

# **MALARIA - A MARITIME PROBLEM**

**2002-2003**

**A GUIDELINE ABOUT MALARIA  
FOR OFFICERS AND SEAMEN  
OF THE MERCHANT MARINE**

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## **MALARIA - A MARITIME PROBLEM**

*"Of all the acute infectious diseases, Malignant Tertian (Falciparum) Malaria is unquestionably one of the most important cause of death in merchant seamen and travellers."*

## MALARIA STILL A MARITIME PROBLEM

Sadly enough the most recent figures about Malaria victims are dramatic: an average of over 4.000 victims per day; the World Health Organization estimates an annual balance between 1.500.000 and 3.000.000 lethal cases. Malaria can be caught in some 100 countries with a total of about 2.300 million inhabitants.

Today we speak about Malaria in a maritime context. It is by passing through those endemic areas that seamen also become potential victims of the female mosquito 'anopheles' who flies miles outward the coastline. Her bite brings the lethal plasmodium parasite into the blood circulation. Malaria is, and will remain for quite some time a dangerous and sometimes lethal disease, which is, nevertheless, fairly easy to prevent or treat. It is because of this high frequency of cases, together with the fact that it is still a Central Africa associated disease that after diagnosis, we sometimes use the slightly ironical phrase: 'Malaria, I presume'

Malaria can kill very quickly. Prevention, recognizing its symptoms and acting accordingly is therefore essential knowledge for maritime officers. We can only guess as to why Malaria has become such an important maritime problem: is it the sailor who neglects prevention? Is it the captain or ship-owner who find prevention too expensive? Is it the ship chandler who delivers wrong medication? Is it the doctor who gives incomplete or faulty information? We do not know, but probably the truth lies somewhere in between.

Through our profession as port doctors we visit a lot merchant ships, and notice regularly that seamen are not well protected against Malaria. It is discouraging to keep on arguing with captains, ship chandlers, ship owners or even medical doctors in attempts to minimize victims. Prevention is so simple that our frustration grows by every new victim

Dr. R. Van Cleempoel

# CONTENT

<b>I. INTRODUCTION</b>	<b>5</b>
<b>II. SOME NOTES ON THE MORBIFIC AGENT</b>	<b>7</b>
<b>III. SYMPTOMS</b>	<b>9</b>
<b>IV. PROTECTIVE MEASURES AGAINST MALARIA</b>	<b>10</b>
<b>A. EXTERNAL PROTECTION</b>	<b>10</b>
<b>B. INTERNAL PROTECTION - CHEMOPROPHYLAXIS</b>	<b>12</b>
<b>Malaria Risk Areas for Seaman (not going into the hinterlands)</b>	<b>14</b>
<b>DOSES :</b>	<b>16</b>
<b>I. CHLOROQUINE - PALUDRINE</b>	<b>17</b>
<b><i>A. ADULTS</i></b>	<b>17</b>
<b><i>B. DOSES ADAPTED TO CHILDREN</i></b>	<b>17</b>
<b>II LARIAM</b>	<b>18</b>
<b>III MALARONE</b>	<b>19</b>
<b>C. WHAT TO DO DURING A POSSIBLE MALARIA ATTACK</b>	<b>20</b>
<b>APPENDIX</b>	<b>28</b>
<b>NAMES OF MALARIA-MEDICATIONS AND SIDE-EFFECTS.</b>	<b>28</b>

## I. INTRODUCTION

Nowadays **MALARIA** is still one of the most frequent and dreadful infectious diseases in the world (one to two million dead a year). Malaria is a serious problem in a growing number of regions in the **TROPICS** and **SUBTROPICS**, because of the extension of the malarious zones and because of the increasing resistance of the malarial parasite to the present medications.

Malaria is of increasing importance in **THE MARITIME WORLD** for the following reasons :

- *unawareness* of the fact that malaria is a serious and potentially fatal disease
- *insufficient information* regarding the clinical picture of malaria tropica or maligna
- *no or insufficient use of* the antimosquito measures and the classical protective medication
- increasing *resistance* of many new malaria strains to the actual medications
- the *fluctuating frequency* of malaria occurrence in the most dangerous areas, which leads to miscalculation of the real risk factors.

Most studies on the protection/treatment of malaria in the maritime world teach us that seaman usually are *uninformed or misinformed* about this disease.

A. The correct use of **PREVENTIVE MEASURES (PERSONAL ANTI-MOSQUITO MEASURES AND ANTI-MALARIAL TABLETS)** cannot be overstressed.

The seaman does not take (or only sporadically) medication or applies external protection against the bite of the malaria-carrying mosquito (e.g. with mosquito repellents).

By his work on board (and not on shore) and at times his long stay in these malarious areas the seaman often **underestimates the problem**

There is still a lot of **misinformation** on malaria, even to the point that many think that the disease has almost been erased, while recent publications to the contrary show an increase in occurrence of the disease. There is no country in the world that has special preventive requirements towards malaria. Many countries even deny the existence of a malaria problem in their countries.

On board there is an increasing problem of **mixed crews** (Filipinos, Europeans, Americans, Africans and Asians). Seamen travelling frequently in tropical areas often have the **false impression that they have almost automatically built up immunity towards malaria**.

In principle, one develops some resistance (immunity) only after repeated contacts with the malaria parasite during a prolonged stay in the tropics. Only people constantly living in an area where there is permanently high malaria transmission may have built up certain immunity. Those people don't need a daily or weekly prevention.

However, prolonged stay in the tropics does not guarantee at all immunity, and most persons residing in the tropics do not obtain considerable immunity. Moreover, this immunity is never a complete immunity. It does not protect against repeated infection, since one is bitten by malaria mosquitoes as much as before. Even though they can have an attack of malaria, which has to be treated according to the classical scheme. Nevertheless, one gets sick less quickly, so that more time becomes available to start proper treatment.

After having left a malaria area for more than 6 months, one loses the acquired immunity for the most part, since it is maintained by repeated malaria infections. Unfortunately these people often have attacks of malaria while adequate preventive and curative treatment is available on board: medication is often not taken because of lack of any knowledge of the disease.

We now notice that mixed and ever changing crews of different nationalities may generate a **decreasing knowledge** of the malaria prevention and treatment. Because of this, sailors expose themselves more frequently to dangerous and even mortal varieties of malaria.

