Buffer with even pressure on the Buffer well (A), Vial must be Vertical



- Place the cassette on table or on flat surface for 20 minutes
- Read the test result in 20 minutes; and the result is interpreted as follows:

Interpretation of the test result**:**

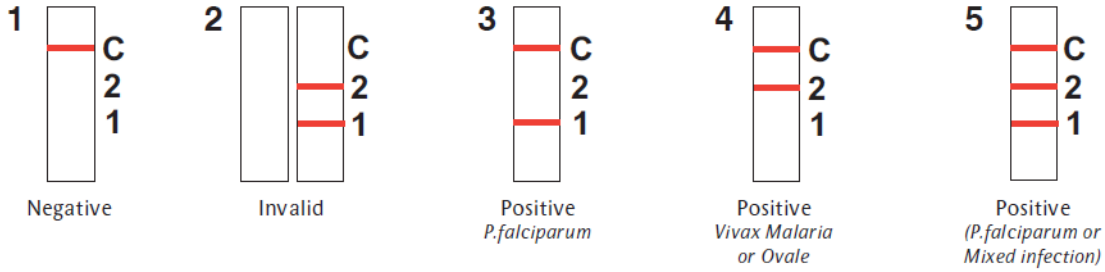


Figure 18: RDT procedure and interpretation

- **Negative reaction:** The presence of only one band in the control area within the result window indicates a negative result.
- **Invalid:** The test is invalid if the line in the control area does not appear. If this occurs, the test should be repeated using a new strip.
- **Positive reaction** - ***P. falciparum***: The presence of three color bands (three bands in the Control, "2" and "1" areas) or two bands (one band in the control area and another band in the "1" area) indicates a positive result for P. falciparum.
- **Positive reaction -*P. vivax, P. malaria, or P. ovale*:** The presence of two color bands (one band in the Control Area and another band in the "2" area) indicates a positive result *for P. vivax, P. malariae, or P. ovale*. The pLDH present in the sample reacts with the pan anti-pLDH conjugate and move through the test strip where the pLDH is captured by pan specific anti pLDH.

- **Positive reaction - Mixed infection *of P. falciparum* and other species** the presence of three color bands (three bands in the Control, "2" and "1" areas) indicates a positive result for *P. falciparum* or mixed infection of *P. falciparum* and other species.

Precaution on the interpretation of RDT results: A positive RDT result does not always signify malaria illness because the antigen of malaria parasites might be sometimes be detected after treatment or due to the persistence of malaria gametocytes in the absence of illness, presence of other substances in the blood might occasionally produce a false-positive result.

Advantage and disadvantages of using RDT:

Advantages

- Easy to use and rapid, on spot test results
- No/little manipulation of sample
- No refrigeration of sample or reagent
- Use of whole blood possible.
- Can detect sequestrated malaria

Disadvantages:

- Short shelf life (storage and distribution)
- Only qualitative result no quantification of malaria parasite
- Inability to identify sexual and asexual parasite stage
- Less accurate on identifying species of the parasite
- Post treatment positive result due to long survival of malaria antigen in peripheral blood
- Sometime presence of abnormal antibody in the patient peripheral blood may block Ag – Ab reaction on nitrocellulose to see visible reaction.
- Band intensity depends on Ag – Ab reaction.

Points to remember when performing RDT

- Product instructions should be strictly followed
- Management plan for results must be in place
- Blood-safety precautions should be followed
- Should be discarded if the envelope is punctured or badly damaged
- The test envelope should be opened only when it has reached ambient temperature
- The RDT should be used immediately after opening
- The result should be read within the time specified by the manufacturer

Quality Assurance of Malaria Laboratory Diagnosis

- **Quality Assurance (QA)** is a system designed to improve the reliability and efficiency of laboratory services.
- **Components of QA:**
    - **Quality Control (QC):** internal monitoring of work practices, technical procedures, equipment, and materials
    - **External Quality Assessment (EQA):** Assessment of laboratory performance by external higher body
    - **Quality Improvement (QI):** the components of malaria microscopy services are analyzed with the aim to identify and permanently correct any deficiencies

External Quality Assessment methods

1- Proficiency testing /PT/

- The laboratory performs malaria microscopy on a set of prepared slides received from the reference Laboratory
- It is used to check the staining procedure as well as the ability of the personnel to recognize and identify any malaria parasite present
- It provides a rapid picture of the proficiency of many laboratories

2- Blinded Rechecking

- It is rereading of randomly selected slides collected from the "testing" laboratory at higher level laboratory
- Detects malaria misdiagnosis in routine work and assess the overall quality of testing
- It reflects a true performance of laboratories offering routine diagnostic services at the peripheral level
- Checks not only the result of the blood film, but also the performance of the stain and quality of blood film
- Feedback to the participant site with comments and recommendation should be given timely

3- Onsite Supervision

- Is comprehensive assessment of essential elements of laboratory quality system
- It is ideal means of obtaining a realistic picture of the conditions and practices in a laboratory
- Provides opportunity for immediately identify sources of errors, provide onsite corrective actions, and implement appropriate measures to resolve problems
- It is done for both microcopy and RDT service facilities

LEARNING UNIT NINE

Supply Chain Management

Learning objectives

By the end of this training, participants should be able to:

- Describe supply chain management
- Define pharmaceutical supply chain management
- Understand logistics cycles
- Define and understand drug quantification
- Fill the different LMIS forms

Overview of Pharmaceuticals Supply Chain

Pharmaceuticals supply chain management: encompasses the planning and management of all activities involved in selection, quantification, procurement, storage, distribution and delivering a final product or service, from the supplier's supplier to the customer's customer. In essence, supply management should integrate supply and demand management within and across the health facilities and supply chain levels.

Logistics: Management of materials in motion and at rest. Some scholars also defined as the flow of material, information, and money between consumers and suppliers or what is happening in the supply chain. Logistics is part of SCM.

The purposes of logistics are to ensure the SIX Rights in order to serving customers, ensuring health commodity security exists for each client:

Ensuring the six rights:

- Right product in the
- Right quantity of the
- Right quality at the
- Right place at the
- Right time for the
- Right cost

Well-functioning supply chains benefit public health programs in important ways by:

- Increasing program impact
- Enhancing quality of care
- Improving cost effectiveness and efficiency.

Logistics Cycles and Activities

The following figure summarizes the logistics cycles and activities.

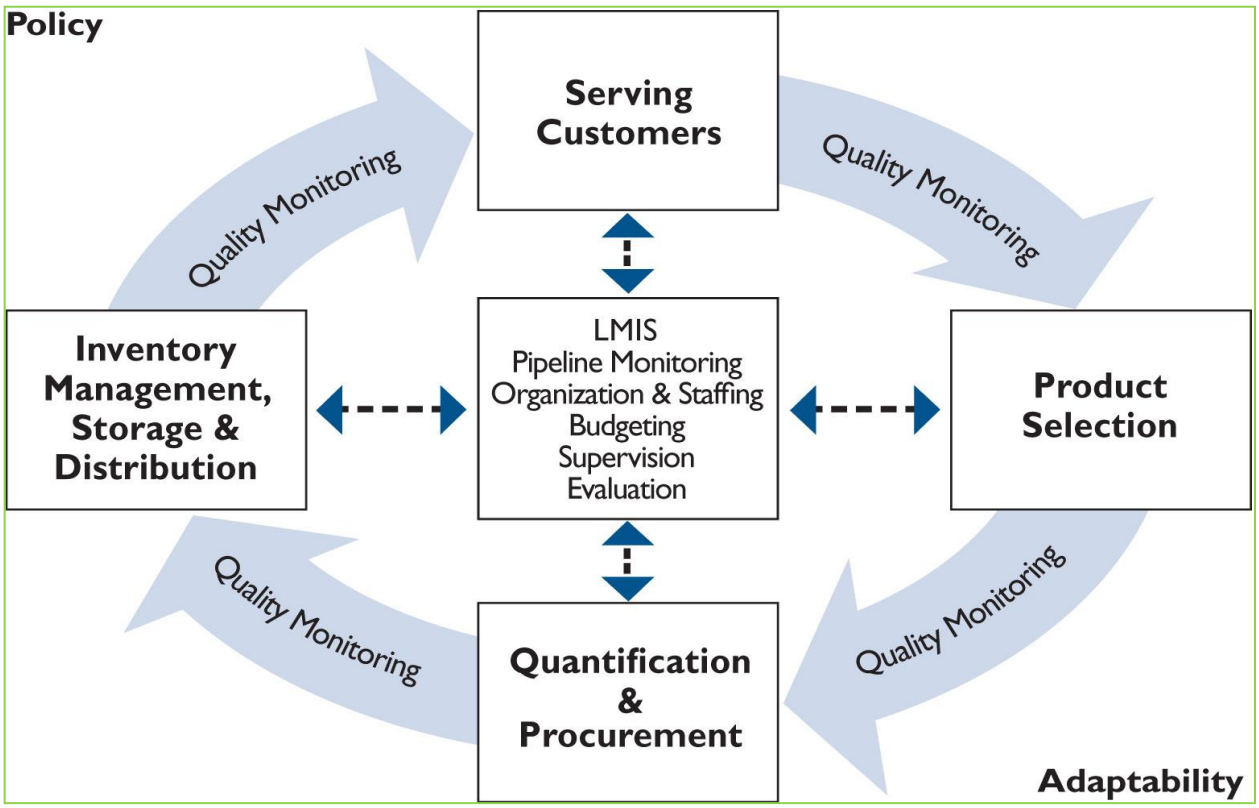


Figure 19: Logistics Cycle and Activities

Product Selection

Product selection is the first "action area" for our pharmaceuticals supply chain system. When we select the products that we intend to put into our system and distribute to the customer, we must take into account things like the capacity of our system: if we are selecting products that require cold chain, for example, then we must ensure that we have the facilities required to safely store and transport those products all the way to the customer. The process expected to be participatory.

