The epidemiological approach to malaria control

Tutor’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.
Learning Unit 1

What you know about malaria in your country or place of work

**Learning objectives:**

By the end of this Unit, the Learner should be able to:

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

It should be made clear to the participants that this Unit is not an examination but is designed to make the learners think about the relationship between the epidemiology of malaria and its control as it pertains to their own country or place of work. Through this process and with your subsequent help as a tutor they will have a better understanding of this relationship. Participants should be encouraged to answer the questions as precisely and briefly as possible and not more than 60 minutes should be allowed for this.

In plenary session open a discussion between the participants regarding their experience in completing the questionnaire, paying particular attention to difficulties encountered and the reasons, and missing information. Approximately one hour should be spent on this activity.

At the end of the day you should then review the papers and identify any specific areas which are the cause of common difficulties and which will need special emphasis in the Units that will follow.
Please remind all trainees to read the next Learning Unit ahead of time; they will be dealt with according to the timetable.
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, the Learner should 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 and immune responses
- 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, by what methods, technically eligible for use in malaria control programmes.

You will need to prepare photocopies and use the overhead transparencies of Figures 2.1 to 2.6 and of Tables 2a and 2b provided.

Diagram of the life cycle of the malaria parasite.

The learners should work in groups and each group should prepare a diagram of the parasite's life-cycle. After they have completed this task they should be given a photocopy of Figure 2.1. Each group is asked to compare it with the one they have prepared and discuss the differences.

Only the zygote and oökinete are diploid, the rest of the cycle is haploid. It matters, because:
1. fertilisation allows recombination between gametes of different genotypes (e.g., resistance to different drugs), and

2. in the haploid state, no allele (e.g., resistance to drug X) is recessive.

Note: This unit presents many exercises overlapping with other learning units (units 4, 6 and 8) and the facilitators should be careful to avoid entering into in-depth discussions of topics which will be dealt with elsewhere in this guide.

Important characteristics of infection with each of the four species of human malaria parasites.

The learners should work in small groups to list and discuss the characteristics of infection with each of the four species of human malaria.

The facilitators should guide them along the lines in Tables 2a and b below:

**Time factors**

Table 2a  Time Factors

<table>
<thead>
<tr>
<th>Characteristics</th>
<th><em>Plasmodium falciparum</em></th>
<th><em>Plasmodium vivax</em> (^2)</th>
<th><em>Plasmodium malariae</em></th>
<th><em>Plasmodium ovale</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Prepatency(^2)</td>
<td>5.5</td>
<td>8</td>
<td>15</td>
<td>9</td>
</tr>
<tr>
<td>Incubation(^3)</td>
<td>9-14</td>
<td>12-17 or longer</td>
<td>18-40 or longer</td>
<td>16-18 or longer</td>
</tr>
<tr>
<td>Time of appearance of gametocytes(^4)</td>
<td>8-15</td>
<td>0-5</td>
<td>5-23</td>
<td>5</td>
</tr>
<tr>
<td>Asexual cycle in the blood</td>
<td>48 hours</td>
<td>48 hours</td>
<td>72 hours</td>
<td>48 hours</td>
</tr>
<tr>
<td>Duration of untreated infection</td>
<td>1 - 2 years *</td>
<td>1½ - 5 years</td>
<td>up to 50 years</td>
<td>Probably the same as <em>P. vivax</em></td>
</tr>
</tbody>
</table>

*assuming uncomplicated infection

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\(^1\) given in days, unless specified otherwise  
\(^2\) from infection to the appearance of detectable parasitaemia  
\(^3\) from infection to the appearance of symptoms  
\(^4\) after the appearance of parasitaemia  
\(^5\) except those strains with prolonged incubation periods
Multiplication factors
Table 2b Multiplication factors

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Plasmodium falciparum</th>
<th>Plasmodium vivax</th>
<th>Plasmodium malariae</th>
<th>Plasmodium ovale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of merozoites per hepatic schizont</td>
<td>30 000</td>
<td>between 8000 and 20 000</td>
<td>15 000</td>
<td>15 000</td>
</tr>
<tr>
<td>number of merozoites per blood schizont</td>
<td>16-32</td>
<td>12-18</td>
<td>6-12</td>
<td>8-10</td>
</tr>
<tr>
<td>number of sporozoites per oocyst</td>
<td>10 000</td>
<td>1 000 - 10 000</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Other differences among parasite species

- "hypnozoites" (intrahepatic parasites with retarded development) exist in *P. vivax* and *P. ovale* but not in *P. falciparum* and *P. malariae*. They are responsible for relapses either at relatively short intervals or after a long period;

- *P. falciparum* invades red blood cells of any age, the other species are more selective (one of the factors that make *P. falciparum* the most dangerous species);

- in *P. falciparum*, parasitized red blood cells are sequestered in various tissues (through cytoadherence to endothelial cells) during the second half of the asexual cycle (another factor making *P. falciparum* so dangerous) and during maturation of gametocytes.

The parasite's life cycle, pathogenesis, and immunity

Fig 2.2 = Fig 2.1, plus main broad ways of pathogenesis.

The main mechanisms of pathogenesis:

a) the rupturing parasitized red blood cells release, in addition to merozoites, malaria toxin(s), which precipitate a complex "cascade" or network of *cytokines* (TNF, etc) and *effectors* (NO = nitric oxide etc), which cause fever;

b) *sequestration* of parasitized red blood cells (*P. f.*), plus the *local* release of toxin(s), cytokines and effectors causes *tissue damage*, in particular cerebral malaria;

c) *anaemia* is caused by destruction of red blood cells by the parasite, plus depression of erythropoiesis (production of new red blood cells) by the effects of toxin(s) released;
The epidemiological approach to malaria control: Tutor's Guide

d) the size of the parasite population aggravates (a), (b) and (c), note that the size of the parasite population may not be reflected by the circulating parasite density (in particular for *P. falciparum*, because of sequestration).

Fig. 2.3 = Fig. 2.2, plus naturally acquired immune responses (IRs)

**Remarks:**

a) IRs include protective and non-protective responses;
b) all the naturally acquired IRs are only to some extent effective;
c) the naturally acquired transmission - blocking immunity acts in the vector’s gut (through antibodies picked up with the gametocytes during the blood-meal).

Fig 2.4 = Fig 2.3, plus expected points of impact of different kinds of potential malaria vaccines.

Remark: transmission-blocking vaccines may contain, in addition to antigens expressed by gametocytes (naturally exposed to the host’s immune system), some antigens expressed only after fertilization, thus not naturally exposed to the host’s immune system.

**The parasite’s life cycle and antimalarial drugs**

Fig 2.5 = Fig 2.1, plus points of impact of the main antimalarial drugs.

**Measurement methods**

Figure 2.6 = Fig 2.1, plus measurement methods.

At this stage we are concerned with a review of existing measurement methods; the selection of measurement methods to be included in a control programme is considered elsewhere.

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*Please remind all trainees to read the next Learning Unit ahead of time; they will be dealt with according to the timetable.*
Learning Unit 3

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, the Learner should be able to:

- describe the life-cycle of 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.

You will need to prepare photocopies and use the overhead transparencies of Figures 3.1, 3.2 and 3.3 provided.

Diagram of the vector’s life cycle

The learners should work in small groups. Each learner should draw a diagram of the life-cycle of the malaria vector. After they have completed this, Figure 3.1 can be handed out to all learners. Time should them be allocated for them to compare the version they produced in the groups with Figure 3.1 and to discuss any major differences. The facilitators and tutor should then invite questions and respond accordingly.

You should point out that Figure 3.1 is very much simplified; in particular:

- it assumes gonotrophic concordance (one oviposition per blood-meal throughout), whereas in reality the first oviposition often requires two blood-meals;
- it ignores split blood-meals, including those split between man and animal;
- it ignores movement between indoors and outdoors resting within the same gonotrophic cycle.

These simplifications are without importance for the present exercise.
Factors affecting the vector's life cycle in relation to malaria transmission, including vector control

Ask the learners to list the factors that have a direct effect on the vector's life-cycle. The expected outcome from this exercise is outlined below.

**Numerical factors**

**Time factors (durations)** are all temperature-dependent; the following are typical of the main African vectors at high temperature.

- from egg to emerging adult 7 days at 31°C (20 days at 20°C)
- from one blood-meal to the next (or from one oviposition to the next) 2-3 days
- expectation of life of the adult female 5-7 days

**Number of eggs** 100 to 200 per oviposition, i.e. every 2 to 3 days at 31°C temperature (partly compensated by high larval mortality)

**Vector behaviour** (determined by genetic factors, by environmental factors and by opportunity)

- choice of host (anthropophily, zoophily)
- choice of feeding place (endophagy, exophagy)
- choice of resting place (endophily, exophily)
- choice of oviposition place.

**Vector-parasite interactions**

There may be differences in the susceptibility of the vector to infection and the physiological ability to transmit. It may be higher in some vectors than in others in the same geographical area. Some vectors may or may not be susceptible to a particular parasite strain, an important question with respect to vectors from north of the Sahara in relation to *P. falciparum* from south of the Sahara.

The duration of sporogony is dependent on the microclimate, e.g. temperature, of the adult resting place as well as on the species of plasmodium. At a temperature of 25°C, 12-14 days are required for *P. falciparum* (or about 4 feeding cycles) somewhat less for *P. vivax* (11-12 days), definitely longer for *P. malariae* and *P. ovale*; thus only a minority of vectors live long enough to transmit (a very small minority for *P. malariae* and *P. ovale*). At lower temperatures, sporogony lasts longer. The duration of

*average; the range of individual values is wide*
sporogony is more sensitive to temperature than the life expectancy of the vector, so that the fraction surviving sporogony increases and decreases with temperature.

The minimum temperature below which sporogony cannot be completed is about 19°C for *P. falciparum*, 16°C and for the other species.

The requirement for relatively high temperatures for the completion of sporogony determines the geographic distribution, with respect to both latitude and altitude, of the transmission of the different species, as well as the seasonal distribution of transmission at cooler latitudes and altitudes.

The duration of sporogony thus increases in the following order: *P. vivax*, *P. falciparum*, *P. ovale*, and *P. malariae*.

The effect of infection on vector longevity is probably insignificant. Loss of infectivity is probably not important, although it has been shown in hibernating vectors infected with *P. vivax* in northern Europe through degeneration of sporozoites.

Probable *density-dependent regulation in the vector*:

- the sporozoite-load developed by a vector is less than proportional to the number of gametocytes picked up. This is due to crowding and effect of transmission-blocking antibodies;

- the number of sporozoites inoculated is also less than proportional to the sporozoite-load, injection of a very small volume of saliva.

**Broad biological differences between vector species relative to malaria transmission**

The vector species may differ mainly with respect to:

- longevity
- behaviour
  - feeding preferences
  - resting sites
  - oviposition sites (suitability of different types of surface water)
- susceptibility to infection

**Physical environment**

Factors affecting vector production include rainfall, type of soil, slope of the land, irrigation systems, urbanization, pollution, afforestation and deforestation, existence of borrow-pits, and presence or absence of shade. Many of these factors affect the types of surface water that will be available. Factors affecting vector survival include
the use of insecticides in agriculture, presence of predators, sudden changes in climatic conditions, etc.

Factors affecting man-vector contact include the siting of settlements, housing, sleeping habits (anophelines bite mostly at night) and the availability of animals, especially cattle, as alternative sources of blood.

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

Learners should have a copy of Figure 3.1 already handed out for them to indicate vector control measures and their points of impact. The outcome should be Figure 3.2 The question in the Learner’s Guide about the effect of different control measures on the transmission of malaria is designed to emphasise that, at every feeding cycle, the vector passes through the feeding, resting and oviposition stages, while it goes through all other stages (egg, larva, adult, mating) only once in a lifetime. Thus indoor residual spraying has a chance of killing the vector after every blood-meal, i.e. four to five times before it can transmit *P. falciparum* assuming a sporogonic cycle of about 8-10 days. Personal protection methods or the diversion of bites from man to animal can interfere twice with transmission, first by reducing transmission from man to vector, second by reducing transmission from vector to man. The other control methods act only once in a vector’s lifetime (aquatic stages) or only once between acquisition and transmission of the infection by the vector (adult stages).

