Malaria

Malaria is one of the world's most common diseases, caused by a parasite that is transmitted to humans by a female mosquito's bite. The discovery of this parasite in mosquitoes earned the British scientist Ronald Ross the Nobel Prize in Physiology or Medicine in 1902. In 1907, Alphonse Laveran received the prize for his findings that the parasite was present in human blood.

Statistics

Malaria is one of the most severe public health problems worldwide. It is a leading cause of death and disease in many developing countries, where young children and pregnant women are the groups most affected.

According to the World Health Organization's World Malaria Report 2005:

- At the end of 2004, some 3.2 billion people lived in areas at risk of malaria transmission in 107 countries and territories.
- Between 350 and 500 million clinical episodes of malaria occur every year.
- At least one million deaths occur every year due to malaria.
- About 60% of the cases of malaria worldwide and more than 80% of the malaria deaths worldwide occur in Africa south of the Sahara.

Geography

Malaria occurs mostly in poor, tropical and subtropical areas of the world; is present in sub-Saharan Africa, southern and eastern Asia, India, Haiti, Mexico, the Middle East, Dominican Republic, Oceania, Central and South America, Vanuatu the Solomon Islands as well as Papua New Guinea.

The population of Africa suffers the most from malaria, and it is reported that 90% of malaria cases are diagnosed in Africa - mainly among young children and pregnant mothers. It is reported that malaria causes the death of an African child every 30 seconds.

Africa south of the Sahara, 80%-90% of the deaths occur due to malaria. This is due to a combination of factors:

- A very efficient mosquito vector (*Anopheles gambiae*) assures high transmission
- The predominant parasite species is *Plasmodium falciparum*, which causes the most severe form of malaria
- Local weather conditions often allow transmission to occur year round
- Scarce resources and socio-economic instability hinder efficient malaria control activities.

In other areas of the world malaria is a less prominent cause of deaths, but can cause substantial disease and incapacitation, especially in rural areas of some countries in South America and Southeast Asia.

People at risk

Persons most vulnerable are those with no or little protective immunity against the disease. In areas with high transmission (such as Africa south of the Sahara), the most vulnerable groups are:

- Children under 5 , who have not yet developed immunity to malaria
- Adults over 65
- Pregnant women, whose immunity is decreased by pregnancy, especially during the first and second pregnancies

- People on long term steroids or those receiving chemotherapy
- Aids patients
- People who have had their spleens removed
- People with porphyry (porphyria), epilepsy and chronically ill patients.
- Travelers or migrants coming from areas with little or no malaria transmission, who lack immunity.

In areas with lower transmission (such as Latin America and Asia), residents are less frequently infected. Many persons may reach adult age without having built protective immunity and are thus susceptible to the disease.

How Malaria Affects People's Health

Malaria can affect a person's health in various ways.

- People who have developed protective immunity (through past infections, as is the case with most adults in high transmission areas) may be infected but not made ill by the parasites they carry
- In most cases, malaria causes fever, chills, headache, muscle ache, vomiting, malaise and other flu-like symptoms, which can be very incapacitating
- Some persons infected with *Plasmodium falciparum* can develop complications such as brain disease (cerebral malaria), severe anemia, and kidney failure. These severe forms occur more frequently in people with little protective immunity, and can result in death or life-long neurologic impairment
- People subjected to frequent malaria infections (such as young children and pregnant women in high transmission areas) can develop anemia due to frequent destruction of the red blood cells by the malaria parasites. Severely anemic patients might receive blood transfusions which, in developing countries, can expose them to HIV and other bloodborne diseases
- Babies born to women who had malaria during their pregnancy are more often born with a low birth weight or prematurely, which decreases their chances of survival during early life
- In developing countries, the harmful effects of malaria may combine with those of other highly prevalent diseases and conditions, such as malnutrition, HIV/AIDS, and anemia of all causes. Such combinations can have severe results, especially if they occur repeatedly.