If giving a daily or weekly prevention with malaria tablets would run into difficulties with multicultural crew, it is better to assign everybody to the classical prevention scheme.

Beware of the dangerous use of homeopathic drugs, which aren't active and may be the cause of lethal evolution.

B. On the other side, one must realise that at present a 100 % protection is no longer possible at this moment, as there isn't any method available to prevent completely malaria. All measures are aimed at reducing the risk of a malaria-attack to a minimum and for this reason, hence **ALL MEASURES HAVE TO BE APPLIED TOGETHER**.

Since the risk is not anymore zero, **THE INFORMATION ABOUT CORRECT TREATMENT DURING A POSSIBLE ATTACK IS INDISPENSABLE.**

Thus the strategy to be followed by anyone who stays in a malaria area, is based on the following 3 interventions: (1) measures to prevent contact with the malaria mosquito (external protection by (mosquito net, mosquito lotion) as well as (2) internal measures: tablets (chemoprophylaxis), that aim to prevent a malaria attack, and also (3) **CORRECT AND TIMELY TREATMENT IN CASE OF BREAKTHROUGH MALARIA** (i.e. malaria in spite of taking tablets correctly). NB. So far, there is no vaccination available.

Usually, for a traveller on land in the case of breakthrough malaria, prompt treatment is available, and we see at regular intervals cases of acute falciparum malaria in seamen who, thanks to their reception in the ports can be helped quickly and efficiently.

However in the event of an attack at sea, things are quite different and it is really of paramount importance to give the appropriate treatment correctly and in time. If not, there is a major risk for the patient to die. In ports we sometimes encounter sailors with serious symptoms of falciparum malaria arriving in a pre-coma state. Urgent hospitalisation and correct treatment can only save them. They usually come from the **West or East Coast of Africa**. In Lisbon three **seamen died** after a trip along the West Coast of Africa. Better information and treatment could have saved their lives.

It happened before that we were able to help with specific malaria advice over the radio, and even to hinder that ships were needlessly led to unforeseen harbours for hospitalisation for the sick sailor. When the patient is still able to swallow medication, we know that most of them can be treated on board with **quinine and doxycycline** (see further).

All seamen who were treated on board for suspected malaria have to consult (when possible with blood slides) the PORT DOCTOR in the next port because of:

- blood-examination and blood-slides (blood smear), etc.
- hospitalisation in case of serious symptoms
- briefing on board about good anti-malaria preventive measures on board

**In consideration of the discussions on board and the frequent occurrence of malaria with seamen** we realise there is a great need for up-to-date knowledge about **MALARIA TREATMENT IN CASE OF BREAKTHROUGH MALARIA**. Only knowledge of the disease and/or **updated guidelines written in an appropriate and comprehensive text** can (in conjunction with **radiomedical advice**) help to save the life of a seaman with severe falciparum malaria. For this reason, viz. to protect himself and his crew, the necessary guidelines are described in this text. At the same time we refer to the "**MEDICAL GUIDE FOR SHIP'S CAPTAINS**" and other **WHO papers**.

**It is the responsibility of EVERY SEAMAN to prevent malaria, both for him and his fellow crewmembers. THIS TEXT is written for the captain and the officers (but in fact even so for every sailor or seaman and every person travelling in the tropics), to protect himself and his crew in the best possible way. The following notes look rather complex, however, the malaria problem is complicated, potentially serious, and world-wide present.**

## II. SOME NOTES ON THE MORBIFIC AGENT

The female mosquitoes of the anopheline genus are transmitting malaria.  
The four species of malaria causing symptoms of the disease in man are:

**PLASMODIUM FALCIPARUM**  
**PLASMODIUM VIVAX**  
**PLASMODIUM OVALE**  
**PLASMODIUM MALARIAE**

Only Plasmodium falciparum is the dangerous, mortal malaria, because in this case a massive infection of the red blood cells may occur through which the small blood vessels in the brains, the liver and the kidneys can get blocked off and causing a break-down of the red blood cells at an accelerated pace. These complications occur especially with persons who never or only sporadically come in contact with **MALARIA** and are not able to build up immunity or self-defence against malaria.

This is now the very specific problem with the **SEAMEN** who stay in the tropics for a short while and still must take medication for at least four weeks after leaving the malaria area. It is precisely carrying on with taking medication for a further four weeks or seven days (Malarone™) that is often being neglected !

**ATTENTION: IN CASE OF A MALARIA INFECTION BY PLASMODIUM FALCIPARUM IRREGULAR PEAKS OF FEVER OCCUR, ESPECIALLY IF IT IS A FIRST MALARIA INFECTION. IN CASE OF AN INFECTION PRODUCED BY PLASMODIUM FALCIPARUM THE PATTERN OF FEVER MAY SHOW A 48-HOUR CYCLE WHEN A PERSON HAS BEEN REPEATEDLY SUFFERING FROM MALARIA INFECTIONS.**

In case of an infection caused by Plasmodium vivax and ovale we see in these typical cases attacks of fever recurring every other day, i.e. at 48-hour intervals (malaria tertiana). In case of Plasmodium malariae the peaks of fever recur every three days, i.e. at 72-hour intervals (malaria quartana).

In most cases different mosquitoes sting a person so that, in principle, one can catch more than one type of malaria. This is an explanation for the fact that after treatment of a specific type another type of malaria may occur later on, viz. caused by one of the other Plasmodium species. These may be responsible of a late attack due to the existence of remaining dormant forms in the liver (P. vivax, P. ovale) or more rarely in the blood vessels (P. malariae) and whose permanent eradication can not be guaranteed by a therapy against P. falciparum alone. Such a late attack does not lead to life threatening complications (on the condition that Plasmodium falciparum is not present), and is mostly characterised by a typical fever pattern. Eradication is nearly always possible for all those forms (with primaquine).

**SUMMARIZING :**

Plasmodium falciparum

= **MALIGNANT tertian malaria** meaning possibly mortal malaria with irregular fever episodes.

Plasmodium vivax

= **BENIGN tertian malaria** meaning a benign malaria with fever every 48 hours (sometimes every 24 hours).

Plasmodium ovale

= **BENIGN tertian malaria** meaning a benign malaria with fever every 48 hours (sometimes every 24 hours).

Plasmodium malariae

= **BENIGN quartan malaria** meaning a benign malaria with fever every 72 hours.