**Efficacy of vector control measures**

The expected impact of residual spraying varies with the degree of uniformity of resting behaviour of the vector population. This can be illustrated by the following example.

Let:

i) half of the blood meals be followed by rest indoors;
ii) rest indoors be lethal;
iii) sporogony lasts four gonotrophic cycles, i.e. there are four opportunities of exposure to the insecticide.

Then:

i) if the resting behaviour is random in the vector population then half escape the first opportunity of exposure, and half of those escape the second time, etc., so that the fraction that residual spraying fails to kill before completion of sporogony is \((0.5)^4 = 0.0625\), i.e. 6.25%.
ii) if this behaviour is not common to all members of the population, the expected impact is smaller, e.g., if half of the mosquitoes are totally exophilic, the other half totally endophilic, then half escape exposure all the time, so that the fraction that residual spraying fails to kill before completion of sporogony is 0.5, i.e. 50%.

The expected impact of diversion of bites to animals increases with the extent to which members of the vector population bite both man and animal. This can be illustrated by the following example.

Let half of the blood-meals be diverted to animals:

Then

i) if the biting behaviour is completely random, then the vector population acquires only half as many infections as before, and each infective vector infects only half as many persons as before, so that transmission is only $(0.5)^2 = 0.25$ of what is was previously;

ii) if behaviour is not random, the expected impact is smaller, e.g., if half of the mosquitoes are totally diverted to animals, the other half not at all, the vector population acquires only half as many infections as before, but each infective vector infects as many persons as before, so that transmission is 0.5 of what is was previously.

There is evidence for the *A. gambiae* complex, the major vector group in Africa south of the Sahara, that both resting behaviour and biting behaviour vary within species and within local populations, and that the variations are at least partly genetically determined.

**Measurement methods of the more important characteristics of vector populations**

At this stage we are concerned with a review of existing measurement methods; the actual selection of methods to be included in a control programme is considered elsewhere.

Fig 3.3 relates vector collection methods to the vector’s life-cycle.
Answers to the three problems of epidemiological interpretation of entomological data:

1.
   a) No, all the collection methods in Fig 3.3 measure density and behaviour, at the same time.
   b) Our measurements of density are therefore only indicators of trend.
   c) It matters for measuring impact of vector control if the control measure(s) affect both density and behaviour, as is the case with impregnated mosquito nets, or also with a residual insecticide which has also a repellent effect.

2.
   a) Entomological sampling fractions are usually very small.
   b) In the example, in addition to the numbers given (20 female mosquitoes, 2 man-nights) we need to know:
      i) size of the village’s human population
      ii) fraction of the vector population feeding per night
      iii) fraction of blood-meals taken on man.
   c) Let village population = 800; fraction of vectors feeding per night = 1/3; fraction of blood-meals taken on man = 1/4; the estimated vector population is (20/2) x 800 x 3 x 4 = 96,000; the sampling fraction is 20/96,000 = 0,0002; it can also be calculated directly from the sampling scheme (i.e. before the collection), as follows: 2/(800 x 3 x 4) = 0,0002.
   d) It is indeed common to find new cases of human infection without finding infected vectors. Suppose case detection identifies 75% of the actual new cases (i.e. sampling fraction = 0.75). If collection on human baits are conducted every 14 nights, the entomological sampling fraction calculated above must be further divided by 14, yielding 0.000015. The ratio between the two sampling fractions is (0.75/0.000015) = 50,000, i.e. case detection is very much more sensitive than the detection of infected vectors (even though it misses 25% of the new cases of infection). Any other plausible numerical example will reach a similar conclusion. The finding of new human cases without finding infected vectors is therefore easy to explain.

3.
   a) Age composition of adult female vectors at a point in time is determined by
      i) the number of females emerging per day over a period equal to the maximum life expectancy, and
      ii) survival
b) If we calculate survival from age-composition at a point in time, we assume that emergence has been constant, over a period equal to the maximum life expectancy.

c) If we calculate survival from average age composition over a period of time, we assume that survival is constant over that period.

Please remind all trainees to read the next Learning Unit ahead of time; they will be dealt with according to the timetable.
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, the Learners should 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.

You will need to prepare photocopies and use the overhead transparencies of the figures 4.1, to 4.4, and of table 4.a provided.

Natural history of malaria in the human host

Working in small groups ask each learner to perform the tasks outlined in the learner’s guide. Give them some guidance in approaching this exercise in a logical manner such as considering infection, disease, recovery, death and immunity and their relationship.

Allow about 30 - 40 minutes for this exercise giving the groups the time to discuss the results on their own, and have each group present its results and discuss the findings, especially any marked differences between their diagram, table, and answers to questions and those of this tutor’s guide, i.e. Fig 4.1, and table 4.a (of which you will distribute copies), and to the answers given in the next paragraph.

1. Moves from one state to another can be very fast. In particular the intervals from onset of symptoms to development of severe malaria, and from onset of severe malaria to death are commonly very short, from a few hours to a few days.
2. The implications for case-management are therefore obvious:
   a) if a simple treatment of uncomplicated malaria can prevent its evolution into severe malaria, the time in which this intervention is possible is very short;
   b) immediate treatment of severe malaria is a major survival factor, suggesting the administration of an interim treatment, by injection or suppository, before transportation to a more appropriate service for further management;
   c) in relation to the time of inoculation, the risk of disease tends to be concentrated in the first few weeks after first patency. The risk of severe disease is even more true in the first few days after first patency;
   d) two types of data are relevant for this last point:
      i) concentration of malarial disease, and more importantly, malaria deaths, in the transmission season, in areas where parasitaemia is common throughout the year, but transmission as such is only seasonal;
      ii) follow-up of neurosyphilitics treated by malariotherapy, which was a recommended method of treatment in the past.

The inoculum's intrinsic factors

1. Number of sporozoites inoculated
   a) An infected vector usually inoculates few sporozoites, perhaps about 10 on average, rarely up to 100.
   b) The number has been estimated by letting an infected vector salivate on a glass slide or in a small vial of liquid nutrient, or by letting the vector feed on blood in vitro, through an animal skin.
   c) Increasing the number of sporozoites inoculated slightly shortens the incubation period, with little or no effect on parasitaemia or disease.
   d) The relevant data came from the follow-up of neurosyphilitics treated by malariotherapy.

2. Differences of “virulence” among parasite species.

Only *P. falciparum* is an important cause of direct mortality (cerebral malaria, severe anaemia, acute renal failure, etc). *P. vivax* can also kill in case of spleen rupture, but this is extremely rare. Death is also rare from *P. malariae*, due to chronic renal insufficiency.

*P. falciparum* invades red cells of all ages, while *P. vivax* tends to invade reticulocytes and *P. malariae* only relatively old red blood cells. This explains why *P. falciparum* reaches higher parasitaemias than the other species. Another major factor of pathogenicity in *P. falciparum* is its sequestration in vital organs, including the brain.
3. Differences of “virulence” within a parasite species or local parasite population

Differences of virulence within a species are suggested by old observations made under malarial therapy for neurosyphilis: e.g. *P. falciparum* from Italy was found more pathogenic than *P. falciparum* from India.

Differences of virulence within a local population of a species are suggested by points (a) and (b) in the learner’s guide. The example works out as follows:

Before superinfection, this child’s circulating population of parasitized red blood cells is $2 \times 10^6 \times 10^3 = 2 \times 10^9$; each mature liver schizont release 30,000 merozoites (see Learning Unit 2); suppose each of these merozoites successfully invade a RBC; the number of parasitized red blood cells added by superinfection is $20 \times 30,000 = 6 \times 10^5$, the ratio of added parasitized red blood cells to preexisting parasitized red blood cells is $(6 \times 10^5) / (2 \times 10^9) = 3 \times 10^{-4}$, i.e. very small. Therefore, in order to cause disease (uncomplicated malaria or severe malaria) the added parasites must be *different*. However, in addition to intrinsic parasite diversity, its interaction with host diversity is probably important (see below).

**The human host’s intrinsic factors**

*Mutations and susceptibility*

<table>
<thead>
<tr>
<th>Genetic Trait</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbS</td>
<td>The heterozygotes have a high degree of protection against the lethal effect of falciparum malaria</td>
</tr>
<tr>
<td>Duffy-red cells</td>
<td>Individuals with erythrocytes lacking the Duffy blood group antigen (Fy^a Fy^b) are resistant to <em>P. vivax</em> infection. Protection is absolute and specific.</td>
</tr>
<tr>
<td>G-6-PD deficiency</td>
<td>Probably impedes the development of the parasite in erythrocytes and restricts parasitaemia.</td>
</tr>
<tr>
<td>Other haemoglobinopathies</td>
<td>HbC in Africa and HbE in Asia seem to protect against <em>P. falciparum</em> infection but this requires further investigation.</td>
</tr>
</tbody>
</table>

An example of a mutation increasing the human host’s susceptibility: homozygotes for a mutation that enhances TNF production carry an increased risk of cerebral malaria.
Acquired immunity (active)

1. Acquisition, loss and effects of active immunity

Active immunity increases after each new appearance of parasites in the blood (infection, relapse or superinfection).

Immunity decreases gradually after the parasites disappear from the blood.

Immunity does not prevent infection, but in case of infection it decreases the risk of illness and in case of disease it decreases the risk of death.

Acquired immunity to malaria is species specific. It induces an accelerated clearance of asexual parasites from the blood, probably combined with partial protective immunity against pre-erythrocytic stages. The acquisition of active immunity is already involved in recovery from the first infection. Subsequent infections tend to increase the level of immunity, while in the absence of inoculation the level tends to decrease.

Loss of immunity results from removal from exposure, as shown by the occurrence of clinical, even severe, malaria in previously immune adults returning from a stay of 1-2 years in a non-endemic area. Upon returning to a malarious area they will need 1-2 years to regain their immunity.

2. Diagram

Fig 4.2 summarizes in a diagram the expected effects of gradual development of active immunity. The diagram does correctly suggest that successive inoculations become progressively less pathogenic and less dangerous. There is no contradiction with the statement about some children developing severe malaria only after many previous inoculations: on a population basis, the fractions developing uncomplicated malaria or severe malaria decreases with successive inoculations; on an individual basis, the probability of developing uncomplicated malaria or severe malaria decreases with successive inoculations, but the actual outcome of an inoculation may also depend on host and parasite diversity and their interaction (see below).

3. Expected effects of different malaria control measures

Antimalarial drugs prevent or delay the acquisition of immunity, but the treatment of cases prevents and reduces mortality at the same time.

The future vaccines against asexual blood-stages might mimic natural immunity, which protects against disease and death more than against infection; but the vaccines should arrive at that result without the morbidity and mortality associated with the development of natural immunity.
The future anti-gamete vaccines will have no direct effect on the host; they will have an indirect effect through the reduction of transmission in the community.

**Passive immunity**

Passive immunity is conferred through maternal antibodies in areas of relatively intense transmission. Such immunity is partial and transient, and is probably lost by the age of 6 months or even before. The effects of passive immunity are also illustrated diagramatically in Fig. 4.2.

**Other human biological factors**

**Pregnancy**

Pregnant women, especially primigravidae, show increased susceptibility to *P. falciparum* malaria, manifested by increased prevalence and density of parasites, anaemia, risk of abortion, stillbirth and decreased birth weight. The main pathogenic mechanism is massive parasite proliferation in the placenta. Malaria experience during one pregnancy protects during subsequent pregnancies.

**Nutritional status**

Malaria has a negative effect on nutritional status by reducing food intake and increasing metabolism, and malnutrition could increase the case fatality rate of malaria by impairing general resistance. On the other hand the correction of severe malnutrition and/or iron deficiency may cause latent *P. falciparum* to flare up.

