The epidemiological approach to malaria control

Learner’s Guide

Communicable Diseases Cluster
Department of Control, Prevention and Eradication
Social Mobilisation and Training Unit
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An introduction to the epidemiological approach to malaria control

The Subject

Epidemiology has been defined as the basic science of public health. The epidemiological approach to disease control, e.g. malaria control, is based on the three main functions which epidemiologists perform, more or less successfully, namely, in order of increasing difficulty and uncertainty:

1. to describe and measure the distribution of disease, e.g. who gets malaria, how much of it, when and where?
2. to explain that distribution by its determinant factors: biological, environmental, social, behavioural and economic.
3. to predict the changes expected in that distribution from human interventions, in particular from control measures.

These three epidemiological functions should constitute important inputs into the planning of malaria control, with the aim of adapting the control strategy to the epidemiological situation.

During implementation of the control strategy, the epidemiologist should continue to be involved and is responsible for epidemiological evaluation, meaning measurement of the national malaria strategy’s impact on the health problem. Evaluation should lead the epidemiologist to a critical review of earlier explanations and predictions, and that review will constitute an important input into replanning, i.e. revision of the plan in accordance with a changing situation and/or better information.

This training module

The module consists, in its present state, of ten units addressing various (overlapping) aspects of the epidemiological approach to malaria control. Each unit consists of a Learner’s Guide and a Tutor’s Guide. The Learner’s Guide proposes a series of exercises and offers hints for some of the problems. The Tutor’s Guide gives guidance to the tutor for answers to the exercises.

The module aims at developing an approach, namely the critical application of epidemiological thinking to malaria control, rather than to convey a body of facts (even though many facts may be conveyed in the process).

No document can, and this module does not, exhaust such a wide subject. It is an introduction to the subject, and an introduction rather than the introduction. The module will be successful if it helps the learner decide to continue to develop the approach as an integral part of his professional activities.
Using the module

The module is designed for 1 week of training, working mainly in small groups, say 2 or 3 groups of 6 to 9 learners each. It is desirable for each group to have its own room, with at least one of the following: overhead projector, whiteboard, blackboard, flipcharts. For each unit the group selects, among its members, a moderator and a rapporteur by rotation, so that, as far as possible, each learner performs each of those two functions at least once.

The learners will usually have different backgrounds, in terms of training and experience, so that they should have much to learn from each other. Each group should be assisted by a facilitator, ideally a person that has been a learner during a previous application of the module, who is expected to help the group perform the exercises, without becoming too directive. Finally, the course tutor has the overall responsibility of coordinating the week's work. This will include rotation among the groups, participating in their discussions if needed or requested.

The learners will have received the Learner's Guide sometime in advance. The facilitators have in addition the Tutor's Guide, out of which they will provide to the groups, as work on the unit proceeds, the relevant graphs, tables, and responses, as referred to in the Learner's Guide. In the course of work on a unit, the tutor will distribute the presentation, in plenary session, of that unit's parts among the groups. After completion of group work on a given unit, each group will present (briefly) in plenary session, its conclusions (on the part assigned to it for presentation), and the presentation will be open to question and comments from learners, facilitators, and tutor. After completion of the plenary on a given unit, each learner will receive that unit's Tutor's Guide (including graphs and tables).

It is rather difficult or even impossible, in one week, to go in detail through every point of every unit. That is not a major problem if one accepts that the goal is to learn an approach rather than any detailed factual content. The tutor will use his judgement in skipping some parts or even whole units. The fact that several parts or units often converge, from different angles, on the same issues, should allow this. The tutor should make a tentative timetable at the beginning of the week, but be ready to adapt it to the way the course actually progresses.

The Learner's Guide can also be used in conjunction with the Tutor's Guide, for individual active self-learning.
What you know about malaria in your country or place of work

Learning objectives:

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

- understand more clearly the relationship between the epidemiology of malaria and its control in your country or place of work.

In the following pages of this Learning Unit you will find a series of questions which you should answer the best you can. This is not an examination but is designed to make you think about the relationship between the epidemiology of malaria and its control as it relates to your own country or place of work. You should answer the questions in the sequence in which they are written because depending on your answer to some of them you may not need to answer some of the questions that follow. Your answers should be in respect to your own country (or the country in which you are, or will be working). If you cannot answer the question relative to the whole country, but can for a part of it, then please do so stating clearly to what part of the country your answer applies.

Answer clearly and briefly those questions on which you have a definite opinion. Where "yes", "no", "do not know" answers are provided then please tick the box for which one of them is appropriate.
Questions
A. The species of human malaria parasites in your country

What species of human malaria parasites are endemic?

Rank them in order of frequency of occurrence:

Rank them in order of importance with respect to public health:

B. The geographic distribution of malaria (infection and disease) in your country

Is the geographical distribution of malarial infection uniform?

Yes  No  Do not know

Is the geographical distribution of malarial disease uniform?

Yes  No  Do not know
What you know about malaria in your country or place of work:  

(If the response to both questions is yes or do not know, then please proceed to Section C).

Are there malaria-free areas?

Yes  
No  
Do not know

If yes, identify them, and state briefly why you think they are malaria-free.

Except for any malaria-free areas, is the distribution uniform?

Yes  
No  
Do not know

If no, is the geographical distribution of malarial infection and disease related to the geographical distribution of other variables?

Yes  
No  
Do not know

If yes, list these variables and describe how they influence the distribution of malaria infection and disease.
Is the geographical distribution of disease the same as that of infection?

Yes  
No  
Do not know

If no, how do they differ, and why?

C. The variation of malaria (infection and disease) over time in your country

Does malaria vary by season?

Yes  
No  
Do not know

If yes, how and why?

Does malaria vary from year to year?

Yes  
No  
Do not know

(If the response is no or do not know, proceed directly to Section D).
Does the variation from year to year show some periodicity?

Yes  No  Do not know

If yes, what kind of periodicity, and why?

__________

__________

__________

Does the variation from year to year show a long-term trend?

Yes  No  Do not know

If yes, is the trend upwards or downwards? (Indicate by an arrow).

How do you explain the trend?

__________

__________

__________

Do malaria epidemics occur in your country?

Yes  No  Do not know

(If no or do not know, then proceed directly to Section D).
What is your definition of a malaria epidemic?

When and where do malaria epidemics occur in your country, and why?

D. **The distribution of malaria (infection and disease) among persons in your country**

Is the distribution of malarial *infection* among persons uniform?

- Yes
- No
- Do not know

Is the distribution of malarial *disease* among persons uniform?

- Yes
- No
- Do not know

(If the response to both questions is *yes* or *do not know*, then please proceed directly to Section E).

Is the distribution of malarial infection and disease among persons related to personal factors?

- Yes
- No
- Do not know
What you know about malaria in your country or place of work:

If yes, which factors, how and why?

Is the distribution of malarial disease among persons the same as the distribution of infection?

Yes [ ] No [ ] Do not know [ ]

If no, how do they differ, and why?

E. Cerebral malaria

Is it an important problem in your country?

Yes [ ] No [ ] Do not know [ ]

If no, or do not know, then please proceed directly to Section F.

If yes, which part of the population is primarily affected, when and where?

--
How do you explain that distribution of cerebral malaria?

F. Malaria mortality

Is it an important problem in your country?

Yes [ ] No [ ] Do not know [ ]

(If no, or do not know, then please proceed directly to Section G).

If yes, which part of the population is affected, when and where?

________________________________________________________________________

________________________________________________________________________

How do you explain that particular distribution of malaria mortality?
G. Epidemiological types of malaria

Can you identify different epidemiological types of malaria in your country?

Yes [ ] No [ ] Do not know [ ]

If yes, list the different types and indicate their main characteristics.

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H. Malaria control measures

Identify malaria control measures that are currently used in your country and for each of these measures, indicate:

(a) the methods used;
(b) who performs the actions required; and
(c) whether it is applied uniformly or not and under what conditions (e.g. where, in what population group and when).