Quantification

Quantification, a critical supply chain management activity, links information on pharmaceuticals demand from the health facility level with program policies and plans at the national level to estimate the quantities and costs of the pharmaceuticals required for a health program. Quantification is important for informing supply chain decisions for financing, procurement, and delivery. It is not a one-time exercise; it should be exercised in a regular manner depending on the pharmaceuticals to be determined. Health facilities are required to forecast their need (estimating the quantity of each product that will be dispensed or used for the next year) and adjust their expected budget. Pharmaceutical needs can be quantified by using one or a combination of more than two standard methods. Consumption and Morbidity method are the two major quantification methods which are relevant and practical at health facility level.

Procurement

Once we know the quantities that we need to meet our needs, then we must obtain those products from our supplier, that is, we must procure our need. Health facilities procure preferentially through PFSA, products which are not found at PFSA can be procured from private suppliers using stock out certificate.

Storage, Inventory Management and Distribution

Once the products have been procured and received in health facility, there should be appropriate storage and distribution within a hospitals and health centers. Storage must be adequate to maintain the quality of our products and storage capacity must be adequate to manage all of the products in our system. The purpose of an inventory control system is to inform personnel when and how much of a pharmaceuticals to order and to maintain an appropriate stock level to meet the needs of patients. A well designed and well operated inventory control system helps to prevent shortages, oversupply, and expiry of pharmaceuticals.

The SOP for the IPLS in health facilities of Ethiopia dictates all hospitals and health centers are required to order on a fixed schedule from PFSA

- Hospitals and health centers place order every 2 months
- Orders are placed using RRF

LMIS: the LMIS is shown at the center of the cycle, and we consider it to be the engine which drives the supply chain system. The LMIS is the means through which we gather and communicate the information that allows managers to make the decisions they need to make in order to ensure product availability and customer service. Every function in the supply chain cycle needs accurate information in order to work. For example, without a properly functioning LMIS:

- We do not know which products are being accepted and used by our customers (which products to continue to select or stop selecting).
- We do not know if we are obtaining the right quantities at the health facility level to serve the customers' needs.
- We do not know if stores are sitting empty or if products are piling up and not being dispensed.
- PFSA do not know what, when and how much products HFs need.

The other activities found at the center of the supply chain cycle are management support activities that are also essential to the functioning of the system as a whole.

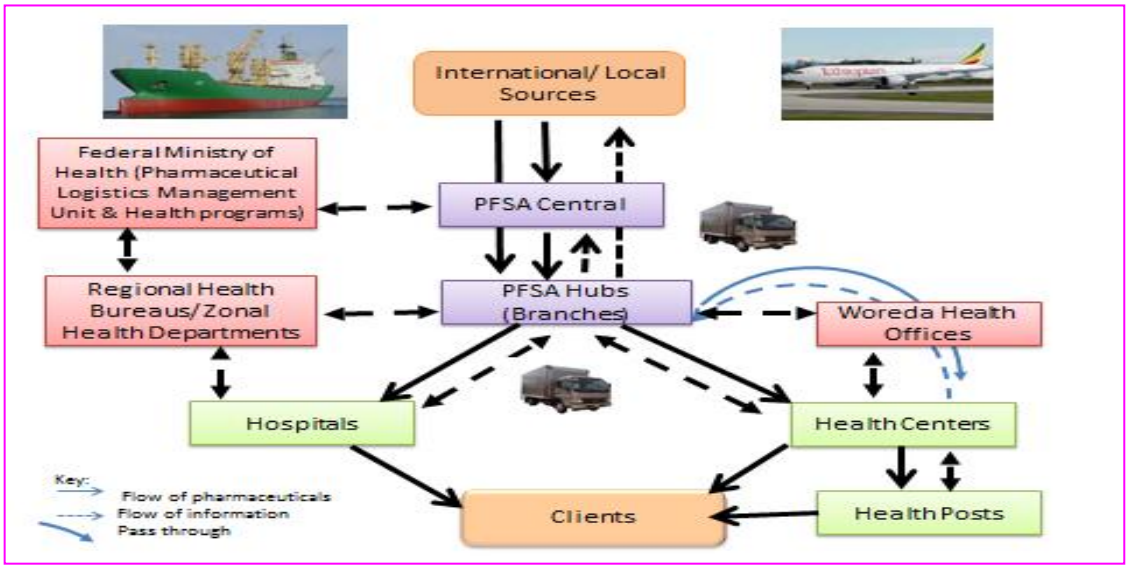


Figure 20: Flow of Pharmaceuticals and Information in the Integrated Pharmaceutical Logistics System

Requesting and Getting Pharmaceuticals from PFSA

In IPLS hospitals and health centers are expected to summit all pharmaceutical transaction reports and orders/requisitions bimonthly by using a form called Report and Requisition Form (RRF) to a nearby PFSA branch. RRF should be completed at the end of the month and sent to PFSA until the 10th day of the month following the end of the reporting period. This report is expected to be

completed by Health Centre or Hospital Store Manager (verified by the Pharmacy Head and Approved by Head of the Health Centre or Hospital.

Unless PFSA receives request from HFs timely and completely/accurately PFSA will face challenge to resupply pharmaceuticals to HFs and this will negatively affect the service.

The role of drug and therapeutic committee (DTC) in inventory management, storage and distribution of pharmaceuticals within health facility includes:

- Monitor the bi-monthly report and requisition form (RRF) is completed timely and sent to PFSA and internal reporting is implemented as indicated by the IPLS SOP manual.
- The DTC should also check and evaluate the quality of the data on the RRF on regular basis.
- Approve pharmaceuticals list of each dispensing units.
- Approve and ensure the implementation of SOPs for guiding the whole process of distribution.
- Monitor the application of storage guidelines in the pharmacy store and dispensing units.
- Make sure that system is in place to monitor stock status at main pharmacy store and dispensing units, and disposal of unfit for use pharmaceuticals is working.

LEARNING UNIT TEN

Malaria Epidemics Detection and Response

Learning Objectives

At the end of this training, participants should be able to:

- Define malaria outbreak and epidemics
- Describe the purpose of malaria epidemic forecasting and early warning
- Explain the basic principles of malaria epidemic detection and response.

Definition

Outbreak: is an increase in number of cases of a disease compared with the expected number. An outbreak lasts for only a short time, or it occurs only in a limited area.

Epidemics: is also an excess number of cases compared with the number expected. However, an epidemic is more general than an outbreak, the increase in the number of cases continues far longer, and the cases are distributed across a wider area.

Malaria epidemics: are the occurrence of numbers of cases above what is expected in a place in a particular time period. Sometimes it is hard to distinguish malaria epidemics from usual seasonal upsurge of malaria. Malaria epidemics can be one of the most serious public health emergencies. Malaria epidemics may occur with little or no warning and may challenge the health system to prevent or effectively respond to the problem and may strain health facilities and systems, and cause public outcry resulting in intense political pressure for rapid and decisive intervention.

Overview of Malaria Epidemics in Ethiopia

A devastating malaria epidemic occurred in 1958, involving about three million cases and 150,000 deaths, and covering about 100,000 square miles (259,000 square kilometers) of highland area. Since 1958, major epidemics of malaria have occurred at approximately 5-8 year intervals, though there has been a trend towards smaller-scale, more frequent, sporadic epidemics and seasonal case build ups. In 1998, a widespread severe malaria epidemic occurred in most highland as well as lowland areas in the country. Many localized but severe outbreaks of malaria occurred in Amhara and SNNP Regional States, leading to widespread epidemic malaria in highland and highland fringe areas (up to 2,500 meters) in 2003. However, there has not been any major malaria epidemic since 2003.

Factors Precipitating Malaria Epidemics

Malaria epidemics can occur as a result of variability or changes in the rate of infection and population immunity. Generally malaria epidemics occur in places where there is low and unstable transmission, and where people have low or no immunity against malaria. There could be epidemics in high transmission areas as well if there is deterioration of health system, interruption of anti-malarial measures or migration of non-immune individuals, such as population movement in search of labor to these areas. Other triggering factors include:

- Unusual local weather phenomena and activities resulting in environmental modification that increase vector population;
- Increased vulnerability of population from famine and malnutrition;
- Interruptions of anti-malarial measures which have kept malaria under control;
- Resistance to anti-malarial medications and/or insecticide used for vector control.

Epidemic Preparedness

Preparedness includes availability of trained human resources, diagnostics, anti-malarial drugs, supplies and insecticides. As a rule, an additional 25% of the annual drug requirement should be kept as contingency at woreda or health center level, since there is always uncertainty regarding where the epidemic will occur. The additional 25% need only be spent until a verified malaria epidemic occurs; following the response to an epidemic outbreak, the contingency stock would have to be replenished.

Contingency supplies must be transported to the various levels well in advance. All RHBs and woredas should plan, request and budget the amount of contingency supplies required at each level as accurately and realistically as possible. This is part of the annual malaria commodity "micro-planning" process. All levels of the public health system should report at least monthly to higher levels the status of their inventories of critical supplies as well as expiry status.

Epidemic Detection

There are two methods of epidemic detection. Method 1 is the classic method, based on norm charts and thresholds. This is currently recommended and probably will continue to be used for some time in areas of higher transmission. Method 2 (cluster mapping) will be tested and gradually introduced, where applicable; as malaria incidence and transmission in an area falls to low levels this new method will improve management of the relatively few clusters of malaria infection that remain within communities.

In a strict sense, an epidemic of malaria is defined as a situation when the number of malaria cases is in excess of the normal number at a specific period of time and place. Therefore, the "normal" expected number has to be estimated. One way to do this is by using past weekly data of up to five previous years to construct a third quartile (second largest number) threshold line in an epidemic monitoring chart.