**Age per se**

Age *per se* affects susceptibility to the two main forms of severe malaria, cerebral malaria and severe malaria anaemia. Cerebral malaria is exceptional below 2 years of age, even under the most intense transmission. Infants, on the other hand, are particularly susceptible to severe malarial anaemia.

**Interaction between parasite diversity and host diversity**

Refer to the questions in the Learner’s Guide.

(a) (i) many antigens;  
(ii) much antigenic diversity;

(b) (i) no;  
(ii) yes;
it is possible that any *P. falciparum* parasite could be dangerous for some host, if the host’s immune repertoire covers too small a part of the parasite’s antigenic repertoire

**Age specific distribution of malaria**

Where there is relatively intense transmission, the age-specific distributions of acute malaria morbidity will appear more or less as in figure 4.3.

If the intensity of transmission increases, the peaks (maxima) occur earlier (at a younger age) and the subsequent decreases are steeper; if the intensity of transmission decreases, it is the opposite.

In fact, exposure to vectors increases with age; if the average exposure is high, its increase with age is probably not very important.

As the intensity of transmission increases, the source of infection, clinical malaria, severe malaria and malaria mortality get concentrated in younger age-groups (this concentration is greatest for severe malaria and malaria mortality). With respect to the source of infection, the size of the adult population partly compensates for the low infectivity of adult individuals. If the intensity of transmission decreases, e.g. under the impact of vector control, uncomplicated malaria and severe malaria may become more common in older age groups.

Figure 4.3 outlines the classical picture of age-specific distribution of malaria morbidity at different levels of endemicity and in epidemic malaria, as described by Boyd in 1949. Immunity is the main factor affecting the age-specific variations of infection and disease.

**Malaria mortality**

The risk of dying is almost certainly greater among children suffering from pneumonia *plus* uncomplicated malaria than among children suffering from pneumonia alone. And similarly for several other diseases. So that, more generally, the addition of malaria is likely to increase the CFR of a number of diseases.

Fig 4.4. is a diagram of the events leading to direct and indirect malaria mortality.

The relative magnitude of direct and indirect malaria mortality is of practical importance: it affects what can be expected from the reduction of transmission (see Learning Unit 9).
Two kinds of data may allow estimation of the relative magnitude of direct and indirect malaria mortality:

a) measurements of malaria-specific mortality from death certificates or from "verbal autopsies" or of the incidence of severe malaria as an alternative indication in a population well covered by an adequate hospital service;

b) measurement of the reduction in mortality from all causes following the removal, or near removal, of malaria by residual spraying or chemoprophylaxis.

The second kind of measurement must correspond to all malaria mortality (direct and indirect), while the first kind of measurement is more likely to reflect direct malaria mortality; the difference might thus represent indirect malaria mortality.

The data actually available may not be as clear cut as one might wish, but they do suggest that total malaria mortality, both direct and indirect, can be 2 to 3 times larger than direct malaria mortality alone.

Two other points could come up in the discussion:

a) The high (total) malaria mortality implicit in the high HbS gene frequency observed in some populations also suggest a large indirect malaria mortality;

b) The usual way to define and measure cause-specific mortality assumes that every death has one cause and one cause only, an assumption which is questionable.

---

1 "Verbal autopsy" assigns a cause to a death on the basis of a standardized interview of close relatives
Table 4a  Classes of factors that might affect the outcome of an inoculation

1. The inoculum’s intrinsic factors
   a) Quantity (the number of sporozoites inoculated)
   b) Quality (the kind of sporozoites inoculated)
      i) differences of “virulence” among parasite species
      ii) differences of “virulence” within a parasite species, or within a local population of a parasite species

2. The human host’s intrinsic factors
   a) mutations that decrease or increase the host’s susceptibility
   b) acquired immunity, active and passive
   c) other human biological factors

3. Interaction between parasite diversity and host diversity

Please remind all trainees to read the next Learning Unit ahead of time; they will be dealt with according to the timetable.
Learning Unit 5

Intensity of malaria

Learning objectives:

By the end of this Unit, the Learners should be able to:

- 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 actual 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.

You will need to prepare photocopies and use overhead transparencies of Figures 5.1 to 5.4, and of Table 5a provided. A copy of Table 5a is to be given to the learners after completion of this Unit.

This Unit will require careful preparation and should certainly be given more time than the other Units, unless you decide to select only those parts which fit the scope of your course. Some of the participants may feel uncomfortable with mathematical formulae, so it is important that these are introduced step by step and that practical examples are given. The numerical exercises given will help the learners to become familiar with the models and to understand how the formulae can be used to describe the determinants of malaria transmission.
Intensity of transmission

Incidence rate
The number of new infections occurring in a given population unit, e.g. per thousand, in a given time period, e.g. one year. Note that the traditional API (annual parasite incidence) is an incidence rate.

Prevalence rate
The fraction of a population infected at a given point in time (sometimes known as a “point prevalence”). Note that the traditional SPR (slide positivity rate) is a prevalence rate among fever cases.

Note that although “incidence” and “prevalence” are sometimes used as synonyms of “incidence rate” and “prevalence rate” they are in fact actual numbers used as numerators in calculating these rates, the denominators being the population at risk.

Entomological inoculation rate
The number of mosquito bites (inoculations) containing sporozoites received by the population unit in a given period of time. It is often expressed as the total number of infective bites per person per day, sometimes as the number of infective bites during a whole transmission season or a whole year.

Vectorial capacity and basic reproduction rate

Vectorial Capacity (C)

The potential number of secondary cases of malaria originating per day from a primary case, assuming that the population is and remains fully susceptible. Note that the term refers to the combination of the components determining the effectiveness of a local mosquito population to transmit malaria and although human infection is the beginning and end of the sequence the term refers to the insect stages, not those occurring in man.

Basic reproduction rate ($R_0$)

The potential number of secondary cases of malaria originating from one primary case, assuming that the population is and remains fully susceptible. Note that the basic reproduction rate is a potential multiplication factor, not an actual secondary attack rate.
Derivation of a formula for the vectorial capacity (C) and the basic reproduction rate ($R_0$)

You should go through the various stages carefully to ensure that the learners have fully understood the steps involved. Both you and the learners should follow the sequence of steps in the Learner’s Guide and you could discuss the steps listed by the learners at an early stage.

**Derivation of a formula for the vectorial capacity (C)**

The steps leading from one primary case to secondary cases can be outlined as follows:

I. The steps leading from one primary case to secondary cases can be outlined as follows:
   
   i) the primary case is bitten by a certain number of vectors per day;
   
   ii) a fraction of these vectors acquire the infection:
   
   iii) some of these vectors survive the parasite’s incubation period in the vector, the sporogonic cycle, and become infective;
   
   iv) each of the latter will live for a certain period of time during which she will bite a certain number of humans before eventually dying;
   
   v) a fraction of the humans bitten by infective vectors become secondary cases.

II/III. The factors that should be included and their algebraic symbols are:

- the vector density in relation to a man, let $m$ = the number of vectors per person;
- the rate at which the vectors feed on man; let $a$ = the number of blood-meals taken on man per vector per day;
- the survival of the vector; the simplest survival model assumes an age-independent death rate; let $p$ = the proportion surviving per day and $(1-p)$ the proportion dying per day; then the (age-independent) expectation of life is approximately:

$$\frac{1}{(1-p)^{1}}$$

For example if $p = 0.9$

$$(1-p) = 0.1, \text{ and } \frac{1}{(1-p)} = 10 \text{ days}$$

- the duration of the incubation period in the vector; let it be $n$ days

---

1 The exact expectation of life is $1/(-\log p)$ but the approximation is easier to grasp, and adequate for the present purpose.
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- the "efficiency" of the system, i.e. the product of the two fractions identified above as steps (ii) and (v); let it be designated by b

IV. Combining the symbols in a formula.

The vectorial capacity must be the product of the five steps; they can be expressed in terms of the individual factors as follows:

step (i) = (m) x (a) = ma

step (ii) x (v) = b

step (iii) = p^n

step (iv) = \[
\begin{bmatrix}
1 \\
(1-p)
\end{bmatrix}
\] \[a = \frac{a}{(1-p)} \]^2

multiplying, we get

\[C = \frac{ma^2bp^n}{1-p} \]^2

In thinking of C as a potential for multiplication, it is usual to assume that b = 1, and to drop it from the formula; such a potential may never be realized, except perhaps at the very onset of an epidemic starting from a small reservoir in a large non-immune population.

Derivation of a formula for the basic reproductive rate R_o

R_o must be equal to C multiplied by the number of days a case is infective. That number is usually expressed as

\[
\frac{1}{r}
\]

where r = the fraction losing infectivity per day.

\[
\text{thus } R_o = \frac{C}{r} = \frac{ma^2bp^n}{r(1-p)} \]^2

When considering R_o as a potential for multiplication, it is usual to assume that b, the efficiency of the system = 1 and to drop it from the formula.

\[2 \text{ the exact expressions are step (iv) a}/(-\log p); C = ma^2bp^2}/(-\log p); R_o - ma^2bp^2}/(-\log p).\]
Vectorial capacity, basic reproduction rate and control of transmission

The following control measure can affect the various component of the vectorial capacity:

(a) residual spraying reduces m and p, it may also reduce a if the insecticide has a repellent effect;

space spraying, source reduction and larviciding reduce m;

reduction of man-vector contact reduces a;

impregnated mosquito nets reduce m, a, and p;

treatment of cases increases r (decreases 1/r).

(b) reduction of m reduces C (or R₀) in the same proportion;

reduction of (1/r) reduces R₀ in the same proportion;

reduction of a is amplified by squaring a in the formula;

reduction of p is amplified much more by putting p to the n\textsuperscript{th} power, i.e. 8\textsuperscript{th} to 10\textsuperscript{th} power for P. falciparum at high temperature, in addition to the roughly proportional reduction of the longevity 1/(1-p).

(c) Solution of the numerical example.

<table>
<thead>
<tr>
<th>m</th>
<th>a</th>
<th>p</th>
<th>n</th>
<th>C (approx)</th>
<th>C (exact)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>0.5</td>
<td>0.8</td>
<td>10</td>
<td>1.34</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>0.5</td>
<td>0.8</td>
<td>10</td>
<td>0.67</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>0.25</td>
<td>0.8</td>
<td>10</td>
<td>0.335</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>0.5</td>
<td>0.4</td>
<td>10</td>
<td>0.0004</td>
<td></td>
</tr>
</tbody>
</table>

(d) With regard to the relative efficacy of different control measures, residual spraying appears much more effective than any other measure and reduction of man-vector contact appears more effective than other control measures, with the exception of residual spraying.
Identification of simplifying assumptions

We have assumed uniform vector behaviour which maximizes the expected effects of residual spraying and of reduction of man-vector contact, as already shown in Learning Unit 3.

The comparison between equal proportional reduction of various factors influencing the vectorial capacity does not correspond directly to an operational option; other factors are neglected, including:
• cost
• effectiveness of control measures in reducing the factors of the vectorial capacity
• quality of operations, and its maintenance
• acceptability, and its maintenance
• insecticide resistance

So far the discussion is concerned with malarial infection and its transmission; we cannot assume that the impact of control measures on malarial morbidity and mortality is simply proportional to their impact on infection and transmission.

Measurement of intensity

The following comments can be made about the actual measurement of the five parameters of the intensity of transmission:

• incidence of infection can be measured by:
  i) case detection i.e. detection of fever cases, from which a blood slide is then taken, if new infections are generally symptomatic. This is may be true at low transmission, but is definitely not true at high transmission; cost is low if one relies on cases detected by the curative services, high if one aims at more complete coverage;
  ii) longitudinal follow-up of a cohort of negatives, e.g newborns, or children given a curative treatment; the estimate obtained in infants is usually called infant conversion rate;
  iii) fitting of a catalytic model to an age-specific prevalence curve among infants; the estimate is usually called force of infection; the prevalence of parasitaemia may be supplemented by prevalence of specific IgM, evidence of post-natal infection as IgM does not cross the placenta.

ii) and (iii) are only applicable on a sample base, and usually restricted to research projects.
Prevalence of infection can be measured by sample survey; technical feasibility and reliability depend on representativeness of sampling and quality of parasitologic examination; cost is moderate as long as prevalence is relatively high.