Areas Where Malaria Is Not Endemic

In countries where malaria transmission has never existed or has been eliminated, such as the United States, the great majority of cases occur in returning travelers or in migrants arriving from areas where malaria is transmitted ("imported" malaria). However malaria remains a health threat for people who live in these countries:

- Most patients have no protective immunity, and when they get malaria they can develop a rapidly severe, even fatal disease
- Health-care providers are unfamiliar with malaria, and this can cause delayed or incorrect diagnosis and treatment of the disease
- Under certain conditions, malaria patients can transmit parasites to local mosquitoes, which can in turn infect local residents. Left unchecked, this course of events can re-introduce malaria in a previously malaria-free area.

Etiology

Malaria is caused by protozoan of the genus *Plasmodium*.

- Infection begins with a bite from an infected mosquito. The infecting agent is the sporozoite, a microscopic spindleshaped cell which is in mosquito's saliva. Thousands of sporozoites may be injected in a single bit. Infection may also be acquired transplacentally and by blood transfusion or inoculation, via the blood stages of the parasite. The sporozoites disappear from the blood within 8 h, and the successful ones enter polygonal liver cells (hepatocytes).

- The parasite travels from the mosquito to the liver, where the parasite begins to reproduce. Inside the liver cell the sporozoite divides by asexual fission to form a cyst-like structure called a pre-erythrocytic (PE) schizont, which contains thousends of merozoites. Each merozoite consists of a small mass of nuclear chromatin within a tiny sphere of cytoplasm. The process by which the malaria parasites multiply asexully is called schizogony, whether it takes place in a hepatocyte or in an erythrocyte.

- The parasite leaves the liver and travels to the bloodstream, where it infects red blood cells. The parasite reproduces in the red blood cells, which destroys the cells and releases more parasites into the bloodstream. When they enter the red cells, the process of blood schizogony begins

- If another mosquito bites an infected person, that mosquito can then carry the infection to someone else.

<u>Prepatent period and relapse: the hypnozoite concept</u>

The time between the bite of the infecting mosquito and the appearance of parasites in the blood is the prepatent period. It is 7-30 days in P. falciparum (usually around 10 days), and longer in the other species. It may be very long – in the case of P. vivax and P. ovale many months or even more than a year. This is believed to be due to the dormant stage of the parasite in the liver. It is as if the sporozoite enters a liver cell and promptly goes to sleep. This dormant stage of the parasite is the hypnozoite. But the dormant parasite has a biological alarm clock, which wakes it from dormancy at a predetermined time. Some strains of parasite "sleep" longer than others.

The hypnozoite concept explains both a prolonged incubation period and the phenomenon of relapse.

Once in the circulation, all species of Plasmodium multiply by asexual multiplication in erythrocytes-blood schizogony (versus tissue schizogony). After entering the red cell, the merozoite begins to feed on the red cell contents, and because it begins to grow, is now called a trophozoite. Feeding is by ingestion of red-cell stroma and its digestion in a food vacuole. Digested haemoglobin gives rise to a characteristic pigment, malaria pigment (haemozoin), which is present in the cell in increasing amounts as the trophozoite becomes mature. The mature trophozoite begins to divide into separate merozoites within 1-3 days depending on the species, and this process of schizogony is completed in 48 h in the case of P. falciparum, P. vivax and P. ovale and 72 h in the case of P. malariae. When fully developed, the schizont ruptires the red cell containing it, and liberates the merozoites into the circulation. These merozoites will then enter new red cells, and this process of asexual replication in the blood tends to proceed, at least in the early stages, in a logarithmic manner.

