



THE PRESCRIBER

Promoting Rational Use of Drugs and Correct Case Management in Basic Health Services

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MALARIA PREVENTION AND TREATMENT

The global malaria burden

AROUND THE WORLD, the malaria situation is serious and getting worse. Malaria threatens the lives of 40% of the world's population – over 2 200 million people. Each year, there are an estimated 300-500 million clinical cases. Malaria is estimated to kill more than 1 million people annually, the majority of whom are young children. Ninety per cent of malaria cases in the world occur in Africa south of the Sahara. Children under 5 years of age and pregnant women are the worst affected by malaria. It is one of the leading causes of death among young children. Together with pneumonia, diarrhoea, measles and malnutrition, malaria is responsible for over 70% of deaths in young children especially in developing countries. Malaria during pregnancy causes severe maternal illness and anaemia, and is also associated with low birth weight among newborn infants, a leading risk factor for infant mortality.

Malaria's cost to human and social well-being is enormous. The mosquito-borne disease typically strikes its victims not once but repeatedly. As a result, workers' output is diminished, and children miss school, often for periods of a week or more at a time. The economic loss from malaria was estimated at US\$2 billion in Africa alone in 1997. Malaria is a major cause of poverty, and poverty exacerbates the malaria situation. Taken together, the effects of malaria on lives and livelihoods are devastating for economic progress in hard-hit countries.

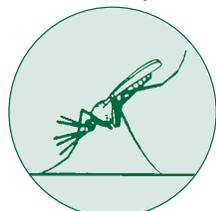
The World Health Organization and the World Bank rank malaria as the largest single component of the disease burden in Africa, causing an annual loss of 35 million future life-years from disability and premature mortality. In Africa, malaria is responsible for about 20-30% of hospital admissions and about 30-50% of outpatient consultations.

Malaria is also a major public health problem in parts of Asia, Latin America, the Middle East, Eastern Europe and the Pacific. In India, epidemics of malaria are frequently reported from areas that previously were not associated with malaria. In Bangladesh, the malaria situation has been steadily deteriorating since the late 1980s. The number of cases increased fivefold between 1988 and 1994. In Latin America, Brazil is worst affected with over 50% of all malaria cases in the Americas.

Malaria is mostly a disease of hot climate. The Anopheles mosquito, which transmits the malaria parasite from one human being to another, thrives in warm, humid climates where pools of water provides perfect breeding grounds. It proliferates in conditions where awareness is low and where health care systems are weak.

THIS ISSUE COVERS THE FOLLOWING:

- The new global Roll Back Malaria partnership
- The global malaria burden
- Strategies to prevent and control malaria
- New risks and new opportunities in the control of malaria
- What malaria mosquitoes look like and how they live
- How to diagnose malaria
- Malaria drug resistance patterns
- Treatment of mild and severe malaria
- Special concerns for pregnant women and young children
- Chemoprophylaxis against malaria
- Personal protection and selective vector control measures
- How to treat mosquito nets with insecticide



NEW RISKS

Widespread drug resistance against commonly used anti-malaria drugs such as chloroquine and pyrimethamine/sulfadoxine (Fansidar) has been reported all over the world. Epidemics are increasing in highland areas where malaria was uncommon, partly due to climatic changes including high rainfall patterns. New development projects such as dams and agricultural irrigation works are creating environmental changes more conducive to mosquito breeding and malaria transmission. Economic activities in frontier areas have partially contributed to increased malaria risk in South East Asia, the area of the world with the most severe resistance to malaria drugs.

Refugees and people who are internally displaced as a result of civil war and natural disasters are particularly vulnerable to epidemics of malaria. Afghanistan recorded over 300,000 cases in a year, as a result of interruption of malaria control activities and the displacement of populations due to war. In Sierra Leone, where health facilities have been destroyed and health staff displaced because of the war, almost half the patients seen at referral hospitals are suffering from malaria.

In Ethiopia, repeated epidemics in highland areas, which were not previously vulnerable, are due to high rainfall patterns and degraded environment. In Kenya

Refugees and people displaced by war and natural disasters are vulnerable to malaria epidemics.

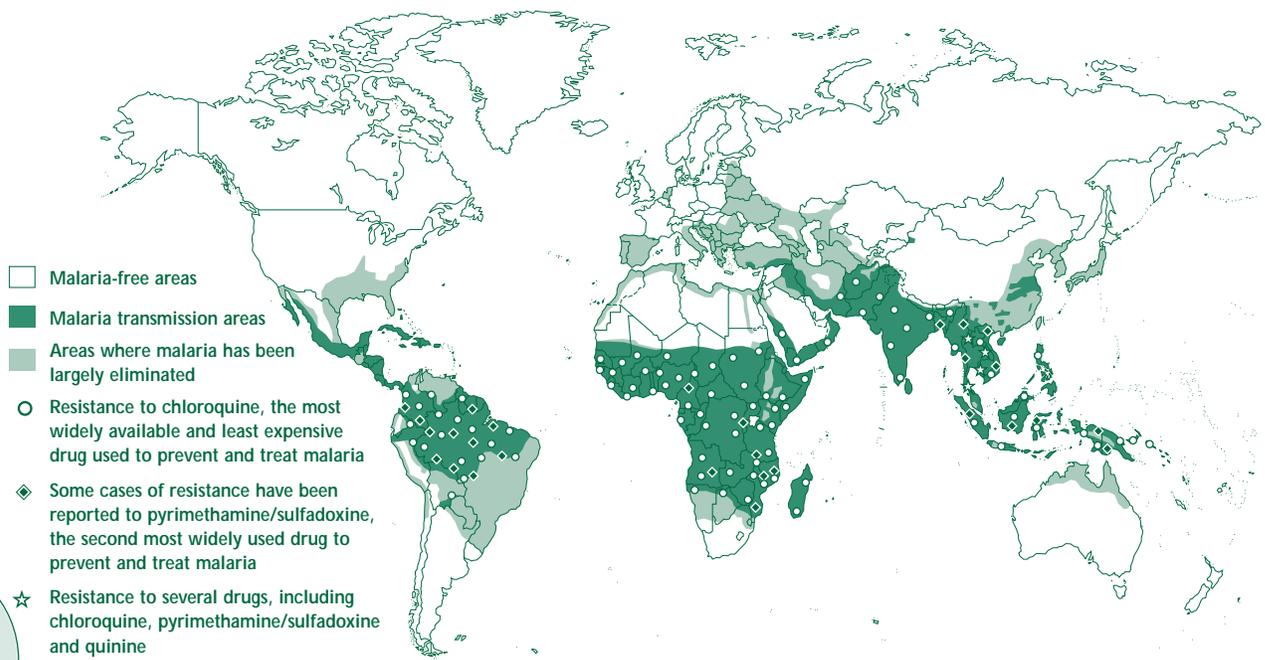
epidemics occurred during 1999 in the highlands of Kisii and Kericho where malaria was uncommon, again mainly because of high rainfall patterns.

ROLL BACK MALARIA

The **Roll Back Malaria (RBM) Initiative** was launched by the United Nations agencies WHO, UNICEF and UNDP, together with the World Bank, on 30 October 1998, as a bold new effort to mobilize global partnerships including governments, donors, non-governmental organizations (NGOs) and communities, to effectively tackle the increasing global problem of malaria. This new initiative is a response to the request by African Heads of State and Government at the 1997 Organization of African Unity (OAU) summit meeting in Harare, when they requested support from the international community, to help them fight the problem of malaria in the African region. The RBM movement has now been accepted by many heads of state in Africa who have expressed strong commitment to intensify malaria prevention and control in their own countries, with the assistance of the international community.

