INTERNATIONAL ASSOCIATION
FOR MEDICAL ASSISTANCE
TO TRAVELLERS

IAMAT

# How To Protect Yourself Against Malaria

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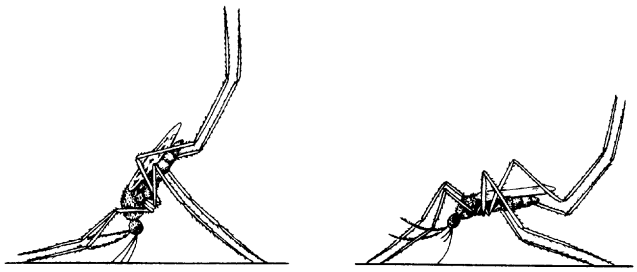
## How to Protect Yourself Against Malaria

**THE ENEMY**

Sunset — the hunt for human blood begins. From dusk to dawn the female *Anopheles*, the malaria-carrying mosquito, searches for a host to supply her with blood. Blood is an absolute necessity for her because it provides the protein needed for the development of her eggs, which she later deposits in her breeding place.

She has a tiny, elegant body, measuring from 8 mm to 1 cm. She has dark spots on her wings, three pairs of long, slender legs and a prominent tubular proboscis with which she draws blood.

The *Anopheles* enters your room at night. You may recognize her by the way she rests on the wall — she stands on her head with the tail-end of her body tilted upwards, protruding into the air like a rocket on a launching pad. She is unlike the common pests of our temperate climates, the *Culicines* (*Culex, Aedes,* etc.), which assume a position parallel to the surface.



*Anopheles* *Culex*

She is your enemy, because only she can harbor the human malaria parasite and carry it from an infected person to a new victim. In fact in East Africa the same word, *umbu*, means both malaria and mosquito. In tropical Africa alone, where half the population is infected with malaria, she kills two million people each year, mostly children.

The unprotected international traveller pays her a heavy toll — she is responsible for infecting thousands with malaria every year. Her bite is the direct cause of death for many who contract the disease in their travels. (Male mosquitoes do not bite.)

The twenty-six hundred species of mosquitoes are grouped into the family of *Culicidae*, of which the genera *Aedes, Anopheles* and *Culex* are the most widespread. Throughout the world, each species of *Anopheles* is peculiar to a localized area. Of the four hundred *Anopheles* species, about sixty are proven carriers of the malaria parasite.

Mosquitoes prey on a variety of hosts — humans, monkeys, lizards, birds — carrying different species of malaria parasites which in turn infect only specific hosts. Of the approximately fifty different species of malaria parasites sharing the genetic name *Plasmodium*, only four infect humans: *Plasmodium falciparum*, the killer; the benign *Plasmodium vivax*; and the less common *Plasmodium malariae* and *Plasmodium ovale*, both benign.

Malaria parasites are older than humankind. They have accompanied the evolution of primates throughout the geological ages from their earliest ancestors up to the emergence of humans. The parasites too underwent adaptive changes, and it is believed that the *Plasmodium falciparum*, which causes the fatal form of human malaria, is the latest evolved species of the parasite, which the benign *Plasmodium malariae*, the oldest on the scale of evolution, may have been the first to invade humans.

**THE BITE**

Now that the burglar has entered your premises she is waiting in a dark corner for the right moment to rob you of your blood. The insidious *Anopheles*, attracted by the warmth of your body and the carbon dioxide you exhale, approaches silently. She does not hum or hover as other mosquitoes do.

In a moment she will land on an exposed part of your body and pull out from her proboscis her armament, consisting of six stylets. First, two needle-pointed stylets will stab your skin, then two blades bearing very fine teeth will lacerate the skin like a microscopic saw, searching for a small vein. Soon she pierces the vessel with a flexible tube, the “food canal” through which blood is conveyed into her mouth. During the feeding, she will introduce into the wound her sixth weapon, a hollow stylet containing a duct which is connected to the salivary glands. Through this duct she injects a few drops of her saliva to act as a local anaesthetic so that you do not feel her bite.

Simultaneously with her saliva she will introduce into your bloodstream hundreds of motile *sporozoites* (Gr.: *sporá*=sowing, seed; *zõon*=animal). These malaria organisms have been multiplying in her intestine for two weeks, the result of having bitten a person infected with malaria.

Soon she will fly away, loaded to twice her unfed weight with blood, to conceal herself in a dark corner of your room. During the forty-eight hours it takes to digest the blood she has taken, her ovaries will completely develop and she will be ready to lay her eggs.

At sundown she will leave your room for her breeding place nearby. She can breed almost anywhere water collects — a footprint, a puddle, a tire track, even a coconut shell or a man-made container. After laying her eggs, her ovarian cycle starts again, and she may return to see you the same night. During her three-month life span she may lay up to three thousand eggs.

This shuttling between blood source and breeding place makes malaria a “focus” disease; that is to say, its area of infective activity is localized and dependent upon the radius of the flight range of the *Anopheles*, usually from a few hundred yards to a mile.

The most dangerous species of *Anopheles* attack human victims between midnight and dawn. This means you are a prime target when you are most vulnerable — asleep.

**THE THREE LIVES OF THE MALARIA PARASITE**

The malaria organism is a *protozoan* (Gr.: *proto*=primitive; *zõon*=animal), that is to say a microscopic, single-celled animal, not to be confused with a bacterium, which belongs to the plant kingdom. The parasite has a complex life-cycle, reproducing first in the liver, then in the red blood cells and finally in the mosquito. During these three cycles the parasite transforms itself and emerges each time with new physical and biochemical characteristics.

**The Liver: Hiding Place of the Parasite**

The malaria organisms (*sporozoites*) injected into the body by the bite of the infected mosquito remain in the bloodstream for only a short period — see the illustration of the Life-Cycle of the Malaria Parasite (1) — usually less than one hour. They disappear from the circulation and establish themselves in the cells of the liver (2a), where they commence cycles of reproduction, a process lasting from six to twelve days, depending on the species. This stage corresponds to the incubation period of the disease. During this time, each *sporozoite* grows through repeated divisions of the nucleus into one large cell named *schizont* (Gr.: *schizein*=to divide; *on ontos*=being), now containing thousands of tiny new parasites (2b).

The increased pressure causes the *schizont* to burst and release these newly formed parasites, called *merozoites* (Gr.: *meros*=part, *zõon*=animal) (2c), which leave the liver and enter the red blood cells where they initiate cycles of reproduction.