Many, if not most, malaria illness in Ethiopia probably represents micro-clustering of local malaria transmission near a home, whereas isolated non-clustered infections might represent importations or relapses (though possibilities of indigenous transmission should be scrutinized and ruled-out). Local "micro-clusters" of malaria infections are defined as three or more indigenous cases of malaria of the same species occurring in homes within 1 km distance of one another within a 28-day interval, indicating probable local transmission. These should be detectable early by the HEW at the health post, when approximate map sector locations of homes of ill persons with malaria are systematically documented in malaria registers along with date of illness (Method 2).

The key principles of epidemic detection and action (using any detection method) are:

- Defining epidemics according to a particular time period and area (usually health facility catchment area). The basic unit of time is a week; epidemics in Method 1 are defined according to a weekly threshold, while Method 2 uses a time window of up to four weeks.
- In both cases, taking actions to avert the epidemic as soon it is detected.
- Both methods use a combination of active surveillance and other containment actions (e.g. promoting LLIN use, other vector control, requesting supplies and further support if needed) once an epidemic has been detected. Method 2 provides an evidence basis for SBCC efforts and other resources focused on areas within the kebele with the most intense recent malaria transmission, i.e. malaria "micro-cluster" hot spots localized to within 1 km sectors.
- There is no need to wait for formal confirmation of an epidemic before starting active surveillance and containment actions. Epidemics which spread beyond the kebele or woreda level may need further support and confirmation from zonal, regional or national levels to release additional resources supplies.

Method 1: Norm charts and thresholds

To establish a threshold for 'normal' for any given week, a health facility's past data by week should be compiled and a threshold determined using the 'third quartile' method. Current data may then be compared with the threshold. If an increase above the weekly threshold is observed, it implies that there may be an epidemic.

Under Method 1, an epidemic is defined as: "*The occurrence in a health facility catchment area of cases of an illness, clearly in excess of normal expectancy*".

Definition involves: clear time, place, and person

For this we need to know:

- *Where?* Which health facility catchment or other defined area
- *When?* What time period ("occurrence")
- *What is "normal expectancy" for that area and time period?*
- *What do we mean by "cases" (case definition)? How many of these and what proportion tested have malaria by RDT or microscopy?*
- *What is regarded as "excess"?*
- *Who has become ill?*

Health post or kebele: is the smallest administrative/operational unit to monitor and will be defining epidemics in its catchment area. Hence, recording the address of people in registers is mandatory as people from other catchment area may prefer your facility for various reasons (e.g. proximity, availability of drugs). Catchment area population may appear to change due to temporary malfunctioning of adjacent facilities or as a result of newly created facilities. However, district health offices, health centers (primary health care units) can also monitor malaria trends using kebele-level disaggregated data, since aggregated data might mask what is happening in individual kebeles.

Time period: the week is the primary time unit. 'Week' is defined in a standard way by WHO week number (**Annex T**).

Normal expectancy: is defined based on that same case definition, catchment and week in previous years. We have two choices, depending on what information we have.

"Normal" is: The third quartile (second highest number from the five previous years' data for that week); and doubling of the previous year's number of cases (in the absence five years data).

Case definition: Choose ONE indicator as the primary one for defining epidemics. Ideally, it would be CONFIRMED malaria cases (either as evidenced by a positive RDT or a positive microscopy slide) in all age groups. If confirmation is not possible in your location then use clinical malaria cases, but these must be classified as presumptive malaria (not parasitologically confirmed). The threshold must be based on the same indicator, which is the most challenging requirement of Method 1, since often at facility-level that malaria cases are diagnosed both clinically as well as parasitologically based on the availability of RDTs or microscopy at facilities.

Note: If you have five years' previous data (all years must be normal years, without an epidemic), you can definitely determine that when malaria cases exceed the third quartile number (or line on the chart) then there is an epidemic for that week. If you have less than five years' data, you can say that any number of malaria cases more than double the number in the same week of last year's data is an epidemic. In a strict sense, if no historical data (the last 5 years) is available at all for the catchment area, an epidemic cannot be detected, since there is no known "normal". However, an alarmingly rapid rise in cases or mortality can be detected by doing a week-to-week comparison of case registers. Alternatively, Method 2 could be used to monitor the malaria situation provided that the system is established.

Why do we need a threshold? It can be very difficult to distinguish an epidemic from a normal seasonal case increase. Once it is apparent that the seasonal case increase is much higher than normal, the epidemic is well underway. Because health staff often move around to different health facilities, they may not be aware of the expected number of cases in the local area.

How to calculate the threshold? The following tables give examples of how to tabulate data for estimating a threshold by two methods. The data in the tables is illustrative and for this example only. **Table 18** is the empty sheet. **Table 19** is filled in with the past five years' data and shows the third quartile threshold. **Table 20** shows what to do if you only have one year's data.

Thresholds can be calculated for any health facility or any other unit including kebele, woreda or zone. However, the heath post catchment area (usually kebele) is defined to be the smallest geographic area for monitoring epidemics. Higher levels could also monitor epidemics provided that the data thresholds for monitoring are disaggregated by health post catchment area.

Table 17 Chart for assessing usual number of weekly cases (confirmed or clinical) and threshold at health facility.

WHO Week No.	Year 1	Year 2	Year 3	Year 4	Year 5	Third Quartile or second largest number or 2x last year's cases	This year's cases
1							
2							
.							
.							
.							
51							
52							
(53)							

Note:

1) Week number: the WHO week number system is used, and weeks run from Monday to Sunday.
2) If 5 years of data are available, the Third Quartile can be filled in (**Table 18**). The Third Quartile is the second highest number from the five values for each week.
3) The current year's data should be added in right column, by week ("this year").
4) If only last year's data is available, a threshold of twice the last year's number for that week should be entered.
5) A new chart must be prepared each year, adding the new annual data (unless an epidemic year) and dropping the oldest year.
6) The data can be plotted manually onto a norm chart with the threshold line and the current year by week (**Table 19**).
7) For higher level health workers with computer capacity, a Microsoft Excel file for the can be used to estimate the third quartile. For example, the formula for third quartile in a second week (row-3) with five years' data (B3 to F3) of a Microsoft Excel work book sheet is given by =QUARTILE(B3:F3, 3). Then, draw charts (**Table 20**) and update the threshold each year.

Table 18 Construction of the threshold (norm) when five years' historical data are available to monitor the current year

WHO Week No.	Year 1	Year 2	Year 3	Year 4	Year 5	Third Quartile or second largest number or 2x last year's cases	This year's cases
1	8	42	6	36	14	36	20
2	12	42	27	38	17	38	22
3	10	42	43	49	21	43	35
4	20	17	34	59	32	34	26
5	34	17	46	20	30	34	25
6	18	10	34	22	23	23	20
7	12	19	33	24	25	25	21
8	37	10	27	61	23	37	25
9	32	18	37	29	26	32	16
10	31	24	28	17	13	28	5
11	22	19	22	12	23	22	15
12	17	39	31	22	43	39	25
13	5	19	19	16	21	19	16
14	22	19	28	25	21	25	30
15	29	16	28	19	13	28	45
16	17	32	25	6	11	25	60
17	28	11	32	8	8	28	62
18	17	34	40	13	9	34	60
19	12	17	27	9	10	17	25
20	16	18	14	1	9	16	10
21	31	34	29	2	8	31	15
22	38	22	23	1	9	23	16
23	29	33	14	1	17	29	17
24	19	32	35	1	32	32	18
25	27	10	25	1	34	27	22
26	36	20	34	1	47	36	30
27	15	32	36	4	62	36	35
28	19	42	44	8	38	42	36
29	52	49	47	10	62	52	101
30	31	44	45	12	73	45	122
31	31	51	53	94	142	94	135
32	97	67	56	114	104	104	176
33	42	73	67	94	67	73	200
34	74	61	71	82	124	82	250
35	53	123	46	57	130	123	261
36	41	58	92	79	129	92	261
37	76	136	118	70	125	125	255
38	116	113	134	37	87	116	244
39	94	145	128	73	138	138	230
40	93	102	194	103	139	139	269
41	108	692	171	52	178	178	267

42	34	178	168	59	208	178	233
43	49	165	232	59	164	165	199
44	27	183	145	44	114	145	145
45	16	283	111	34	103	111	67
46	55	141	150	40	105	141	53
47	33	133	112	20	105	112	52
48	40	122	87	25	81	87	45
49	40	95	102	30	42	95	
50	19	67	71	30	33	67	
51	26	56	21	38	27	38	
52	23	55	34	29	6	34	
(53)							

Note: The threshold is the 3rd quartile. The epidemic weeks in the current year are shaded in the right column.

Table 19 Construction of threshold (norm) with single recent year morbidity data

WHO Week No.	Year 1	Year 2	Year 3	Year 4	Year 5	Threshold (norm) = 2x last year's cases	This Year's cases
1					14	28	20
2					17	34	22
3					21	42	35
4					32	64	26
5					30	60	25
6					23	46	20
7					25	50	21
8					23	46	25
9					26	52	16
10					13	26	5
11					23	46	15
12					43	86	25
13					21	42	16
14					21	42	30
15					13	26	45
16					11	22	60
17					8	16	62
18					9	18	60
19					10	20	25
20					9	18	10
21					8	16	15
22					9	18	16
23					17	34	17
24					32	64	18
25					34	68	22
26					47	94	30
27					62	124	35
28					38	76	36
29					62	124	101
30					73	146	122
31					142	284	135
32					104	208	176
33					67	134	200
34					124	248	250
35					130	260	261
36					129	258	261
37					125	250	255
38					87	174	244
39					138	276	230
40					139	278	269
41					178	356	267
42					208	416	233

WHO Week No.	Year 1	Year 2	Year 3	Year 4	Year 5	Threshold (norm) = 2x last year's cases	This Year's cases
43					164	328	199
44					114	228	145
45					103	206	67
46					105	210	53
47					105	210	52
48					81	162	45
49					42	84	
50					33	66	
51					27	54	
52					6	12	
(53)							

Note: The threshold (norm) is 2x the previous year's value for the week. The epidemic weeks in the current year are shaded in right column.