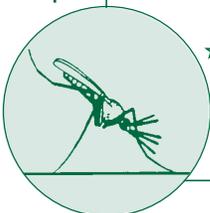
RBM aims at reducing overall mortality due to malaria by 50% by the year 2010. The partnership will work closely with governments to strengthen national health systems as part of health sector development.

MALARIA: KEY AFFECTED AREAS



Source: Adapted from the World Health Organization

Note: This map does not reflect a position by UNICEF on the legal status of any country or territory or the delimitation of any frontiers



In Latin America, those living close to forested areas which have recently been opened up for agriculture or mining face an increasing threat. Epidemics of severe malaria are common in such environments. In Brazil, an estimated 6,000-10,000 deaths per year caused by malaria are in new settlement and mining forest areas. The situation is similar in areas of Cambodia, Lao People's Democratic Republic, Myanmar, Thailand and Viet Nam as a result of environmental disturbance due to illicit mining and civil unrest.

Declining health services and increasing poverty in parts of Africa and South Asia are also playing an important part in malaria's comeback. Where improvements in the malaria situation have taken place in the past, they have been largely due to the development of the health services and socio-economic development taking place at the same time. The more people are aware of the risks of malaria and can afford to be treated promptly and take necessary personal protection measures, the less malaria is able to spread.

OPPORTUNITIES FOR SUCCESS

Technology now available to health workers and to households has made malaria control a real possibility. One increasingly promoted technology is the use of insecticide-treated mosquito nets and other materials such as curtains and screens on windows and doors. The success of three large trials on insecticide-treated mosquito nets conducted in the Gambia, Kenya and Ghana and another one using treated curtains in Burkina Faso, have demonstrated that the use of insecticide-treated materials can reduce all-cause child mortality by about 25%.

Secondly, changes in treatment regimen in areas of chloroquine resistance are possible. Alternative drugs, such as pyrimethamine/sulfadoxine, mefloquine, quinine and artemisinin derivatives, provide effective cure in many of the cases in which chloroquine fails to achieve a cure. Combination

The technology now available has made malaria control a real possibility.

GLOBAL STRATEGIES TO PREVENT AND CONTROL MALARIA

WHO has prioritized four main strategies for malaria control, which were endorsed by the Global Malaria Conference for Health Ministers, held in Amsterdam in 1992:

- Provision of early diagnosis and prompt treatment
- Planning and implementation of selective and sustainable prevention measures including vector control
- Early detection, containment and prevention of epidemics
- Strengthening of local capacities in basic and applied research, for regular assessment of the malaria situation within countries

drug therapies provide effective cure and slow down the emergence of drug resistance.

Finally, the Integrated Management of Childhood Illness (IMCI) approach, recently developed by WHO, UNICEF, USAID and other partners, will play a crucial role in malaria control. IMCI not only encourages management coordination of a range of childhood illnesses at the health facilities, it also emphasizes prevention and health promotion within families and communities, aiming to increase the general care skills of parents, caregivers and health workers. IMCI has already begun integrating malaria into a broader disease control approach within public health programmes.

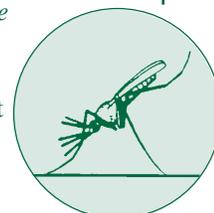
UNDERSTANDING MALARIA

HOW PEOPLE BECOME INFECTED WITH MALARIA

Malaria is transmitted through the bite of an infected, female Anopheles mosquito and occasionally through blood transfusion. When a mosquito bites a person it sucks up blood. If the person has malaria, some of the parasites in the blood will be sucked into the mosquito. The malaria parasites multiply and develop in the mosquito. After 10-14 days they are mature and ready to be passed on to someone else. If the mosquito now bites a healthy person, the malaria parasites enter the body of the healthy person. The

parasites are transported in the bloodstream to the victim's liver where they multiply and then re-enter the bloodstream. The malaria parasites can multiply 10 times every 2 days, destroying red blood cells and infecting new cells throughout the body.

There are four main species of these parasites: *Plasmodium falciparum* which causes the severest type of malaria, and *Plasmodium vivax*, *ovale* and *malariae* which cause less severe symptoms. The person infected by the mosquito bite will become ill with malaria, symptoms appearing anywhere from about a week to several months after infection, but usually in 7-21 days.



HOW MALARIA MOSQUITOES LIVE

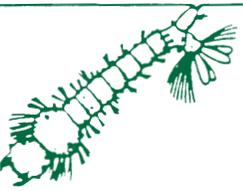
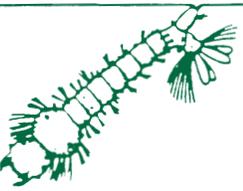
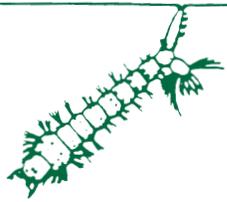
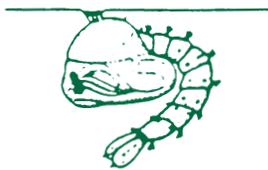
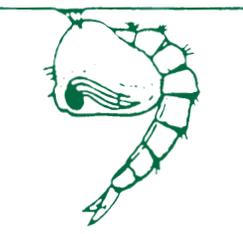
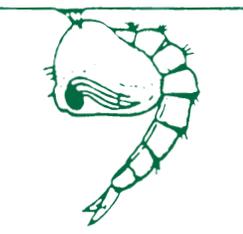
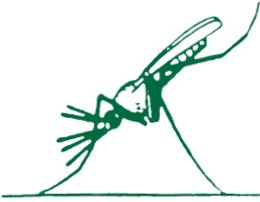
Although many different kinds of mosquitoes exist, only female Anopheles mosquitoes can pass on malaria parasites. The Anopheles mosquito can be recognized by its upturning tail (see drawing). They need blood to produce eggs. The eggs are very small but can be seen as small (2-5mm wide) black spots on the surface of water. The malaria mosquito chooses stagnant or slow-flowing water in which to lay her eggs.

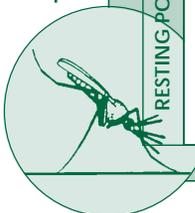
Two or three days after the eggs are laid on the water, a mosquito larva will come out of each egg. The larva feeds on microscopic organisms and plants in the water, and grows until it becomes a pupa. The pupa remains in the water, but does not feed. After a few days the adult mosquito will come out of the pupa and fly away. After feeding, the mosquito usually rests on a nearby surface before it flies away. Then it will lay eggs and

everything starts all over again. It takes 7-14 days for a mosquito to grow from an egg to an adult mosquito.

A mosquito egg, larva or pupa does not have malaria parasites inside it. Adult mosquitoes may have malaria parasites in their bodies, but only if they have bitten someone who has malaria. Life for the parasite inside the mosquito is a race against time. The average lifespan of the mosquito is roughly the same as the time taken for the parasite to go through its growth and development. This period is shorter in cooler environments and lengthens as the temperature rises. Thus the survival of the parasite depends upon the weather. Once the average temperature drops below a certain point, the mosquito tends to die before it can transmit malaria.