Some of the merozoites entering red cells do not develop into schizonts, but develop more slowly into solid-looking parasites called gametocytes. These may persist in the circulation for many weeks without destroying the red cells containing them, and they are the forms infective to the mosquito. In each species of malaria, the gametocytes are differentiated into male and female. When the female mosquito swallows the male and female gametocytes in her blood meal, they develop further in her stomach. The male gametocytes rapidly develop to produce spermatozoon-like microgamete, and the female gametocyte becomes the egg like macrogamete.(sexual cycle)

Fertilization takes place when a microgamete unites with the macrogamete, and this union produces a motile zygote, the ookinete. The ookinete penetrates to the outer surface of the mosquito's stomach and there develops into an oocyst, which comes to contain thousands of sporozoites. When mature, the oocyst ruptures and liberates the sporozoites into the mosquito's body cavity. The sporozoites then migrate forwards to the salivary glands, and are then ready to infect another victim when the mosquito bites. The time elapsing between the ingestion of the gametocytes and the saliva of the mosquito becoming infective by containing sporozoites is called the extrinsic incubation period. It is variable in the different species of parasite, with different mosquito vectors, and with environmental factors, especially temperature. It is never shorter than 10 days and often much longer.

- There are 4 species of *Plasmodium* that infect humans:
    - *P vivax* – (benign tertian malaria) Most common in India and Central and South America but found worldwide. It has an incubation period of 8-13 days. Infections can sometimes lead to life-threatening rupture of the spleen. In people treated only with chloroquine (Aralen), this type of malaria can hide in the liver and return later.
    - *P ovale* –(ovale tertian malaria) Rarely found outside Africa. This form of malaria has an incubation period of 8-17 days and can hide in the liver of partially treated people and return later.
    - *P malariae* – (quarten malaria) Found worldwide but less common than the other forms. This form of malaria has an incubation of 2-4 weeks. If untreated, the infection can last many years.
    - *P falciparum* – (malignant tertian malaria) Common worldwide, this is the most life-threatening form of malaria. This parasite has an incubation period of 5-12 days. Resistance to many of the drugs used to treat or prevent malaria is becoming very common.
- Although most people acquire malaria through mosquito bites, in some countries the disease can have other sources.
    - Every year a handful of people are infected through blood transfusions or organ transplants.
    - IV drug users can develop malaria from sharing needles.
    - Each year a few babies are born to mothers who did not know they were infected. The babies then develop malaria.

Clinical features

More commonly, the patient presents with a combination of the following symptoms:

- Fever, Chills, Sweats, Headaches, Nausea and vomiting, Body aches, General malaise.

In countries where cases of malaria are infrequent, these symptoms may be attributed to influenza, a cold, or other common infections, especially if malaria is not suspected. Conversely, in countries where malaria is frequent, residents often recognize the symptoms as malaria and treat themselves without seeking diagnostic confirmation ("presumptive treatment").

Physical findings may include:

- Elevated temperature, perspiration, weakness, enlarged spleen.

Infections with all the four different malaria species have many clinical features in common. These are related to the liberation of fever-producing substances, especially during schizogony, and the fact than every red cell containing a trophozoite will be destroyed within 48-72 h. the common features are:

- *Fever:* often irregular. Fever is believed to be mediated by host cytokines, which are secreted by leucocytes and other cells in response to a pyrogen or toxin released by rupturing schizonts. The pattern of regularly periodic fever often does not occur until the illness has continued for a week or more. It depends on synchronized schizogony. Why schizogony should ever become synchronized is unknown, but an intriguing explanation has been suggested. High temperatures slow the growth of mature, more than of young, parasites. Fever itself may therefore allow young parasites to ‘catch up’ with older ones, leading to increasing synchrony with successive cycle.
- *Anaemia.* This is haemolytic in type. It is usually most severe in P. falciparum because in this infection cells of all ages can be invaded and even unparasitized red cells may undergo hemolysis. Also, the parasitemia in this infection can be much higher than in others malarias.
- *Splenomegaly.* The spleen enlarges early in the acute attack in all sorts of malaria. When a patient has had many attacks, the spleen may be of enormous size and lead to secondary hypersplenism.
- *Jaundice.* A mild jaundice due to hemolysis may occur in all types of malaria. Severe jaundice only occurs in P. falciparum infection, and is due to specific liver involvement.