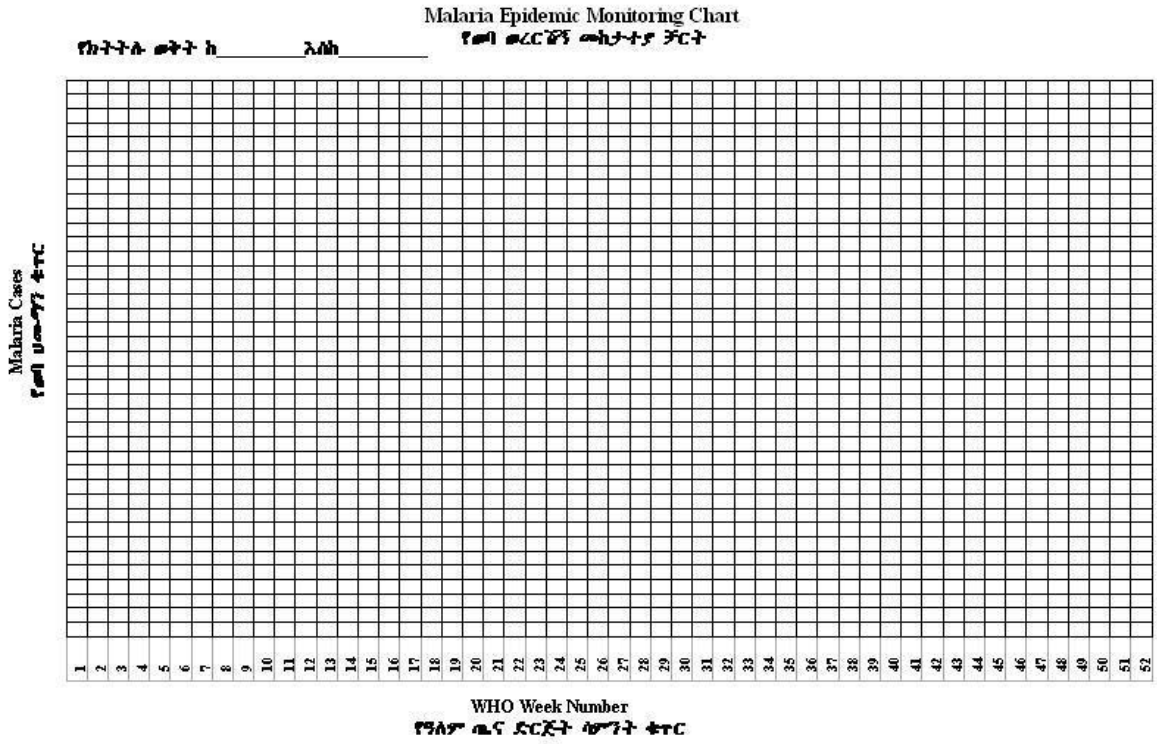


Figure 21: Norm chart for plotting weekly morbidity data: confirmed cases

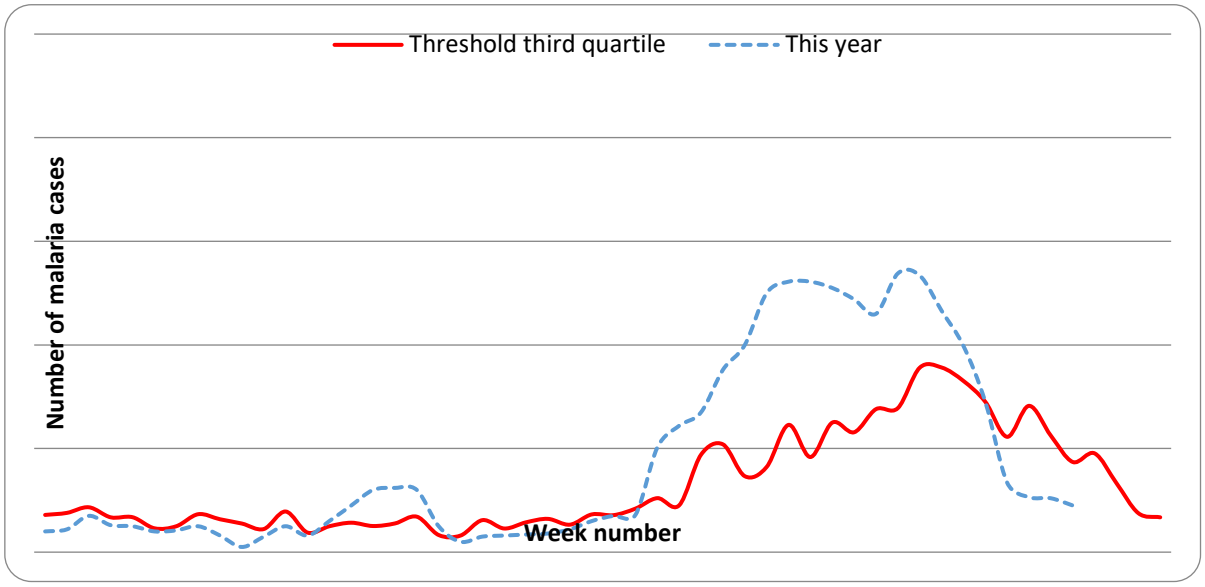

Threshold third quartile
This year
Number of malaria cases
Week number

Figure 22: Chart drawn from Table 19 showing epidemic weeks in current year above third quartile threshold

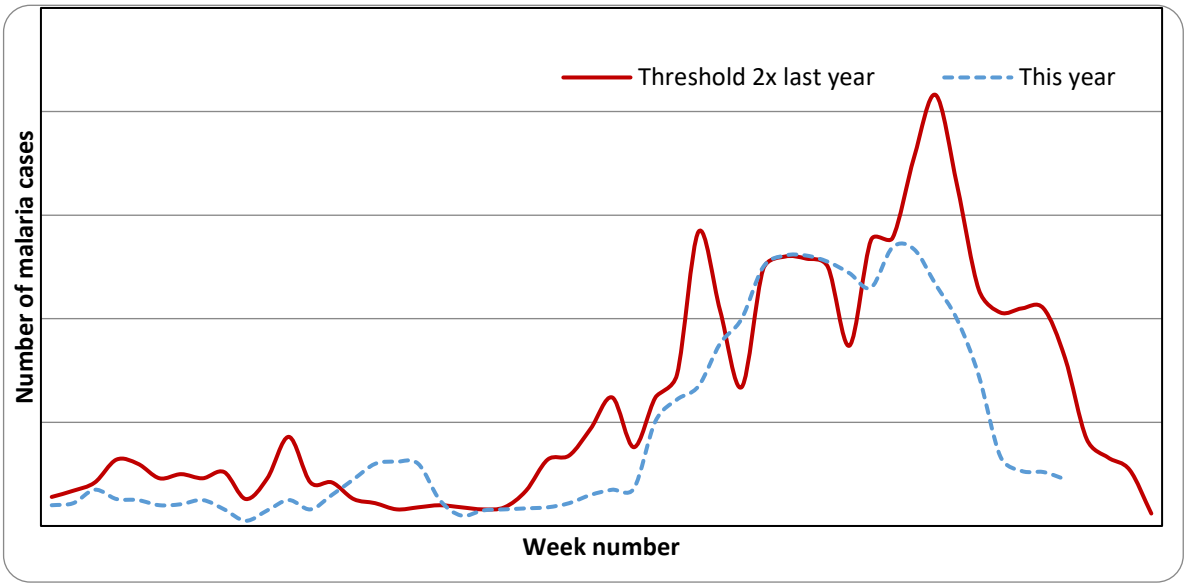


Figure 23: Chart drawn from Table 20 showing epidemic weeks in current year based on threshold of twice last year's weekly data.

Epidemic Confirmation

Epidemics detected through health facility registers using norm charts (Method 1) are by definition epidemics and do not need additional confirmation, assuming that they were based upon RDT or laboratory confirmed cases. Epidemics detected by mapping of micro-clusters of cases (Method 2) also assume RDT or microscopy verification, and should be handled immediately by HEWs. In both situations, large epidemics will require that microscopy slides be collected for analysis by FMOH (EPHI) experts; and in certain cases dried blood spots on filter paper may be collected for serological analysis.

Initially, the most important information needed for an assessment will be:

a) How many suspected malaria cases (persons) were documented within a specified time interval (week, month) within a specific district or kebele (place)?
b) How many of these suspected malaria cases were tested by RDT or microscopy?
c) How many of the suspected malaria cases tested were also diagnosed as positive for malaria
d) How many laboratory-confirmed malaria cases were *P falciparum* and how many were *P. vivax*?
e) How many deaths, hospitalizations and severe malaria cases occurred?

f) Are there adequate supplies of RDTs, AL and chloroquine (and quinine, rectal artesunate, IV artesunate)?
g) If available, compare current malaria case numbers with previous malaria registry data.

For large epidemics (several woredas or zones), a detailed emergency plan of action should be rapidly, but carefully, prepared in order to optimally use available personnel, finance, transportation, supplies and time. In this plan, the responsibilities, localities to be covered and schedule of work for each control team should be shown clearly and shared as appropriate at the kebele, zonal and regional levels.

Response to Malaria Epidemics

Whether an epidemic is detected by Method 1 or 2, certain active surveillance and other control actions are triggered and should continue for up to one month or until no further cases are detected for at least two months. At the end of the four-week period, epidemic status should be reassessed and a decision made to continue active surveillance or revert to normal passive surveillance and treatment. If an epidemic is detected, the active surveillance should be as follows:

Mass fever testing and treatment (MFTT): Test everyone with fever and treat those with confirmed malaria. This step should be taken when sufficient RDTs are in stock and as long as RDT positivity is below 50%, upon examination of 50 febrile patients. Treatment must be species-specific (refer to **Learning unit three)**.