It is now well established that on entering the liver, all sporozoites of *Plasmodium falciparum*, the most dangerous of malaria parasites, and of *Plasmodium malariae*, one of the benign forms, immediately enter into a reproductive phase which exhausts itself after one generation. If you are harbouring an infection caused by these parasites, suppressive medication will eliminate the parasites from the red blood cells, and because no new invasions from the liver can occur, you will be completely cured of the infection. (2a, 2b, 2c)

However, *Plasmodium vivax* and *Plasmodium ovale*, the other two benign forms of parasites, enter the liver cell as two different forms of sporozoites: one strain immediately enters into a phase of reproduction (2a, 2b, 2c); and one, called *hypnozoite* (Gr.: *hypno*=sleep, *zõon*=animal), lies dormant in the liver cell (2d red cell). The *hypnozoites* enter into reproductive phases at different times (2e, 2f), even after months or years, depending upon the species, and are therefore responsible for the well-known relapses of *Plasmodium vivax* and *Plasmodium ovale*. These relapses may persist for months or years, even though an antimalarial regimen has been meticulously followed.

**The Red Cell: Life at the Expense of the Red Corpuscle**

From the liver, the *merozoites* enter the bloodstream and penetrate the red blood cells (3g), where they multiply in cycles. Each *merozoite*, feeding at the expense of the red cell, grows into a ring-shaped parasite called *trophozoite* (Gr.: *trophé*=nourishment; *zõon*=animal) (3h). Upon reaching its full size (about .016 mm), each *trophozoite*, through repeated divisions of the nucleus, forms a *schizont*, a cluster containing sixteen to twenty-four new oval-shaped parasites, again called *merozoites* (3l). When the infected red blood cells burst, the *merozoites* flood the circulation and invade fresh red blood cells to start new cycles of reproduction (3m, n, o, p). These cycles repeat themselves every two to three days depending on the species. The rhythmic release into the circulation of so many parasites — estimated at a quarter of a billion — coincides with the characteristic clinical picture of malaria: periodic high fever, preceded by shivering and followed by profuse sweating.

**The Mosquito: The Sexual Life of the Parasite**

Some *merozoites* are distinguished from others in that they grow in the red blood cell without dividing. They transform themselves into sexual cells, the male and female *gametocytes* (Gr.: *gameté*=wife, *gamétes*=husband; *kútos*=cell) which are necessary for the perpetuation of the parasite (3q). However, they can mature only outside the human body, and because they cannot leave the bloodstream on their own, they need outside help — the *Anopheles* mosquito. During evolution an affinity has developed between the malaria parasite and the *Anopheles*: the *Anopheles* requires blood for the protein she needs to lay her eggs, and the parasite requires a host in which it can reproduce.

When the *Anopheles* bites an infected person, the *merozoites* drawn from the bloodstream are digested in the stomach of the mosquito, while the *gametocytes* (4q) develop in the intestine into mature cells called *gametes*, the female ovule and the male spermatozoon (4r). The fertilized eggs, *ookinete* (Gr.: *õon*=egg; *kinesis*=motion) (4t), moves to the outside wall of the mosquito gut where, by secreting a cyst wall around itself, it develops into an *oocyst* (4u, v), which will give rise to a myriad of new parasites, the *sporozoites*. As soon as these *sporozoites* (4z) are released from the *oocyst* they migrate to the salivary glands of the *Anopheles*, waiting to be injected into the next victim. The endless cycle starts all over again.

## HOW TO AVOID *ANOPHELES'* BITE

**The World of *Anopheles***

To visualize the mechanism of malaria transmission in a given area, one must take into consideration the behavior of the local species of *Anopheles*. The knowledge of her habits will give you a better chance to protect yourself against her bite.

Like humans, anopheline mosquitoes are concerned with food, shelter and reproduction. Will she feed on humans or on domestic animals? Will she enter human dwellings to bite or will she feed outdoors? Does she prefer to bite soon after dusk, late at night or at dawn? Will she use houses as a daytime resting place or will she seek shelter in dense vegetation? Will she breed in peridomestic waters such as small ponds, footprints or artificial containers, or far away in large bodies of water? Different preferences characterize each species. Take for instance *Anopheles gambiae*, the mosquito responsible for so many deaths in Africa south of the Sahara. She chooses her breeding place a few yards from your habitation. She may even be travelling with you by car, plane or boat. In fact she once crossed the Atlantic by boat and spread misery and death along the northeastern coast of Brazil. On the other hand, the main vector of malaria in the Philippines, the *Anopheles minimus flavirostris*, has different habits. She prefers to breed along the margins of foothill streams and lakes, and her presence is confined to rural areas. That is why, although there is no malaria in large cities like Manila, there is malaria transmission in African cities south of the Sahara.

Two factors influence the reproduction of *Anopheles*: rainfall and temperature. The rainy season, bringing an increase in the anopheline population, will determine the annual high-risk period of malaria transmission. Lower temperatures will decrease the *Anopheles* population and, more important, will arrest the development of parasites in the mosquito gut. Since temperature lowers with increased altitude, transmission of the disease is not possible over a certain height above sea level. (See IAMAT's publication WORLD MALARIA RISK CHART.)

**The Super *Anopheles***

With the knowledge of the habits of the *Anopheles*, humans learned to fight her by poisoning her resting places with DDT. A single indoor spraying, leaving a layer of microscopic crystals, made surfaces lethal to mosquitoes for months. But, although this residual insecticide reversed the odds in the struggle, within a few years the *Anopheles* had developed a resistance to these chemicals. Other pesticides followed, always with the same inglorious result. Today, forty-five species of *Anopheles* have been reported resistant to traditional insecticides. The more recent insecticides, the carbamate compounds, are not suitable because of their high cost (ten times that of DDT) and short residual action period (two weeks only). Furthermore, some *Anopheles* are already showing resistance to these new compounds. Because of these new "super *Anopheles*", malaria is now making a comeback in areas previously considered conquered. This situation puts a renewed emphasis on the mechanical forms of protection.

## MECHANICAL PROTECTION

Mechanical forms of protection are still the most effective means of preventing the spread of malaria.

**Window and Door Screens**

Ensure that the window and door screens of your room fit tightly and are free of holes. At the same time check the screens to be sure the mesh is small enough to prohibit the entrance of any mosquitoes.

**The Mosquito Bed Net**

In malarious areas, unscreened bedrooms require mosquito bed nets except in buildings with sealed windows and central air conditioning. If possible, bed nets should be rectangular rather than cone-shaped to prevent skin contact with the netting allowing the *Anopheles* to bite through. Netting should be of stiff cotton or synthetic thread to allow the movement of air. The net must be white to allow mosquitoes to be seen against the background, and should have a wide, tightly woven border to be tucked under the mattress.