Entomological inoculation rate can be measured by the man biting rate (number bites/man/night) and the sporozoite rate; it is technically feasible, but reliable only with relatively intensive sampling in time and space, which makes it expensive. In the future, anti-sporozoite antibody profile is likely to become a practical and useful indicator of past entomological inoculation rate.

In principle the vectorial capacity can be measured:

ma can be measured by collections on human baits

a can be calculated by dividing the proportion of blood meals taken on man by the interval between consecutive blood meals, the said proportion is measured by the precipitin test; the said interval can be measured by various methods.

p can be calculated from the age composition of the population.

n can be calculated from the temperature and the known relationship between n and temperature.

The measurement of $R_0$ requires in addition a value for $r$ and $(1/r)$. Values can be found in the literature but they are not very satisfactory. However a new estimation, by following untreated infections, would be unethical, except with asymptomatic infections which are likely to be atypical.

In practice, measurements of C and $R_0$ are expensive and not very reliable.

However, these concepts can be useful, even in the absence of actual measurements, for understanding certain principles of the epidemiology and control of malaria, as attempted in this exercise.

Furthermore, even a very crude estimation might be useful and obtainable indirectly (see Figure 5.3).

**Relationship between prevalence and incidence**

Prevalence (of a phenomenon) is determined by its incidence and its duration

$$P = I \times D \text{ or } I = P/D$$

where P = prevalence

I = incidence
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\[ D = \text{duration} \]

Example using the formula \( I \times D \):

if the incidence rate is 200 per thousand or 0.20 per year, and the duration of a case is 2 months or (2/12) or a year, then the expected prevalence is \( 0.20 \times (2/12) = 0.033 \) or 3.3 per cent.

*Note that \( I \) and \( D \) have to be expressed in the same time unit.*

**Qualitative relationships between the different dimensions of intensity of malarial infection and its transmission (Fig 5.1)**

The vectorial capacity and the prevalence rate together determine the entomological inoculation rate. This rules the incidence rate which in turn determines the immunity level, and this, together with the basic (non-immune) recovery rate, determines the actual recovery rate, i.e. the actual duration of infection. The incidence rate and the actual recovery rate together determine the prevalence rate, whilst the vectorial capacity and the basic recovery rate together define the basic reproduction rate.

In Figure 5.1 infection and infectivity are not distinguished.

**Quantitative relationship between the prevalence rate and vectorial capacity**

a) Let the groups reach their own conclusions about the relationships between the prevalence rate and vectorial capacity.

b) The relationship has the general shape shown in Figure 5.2.

The logic behind the formula \([1]\) is as follows: the prevalence at time \((t + 1)\) is equal to the prevalence at time \(t\), plus the new cases occurring in the interval and minus the old cases recovering in the interval.

According to Ross’s model the population is divided into negative and positive fractions: the negatives become positive at a rate which is the product of the fraction positive \((y)\) multiplied by a contact rate \((C)\) [which is equivalent to the vectorial capacity] and the positives become negative at a constant rate \((r)\).

and d) In equilibrium \(y = (t + 1)\) must equal to \(y(t)\); the added and subtracted terms should be equal:

\[ y(t)C[1-y(t)] = ry(t), \text{ hence formula [2]} \]

e) A graph of formula [2] looks like the upper line in Figure 5.2; the endemic level \((y)\) reaches zero for \(C = r\)
f) formula [2] becomes:

\[ y = 1 - \frac{1}{R_0} \]

In the graph \( R_0 \) replaces \( C \), and the endemic level reaches zero for \( R_0 = 1 \) (intuitively, malaria can be endemic only if the basic reproduction rate is greater than one).

g) Ross's model yields important epidemiological insights:

- there is a non-zero critical value of the vectorial capacity below which malaria cannot maintain itself. When Ross said that malaria could disappear without elimination of all the vectors, few "experts" believed him;

- above that threshold, the relationship is non-linear - i.e. not proportional - close to the threshold, a small change in vectorial capacity produces a large change in the endemic level; far above the threshold, large changes in vectorial capacity produce little or no change in the endemic level;

- close to the threshold malaria is naturally unstable, and there is a risk of epidemics; far above the threshold it is naturally stable. The public health problem is likely to be more obvious at relatively low vectorial capacities;

- close to the threshold, vector control has a great impact on prevalence of infection; far above the threshold, it may have little or no impact, even if it has a big impact on the vector.

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

a) At the critical level \( y = 0 \), and so

\[ 1 - \frac{r}{C^*} \text{ must be zero} \]

i.e. \( C^* = r \)

From this we can derive that the critical vectorial capacity is lower for longer lasting infections, it is lower of \( P. vivax \) than for \( P. falciparum \), because the recovery rate (r) for \( P. vivax \) is lower than for \( P. falciparum \).

b) the critical value of the vector density can be derived from the formula:

\[ C^* = \frac{m^* a^* p^*}{1 - p} = r \]
from which:

\[ m^* = \frac{r(1-p)}{a^2p^a} \]

3

c) The critical value of the vector density \((m^*)\) for the given values will be calculated as:

<table>
<thead>
<tr>
<th>“good vector”</th>
<th>“bad vector”</th>
</tr>
</thead>
<tbody>
<tr>
<td>(m^*)</td>
<td>0.011</td>
</tr>
<tr>
<td></td>
<td>0.012</td>
</tr>
</tbody>
</table>

(approximate formula)
(exact formula)

The expected relationship among the possible measures of “intensity” is shown in the graph in Figure 5.3. The graph, based on the Garki model, is meant to show the approximate shape of the relationships, not their exact numerical values.

With respect to the diagnosis of malaria situations, one would like to know how close one is to the threshold of either \(C\) or \(R_0\). A crude indirect estimation of \(C\) or \(R_0\) may be possible along the following lines: close to the threshold, parasitological and serological measurement (prevalence, incidence) are sensitive and informative, instability is likely to be obvious, while entomological measurements (entomological inoculation rate, vectorial capacity) are insensitive; far above the threshold, it is the reverse: entomological measurements are sensitive and informative, parasitological and serological, measurements are insensitive, and stability is likely to be obvious. Recent studies measuring anti-sporeozoite antibody titres suggest that these are likely to become a good indicator of the entomological inoculation rate, more stable and less costly than the direct measurement.

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

This exercise shows two other major insights given by Ross’s model, i.e. the expected impact of a reduction in prevalence or in vectorial capacity. The correct answers to exercise a) and b) are:

a) prevalence is expected to return to its original level, unless the reservoir has been reduced to zero;

b) the prevalence will decrease towards a new equilibrium value - non zero, unless the vectorial capacity has been reduced below its threshold level; the rate of decrease is not constant but progressively slowing down. Do not expect the decline to continue at its initial rate.

\[ m^* = \frac{r(1-p)}{a^2p^a} \]
Leave the groups to reach their own conclusions and do not try to force any specific resolution. Their results will be compared with Fig 5.4. Effects of a reduction in prevalence or in vectorial capacity.

Is there a place for models in planning malaria control?

Statements a) to d) are all correct. However:

a): our knowledge of facts is - and will remain - incomplete, and planning always involves some kind of model. The model may be intuitive and implicit, rather than mathematical and explicit, but it is there, and it is preferable to make it explicit, so that it can be considered critically.

b) and c): questioning the assumptions and numerical values which underlay our projections is part and parcel of modelling. Once our model is explicit, we can vary its assumptions, and the numerical values, to evaluate how sensitive our conclusions are to such variation i.e. we can conduct a sensitivity analysis. For example we have seen above (see also Unit 3), that the calculated impact of residual spraying is very sensitive to the assumption made about the distribution or resting behaviour among the vector population.

d): we should probably not use models to make absolute predictions about the future, only relative predictions to compare, or eventually rank, the outcomes of the small number of operationally realistic options.

The relationship between intensity and disease

Among the five measures of intensity, only incidence and prevalence are applicable to malaria in terms of disease.

Other applicable concepts:

i) incidence of severe malaria;

ii) average duration of episodes of malarial illness;

iii) absenteeism from school or work.

Measurement of the intensity of disease

a) Health services can relatively easily collect data on:

i) incidence of malarial illness;

ii) incidence of severe malaria.
They could perhaps also collect data on the duration of episodes of malarial illness or on the interval between first symptoms and treatment.

Schools and employers can relatively easily collect data on absenteeism; they could perhaps also collect data on its suspected causes, in particular malaria.

b) The main problems are that:
   
i) the geographical distribution of malaria and of the coverage by health services vary, and also vary more or less independently of each other;
   
ii) coverage of the population by services is incomplete, irregular and changing (hopefully increasing);
   
iii) utilization of the services is changing (hopefully increasing);
   
iv) different diagnostic criteria are used at different levels or types of institution;
   
v) even within a given level (or type of institution), diagnostic criteria may not be standardized.

c) Possible solutions include:
   
i) geographical subdivision of the data;
   
ii) standardize diagnostic criteria at each level;
   
iii) present separately data obtained with different diagnostic criteria;
   
iv) include coverage in reporting; the “population covered” may be unknown; some idea of coverage may be given by providing the number of institutions or administrative units reporting;
   
v) relate cases to available measures of utilization of services, e.g. total number of patients at different levels or types of institutions.

Quantification of mortality from malaria

a) Malaria-specific mortality rate = the number of malaria deaths in a time period (usually one year) in a population unit (usually 100 000)

See the discussion of direct, indirect, and total malaria mortality in Learning Unit 4.

Malaria cases fatality rate (CFR) = the number of malaria deaths in a time period, divided by the number of malaria cases in the same period; the ratio is usually multiplied by 100, to express the CFR as a percentage.
b) the main problems with respect to the measurement of malaria mortality are:
   i) the enumeration of deaths and their attribution to causes is incomplete, irregular and changing;
   ii) the correct attribution of deaths to malaria is technically difficult under any circumstance;
   iii) the "number of malaria cases" may be poorly defined and is either not measured very well or not at all.

Some hints to overcome these problems:
   i) review critically what information is really needed about malaria mortality;
   ii) cooperate with national demographers, who are usually not under the Ministry of Health. This may include the use of retrospective sample surveys and so-called "lay reporting" of death;
   iii) try to make the best use of the limited data available, e.g. malaria deaths as a percent of all certified deaths; CFR of hospitalized severe malaria cases.