Mass presumptive fever treatment (MPFT): When, upon examination of 50 febrile patients, RDT positivity is equal to or greater than 50%, action should switch to MPFT (treat all persons with fever presumptively). This should be done when stocks of RDTs are low (while waiting for supply), or if RDT positivity among at least 50 actively detected and tested suspected cases increases to more than 50%. MPFT indicates treatment with AL plus PQ, unless the cause of the epidemic is definitely confirmed to be *P. vivax* only.

Both MFTT and MPF are most rational within malaria 'hot zones' (i.e. households especially within 500 meters of a cluster of known recent malaria transmission/cases) beginning with the nearest homes. Registers must be kept of persons actively tested and treated.

Other interventions to be taken simultaneously with MFTT and MPF: Treat and refer severe malaria cases; request more supplies to replace those expended; use effective anti-malarial medication that are closest to expiry date; SBCC for improving LLIN use; consider IRS if evidence

from epidemiological analysis ensures that transmission will continue despite treatment interventions.

Reporting

Listings of persons tested and treated during ‘mass fever treatment’ or ‘mass test and treat’ active surveillance must be reported. The following table may be used for recording ‘mass fever treatment’ or ‘mass test and treat’.

Starting from one randomly selected household in the highly affected part of the village, take 20 houses in sequence and fill in the following format:

Table 20 Reporting form for active surveillance and treatment

HH No.	Total no. of HH members	No. of sick (febrile) household members	No. of blood samples (RDT or microscopically) examined		No. and proportion of positives out of examined (if applicable)		Treatment given
			RDT	Microscopy	RDT	Microscopy	
1							
2							
.							
.							
20							
Total							
Note: Indicate the type of diagnosis, i.e. RDT or microscopy. Then determine fever rate and test positivity rate from the sampled households. Health posts should also report status of malaria supplies inventory.							

Whether an epidemic is detected by Method 1 or 2 anywhere in the satellite health post’s catchment area, the report must be immediately relayed to all responsible higher levels. The mitigation activities initiated by the health post must be supervised and leveraged by the health center and woreda health

office. Any epidemics beyond the capacity of the health center should be handled at the woreda level using local contingency supplies. Progress on mitigation activities and gaps must be reported to higher levels on a daily and weekly basis.

When an epidemic is detected and reported by any primary health care units, this must be immediately relayed to all responsible higher levels. The mitigation activities initiated must be followed-up and supportive supervision planned and implemented if necessary. Any epidemics beyond the capacity of the woreda should be handled by the zone/RHB. Progress on mitigation activities and gaps must be reported to higher levels on a daily/weekly basis throughout the mitigation process. Once an epidemic is evident at the woreda level, the situation is probably quite serious and the zone as well as the RHB must be informed. The epidemic report form (PHEM form) must be completed and disseminated to higher levels.

Case Management (See Case Management Guidelines for detail)

***P. falciparum* epidemics:** AL+PQ is the first-line anti-malarial drug recommended for the treatment of uncomplicated *P. falciparum* malaria. Oral quinine is recommended for the treatment of pregnant women in the first trimester with uncomplicated malaria.

***P. vivax* epidemics:** Use chloroquine if the cause of the epidemic has been established as only *P. vivax*.

Mixed *P. falciparum* and *P. vivax* epidemics: Use AL+ PQ treatment for mixed *P. falciparum* and *P. vivax* infections.

Management of severe malaria in epidemic situations should take place in hospitals and health centers using intravenous medications, whenever possible. Hence, severe malaria cases diagnosed in health posts or community level should be referred to the nearby health center or hospital as promptly as possible.

Stabilizing therapy, such as artesunate suppositories or IM artemether or IM quinine, may be needed in temporary posts or situations in which staff shortages and high workloads make intensive care monitoring difficult. The following should be done before referral of the patient:

- Always nurse patients in a coma in a lateral position to avoid aspiration;
- Give 40% or 50% glucose to all patients with severe manifestations;
- Use tepid sponging as needed,

Record all your findings and drugs given in a referral slip and refer the patient to the nearest health center or hospital.

Exercise:

Group work: The following two tables contains last year's and five year's weekly data on malaria cases. Study the table and then answer the questions below it.

Identify the threshold for each scenarios?

Draw the chart using the give data?

Interpret the result?

Exercise 1: One year data

Week no. (EFY)	Week no (WHO)	2007	doubling Previous year data	This year (2008)
1	28	38		36
2	29	62		101
3	30	73		122
4	31	142		135
5	32	104		176
6	33	67		200
7	34	124		250
8	35	130		261
9	36	129		261
10	37	125		255
11	38	87		244
12	39	138		230
13	40	139		269
14	41	178		267
15	42	208		233
16	43	164		199
17	44	114		145
18	45	103		67
19	46	105		53
20	47	105		52
21	48	81		45
22	49	42		18
23	50	33		22
24	51	36		30
25	52	38		35
26	1	24		20

Week no. (EFY)	Week no (WHO)	2007	doubling Previous year data	This year (2008)
27	2	20		22
28	3	21		35
29	4	32		26
30	5	30		25
31	6	23		20
32	7	25		21
33	8	23		25
34	9	26		16
35	10	13		5
36	11	23		15
37	12	43		25
38	13	21		16
39	14	21		30
40	15	13		45
41	16	11		60
42	17	8		62
43	18	9		60
44	19	10		25
45	20	9		10
46	21	8		15
47	22	9		16
48	23	17		17
49	24	32		
50	25	34		
51	26	47		
52	27	62		

Exercise 2: Five years data

Week no. (EFY)	Week no (WHO)	2003	2004	2005	2006	2007	second largest number	This year
1	28	19	42	44	8	38		36
2	29	52	49	47	10	62		101
3	30	31	44	45	12	73		122
4	31	31	51	53	94	142		135
5	32	97	67	56	114	104		176

Week no. (EFY)	Week no (WHO)	2003	2004	2005	2006	2007	second largest number	This year
6	33	42	73	67	94	67		200
7	34	74	61	71	82	124		250
8	35	53	123	46	57	130		261
9	36	41	58	92	79	129		261
10	37	76	136	118	70	125		255
11	38	116	113	134	37	87		244
12	39	94	145	128	73	138		230
13	40	93	102	194	103	139		269
14	41	108	692	171	52	178		267
15	42	34	178	168	59	208		233
16	43	49	165	232	59	164		199
17	44	27	183	145	44	114		145
18	45	16	283	111	34	103		67
19	46	55	141	150	40	105		53
20	47	33	133	112	20	105		52
21	48	40	122	87	25	81		45
22	49	40	95	102	30	42		18
23	50	19	67	71	30	33		22
24	51	26	56	21	38	27		30
25	52	23	55	34	29	6		35
26	1	8	42	6	36	14		20
27	2	12	42	27	38	17		22
28	3	10	42	43	49	21		35
29	4	20	17	34	59	32		26
30	5	34	17	46	20	30		25
31	6	18	10	34	22	23		20
32	7	12	19	33	24	25		21
33	8	37	10	27	61	23		25
34	9	32	18	37	29	26		16
35	10	31	24	28	17	13		5
36	11	22	19	22	12	23		15
37	12	17	39	31	22	43		25
38	13	5	19	19	16	21		16
39	14	22	19	28	25	21		30
40	15	29	16	28	19	13		45
41	16	17	32	25	6	11		60
42	17	28	11	32	8	8		62
43	18	17	34	40	13	9		60

Week no. (EFY)	Week no (WHO)	2003	2004	2005	2006	2007	second largest number	This year
44	19	12	17	27	9	10		25
45	20	16	18	14	1	9		10
46	21	31	34	29	2	8		15
47	22	38	22	23	1	9		16
48	23	29	33	14	1	17		17
49	24	19	32	35	1	32		
50	25	27	10	25	1	34		
51	26	36	20	34	1	47		
52	27	15	32	36	4	62		

Weekly malaria cases in 2004–2008 (EFY).

Week no. (EFY)	Week no (WHO)	2003	2004	2005	2006	2007	2008	second largest number	This year (2009)
1	28	16	42	105	36	14	42		33
2	29	12	42	100	38	17	22		35
3	30	16	42	103	49	21	34		40
4	31	20	17	134	59	32	40		39
5	32	34	17	146	20	30	39		33
6	33	18	10	134	29	23	27		30
7	34	30	19	133	24	25	25		29
8	35	37	10	127	41	23	42		42
9	36	32	18	137	29	26	29		35
10	37	31	24	128	17	13	32		30
.		.	.	.	.	.	.		.
51	26	26	40	134	32	39	39		.
52	27	23	35	110	27	25	33		.

a. Which year do you think the data shows an abnormally high number of malaria cases? What do you do with this year before you start identifying the second largest number?

b. Identify the second largest number for the six years of data (2003 –2008) and fill in the column in the table.

c. Use the blank epidemic monitoring chart and plot a reference line of the second largest numbers and the data for the year 2009 against it.

d. Does the graph show weeks when an epidemic occurred? If yes, in which weeks?

LEARNING UNIT ELEVEN

Monitoring and Evaluation

Learning Objectives

By the end of this session, participants will be able to:

- Identify the definition and purpose of M&E.
- Explain the Ethiopian Malaria Program M&E framework
- Recognize national malaria related indicators and how they are generated
- Recognize the importance of evidence-based decision making
- Demonstrate how to fill different M&E forms

Definition and purpose of M&E

Definition: Monitoring and Evaluation refers to a process by which data are collected and analyzed in order to provide the information necessary for effective program planning and management.

Monitoring is a process of measuring progress towards program/project objectives through tracking activities conducted, resource utilization, and the outputs generated.