Differences between the anopheline mosquito (malaria vectors) and other common mosquitoes (non-malaria vectors)

	ANOPHELINES		CULICINES	
	ANOPHELES	AEDES	AEDES	CULEX
EGGS				
LARVA				
PUPA				
HEAD	 	 	 	 
RESTING POSITION				



DIAGNOSING MALARIA

UNCOMPLICATED MALARIA

Children and adults infected with malaria commonly suffer from high fever and severe aches but symptoms may also include cough and diarrhoea.

Any child who presents with fever in a malaria endemic region or who recently visited such a region, must be assumed to have malaria until proven otherwise, and requires urgent treatment. The most important feature of malaria is fever. Early diagnosis and treatment will save lives and prevent the development of

complications. All parents and caregivers should be made aware of malaria symptoms and urged to seek prompt treatment.

SEVERE OR COMPLICATED MALARIA

Untreated malaria in a young child or in a non-immune individual may become complicated: the patient presents with very high body temperature, drowsiness, convulsions and coma indicating heavy parasitaemia and cerebral malaria. Other complications may include bleeding, jaundice, diminished urine output, all signifying liver and/or kidney failure.

HOW TO RECOGNIZE MALARIA

It is difficult to tell whether a sickness is caused by malaria or some other disease, because the features may be similar. Ask the patient, or the adult accompanying a young patient, whether there has been any fever at any time during the past 2-3 days. The patient has a fever when the forehead feels hot, or more precisely when his or her temperature is more than 37.5 degrees centigrade on a thermometer. Very young children with malaria may present with low body temperatures or hypothermia. Patients who have had fever during the last 2-3 days may have malaria. In this case, ask and then look for danger signs.

DANGER SIGNS OF SEVERE MALARIA

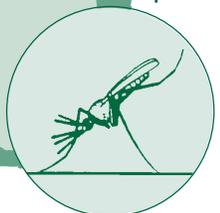
Look for the following signs of malaria, and ask the following questions to each patient, or parent or care-giver accompanying a child:

- if he/she is able to drink
- if he/she has had fever at home
- if he/she has had convulsions (fits)
- does he/she vomit repeatedly or have diarrhoea or a cough
- how much urine he/she has passed – very little, none at all? Is it dark or blood coloured?

LOOK FOR:

- changes in behaviour (convulsions (fits); unconsciousness; sleepiness; confusion; inability to walk, sit, speak or recognize relatives)
- repeated vomiting; inability to retain oral medication; inability to eat or to drink
- passage of small quantities of urine or no urine, or passage of dark urine
- severe diarrhoea
- unexplained heavy bleeding from nose, gums, or other sites
- high fever (above 39 degrees centigrade)
- severe dehydration (loose skin and sunken eyes)
- anaemia (look at the patient's facial colour and hands – the palms of a patient with anaemia do not have the redness of a healthy person's palms)
- yellowness of the eyes.

If you identify any of the danger signs, urgent treatment is needed at a clinic or hospital to save the patient's life.



Each attack may last several hours and often begins with shivering (body shaking). Next, there is a period of fever, and finally there is profuse sweating. During an attack, the patient often complains of headache and pain in the back, joints and all over the body. There may also be loss of appetite, vomiting and diarrhoea. Alternatively, the child may present with symptoms of severe malaria such as loss of consciousness, drowsiness and/or convulsions, diarrhoea, dark urine and reduced urine output (anuria).

If untreated (or inadequately treated), malaria may cause several weeks or months of poor health because of repeated attacks of fever, anaemia and general weakness. Malaria symptoms can mimic many illnesses and can affect most organs in the body.

It is particularly important to make an early diagnosis of malaria in young children and in pregnant women. These two groups may rapidly become very ill and may die within a few days. Pregnancy reduces the immune status of individuals and hence makes them more susceptible to malaria infection. Malaria during pregnancy is more difficult to treat, because the parasites tend to hide in the placenta, making diagnosis and treatment difficult.

BLOOD TESTS

Examining a stained blood film under a microscope will show whether a patient has malaria parasites in the blood (parasitaemia). This does not prove the parasites are causing the illness. However, the more dense the parasitaemia, the more likely it is to be the cause of the disease. For example, a patient with more than 10% of red cells containing

parasites, in an endemic area (or more than 4% in a non-endemic area) is at increased risk of developing severe malaria. Repeat testing will show whether or not the percentage of parasites in the red cells is increasing.

DISTINGUISHING MALARIA FROM OTHER SERIOUS CONDITIONS

Complications of severe malaria may be similar to those caused by other diseases. For each complication, examine the patient carefully and think of other possible causes. For example, a lumbar puncture may distinguish malarial coma from meningitis; careful examination of the chest may distinguish malarial breathing from pneumonia. Other conditions which may present with similar symptoms to malaria include: hepatitis – causing jaundice; acute renal (kidney) failure – causing diminished urine output; diabetes – causing deep acidotic breathing. Complications due to malaria may mimic many diseases, so a good history and physical examination are critical, followed by blood examination to confirm the diagnosis.

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MALARIA DRUG RESISTANCE PATTERNS

WHAT IS DRUG RESISTANCE?

Drug resistance is the degree to which a disease or disease-causing organism remains unaffected by a drug which was previously able to eliminate it. In the case of malaria, it is the resistance of the malaria parasite, *Plasmodium falciparum*, to chloroquine or other anti-malarials.

Reports of chloroquine resistant strains of *P. falciparum* are being documented in all regions of the world where malaria is endemic. Resistance to anti-malaria drugs other than chloroquine is also occurring at an alarming rate. All malaria endemic countries are therefore recommended to assess the level of chloroquine resistance including other commonly used anti-malarial drugs, using WHO recommended protocols, and change their drug policy if significant chloroquine resistance is documented.

Malawi and Kenya recently changed their first line anti-malaria drug treatment from chloroquine to pyrimethamine/sulfadoxine (Fansidar) because of documented widespread chloroquine resistance.

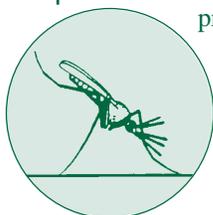
Chloroquine resistant strains of *Plasmodium falciparum* have been documented in all areas of the world except the following: North Africa; the Middle East (though cases have been reported in Oman, Yemen and Iran); Haiti; Dominican Republic; rural areas of Mexico; and Central America, north and west of the Panama canal.

Pyrimethamine/sulfadoxine (Fansidar) resistance has been documented in: South East Asia; the Indian sub-continent; the Amazon basin; many countries in Africa south of the Sahara; and Oceania.

Mefloquine resistance has been documented in: South East Asia especially in Thailand; parts of Africa and South America; the Middle East; and Oceania.

Quinine resistance has been reported in: South East Asia; parts of Africa; Brazil; and Oceania.

Halofantrine resistance has been noted in Thailand and shows cross resistance with mefloquine.



A CHANGE IN DRUG TREATMENT

Each country needs to review its drug policy on malaria, taking into account the distribution of malarial mosquitoes and the level of drug resistance. Research in the Gambia has revealed that chloroquine resistance is likely in about 20% of cases. At this level, its use as a first line drug is still recommended. In Malawi, when it was revealed that 30% of children treated with chloroquine had symptoms again within 14 days, the decision was made to change the first line treatment from chloroquine to pyrimethamine/sulfadoxine (Fansidar).