<u>Classical stages of fever</u>

In a paroxysm of malaria, the patient may notice the following stages:

1. A cold stage (the patient shivers or has a frank rigor; the temperature rises sharply)
2. A hot stage (the patient is flushed, has a rapid full pulse, and a high temperature is sustained for a few hours).
3. A sweating stage (the patient swears freely, or is even drenched, and the temperature falls rapidly).

These stages are most often recognized in P. vivax infection. In rare cases, the patient may be afebrile in the presence of a very severe P. falciparum infection. Hyperpyrexia may complicate malaria, especially in attacks of P. falciparum.

Progress of the untreated attack

The natural history of untreated malaria differs with each species.

P. falciparum

Following a single exposure to infection, the patient will either die in the acute attack 8a common event) or survive with the development of some immunity and residual anemia. Attacks may recur over the course of the next year 8 a phenomenon called recrudescence, due to the persistence of blood forms in small numbers between attacks) but then die out spontaneously in the absence of reinfection.

P. malariae

Following a single exposure to infection, and an incubation period that may extend to many weeks, the patient develops a recurrent fever, which occurs at increasing intervals. There may be considerable anemia, and enlargement of the liver and spleen. If no treatment is given to clear the blood forms of the parasite, recrudescence may occur from time to time for more than 30 years. The severity of the attacks tends to diminish as time goes by, until bouts of fever last only a few days.

P. vivax and P. ovale

P. vivax and P. ovale malaria cause very similar illnesses, with bouts of fever which relapse periodically but irregularly over a period of up to 5 years. These are true relapses and not simple recrudescences, because they may occur despite treatment with drugs that entirely eliminate the parasites from the blood. The relapses are due to reinvasion of the blood by merozoites produced when hypnozoites awake from dormancy and develop into PE schizonts.

Severe Malaria

Severe malaria occurs when *P. falciparum* infections are complicated by serious organ failures or abnormalities in the patient's blood or metabolism. The manifestations of severe malaria include:

- Cerebral malaria, with abnormal behavior, impairment of consciousness, seizures, coma, or other neurologic abnormalities
- Severe anemia due to hemolysis
- Hemoglobinuria due to hemolysis
- Pulmonary edema or acute respiratory distress syndrome (ARDS), which may occur even after the parasite counts have decreased in response to treatment
- Abnormalities in blood coagulation and thrombocytopenia
- Cardiovascular collapse and shock

Other manifestations that should raise concern are:

- Acute kidney failure
- Hyperparasitemia, where more than 5% of the red blood cells are infected by malaria parasites
- Metabolic acidosis, often in association with hypoglycemia
- Hypoglycemia. Hypoglycaemia may also occur in pregnant women with uncomplicated malaria, or after treatment with quinine.

Severe malaria occurs most often in persons who have no immunity to malaria or whose immunity has decreased. These include all residents of areas with low or no malaria transmission, and young children and pregnant women in areas with high transmission.

In all areas, severe malaria is a medical emergency and should be treated urgently and aggressively.

Malaria Relapses

In *P. vivax* and *P. ovale* infections, patients having recovered from the first episode of illness may suffer several additional attacks ("relapses") after months or even years without symptoms. Relapses occur because *P. vivax* and *P. ovale* have dormant liver stage parasites ("hypnozoites") that may reactivate. Treatment to reduce the chance of such relapses is available and should follow treatment of the first attack.

Fortunately, the most common type of malaria is the *P. falciparum* strain that has no relapsing phase, so malaria medications will prevent any symptoms of this infection. However, it is necessary to continue such medications for four weeks after a possible exposure to ensure that the infection has run its course before the medication can be safely stopped.