On board in the tropical regions, however, it is impossible on the basis of clinical symptoms solely to distinguish between the four forms

Therefore: EVERY FEVER

→ MALARIA

→ POTENTIALLY FALCIPARUM MALARIA

→ POTENTIALLY RESISTANT FALCIPARUM

MALARIA

**CHOOSE ALWAYS FOR THE WORST POSSIBLE SCENARIO:**

**® RESISTANT FALCIPARUM MALARIA**

### III. SYMPTOMS

A classic malaria attack is being characterised by suddenly arising fever, which lasts several hours. Three successive and clearly distinctive stages may be observed.

1. **Cold stage (chill)** rising fever, patient feels cold, ashen colour, temperature is increasing rapidly, seeks more covering with blankets on bed.
2. **Hot stage**, throws off all blankets, looks red and congestive, very warm, high temperature, splitting headache and severe neck pains.
3. **Sweat stage**, patient suddenly breaks out in perspiration, clothes and bed are wet with sweat, temperature is falling quickly, patient feels better, often gets appetite back and falls asleep.

An attack in its whole lasts no longer than 10-12 hours. It is necessary to take the temperature every 3 or 4 hours in order to discover such an attack with a person who possibly may have malaria. Beginning attack of malaria at night is missed in most cases, because at night the temperature is not taken.

A person who is developing an attack of malaria is best assisted and controlled by one of the officers. When the temperature is rising the patient shall be covered and if necessary, in the second stage the blankets shall be removed, in the third stage pyjamas and sheets shall be changed. The patient can be given cool drinks in small quantities and cold or preferably tepid water compresses can be applied on the forehead.

At the same time the psychic condition should be observed.

During an attack the patient may be confused and consequently requires continued control, because in his confusion he can get overboard. In the event of convulsions the patient must be administered intramuscularly one ampoule of Valium, he must be cooled down and can then be given antipyretic tablets or suppo's: preferably paracetamol (500 mg 2/3 times a day). Avoid taking aspirin! In case someone has got convulsions, it is of importance to keep the temperature low and to strictly follow the **treatment scheme** of the malaria attack.

Any fever in tropic areas is a suspected case of malaria until proven the contrary.

The more so, when the patient has been careless in taking his preventive antimalarial medication or when on account of gastro-enteritis he has vomited or insufficiently absorbed the medication because of diarrhoea. But even if he took his pills regularly, the diagnosis of malaria may not be discarded.

It speaks for itself that at any rate malaria should be prevented and one should continue to take antimalarial tablets long enough and in time.

In case a seaman dies on board quite unaccountably after having left a malaria area (after the usual legal ascertainment by the captain and the officers) one shall always consider that cerebral malaria (*Plasmodium falciparum*) may be the cause of death. The corpse shall be kept in deepfreeze storage (container) because, later on an anatomopathological examination can still reveal if it was a malaria case or not, even so when the body is already decomposing. The ascertainment of natural death caused by a disease or an accident is of utmost importance for the ship owners, the insurance company and the next-of-kin.

## IV. PROTECTIVE MEASURES AGAINST MALARIA

The fight with malaria is going on in three fields:

- A One shall try literally to hold the mosquitoes at bay by **EXTERNAL PROTECTIVE MEASURES (p.9)**
- B One shall take in advance (preventively) antimalarial tablets (chemoprophylactic) so that a barrier is being built up in the blood in order to prevent the malarial parasite to multiply, in the event the mosquitoes should nevertheless bite one. In other words, to prevent an attack of malaria. This is the **INTERNAL PROTECTION (p.11)**.
- C If an attack of malaria should nevertheless break through, one should **KNOW AT ONCE WHAT TO DO TO STOP THIS MALARIA (p.17)**.

### A. EXTERNAL PROTECTION

It is aimed to avoid contact of the mosquito with the human skin, whereby one should remember two important aspects :

- **These female anopheles mosquitoes bite almost exclusively between dusk and dawn with emphasis on a few hours before sunrise.**
- **It is not because no mosquitoes can be perceived that it should mean there aren't any. Anopheles mosquitoes don't buzz loudly!**

The prevention of contact with the mosquito is of utmost importance, because, on its own, this is very effective for the prevention of malaria.

Following measures are important:

- In the cabins an insecticide based on pyrethrum by spraying, evaporation (by electrically heated plates), or by burning of an anti-mosquito coil. An insecticide with long duration (12 months) of effect (**DELTAMETHRINE**) can be applied **ON THE MOSQUITO NETS**.
- One has to use an undamaged bed net. The borders of the bed net have to be put under the mattress, and the bed net has to be fixed to supports on the 4 corners of the bed. The bed net has to be checked regularly for holes. In case there are children on board mosquito netting shall be put over the cradle and the easy chair. The bed net can be treated (impregnated) with an insecticide like permethrine or deltamethrine, which remains as a thin film on the fibers of the net. Consequently, mosquito's in contact with the net will be killed or chased before they can bite, and mosquito's in the room will be eliminated. These products are safe for human beings, even for small children. When covered over a baby bed, one has to make sure that the baby can not catch hold of the net, or suck on it. These products remain effective for many months (Deltamethrine: 12 months) on condition the bed net is not washed.
- Sleeping spaces or cabins shall be kept closed and ventilated via ventilation holes covered up with mosquito netting.
- The kitchen shall be well ventilated but doors and windows shall be covered up with mosquito netting.