When a national policy changes because drug resistance is more widespread, treatment costs rise. In the past, malaria was often diagnosed and treated with chloroquine whenever other likely causes of fever or illness had been excluded. Use of more expensive drugs can be justified because it reduces the number of treatment failures and shortens hospital stay. Whenever possible, use of more expensive and toxic drugs should be preceded by confirming the diagnosis of malaria with a blood slide examination.

TREATMENT

(Also see treatment charts, page 11)

Early diagnosis and treatment of malaria can prevent it developing into a severe condition which could be fatal. **In view of widespread drug resistance, treatment should follow national recommended protocols as indicated above.**

UNCOMPLICATED MALARIA

In areas where chloroquine resistance is still low, chloroquine is used to treat uncomplicated malaria cases. **In many regions of the world, chloroquine is no longer effective in treating malaria, hence second line anti-malarial drugs are often used.**

Most cases of mild malaria can be cared for at home but the patient or caregiver should be aware of the following:

- dosage and frequency of the medication
- symptoms will return if treatment is not completed (even if symptoms disappear immediately after first medication)
- vomiting soon after medication may require more treatment
- fever which persists during treatment or which returns after a few days of completed anti-malaria treatment may indicate treatment failure.

If treatment fails, it may either be because the patient received incomplete treatment (e.g. vomited or forgot to take the medication) or because the malaria might be resistant to

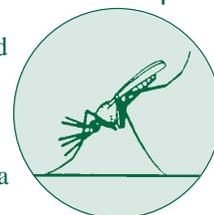
the drug. Discuss the possibilities of incomplete compliance with the patient or guardian and check national guidelines for alternative anti-malaria drug therapy.

ALTERNATIVE TREATMENT

If chloroquine fails to clear the malaria infection, an alternative drug needs to be used. If resistance to chloroquine is known to exist, other treatment is recommended. For example, **pyrimethamine/sulfadoxine (Fansidar) or mefloquine may be used as first line drugs** in areas of chloroquine resistance. Mefloquine is effective in the treatment of many cases of drug-resistant malaria, though resistance to mefloquine is growing in South East Asia. In addition, adverse reactions have been reported. Artemisinin is a natural product developed by Chinese scientists from the wormwood plant, *Artemisia annua*. **Artemisinin clears the parasite from the body more quickly than chloroquine or quinine.** It is also considered to be less toxic than quinine. Combination drug therapies are being advocated for treatment of malaria, e.g. mefloquine plus artemisinin.

SEVERE OR COMPLICATED MALARIA

The recommended treatment of severe complicated malaria is intravenous quinine or artemisinin derivatives. Intravenous infusion of quinine should be given slowly over 8 hours to avoid cardiac complications. This should be followed by oral quinine tablets for a total of 7 days once the patient is conscious and can drink. Although treatment may start at the health centre, the patient should then be immediately referred to a



The patient must be monitored closely to recognize, prevent and treat complications such as severe anaemia, convulsions and hypoglycaemia. Avoid blood transfusions wherever possible.

district hospital. Artemisinin, if available, can be given in suppository form in young children and to patients who are unconscious.

To bring down the fever, give paracetamol or aspirin. Take off most of the patient's clothes. Moisten the body with slightly warm water, using a sponge or cloth. Ask

someone to fan the patient continuously (including during the journey to the hospital). Protect the patient from direct sunlight. A note should be sent with the patient which clearly states the drugs already given with the dosage, route, date and time of administration. A brief clinical history and details of examination findings should also be included in the note. Findings from laboratory tests for parasite counts, haemoglobin or haematocrit, and glucose levels are also useful.

At the hospital, the patient's condition should be quickly assessed with the help of the note from the health centre and

TREATING SEVERE MALARIA

Treat convulsions with diazepam (Valium) given rectally if the intravenous route is not available:

Dose for	
child 1-3 years	5mg
child over 3 years	10mg
adult	10-30mg
elderly person	10mg

Give quinine intravenously (see page 11)

Treat anaemia with ferrous sulphate tablets (200mg salt; 65mg elemental iron):

Dose for	
child 6 months-2 years	6mg/kg daily in 3 divided doses
child 2-6 years (less than 20kg)	half a tablet a day
child over 6 years	1 tablet a day
adult	3 tablets a day

Hypoglycaemia can be prevented by encouraging food and drink intake when the patient is conscious, or by giving an infusion of 5% dextrose

by checking present clinical symptoms and signs of other diseases. Regular checks of the intravenous drip, urine output and hydration, pulse, respiratory rate and rhythm and coma score, haemoglobin or haematocrit, and blood sugar level need to be made. The patient must be

THE MOST VULNERABLE

In areas where malaria occurs frequently, individuals may be bitten by infected mosquitoes 1,000 times a year. Many people slowly acquire natural immunity. This keeps them from developing severe symptoms. However, until they acquire this personal defence mechanism, newcomers such as migrants and travellers arriving in malaria areas are highly vulnerable. Young children under 3 years have insufficient natural immunity and are therefore in special need of protection. Pregnant women, especially primigravidas, are also very susceptible because their natural immunity against the disease often declines during pregnancy.

monitored closely to recognize, prevent and treat complications such as severe anaemia, convulsions and hypoglycaemia.

Avoid blood transfusions wherever possible. Even adults and children with extremely low haemoglobin (less than 5g/dl) who are clinically stable do not require transfusion. Carefully transfuse with whole blood or with packed cells if there are signs of cardiac or respiratory insufficiency.

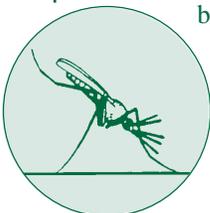
MALARIA IN CHILDREN

Chloroquine is the recommended treatment for uncomplicated cases in areas where resistance is low or non-existent. Fansidar is the recommended treatment in areas of high chloroquine resistance where Fansidar is still effective. To mask the bitter taste of chloroquine, crushed tablets can be given to the child with banana or other local food. **Quinine is the standard treatment for children with severe malaria.**

All children with high fever (over 38.5 degrees centigrade) should be given paracetamol (15mg/kg). When the fever has reduced and the child is calm, give the anti-malaria drug with a spoon, after the tablets have been crushed and mixed with water. A sweet drink or breastmilk should be given immediately after the medicine has been swallowed. The child should be observed for 1 hour.

If the child vomits during that time, treatment should be repeated (full dose if the drug is vomited before 30 minutes, half dose if vomited between 30 minutes and 1 hour). If the child vomits repeatedly, he or she must be hospitalized.

Chloroquine is the recommended treatment for uncomplicated cases in areas where resistance is low. Quinine is the standard treatment for children with severe malaria.



The Prescriber will keep you updated on important developments in the prevention and treatment of malaria. If you need more information right away, write to the Division of Control of Tropical Diseases, World Health Organization, Avenue Appia, 1211 Geneva 2, Switzerland.

Children with malaria may have other infections at the same time, such as meningitis or pneumonia. If coma and fever persist, it may be a result of the common association of severe malaria with meningitis, pneumonia or sepsis. Children must be carefully examined at least twice a day and at any time that their condition does not improve or becomes worse. The child should be placed in a bed where the nurses can observe him or her easily and frequently. An unconscious child should be made to lie on his or her side. The mother can be encouraged to turn the child every 2 or 3 hours, and to change soiled or urine-soaked linen. Clean the child's eyes and mouth regularly. When the child is conscious, encourage liquid intake or breastfeeding.