Further reading:


Please remind all trainees to read the next Learning Unit ahead of time; they will be dealt with according to the timetable.
Table 5a: Factors composing the vectorial capacity of a mosquito population and the basic reproduction rate of malaria (after Black, 1968)

<table>
<thead>
<tr>
<th>Factor</th>
<th>Definition of index</th>
<th>Common name of index</th>
<th>Method of obtaining the index</th>
<th>Macdonald's (1957) expressions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Bites <em>per man</em> per night by vector population</td>
<td>Man-biting rate</td>
<td>Night-biting captures on human baits, e.g. 10 bites per man.</td>
<td>$ma$</td>
</tr>
<tr>
<td>2</td>
<td>$(\text{Bites per mosquito per night}) \times (\text{Proportion of bites on man (&quot;human blood index&quot;})$</td>
<td>Man-biting habit</td>
<td>Composed of: (i) the feeding frequency based on the observed gonotrophic cycle in nature, e.g. 0.4 where the female oviposits and feeds once in 2.5 days on an average; and (ii) the human blood index, assessed by the precipitin test applied to daytime resting samples, e.g. 0.5: $a = 0.4 \times 0.5 = 0.2$</td>
<td>$a$</td>
</tr>
<tr>
<td>3</td>
<td>Probability of vector's survival through sporogonic period of parasite</td>
<td></td>
<td>Based on age-grading or proportion parous, and knowledge of gonotrophic cycle duration, e.g. 0.60 days.*</td>
<td>$p^n$</td>
</tr>
<tr>
<td>4</td>
<td>Expectation of life of female vectors</td>
<td></td>
<td></td>
<td>$\frac{1}{-\log_e p}$</td>
</tr>
<tr>
<td>5</td>
<td>Expected inoculations of man per infective case per day</td>
<td>Vectorial capacity of vector population</td>
<td>Multiplication of factors $1 \times 2 \times 3 \times 4$. e.g. $10 \times 0.2 \times 0.6 = 1.2$. When this value descends below 0.01, basic reproduction rate is 1 for <em>P. falciparum</em>.</td>
<td>$ma^2p^n$</td>
</tr>
</tbody>
</table>

To obtain the basic reproduction rate:

| 6      | Proportion of vector females developing parasite normally following ingestion of gametes | Mosquito’s receptivity (susceptibility) to infection | Only assessable by infections of captive samples on malaria cases, e.g. 0.9. | $b$ |
| 7      | Days of infectivity per case (i.e. reciprocal of proportion of cases recovering in one day) | Reciprocal of recovery rate | Longitudinal observations of local cases of malaria in the absence of transmission, e.g. 100 days. | $\frac{1}{r}$ |
| 8      | Expected new infections per case in the absence of immunity | Basic reproduction rate of parasite | Multiplication of factors $5 \times 6 \times 7$, e.g. $1.2 \times 0.9 \times 100 = 108$. | $ma^2np^n$ |

* To compute the factors from the proportion parous it is necessary to know also the mean difference in age between the nulliparous and the youngest parous females in the sample, and the sporogonic period of the parasite. Graphs are available to enable the field worker, who has observed these parameters, to read off from his data the proportion surviving one day, the expectation of infective life and the expectation of life.

Note: $e$ is the base of natural logarithms (2.718).
Learning Unit 6

Case management in a malaria control programme

**Learning objectives:**

By the end of this Unit, the Learners should be able to:

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

You will need to prepare photocopies and use the overhead transparencies of Figures 6.1 and 6.2 and Tables 6.d and 6.e provided.

**Introduction**

The present exercise is concerned with the implementation of the recommendation for the control of malaria by the treatment of sick persons, with the objectives of reducing/shortening illness and preventing death by means of the epidemiological approach.

The recommendation that the first priority in the control of malaria should be the treatment of sick persons could be discussed in contrast with the opinion the first priority of malaria control is the reduction of transmission”, or with the opinion “the first priority of malaria control is the reduction of the endemic level”.

**First line treatment: the current situation**

The specific questions of this exercise will help the participants in defining the factors that influence the relationships between those who need treatment and those who get if effectively.
The factors that play a role

Peripheral reasons
Geographic distribution of the “providers of health care”
Drugs available
Cost to the “consumer”
Knowledge, attitudes and practices of the “consumers”
Knowledge, attitudes and practices of the “providers”

Underlying causes
Policies concerning:
Health
Education
Trade

Treatment failures

What is treatment failure?

An operational definition of a treatment failure, based on clinical manifestations can be: no clearance of fever 48 hours after treatment. Compare this definition with others, i.e. those based on parasitological clearance, and make the participants select the best for a malaria programme based on case management.

Table 6.d. Methods for detecting treatment failures and their causes

<table>
<thead>
<tr>
<th>Method</th>
<th>relative reliability</th>
<th>relative simplicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>history and observation</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>clinical examination</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>trial of another treatment, based on another diagnosis</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>parasitologic examination</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>detection/measurement of antimalarials in urine</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>detection/measurement of antimalarials in blood</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>drug sensitivity test <em>in vivo</em></td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>drug sensitivity test <em>in vitro</em></td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>quality control of drug preparation</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>tests of abnormal metabolism</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

Facilitators should assist the participants in the definition of possible causes of treatment failures, and methods of prevention.

Possible causes of treatment failure.

- diagnostic error
- defective drug preparation
- inadequate dosage
- failure to take the drug (poor patient compliance)
- failure to absorb the drug - vomiting, diarrhoea?
- drug-resistant parasites
- genetically determined abnormal metabolism, e.g. affecting sulphonamides

For each of the possible causes of treatment failure listed above, participants can identify the remedial action to be taken. Focus first on practical solutions before discussing more theoretical ones.

**Severe malaria**

Severe malaria (life-threatening malaria) has different clinical forms. In children the most common are cerebral malaria, severe malarial anaemia and acidosis. Cerebral malaria (See Fig 6.2) is defined as unrousable coma not attributable to any other cause in a patient with *P. falciparum* malaria. In severe malaria there is a sequestration of red blood cells parasitized with the later stages of the malaria parasite in the deep tissue post-capillary venules, in the brain in the case of cerebral malaria.

It affects predominantly non-immune patients. Persons with certain haemoglobinopathies are to some extent, protected even if not immune.

It requires parenteral antimalarial treatment, and other forms of intensive care, such as correction of fluid and electrolyte disturbances, and meticulous nursing care.

Treatment is ideally provided by well-trained medical personnel in the hospital, or an appropriately staffed and equipped health facility; in certain circumstances, the dispensary can administer parenteral drugs before transportation of the patient to the hospital.

Given the rapid evolution of severe malaria, the limited accessibility of the health services, and their relative inadequacy for the management of these cases, it is likely that many cases of severe malaria do not reach the health services and that an important fraction of those that reach the services reach them too late or do not receive the most appropriate treatment.

The early and effective treatment of malarial illness should reduce the incidence of severe malaria. But severe malaria commonly develops within 48 hrs of the onset of symptoms, so that the time available to prevent the evolution of uncomplicated malaria into severe malaria is very short.
The control of transmission may reduce immunity so that in case of resurgence of transmission, severe malaria, including cerebral malaria, may affect older age groups than previously.

**Microscopic diagnosis**

Microscopic diagnosis can serve three objectives:

- guide individual treatment, maybe selectively: treatment failures, severe cases
- measure the incidence and prevalence of malaria
- assess the sensitivity of the parasites to drugs

The three objectives are relevant in all control programmes. Programmes have limited diagnostic resources, that should thus be used and distributed in relation to the objectives.

There is no perfect relation between parasitaemia and malarial illness:

- immune persons may show parasitaemia, even relatively high, without symptoms
- one can suffer from malarial illness and have temporarily so few parasites in the peripheral blood that they are likely to be missed; in case of doubt, repeat the examination and/or treat as malaria.

Quality control should be concerned with:

- the preparation and staining of the slides, and the condition of the microscopes;
- the results of the slide examination which can be ascertained by the re-examination of a sample of positive and negative slides by a more experienced microscopist; preferably ignoring the result of the first examination.
Table 6.1 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>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 and complicated 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 <em>falciparum</em> malaria</td>
<td>←</td>
</tr>
</tbody>
</table>

Objectives

Epidemiological objectives are the maximum reduction of:

- malaria mortality
- incidence of severe malaria
- days of illness due to malaria.

Operational objectives are the correct management of:

- all cases of malarial illness, including severe malaria
- all therapeutic failures.

These examples should clarify the distinction between epidemiological and operational objectives.

These objectives are not to be attained “at any cost”. They should as far as possible be combined with:

- an acceptable cost
- a minimum of undesirable side-effects
- a minimum of pressure for selection of drug-resistant parasites. See following exercise in Unit 8.

* paradoxical effect: initial increases by better detection
** difficult to foresee, because both numerators and denominators will change
Evaluation

Evaluation should be adapted to the objectives, i.e. measure variables that correspond to the objectives.

Questions a) to f), in the learner’s guide, can be answered as follows:

a) No
b) Yes - the main sources or error are:
   - by excess: to consider as “malarial illness” all cases of unexplained fever or all cases of patent parasitaemia;
   - by default: the services are not accessible to all, or are not utilized by all those to whom they are accessible.

c) Yes to all three
d) No to both
e) It would involve the investment of considerable resources, and that is neither necessary nor possible.
f) No, examples of important differences:
   - the species of *Plasmodium*
   - the severity of disease
   - diagnostic criteria, e.g. microscopic examination
   - the level of the service making the diagnosis

*In this exercise participants are asked to define responsibilities for a malaria case management programme first in an ideal situation and then to compare with a real situation to identify major problems and priority areas for action. Remember that, again, this is not a planning exercise, but participants should be concerned with the application of basic principles to a malaria control programme.*

Selection and utilization of antimalarial drugs

Factors to be taken into account as far as possible

- effectiveness of the drugs
- operational feasibility (e.g. simplicity of regimens)
- toxicity
- acceptability (in particular in terms of minor side effects)
- impact on immunity
- impact on resistance
- cost
- availability
Please remind all trainees to read the next Learning Unit ahead of time; they will be dealt with according to the timetable.
Learning Unit 7

Social and economic aspects of malaria

*Learning objectives:*

By the end of this Unit, the Learner should be able to:

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

The participants should discuss the three opinions first in their groups and then all together. The idea behind this exercise is to bring out the participants’ opinions and experiences concerning the social and economic aspects of malaria in order to complement the biological aspects of malaria dealt with in Units 2, 3, and 4. The facilitators and the tutor should share their own opinions and experiences with the participants.

The exercises try to define the relationships between social and economic factors and malaria and its control. Discussion should concentrate on the analysis of the different mechanisms that are involved.

In the last exercise, problem analysis should focus on a practical example which can either be provided by you or proposed in each group by the participants. In this case emphasis should be on the definition of practical approaches and solutions to solve the problems analyzed.
Drug resistance and the rational use of drugs

Learning objectives:

By the end of this Unit, the Learner should be able to:

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

You will need to prepare photocopies and we use an overhead transparency of figure 8.1 provided.

Drug resistance

In discussing the results of their work, you should ensure that their definition is either "an inadequate response of parasitaemia to a standard treatment regime", or "an inadequate effect of a given drug concentration on the parasites". Remember that there are both (a) degrees of resistance and (b) geographical variations in response. In discussing the response of *P. falciparum* to a given antimalarial, point out that all four combinations can occur. It is also important to stress that:

- the fever may subside even if the parasites are resistant, under the effect of immunity;
- the fever may persist even if the parasites are sensitive. See the other causes of treatment failure, Unit 6.
The standard tests

Characteristics of the tests, with respect to the 4 points raised in the learner’s guide.

The in vivo test:

- the test measures the clinical and parasitological responses of a malaria patient to an antimalarial treatment;
- the test should therefore be applied to patients with malaria, not to asymptomatic carriers;
- the test is applicable to all species of human malaria;
- the test is applicable to all antimalarial drugs that are active against the asexual blood stages (blood schizonticides), but only one treatment can be tested in any given patient.

The in vitro test:

- the test measures the parasitologic response of an isolate (the parasites growing out of a blood sample) to a drug;
- it is equally applicable to patients and to asymptomatic carriers;
- currently the test is applicable only to P. falciparum, the only species that can be cultivated in vitro;
- it is fully operational for chloroquine, amodiaquine, quinine, mefloquine, sulfadoxine and pyrimethamine, and also applicable to the other blood-schizonticides. The same isolate can be tested simultaneously against several drugs.

The correlation between the results of in vivo and in vitro tests:

- there should be good correlation at the population level, but at the individual level, because of immunity, the same infection can be sensitive in vivo and resistant in vitro.

Monitoring drug resistance

Objectives

The primary objective is to adapt drug policies (see WHO/MAL/94.12070) to changes of treatment efficacy, clinical and parasitological, in order to ensure adequate treatment of malaria patients. Possible secondary objectives include research on the epidemiology of resistance, including cross-resistance and the evaluation of measures designed to control the development of resistance.
Tests for monitoring drug resistance.

Question a) to f) in Learner's Guide can be answered as follows:

a) and b): the two types of test are complementary. The assessment of the *in vivo* response is indispensable and the first priority in a control programme, while the *in vitro* test is supplementary. For certain research activities, the *in vitro* test is preferable:

i) to assess possible geographical variation of the response to new antimalarials before their large-scale utilisation;

ii) to assess a possible decrease of resistance to an antimalarial when its consumption decreases;

iii) to assess multiple resistance (testing the same case with different drugs is only feasible *in vitro*).

c) and d) are not true.

d): it is not feasible at an acceptable cost, and what should be detected as soon as possible is a change in drug-response which is sufficiently large to require intervention.

e) and f): in recent years WHO has co-ordinated the development and validation of a simplified *in vivo* test, adapted to the needs of malaria control programmes.