Other Manifestations of Malaria

- Neurologic defects may occasionally persist following cerebral malaria, especially in children. Such as: ataxia, palsies, speech difficulties, deafness, and blindness.
- Recurrent infections with *P. falciparum* may result in severe anemia. This occurs especially in young children in tropical Africa with frequent infections that are inadequately treated.
- Malaria during pregnancy (especially *P. falciparum*) may cause severe disease in the mother, and may lead to premature delivery or delivery of a low-birth-weight baby.
- On rare occasions, *P. vivax* malaria can cause rupture of the spleen or acute respiratory distress syndrome (ARDS).
- Nephrotic syndrome can result from chronic or repeated infections with *P. malariae*.
- Hyperreactive malarial splenomegaly (also called "tropical splenomegaly syndrome") occurs infrequently and is attributed to an abnormal immune response to repeated malarial infections. The disease is marked by a very enlarged spleen and liver, abnormal immunologic findings, anemia, and a susceptibility to other infections (such as skin or respiratory infections).

Diagnosis of malaria can be difficult:

- Where malaria is not endemic any more (such as the United States), health care providers are not familiar with the disease. Clinicians seeing a malaria patient may forget to consider malaria among the potential diagnoses and not order the needed diagnostic tests. Laboratorians may lack experience with malaria and fail to detect parasites when examining blood smears under the microscope.
- In some areas, malaria transmission is so intense that a large proportion of the population is infected but not made ill by the parasites. Such carriers have developed just enough immunity to protect them from malarial illness but not from malarial infection. In that situation, finding malaria parasites in an ill person does not necessarily mean that the illness is caused by the parasites.
- In many malaria-endemic countries, lack of resources is a major barrier to reliable and timely diagnosis. Health personnel are undertrained, underequipped and underpaid. They often face excessive patient loads, and must divide their attention between malaria and other equally severe infectious diseases such as pneumonia, diarrhea, tuberculosis and HIV/AIDS.

Clinical Diagnosis

Clinical diagnosis is based on the patient's symptoms and on physical findings at examination. The first symptoms of malaria (most often fever, chills, sweats, headaches, muscle pains, nausea and vomiting) are often not specific and are also found in other diseases (such as the "flu" and common viral infections). Likewise, the physical findings are often not specific (elevated temperature, perspiration, tiredness).

In severe malaria (caused by *Plasmodium falciparum*), clinical findings (confusion, coma, neurologic focal signs, severe anemia, respiratory difficulties) are more striking and may increase the suspicion index for malaria.

Thus, in most cases the early clinical findings in malaria are not typical and need to be confirmed by a laboratory test.

"Presumptive Treatment"

In highly endemic areas (particularly in Africa), the great prevalence of asymptomatic infections and lack of resources (such as microscopes and trained microscopists) have led peripheral health facilities to use "presumptive treatment". Patients who suffer from a fever that does not have any obvious cause are presumed to have malaria and are treated for that disease, based only on clinical suspicion, and without the benefit of laboratory confirmation.

This practice is dictated by practical considerations and allows the treatment of a potentially fatal disease.

But it also leads frequently to incorrect diagnoses and unnecessary use of antimalarial drugs. This results in additional expenses and increases the risk of selecting for drug-resistant parasites.

Microscopic Diagnosis

Malaria parasites can be identified by examining under the microscope a drop of the patient's blood, spread out as a "blood smear" on a microscope slide. Prior to examination, the specimen is stained (most often with the Giemsa stain) to give to the parasites a distinctive appearance. This technique remains the gold standard for laboratory confirmation of malaria. However, it depends on the quality of the reagents, of the microscope, and on the experience of the laboratorian.

Alternate methods for laboratory **diagnosis** include:

Antigen Detection

Various test kits are available to detect antigens derived from malaria parasites. Such immunologic ("immunochromatographic") tests most often use a dipstick or cassette format, and provide results in 2-10 minutes. These "Rapid Diagnostic Tests" (RDTs) offer a useful alternative to microscopy in situations where reliable microscopic diagnosis is not available. Malaria RDTs are currently used in some clinical settings and programs. However, before malaria RDTs can be widely adopted, several issues remain to be addressed, including improving their accuracy; lowering their cost; and ensuring their adequate performance under adverse field conditions. Malaria RDTs are currently not approved by the U. S. Food and Drug Administration (FDA) for use in the United States. The World Health Organization's Regional Office for the Western Pacific (WHO/WPRO) provides technical information, including a list of commercially available malaria RDTs.