A netting with twenty-six holes per square inch will prevent even the smallest *Anopheles* from penetrating. (This figure is obtained by adding the number of holes along the bottom line of a square inch of net and the number of holes along the diagonal.) Not one single tear should be permitted, since mosquitoes will spend hours searching for an opening.

There are several good reasons for using bed nets in addition to preventive medication.

- Because the bed net gives protection when the *Anopheles* is most active, chances of infection are reduced. Some malariologists estimate that with proper use of bed nets malaria cases could be reduced by two-thirds.
- The bed net offers protection from other diseases transmitted by mosquitoes, such as filariasis, known for massive swelling of the limbs.
- Bed nets also protect against ticks, beetles, flies, bed-bugs and other insects which may enter your bed.

To accommodate a real need for a practical bed net, IAMAT has designed La Mosquette,™ a light-weight, portable free-standing aluminum frame and a rectangular bed net. It is available at cost of U.S. $110.00 (CAN. $145.00) plus postage.

If you are contemplating a long residency in a high risk malarious area, you might like to soak your bed net in an insect repellent solution, which will impregnate the net for up to six months. (Brand names: Coulston's Permethrin Arthropod Repellent; Duranon permethrin clothing repellent; Permanone Tick Repellent). These products are available through pharmacies and out-door equipment stores). These solutions have proven to be very effective binding itself tightly to the fabric and remaining effective through several washings. Outer clothing (vests, jackets, hats) may also be treated with this solution.

## FOUR STEPS TO MOSQUITO PROTECTION

The following precautions require self-discipline, and should be taken every day beginning at sunset by everyone visiting the tropics.

**Step one: protective clothing**

Beginning at sunset, wear long-sleeved shirts and long trousers in light colors such as beige or yellow. Dark clothing attracts mosquitoes, as does the scent of perfume or after-shave lotion.

**Step two: mosquito repellent**

Apply mosquito repellent, available in sprays, lotions and towelettes, to all exposed areas of skin, as well as thin clothes, avoiding eyes and mouth. The active ingredient keeps mosquitoes away but does not kill them. Since repellent gradually evaporates and some will be lost through perspiration, swimming and active exercise, re-apply every few hours accordingly to the manufacturer's directions for continuous protection. (Caution: repellent may damage plastic items such as eye-glass frames, watch crystals, nail-polish, etc.)

**Step three: pyrethrin insecticides (brand name: Raid)**

Pyrethrin insecticides (active ingredient pyrethrin, extracted from the pyrethrum flower, a member of the chrysanthemum family) kills mosquitoes instantly by acting on the central nervous system. Frequent spraying is necessary since pyrethrin dissipates when exposed to air. Spray bed net and under the bed, as well as walls, baseboards, corners, furniture, behind pictures and inside closets in the bedroom, and under the sink in the bathroom. Cover any food and cooking utensils. Do not open windows while spraying, and allow vapor to settle before returning to the room.

**Step four: preparing your bed for the night**
During the day, the bed net should be left hanging in a knot from the ceiling. Before retiring lower the net and search carefully for mosquitoes hidden inside. Mend any holes or tears with adhesive tape or thread. Tuck the edge of the bed net under the mattress, making sure there are no openings.

If you are camping, avoid campsites near native villages or any kind of habitation, even when empty. Before camping check surrounding area for possible *Anopheles* breeding places.

## ANTIMALARIAL DRUGS

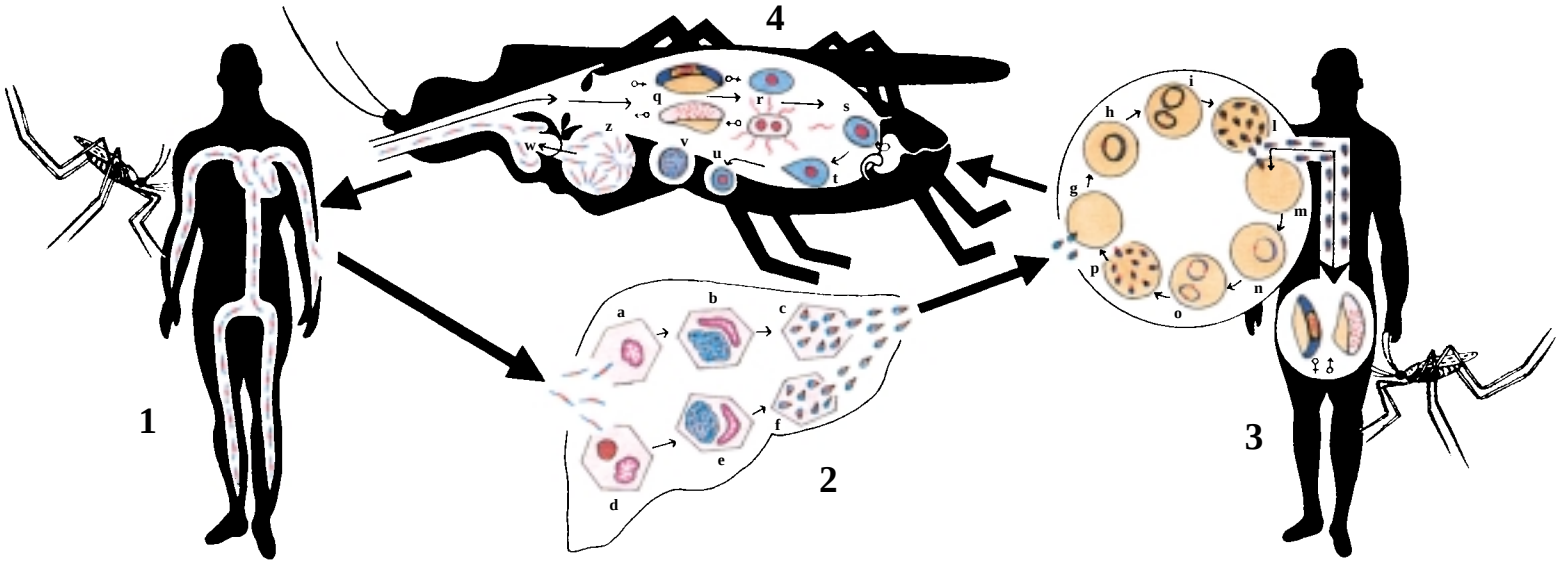
The most widely used antimalarial drugs will suppress the clinical symptoms of malaria but will not prevent the establishment of malaria infection. If anti-malarial drugs were true prophylactics (Gr.: *prophylasso*=to guard before) they would prevent malaria infection by killing the parasites (*sporozoites*) the moment they are introduced into your bloodstream by the bite of the *Anopheles*. Instead, they act by eliminating the parasites during their multiplication phase in the red blood cells (*red cell cycle*). Suppressive medication will eliminate the infection caused by *P. falciparum* and *P. malariae*, but will not always prevent a delayed first attack or relapses caused by *P. vivax* and *P. ovale*, which may appear months or years after discontinuing the suppressive drug.