<table>
<thead>
<tr>
<th>Malaria control measure</th>
<th>Method used</th>
<th>Who performs the actions required</th>
<th>Applied uniformly or not?</th>
<th>Under what conditions?</th>
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Outline the distribution of responsibilities for malaria control activities at different levels in your country.

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What are the aims of malaria control in your country? *If different objectives are pursued in different geographic areas or population groups, subdivide your answer accordingly.*

Were malaria control measures other than the current ones applied in the past in your country?

- Yes  
- No  
- Do not know

If yes, which ones, in what part of the country, and with what objective(s)? With what success? Why were they discontinued?

Is malaria being controlled satisfactorily in your country, given the epidemiological conditions and resources?

- Yes  
- No  
- Do not know
Is it improving, deteriorating or unchanged? If deteriorating then what are the main obstacles to achieving a good level of control?
I. Information concerning malaria in your country

Indicate briefly what kind(s) of information (not the actual numbers) is (are) available on the aspects of malaria listed in the table below. For each kind of information rate its reliability, coverage, potential usefulness and actual utilization using the symbols "- ±, +" * and complete the table with other information that you may have and consider useful in understanding the malaria situation.

* - no
± may be / possibly
+ yes

<table>
<thead>
<tr>
<th>Kind of information</th>
<th>Reliable?</th>
<th>Coverage complete?</th>
<th>Potentially useful?</th>
<th>Actually used?</th>
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<td>Economic</td>
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<td>Prevalence/infection rates</td>
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<td>Vector</td>
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<td>Groups at risk</td>
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<td>Severe malaria</td>
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<td>Mortality</td>
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<td>Drug consumption/usage</td>
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Outline, for your country, the distribution of responsibilities at different levels with respect to the collection and analysis of information concerning malaria.

Is the information available on malaria in your country satisfactory, given the epidemiological conditions and resources?

Yes

No

Do not know

If the answer is no, why? How can it be improved?
Learning Unit 2

The life cycle of the malaria parasite and its relationship to pathogenesis, immune responses, antimalarial drugs and field measurements

*Learning objectives:*

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

- describe the life-cycle of human malaria parasites
- describe some important characteristics of infection with each of the four species of human malaria parasite
- relate the parasite’s life cycle to pathogenesis, immune responses and potential vaccines
- identify, in the parasite’s life cycle, the points of impact of the main antimalarial drugs
- identify in the parasite’s life cycle what can be measured and by what methods, technically eligible for use in malaria control programmes.

*Diagram of the life cycle of the malaria parasite.*

Working as a small group discuss with your colleagues ways of preparing a schematic representation of the life-cycle of the malaria parasite. Review the different viewpoints of your colleagues before preparing your own diagram (each individual learner).

Like all sexually reproducing organisms the malaria parasite is diploid during part of its life-cycle, haploid during the rest of the cycle. Identify in what parts of the cycle the parasite is diploid and haploid, respectively. Discuss whether it matters.

Study the diagram of the life-cycle of the malaria parasite presented to you by the tutor (Fig 2.1) and compare it with the one you have prepared. If there are major differences between the two presentations discuss these differences with your facilitator.
Characteristics of infection with the four species of human malaria parasites.

Working as a small group list the different characteristics of an infection with each of the four species of human malaria parasites.

Draw:

a) a table of time factors (e.g. duration of incubation period, duration of asexual cycle in the blood, total duration of untreated infection) for the different species;
b) a table of multiplication factors (e.g. numbers of merozoites per hepatic schizont and per blood schizont) for the different species;
c) a short list of other important differences among the species.

Compare the results of your exercise with the tables and list presented by the tutor.

Discuss the differences.

The parasite's life cycle, pathogenesis, and immunity

- On a copy of the diagram of the parasite’s life cycle (fig 2.1), indicate the main ways in which the parasite can produce disease. List the main mechanisms of pathogenesis. Compare to the tutor’s Fig 2.2. Discuss differences and implications.
- On a copy of Fig 2.2, indicate the main categories of naturally acquired immune responses (IRs) to the malaria parasite. For each category of IR, indicated by what parasite life stage(s) it is stimulated, and in what part of the life-cycle it exerts it impact. Compare to the tutor’s Fig. 2.3. Discuss the differences and implications.
- On a copy of Fig 2.3, indicate the expected points of impact of different kinds of potential malaria vaccines. Compare to the tutor’s Fig 2.4. Discuss differences and implications.

The parasite's life cycle and antimalarial drugs

On a copy of the diagram of the parasite’s life cycle (Fig 2.1), indicate the points of impact of the main antimalarial drugs. Compare to the tutor’s Fig 2.5. Discuss differences and implications.

Epidemiological measurements

On another copy of the same diagram (Fig. 2.1) identify the possible epidemiological measurements. Indicate, from a technical point of view, what can be measured, and state by what methods. Compare with the Tutor’s Figure 2.6. Discuss differences and implications.
Please read carefully the next Unit of this module before commencing the session to which it relates.
The life cycle of the vector and the factors that affect it in relation to malaria transmission

Learning objectives:

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

- describe the life-cycle of the malaria vectors
- describe the factors affecting the vector’s life-cycle in relation to malaria transmission (including vector control)
- relate vector collection methods to the vector’s life-cycle, and entomological data to their epidemiological interpretation

The vector’s life cycle

Discuss with your colleagues ways of preparing a diagram of the life-cycle of the malaria vector. Review the different viewpoints of your colleagues before preparing your own diagram.

Study the diagram of the life-cycle of the malaria vector presented to you by the tutor (Fig 3.1), and compare it with the one that you drew. If there are major differences between the two presentations, discuss these differences in your group and with your facilitator.

Factors affecting the vector’s life-cycle in relation to malaria transmission

Working as a small group, list the major factors that have a direct effect on the vector’s life-cycle, then try to organize these factors into appropriate groups.

You might consider the following groups:

- numerical factors e.g. duration of life-stages
- vector behaviour
vector-parasite interactions, including perhaps possible density-dependent regulation in the vector
- differences among vector species
- factors of the physical environment, perhaps subdivided according to type of effect on the vector's life-cycle, e.g. vector production, vector survival, man-vector contact, etc.

Compare the results of your exercise with the grouping presented by the tutor. Explain how each listed factor affects the vector's life-cycle.

**Vector control measures and their point of impact**

Group vector control methods according to their nature - e.g. chemical - and to the stage of the vector's life-cycle to which they are applicable; also consider methods for reducing man-vector contact.

Then on a copy of the diagram of the life-cycle of the malaria vector (Fig 3.1) indicate the points of impact of the different control measures. Compare your diagram to the one presented by the tutor (Fig 3.2).

**Efficacy of vector control measures**

Do all control measures have the same effect on the transmission of malaria? If not, how and why do they differ?

Do you need a hint? Try to imagine the path followed by a vector acquiring, incubating and transmitting the infection.

Do you need a second hint? Think of the number of times the same individual vector passes through the various stages represented on the diagram (Fig. 3.2).

Are your conclusions about the expected efficacy of certain control methods affected by the assumption that all the mosquitoes in a given population may or may not behave in the same way?

For instance a given amount of exophilic behaviour (outdoor resting after a blood-meal) may be a function of the whole vector population or only concentrated in a part of that population (exophilic subpopulation). Would that affect the efficacy of indoor residual spraying?

Similarly a given amount of behavioural change resulting in a decrease in the proportion of bites on man and an increase in the proportion of bites on animals could be a characteristic of the total population or concentrated only in a subpopulation; would that affect the impact of a control measure on transmission? Discuss within your group.
Measurement methods

On another copy of the same diagram of the vector’s life-cycle, indicate the main vector collection methods that are technically feasible in a control programme.

A number of variables can be measured in the samples collected, e.g. sex, species, number, age-class of females, nulliparous or parous, infection, etc., and from these measurements various indicators can be calculated, e.g. man-biting rate, sporozoite rate, survival rate, etc. Measurement of the variables and calculation of the indicators are covered in courses of medical entomology.

Compare your diagram with the one presented by the tutor (Fig. 3.3).