Evaluation is a process of determining systematically and objectively the relevance, effectiveness, and impact of interventions in relation to their objectives.

Purpose: The overall purpose of monitoring and evaluation of malaria program is to improve the program based on evidence regarding the effective and efficient use of program resources. M&E also helps to track changes in the services provided, and in the desired outcomes. It also generates new knowledge by identifying factors (individual, community, programmatic) that influence health outcomes, and justifying use of allocated resources (increasing cost-effectiveness). Furthermore M&E helps to meet an organizational requirement (e.g., reporting to development partners). Hence, M&E is a backbone of malaria program that enables effective and efficient implementation of interventions.

The Difference between Monitoring and Evaluation

Monitoring

Monitoring involves the routine tracking of progress of the implementation of a program's activities and changes in program performance over time. It is a continuous oversight of the implementation

of a program's activities. Its purpose is to allow the program's stakeholders to understand if the program is achieving its objectives and utilizing its resources efficiently. Examples of monitoring questions are indicated below.

- Were inputs made available to program/ project in the quantities and at the time specified by the program/project work plan?
- Were the scheduled activities carried out as planned?
- How well were they carried out? Did the expected changes occur at the program/project level, in terms of people reached, materials distributed?

Monitoring seeks to establish if the resources invested (inputs), the activities undertaken, the quality of those activities (processes), and number of activities performed (outputs) are proceeding according to plan. It also includes the regular collection and analysis of data to assist in timely decision-making, to aid in program planning and management, to ensure accountability and lastly, to provide a basis for evaluation and learning.

Evaluation

Intends to measure how well the program activities have met their expected objectives and/or whether the changes in the outcomes observed can be attributed to the program. Evaluation entails the process of determining the worth or significance of a program or intervention.

Evaluation answers the question "what have we achieved?" Questions to be asked in evaluation:

- Did the LLINs national distribution program reduce inequity in household ownership of insecticide-treated nets?
- Was the program effective in increasing the population's knowledge of the proper use of LLINs?
- Did the program's activities to increase access to ACT treatment for children under five-age lead to a decline in malaria-specific mortality?

Summary of the difference between M&E

Monitoring	**Evaluation**
Routine and continuous	Time bound
Internal to program	External or internal
Regular	Periodic assessment
Measures actual performance	Impact Evaluation
Tracks cost	Evidence of changes due to program
Done by those in the program	Rigorous and requires a design

Monitoring and Evaluation Frameworks

Frameworks are useful in helping us understand the relationships between each element of the program; inputs, processes, outputs, outcomes and between the program activities and the environmental context where the program will be implemented.

Inputs: The resources invested in a program, for example, technical assistance, financial resources, infrastructure and equipment.

Processes: The activities carried out to achieve the program's objectives, such as training and outreach.

Outputs: The immediate deliverables of a program achieved through implementation of activities, such as providers trained or bed nets distributed.

Outcomes: Short-term and intermediate results at the population level achieved by the program through the implementation of program activities, such as changes in people's knowledge, attitudes or behavior.

Impact: The long-term effects of a program, for example, changes in health status.

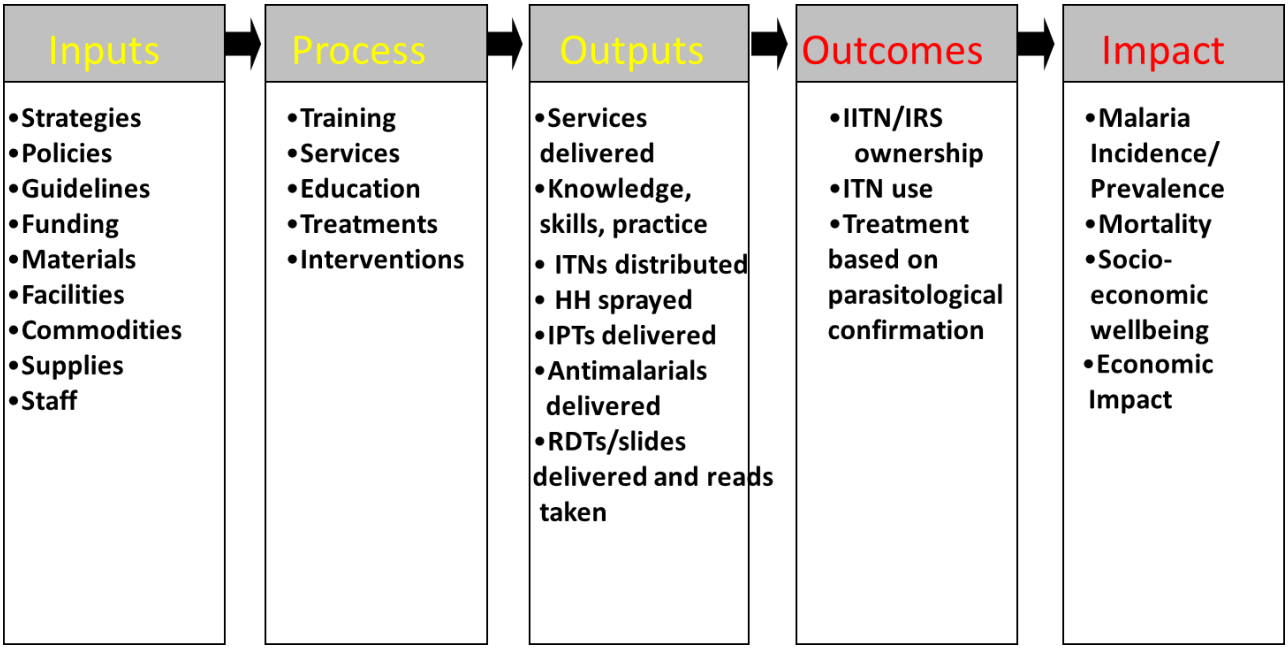


Figure 24: Logical framework for monitoring and evaluation

Ethiopian Malaria Program M&E system

The Ethiopian malaria monitoring and evaluation system is based on data collected through regular reporting systems (PHEM and HMIS) and surveys and evaluations conducted periodically which includes MIS, malaria program review and drug efficacy studies.

Information collected through HMIS is organized under the following data flow structure for all health related data according to the national HMIS guidelines: health posts and health centers

(PHCU) report to the woreda. Woreda-based hospitals report to the woreda in which they are located. Other hospitals report to the zone or to the region. Woredas report to the zone or the region. Zones report to regions. Regions report to the FMOH

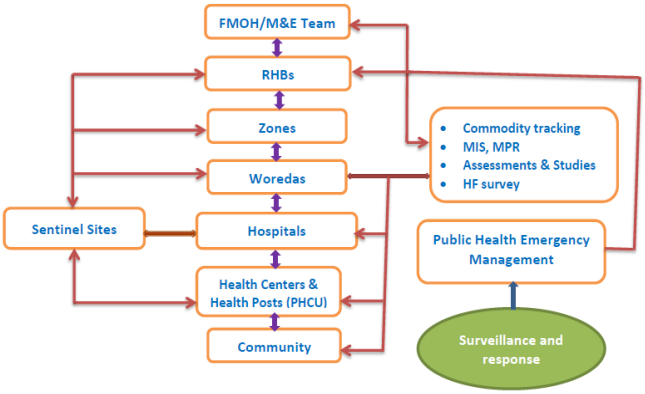


Figure 25: Regular reporting system (PHEM and HMIS)

The national malaria program M&E plan has identified M&E related targets during the control and elimination phases. The realization of these targets is vital for the overall achievement of the national vision of seeing malaria free Ethiopia. The targets identified are:

Control Phase

- 100% of health facilities and health offices engaged in malaria control phase send weekly malaria report to the next higher level
- 100% of health facilities in epidemic prone areas adhere to the national epidemic and response plan.
- 100% of health facilities in epidemic prone areas have developed epidemic thresholds defined by time period using all available past data of confirmed cases.
- 100% of health facilities and Woreda health offices using epidemic monitoring charts based on confirmed cases.
- 100% of all detected malaria epidemics properly controlled per the national epidemic and response plan within two weeks of onset.

Elimination Phase

- 100% of facilities in the selected elimination districts will have standardized data capturing tools.
- 100% of the clusters/*Kebeles* in selected elimination districts will have a trained functional surveillance assistant.

- 100% of health facilities in selected elimination districts will report weekly malaria data using rapid reporting system.
- 100% of index cases family and neighbors will be traced and tested.

Sources of Routine Data Collection

1. **Health Management Information System:** should be complete, timely and reliable at all levels

2**. Public Health Emergency Management/ Surveillance:** encompasses reporting of morbidity and mortality data from health posts, health centers and hospitals through PHEM, including clinical malaria (outpatient and inpatient), confirmed malaria by species and severe malaria.

3. **Integrated Pharmaceuticals Logistical System (IPLS):** developed to track all health commodities from procurement to distribution to the Woredas level.

4. **Activity and Performance Reports:** Tracking program performance, and ensuring availability of financial, human and other resources. Determining the level of service delivery that is achieved during implementation efforts.

National malaria case management related indicators

Morbidity attributed to malaria: this indictor is defined as, Malaria cases per 1000 population and the source of data are Patient register at HP; outpatient/ inpatient service-based registers

Facility-based malaria deaths: this indictor is defined as: Percentage of all deaths due to malaria (according to confirmed malaria diagnosis). Data for this indicator are generated from Inpatient register at health centers and hospitals.