MALARIA IN PREGNANCY

Pregnant women in malaria endemic areas are more susceptible to malaria infections because of their reduced natural immunity and may therefore develop complications such as fever and severe anaemia. In some countries, national policies recommend routine use of anti-malarial drugs during pregnancy. Difficulties arise in providing pregnant women with prophylaxis in areas where there is resistance to

OTHER DRUGS USED IN THE TREATMENT OF MALARIA

Primaquine phosphate

Used to prevent relapse of *Plasmodium vivax* and *ovale* infections by eliminating the liver stages of both species, which can cause malaria symptoms long after leaving a malaria endemic zone.

Dosage: Adults: 15mg (base) daily for 14 days
Children: 0.3mg (base)/kg for 14 days

26.3mg tablet of primaquine phosphate equals 15mg of base

Side effects: (include) headache, dizziness, jaundice and neutropenia

All patients, especially persons of African and Mediterranean origin, should have blood tests done to rule out G6PD deficiency which can cause haemolytic anaemia, before being treated with primaquine. **Avoid use during pregnancy.**

Doxycycline

Used as treatment against chloroquine resistant *Plasmodium falciparum*, *ovale* and *malariae*, and can be combined with quinine. Can also be used as prophylaxis against malaria.

Dosage (as prophylaxis): Adults: 100mg tablet daily starting 1-2 days before travel and continued for 4 weeks after return from a malaria endemic area
Children over 8 years: 2mg/kg orally, once daily, as in adults

Side effects: nausea, vomiting, abdominal pain, photosensitivity

Avoid use in children under 8 years of age, during pregnancy, during breastfeeding and in patients with liver problems.

Halofantrine

Used in treating all four species of malaria, including multi-drug resistant *Plasmodium falciparum*.

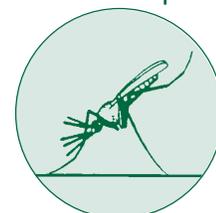
Dosage: Adults: 500mg 3 times a day (at 6-hourly intervals)
Repeat the 1-day course in 1 week

Side effects: abdominal pain, diarrhoea, cough, rash, itching

Avoid taking with meals (fatty foods delay absorption), avoid using with mefloquine, avoid using during pregnancy.

chloroquine. Pyrimethamine/sulfadoxine (Fansidar) has been used as prophylaxis/intermittent treatment in Malawi and in Kenya with good preliminary results.

In addition, all pregnant women should attend routine pre-natal clinic and should be protected from malaria by sleeping under treated mosquito nets. They should also receive ferrous sulphate and folic acid daily, to treat and prevent anaemia. When pregnant women become ill with malaria, treatment depends on national guidelines. Chloroquine, amodiaquine and quinine can all be safely given during pregnancy.



Concern has been expressed about the safety of mefloquine use during pregnancy. However clinical trials have shown that it can be given with confidence during the second and third trimesters. Artemisinin and its derivatives are also safe from the fourth month of pregnancy onwards, though it is not recommended during the first 3 months of pregnancy.

TREATMENT COSTS

Chloroquine is cheap and widely available although no longer effective in many countries. All other treatments are more expensive, and mefloquine is very expensive. Because of its high cost, mefloquine should only be used when infection is due to *P. falciparum* malaria and when resistance to chloroquine or pyrimethamine/sulfadoxine is known or suspected.

MALARIA TREATMENT DURING PREGNANCY

Uncomplicated malaria

- chloroquine – except in countries where it is no longer effective
- pyrimethamine/sulfadoxine (Fansidar)
- quinine
- mefloquine – second/third trimesters only
- artemisinin derivatives – second/third trimesters only

Severe or complicated malaria

- artemisinin derivatives – second/third trimesters only
- quinine – beware of hypoglycaemia (low blood sugar)

Anti-malarial drugs contraindicated during pregnancy

- tetracycline, doxycycline, halofantrine and primaquine

CHEMOPROPHYLAXIS AGAINST MALARIA

A course of tablets to prevent malaria is recommended for all migrants and travellers moving to endemic malaria areas from non-endemic areas. Such people do not have the natural immunity to prevent malaria.

In addition, chemoprophylaxis and/or intermittent treatment may be recommended for women to protect them from malaria during pregnancy when they have reduced immunity, and for certain medical conditions, e.g. children with sickle cell anaemia, who are also very prone to malaria infections. Chemoprophylaxis is an effective strategy for a limited time (ranging from a few weeks to a few years). However, it does not offer lifelong protection because of the high costs and the potential for the development of drug resistance.

USE OF CHLOROQUINE AND MEFLOROQUINE

In the **few countries** where *P. falciparum* is still sensitive to chloroquine, it remains the drug of choice for chemoprophylaxis. Recommended dose is 500mg chloroquine (300mg base) given as a single weekly dose starting 1 week before leaving for a malaria endemic area and continued for 4 weeks after leaving the malaria endemic region. Children should be given a weekly dose of 5mg/kg. Hydroxychloroquine is recommended for patients who are unable to take chloroquine. **It must be cautioned that because of the danger of chloroquine resistance in many countries, chloroquine is no longer the drug of choice for prophylaxis in many regions of the world.**

Weekly chloroquine prophylaxis is often combined with daily proguanil, 200mg orally daily and continued for 4 weeks after leaving a malaria area. This regimen can be safely given during pregnancy.

In regions where chloroquine resistance is high alternative drugs can be given. Mefloquine is the first drug of choice. The recommended dose is 1 tablet (250mg) weekly starting 1-2 weeks before departure to malaria endemic regions and continued for 4 weeks after return.

For children the dose is:

Weight over 45kg	1 tablet weekly
31-45kg	three-quarters of a tablet weekly
20-30kg	half a tablet weekly
5-19kg	quarter of a tablet weekly

again continued for 4 weeks after leaving a malaria area.

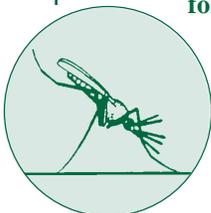
Side effects of mefloquine are: nausea, vomiting, abdominal pain, diarrhoea, headache, dizziness, abnormal heart rhythm and liver dysfunction. It is contraindicated in patients with liver abnormality, heart conduction abnormalities, psychiatric disorders and epilepsy.

ALTERNATIVE DRUGS FOR CHEMOPROPHYLAXIS

Doxycycline: Dosage 100mg daily for 2 days before departure and continued for 4 weeks after return from a malaria zone. It is contraindicated in children under 8 years of age. Side effects include nausea, vomiting, abdominal pain and in women it may cause frequent vaginal candida infections. It is contraindicated during pregnancy.

Pyrimethamine/sulfadoxine (Fansidar), is no longer recommended for routine weekly prophylaxis, because of the danger of severe cutaneous reaction and sudden death.

During pregnancy doxycycline and primaquine are contraindicated, and Fansidar may be given as single dose intermittent/prophylactic treatment once in the second and third trimesters when indicated.