**Three problems of epidemiological interpretation of entomological data will be considered here.**

1. **Representativeness** of entomological measurements: relationship between the actual measurement and the reality it is intended to measure.

We would like to measure vector density and vector behaviour.

   a) Do our collection methods allow us to measure them independently of each other?
   b) If the answer is no, do we measure “true” density or only indicators of trend?
   c) Does this matter for measuring impact of vector control, e.g. entomological impact of the introduction of impregnated mosquito nets?

2. **The ratio between sample size and population size**

   a) Are entomological sampling fractions usually large, small, or very small?
   b) Consider the following example. In an isolated village, during one whole night, 20 female mosquitoes of species X are collected on two human baits. What other variables do you need to know to calculate the mosquito population of that night in that village?
   c) Attribute some plausible value to each of these variables, and calculate the mosquito population size and the sampling fraction.
   d) Is it common to find new cases of human infection without finding infected vectors? Can you compare the sampling fraction of the two measurements? Start from the example just calculated, does the comparison explain the discrepancy?
3. Calculating survival from age-comparison
   
a) Name the two variables that determine age-composition of adult female vectors at a given point in time.

b) What are we assuming if we calculate survival from age-composition at a given point in time?

c) What are we assuming if we calculate survival from average age-composition over a period of time, e.g. a transmission season?

Please read carefully the next Unit of this module before commencing the session to which it relates.
Learning Unit 4

The natural history of malaria in the human host and the factors that affect it

Learning objectives:

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

• describe the natural history of malaria in the human host

• describe the factors that have an effect on the natural history of malaria in the human host, including immunity and malaria control measures

Natural history of malaria in the human host

1. Working in a small group, discuss with your colleagues ways of preparing a diagram of the natural history of malaria in the human host. Start with a flow-chart from inoculation to death, including intermediate states and reversible steps.

Review the different viewpoints of your colleagues before preparing your own diagram. Each learner should draw his/her own diagram of the natural history of malaria in the human host.

Study the flow chart (Fig. 4.1) presented to you by the tutor and compare it with the one you have drawn. If there are major differences between the two, discuss these differences with your facilitator.

2. a) How fast do persons move from one state to another?
   b) Does it matter for case-management?
   c) Does the risk of disease and the risk of severe disease change in the course of time after inoculation?
   d) What kind of data are relevant for addressing this last question?
Discuss these four questions in a small group, draft individual answers, and compare them to the tutor’s.

3. Not every case proceeds all the way from inoculation to death and different cases stop at different intermediate states. Discuss in group what factors might affect the outcome of an inoculation, and how to classify the factors in a meaningful table. After that, each learner will draw a table. Note that at this stage we are only concerned with identification and classification of factors; subsequent sections will consider the different classes of factors, their possible importance and mode of action. Compare your table with the one presented by the tutor (Table 4a). Discuss the differences.

The inoculum’s intrinsic factors

Address the following questions in small group discussion, and draft individual answers.

1. Number of sporozoites inoculated
   a) How many sporozoites does a vector inoculate?
   b) How can the number be measured?
   c) Does the number affect the outcome?
   d) How does one know?

2. Differences of “virulence” among parasite species

Why is *P. falciparum* the most pathogenic? (see Learning Unit 2). Do other species of *Plasmodium* cause lethal forms of malaria?

3. Differences of “virulence” within a parasite species or local parasite population.

What observations suggests that there are such differences, within a species? And within a local population of a species? Consider the following:

   a) some children develop severe malaria presumably after a recent inoculation have received many previous *P. falciparum* inoculations without developing severe malaria;
   b) some asymptomatic parasitaemic children develop clinical malaria (uncomplicated malaria or severe malaria) following superinfection; can you explain that by the quantity of parasites added? As an example, imagine a child with an asymptomatic parasitaemia of 1000 parasitized red blood cells/µl, and a blood volume of 2000 ml, in which superinfection leads to the successful maturation of 20 liver schizonts;
   c) if you conclude that the outcome - disease or no disease, uncomplicated malaria or severe malaria - is related to the quality of the parasites
rather than their quantity can you further conclude that the parasite’s variable intrinsic virulence is a sufficient explanation of such differences of outcome?

Discuss all your answers with the tutor. Discuss the discrepancies.

The human host’s intrinsic factors

*Mutations and susceptibility*

List and discuss briefly examples of mutations that decrease or increase the human host’s susceptibility.

*Acquired immunity (active)*

1. What stimulates it? Is it “all or nothing” or gradual? Is it species-specific? Is it reversible? If so, how? Discuss the questions in group, then draft individual answers.

2. Draw a diagram of the effect(s) of active immunity on the natural history of malaria in the human host. Discuss the matter in group, then draw individual diagrams. Suggestion: take another copy of the flow-chart of malarial states (Fig 4.1); draw, to the right of the flow-chart, two additional, modified, flow-charts corresponding to “intermediate” and “high” levels of active immunity. Compare your diagram to the tutor’s (Fig 4.2). The diagram suggests that successive inoculations are progressively less pathogenic and less dangerous. However, according to a previous statement (see above): “some children developing severe malaria, presumably after a recent inoculation, have received many previous *P. falciparum* inoculations without developing severe malaria”. *Is there a contradiction? Discuss.*

3. Discuss, in relation to the diagram, the expected effects of different malaria control measures, such as vector control, control of man-vector contact, chemoprophylaxis, treatment of cases, potential vaccines.

*Acquired immunity (passive)*

1. How is it acquired? Is it reversible? If so, how? Discuss in group, then answer individually.

2. Draw a diagram of the effect(s) of passive immunity. Discuss in group, then draw individual diagrams. Suggestion: take the copy of Fig 4.1 on which you have already sketched the effect(s) of active immunity, and add, to the left of the original flow-chart, a modified flow-chart, corresponding to passive immunity.

3. Compare your answers and diagrams with the tutor’s, in particular to Fig. 4.2.
Other human biological factors

Discuss how pathogenesis is affected by:

- pregnancy
- nutritional status
- age per se (i.e. over and above its association with immunity)

Interaction between parasite diversity and host diversity

1. It appears that intrinsic parasite and host factors can explain only part of the variation in outcome of host parasite encounters, and that interaction may be important.

   a) Consider the parasite:

      i) does a parasite present one, a few, or many antigens to the host?
      ii) do different parasites of the same species present much antigenic diversity, or a little or none?

   b) Consider the human host:

      i) can every host respond to every antigen?
      ii) does the set of antigens, to which a host can respond, i.e. the host's potential immune repertoire, vary among hosts?

   c) Do the answers to (a) or (b) suggest something about pathogenesis, over and above the intrinsic virulence of the parasite and the intrinsic susceptibility of the host?

Age-specific distribution of malaria

Working as a small group with your colleagues, carry out the following exercise. Suppose that exposure (to vectors) does not vary with age; show on a diagram the kinds of age-specific distributions you expect for:

- malarial infection (parasitaemia)
- malaria disease
- malaria deaths.

How do you expect those distributions to change if transmission increases or decreases? Try to show on a separate diagram the effect of transmission changes.

Does exposure to vectors vary with age? Does it matter?
What will the diagram look like in case of sudden exposure of a non-immune population to intense transmission?

**Malaria mortality**

Refer to Figures 4.1 and 4.2. According to those diagrams, malaria (P. falciparum) kills through severe malaria, i.e. clinical forms of malaria such as cerebral malaria, likely to be lethal if left untreated. Is that the only kind of death for which malaria is responsible? Think of the risk of death associated with some other diseases, e.g. pneumonia, measles, malnutrition; among children suffering from pneumonia, for example, some may suffer from uncomplicated malaria at the same time; is the risk of dying the same among the children suffering from pneumonia plus uncomplicated malaria, as among the children suffering from pneumonia alone? More generally, is the addition of uncomplicated malaria likely to affect the case fatality rate (CFR) of some other diseases?

If you think that the addition of uncomplicated malaria increases the CFR of some other diseases, the additional deaths may be called *indirect malaria deaths*, while the deaths by severe malaria may be called *direct malaria deaths*, and the sum of the two may be called *total malaria deaths*. Try to add these concepts to Fig 4.1. Compare your new diagram to the tutor's Fig. 4.4. Discuss the differences.