- After darkness has set in, all doors shall be kept closed, windows shall only be left open when mosquito netting is in front of it.
- Should nevertheless in spite of these measures, mosquitoes have penetrated into the room or cabin one shall try to kill them with an insecticide spray (pay attention to young children). Spray shall be used especially under tables, chairs and dark corners. After use of insecticide spray one shall wait a little while before sleeping in this room or cabin.
- On ships without air conditioning the ventilation grid - vent holes and all openings through which the mosquitoes can penetrate shall be covered up with the usual mosquito netting, large vent holes or covering grids shall be covered up with clothing.
- On deck or on shore, one shall wear clothing preferably of a light colour, covering the legs as much as possible (mosquitoes avoid sitting on a white surface). At the same time the remaining uncovered parts of the body (hands, wrists, ankles) which are exposed to mosquito bites shall be smeared with mosquito repellent, products on the basis of **DIETHYL-M-TOLUAMIDE (DEET)**, to be renewed every four/six hours.
- Bear in mind that on anchoring off shore mosquitoes may appear on board even at a distance of 2 to 3 km away from the shore. Cases of malaria have occurred sailing within this area parallel with the coastline.
- Avoid being outside after sunset and especially avoid parties near swimming pools and lakes.
- Avoid ointments that are simply perfumed and locally produced insect repellents. Mosquito repellents, however, of well know compositions (with DEET) are strongly recommended
- To sleep on deck (unless under a mosquito net) is strictly prohibited!
- Clear light on board shall be covered up : the light attracts the mosquitoes.
- No receptacles or places where water can stagnate and dew water can collect. In these small quantities of water, mosquitoes can lay their eggs. Especially, lifeboats must be kept dry and rain pools must be removed or emptied and swabbed.
- Refuse and small puddles on deck especially attract mosquitoes - for this reason deck and corridors shall be kept clean and dry.
- **THE REFUSE BAGS** (best are plastic bags) or **DRUMS SHALL BE SEALED PROPERLY**: in this way the mosquito plague often goes down spectacularly, especially on ships lying a few meters off shore.

## B. INTERNAL PROTECTION - CHEMOPROPHYLAXIS

This means the taking of medication to prevent a malaria attack. This medication doesn't stop the malaria parasite from getting into the bloodstream but prevents the acute attack of malaria on the condition that the medication is taken correctly.

In case someone has **never** taken anti-malarial medication the best way is to start a full week or even (in case of mefloquine) 2- 3 weeks in advance, to see if these products don't give adverse reactions. This tolerance test is not necessary with Malarone™.

**The medication shall be taken until at least four weeks (seven days for Malarone Ô) after having left the coast** or eventually one to two weeks longer in case mosquitoes have still been found on board. To continue taking malaria medication after having left the malarial area is necessary, because the incubation period of malaria in the human body can take several weeks. This means that many seamen, as well as people living full time on shore must take antimalarial drugs for several months.

**THE CAPTAIN AND THE OFFICERS HAVE TO SEE TO IT THAT THE CREW EFFECTIVELY TAKES THE PREVENTIVE MEDICATION.** The best way is to indicate one man (for instance the second officer) charged with controlling the taking and the time of the taking shall be mentioned in the medical logbook. In case a seaman refuses to take the antimalarial drugs this shall be mentioned in the medical logbook and the seaman as well as the captain and the second officer shall be asked to sign.

There still remains the problem of the mixed Asian, South American or African crew. Some of these people have acquired a partial immunity from Malaria: which may be specific for their region, and which will be reduced after leaving. On the other hand, these people are also in danger when calling at the East Coast of Africa or Thailand (see further on, zone C).

In former times prevention was very simple. **CHLOROQUINE (NIVAQUINE)** was always and everywhere effective against the main and most dangerous form of malaria i.e. the one caused by *Plasmodium falciparum*. Since increasingly resistance has occurred, that is spreading continuously, this is not anymore the case. However, there are gradations in this increasing resistance.

- a) Resistance doesn't mean that there isn't any effect of chloroquine at all; in a number of cases there is still enough activity to reduce the symptoms of the disease or even to suppress them totally for a short period, but which unfortunately seems to be insufficient to eradicate malaria, even after taking a higher dose of chloroquine. Nivaquine often still slows down the evolution to dangerous complications – unfortunately more and more less frequently.
- b) The fact that there is resistance against chloroquine in a certain area doesn't mean that 100 % of the malaria strain, is less or totally unsusceptible. So far, it is only a percentage that will certainly increase in the years to come. In some places it may already be as high as 100 %.

Consequently, chloroquine remains partly active in areas where there is chloroquine resistance, and offers approximately a 100 % protection from the other species of malaria (see below).

At present chloroquine is keeping its place as a prophylactic medicine but it must be supplemented with other medication, viz. **PROGUANIL (PALUDRINE®)**. Taking a higher dose of chloroquine as sole remedy (e.g. 100 mg Nivaquine a day) is abandoned in favour of the combination Chloroquine + proguanil. In France Savarine® is commercialised, combining in 1 tablet 200 mg paludrine and 100 mg chloroquine, in a dosage of 1 a day.

The choice of these two drugs out of all other medicines (such as Camoquin® or Flavoquine®, Daraprim®, Maloprim® and Fansidar®) is motivated by the fact that they are very safe medicines that are sufficiently effective. All other drugs have a very small but real chance to cause serious and even mortal side effects. Although the prevention is not a total one, it is in our opinion the most optimal.

Nivaquine alone is still sufficient in a few malarial areas (a.o. North Africa and Central-America).

**MEFLOQUINE 250 mg per week (LARIAM®**, see further on) is part of the range of chemoprophylaxis, and if it is really necessary, it can be taken for months or even years. In some cases **DOXYCYCLINE 100 mg per day** is an option (can be taken for some months). **MALARONE® 250/100 mg daily** is beside Lariam a good prevention for malaria, there are no side effects and can be taken for about 28 days, and after leaving the malaria zone only 7 days to take instead 4 weeks; this can be very interesting for many seamen going in and out malaria zones during several months.

<b>Product</b>	<b>Dose</b>	<b>Start before departure</b>	<b>to take after the malaria zone</b>
<b>Nivaquine</b>	<b>300mg/week</b>	<b>1 week</b>	<b>4 weeks</b>
<b>Nivaquine and Paludrine</b>	<b>300mg/week and 200mg/day</b>	<b>1 week</b>	<b>4 weeks</b>
<b>Nivaquine and Paludrine</b>	<b>100mg/day and 200mg/day</b>	<b>1 week</b>	<b>4 weeks</b>
<b>Mefloquine</b>	<b>250mg/week</b>	<b>1 (at least) - 3 weeks</b>	<b>4 weeks</b>
<b>Doxycycline</b>	<b>100 mg/day</b>	<b>1 day</b>	<b>4 weeks</b>
<b>Malarone (atovaquone /proguanil)</b>	<b>250mg/100mg = 1 tablet/day</b>	<b>1 day</b>	<b>7 days</b>

## **Malaria Risk Areas for Seaman (not going into the hinterlands)**

- It can be stated that all port areas (ports and hinterland) of Africa, Asia, Central and South America

situated **between 25° NB and 25° SB** are **potentially contaminated**.