- *It is mandatory that you take the medicine at regular intervals throughout your stay in a malarious region, and you should continue to do so for 4-6 weeks after leaving the area.*
- Taking the full course of suppressants is essential even for a short stay. *Remember, one single bite is sufficient to infect you*.
- If you are on a weekly regimen, always take your suppressant the same day and at the same hour soon after your meal. Establish this as a habit so you will not forget. Take the suppressant with plenty of liquids to reduce stomach discomfort which may occasionally occur.
- Since an adequate concentration of the drug in the blood is reached a few hours after ingestion, you may start the medication on the day of your departure. However, it is advisable to start your regimen one to two weeks before leaving — while still at home you will acquire confidence with the drug and you can seek the advice of your family physician in case of any adverse reaction.
- It would be ideal to take a complete supply of medication with you to avoid any confusion which might arise in the new country.

**In offering guidance on the choice of antimalarial drugs the main concern is to provide protection against *Plasmodium falciparúm* malaria, the most dangerous and often fatal form of the disease.**

**The appearance of chloroquine-resistant and multi-drug-resistant *Plasmodium falciparum* in many malarious areas makes the choice of suppressive drugs problematic as none of the medications currently used is 100% effective. Regardless of which medication is being used for malaria prophylaxis, it is of utmost importance for travellers and their physicians to consider fever and flu like symptoms appearing seven days to 3 months after leaving a malarious area as a malaria breakthrough. Early diagnosis is essential for successful treatment of such an infection.**

Reliable information on malarious areas and a sound knowledge of geography of the area to be visited, including knowledge of the feeding and breeding habits of the local anopheles mosquitoes, will help you to take the appropriate antimalarial measures. (See IAMAT's publication WORLD MALARIA RISK CHART).




**THE LIFE-CYCLE OF THE MALARIA PARASITE**

## SUPPRESSIVE MEDICATION IN AREAS WHERE *P. FALCIPARUM* IS SENSITIVE TO CHLOROQUINE

Travellers to areas with chloroquine-sensitive *P. falciparum* malaria should follow the following regimen:
USE CHLOROQUINE (ARALEN) IN WEEKLY DOSES OF 500mg (300mg base). START ONE WEEK BEFORE ENTERING MALARIOUS AREA, CONTINUE WEEKLY DURING YOUR STAY AND CONTINUE FOR FOUR WEEKS AFTER LEAVING. TAKE IT AFTER A MEAL TO AVOID STOMACH UPSETS.

**CHLOROQUINE (Chloroquine diphosphate (brand names: ARALEN by Winthrop, AVLOCLOR by ICI, RESOCHIN by Bayer); Chloroquine sulfate (brand name: NIVAQUINE by Société Spécia)**

Chloroquine is the antimalarial drug used most commonly around the world for the suppression of falciparum malaria in areas where the parasites are still sensitive to it. In case of infection, chloroquine will completely cure malaria caused by sensitive strains of *P. falciparum*. For chloroquine-sensitive malarious areas see IAMAT's publication WORLD MALARIA RISK CHART.

Chloroquine is also the drug of choice for the suppression of malaria caused by *P. vivax*, *P. ovale* and *P. malariae*, the benign forms of the disease. Travellers should be aware that chloroquine will not always prevent delayed first attacks or relapses of malaria months to years after departure from malarious areas even when the chloroquine regimen has been followed meticulously. Depending on the strain (subspecies) of the parasite these delayed attacks develop in 30 to 70% of persons. *Inconveniences:* The bitter taste makes the drug unpalatable. Minor stomach upsets, itching skin, nausea and diarrhea may occur; it may also cause blurring of vision and a transitory headache. *CAUTION: Since chloroquine is deposited in high concentration in the liver and white blood cells, it should be used with caution by persons with a liver condition, alcoholism or blood disorder. Patients on phenylbutazone should discontinue this drug while taking chloroquine since it may enhance the chances of dermatitis. It may also aggravate the condition of persons suffering from porphyria and psoriasis. Due to the adverse effect of chloroquine on the optic nerve, persons with diseases of the retina and optic nerve (diabetic retinopathy, optic neuritis, etc.) should not use this drug. Persons contemplating a prolonged course with chloroquine should have an eye examination at least once a year to detect any changes in the retina. Persons with a history of epilepsy should not take chloroquine.*

## SUPPRESSIVE MEDICATION IN AREAS WHERE CHLOROQUINE-RESISTANT *P. FALCIPARUM* (CRPF) MALARIA IS PRESENT BUT ACCOUNTS FOR LESS THAN 20% OF TOTAL MALARIA CASES

(Afghanistan, Bolivia, Tajikstan — see IAMAT's Malaria Risk Chart)

In areas with chloroquine-resistant *Plasmodium falciparum* (CRPF) malaria accounting for less than 20% of total malaria cases, a first-choice prophylactic regimen of chloroquine should be followed. It is the drug of choice for benign forms of malaria, and it will lessen the severity of a breakthrough with resistant *P. falciparum* strains and thus prevent fatal malaria.

However, in case of flu-like symptoms — general malaise, fever, headache, nausea — appearing about 7 days or later after entering the malarious area, immediate medical attention should be sought as these symptoms may signify a malaria breakthrough.

In case medical attention cannot be reached within 24 hours, adult individuals with no history of sulfonamide intolerance should take one treatment dose of three tablets of Fansidar (sulfadoxine + pyrimethamine) carried from home as a self-treatment for the presumptive diagnosis of a malaria breakthrough. Medical attention should be sought as soon as possible.

**PROPHYLACTIC REGIMEN:**
TAKE CHLOROQUINE (ARALEN) IN WEEKLY DOSES OF 500mg (300mg base). START ONE WEEK BEFORE ENTERING MALARIOUS AREA, CONTINUE WEEKLY DURING YOUR STAY AND CONTINUE FOR FOUR WEEKS AFTER LEAVING.
CARRY WITH YOU A TREATMENT DOSE OF THREE TABLETS OF SULFADOXINE-PYRIMETHAMINE (**FANSIDAR**) TO BE TAKEN IN A SINGLE DOSE **OR** 4 TABLETS AS A SINGLE DOSE DAILY FOR THREE DAYS OF **MALARONE** FOR THE SELF-TREATMENT OF A PRESUMED *P. FALCIPARUM* MALARIA BREAKTHROUGH.