TREATMENT CHARTS

Chloroquine phosphate

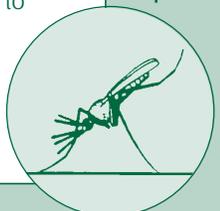
Brand names	Aralen, Avlochlor, Nivaquine, Resochin and many others
When to use	Uncomplicated chloroquine-sensitive <i>P. falciparum</i> malaria <i>Vivax, malariae</i> and <i>ovale</i> malaria
Possible risks/ side effects	Itching; will disappear when treatment finishes Skin reactions, urticaria Headaches, nausea Blurred vision, ocular damage with prolonged use Overdose: 5 x 150mg tablets in a single dose can be fatal for children
Contraindications	Avoid if a child has already taken the correct dose of chloroquine for the current illness for 3 days without success Contraindicated in patients with psoriasis and liver damage
How to give	Oral, with a meal and plenty of water. If the patient vomits within 30 minutes, repeat the full dose; if the patient vomits between 30 and 60 minutes later, give an additional half dose IM Chloroquine can also be given intramuscularly in a reduced dose 2.5mg/kg 3 times a day
Preparations	Tablets 100mg, 150mg, 300mg base as phosphate/sulphate
Frequency of dosage	Once a day for 3 days: 10mg/kg orally on the first and second days, 5mg/kg on the third day (total dose 25mg/kg) Adult dose 600mg (4 tablets) start, then 300mg after 6 hours, then 300mg daily for 3 days
Storage	Store in a closed container in a dry place, away from light

Quinine

(DIHYDROCHLORIDE, HYDROCHLORIDE, SULPHATE)

Brand names	Many
When to use	IV/IM Severe and complicated malarial

Possible risks/ side effects	Oral Follow-up treatment for severe and complicated malaria In selected areas: oral treatment of uncomplicated, multi-drug resistant <i>P. falciparum</i> malaria Tinnitus, muffled hearing, vertigo or dizziness; normally reversible Headache, nausea, visual disturbances, deafness, skin rashes Hypoglycaemia occurs frequently Severe hypotension if infused too rapidly, cardiotoxic Overdose: 1g can be fatal in children
Contraindications	Known hypersensitivity (quinine is safe in pregnancy) IM Injections should not be given in children
How to give	IV Give SLOWLY. Never give a dose in less than 4 hours Beware of hypoglycaemia IM Dilute to a concentration of 60mg/ml Give single dose before referral, divided into two halves Oral Start as soon as possible; give with a meal and plenty of water
Preparations	Quinine hydrochloride 2ml ampoules containing 150mg/ml Quinine dihydrochloride 2ml ampoules containing 150mg/ml or 300mg/ml Tablets quinine sulphate 200mg, 300mg
Quinine dihydrochloride salt Frequency of dosage	IV Give 10mg/kg in 500ml of 5% glucose solution slowly over 4 hours. Repeat every 8 hours until oral therapy is possible (maximum of 1 800mg per day). After 48 hours of IV therapy, reduce dose to 5mg/kg if IV therapy is still required. Ideal fluid requirements for children: 100 ml/kg per day In severe cases of malaria give an initial loading dose of 20mg/kg IV slowly over 4 hours (reduce to 10mg/kg if patient has received quinine within the past 24 hours or mefloquine within the past 7 days)



IM Always dilute IM quinine to a concentration of 60mg/ml. Dilute 2ml ampoules containing 150mg/ml with 3ml 0.9% sodium chloride injection. Dilute 2ml ampoules containing 300mg/ml with 8ml 0.9% sodium chloride injection. Give 10mg/kg, repeat after 4 hours, repeat again 4 hours later, then repeat dose every 12 hours until the patient can swallow oral medication

Oral 10mg/kg 3 times daily for 7 days (including time on IV or IM therapy)

Storage Protect from light

Note: Quinidine gluconate has similar characteristics as quinine

Pyrimethamine/sulfadoxine

PYRIMETHAMINE 25Mg Sulfadoxine 500Mg

Brand names	Fansidar
When to use	Areas with highly developed resistance of <i>P. falciparum</i> to chloroquine
Possible risks/ side effects	Skin irritations High doses are potentially fatal, jaundice
Contraindications	Known hypersensitivity to sulfa drugs Severe hepatic or renal dysfunction (except when benefits exceed the risk involved) Infants in the first 2 months of life First trimester of pregnancy and 4 weeks before delivery
How to give	Oral is preferred
Preparations	Tablets 500mg sulfadoxine and 25mg pyrimethamine Ampoules containing 500mg sulfadoxine and 25mg pyrimethamine in 2.5ml injectable solution
Frequency of dosage	Single oral dose Adults: 3 tablets as a single dose Children: pyrimethamine 0.5-0.75mg/kg as single dose

Amodiaquine

When to use	Uncomplicated, chloroquine resistant <i>P. falciparum</i> malaria
Possible risks/ side effects	Adverse reactions include nausea, vomiting, abdominal pain, diarrhoea and itching

Fatal adverse reactions (toxic hepatitis and severe agranulocytosis) have been reported in travellers using this drug for prophylaxis

Contraindications

Known hypersensitivity
Not recommended for chemoprophylaxis
Persons with hepatic disorders

How to give

Preparations

Oral
Tablets 200mg, 600mg amodiaquine base as hydrochloride or 153.1mg base as chlorhydrate

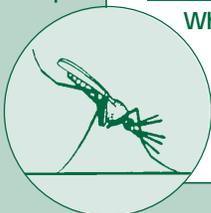
Syrup 10mg/ml amodiaquine base as hydrochloride or chlorhydrate

Frequency of dosage

Over 3 days at total doses ranging between 25mg and 35mg of amodiaquine base/kg in dosage regimes similar to those of chloroquine

Mefloquine hydrochloride

Brand names	Lariam
When to use	Only after microscopical or careful clinical diagnosis of <i>P. falciparum</i> infections known or suspected to be resistant to chloroquine or pyrimethamine/sulfadoxine combinations
Possible risks/ side effects	Nausea, vomiting, abdominal pain, diarrhoea, headache, syncope Heart conduction abnormalities Psychiatric problems and dizziness
Contraindications	History of allergy to mefloquine Pre-existing neurological or psychiatric disease History of severe neuropsychiatric disease Concomitant quinine, quinidine or halofantrine treatment Treatment with mefloquine in the previous 4 weeks Persons undertaking fine coordination and spatial discrimination e.g. air crew Avoid during first trimester of pregnancy
How to give	Oral



Preparations	Tablets 274mg hydrochloride, equivalent to 250mg mefloquine base
Frequency of dosage	Adults: 5 tablets (1 250mg) as a single dose Children: 20mg/kg (of mefloquine base) as a single dose (up to maximum of 1 250mg) or preferably as two divided doses

Artemisinin (qinghaosu)

When to use	Severe malaria in areas of multi-resistant <i>P. falciparum</i> malaria
Possible risks/ side effects	Nausea, vomiting, itching and drug fever Abnormal bleeding, dark urine
Contraindications	Not used for malaria prophylaxis Not recommended during first trimester of pregnancy

How to give Oral – where compliance may pose problems, combination with mefloquine is indicated. The dose of mefloquine depends on the sensitivity of the parasite to mefloquine (Artemisinin: 10mg/kg once a day for 3 days, plus mefloquine (15-25mg base/kg) as a single dose on second or third day)

Preparations Tablets: artemisinin
Suppositories: Artesunate

Frequency of dosage Artemisinin: 10mg/kg once a day for 5 days, with a double divided dose administered on the first day
Artesunate: 2mg/kg once a day for 5 days, with a double divided dose administered on the first day
Artemether: 2mg/kg once a day for 5 days, with a double divided dose administered on the first day
Dihydroartemisinin: 2mg/kg once a day for 5 days, with a double divided dose administered on the first day

Abbreviations **IV** intravenous **IM** intramuscular **Mg** milligrams **ml** millilitres

PERSONAL PROTECTION AND SELECTIVE VECTOR CONTROL MEASURES

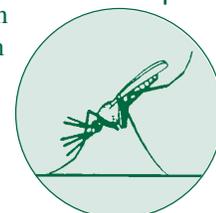
USE OF INSECTICIDE-TREATED MOSQUITO NETS

The promotion and use of insecticide-treated mosquito nets has become a leading strategy in malaria prevention and control. Surveys have shown dramatic reductions in the number of cases of malaria in communities using insecticide-treated mosquito nets. Regular use of treated nets has been shown to reduce child mortality by about 25%. Children sleeping under treated mosquito nets are less prone to anaemia, malnutrition and severe malaria.