If there is both direct and indirect mortality from malaria, is their relative magnitude of practical importance, and, if so why? What kind of data would allow to estimate their relative magnitude? Do you know of such data, and what do they show?

Please read carefully the next Unit of this module before commencing the session to which it relates.
Learning Unit 5

Intensity of malaria

Learning objectives:

- define the major parameters of intensity of transmission which are used in malaria epidemiology
- identify the relationships between the vectorial capacity, the basic reproduction rate, the inoculation rate, and the incidence and prevalence of malaria infection
- describe the expected impact of mass drug administration and/or vector control activities on malaria transmission at different levels of endemicity
- distinguish what models can or cannot contribute to the planning of malaria control
- indicate the epidemiological methods for measuring malaria morbidity and mortality and how information can be collected
- describe how the relationship between vectorial capacity and other concepts of the intensity of malaria influence the selection of control methods in different epidemiological situations.

Intensity of transmission

The concept of “intensity” can be applied to the transmission of the malarial infection, to the disease, and to the related mortality. Name and define the different concepts of intensity that you think are applicable to malaria infection and to its transmission. After you have completed the exercise, compare your ideas with those of the other groups.

Vectorial capacity and basic reproduction rate

Vectorial capacity (C)

Derive a formula for the vectorial capacity C. You will probably find it helpful to start from the verbal definition of the vectorial capacity. The vectorial capacity (C) is defined as the “potential number of secondary cases originating per day from one
primary case, assuming that the population is and remains fully susceptible”. Proceed in the following order:

I. list the steps leading from a primary case to one or more secondary cases
II. list the factors that should be included and define them
III. designate each factor by a symbol
IV. combine the symbols into a formula.

The vectorial capacity is a measure of the efficiency of a local vector population. Does the derivation of the formula for C assume the actual presence of the parasite in the locality? In other words, can we calculate the vectorial capacity of the anopheline population present in an area in which there is no local malaria transmission?

**Basic reproduction rate (R<sub>0</sub>)**

The basic reproduction rate R<sub>0</sub> is defined as “the potential number of secondary cases of malaria originating from one primary case, assuming that the population is and remains fully susceptible”.

You could start by comparing the verbal definition of the vectorial capacity C and the one of the basic reproduction rate R<sub>0</sub> given above. R<sub>0</sub> must be equal to C multiplied by the number of days a case is infective.

How could the last factor be expressed algebraically? How is it usually done? If you know the traditional formulae for both C and R<sub>0</sub>, their comparison should give the answers.
Vectorial capacity, basic reproduction rate and control of transmission

There are a number of deductions concerning malaria control that can be made from the formulae for the vectorial capacity and the basic reproduction rate.

a) Complete the following table, identifying for each control measure the factor(s) affected.

<table>
<thead>
<tr>
<th>Control measures</th>
<th>Factors affected (among ( m, a, p, n, b, 1/r ))</th>
</tr>
</thead>
<tbody>
<tr>
<td>residual spraying</td>
<td></td>
</tr>
<tr>
<td>space spraying</td>
<td></td>
</tr>
<tr>
<td>source reduction</td>
<td></td>
</tr>
<tr>
<td>larviciding</td>
<td></td>
</tr>
<tr>
<td>reduction of man-vector contact</td>
<td></td>
</tr>
<tr>
<td>impregnated mosquito nets</td>
<td></td>
</tr>
<tr>
<td>treatment of cases</td>
<td></td>
</tr>
</tbody>
</table>

b) On the basis of formulae for \( C \) and \( R_0 \) evaluate the extent to which the variation in the different factors listed above affects the magnitude of the vectorial capacity or the basic reproduction rate;

c) Do the following exercise: calculate \( C \), given \( m = 10, a = 0.5, p = 0.8, n = 10 \). Calculate the effect on \( C \) of reducing either \( m, a \) or \( p \) by half. Why is a reduction of \( n \) not included in the exercise?

d) What is your conclusion concerning the relative efficacy of different control measures?

Identification of simplifying assumptions

In deriving the formulae of the vectorial capacity and the basic reproduction rate, and in making deductions about control, some simplifying assumptions were made. Can you identify them? Do they matter? (see Learning Unit 3).

Measurement of intensity

---

\(^1 m = \) vector density in relation to man; \( a = \) vector’s biting rate on man; \( p = \) survival of the vector; \( m = \) incubation period (in the vector); \( b = \) efficiency of the system; \( 1/r = \) duration of infectivity (in man)
With the colleagues of your working group, consider successively the five kinds of "intensity" identified at the start of this Unit. For each one, go through the following exercise:

a) can it be measured?
b) if so, how?
c) discuss with your colleagues the measurements in terms of:
   − technical feasibility
   − cost
   − reliability

Can the concepts - especially those of vectorial capacity and basic reproduction rate - be useful in the absence of the corresponding measurements?

Relationship between prevalence and incidence

With the colleagues of your working group, discuss the relationship between prevalence and incidence.

Can you express the relationship by a formula?

Can you give a numerical example? For example: if the incidence rate is 200 per thousand per year, and a "case" lasts on the average two months, what is the expected prevalence rate?

Qualitative relationships between the different types of intensity of malarial infection and its transmission

Working as a small group, construct a diagram in which the five dimensions of intensity previously identified are connected by arrows indicating what determines what; you may need to introduce some other factors, perhaps the duration of infection, immunity?

Discuss with your colleagues the relationships between the parameters of intensity of malaria shown in the figure given out (Fig 5.1).

Quantitative relationship between the prevalence rate and the vectorial capacity.

Discuss with your colleagues the quantitative relationship between the prevalence rate and the vectorial capacity. Working as a small group complete the following exercise. You may ask the facilitator for help.

a) Let \( y \) designate the prevalence of infection, expressed as a proportion rather than a percentage; draw a graph of \( y \) as a function of the vectorial capacity \( C \).
What is the relationship between the prevalence of infection and the vectorial capacity?

b) Ronald Ross was not only the first to show that malaria was transmitted by mosquitoes, he was also the first to formulate a mathematical model of the transmission of malaria; his model can be represented as follows:

\[
\begin{array}{c}
\text{negatives} \\
1 - y \\
\end{array} \quad \Rightarrow \quad \begin{array}{c}
\text{positives} \\
y \\
\end{array}
\]

\[y(t+1) = y(t) + y(t) \cdot C \cdot [1 - y(t)] - ry(t) \quad [1]\n
where

\[y = \text{proportion of positives in the human population}\]
\[1-y = \text{proportion of negatives in the human population}\]
\[C = \text{vectorial capacity (per time unit)}\]
\[r = \text{recovery rate (per time unit)}\]
\[t = \text{time}\]
\[t + 1 = \text{time } t + 1 \text{ time unit}\]

Do you understand the logic behind formula [1]? What does the added term \(y(t) \cdot C \cdot [1 - y(t)]\) represent? How is it derived?
What does the subtracted term (- y(t)) represent? How is it derived?

c) Imagine that the situation is in equilibrium, i.e. that the endemic level does not change; can we use formula [1] to derive a formula for y as a function of C?

**Hint:** in equilibrium \( y(t+1) \) must be equal to \( y(t) \); should the added term (the addition of new cases) be larger than, equal to or smaller than the subtracted term (the loss of old cases)?

d) You should get: \( y = 1 - \frac{r}{C} \) \[2\]

e) Use formula [2] to draw a graph of y as a function of C; compare to the graph you drew previously. See a) above.

f) Can you translate the formula [2] and the graph in terms of the basic reproduction rate \( R_0 \)?

g) What does the graph imply with respect to the following:
- is (are) there any threshold(s) or critical value(s)?
- what is the shape of the relationship - is it “linear” i.e., proportional?
- the stability of malaria under natural conditions?
- the expected impact of vector control?