A high degree of **awareness** for the problem of malaria is needed, so in these regions the **possible need for preventive measures** should always be considered :

- 1) Protective measures against mosquito bites at night,
- 2) **Standby treatment** (also for the 3 month's after leaving an endemic region),
- 3) Probably (but certainly not always) **chemoprophylaxis** (which has to be continued for four weeks after leaving a malarious region, only seven days when taking Malarone™).

- The risk is often considerably less in coastal regions (seamen are not likely to travel in the country). This is not true in sub-Saharan Africa.

- The risk is often extremely low in the centre of urban areas (but not necessarily in the outskirts). This is certainly not true in Sub-Saharan Africa.

### **NORTH AFRICA**

Here the risk is very to extremely low in major cities.

No chemoprophylaxis indicated.

### **SUB-SAHARAN AFRICA**

- East Africa: from Port Sudan to Richard Bay (South Africa). However, the malaria risk on the Red Sea coast is very limited.
- West Africa : from Nouakchott (Mauritania) to the Kunene river (at the border of Namibia with Angola).

Here the risk is particularly high, chloroquine resistance is widespread and several fatalities occur annually. There are seasonal variations in the north and the south, but in general the risk exist throughout the whole year.

Chemoprophylaxis indicated = zone C = chloroquine + proguanil or mefloquine or Malarone™.  
Standby treatment if yet malaria attack

### **NEAR AND MIDDLE EAST, AND THE INDIAN SUBCONTINENT**

- In the ports of Iran, Pakistan, India, Bangladesh : the risk is present but variable, and chloroquine resistance present but usually moderate. Chemoprophylaxis indicated = zone B = chloroquine + proguanil.
- Colombo and Galle in Sri Lanka are malaria free.

### **SOUTH EAST ASIA**

- In the ports of Myanmar (Rangoon) the risk is probably substantial: chemoprophylaxis is indicated = zone C = mefloquine (Lariam) or Malarone™.
- Nivaquine-Paludrine combination is no longer active in the South East Asia and Oceania.
- The risk is not existent to very low in the major ports of Indonesia, Malaysia, Thailand and also in Manila: No chemoprophylaxis indicated.
- The risk is also low in the main ports of Vietnam and Cambodia. No chemoprophylaxis indicated, but attention should always be paid to the other preventive measures.

## OCEANIA

- The transmission of malaria is intense in Papua New Guinea, the Solomon Islands and Vanuatu; multiple drug resistance is a major problem in Papua New Guinea. Zone C.
- No malaria risk however in Kiribati.

## LATIN AMERICA

- From Mexico to the Panama Canal: benign forms of malaria only, very low risk; no chemoprophylaxis indicated but be alert.
- **No malaria risk in the Panama Canal itself, high risk in some areas inland.**
- Chloroquine resistance is present in some areas on the east coast : in South Panama, Columbia (only a small area), some areas in Venezuela (at the Orinoco-delta) and in British Guyana, and finally in Brazil (the coastal area north of Fortaleza);
- At the west coast it is present from South Panama to the north of Equator, plus at the border Ecuador-Peru; The risk is very low on the coast of the remainder of Ecuador and again very low on the coast of Peru.
- Hence, there is no risk at all in the coastal areas south from Fortaleza on the East Coast and south from the Ecuadorian-Peruvian Border on the West Coast (Malaria Map WHO 2000).

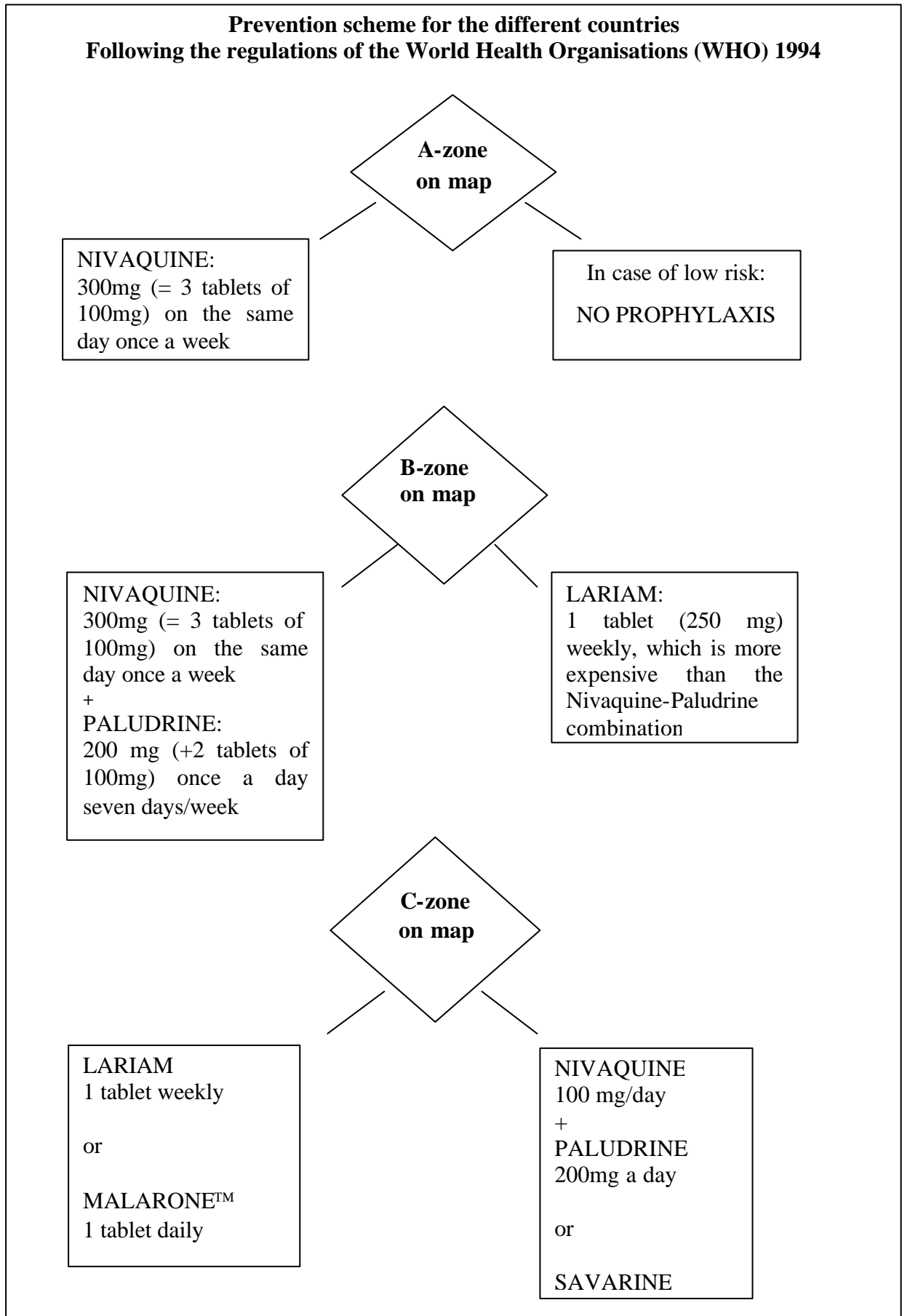
*Although the north of South-America is zone A on the WHO-map, WHO advises the intake of the combination chloroquine and paludrine (as in Zone B)!*