In communities where a substantial proportion of people are using nets, fewer people are being bitten and this provides some community protection. In many countries mosquito nets and their re-treatment are still relatively costly. This is often due to high taxes and import duties levied on mosquito netting materials and insecticides by governments. To be most effective, mosquito nets must be re-treated with recommended insecticides at least every 6 months to give maximum protection. They also protect against bites and

stings of other insects. However, studies (see the case study entitled The Gambia: a question of price, on page 16 of this issue) have shown that if people have to pay for the net re-treatment service, they are less likely to spend the necessary time and money having their nets dipped regularly in insecticides.

This issue of *The Prescriber* describes how to treat nets with insecticide, and describes an example of involving community funds in managing bednet sales and treatments (see the case study entitled Laos: success for the women's union, on page 16 of this issue). Local communities can lobby their municipalities, governments, non-governmental organizations (NGOs), private companies etc. to mitigate the effects of public works projects, to fill up pits dug in the ground, to drain swamps, and to minimize deforestation and mining projects and/or movements of people which may trigger malaria epidemics. Health workers can encourage use of bednets and organize community action to fill in pools of water around the village, keep houses clean and put up curtains or screens on windows and doors.



PERSONAL PROTECTION MEASURES

Mosquito coils and body repellents (sprays and lotions) are often used for individual protection but they are not effective for general use as a control measure and are relatively expensive. In particular, they may be useful to protect an individual from a non-endemic area or a primigravida. It is advisable for everyone to wear long protective clothing while outdoors to prevent mosquito bites, and to put wire screens on windows.

INSECTICIDE SPRAYING

During the 1950s and 1960s, the principal strategy in controlling malaria was vector control. The vector of malaria is the Anopheles mosquito; the aim was to eradicate this mosquito, mainly through spraying with insecticides. Three problems arose: spraying was expensive; there were environmental problems with insecticides (especially DDT); and the mosquitoes became increasingly resistant to the insecticides. However, some vector control programmes were quite effective, especially in Latin America, and selective spraying continues to be used in certain circumstances. For example, it is still a recommended strategy for epidemic prevention and control amongst specifically targeted groups and areas, such as refugee populations or in urban settings. To be effective, vector control interventions must be targeted and have

The Prescriber will update you on developments in the prevention and treatment of malaria, including the Roll Back Malaria Initiative, launched by UNICEF and other UN agencies.

clear objectives, especially when used to prepare for an expected malaria epidemic. Globally, DDT is targeted to be phased out and replaced by more environmentally friendly insecticides during the next 10 years. Many countries in Europe and North America have already banned the use of DDT.

THE ROLE OF THE HEALTH WORKER

The two main ways to reduce the spread of malaria are the use of insecticide-treated mosquito nets, and early diagnosis and prompt treatment of malaria cases. The health worker plays an enormously important role in both these approaches. His or her ability to increase understanding about malaria and then promote the use of bednets can reduce the mortality rates of children within any community. The health worker also needs good knowledge of the diagnosis of malaria, and familiarity with the correct treatment recommended in each country, to reduce infections and save lives.

Having good knowledge of malaria is probably the single most important aspect of a health worker's skills in preventing and controlling malaria. Sharing that knowledge with others is also important. Many people in malaria affected areas do not know enough about the disease to protect themselves from infection. UNICEF considers the training of health workers and support for community awareness and participation in malaria programmes as top priorities.

Information *More information about controlling malaria is contained in Child Health Dialogue, 1st quarter 1997, Issue 6. Copies are available free of charge to readers in developing countries from Healthlink Worldwide, Farringdon House, 29-35 Farringdon Road, London EC1M 3JB, UK. For other information materials on malaria, write to Division of Control of Tropical Diseases, World Health Organization, Avenue Appia, 1211 Geneva 2, Switzerland.*

Resources *A directory of suppliers of insecticides and mosquito nets is available from Healthlink Worldwide. Single copies are available free of charge from Healthlink Worldwide, Farringdon House, 29-35 Farringdon Road, London EC1M 3JB, UK.*

HOW TO TREAT MOSQUITO NETS WITH INSECTICIDE

TREATING A BEDNET WITH INSECTICIDE

Nets are treated by dipping them into a mixture of liquid insecticide and water. There are five steps to follow:

1. Preparation

Wash and dry all used nets before treatment. Collect a small measuring container, a large measuring container and a mixing container – a bowl or bucket. Treat nets outside wearing long rubber gloves to protect the skin.

2. Measure and dilute

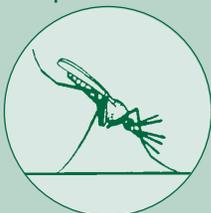
You need to know:

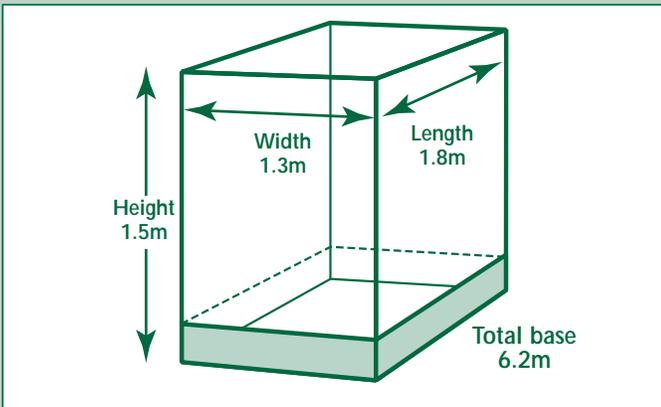
- how many nets need dipping
- what sizes they are
- how much water they absorb
- how much insecticide is required.

Here is how to work out the size, or surface area, of a rectangular net in square metres. Measure the sides and the ends and the height of the net.