Malaria positivity rate: Percentage of slides or rapid diagnostic tests found positive among all slides and rapid diagnostic tests performed and data are generated from Laboratory register at health centers and hospitals, patient register at HP

Confirmed malaria cases (number and rate): Number of confirmed malaria cases (by microscopy or RDT) divided by Mid-year resident population by age per 1000 persons at risk of malaria

Percentage of out-patient malaria cases that received appropriate anti-malarial treatment according to national policy: this is defined as number of outpatient malaria cases receiving ant malarial treatment at health facility divided by number of outpatient patients malaria cases expected to be treated at health facility level with appropriate treatment x 100 and the source of data are Health facility records and registers

Table 21 List of Health Management Information System (HMIS) formats

S/n	Name of the Reporting Form	Data generated from
1	Health Centre OPD Disease Monthly Report	OPD registrations book
2	Health Centre Monthly Service Delivery Report	Laboratory registration book
3	Health Centre IPD Disease Morbidity And Mortality Monthly Report	IP registrations book
4	Health Centre/ Hospital Quarterly Service Delivery Report	Monthly service delivery report
5	Health Post Monthly Disease Report form	OPD registrations book
6	Health Post Monthly Service Delivery Report form	OPD registrations book

Public Health Emergency Management/ Surveillance Form: takes account of Data generated from Morbidity and mortality data from health posts, health centers and hospitals through PHEM, including clinical malaria (outpatient and inpatient), confirmed malaria by species and severe malaria**.** The recording format is indicated blow;

Table 22 PHEM Weekly Disease Report Form for Outpatient and Inpatient malaria Cases and Deaths

Indicator		Out - Patient	In - Patient	
		Cases	Cases	Deaths
Total Malaria (confirmed andclinical)				
Total malaria suspected fever cases examined by RDT or Microscopy				
Number cases positive for malariaparasites (either by RDT or Microscopy)	P. falciparum			
	P. vivax			

Source: National PHEM Guidelines, 2012

LEARNING UNIT TWELVE

Health Facility Visit

Learning Objectives

By the end of this session, participants will be able to:

- Describe the profile of malaria patients with uncomplicated and severe malaria seen in the hospital in the past month or quarter
- Take a history and conduct a clinical examination of (a) a child with fever at Pediatric outpatient, (b) a patient with an uncomplicated febrile illness, and (c) a patient with severe malaria, who are being treated in the hospital
- Assess the basis for diagnosis and the details of the management of the patients reviewed in the second bullet above
- Describe the Integrated Pharmaceutical Logistics' System
- Describe completeness, timeliness and consistency of Health Management Information System (HMIS) and Public Health Emergency Management (PHEM) hospital data.

Activities

Divided into five groups consists of 5 to 8 members.

Use the checklists and complete using:

- Feverish child (under five years) at paediatric outpatient department
- Febrile adult at adult outpatient department
- Very severe febrile disease (in patients)
- HMIS (OPD, Lab and other relevant team member
- Pharmaceutical Logistics Department

Checklist for Health Facility Visit

Malaria data management

Review the data from the previous reporting period

1. HMIS
    a. OPD HMIS register
        i. Number of malaria suspected cases _____
        ii. Number of malaria cases
            1. *Plasmodium falciparum* _____
            2. *Plasmodium vivax* _____
            3. Mixed infection (*p.falciparum* and *p.vivax*) _____
    b. Tally sheet
        i. Number of clinical malaria cases _____
        ii. *Plasmodium falciparum* _____
        iii. *Plasmodium vivax* _____
        iv. Mixed infection (*p.falciparum* and *p.vivax*) _____
    c. Laboratory register
        i. Number of patients tested for malaria _____
        ii. *Plasmodium falciparum* _____
        iii. *Plasmodium vivax* _____
        iv. Mixed infection (*p.falciparum* and *p.vivax*) _____
    d. HMIS reporting form
        i. Number of patients suspected for malaria _____
        ii. Number of patients tested for malaria _____
        iii. *Plasmodium falciparum* _____
        iv. *Plasmodium vivax* _____
        v. Mixed infection (*p.falciparum* and *p.vivax*) _____
    e. Give your comments with regard to data completeness, consistency
    _____
    _____
2. PHEM
    a. Review the PHEM book
        i. Number of patients suspected for malaria _____
        ii. Number of patients tested for malaria _____
        iii. *Plasmodium falciparum* _____
        iv. *Plasmodium vivax* _____
        v. Mixed infection (*p.falciparum* and *p.vivax*) _____
    b. Give your comments with regard to data completeness
    _____
    _____
3. Epidemic monitoring chart
    a. Comment on threshold, is it updated? What is the interpretation?

Checklist for Health Facility Visit
Malaria drug supply management

Visit pharmacy

Review RRF and IRRF forms of the previous reporting period

- Are all columns filled appropriately? _____

Check availability of drugs

- Artemether-lumefantrine
    - AL 1 x6 _____
    - AL 2x6 _____
    - AL 3x6 _____
    - AL 4x6 _____
- Chloroquine
- Artesunate injection
- Quinine tablets
- Quinine injection
- Primaquine
- RDT

If there is drug shortage, find out the reason _____

Checklist for Health Facility Visit

Fever in adult patient and severe malaria

Identify a patient with acute fever or a patient with severe febrile disease

Age _____ sex _____ Address _____

Chief compliant:

History of present illness:

Systemic review

	Normal or abnormal?	Describe if abnormal
General		
HEENT		
Respiratory		
Cardiovascular		
Gastrointestinal		
Genitourinary		
Integumentary		
Musculoskeletal		
CNS		

Differential diagnosis:

Laboratory investigations that you order:

Actual laboratory findings:

Most likely diagnosis:

Treatment:

Checklist for health facility visit, IMNCI

<table>
<tr><td colspan="3">MANAGEMENT OF THE SICK CHILD AGE 2 MONTHS UP TO 5 YEARS

Child's Name: _____ Age_____ months Sex _____ Weight: _____kg
Lt/Ht _____ cm Temp _____^{0}C
ASK: What are the child's problems? _____ Initial visit? _____ Follow-up visit? ____
ASSESS (Circle all signs present, tick or fill dashes/spaces)

CLASSIFY</td></tr>
<tr><td colspan="2">CHECK FOR GENERAL DANGER SIGNS
NOT ABLE TO DRINK OR BREASTFEED
CONVULSING NOW
VOMITS EVERYTHING
LETHARGIC OR UNCONSCIOUS
History of CONVULSIONS</td><td></td></tr>
<tr><td colspan="2">DOES THE CHILD HAVE COUGH OR DIFFICULT BREATHING?
Yes _____ No_____</td><td rowspan="2"></td></tr>
<tr><td>For how long? _____ Days</td><td>□ Count the breaths in 1 minute. _____ breaths/minute. Fast breathing?
□ Look for chest indrawing.
□ Look and listen for stridor.</td></tr>
<tr><td colspan="2">DOES THE CHILD HAVE DIARRHOEA? Yes _____ No____</td><td rowspan="2"></td></tr>
<tr><td>For how long? _____ Days

Is there blood in the stool?</td><td>□ Look at the child's general condition. Is the child: Lethargic or unconscious? Restless and irritable?
□ Look for sunken eyes.
□ Offer the child fluid. Is the child: Not able to drink or drinking poorly? Drinking eagerly, thirsty?
□ Pinch the skin of the abdomen. Does it go back: Very slowly (> 2 seconds)? Slowly?</td></tr>
<tr><td colspan="2">DOES THE CHILD HAVE FEVER? (by history/feels hot/temperature ≥37.5^{0}C)
Yes___ No____</td><td></td></tr>
</table>

- Decide MALARIA risk: High/Low No, - If "low or no" malaria risk, Has child traveled to malarious area in the last 30 days? - For how long has the child had fever? _ Days -If >7 days, has fever been present every day? - Has child had measles within the last 3 months?	□ Look or feel for stiff neck. □ Look for bulging fontanel □ Look for runny nose □ Look for signs of MEASLES NOW : Generalized rash, And one of these: Cough, Runny nose or Red eyes. □ Blood Film or RDT: Positive___ Negative___ Not Done ____	
If the child has measles now or within the last 3 months:	□ Look for mouth ulcers: If Yes, are they deep and extensive? □ Look for pus draining from the eye. □ Look for clouding of the cornea.	

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Annexure

A. BIN CARD

Name of Health Facility: _____

Product Name, Strength and Dosage orm _____

Unit of issue: _____

Maximum Stock Level: _____ Emergency Order Point: _____

Average Monthly Consumption (AMC):_____

Date	Doc. No. (Receiving or Issuing)	Received from or Issued to	Quantity				Batch No.	Expiry Date	Remarks
			Received	Issued	Loss/Adj	Balance			

B. STOCK RECORD CARD

Name of Health Facility: _____

Product Name, Strength and Dosage Form: _____

Unit of Issue: _____ Location: _____

Maximum Stock Level: _____ Emergency Order Point: _____

Average Monthly Consumption (AMC):_____

Date	Doc. No. (Receiving or Issuing	Received from or Issued to	Quantity				Price		Expiry Date	Remarks
							Unit Price			
			Received	Issued	Loss/Adj	Balance	Birr	Cent		

C. Health Post Monthly Report and Re-supply Form

Name of the Health Post: _____ Health Post ID Code: _____

Supplying Health Centre: _____ Health Center ID Code: _____

Ser. No.	Product Code/Product Name/Unit	Unit of issue	Completed by Health Post				Completed by Health Centre				
			Beginning Balance	Quantity Received	Loss / Adjustment	Ending Balance	Calculated Consumption this month E = A+B+/-C-D	Calculated Consumption last month	Maximum Quantity G = E + F	Quantity Needed to Reach Max. H = G – D	Quantity to be Supplied
			A	B	C	D	E	F	G	H	I
1	Product description (pre-printed)										
2											
3											
Remarks:											
Completed by (Name, Date and Signature)							Completed by (Name, Date and Signature)				
Approved by (Name, Date and Signature) :											

Reporting Period From: (month/day/year) To: (month/day/year) Maximum Level: 2 months of stock