Monitoring systems

**Epidemiology of drug resistance**

See question a) to e) in the learner’s guide.

a) The history and geography of drug resistance are described in many publications and WHO documents.

b) One may say “new” if it is proven that there was no resistance before; one may say “focus” if it is proven that there is no resistance in the surrounding area; usually these conditions are not fulfilled, and one should keep in mind that a small sample size may not accurately represent the entire area.

c) Those maps do not show the number of tests, nor the frequency of resistance, nor its degree; they can be misleading by suggesting that resistance is “all or none”, so that, where there is resistance to an antimalarial the latter has no place anymore; they can also suggest that resistance, detected in one locality, extends to the whole country.
d) The factors involved include:

i) spontaneous mutations toward resistance;

ii) sexual reproduction of the parasite in the vector allows genetic recombination between parasites; that can increase the level of resistance and the frequency of cross-resistance by addition of mutations, and lower them by their dissociation;

iii) drug pressure selects resistant parasites;

iv) the intensity of transmission acts in two opposite directions: it enhances firstly recombination in the vector and secondly immunity which may reduce recombination, decrease the drug pressure, and mask resistance;

v) the movements of population may import resistant parasites, and bring together different mutations, thus allowing their recombination in the vector;

vi) even before the introduction of a drug, there is geographic variation in the parasites’ response to that drug.

A tentative combination of the factors involved in a coherent conceptual model is shown in Figure 8.1 the three arrows marked 5 represent the deceleration effect of immunity; the other arrows represent acceleration effects.

e) Increases in the following can be expected:

i) morbidity (duration of clinical episodes);

ii) incidence of severe cases;

iii) malaria mortality;

iv) incidence of drug side-effects/toxicity (if the replacement drugs are more toxic);

v) cost (if the replacement drugs are more expensive).

Control measures

a) It is false; the following should be taken into account:

i) the relative cost of chloroquine compared with replacement drugs;

ii) the relative toxicities of replacement drugs;

iii) the practical level of resistance, in terms of the clinical usefulness of chloroquine;

iv) the ability of the health services to detect and manage therapeutic failures.

b) It is false; it would lead to rapid rejection of all available antimalarials.
c) It is false; it is an illusion to believe that limited "foci" are detected soon enough; the attempts to eliminate them, or even to contain them geographically are probably a waste of resources, and furthermore the real importance of the geographic propagation of resistant strains is unknown.

d) It is false; it would lead to great confusion.

e) It is probably exaggerated. There probably is a certain intensity of transmission below which an increase in resistance through recombination of genotypes in the vector becomes very rare, and in that sense a reduction of transmission may be crucial. It is also likely that the utilization pattern of antimalarial drugs affects the selection of resistance. It is conceivable that this pattern could be manipulated so as to slow down the selection of resistance even if at present we do not know how to do it.

The concept of "control of drug resistance" does indeed cover two very different kinds of "control":

i) control of treatment failures;

ii) control of the development of drug resistance.
Vector control

**Learning objectives:**
At the end of this Unit, the Learner should be able to:

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

You will need to prepare photocopies and use overhead transparencies of Figures 9.1 and 9.2 provided.

The learners should work through the questions in the Learner’s Guide and then discuss the conclusions reached by the groups. The following points should be brought out in the general discussion:

a) It is false. The objective is to reduce diseases and deaths due to malaria. Disease and death come at the end of a long chain of causes and effects, and intervention can take place at different stages. For instance, vector control intervenes at the beginning of the chain and treatment of the sick towards its end. (see Fig. 6.2). In practice, the first component of any control programme should be the treatment of malarial illness which has a direct and immediate impact. The other control methods, in particular vector control, may or may not be added depending on the epidemiological situation and the resources available.

b) It requires qualification. For vector control, it is the method of choice in the short and medium term, and on condition that there are not too many exophilic vectors. For malaria control, see above (a).

c) It requires qualification. Depending on the vectorial capacity (and the corresponding stability), and the degree of endophily of the vector, a coverage of less than 80% will have a major effect on prevalence in certain cases, while in some other cases even a coverage of more than 80% will have very little effect.
d) Under reduced transmission, immunity will indeed develop more slowly, and malaria morbidity and mortality will indeed affect older age groups than before. It is even possible that the total number of attacks of uncomplicated malaria suffered by a cohort will be the same, as suggested by a geographical comparison. Even so, many - but not all - experts expect the cohort’s total malaria mortality to decrease, because:

- the probability of timely and effective treatment is likely to increase with a child’s age;

- indirect malaria mortality (see Learning Unit 4, in particular Fig 4.4) is likely to decrease. The diseases that, in association with uncomplicated malaria, cause indirect malaria mortality, are, like uncomplicated malaria, concentrated in the early years of life; delaying uncomplicated malaria for a few years will reduce the frequency of the association;

- one might discuss, at this stage, whether the burden of mortality is best measured in terms of number of deaths, regardless of age, or in number of years lost;

e) It is indeed probable that a reduction from very intense to relatively intense transmission may lead to an increased incidence of severe malaria. Even so, the cohort’s total malaria mortality may decrease, for the reasons given under (d).

The elements of truth in points (d) and (e) are strong arguments for making improved case-management the first priority of malaria control programmes.

If time allows, it may be worth discussing, in relation to points (d) and (e), the limitations of geographical comparisons as predictors of the impact of vector control. Is the effect of intensity of transmission independent of its seasonal variation? What does one assume about measurements, and about the impact of antimalarial drugs, in the different areas?

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

See Figure 3.2 in Unit 3. The three main classes of vector control are:

i) larval control;

ii) adult control; and

iii) control of man-vector contact.
Larval control

Source reduction

- through permanent environmental modification, e.g. permanent drainage system;
- through repetitive environmental manipulation, e.g. intermittent irrigation. Principle: let surface water be available for less time than is required for development from oviposition to emergence.

Larviciding (killing the larvae)

- mechanical: obstructing the larval respiratory channels by use of oils or monolayers;
- synthetic larvicides, e.g. temephos;
- biological larvicides; e.g. bacterial toxins, applied as dead bacilli;
- biological control, in the strict sense: e.g. by using larvivorous fish.

Adult control

- residual spraying of insecticides indoors;
- space spraying of insecticides outdoors, or, less commonly, indoors.

Control of man-vector contact

- zooprophylaxis: diversion of vector bites from man towards domestic animals. Can be manipulated by modifying the number of domestic animals, by their positioning at night, e.g. between vector breeding places and human dwellings, and by the relative accessibility of human and animal dwellings;
- siting of human dwellings, e.g. upwind of breeding sites or more than 2 km away from them;
- screening of human dwellings, either purely mechanical, (i.e. netting doors and windows), or partly chemical (curtains impregnated with synthetic pyrethroids);
- mosquito coils;
- bednets; they may be impregnated with synthetic pyrethroids;
- repellents applied on the skin or on clothes.

Larval and adult control may give protection at the community level.
Control of man-vector contact may give protection at the community level, at the household level or at the personal level.

Zooprophyaxis and siting of human dwellings are applicable at the community level.

Screening of dwellings and use of mosquito coils are applicable mainly at the household level; insecticide impregnation of screens improves protection at the household level and may in addition have an impact on the vector population, i.e. at the community level.

Bednets and repellents are applicable mainly at the individual level. Insecticide impregnation of bednets improves protection at the individual level and may in addition have an impact on the vector population, i.e. at the community level.

Effects of vector control on malaria at the community level

Vector control at the community level reduces the vectorial capacity.

The effect on infection

Qualitative: see Figure 5.1 in Unit 5. A reduction in the vectorial capacity is expected to reduce the entomological inoculation rate, the incidence and prevalence of infection, and the immunity of the population.

Quantitative: see Figure 5.3 in Unit 5. Each subdivision of the lower horizontal axis (log scale) represents a tenfold change in vectorial capacity. The corresponding change in the entomological inoculation rate is roughly proportional. The corresponding curve would be close to a straight line if both axis were arithmetic or logarithmic. The corresponding change in incidence and prevalence of infection can be much less than proportional on the right of the figure, stable malaria, much more than proportional on the left, unstable malaria. If the vectorial capacity is reduced below its critical level for a time sufficient for exhaustion of the reservoir through spontaneous cures and treatment, malaria should disappear.

Fig 9.1 shows the expected age-specific prevalence of infection at high, medium and low intensities of transmission. Fig 9.2 show the expected age-specific prevalence of infection, gametocytæmia and high parasite density, under intense transmission. Fig 9.1 indicates that under vector control, the distribution of infection may shift to older age groups, and immunity may be acquired more slowly.

The expected effect on disease and death

If vector control eliminates (eradicates) the infection, the elimination of disease and death due to malaria follows.

If vector control reduces infection and superinfection without eliminating it, the effect on disease and death might be proportional or even more than proportional (see
above); the distribution of disease and death may shift to older age-groups, because of a slower acquisition of immunity.

**Finding out the effects to be expected**

The three basic approaches, their advantages and disavantages are as follows:

- **Try it out** in the given situation.
  - *advantage*: it is, in principle, the most reliable way to find out;
  - *disadvantage*: it is prohibitively expensive to try all methods, and their combinations, in all situations.

- **Find out what effects** were obtained elsewhere in a similar situation.
  - *advantage*: it is, in principle, the next most reliable, after the previous one (which is too expensive);
  - *disadvantages*:
    - no trial in a similar situation may be available;
    - no two situations are identical, the minimum acceptable degree of similarity, not only epidemiological, but also social and economic, is hard to define and to assess; significant dissimilarities may become manifest only after local trial;
    - experiences are poorly evaluated and documented. One of the objectives of the epidemiological approach to malaria control should be to remedy precisely this defect.

- **Apply a model** that simulates the behaviour of malaria in different situations, including its response to different interventions.
  - *advantage*: it is in principle the most appropriate and most widely applicable method of extrapolation;
  - *disadvantages*:
    - models simulate only part of the whole, e.g. transmission models may calculate infection in man from the vectorial capacity, but not what comes before, e.g. residual spraying, or after, e.g. disease and death;
    - even the part they simulate is simplified. See for instance the previous discussion about residual spraying and the uniformity/non uniformity of resting behaviour. (Learning Units 3 and 5):
data may be insufficient to define the situation; the vectorial capacity may be too difficult or expensive to measure; however, we should learn to make better use of simple and inexpensive indirect indicators of the intensity of transmission, such as the past stability of the situation and the age-distribution of infection and disease, e.g. the median ages of cases of uncomplicated malaria and of cases of severe malaria;

there may be no data on the expected intermediate effects of vector control, i.e. its effect on the entomological situation, that is however easier, quicker and cheaper to evaluate than the epidemiological impact.

The three approaches are complementary. Eventually, vector control has to be evaluated in the given situation, the first approach. However, prior to that, the second and third approaches are useful, and nearly always used, albeit only implicitly, for identifying clearly what is worth evaluating in a given situation.

**Intersectoral co-operation**

Intersectoral cooperation would be valuable. Examples of possible areas for cooperation include:

- **Agriculture**
  - control of the use of agricultural insecticides, to reduce the potential development of insecticide resistance
  - use of intermittent irrigation to reduce mosquito breeding sites

- **Public works**
  - road construction and other works in order to reduce the creation of vector breeding sites
  - draining systems of cities

- **Education**, e.g. what is taught about malaria transmission in primary school

- The media, e.g. on the possible role of the community in vector control.

**Community participation**

Examples of vector control methods for which community participation is especially needed include the impregnation and use of bednets and correct irrigation practices to minimize vector breeding.
Control of malaria epidemics

Learning objectives:

By the end of this Unit, the Learner should be able to:

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

You will need to prepare photocopies and overheads of Figures 10.1 and 10.2 provided.