**CHLOROQUINE** — see description above.

**SULFADOXINE+PYRIMETHAMINE (brand name: FANSIDAR by Hoffmann-LaRoche)**
Fansidar is a very effective drug for the treatment of chloroquine-resistant *Plasmodium falciparum* malaria. At this time, it is not recommended for weekly prophylaxis because of potential serious side effects which may develop after multiple doses.
*Caution: Persons with known allergies or intolerance to sulfonamides should not take this drug. The intolerance, which affects five percent of the population, becomes apparent with a skin rash, sometimes due to photosensitivity after prolonged exposure to sunlight. Fever may develop, accompanied by itchiness, nausea and general malaise. These symptoms will disappear when the drug is discontinued.*
Seek medical attention as soon as possible even when you have taken the stand-by treatment regimens.
**MALARONE** — see description below.

## SUPPRESSIVE MEDICATION IN AREAS WITH A HIGH INCIDENCE OF CHLOROQUINE-RESISTANT AND SULFADOXINE PYRIMETHAMINE-RESISTANT *P. FALCIPARUM* MALARIA

Travellers to areas with a high incidence of chloroquine-resistant and sulfadoxine-pyrimethamine-resistant *P. falciparum* malaria should follow **ONE** of the following regimens:

1) **FOLLOW A LARIAM (MEFLOQUINE HYDROCHLORIDE) REGIMEN:** TAKE ONE TABLET OF LARIAM 250mg (adult dosage) ONCE A WEEK. START ONE TO TWO WEEKS BEFORE ENTERING THE MALARIOUS AREA, CONTINUE WEEKLY DURING YOUR STAY AND CONTINUE FOR FOUR WEEKS AFTER LEAVING. (See below for description of drug.)
   **OR**
2) **FOLLOW A MALARONE (ATOVAQUONE+PROGUANIL) REGIMEN:** TAKE ONE TABLET OF MALARONE DAILY (atovaquone 250mg+proguanil 100mg adult dosage). START ONE TO TWO DAYS BEFORE ENTERING THE MALARIOUS AREA, CONTINUE DAILY DURING YOUR STAY AND CONTINUE FOR 7 DAYS AFTER LEAVING. (See below for description of drug.)
   **OR**
3) **FOLLOW A DOXYCYCLINE REGIMEN:** TAKE ONE TABLET OF DOXYCYCLINE DAILY (100mg adult dosage). START ONE DAY BEFORE ENTERING MALARIOUS AREA, CONTINUE DAILY DURING YOUR STAY AND CONTINUE FOR FOUR WEEKS AFTER LEAVING. (See below for description of drug.)
   **OR**
4) **FOLLOW A CHLOROQUINE REGIMEN:**
   Persons for whom the above medications are contraindicated should follow a CHLOROQUINE REGIMEN: TAKE CHLOROQUINE (ARALEN) in weekly doses of 500mg (300mg base). START ONE WEEK BEFORE ENTERING THE MALARIOUS AREA, CONTINUE WEEKLY DURING YOUR STAY, AND CONTINUE FOR FOUR WEEKS AFTER LEAVING. IT IS IMPERATIVE THAT YOU USE A MOSQUITO BED NET TO AVOID THE BITE OF THE NOCTURNAL ANOPHELES MOSQUITO. USE REPELLENTS AND INSECTICIDES AS DESCRIBED ABOVE UNDER SECTION "MECHANICAL PROTECTION".
   IN COUNTRIES WITH HIGHLY CHLOROQUINE-RESISTANT *P. FALCIPARUM MALARIA*, A REGIMEN OF PALUDRINE (PROGUANIL HYDROCHLORIDE) 200mg DAILY (ADULT DOSE) SHOULD BE ADDED TO THE WEEKLY CHLOROQUINE REGIMEN.
   PERSONS FOLLOWING A CHLOROQUINE OR A CHLOROQUINE PLUS PROGUANIL HYDROCHLORIDE REGIMEN MUST BE AWARE THAT THESE DRUGS ARE LESS EFFECTIVE THAN LARIAM, MALARONE OR DOXYCYCLINE. THEY MUST SEEK IMMEDIATE MEDICAL ATTENTION IN CASE OF FLU-LIKE SYMPTOMS — FEVER, HEADACHE, NAUSEA, GENERAL MALAISE — APPEARING ABOUT SEVEN DAYS OR LATER AFTER ENTERING MALARIOUS AREA.

Persons travelling to or working in remote areas where medical attention cannot be sought within 24 hours should consult with a specialist before leaving their home country for advice on a possible self-treatment regimen in case of a malaria breakthrough attack.

**CHLOROQUINE** — see description above.

**MEFLOQUINE HYDROCHLORIDE (brand names: LARIAM, MEPHAQUIN, ELOQUIN)**
Mefloquine hydrochloride is very effective for the prevention of chloroquine-resistant and multi-drug-resistant *Plasmodium falciparum* malaria. However, it may not always prevent a delayed first attack or relapses caused by *Plasmodium vivax*.
*CAUTION: Lariam is generally well tolerated. Mild side effects include nausea, headache, dizziness. Serious side effects such as skin rashes, seizures, psychosis, and diarrhea have been rarely reported when Lariam is taken for prophylaxis.*
*CONTRAINDICATIONS:* Persons suffering from coronary heart diseases, liver and kidney diseases, epilepsy or psychiatric disorders such as severe depression, should not use this drug. Lariam may interact with beta blockers, digoxin, calcium channel blockers, metaclopramide, etc. Lariam should not be taken concurrently with chloroquine, quinine or quinidine. If treatment of severe malaria was initiated with these drugs, Lariam should not be started before an interval of 12 hours and only under close medical supervision. Lariam is contraindicated for pregnant women and children under 30 lbs. (15 kg) in weight. If Lariam has been used for prophylaxis and a malaria breakthrough occurs, Lariam should not be used for treatment. If Lariam is taken for longterm prophylaxis periodic liver function tests and ophthalmic examinations should be performed.
Lariam is available by prescription in Canada and the U.S.A.