Internal Facility Report and Resupply Form

Name of Dispensing Unit: _____ Reporting Period From: _____ To: _____

Maximum Level (ML):_____

Ser. No.	Item	Unit of issue	COMPLETED BY UNIT				COMPLETED BY STORE			
			Beginning Balance	Quantity Received	Loss/ Adjustment	Ending Balance	Calculated Consumption E = A+B+/-C-D	Maximum Quantity F =E * 2	Quantity Needed to Reach Max. G = F – C	Quantity to be Supplied
			A	B	C	D	E	F	G	H
1										
2										
3										
4										
5										
Remarks :										
Completed by (Name, Date and Signature) :							Completed by (Name, Date and Signature) :			
Approved by (Name, Date and Signature) :										

D. Report and Requisition Form for Program Drugs

Health Facility: _____	Region: _____ Zone:_____ Woreda:_____
Supplying Branch:_____ _	Maximum Stock Level = 4 Months of Stock
Reporting Period: From:_____To: _____	Emergency Order Point = 0.5 Months of Stock

SN	Product Description	Unit of Issue	**Report Part**							**Requisition Part**		
			Beginning Balance	Quantity Received	Losses/ Adjustments	Ending Balance		Calculated Consumption	Days Out of Stock	Maximum Stock Quantity	**Quantity Needed to Reach Max**	Quantity Ordered
						DU	Store					
			A	**B**	**C**	**D**	**E**	**F = A + B +/- C – D –E**	**F**	**G = (120*F) /(60 – F)**	**H= G-D-E**	
1												
2												
3												

Products with shelf life < 6 months (S/No, Quantity and Expiry date):	Remarks:

Completed by:_____ Signature:_____
Date:_____

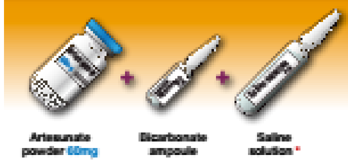
Verified by:_____ Signature:_____
Date:_____

Approved by:_____ Signature:_____
Date:_____

Annex xx. Artesunate Injection Poster

GUIDELINES FOR ADMINISTRATION OF INJECTABLE ARTESUNATE FOR SEVERE MALARIA

WHO RECOMMENDED TREATMENT [2]



PRODUCT DESCRIPTION [1]

Dose: For children < 20 kg: 3.0 mg/kg
For children > 20 kg and adults: 2.4 mg/kg

Can be given by intravenous route (IV) or intramuscular route (IM).
IV is the preferred route of administration.
Please refer to the patient information leaflet for more information.
* Water for injection is not an appropriate diluent

1 WEIGH THE PATIENT

2 DETERMINE THE NUMBER OF VIALS NEEDED

Weight	less than 25 kg	26-50 kg	51-75 kg	76-100 kg
60 mg vial	1	2	3	4

3 RECONSTITUTE

- Activate the drug: artesunate powder + bicarbonate ampoule (immediately before use)

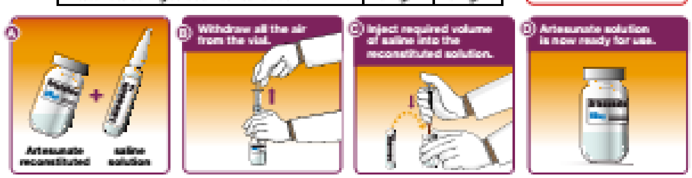
4 DILUTE

- Reconstituted artesunate + saline solution (or dextrose 5%)
- Volume for dilution

	IV	IM
Bicarbonate solution volume	1 ml	1 ml
Saline solution volume	5 ml	2 ml
Total volume	6 ml	3 ml
Artesunate 60 mg solution concentration	10mg/ml	20 mg/ml

IMPORTANT

Water for injection is not an appropriate diluent



5 CALCULATE THE DOSE

- Calculate and withdraw the required dose in ml according to route of administration:

Less than 20 kg

For intravenous route (IV)

Concentration: 10 mg/ml

$$\frac{3.0\text{ mg} \times \text{body weight (kg)}}{\text{IV artesunate solution concentration 10 mg/ml}}$$

Round up to the next whole number

Example:
Dose needed (ml) for 8 kg child:

$$\frac{3.0 \times 8}{10} = 2.4\text{ ml}$$

2.4 ml rounded up to 3 ml

Weight kg	Dose mg	Dose ml
6 - 7	20	2
8 - 10	30	3
11 - 13	40	4
14 - 16	50	5
17 - 20	60	6

For intramuscular route (IM)

Concentration: 20 mg/ml

$$\frac{3.0\text{ mg} \times \text{body weight (kg)}}{\text{IM artesunate solution concentration 20 mg/ml}}$$

Round up to the next whole number

Example:
Dose needed (ml) for 8 kg child:

$$\frac{3.0 \times 8}{20} = 1.2\text{ ml}$$

1.2 ml rounded up to 2 ml

Weight kg	Dose mg	Dose ml
6 - 7	20	1
8 - 10	30	2
11 - 13	40	2
14 - 16	50	3
17 - 20	60	3

More than 20 kg

Concentration: 10 mg/ml (IV)

$$\frac{2.4\text{ mg} \times \text{body weight (kg)}}{\text{IV artesunate solution concentration 10 mg/ml}}$$

Round up to the next whole number

Example:
Dose needed (ml) for 26 kg child:

$$\frac{2.4 \times 26}{10} = 6.24\text{ ml}$$

6.24 ml rounded up to 7 ml

Weight kg	Dose mg	Dose ml
20 - 25	60	6
26 - 29	70	7
30 - 33	80	8
34 - 37	90	9
38 - 41	100	10
42 - 45	110	11
46 - 50	120	12
51 - 54	130	13
55 - 58	140	14
59 - 62	150	15
63 - 66	160	16
67 - 70	170	17
71 - 75	180	18
76 - 79	190	19
80 - 83	200	20
84 - 87	210	21
88 - 91	220	22
92 - 95	230	23
96 - 100	240	24

Concentration: 20 mg/ml (IM)

$$\frac{2.4\text{ mg} \times \text{body weight (kg)}}{\text{IM artesunate solution concentration 20 mg/ml}}$$

Round up to the next whole number

Example:
Dose needed (ml) for 26 kg child:

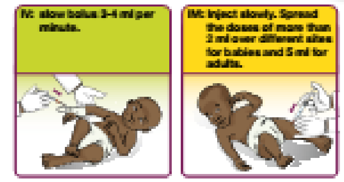
$$\frac{2.4 \times 26}{20} = 3.12\text{ ml}$$

3.12 ml rounded up to 4 ml

Weight kg	Dose mg	Dose ml
20 - 25	60	3
26 - 29	70	4
30 - 33	80	4
34 - 37	90	5
38 - 41	100	5
42 - 45	110	6
46 - 50	120	6
51 - 54	130	7
55 - 58	140	7
59 - 62	150	8
63 - 66	160	8
67 - 70	170	9
71 - 75	180	9
76 - 79	190	10
80 - 83	200	10
84 - 87	210	11
88 - 91	220	11
92 - 95	230	12
96 - 100	240	12

Remark: the upper limit for each weight band is 0.9 kg e.g. 14 - 16 kg covers 14 - 16.9 kg.

6 ADMINISTER



7 DOSING SCHEDULE

1. Give 3 parenteral doses over 24 hours as indicated in the opposite table

2. Give parenteral doses for a minimum of 24 hours once started irrespective of the patients ability to tolerate oral treatment earlier.

- Day 1 Dose 1: on admission (0 Hours)
  Dose 2: 12 hours later
- Day 2 Dose 3: 24 hours after first dose

- When the patient can take oral medication, prescribe a full 3-day course of recommended first line oral Artemisinin Combination Therapy (ACT).
  The first dose of ACT should be taken between 8 and 12 hours after the last injection of artesunate.
- Until the patient is able to take oral medication, continue parenteral treatment (one dose a day) for a maximum of 7 days.
- A course of injectable artesunate should always be followed by a 3-day course of ACT.

- Evaluate the patient's progress regularly.

IMPORTANT

- Prepare a fresh solution for each administration.
- Discard any unused solution after use.

This document is intended to demonstrate to health workers how to prepare and administer injectable artesunate, a treatment for severe malaria. It is not intended to provide personal medical advice. The responsibility for the interpretation and use of this material lies with the reader. In no event shall MMV be liable for damages arising from its use.

Annex Malaria OPD Form

SNO	Disease Facility	Regions/ zone/woreda/HF	Age breakdown						Total
			Male			Female			
			Male<=4	Male 5-14	Male >=15	Female <=4	Female 5-14	Female>=15	
101	Malaria (clinical without laboratory confirmation)								
102	Malaria (confirmed with P. falciparum)								
103	Malaria (confirmed with species other than P. falciparum)								

Annex Malaria
IPD form

Sn	Disease Facility	Regions/ zone/woreda/ HF	Age breakdown												**Total**
			Male			Female			Male			Female			
			Morbidity Male <=4	Morbidity Male 5To14	Morbidity Male >=15	Morbidity Female <=4	Morbidity Female 5To14	Morbidity Female >=15	Mortality Male <=4	Mortality Male 5To 14	Mortality Male >=15	Mortality Female <=4	Mortality Female 5To14	Mortality Female >=15	
101	Malaria (clinical without laboratory confirmation)														
102	Malaria (confirmed with P. falciparum)														
103	Malaria (confirmed with species other than P. falciparum)														

Annex Malaria **Service Delivery**

Sn	**Activity** / **Malaria**	Month / Regions													
C1.4.2.5.3	**Malaria positivity rate**														
4.2.5.3.1	Number of slides or RDT positive for malaria														
4.2.5.3.1.1	Less than 5 years : males														
4.2.5.3.1.2	: females														
4.2.5.3.1.3	5-14 years : males														
4.2.5.3.1.4	: females														
4.2.5.3.1.5	Greater than or equal to 15 years : males														
4.2.5.3.1.6	: females														
4.2.5.3.1.7	Total number of slides or RDT performed for malaria diagnosis														