**The value of the vectorial capacity below which malaria transmission cannot be maintained.**

Discuss with your colleagues why malaria transmission cannot maintain itself if C is below a certain value. Working as a small group complete the following exercise.

a) What is the critical value of C, i.e. the value below which malaria cannot maintain itself? Call it \( C^* \)

b) What is the critical value of the vector density? call it \( m^* \).

c) Calculate \( m^* \) for a “good” and “bad” vector respectively, using the following numerical values:

\[
\begin{align*}
  r &= 0.01 \\
  n &= 10 \\
  a &= \begin{array}{c}
  \text{"good vector"} \\
  \text{"bad vector"}
  \end{array} \\
  p &= \begin{array}{c}
  0.5 \\
  0.1 \\
  0.9 \\
  0.5
  \end{array}
\end{align*}
\]
Can you add on the graph the incidence rate, the entomological inoculation rate and the proportion seropositive as functions of $C$ or $R_0$?

What does the graph imply in terms of selection of measurement methods to describe malaria situations? What would one like to know? Can one get a useful approximation of the vectorial capacity (or of the basic reproduction rate) indirectly, i.e. without actually measuring them?

**Effects of a reduction in prevalence or in vectorial capacity**

Discuss with your colleagues the effects of a reduction in prevalence or in vectorial capacity. Working as a small group complete the following exercise.

a) Suppose that the prevalence of infection (or, if you like, the “parasite reservoir”) has been suddenly reduced to a low level by a single mass drug administration; what do you expect to happen to the prevalence after that?

b) Suppose that the vectorial capacity has been suddenly and permanently reduced to a lower level; what do you expect to happen to the prevalence after that?

c) Ross used the model represented by formulas [1] and [2] to explore these two questions, and reached conclusions which are generally accepted today; you could try to do the same.

Formula [1] is easy to do on a pocket calculator, especially a programmable one, but Ross had only pencil and paper.

To explore question a), you could use $C = 1$ and $r = 0.5$, start at $y(0) = 0.5$; calculate $y(1)$, $y(2)$, $y(3)$, $y(4)$, $y(5)$; change arbitrarily $y(5)$ to 0.1, calculate $y(6)$, $y(7)$ etc, and see what happens - you may find it helpful to plot the values on a graph.

To explore question b), you could do the same, up to $y(5)$; then, instead of changing $y(5)$, you reduce $C$ from 1 to $2/3$; then calculate $y(6)$, $y(7)$ etc. and see what happens - again, you may find it helpful to plot the values on a graph.

**Is there a place for models in planning malaria control?**

Are the following statements a) to d) correct?

a) “Facts are preferable to models”

b) “Models make questionable assumptions”

c) “Models use questionable numerical values”

d) “Models have failed - and will continue to fail - to make accurate predictions”

If some (or all) of the statements are correct, is there any place left for the use of models in planning malaria control?
**Relationship between intensity and disease**

Of the five concepts applicable to the “intensity” of malaria in terms of infection, which ones are applicable to malaria in terms of disease?

Do you see any other concept(s) that could be applicable to the quantification of malarial disease in a population?

**Measurement of the intensity of disease**

After discussion with your colleagues how to measure the intensity of a disease, complete this exercise:

a) What sort of data could be collected by the health services or by other organisations?

b) What are the main problems with respect to those measurements?

c) What can be done about them?

**Quantification of mortality from malaria**

Discuss with your colleagues how malaria mortality can be quantified, then complete the following exercise:

a) How could the mortality from malaria be quantified?

_A hint: malaria deaths could be related either to the population or to the cases of malaria._

b) What are the main problems with respect to those measurements, and what can be done about them?

**Further reading:**

_The Garki Project. Research on the Epidemiology and Control of Malaria in the Sudan Savanna of West Africa, by L. Molineaux and G. Gramiccia; WHO, 1980, 310 pages (E,F); ISBN 92 4 15606 1 4; World Health Organization, Geneva._

**Please read carefully the next Unit of this module before commencing the session to which it relates.**
Learning Unit 6

Case management in a malaria control programme

**Learning objectives:**

By the end of this Unit, you will know how to:

- improve diagnosis and treatment services at intermediate and peripheral levels to reduce morbidity and prevent deaths due to malaria

Working in small groups with your colleagues, discuss the following three alternative priorities for the control of malaria

i) the first priority should be the treatment of sick persons, with the objectives of reducing/shortening illness and preventing death

ii) the first priority should be the reduction of transmission

iii) the first priority should be the reduction of the endemic level.

**Relationship between those who need malaria treatment and those who get it effectively**

Select and define a malaria control programme, preferably using an actual situation that you know. Failing that, imagine one that is plausible on the basis of what is known about malaria. In this case facilitators may help.

The programme chosen should include information on at least the following:

a) the geographic location and type of climate

b) the type of human settlement; you could choose one of the following:
   - urban and suburban
   - rural sedentary with traditional agriculture
   - rural sedentary with modern irrigation

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- nomadic
- labour camps (e.g. migrant agricultural labour, construction projects)

c) type of transmission; you could specify the following:
- seasonal or perennial
- stable or unstable (from one year to the next)
- intense (with strong population immunity) or not.

Note that some combinations are not plausible, e.g. nomadic and perennial, or unstable and intense.

The exercise is concerned with basic principles, not actual numbers, it is not a planning exercise concerning a population of defined size or within a defined budget.

First-line treatment: the current situation.

Define as far as you can those variables affecting first line treatment. In this context, “first-line treatment” refers to the first treatment a person suffering from malaria is likely to get, from whatever source. The following list of questions can be used as a guide.

- Who needs antimalarial treatment, when and where?
- Who provides antimalarial treatment to the patients. If there are several sources, try to give a detailed list, and also to indicate their relative importance?
- How is the treatment obtained? How is contact made between patients and providers? How is the therapeutic decision reached?
- Who gets treatment? Compare with those who need it, both qualitatively, in terms of population subgroups, and quantitatively, in terms of coverage.
- What antimalarials (drug and route of administration) are available? What treatment regimens are most commonly used? If several first line treatments are available, on what grounds is a choice between them made? The answer to these three questions may vary according to the category of provider.
- Do the health services sometimes run out of antimalarials? How often? Why?
- What determines the list of antimalarials available?
- Is the treatment given usually appropriate? What are the criteria for an appropriate treatment?
- Who pays for first-line antimalarial treatment? If the patient has to pay, is the price fair according to the local situation? What determines the price?
- What is the current health impact of antimalarial treatment? What are the main problems associated with antimalarial treatment?
- What changes, if any, would be both beneficial and feasible, at the different levels, with respect to the first-line treatment of malaria?

Develop a diagram of the expected relationship between those who need antimalarials and those who receive them. In the light of your answers to the question “Who gets
treatment?” above, if necessary, redraw the diagram to represent your situation. Also list the factors that play a role in the distribution of treatment. Compare your diagram and list to the tutor’s (Fig. 6.1).

**Treatment failures**

What is treatment failure?

What are the possible causes of treatment failure?

Draft a table of possible methods for detecting treatment failures, and their causes, and indicate how reliable and how simple the different methods are. Compare your table to the tutor’s (Table 6.d)

What remedial actions in terms of prevention or cure, are taken against treatment failures and what else do you think should be done?

**Severe malaria**

What is severe malaria?

Who gets it, when and where?

What kind of care is required?

Who provides that kind of care?

Which cases get the appropriate care? How are they found and how do they get to the appropriate care? What is the relationship between those who get severe malaria - and need the appropriate care - and those who get that care?

Is prevention of severe malaria and malaria mortality possible? How?

Make a diagram showing the relationship of severe malaria and malaria mortality to the natural history of malaria in the human host and to the points of impact of various malaria control measures. Suggestion: start with a copy of Fig 4.4., from learning Unit 4. Compare your diagram to the tutor’s (Fig 6.2).

What is the current impact of malaria control activities (preventive or curative) on severe malaria? How could it be improved?

**Microscopic diagnosis**

What are the objectives of microscopic diagnosis?
How is microscopic diagnosis being currently used in your country?

What is the relationship between parasitaemia and illness?