Then add the area of:

- 2 sides (2 x length of side x height)
- 2 ends (2 x width of end x height)
- 1 top (1 x width of end x length of side)





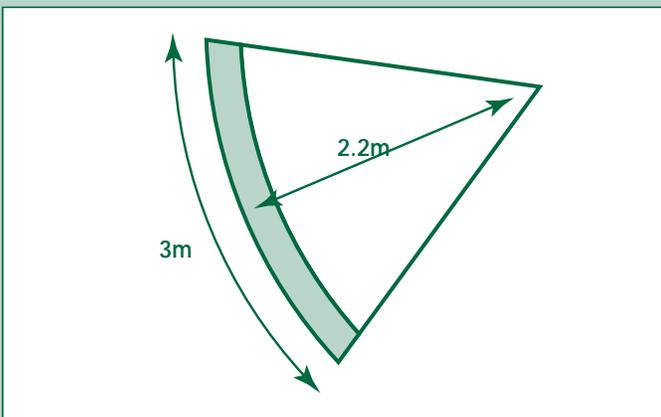
Example:
 $2 \times 1.8\text{m} \times 1.5\text{m} = 5.4$ square metres
 $2 \times 1.3\text{m} \times 1.5\text{m} = 3.9$ square metres
 $1 \times 1.3\text{m} \times 1.8\text{m} = 2.34$ square metres

Total surface area is $5.4 + 3.9 + 2.34 = 11.64$ square metres

For a circular net, lay the net flat. Measure the curved base and the height, and multiply the length of the base by the height to measure the total surface area.

Example:
 Height (2.2m) x base (3m) = 6.6 square metres

Total surface area is $2.2 \times 3 = 6.6$ square metres



Currently recommended insecticides for treating mosquito nets (Revised annually by WHO)

Insecticide	Formulation	Dosage (in mg/m ² of netting)
Alpha-cypermethrin	SC 10%	20-40
Cyfluthrin	EW 5%	50
Deltamethrin	SC 1% WT 25%	15-25
Etofenprox	EW 10%	200
Permethrin	EC 10%	200-500

SC = suspension concentrate
 EW = emulsion, oil in water
 WT = water dispersible tablet (specifications currently being developed)
 EC = emulsifiable concentrate

HOW MUCH WATER DOES EACH NET SOAK UP?

Cotton nets will absorb a lot more water than polyester nets. To find out how much, measure an exact amount of water into the bucket or bowl – for example, 2 litres. Soak the net in the water. Then wring into the bowl and let the net continue to drip into the bowl until the dripping stops. Measure how much water is left. Subtract this amount from the 2 litres. Now you know how much liquid one net will hold. If all the nets are of similar material, take this figure and multiply it by the number of nets to be dipped. Add a little extra (say 10%) for safety.

For example,
 if there are 15 nets to be treated and each soaks up 300ml (one-third of a litre):
 $300\text{ml} \times 15 = (4\ 500\ \text{ml or } 4.5\ \text{litres})$ plus 10% (450ml) = 5 litres.

Permethrin and Deltamethrin* are the most commonly used insecticides. Permethrin goes by the trade names of Peripel, which has a concentration of 20% (or 200g/litre), and Imperator, which has a concentration of 50% (or 500g/litre). The correct amount of insecticide to put into the water is equal to the recommended dose (200 milligramme (mg)/square metre for permethrin) times area of net (rectangular net 11.5 square metres) divided by the concentration of the insecticide (Imperator 50%) times 10.

The total amount is 200×11.5 divided by $(50 \times 10) = 4.6\text{ml}$ of insecticide.

Multiply this amount by the number of nets to be dipped and add 10%. Measure this amount of insecticide and mix it with the amount of water previously measured (5 litres in the example).

3. Dip

Nets should be clean and dry. Soak each net in the diluted insecticide until thoroughly wet. Wring the net well and allow to drip into the bowl until it stops. If you are treating several nets, each one can be wrung, then placed on a plastic bag and carried home to dry.

4. Dry

Nets can be hung up or laid over beds to dry. Placing over beds has the advantage of killing bedbugs! As they dry, turn them a few times to make sure the insecticide is evenly distributed.

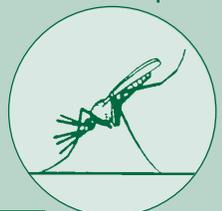
5. Clean up safely

Packaging and leftover insecticide should either be placed in a pit latrine or buried in a pit. Never put into a river or pond. Thoroughly wash all equipment, hands and clothes with soap and water.

Increased protection

Nets should be treated twice a year with insecticide. It is best not to wash them in between as this reduces the amount of insecticide.

Material adapted from articles by Professor Curtis, London School of Hygiene and Tropical Medicine published by Footsteps (Number 33, December 1997) and Child Health Dialogue (1st quarter 1997, Issue 6) newsletters.



CASE STUDIES

THE GAMBIA: A QUESTION OF PRICE

Dramatic results were achieved when mosquito nets treated with insecticides were offered free of charge in a small trial in the Gambia. The mortality of children aged 1-5 years dropped by close to 60%. Encouraged by this success, a national programme was launched to introduce mosquito nets to selected villages within a 3-year period. Later, to help the programme to have the best chance of continuing, villagers would be charged for the nets and for each treatment of the net with insecticide. During the first year, insecticides were delivered free of cost to half of the selected villages. A 25% reduction in overall mortality in children between 1 and 9 years was reported. During the second year, charges for insecticides were introduced in villages that had previously received free insecticides. The result was a sudden drop in the frequency of insecticide treatment. A national survey showed that only 14% of the beds were protected after the fee was introduced (US\$0.50 per net re-treatment), compared with 77% coverage when free insecticide was available.

In the Gambia 70% of households have mosquito nets. With long experience of using mosquito nets, net re-treatment was high (up to 80%) when it was subsidised and fell to 14% once subsidies were withdrawn. Although health experts consider insecticide-treated mosquito nets to be cost effective as a public health measure, the cost of net re-treatment is considered high and discourages many people from bringing their nets for re-treatment. The Gambia's Medical Research Council is currently trying to identify a cheaper insecticide than permethrin, and other options to reduce costs.

LAOS: SUCCESS FOR THE WOMEN'S UNION

In 1994, a village chief asked a local member of the Lao Women's Union to accompany him to a malaria workshop. At that time, five or six people in his village were dying each year of malaria out of a total population of 300. At the workshop, sponsored by the district health authorities and UNICEF, participants learned about how malaria is spread, and about how mosquito nets treated

with insecticide could control the spread of the infection. When they returned to the village, they set up a bednet project which became very successful.

Not long afterwards, the Lao Women's Union took over the management of the project and encouraged their members in different parts of the country to become involved. Members began to sell nets at US\$4, and insecticide treatments at US\$1 per service. The Union also started a UNICEF-backed credit system that allowed villagers to spread payments for nets and treatments over 6 months. An awareness campaign educated families about prevention and treatment, and a training programme instructed health workers in the use of anti-malarial drugs.

By the end of 1997, the number of malaria cases in participating communities had declined by around 25%. Many people increased their knowledge about the disease. For example, in a study of one targeted community the proportion of people who knew how malaria was transmitted had increased from 18% to 90% in the course of a year. Between 1994 and 1997, members of the Lao Women's Union sold US\$32,000 worth of nets.

HOPE FOR A VACCINE?

The possibility of developing a safe and effective vaccine against malaria within the not too distant future is still remote. Several years ago, much excitement followed announcements of the Spf66 vaccine produced by Colombian Professor Manuel Patarroyo. In trials in Tanzania in 1994, the vaccine was shown to reduce the number of malaria cases in children. Unfortunately, subsequent tests in the Gambia and Thailand with the same vaccine failed to show much protective effect. A new form of Patarroyo vaccine is being tested. Hopes remain for a recombinant DNA (genetically engineered) vaccine. But it is likely to be a minimum of 10 years before a vaccine for routine use can be expected.

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