As the risk is generally not existent to low in most of the Latin American ports, no chemoprophylaxis is indicated. For Colombia and Equator special attention needs to be given as the risk for coastal falciparum malaria transmission is focally fairly high.

NOTE:

There is also a risk for seamen travelling by air to join the ship or repatriation when they make a stopover in infected malaria regions (especially when arriving at night in Sub-Saharan African airports).
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As many different areas may be visited during a trip, traversing zone A, B and C, the final advice about which malaria chemoprophylaxis to be taken for the whole route of travel need preferably to be decided in communication by an expert in the field of Travel Medicine.



## DOSES :

### I. CHLOROQUINE - PALUDRINE

#### A. ADULTS

##### ZONE B:

**Chloroquine (NIVAQUINE®):** 3 × 100 mg tablets to be taken at one time, once a week, e.g. on Sundays. If tablets of 250 mgr. Chloroquine use 2 × 250 mgr. weekly. It is best to take this medication in the course of the meals.

+

**Proguanil (PALUDRINE®):** 2 × 100 mg tablets a day at one time, after breakfast, this to prevent a malaria eruption in chloroquine resistant areas.

##### ZONE C: (when LARIAM was not taken)

**SAVARINE** (=100 mg Chloroquine + 200 mg Proguanil): 1 tablet daily

or daily 1 tablet Chloroquine (100 mg) + 2 tablets Proguanil (2 x 100 mg)

#### B. DOSES ADAPTED TO CHILDREN

**Chloroquine (NIVAQUINE®):** 5 mg per kg body weight a week, to be taken at one time

+

**Proguanil (PALUDRINE®):** 3-4 mg per kg body weight per day, at one time to be rounded off upwards.

	<b>Paludrine®</b>		<b>Nivaquine®</b>
WEIGHT	DAILY DOSE	WEIGHT	WEEKLY DOSE
	in mg/in 100 mg tabl.		in mg base/in 100 mg base tabl.
5-8 kg	0,25	5-6 kg	0,25
9-16 kg	0,5	7-10 kg	0,5
		11-14 kg	0,75
		15-18 kg	1
17-24 kg	0,75	19-24 kg	1,25
25-35 kg	1	25-35 kg	2
36-50 kg	1,5	36-50 kg	2,5
> 50 kg	2	> 50 kg	3

*"International Travel and Health - Vaccination requirements and health advice", WGO*

N.B. The chloroquine tablets have to be kept out of reach of children! Regularly fatal poisoning cases have been reported with children taking accidentally an overdose.

Some remarks concerning the functioning of these malaria medicines:

Chloroquine does not prevent a malaria infection, but acts upon the young parasites, that affect the red blood cells after they have matured in the liver. Therefore, it avoids that the malaria develops a real disease attack. Since chloroquine has a fast action, it can also be used as treatment, but in higher doses, at least in those cases where it is still effective (see further). Proguanil acts very slowly, and therefore it is only active preventively. Consequently, it can not be used to treat an attack.

### Side effects:

These medicines are very safe. Both can cause some stomach and intestinal discomfort. Nivaquine can also cause some complaints of slightly diminished visual acuity. Rarely itching and/or skin rash occurs. These discomforts cease after stopping medication.

After 5 years usage of Nivaquine with the above mentioned dosage, it is advisable to consult an ophthalmologist to detect possible irreversible eye damage in the early stage.

However, generally we can state that both medicines are very safe (certainly in comparison with others) and that possible side effects can be controlled.

Pregnant women definitely have to take medicines for malaria prevention. There isn't any contra-indication. The low dosage hasn't any disadvantageous effect. Contrarily, a possible malaria attack is much more dangerous for either the mother or the foetus.

## **II . LARIAM**

Mefloquine prophylaxis, if tolerated, may be taken for many months. The first dose should be taken one to three weeks before arrival in an endemic area. It means one week before for somebody who already took it and did tolerate it; start three weeks before for those who never took Lariam before (to prevent side effects as dizziness, excitability, insomnia, nightmares, over-anxiety or palpitations). Subsequent weekly doses should always be taken on the same day of the week and should be continued for four additional weeks after leaving an endemic area.

### Infants:

<b>Lariam®</b>	
<b>Weight</b>	<b>Weakly dose - Tablets of 250 mg</b>
<5 kg	Not given
5-12 kg	1/4 tablet a week
13-16 kg	1/3 tablet a week
17-24 kg	1/2 tablet a week
25-35 kg	3/4 tablet a week
>36 kg	1

*"International Travel and Health – Vaccination requirements and health advice", WGO*

Patients with a past history of psychiatric disturbances or convulsions should not be prescribed Lariam prophylactically neither for those with cardiac arrhythmia. Look further for notes on side effects of LARIAM/MEFLOQUINE.

Lariam is not given to pregnant women in their first trimester (hence, in certain circumstances it can be taken from the 4th month of pregnancy onwards) and also not to children with weight below 5 kg. Women that took Lariam as prevention or treatment, have to administer tight contraceptive measures for 3 months after the last intake.

### N.B.

The above explained malaria prevention aims predominantly at preventing a malaria attack by Plasmodium falciparum. There are other forms of malaria (by Plasmodium vivax, ovale, malariae), that eventually can lead to severe disease symptoms, but that can only be dangerous in very rare circumstances. Until now these forms of malaria are still sensitive to chloroquine, while sometimes they are insensitive to proguanil.