Is the current use of microscopic diagnosis satisfactory? If not, what changes would be both beneficial and feasible?

Is quality control of the microscopic diagnosis currently applied? What is the procedure? Is it satisfactory? What changes, if any would be both beneficial and feasible?

**Expected impact of improved diagnosis of treatment of malarial illness**

In an area of intense transmission of *P. falciparum*, a programme of improved diagnosis, treatment and reporting of malarial illness and of severe and complicated malaria is introduced. Indicate in the adjoining Table 6.a, what change you expect in the various variables listed. Present separately what you expect in reality from what you expect to receive in reported information. Indicate expected change by arrows. If you wish to indicate the change expected in other variables, add them to the list.

Once you completed table 6.a then compare it with the one provided by the tutor.

**Table 6.a Expected impact of improved diagnosis and treatment of malarial illness**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Expected change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>In reality</td>
</tr>
<tr>
<td>incidence of infection</td>
<td></td>
</tr>
<tr>
<td>prevalence of infection</td>
<td></td>
</tr>
<tr>
<td>incidence of disease</td>
<td></td>
</tr>
<tr>
<td>prevalence of disease</td>
<td></td>
</tr>
<tr>
<td>incidence of severe malaria</td>
<td></td>
</tr>
<tr>
<td>death rate (all causes)</td>
<td></td>
</tr>
<tr>
<td>malaria mortality</td>
<td></td>
</tr>
<tr>
<td>case fatality rate of malaria</td>
<td></td>
</tr>
<tr>
<td>case fatality rate of severe malaria</td>
<td></td>
</tr>
</tbody>
</table>
Objectives

What are the objectives of a programme of diagnosis and treatment of malaria (the disease)? Suggestions:

- the discussion of the preceding points should help you
- the objectives can be epidemiological and/or operational, discuss that distinction
- identify precisely a small number of epidemiological and operational objectives.

Evaluation

What is the desired relationship between evaluation and objectives?

Evaluation uses indicators. An indicator is a ratio between two numbers; e.g. annual incidence rate of uncomplicated malaria = number of cases of uncomplicated malaria in 1 year/population at risk. Table 6.b lists numbers that could be used for the calculation of indicators. Note the distinction between real - but unknown - numbers, and the accessible numbers that could be used instead. Table 6.c lists indicators that could be calculated on the basis of the numbers listed in Table 6.b. The purpose of the tables is not to recommend the measurement/calculation of all numbers/indicators listed, but to help you to:

i) discuss the relationship of indicators to reality

ii) select a small number of indicators, appropriate for the evaluation of a particular control programme with respect to its objectives.

Table 6.b Potentially relevant numbers

<table>
<thead>
<tr>
<th>Real numbers (unknown)</th>
<th>Numbers that are (or can) be known (and can be used instead of the real numbers)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) number of cases of malarial illness</td>
<td>g) number of cases treated as such</td>
</tr>
<tr>
<td>b) number of cases of severe malaria</td>
<td>h) number of cases treated as such</td>
</tr>
<tr>
<td>c) number of deaths due to malaria</td>
<td>i) number of deaths attributed to malaria</td>
</tr>
<tr>
<td>d) population at risk*</td>
<td>j) estimated population at risk</td>
</tr>
<tr>
<td>e) total number of deaths</td>
<td>k) total number of consulting patients</td>
</tr>
<tr>
<td></td>
<td>l) total number of hospitalized patients</td>
</tr>
<tr>
<td></td>
<td>m) total number of registered deaths</td>
</tr>
<tr>
<td></td>
<td>n) total number of deaths attributed to a cause</td>
</tr>
</tbody>
</table>

* depending on the context, either the total population or only a part of it
Table 6.c  Potentially relevant indices

<table>
<thead>
<tr>
<th>Real Rates (unknown)</th>
<th>Alternative (measurable) indices</th>
</tr>
</thead>
<tbody>
<tr>
<td>incidence of malaria illness (a)/(d)</td>
<td>(g)/(j); (g)/(k)</td>
</tr>
<tr>
<td>incidence of severe malaria (b)/(d)</td>
<td>(h)/(j); (h)/(k); (h)/(l)</td>
</tr>
<tr>
<td>proportion of severe malaria (b)/(a)</td>
<td>(h)/(g)</td>
</tr>
<tr>
<td>mortality rate (all causes) (c)/(d)</td>
<td>(m)/(j)</td>
</tr>
<tr>
<td>malaria mortality rate (c)/(d)</td>
<td>(i)/(j)</td>
</tr>
<tr>
<td>proportion of deaths due to malaria (c)/(e)</td>
<td>(i)/(n)</td>
</tr>
<tr>
<td>malaria case fatality rate (c)/(a)</td>
<td>(i)/(g)</td>
</tr>
<tr>
<td>case fatality rate of severe malaria (c)/(b)</td>
<td>(i)/(h)</td>
</tr>
</tbody>
</table>

After studying the table consider the following issues:

a) Is the information reported (e.g. the reported incidence of malarial illness) equivalent to the reality to which it refers (e.g. the true incidence of malarial illness)?

b) If there is a difference, can it be in either direction? What are the principal explanations for errors by excess and by default, respectively?

c) Could the difference between reality and reports vary between:
   - different places?
   - different times in the same place?
   - different indices, e.g. incidence of malarial illness, incidence of severe and complicated illness, malaria mortality?

d) Is it necessary to improve the collection and reporting of information until it becomes equivalent to the reality represented? Would it be possible?

e) What would be required to make reported information equivalent to reality? Is that necessary? Is it possible? How could one take into account the imperfections of reported information?
f) Are all reported cases of malarial illness sufficiently similar to each other to be counted together in reports? If not, how do they differ from each other? You might distinguish true differences from differences of assessment. Can the main differences be taken into account in reporting? If so, how?

Outline the staffing, tasks and responsibilities appropriate at different levels for the effective treatment of malarial illness as a public health measure.

In terms of levels, you might distinguish four levels: the community, the first peripheral health unit, the first referral level and the second referral level.

In terms of tasks and responsibilities, you might distinguish the following categories:

- diagnosis and treatment
- recording and reporting
- direction, supervision, and education
- assignment of staff
- supplies

At what level, if any, are full-time malaria specialists useful or necessary in the above scheme?

What could intersectoral cooperation contribute to a more effective use of diagnosis and treatment?

Under the sections on evaluation, staffing, tasks and responsibilities at different levels mentioned above, you have outlined an ideal situation. The current situation is likely to fall short of that ideal. Try to outline the priority action likely to be most effective in bringing the current situation closer to the ideal.

Selection and utililization of antimalarial drugs

What factors should one take into account?

Please read carefully the next Unit of this module before commencing the session to which it relates.
Learning Unit 7

Social and economic aspects of malaria

Learning objectives:
By the end of this Unit, you will be able to:

- define the ecological factors influencing the malaria situation and its control
- identify the major social and economic impacts of malaria and malaria control

1. With your colleagues in the working group, discuss the following opinions. Review the different points of view before having a plenary discussion. The facilitators and the tutors will share their own experience and points of view.

   a) "Malaria eradication has succeeded in countries that were relatively advanced in their social and economic development but failed in the others. As a matter of fact, it succeeded in countries in which malaria was already steadily declining under the impact of social and economic development. Therefore: (i) a similar steady decline of malaria can be expected in other countries, if they go through a similar social and economic development; (ii) resources spent on malaria control would be more usefully spent on social and economic development, even from the point of view of malaria control".

   b) "The correlations of mortality before 2 years of age with a number of other variables were investigated in an African country highly endemic for malaria, and in which it is probable that malaria makes an important contribution to that mortality. The strongest correlation was a negative correlation with the mother's education; the next strongest correlation was a negative correlation with the father's income; correlations with other factors were weaker. In a multiple correlation analysis, the first two factors left practically nothing, statistically speaking, to be explained by the other factors. Therefore: (i) in our conceptual models of the epidemiology of diseases, including malaria, social and economic factors should be considered as the primordial factors, while biological factors should be considered as intermediate factors, through which the primary factors exert their effects; (ii) the resources spent on primary health care services (including their malaria component) would be spent more usefully on education of mothers and future mothers,"
even from the point of view of disease control, including malaria control”.

c) "Whereas, in the long run, social and economic development is usually accompanied by a decline in malaria, in the short run economic development is often accompanied by an increase in malaria”.