The learners should work through the questions in the Learner's Guide. The points to be brought out in the general discussion should include the following:

What is the general definition of an epidemic?

An epidemic is the occurrence of cases in excess of the number expected in a given place and time period.

Note that the definition does not exclude non-infectious diseases, nor slow increases.

Practical problems in using the definition, in the case of malaria, include difficulty in knowing what is the "expected", and in ascertaining that it has been exceeded.

Endemic malaria commonly shows different kinds of variation in time:

- **seasonal**: usually determined by rainfall in tropical areas, and by temperature in sub-tropical or temperate areas;

- **periodic**: cycles of several - often 8 to 10 years usually determined by rainfall and amplified by loss of immunity in periods of low rainfall and hence low transmission;
• *secular*: long-term trends, e.g. downward trend in northern temperate zone in the period 1900-1940.

Epidemics are "unexpected" increases superimposed on the above more or less "expected" kinds of variation.

There is however some overlap between "epidemics" and the three other kinds of variation: (a) an exaggerated seasonal increase; or (b) an exaggerated "periodic" increase; or (c) an acceleration of a "secular" upward trend, could all qualify as "epidemics".

In non-endemic areas, any transmission constitutes an epidemic. Depending on local receptivity, basic reproduction rate, the potential size of such epidemics may vary from very small (and self-limited) to very large.

From the above, it is obvious that there are different kinds of malaria epidemics; an additional important variable is the parasite species.

**Consequences**

An epidemic of *P. vivax* causes disease in all age groups, while an epidemic of *P. falciparum* causes disease and death in all age groups. Both kinds have, in addition, social and economic effects, through incapacitating disease, the workload put on health services, and the costs of treatment and/or control.

**Causes**

a) No.

b) Situations of unstable malaria (see exercise on intensity of malaria, Learning Unit 5).

c) They can be natural, e.g. irregular rainfall in an arid zone, or man-made (e.g. drastic reduction of the vectorial capacity through residual spraying for several years without change in availability of vector breeding sites or in opportunities for man vector contact).

d) No to both questions.

e) No, they do not occur completely at random. It should be possible to monitor the risk, because the nature of epidemic prone situations is relatively well known, as well as the factors likely to precipitate epidemics in such situations. "Advance warning" would obviously be useful for management.

f) No.

g) Possible precipitating factors of malaria epidemics include
Control of malaria epidemics:

- increase of vectorial capacity.
  - importation of a more potent vector, e.g. *A. gambiae* s.l. in Brazil and Egypt;
  - natural increase, mainly through abnormal rainfall, usually excess, sometimes deficit; other natural factors may be elevation in temperature which accelerates larval development and hence the emergence of vectors; shortens the malaria incubation period in the vector, hence increases the fraction of infective vectors surviving that period and humidity which increases adult longevity;
  - man-made increase:
    * deterioration of vector control operations;
    * inadequate management of surface waters;
    * insecticide resistance;
    * destruction of cattle and/or houses, e.g. through disaster or war, leading to increased man-vector contact.

- immigration of non-immunes into an endemic area;
- immigration of infectives into a receptive non-endemic area;
- resistance to antimalarial drugs, probably responsible for an increase of severe malaria in countries such as Thailand.

h) Often epidemics are precipitated by several factors in combination, e.g. a natural disaster or war may destroy houses and cattle, cause population movements (see comments about immigration in (g) above) and deterioration of vector control operations; or excessive rainfall may be combined with raised humidity and inadequate management of surface waters.

**Monitoring**

The main kinds of epidemic-prone areas are well known, and more or less easy to identify on the map:

- areas of naturally unstable endemic malaria are usually marginal with respect to rainfall or temperature, including lower temperature due to altitude, and their instability is well known from their past history;
- endemic areas made unstable by vector control but without a change in the potential for vector breeding and for man-vector contact may be tentatively
identified from their past history, but the potential may have been reduced more than is realized;

- it should be possible to anticipate/monitor non-immunes migrating to endemic areas: in certain cases, the migration is controlled;

- most non-endemic areas have low or zero receptivity so that infectives migrating to non-endemic areas may not be of great consequence. However, some non-endemic areas at the margin of the current geographical distribution of malaria are receptive, although it may be difficult to assess: man-vector contact may have decreased and local vectors may have low or no sensitivity to foreign parasites, as highlighted by current research on the receptivity of vectors of north Africa to *P. falciparum* of tropical Africa.

A list of factors that *could* be monitored include:

- **Environment**
  - rainfall, in some cases local surface waters depend on rainfall - or snowfall - upstream;
  - temperature;
  - humidity;
  - surface water (however, the type of surface water suitable for breeding varies with the vector species).

- **Entomological situation, i.e. the vectorial capacity or its components or immediate antecedents:**
  - density of larvae;
  - density of adults;
  - longevity;
  - frequency of feeding on man;
  - duration of incubation in the vector.

- **Cases of infection and/or disease in man:**
  - general population surveys;
  - detection of symptomatic cases;
• Deaths: epidemics of *P. falciparum*

These form a time sequence but only the environmental and entomological changes precede the epidemic.

In practice monitoring can only be selective and possible criteria for selection include

i) any relevant information that is already collected for other purposes;

ii) cost of the additional information;

iii) technical measurement problems;

iv) sampling problems (where? how often?);

v) reliability of warning (avoiding errors of prediction in both directions);

vi) timeliness of warning (time available for action).

Discussion of statements (a) to (e) given in the learner’s guide.

a) this singles out criterion (vi) from the others; in practice, environmental monitoring is satisfactory by criteria (i) to (iv), but the predictions are of moderate reliability;

b) this singles out criterion (v) from the others; in practice close monitoring of the number of symptomatic cases, in comparison with the number expected on the basis of past experience, should give reliable warning; it is also satisfactory with respect to criteria (i) to (iv); its weakness is that it is relatively late; in general reliability and timeliness of warning are likely to be inversely correlated;

it does unfortunately happen that an epidemic is detected only through an excess of deaths, and, worse, that the excess is detected by the press before the health services;

c) these two measurements have little place in practical monitoring of epidemic risk, because of measurement and sampling problems (see criteria (iii) and (iv));

d) the most difficult to monitor are the two mentioned in (c); among the easiest is rainfall; among those of intermediate difficulty are surface water and cases. Yes, that should be a selection factor;

e) yes, those three criteria are important.
The following may be suggested:

Routine:

- identify epidemic-prone areas from past occurrence;
- identify the probable precipitating events/factors of past epidemics;
- monitor those events/factors, such as the rainfall, that can be detected at low cost;
- monitor the incidence of symptomatic cases

Conditional: investigate the situations identified as threatening through the last two of the above, for confirmation, explanation and corrective measures.

**Diagnosis**

In endemic areas, they are likely to be right; confirmation involves clinical history, clinical and parasitological examination, circumstantial evidence: is a malaria epidemic likely at that time - e.g. season - and place?

In areas of relatively stable to unstable malaria, a majority of fevers from other causes may have malaria parasites as well; this happened with an Ebola virus epidemic in Sudan.

The usual parameters include:

- where? Check the numbers of cases detected in adjacent areas;
- when? Determine when the number of cases was first unusually large;
- who? Is any particular group affected, e.g. immigrant labour;
- why? Try to explain the epidemic in terms of the possible causal factors (see above); use your tentative explanation to try to project the future of the epidemic in terms of area, time period, population groups. Project your answers to where, when, and who, into the future.
Selection of short-term control measures

a) A compromise between both.

b) Fig 10.1 is a diagram of the states into which the human and vector populations are distributed, in relation to malaria transmission. In fig 10.2, the points of impact of different categories of control measures have been added.

The epidemic was detected by an excess of cases (infectives, at least potentially); there is likely to be an even larger number of incubating persons, and a large number of infected vectors, also with a larger number of incubating than infective vectors.

Discussion of individual measures:

- Larval control:
  - low feasibility as an emergency measure;
  - delayed impact: the whole cycle of transmission continues for sometime.

- Adult vector control:
  - feasibility relatively good;
  - delayed impact: incubating persons continue to become cases.

- Control of man-vector contact:
  - low feasibility as an emergency measure;
  - delayed impact: incubating persons continue to become cases.

- Diagnosis and treatment of cases:
  - feasibility good;
  - limited impact: incubating persons continue to become cases.
• Mass drug administration, with long-acting schizonticide, may have to be repeated:
  – feasibility relatively good;
  – most rapid and complete impact.

c) The cost, and the operational possibility of achieving rapidly a high coverage.

d) The first emergency measure is mass drug administration; if possible start to plan vector control at the same time.

e) All epidemics would eventually wane spontaneously by exhaustion of susceptible and/or natural decline of vectorial capacity. No "ideal" comparison is possible, i.e. one that is scientifically fully satisfactory, but a careful review of the history of the epidemic, probable causal factors and interventions may allow plausible evaluation of the effectiveness of the interventions.

f) Careful consideration of factors which might result in resurgence.

Medium- or long-term control

Long-term changes, e.g. in housing, relative numbers and accessibility of domestic animals, management of surface waters may eventually prevent malaria epidemics, but are unlikely to be planned for that purpose.

Monitoring the risk (see above); build up the capacity to investigate suspected epidemics and to plan and implement emergency measures.
Example of multiple-choice type question

Evaluation by the use of multiple choice type questions has the advantage of some form of standardization of the monitoring, is less time-consuming for both learner and tutor and is beneficial for those who have difficulty in expressing themselves in the language being used or even in their mother tongue. It has the disadvantage of not being able to express alternative scenarios and this is a drawback especially in medicine where variations are rife. It is therefore a compromise that it is suggested, that the evaluation of the trainees’ progress be measured by means of a series of multiple choice questions.

However, it must be said that in order to validate the questions they must be properly written, meaningful and as much as possible problem solving rather than recall of memory. Further, to be really valid they should not be designed in such a way as to offer a set choice. That is to say if the questions say which one of the following are correct then without knowing anything about the subject, you can achieve the correct answer in 20% of cases. To eliminate the bias and distinguish more clearly those who really know the subject and those who are guessing right, one would not indicate how many of the five might be correct but then negative marking will have to be introduced otherwise by checking all five total marks could be obtained. Negative marking however makes it much harder and is more complex to apply. It is suggested that for each wrong answer 0.5 of a mark or less be deducted and fore each correct answer 1 mark be given.

Two other issues arise. The first is that if equal marking is to be used then the question and answer must have equal difficulty. The second is that to measure progress the pre- and post-test must be of equal difficulty. This can be achieved by offering the same questions in the pre- and the post-test by rearranging the proposed answers and questions in a different sequence.
If certain rules are adhered to, then writing multiple-choice questions is greatly facilitated although still a difficult task. The following are some suggestions:

- The body of each question should be a complete statement (not just a single word) and the answer should not be dependent on the answer to any other questions on the page.
- Do not overburden the question with unrelated details and avoid negative statements, but if unavoidable then highlight them to draw them to the attention of the trainees.
- Use plausible or logical distracters in the possible answers, and each distracter must appear to have something to do with the question otherwise it looks nonsensical.
- Ensure that the distracters and the correct response are fairly similar in content or in the total number of words.
- Avoid clues that may suggest the correct answer and be cautious about the use of “some of the above” as a distracter or correct answer. This is especially important if you use the same question for the pre- and post- tests but then rearrange the sequence of possible answers.
- If it is not possible to obtain more than three plausible responses, do not waste time trying to invent others.
- Items that have numerical answers should have them arranged in order from large to small or vice-versa.
- Review the test paper as a whole and ensure that no letter or number corresponding to the correct answer appears more frequently than some other letter.

The following are some example types of multiple-choice questions. It is good practice to mix several different types in one examination paper.
One “best” response type

Question 1

Careful programmatic planning and replanning are essential for effective malaria control and involves a series of coordinated activities. Which of the following does planning involve?