Therefore, also for this reason chloroquine continues to be useful as part of chemoprophylaxis in areas with chloroquine resistant malaria.

These 3 Plasmodium types can be responsible for late attacks or relapse of malaria, e.g. after return in the country of origin. In fact, the parasite can remain present for many months to years as a dormant form in the liver (*P. vivax*, *P. ovale*) or in the blood (*P. malariae*), before it can cause a new attack. When this occurs, the necessary treatment (3 days of chloroquine, followed by 14 days of primaquine) has to be initiated in a centre familiar with malaria treatment.

### III. MALARONE

Malarone™ is a combination of atovaquone 250 mg and proguanil 100 mg. It is well tolerated and very active for malaria prevention in WHO zone C.

Prevention doses:

#### **Adults and children over 40 kg:**

1 tablet daily to start 1 day before arriving in endemic malaria area. Always take the tablet at the same time and if possible together with a meal or a milky drink. After leaving the endemic malaria country, it is necessary to continue for 7 days with Malarone. Formerly it was believed that the maximum period to take the tablets was not longer than 28 days (+ 7 days after leaving the endemic area), but now it is considered safe to take them several weeks or months without complications.

In case of vomiting within 1 hour after taking the tablet, a new tablet has to be taken. Not to be used for pregnant women, or mothers with breastfeeding.

Malarone™ is a safe and well tolerated medication.

Malarone™ provides excellent prevention for seamen going in and out malaria zone C.

Contra indications:- Patients with insufficient kidney function cannot use this medication

- Patients taking medication like tetracycline, rifabutine, indinavir or metoclopramide (primperan, medication to prevent nausea and vomiting) cannot take this in combination with Malarone as it reduces the concentration of atovaquone in the blood.

In case adults or children change from another antimalarial drug to Malarone during the time they are in endemic malaria area, they have to take Malarone for 4 weeks (instead of 7 days).

**Children < 40 kg and >11 kg**

**For children > 12 kg a specific tablet of MALARONE JUNIOR is available**

Weight kg                      daily doses in tablets

<11 kg	not use
11- 20 kg	1 tablet Malarone Junior
21- 30 kg	2 tablets Malarone Junior
31- 40 kg	3 tablets Malarone Junior
>40 kg	1 tablet normal dosis Malarone

## **C. WHAT TO DO DURING A POSSIBLE MALARIA ATTACK**

### **STAND BY OR EMERGENCY TREATMENT!**

Every attack of fever longer than 24 hours (keep always a thermometer at hand!) occurring during or after a stay in an area where malaria is found, has to be considered as a malaria attack, until the contrary is proven, and needs a quick medical action.!!!

Nevertheless, many infectious diseases do start with similar symptoms (feeling of flu, with or without fever), which means that in case of fever also has to be thought on other infectious diseases. Try to have RADIO-MEDICAL contact in order to receive advice from a tropical doctor, and to discuss the treatment. Radio-medical contact is also important to prevent jurisdictional problems for captains and officers treating malaria patients.

A correct medication scheme shall be followed, if not, the patient may fall into coma and even die. Most of the ships have quinine or tetracycline or doxycycline on board.

When regularly chloroquine prevention has been taken, and when malaria is confirmed or very probable, the chance that we are dealing with a **CHLOROQUINE RESISTANT MALARIA** is very high. One has then the choice out of the following treatment schemes:

- A. MALARONE<sup>®</sup>**
- B. QUININE + TETRACYCLINE or DOXYCYCLINE**
- C. QUININE + FANSIDAR<sup>®</sup>**
- D. ARTEMETHER (PALUTHER<sup>®</sup>)**
- E. LARIAM<sup>®</sup>**
- F. HALFAN<sup>®</sup>**

These 6 schemes have been selected since their effectiveness approximates 100 %. Many other schemes are possible, but they are definitely less effective!

<b>SCHEME A</b>	<b>MALARONE<sup>®</sup></b>
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A new very active medicine which is used in case of non-complicated malaria is Malarone<sup>™</sup> (one tablet contains 2 active substances: 250 mg atovaquone + 100 mg proguanil) (about €43,38). One box contains 12 tablets, and an adult should take 4 tablets at once/day, for three days running at the same time, with some food. Not use for pregnant women. Sometimes the intake of this medicine can cause vomiting. For children (body weight > 11 kg) the dose must be adapted.

11-20 kg	1 tablet/day, during the next 3 days
21-30 kg	2 tablets/day at once, during the next 3 days
31-40 kg	3 tablets/day at once, during the next 3 days

<b>SCHEME B</b>	<b>QUININE + TETRACYCLINE / DOXYCYCLINE</b>
-----------------	---------------------------------------------

1.	Start with <b>QUININE</b> (mostly capsules of 500-mg quinine sulphate) or <b>QUINIMAX<sup>®</sup></b> (tablets of 100 mg,) every 8 hours. This means for an average adult <u>3 tablets of 500 mg quinine or 3 x 7 tablets of 100 mg Quinimax per day</u> (1 tablet of 100 mg contains only 70 mg active quinine). Same dosage to continue <b>for 4 days</b> . When fever drops slowly, it is advisable to continue quinine for another 3 days, 1 capsule every 12 hours. In Southeast Asia one has to take quinine for 7 days.
2.	At the same time, start with (in case retching or vomiting are present, postpone this part of the treatment until third day) : <ul style="list-style-type: none"> <li>- Either <b>TETRACYCLINE</b> 20 mg/kg (max. <u>3 x 500 mg/day</u>) for 7 days.</li> <li>- Or <b>DOXYCYCLINE</b> (VIBRAMYCIN, VIBRATAB or DOXYLETTS) <u>2 tablets of 100 mg (=3.5 mg/kg) the 1<sup>st</sup> day, followed by 1 tablet of 100 mg (= 2 mg /kg) per day during the next 6 days.</u></li> </ul>

<b>This scheme is actually the most effective (and still 100% effective in Africa !)</b>
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The adjustment of dosage for children above 8 years is according to the body weight (quinine: identical scheme as for adults; 10 mg/kg every 8 hours).

In case the medication is vomited, quinine = **QUINIMAX<sup>®</sup>** shall be injected intramuscularly (in the femoral muscle) every 8 hours (3 injections a day); this during 4 days.

Tetracycline and doxycycline alone as antimalarial drugs are too weak. Therefore, they always have to be combined with quinine.