2. Consider the following diagram:

To which of the 6 arrows can you give a meaning? Specify the meanings.

Arrow A in the above diagram represents the effect of social and economic factors on the malaria situation. List the main factors involved, try to organize them in a meaningful way, and briefly indicate in what direction and through what mechanism they affect the malaria situation.

Arrow C in the above diagram represents the effect of social and economic factors on malaria control activities. List the main factors involved, try to organize them in a meaningful way, and briefly indicate in what direction and through what mechanism they affect malaria control activities.

At this stage you may wish to re-discuss the opinion: "Whereas, in the long run, social and economic development is usually accompanied by a decline in malaria, in the short run economic development is often accompanied by an increase in malaria”.

What are the practical implications of the relationships between malaria and social and economic factors in your own country? Try to give short, precise answers.

Please read carefully the next Unit of this module before commencing the session to which it relates.
Drug resistance and the rational use of drugs

Learning objectives:
By the end of this Unit, you will be able to:

- describe methods to measure parasite resistance to antimalarial drugs and how to use this knowledge to guide towards the best use of these drugs.

Drug resistance

Discuss with your colleagues about drug resistance. Is there any drug resistance in your country or the country where you will be working?

Working as a small group answer the following questions and produce a short paper that will be discussed with the facilitators.

- How do you define drug resistance?
- Is it an “all or nothing” phenomenon or are there grades of resistance?
- Does the concept apply to an individual parasite, or to the parasite population in an infected person, or to both?
- Is there geographic variation in drug response, even in the absence of resistance?
- How does resistance of *P. falciparum* to a given antimalarial relate to the success or failure of the treatment of fever cases by that same antimalarial?

A hint: drug - resistance is either present or absent; after treatment fever either subsides or not; there are thus in theory four possible combinations. Identify those that exist in reality and explain their existence.
The standard tests

Discuss with the colleagues in your working group what you know about standard tests. Review the different viewpoints of your colleagues before completing the following exercises.

Discuss with the facilitator the outcome of your exercise.

There are standard in vivo and in vitro tests. They are described in detail, including the techniques, the inclusion/exclusion criteria, the interpretation of the results, in several WHO documents. Here we are concerned with their applications in epidemiological settings. Characterize in vivo and in vitro tests with respect to:

- the basic variable(s) measured by the test
- whether the test is best applied to malaria patients or to asymptomatic carriers
- the parasite species to which it is applicable.
- the antimalarials to which it is applicable.

What correlation do you expect between in vivo and in vitro test results:

- at the population level?
- at the individual level?

What is the main biological cause of discrepancy?

Monitoring drug resistance

Objective(s)

Is it useful to monitor the response of malaria parasites to antimalarials? If so, what is (are) the objective(s)?

Tests for monitoring drug resistance

Discuss with the colleagues in your working group the following opinions about tests of drug resistance; then after a revision of the different viewpoints produce a document that you will discuss with the facilitator.

a) “the in vitro test is superior to the in vivo test because it is better standardized, performed by better trained specialists, and is not affected by immunity”;
b) “the decision to change the rules about what drugs to use cannot be taken without evaluation of the response in vivo; therefore, the in vitro test is redundant, indeed useless”;

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c) "the only really useful sensitivity test would be one providing guidance for
individual treatment, by analogy with the use of tests of the sensitivity of bacteria
to antibiotics; the standard tests do not allow this; therefore, they are useless";
d) "the first aim of a monitoring system should be to detect as early as possible any
decrease in the sensitivity of the parasites";
e) "the standard tests are too complicated to be used in public health programmes (as
distinct from research projects)";
f) "an adequate coverage by the standard tests would utilize too large a fraction of the
resources available for malaria control".

**Monitoring systems**

Is drug response to antimalarials being monitored currently in your country? If so,
outline the monitoring system(s), including the tests used, the sampling scheme, and
who performs the tests?

Is the monitoring system for drug resistance currently in use in your country
satisfactory? If not, why not?

Outline a satisfactory monitoring system in terms of objectives, sampling scheme,
tests and distribution of responsibilities.

**The epidemiology of drug resistance**

Working as a small group carry out the following exercise. Produce a document that
your group will discuss with the facilitator.

a) Outline what you know about the history and geographical distribution of drug
resistance.

b) One often hears statements of the following kind: "A new focus of resistance has
been discovered in CountryX." Under what conditions is such a statement
justified? Are those conditions usually satisfied?

c) Some maps of the distribution of drug resistance, e.g. of *P. falciparum* to
chloroquine, show by dots locations where resistance has been reported; other
maps show in a different colour countries in which resistance has been reported.
Comment on these two kinds of maps. In particular, what relevant information do
they fail to show? Can they be misleading?

d) How would you explain the origin and the distribution, history and geography of
drug resistance, e.g. of the resistance of *P. falciparum* to chloroquine?

*Hint: list the factors involved - think of the parasite, of the use of drugs, and
of the epidemiological situation, outline how each factor is likely to affect
resistance, and try to combine the factors into a diagram. Compare your
diagram with Fig 8.1 in the tutor’s guide.*
Control measures

Discuss with your colleagues in the working group the following opinions, then after a revision of the different viewpoints involve the facilitator in the discussion.

a) “As soon as resistance of *P. falciparum* to chloroquine has been detected somewhere, it should be replaced by a more effective drug, because otherwise patients have an increased risk of mortality”.

b) “As soon as resistance of *P. falciparum* to chloroquine has been detected somewhere, it should be replaced by a more effective drug, because otherwise the resistance will rapidly increase and spread under chloroquine pressure”.

c) “As soon as a new focus of resistance has been detected, a major effort should be made to eradicate it”.

d) “The best policy is to make the widest possible variety of antimalarials as widely available as possible; this will allow every case to find an appropriate treatment, by trial and error; it will also delay the selection of resistance by reducing the pressure exerted by any one drug”.

e) “If you cannot effectively reduce transmission by vector control, nothing will slow down the selection of resistance”.

Is the concept of “control of drug resistance” ambiguous, covering two very different kinds of “control”?

*A hint: contrast the justifications of opinions a) and b) above. Are the two kinds of control equally feasible?*

Please read carefully the next Unit of this module before commencing the session to which it relates.
Vector control

**Learning objectives:**

By the end of this Unit, you will be able to:

- list different types of vector control methods and select the most appropriate according to the prevailing conditions.

Discuss with the colleagues in your working group the following opinions. Review the different viewpoints of your colleagues and then prepare a document with the conclusion reached by your group. Discuss your result with the facilitator.

a) "Vector control strikes at the root of transmission and it should therefore be the backbone of any malaria control programme. Indeed, it is incorrect to speak of malaria control in the absence of vector control";

b) "The vectorial capacity is highly sensitive to the longevity of the vector, and longevity is highly sensitive to residual insecticides. Therefore, residual spraying is the method of choice for vector control, indeed for malaria control";

c) "The impact of residual spraying on the prevalence of infection depends on coverage; unless coverage reaches 80%, there will not be much of an impact";

d) "A human cohort, born and living under relatively intense transmission, will, by a certain age, have acquired strong immunity against malaria-associated disease and death. Before reaching that state the cohort will have suffered a number of malaria attacks and a number of malaria deaths. Now suppose we control transmission, but not to a very low level. A second cohort of equal size, born and living under the new situation, will go through the same process, only more slowly; strong immunity will be reached at a later age, but, before reaching it, the second cohort will have suffered the same number of malaria attacks and the same number of malaria deaths as the first cohort. The only effect of the control of transmission will have been to delay part of the attacks and part of the deaths to a later age. Therefore the control of relatively intense transmission is useless, unless it can reduce transmission to a very low level";
The epidemiological approach to malaria control: Learner’s Guide

e) “Under very intense transmission severe malaria and malaria deaths are concentrated in the very young (median age less than 2 years), the main form of severe malaria is severe malarial anaemia, while cerebral malaria is very rare. Under somewhat lower, but still relatively intense, transmission, severe malaria and malaria deaths are less concentrated in the very young - median age 3 - 4 years. The incidence of cerebral malaria is definitely higher, and the total incidence of all forms of severe malaria is perhaps higher. Therefore, the reduction of transmission from very intense to relatively intense may be indeed harmful.