A. Setting priorities
B. Selecting tactical variants
C. Deploying field personnel
D. Conducting field research
E. Arranging meetings

Multiple type response

Question 2

An implementation plan should include certain sections. Five suggested sections are listed below (A - E). Select the sections which should be included in an implementation plan and indicate your answer in the boxes provided.

A. The stratification process
B. A description of strata
C. The objectives set in each stratum
D. The approaches formulated to achieve the objectives
E. The operational targets

(i) only A and B are correct
(ii) only B and C are correct
(iii) only B, C, and D are correct
(iv) only B, C; D and E, are correct
(v) all are correct
The “matching” type

These are more difficult to construct but in doing so remember to:

- Limit the number of entries to 10 or less
- Do not break items at the bottom of a page
- Have a longer list of questions than of possible answers but state in the directions that they may be used more than once

Questions 3 - 8

The group of questions (3-8) below, consist of numbered items and a list of lettered components of a definition for each numbered item. Select the one element of a definition that is most clearly associated with it and mark that letter in the answer column against the numbered item. Each letter heading may be selected once, more than once, or not at all.

3. Planning environment  
4. Planning process  
5. Analysis of the malaria situation  
6. Stratification process  
7. Criterion for selecting malaria control measures  
8. Implementation plan

   a) Safety to people and environment
   b) Objectives
   c) Lack of data
   d) Past malaria control activities
   e) Interpretation of data
The comparison type

The comparison type questions permit one to compare and contrast situations or events.

Each set of letter headings below is followed by a list of number words or phrases. Mark the answer column against each numbered word or phrases the following:

a) If the item is associated with (a) only
b) If the item is associated with (b) only
c) If the item is associated with both (a) and (b)
d) If the item is associated with neither (a) nor (b)

Questions 9 - 12

a) Panning and replanning
b) Description of strata
c) Both
d) Neither

9. Evaluation (a)
10. Implementation plan (b)
11. Analysis of malaria situation (c)
12. Operational research (d)

True-false type questions should not be used and have never been included here. Where possible for the planning examination try to pose a problem situation, based on your own experience for instance, and then ask searching questions about what you would do and suggest the answers. The question can be of any of the types noted above.

* * *
Questionnaire for evaluation of training

Instructions for completion of questionnaire

Use the following code to indicate the extent to which you agree or disagree with each of the statements made in the questionnaire:

1   Disagree strongly
2   Disagree
4   Agree
5   Agree strongly

These numbers are printed alongside each question. You should circle the number that corresponds most closely to your opinion.

The difference between options 1 and 2 and between options 4 and 5 is one of degree only. To oblige you to express a definite opinion, no code 3 has been included (except for question 12); this allows a "satisfaction index" to be calculated for each question.

Take your time over completing the questionnaire. You do not have to put your name on it if you would rather not, but please answer the questions as frankly as possible.
Section I. Overall assessment of the training activity

1. Overall the organization of the training programme was satisfactory.

2. The training programme covered all the subject matter in adequate detail. (If you disagree with this, state which subjects should have been given greater coverage.)

Comments:

________________________________________

________________________________________

________________________________________

________________________________________

3. The tutors and facilitators for this training course had sufficient knowledge and teaching ability to provide you with the necessary skills and competence.

Comments:

________________________________________

________________________________________

________________________________________

________________________________________

4. The time allocated to each part of the training was adequate relative to the total time available. (If you disagree with this, state which particular topic should have been allotted more or less time.)

Comments:

________________________________________

________________________________________

________________________________________

________________________________________

1245 1245 1245 1245
Section II. Relevance and usefulness of the different teaching methods

5. Overall, the teaching methods used in this training course were effective.

Comments:

6. The use of the various teaching methods listed below was quite appropriate.

Large group presentations

Comments:
The epidemiological approach to malaria control: Tutor's Guide

Practical demonstrations (laboratory)

Comments:


Laboratory work and facilities (including equipment)

Comments:


Field work

Comments:


Small group discussions

Comments:

Self-study

Comments:

Quizzes, tests and other evaluation exercises

Comments:
Section III. Assessment of teaching materials

7. The audio-visual materials (slides, overhead projection transparencies) used in the training were very helpful.

Suggestions for improvement:

8. The teaching materials provided were satisfactory in all respects.

Suggestions for improvement:

Section IV. Implementation of training; attitude of tutor and facilitators

9. The general atmosphere of the training course made this a good learning experience.

Comments:
10. Every effort was made to help you achieve the learning objectives.

Comments:

11. You were able to achieve all the learning objectives of the training programme.

Comments:
Section V. Overall evaluation of the training

12. What overall rating would you give to this training programme? (Circle your response)

1  2  3  4  5
Lowest  Highest

13. With regard to this training experience, state the following giving actual examples):

(a) the three aspects that impressed you most favourably

________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________

(b) the three aspects that impressed you least favourably

________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
14. Do you have any additional comments regarding any aspect of the training programme? If so, please make them below.

__________________________________________________________________________

__________________________________________________________________________

__________________________________________________________________________

__________________________________________________________________________

__________________________________________________________________________

__________________________________________________________________________
The epidemiological approach to malaria control: Tutor's Guide

Analysing response to the questionnaire.

The following method will allow you to analyse the responses to the questionnaire quite simply and quickly. Take a fresh (uncompleted) copy of the questionnaire; against each question, mark the learners' responses:

**Example**

**Question.** Overall, the teaching methods used in this training course were effective.

\[
\begin{array}{cccc}
1 & 2 & 4 & 5 \\
| & | & | & | \\
| & | & | & | \\
| & | & | & | \\
| & | & | & | \\
& & & & \\
\end{array}
\]

This shows that two learners considered the teaching methods were not effective while 28 agreed that they were effective.

Now multiply the number of answers by the corresponding coefficient:

\[
(2 \times 2) + (10 \times 4) + (18 \times 5) = 4 + 10 + 40 + 90 = 134
\]

The "satisfactory index" is calculated as a percentage. For the above example, the number 134 is multiplied by 20 (i.e. 100 divided by the maximum coefficient, 5) and divided by 30 (the number of learners):

\[
\frac{134 \times 20}{30} = 89.3\%
\]

Since the satisfaction index is calculated in such a way that 60% represents "average" satisfaction, you should make a note of any questions for which the index is below 60% (if there is none, identify the five questions for which the index is lowest and the five for which it is highest). Let the learners know the results of this questionnaire at the final evaluation session on the last day of the training programme.
Commonly used methods of teaching and their objectives

<table>
<thead>
<tr>
<th>Teaching method</th>
<th>Purposes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Audio tapes</strong></td>
<td>• To guide practical work.</td>
</tr>
<tr>
<td></td>
<td>• As a variation in the method of</td>
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<td></td>
<td>presentation of material.</td>
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<td></td>
<td>• For the acquisition of new knowledge.</td>
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<tr>
<td><strong>&quot;Brainstorming&quot;</strong></td>
<td>• For developing new and creative ideas.</td>
</tr>
<tr>
<td></td>
<td>• As a prelude to detailed, in-depth</td>
</tr>
<tr>
<td></td>
<td>problem-solving.</td>
</tr>
<tr>
<td><strong>&quot;Buzz-groups&quot;</strong></td>
<td>• To encourage all learners to participate.</td>
</tr>
<tr>
<td></td>
<td>• To develop group cohesion and encourage</td>
</tr>
<tr>
<td></td>
<td>learners to help one another.</td>
</tr>
<tr>
<td></td>
<td>• To &quot;rehearse&quot; understanding and thus</td>
</tr>
<tr>
<td></td>
<td>consolidate factual learning.</td>
</tr>
<tr>
<td></td>
<td>• To stimulate creative thinking.</td>
</tr>
<tr>
<td><strong>Case discussion</strong></td>
<td>• To help in understanding the facts</td>
</tr>
<tr>
<td></td>
<td>underlying the problems and to eliminate</td>
</tr>
<tr>
<td></td>
<td>misconceptions.</td>
</tr>
<tr>
<td></td>
<td>• To show how various principles are</td>
</tr>
<tr>
<td></td>
<td>applied to real problems.</td>
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<tr>
<td><strong>Controlled discussion</strong></td>
<td>• To provide further consideration of factual</td>
</tr>
<tr>
<td></td>
<td>learning.</td>
</tr>
<tr>
<td></td>
<td>• To bring together and synthesize the</td>
</tr>
<tr>
<td></td>
<td>contents of a lecture and provide feedback</td>
</tr>
<tr>
<td></td>
<td>to tutor and learners.</td>
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</tbody>
</table>
Demonstrations
Certain procedures are performed by the tutor to demonstrate skills that must be acquired by learners.

- To help develop learners' power of observation.
- To provide knowledge of principles as a prelude to learners practising the skills for themselves.

Video tapes

- For development of skills in interviewing, counselling, etc.
- To allow learners to see themselves "in action".
- To provide learners with direct feedback.

Free group discussion
Discussion in which the content and direction are principally under the learners' control. The role of the tutor is that of an observer.

- To develop effective small-group functioning.
- To help learners establish the practice of self-learning.
- To allow the tutor to observe developments in the learners' problem-solving skills.

Group tutorial
Tutorial with 12-15 learners. The subject and direction are usually, but not invariably, under the control of the tutor.

- To facilitate understanding of particular topics, and bring together ideas.
- To develop group-functioning skills.

Projects
Varied in format and content, but generally submitted as a written exercise by a small group of learners or by individuals.

- To develop skills in gathering organizing, applying and illustrating information in the context of a particular problem.
- To provide practice in the presentation of data.

Private reading

- To assist in acquiring and understanding new information.
- To assist the development of critical thinking skills.
- To develop an ability to select and retrieve relevant information.

Role-playing
Learners are assigned or select certain roles (e.g. village leader, mosquito collector), then create and act out typical situations. It is essential that the content of the role-play is discussed at length by participants and observers; without this, the exercise has little value.

- To develop "self-awareness", i.e. to help the learner appreciate the effect that his or her attitudes have on other people.
- To improve attitudes and behaviour by encouraging the learner to "get into the skin" of another person.
Seminar
Presentation of material by one learner to a group of fellow learners, followed by critical analysis and discussion. It is not essential that the tutor be present.

Individual tasks
The type of task assigned to the individual learner may vary, but it will generally be a problem to be solved within or outside the classroom situation.

Lecture
The "classical" lecture is an uninterrupted talk by the tutor to a group of learners, generally lasting about 1 hour. The form may be modified and used in conjunction with "buzz groups", syndicate groups, etc. into a coherent whole.

Practical classes
Learners perform experiments, write up their results, and draw appropriate conclusions.

Problem-centred groups
Problem solving in the classroom situation by groups of 4-8 learners, partly under the direction of the tutor.

Step-by-step lecture
A lecture format linked to an organized around, for example, a set of 35-mm slides or a number of multiple-choice question.

Step-by-step discussion
Working with a small group (8-10) of learners, the tutor directs a discussion centred on a particular issue or a set of pre-prepared questions. The intention is to draw out from the learners the required information.

- To present new information.
- To help with understanding of new material.
- To foster active, direct learning.
- To develop problem-solving skills.
- To provide a context in which the tutor can help learners to remedy particular weaknesses.
- To transmit information.
- To impart general background knowledge of a particular subject.
- To synthesize a wide variety of information.
- To develop powers of observation.
- To develop familiarity with equipment and skill in its use.
- To develop problem-solving through collection, analysis and evaluation of data.
- To develop skills in analysing and solving problems and in decision-making.
- For practice in applying theoretical knowledge to "real" problems.
- To impart new information and reinforce its understanding.
- To present a new factual material.
- To help learners in the process of scientific and deductive reasoning and of drawing appropriate conclusions.
Syndicate group

The class is divided into groups of 4-6 people; all groups work on the same, or closely related, problems, with occasional teacher contact. Each group prepares a report, which is presented to the rest of the class. The syndicate group technique can be used in conjunction with tutorials.

- To develop skills in seeking out, organizing and presenting information.
- To foster cooperation between learners in planning, writing and presenting a report.