Molecular Diagnosis
Parasite nucleic acids are detected using polymerase chain reaction (PCR). This technique is more accurate than microscopy. However, it is expensive, and requires a specialized laboratory (even though technical advances will likely result in field-operated PCR machines).

Serology Serology detects antibodies against malaria parasites, using either indirect immunofluorescence (IFA) or enzyme-linked immunosorbent assay (ELISA). Serology does not detect current infection but rather measures past experience.

Drug Resistance Tests
Drug resistance tests are performed in specialized laboratories to assess the susceptibility to antimalarial compounds of parasites collected from a specific patient. Two main laboratory methods are available:

- In vitro tests: The parasites are grown in culture in the presence of increasing concentrations of drugs; the drug concentration that inhibits parasite growth is used as endpoint;
- Molecular characterization: molecular markers assessed by PCR or gene sequencing allow also the prediction, to some degree, of resistance to some drugs; however, the predictive values of these molecular tests are still being evaluated

Treatment: general
The treatment of a patient with malaria is supportive and specific.
Supportive treatment
Supportive treatment may include:

1. Reducing the temperature if hyperpyrexia is present-especially common with P. falciparum infection.
2. Rehydration, especially when vomiting and diarrhoea have been prominent. Overhydration must be carefully avoided, by weighing the patient if possible.
3. Monitoring renal output and taking corrective measures if necessary.
4. Monitoring the hemoglobin: blood transfusion, which is sometimes life-saving should only be given when there are strong clinical indications. In most patients the hemoglobin rises rapidly when the attack has been terminated by specific chemotherapy.
5. Terminating convulsions with appropriate drugs.
6. Monitoring of blood glucose and correction of hypoglycemia where necessary.
7. Treating DIC if this complication is severe enough to cause bleeding; fresh whole blood, platelet-rich plasma and fresh frozen plasma may be given according to availability.
8. Reducing acidemia: usually rehydration and antimalarial therapy are sufficient for this purpose. The use of bicarbonate infusion is not of proven benefit, but may be attempted with care in severe acidosis.

Specific chemotherapy
Specific treatment is directed to terminating the parasitemia as rapidly as possible. The drug of choice depends on national policy in the country where you work, and on the likely place of origin of the patient's parasites. Drug resistance is an increasing problem throughout the world, and the picture changes with time; in some countries multidrug resistance threatens to make malaria untreatable, and new additions to the armamentarium of drugs are urgently needed.

Drugs that prevent the development of the blood stages that are causing the illness are traditionally called schizonticides. Some of them also act against the gametocytes of some species, but this has no relevance to the clinical situation. Some of the schizonticides have useful anti-inflammatory effects also.

The most widely used schizonticides has until recently been chloroquine, but the spread of parasite chloroquine resistance has limited the use of this drug in recent years. However, chloroquine remains the first-line treatment for non-severe falciparum malaria in some semiimmune populations in Africa, and it is the drug of choice for all non-falciparum malarias, although early reports of P. vivax resistance to chloroquine are appearing.

Effective drugs:

- Chloroquine, Amodiaquine, Quinine, Fansidar (sulfadoxine-pyrimethamine) – for treatment of chloroquine resistant P. falciparum infections, Mefloquine (effective against most multidrug-resistant strains of P. falciparum), Halofantrine (also active against multidrug-resistant P. falciparum), Primaquine (for radical cure of relapsing forms of malaria)

Chemoprophylaxis

Chemoprophylaxis of malaria involves the regular administration of drugs to prevent clinical symptoms. Drugs taken this way act in two ways: as schizonticides, so that when the parasites enter the red cells they are destroyed, and causal prophylactics. Causal prophylactics prevent the development of the PE schizonts in the liver, and they may also have blood schizonticidal effects. The practical importance of these two modes of action has only become apparent fairly recently, when it was discovered that some drugs might have a much greater effectiveness when given as causal prophylactics, i.e. before sporozoite challenge rather than afterwards.