Methods of vector control and of control of man-vector contact

Working as a small group, make an ordered list of the different kinds of methods for vector control and for control of man-vector contact.

Hint: see exercise on the vector’s life-cycle in Unit 3; identify in a broad sense three main classes of “vector control.

Which of these methods can be applied

• at the community level?
• at the household level?
• at the personal level?

Discuss the various points on your list with the facilitator.

Effects of vector control on malaria at the community level

Working as a small group, write down what are the expected medium-term effects of vector control on malaria at the community level.

Hints:

• consider the different variables that might be affected, such as infection, disease, death, and their distribution by age
• consider whether the expected effects are always the same, and if not, how much they may vary and why

Discuss with the facilitator the outcome of your exercise.
Expected effects of different vector control methods

Without repeating, reconsider the discussion around this topic in Learning Units 3 and 5.

Discuss with your colleagues the expected effect of vector control methods. Share with your colleagues your own experience on this matter, then working as a small group, complete the following exercise, producing a document that you will discuss with the facilitator.

How could one find out what medium-term effects to expect from the use of a given vector control method in a given situation?

Hints:

- think first of what you need to know;
- think next of practical approaches in which you may have to replace what you need to know by an acceptable substitute that you would be able to learn;
- if there are several approaches, discuss their advantages and disadvantages;
- can and should the different approaches be combined?

Do you need an additional hint regarding approaches? think of the following:

- try it out;
- find out what effects were observed elsewhere;
- what effects would you expect?

List the main types of malaria situations that occur in your country, or a country or region selected by the working group. Under each type, discuss the possible utilization of vector control, and the possible choice of vector control method(s).

Intersectoral cooperation

Discuss with you colleagues about the value of intersectoral cooperation and the possible areas for its application. Then complete the following exercise, and discuss the outcome with your facilitator.

Would better intersectoral cooperation be useful for vector control? If so describe how by giving examples.

Would better community participation be useful for vector control? If so what could the community do, and what could the community not do?
Please read carefully the next Unit of this module before commencing the session to which it relates.
Control of malaria epidemics

Learning objectives:
By the end of this Unit, you will be able to:

- recognize epidemic situations, develop preparedness measures and select appropriate measures for the control of outbreaks

With your colleagues in the working group, work through the questions on malaria epidemics. You may wish to involve your facilitator in this team effort.

The result of your activity will be discussed in plenary.

Definition

What is the general definition of an epidemic?

What is a malaria epidemic?

Hints:

a) try to apply the general definition of an epidemic to a malaria epidemic, and

b) try to distinguish malaria epidemics from other temporal variations, such as seasonal, periodic, secular.

Is there only one kind of malaria epidemic? If there are several, explain.

Consequences

What are the effects of malaria epidemics on health?

What else besides health, is affected by a malaria epidemic?
Causes

a) Do malaria epidemics occur at random in any malarious area or in any population at risk of malaria?

b) If not, what underlying situation(s) is (are) epidemic-prone?

c) Are epidemic-prone situations natural, or man-made, or both? Discuss the respective roles of natural and man-made factors in producing epidemic-prone situations.

d) In an epidemic-prone situation, do epidemics occur with mathematical regularity? If they did, would they still be "epidemics"?

e) Do they occur completely at random? If they do, how feasible and useful is it to monitor for advance warning of their occurrence?

f) If there are precipitating factors, are they the same for all malaria epidemics?

g) List possible precipitating factors of malaria epidemics; try to classify the factors in a meaningful way. Discuss how each factor does or could precipitate an epidemic.

h) Do the factors act in isolation or in combination? Can you give examples of this?

Monitoring

In practice, is it possible to identify epidemic-prone areas or situations? How would you do this?

In the epidemic-prone areas or situations, is it possible to monitor the epidemic risk?

What variables could, in theory, be used for monitoring the epidemic risk? Group them in a meaningful way.

*A hint for grouping the variables is to think of a malaria epidemic as a sequence of events, and of the possibly relevant variables at the different stages of the sequence.*

*A hint for the sequence: environmental changes - changes in the entomological situation - increase in the number of cases - increase in the number of deaths.*

In practice, which variables should be used for monitoring the epidemic risk? As many as possible to get the most and best possible information about the risk, or as few as are indispensible to decide among a limited number of possible actions? What selection criteria could be used?

First state your own criteria, then identify and discuss the criteria that are implicit or
explicit in the following statements.

a) "The most useful warning is the earliest; therefore monitoring should get as close as possible to the beginning of the sequence of events leading to an epidemic."

b) "The most useful warning is the most reliable, i.e. the one that makes the fewest false predictions, either by excess or by default; therefore, monitoring should get as close as possible to the actual onset of the epidemic, and eventually be concentrated on early detection after the actual onset."

c) "Analysis of the formula of the vectorial capacity (or of the formula of the basic reproduction rate) shows that the multiplication potential of a malaria case is exceptionally sensitive to two variables, namely the longevity of the vector and the duration of the incubation period of the vector; therefore these are the variables of choice for monitoring the epidemic risk."

d) "Not all the variables are equally easy to measure technically; how meaningful are the differences in this respect? Should that be a selection factor?"

e) "The most useful warning system is the one that best covers the epidemic-prone areas or situations; therefore the following criteria merit priority:

- practical possibility of a sampling scheme giving adequate coverage
- possibility of basing monitoring on activities routinely performed anyway, with a minimum of additional investment
- the overall cost."

As a conclusion to the discussion above can you outline practical guiding principles for monitoring the epidemic risk?

In theory, certain components of monitoring could be routinely be done, while others would be conditional (depending on the routine findings). Would that be useful in practice? If so, how? Can you give examples?

**Diagnosis**

If a community or the most peripheral health services report an epidemic of malaria, are they right?

What could be done to confirm the diagnosis of a reported epidemic of malaria?

If the majority of cases of epidemic fever have patent parasitaemia, does that establish that the epidemic fever is malaria?

If the existence of a malaria epidemic has been clearly established, what other characteristics of the epidemic is it useful to determine, in view of control?
A hint: use some of the most usual epidemiological questions, i.e. where? when? who? why?

Selection of short-term control measures

a) Should the selection of short-term (emergency) control measures be based on the relative epidemiological effectiveness of the different possible measures, or on their relative operational feasibility, or on a compromise between both?

b) Make a diagram of the states into which the human and vector populations are distributed, in relation to malaria transmission. Compare your diagram to the tutor’s Fig. 10.1.

Indicate on the graph the points of impact of different categories of control measures.

A hint: you could use the following categories: larval control, adult vector control, control of man-vector contact, diagnosis and treatment of cases and mass drug administration, regardless of the parasitological status.

With the help of the graph, evaluate the relative effectiveness of the different categories of control methods, both immediately and later.

A further hint: think of the relative numbers in different states - e.g. incubating and infective - during the ascending phase of an epidemic.

c) With respect to feasibility, what operational criteria are relevant to the selection of control measures?

d) Present your conclusions with respect to selection of short-term (emergency) control of malaria epidemics

e) How would you evaluate the effectiveness of your control measures? To evaluate them properly would it be sufficient to show that the incidence rate decreases, or decreases drastically, after intervention? What would be the ideal comparison? Can such a comparison be performed in reality?

f) How would you decide when the emergency measures can be stopped?

Medium- or long-term control

Discuss the possibility of long-term prevention of malaria epidemics.

Short of actual prevention what medium-term measures, beyond the short-term (emergency) measures, would be useful for the control of malaria epidemics?