**ATOVAQUONE+PROGUANIL (brand name: MALARONE by GLAXO)**
Atovaquone 250mg+proguanil hydrochloride 100mg is effective for the prevention of chloroquine-resistant and multi-drug resistant *P. falciparum* malaria. It is less effective against vivax malaria, and a malaria breakthrough with *P. vivax* may occur.
*CAUTION:* MALARONE may cause mild side-effects when used for prophylaxis such as stomach upsets, vomiting, headaches, nausea. MALARONE should be taken with food or milk.
*CONTRAINDICATION:* Persons suffering from renal (kidney) disorders or with known allergies to atovaquone or proguanil should not use this drug. The safety of this drug in pregnancy, nursing mothers and children weighing less than 11kg (24 lbs) has not been established.
MALARONE is available by prescription for prophylaxis and treatment in the U.S. In Canada it is available for treatment; the application for use as prophylaxis is pending.

**DOXYCYCLINE (brand name: VIBRAMYCIN)**
Doxycycline belongs to the tetracycline group of antibiotics and has proven effective in preventing malaria in multi-drug resistant areas. It is also used in combination with quinine for the treatment of severe and multi-drug resistant malaria.
*CAUTION:* Doxycycline may cause photosensitive skin reactions (avoid exposure to direct sunlight and use sun-screen with high protection against UVA (long range ultraviolet radiation) to minimize risk of photosensitive reaction). It may also cause vaginal yeast infections in women, and produce antibiotic-resistant pathogenic bacteria. Antibiotic associated colitis, a severe form of diarrhea, can also follow a prolonged use of this drug class.
*CONTRAINDICATIONS:* Doxycycline should not be used by persons with known photosensitive skin reactions. It is contraindicated for pregnant and lactating women and children under 8 years of age. Tetracyclines permanently stain the teeth of unborn fetuses, infants and children up to eight years of age.

## SUPPRESSIVE MEDICATION IN AREAS WITH HIGHLY CHLOROQUINE FANSIDAR AND LARIAM RESISTANT *P. FALCIPARUM* MALARIA (Border areas of Thailand–Cambodia, Thailand–Myanmar)

Persons travelling to multi-drug-resistant *P. falciparum malaria* areas should follow a MALARONE or DOXYCYCLINE antimalarial regimen as described above. Persons who cannot follow one of these regimens or contemplate a long term visit to these areas should seek advice from a specialist in tropical diseases for a possible alternative drug regimen. Contact IAMAT for referrals to specialists.

Treatment of a breakthrough of multi-drug-resistant malaria should be given under medical supervision and may include a variety of drugs in different combinations. Fast medical attention is imperative to successful treatment.

## THE FOLLOWING IS A SHORT DISCUSSION OF MALARIA SUPPRESSANTS AVAILABLE IN DIFFERENT AREAS:

**AMODIAQUINE**
**Amodiaquine dihydrochloride (brand names: CAMOQUINE, FLAVOQUINE)**
Belonging to the same chemical family as chloroquine (4-Amino-quinolines) this drug offers protection similar to chloroquine, but unfortunately experience has shown that it causes serious side effects such as hepatitis and agranulocytosis. It should not be used for malaria prophylaxis.

**ARTEMISININ, ARTEMETHER** and **ARTESUNATE**
These drugs are derivatives from the Chinese plant Qinghaosu, and are used for the treatment of multi-drug resistant *P. falciparum* malaria. It should not be used for prophylaxis. They are not available in Canada or the U.S.A.

**CHLOROQUINE-PROGUANIL (brand name: SAVARINE by Zeneca)**
This combination drug eliminates the difficulty of taking chloroquine on a weekly basis and proguanil on a daily basis. However, the usefulness of this drug is compromised by the high resistance of *P. falciparum* malaria to both drugs. This drug is not available in Canada or the United States.

**DAPSONE-PYRIMETHAMINE (brand name: MALOPRIM)**
An alternative to Fansidar, this drug is not available in Canada or the United States.

**HALOFANTRINE (brand name: HALFAN by SmithKline Beecham)**
Halofantrine is effective for the treatment of chloroquine-resistant and sulfodoxine-pyrimethamine-resistant *Plasmodium falciparum* and *Plasmodium vivax* malaria. It is less effective for the treatment of mefloquine-hydrochloride-resistant **P. falciparum** malaria.
CONTRAINDICATIONS: Halfan should not be used for prophylaxis but only for the treatment of multi-drug-resistant malaria. It is contraindicated for pregnant and nursing women and children under 3 months of age. Halfan is contraindicated for persons with cardiac condition defects (congenital or pre-existing Q-T wave prolongation on an electrocardiogram or persons on medications known to prolong Q-T wave intervals), persons taking beta-blockers, dioxin, calcium-channel blockers, or on quinidine; or persons suffering from thiamine deficiency or severe electrolyte imbalance. Halfan should not be taken concomitantly with mefloquine hydrochloride, quinine or tetracyclines.
NOTE: Halfan must be taken on an empty stomach (1 hour before or 2 hours after a meal). It should be administered under medical supervision and monitored by ECG's before and 4 hours after treatment.

**PRIMAQUINE**
This drug is used for the eradication of liverstage malaria parasites of *P. vivax* and *P. malariae* to prevent future malaria attacks. Primaquine is also used for prophylaxis for persons living for extended periods in highly malaria endemic areas. It is contraindicated for persons suffering from glucose-6-phosphate dehydrogenase deficiency (G6PD), and patients must be screened before this drug is prescribed or administered.

**PROGUANIL (brand name PALUDRINE by Ayerst)**
Although proguanil hydrochloride is the oldest and safest of malaria suppressants, *Plasmodium falciparum* has become so highly resistant to it that its usefulness is now seriously compromised in all malarious areas. Recent studies have shown that proguanil is less effective against the benign forms of malaria *(P. vivax, P. ovale* and *P. malariae)* than chloroquine. In areas with a high incidence of multi-drug-resistant *P. falciparum*, proguanil may be added to a chloroquine regimen in daily doses of 200mg (adult dosage). It should not be used alone as a malaria suppressant. Caution: Mouth ulcers are a common side effect.
Proguanil is not available in the U.S.A.

**QUININE (alkaloid of cinchona bark)**
Quinine is used in combination with other antimalarial drugs (such as primaquine, tetracycline and others) for the treatment of relapsing *Plasmodium vivax* malaria and multi-drug-resistant *Plasmodium falciparum* malaria. It cannot be used for prophylaxis, and it should be administered under close medical supervision because of potential serious side effects. A 7-day course (8mg base/kg orally 3 times daily) of quinine may be prescribed as a stand-by treatment for chloroquine-resistant *P. falciparum* malaria for travellers who spend prolonged periods of time in remote areas.