One must always remember that chemoprophylaxis never provides complete protection against malaria. Everyone embarking on it should be aware of this.

Proguanil – is the safest of all antimalarials. It is used a prophylactic only.

Pyrimethamine (Daraprim, Malocide) – it is used by itself for suppression only.

Mefloquine propylaxis

- As a result of the spread of chloroquine resistance around the world, mefloquine (alone) is now the prophylactic drug of choice for many areas. Initial anxieties about drug accumulation have diminished, and it is now acceptable to recommend an adult dose of 250 mg weekly for periods of a year or more.

Doxycycline

- This long-acting tetracycline is an effective prophylactic against malaria in a dose of 100 mg daily. It is useful in areas where there is resistance to both chloroquine and mefloquine. It should not be used in pregnancy or lactation, or in young children. An occasional toxic effect is a rash due to photosensitization.

Pyrimethamine-dapsone (Maloprim)

- This combination drug has occasionally caused agranulocytosis. Its use in prophylaxis is therefore limited to areas where P. falciparum is resistant to both chloroquine and mefloquine, and where the risk of contracting P. falciparum infection is high. The dose of Maloprim should not exceed one tablet per week.

Fansidar is not used for prophylaxis because of the risk of Stevens-Johnson syndrome.

Amodiaquine should be avoided because of a risk of marrow aplasia.

Prevention

There are two important measures to prevent malaria infection: avoiding mosquito bites and using antimalaria medication.

Recommendations

Personal measures to avoid mosquitoes

Any measure that reduces exposure to dusk-to-dawn biting mosquitoes during their feeding will also reduce the risk of acquiring malaria. These measures include:

Protective clothing

- Wear clothing that reduces the amount of exposed skin.
- Wear light-coloured, long-sleeved shirts, long pants, socks and shoes when outdoors between dusk and dawn (note: dark colours attract mosquitoes).
- Impregnate all clothing with 0.5% permethrin to make them repellant.

Screens and bed nets

- Sleep inside screened areas, under a mosquito net or in an air-conditioned room.
- Use bed nets that are rectangular in size, impregnated with permethrin every six months and tucked tightly under the mattress before dusk (note: treated bed nets are available in Canada).

Insect repellent

- apply DEET-containing insect repellent to exposed skin when outdoors between dusk and dawn.

Of the insect repellents, those containing 'N, N diethyl-m-toluamide' (DEET) are the most effective. Although the concentration of DEET varies from product to product, repellency rates are largely equivalent. In general, higher concentrations protect for longer periods of time, but there is little advantage in the duration of repellence with DEET concentrations greater than 50%, and there may be additional risk of toxicity with higher concentrations.

Antimalarial medication (prophylaxis)

While no vaccine is available, there are several drugs for the prevention of malaria. Antimalarial medications decrease the risk of developing symptomatic malaria; however, they do not provide 100% protection against the disease. In most cases, antimalarial medication must be taken both before and after travel. As with all drugs, these drugs can have potential side effects and contraindications. With an individual risk assessment the appropriate preventive anti-malarial medication for each traveller can be determined. Each drug has its own dosing regime that should be strictly followed.

Multi-drug resistant strains of malaria are now common in several regions of the world. Because of these strains, medications for the prevention and/or treatment of malaria will differ. For instance, there is widespread resistance of *P. falciparum* to the antimalarial drug cholorquine in all malarious areas except the Caribbean, Central America (west of the Panama Canal) and parts of the Middle East.

There are many misconceptions about malaria. The **prevention** of malaria in travellers through the use of prophylactic drugs (including mefloquine) does **not** lead to the development of drug-resistant malaria parasites. When preventive drugs are appropriately used, they can actually reduce the disease's resistance to treatment by lowering the overall number of cases of malaria.

Travellers may receive conflicting information about antimalarial drugs while they are overseas. However, it is essential that travellers who have been prescribed medication continue to take it according to directions unless they experience moderate to severe adverse effects. In such cases, travellers should seek medical help promptly.