## ANTIMALARIAL REGIMEN IN CHILDREN

Chloroquine is the best antimalarial drug for children. The liquid form, not available in Canada or the United States, may be purchased in some countries in Europe and malarious regions (Nivaquine by Société Spécia, Paris, France). Parents are warned to keep chloroquine out of the reach of children since misuse has resulted in some fatalities. Breast-fed infants are not protected by their mother's prophylactic regimen, but must be given their own dosages according to their weight and/or age. Children should always sleep under a bed net. Special care should be taken with the application of anti-mosquito lotion, especially on infants, overuse may produce neurological symptoms. Infants and small children should not travel to areas with chloroquine and multi-drug-resistant *P. falciparum* malaria.

Fansidar (sulfadoxine + pyrimethamine) and Halfan (halofantrine) are contraindicated for children under 3 months of age. Lariam (mefloquine hydrochloride) is contraindicated for children under 30 lbs. (15 kg) in weight. Vibramycin (doxycycline) is contraindicated for children under eight years of age.

Malarone (atovaquone+proguanil) is contraindicated for children weighing less than 11 kg (24 lbs).

Schoolage children are very vulnerable to malaria, as proven by the high incidence of the disease among this group. Children on holiday visits to parents working in the tropics should be watched to ensure that they continue the suppressive treatment for 4-6 weeks after their return to school. Their guardians must be warned that fever and flu-like symptoms appearing 7 days to several months after their return may signify a malaria breakthrough and early diagnosis are imperative for successful treatment.

## ANTIMALARIAL REGIMEN DURING PREGNANCY

Since all drugs taken by a pregnant woman reach her unborn child, it is never advisable to take medication during pregnancy. However, if travel to malarious regions cannot be avoided, the risk of miscarriage or premature delivery as a result of contracting malaria far outweighs the risk of possible side effects from antimalarial drugs. Chloroquine and proguanil are considered safe during pregnancy in doses used for malaria prophylaxis. Pregnant women should not travel to chloroquine-resistant and multi-drug-resistant areas. If travel cannot be avoided, mechanical anti-mosquito measures should be followed meticulously to minimize the possibility of infection. Sulfadoxine + pyrimethamine (Fansidar), mefloquine (Lariam), Malarone (atovaquone+proguanil), halofantrine (Halfan), quinine and tetracyclines (doxycycline) are contraindicated in pregnancy. If you have taken Lariam, Fansidar or Halfan for prophylaxis avoid becoming pregnant for 3 months, after a doxycycline regimen wait for about a week.

## WHEN YOU RETURN…

Back home from the tropics you may feel a general malaise, headache and some fever, all symptoms usually associated with flu. But you should be aware that falciparum malaria, the malignant form of this disease, may simulate flu, and that you may be having a breakthrough of malaria due to laxity during your antimalarial regimen or the appearance of strains of *P. falciparum* resistant to your medication. Remember to tell your doctor where you have been even if the fever develops months after your return, since such an episode could be a delayed first attack or a relapse of vivax malaria. For the same reason blood is not accepted from donors who have taken malaria suppressant medication within the preceding two years.

## THE SEARCH FOR THE KILLER

**November 6, 1880, Constantine, Algeria: the end of a superstition**

Thousands of years of superstition attributing malaria (L.: *mala aria*=bad air) to some kind of air-borne poison is overthrown by a French army surgeon. Charles Louis Alphonse Laveran. He identified the malaria parasite for the first time while examining with the aid of a microscope the fresh blood of a patient infected with falciparum malaria. But Laveran's times were under the spell of the genius Louis Pasteur, and the bold idea that malaria was caused by the presence of millions of minute animal parasites in the blood, and not by bacteria, was difficult to accept. It took six years for the skeptical medical profession to recognize the importance of his discovery.

**1886, Pavia, Italy**

Camillo Golgi definitively identified two human malaria parasites: *Plasmodium vivax* and *Plasmodium malariae*. He described the asexual multiplication of the parasite in the red corpuscle of the blood and demonstrated its relationship to the periodic appearance of the fever characteristic of malaria.

**1889, Rome**

Three years later, Ettore Marchiafava differentiated a third species of human malaria parasites, *Plasmodium falciparum*, named for the crescent shape of the sexual form of the parasite (L.: *falx*=sickle; *parere*=to bring forth). However the mechanism of transmission of the disease was still a mystery.

**1894, London: Patrick Manson, the grey eminence behind malaria research**

Patrick Manson, an eminent English physician, had discovered that mosquitoes could suck up the microscopic threadlike worms from the blood of patients infected with a disease called filariasis. He believed that mosquitoes might also draw out the malaria parasites from human blood, and that transmission would occur by ingestion of water contaminated by infected mosquitoes.

**July 4, 1898, Calcutta: Ronald Ross, "It is the bite"**

Manson, realizing he could never experiment enough in England to prove his theory, convinced Ronald Ross, a British army surgeon who visited him in 1894, to carry on this research. Together they planned a series of experiments which Ross was to carry out upon his return to India. Ross began by raising *Culex* and *Aedes* larvae, and let the adult mosquitoes feed on patients with malaria. Then he let these mosquitoes bite volunteers, but with no result — since he wasn't an entomologist he wasn't aware that he was using the wrong species of mosquito. After several unsuccessful experiments, in April 1897, while working in Ootacamund near Madras, he saw for the first time the dapple-winged *Anopheles*, and started to experiment with this species. On August 20, 1897, looking through his microscope at the gut of mosquitoes which had fed on a patient with malignant malaria, he saw for the first time the human malaria parasite growing in the gut of *Anopheles*.

Unwillingly he had to interrupt his investigations, and when moved to his new post in Calcutta he started working with the avian malaria parasites, which are transmitted by a *Culex* species. He proved that the spindle-shaped malaria organisms (*sporozoites*), freed by the rupturing of the fertilized eggs, migrate from the gut of the mosquito to its salivary glands, to be injected into the victim when the insect bites. To Ross goes the credit for the discovery that malaria is transmitted by mosquito bite.

**1898, Baltimore**

Later in the same year William George McCallum, a Canadian pathologist also working with birds, was able to interpret and describe the fertilization process of the parasite taking place in the gut of the mosquito.

**1886-1899, Rome: the magnificent four**

Simultaneously, a group of Italians were working to solve the puzzle of the transmission of malaria in humans. During the decade 1886 to 1896, G. Bastianelli, A. Bignami, A. Celli and G.B. Grassi had been actively investigating the life-cycle of the human malaria parasites and making accurate descriptions of the lesions produced by the parasites in the different organs of the body. A break-through came with the observations of Giovanni Battista Grassi, a physician with a keen interest in zoology, particularly mosquitoes. He noticed that when malaria was present there was always a large population of *Anopheles*, while in areas of large *Culex* populations there was no malaria.

From the Campagna Romana near Rome he collected *Anopheles* mosquitoes, which his colleague, Amico Bignami, allowed to feed on a volunteer patient from the Santo Spirito Hospital, a few steps away from St. Peter's Basilica. On November 1, 1898, the patient, Abele Sola, developed the classic symptoms of falciparum malaria. Together with Giuseppe Bastianelli and Angelo Celli, they were able to reproduce malaria infections in other volunteers and prove that only the *Anopheles* mosquito, and no other species, transmits malaria in humans.

**1936, Rome: Giulio Raffaele discovers the liver cycle**

It was soon discovered that a link was missing in the knowledge of the life-cycle of the malaria parasite. Still unexplained was the time elapsed between the introduction of the parasites through the bite of the mosquito and the appearance of the symptoms of malaria. Raffaele discovered while working with birds that malaria parasites entering the host first undergo a cycle of transformation within the blood-forming cells of the liver.

**1948, London: the final touch**

Now the road was open for British researchers Colonel H.E. Shortt and P.C.C. Garnham to demonstrate the liver cycle of the malaria parasite in humans. Following a period of extensive trials on monkeys, in 1948 a human volunteer — a Mr. Howard — was bitten during three days by nearly eight hundred *Anopheles* infected with *Plasmodium falciparum*. On the fifth day, a surgeon removed a small piece of tissue from his liver which, examined under the microscope, demonstrated the growth of the parasites in the liver cells. The last mystery of the life-cycle of the malaria parasite was finally unraveled.

## PROPHYLACTIC ADULT DOSAGES OF ANTIMALARIAL DRUGS

| Countries where sold | Brand Name | Manufacturer | Generic name | Salt content per tablet | Base (active compound) | No. of tablets ★ | Frequency |
|---|---|---|---|---|---|---|---|
| Canada and overseas | ARALEN | Winthrop | chloroquine diphosphate | 250 mg | 150 mg | 2 | once a week |
| United States | ARALEN | Winthrop | chloroquine diphosphate | 500 mg | 300 mg | 1 | once a week |
| Europe and some malarious areas | RESOCHIN | Bayer | chloroquine diphosphate | 250 mg ★★ | 150 mg | 2 | once a week |
| France and some malarious areas | NIVAQUINE | Société Spécia | chloroquine sulfate | 410 mg ★★ | 300 mg | 1 | once a week |
| United States, France, Switzerland and some malarious areas | LARIAM | Hoffmann-LaRoche | mefloquine hydrochloride | 250 mg | 228 mg | 1 | once a week |
| United States, Europe | MALARONE | GlaxoSmithKline | atovaquone 250 mg +proguanil 100 mg | | | 1 | daily ★★★ |
| World-wide | VIBRAMYCIN | Pfizer | Doxycycline | 100 mg | | 1 | daily |
| Canada, United Kingdom Europe, some malarious areas | PALUDRINE | Ayerst | proguanil hydrochloride | 100 mg | | 2 | daily ★★★★ |

★ See text for details; take after a meal, with at least 240 ml / 8 oz. of water.
★★ Other formulations are available.
★★★ Take with food or milk.
★★★★ Proguanil should not be taken alone as a malaria suppressant. See text.

## STANDBY TREATMENT DOSAGES OF ANTIMALARIAL DRUGS FOR ADULTS

If a malaria breakthrough occurs, medical attention should be sought immediately. The following treatment dosages are recommended when medical attention cannot be reached within 24 hours.

| Countries where sold | Brand Name | Manufacturer | Generic name | No. of tablets | Frequency |
|---|---|---|---|---|---|
| United States, most malarious areas | FANSIDAR | Hoffmann-LaRoche | sulfadoxine 500 mg +pyrimethamine 25 mg | 3 | in one dose* |
| Canada, United States, Europe | MALARONE | GlaxoSmithKline | atovaquone 250 mg +proguanil 100 mg | 4 | in one dose for 3 days** |

* See text for details; take after a meal, with at least 240 ml / 8 oz. of water.
** Take with food or milk

## PEDIATRIC PROPHYLACTIC DOSAGES

| | | Under 1 year | 1-4 years | 5-8 years | 9-12 years | Frequency |
|---|---|---|---|---|---|---|
| NIVAQUINE Sirup ■ | | 1 1/2 tsp. | 1 tbsp. | 2 tbsp. | 3 tbsp. | once a week |
| ARALEN tablets ■■ | | calculate 8mg per kilogram of body weight | | | | once a week |
| LARIAM ■■ | Under 30 lbs. Contraindicated | 30-40 lbs. 1/4 tablet | 40-60 lbs. 1/2 tablet | 60-90 lbs. 3/4 tablet | 90 lbs. + 1 tablet | Frequency once a week |
| MALARONE | Under 24 lbs. Contraindicated | 24-45 lbs. 1 pediatric tablet | 46-67 lbs. 2 pediatric tablets | 68-88 lbs. 3 pediatric tablets | 88 lbs. + 1 adult tablet | daily ■■■ |

## PEDIATRIC TREATMENT DOSAGE (TO BE USED IF MALARIA BREAKTHROUGH OCCURS AND MEDICAL ATTENTION CANNOT BE REACHED WITHIN 24 HOURS) See text.

| | Under 3 months | Under 1 year | 1-3 years | 4-8 years | 9-14 years | 14y. + | Frequency |
|---|---|---|---|---|---|---|---|
| FANSIDAR ■■ | Contraindicated | 1/4 tablet | 1/2 tablet | 1 tablet | 2 tablets | 3 tablets | in one dose |
| | Under 24 lbs. | 24-45 lbs. | 46-67 lbs. | 68-88 lbs. | 88 lbs. + | | in one dose for |
| MALARONE | Contraindicated | 1 adult tablet | 2 adult tablets | 3 adult tablets | 4 adult tablets | | three days ■■■ |

■ 1 teaspoon (tsp.) = 5 ml = 25 mg of chloroquine base; 1 tablespoon (tbsp.) = 3 tsp.
■■ Your pharmacist will be able to crush tablets and prepare children's dosages in gelatine capsules as needed. These dosages are to be used as a guide only. Check with your pediatrician before leaving the country.
■■■ Take with food or milk

*The recommendations outlined in this document are intended as guidelines only. For a prophylactic malaria regimen tailored to your needs, seek further advice from your physician or travel clinic.*