On the other hand, when a malaria attack is treated solely with quinine (e.g. by injecting **QUINIMAX<sup>®</sup>** ) there is always a real chance of relapses of malaria later on, because it is not always possible to eradicate the last parasite. Therefore, a combination of quinine with tetracycline of Fansidar is preferred.

Taking of tetracycline or doxycycline can cause hypersensitivity reactions, when exposed to sunlight. Therefore, be careful with direct exposure to sunlight.

Tetracycline and Doxycycline are not recommended for children under the age of 8 years or during pregnancy (because of possible discoloration of teeth). In case of Fansidar-resistance or sulfamide-allergy and unavailability of mefloquine, quinine can with this group be continued for 7 days, followed by correct chemoprophylaxis. When the malaria attack is being treated with quinine only (e.g. only **QUINIMAX<sup>®</sup>** injections), there is always a small chance for later relapse, since all parasites are not always eradicated.

Infants can be administered quinine drops (see scheme I).



<b>SCHEME C</b>	<b>QUININE + FANSIDAR®</b>
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- |    |                                                                                   |
|----|-----------------------------------------------------------------------------------|
| 1. | Start with <b>QUININE</b> or <b>QUINIMAX®</b> for at least 4 days as in scheme B. |
| 2. | On the 3rd day <b>FANSIDAR®</b> has to be taken, 3 tablets at once                |

When the fever decreases slowly, it is recommendable to take quinine a few days longer (up to 7 days).

With children the adaptation of the dose of **Fansidar®** is to be made as follows (in function of the body weight):

< 10 kg	½ tablet
10-20 kg	1 tablet
20-30 kg	1 ½ tablet
30-50 kg	2 tablets
>50 kg	3 tablets

Infants from 0 - 2 months shall not be given **Fansidar®**.

Such infants can be given quinine drops in a dose of 10 mg (= 1 drop) per kilogram every 8 hours (= 3 x a day) during 7 days (the indicated dose shall not be exceeded).

The prescription is as follows:

- R/ Quinine bichlorhydrate 6 g  
 Natrium metabisulfite 15 mg  
 Aqua ad 30 ml in brown coloured vial  
 To be renewed two times
- S/ one drop per kg, per day (with a dropper of 20 drops per ml).

A vial with concentrated quinine solution contains 30 ml and each drop contains 10 mg quinine. One drop per kg body weight is administered three times a day (e.g. ± 4 kg = 4 drop, ± 5 kg = 5 drops, etc.). After opening a vial can be kept for three months; a sealed vial can be preserved for maximum one year.

These drops can also be used for the prevention of a malaria attack during the first three months of life. However, we repeat that the most important preventive measure for infants is the correct use of a mosquito net.

**Fansidar®** shall only be taken when it is well known that there doesn't exist an allergy for Sulfamides. When only a slight, uncomplicated malaria attack is concerned, a treatment exclusively with **Fansidar®** can be started. However, one shall take into account that in most cases there will pass still one to two days before the effect of **Fansidar®** is clearly noticeable. This is the main reason why **Fansidar®** should be combined with quinine especially when the symptoms of the disease are clearly noticeable.

When there are some **alarming symptoms**, e.g. fever for longer than 3 days, dark coloured urine, jaundice or diminished consciousness, hospitalisation is necessary as quickly as possible.

The areas where **Fansidar®**-resistance has been signalled are growing! Especially in South East Asia, where **Fansidar** should not be used.

**NB. TREATMENT DURING PREGNANCY:**

- + During the first trimester and during the last weeks of the pregnancy: quinine, 3 x per day, for 7 days.
- + During the second trimester of the pregnancy malaria can be treated either with quinine alone (for 7 days) or with scheme C (**Fansidar/Metakelfin** is not contra-indicated during this period).

<b>SCHEME D</b>	<b>ARTEMETHER : PALUTHER®</b>
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The new medicine ARTEMISININ and derivatives of it (e.g. Artenam ®, Riamet ®) are currently available in many countries in the Far East (e.g. Vietnam, Thailand and Myanmar), and also in several countries in sub-Saharan Africa. This very effective medicine can replace quinine in the different above-mentioned combinations for treatment of resistant malaria.

The initial dose of Artenam® is 6 tablets of 50 mg the first day, followed by 2 tablets per day during the next 4 days. When the medicine is used alone, there is a small risk for relapse. Therefore, (especially in the Far East) the combination with doxycycline or even mefloquine, as with quinine, is recommended.

<b>Injectable form = ARTEMETHER : PALUTHER® : pack of 6 ampoules of 1 ml = 80 mg.</b>
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Adults: 2 ampoules by IM infection on day 1, followed by 1 ampoule IM daily the next 4 days (the instructions mention the correct dose for children).
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<b>SCHEME E</b>	<b>LARIAM®</b>
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**LARIAM®** (mefloquine tablets of 50 mg and 250 mg).

Only intake by mouth is possible : so only for uncomplicated malaria.

To be taken in a single dose of 25 mg/kg, spread over 3 intakes every 8 hours (respectively 12,5 - 7,5 - 5 mg/kg).

This means for average adult respectively 3 tablets of 250 mg - 2 tablets of 250 mg - 1 tablet of 250 mg, with intervals of 8 hours in between. The maximum total dose amounts to 1500 mg (6 tablets of 250 mg).

The child dose shall be adapted in proportion to the body weight.

For children the dosage adjustment is in function of the body weight: 12,5 mg per kg, followed by 7,5 mg per kg, followed by 5 mg per kg, with every time 8 hours in between.

After intake of mefloquine the fever does not disappear immediately, but can still continue for approximately 3 days. In case of serious illness, or high risk of vomiting medication, it is advisable to start for a few days with QUININE (as in scheme B, preferably intravenously or intramuscularly), and to continue with mefloquine only 12 hours after the last quinine intake (this in contrast with Fansidar/Metakelfin, that can be taken together with quinine).

Mefloquine can have very annoying side-effects (gastro-intestinal disorders, dizziness, sleeplessness). The World Health Organisation advises for an adult, who takes Lariam as emergency treatment according to his own initiative, the following dosage: 2 tablets of 250 mg, followed by 2 tablets of 250 mg after 8 hours. This dosage is smaller than the one mentioned on the guide in the packing! This dosage is adjusted because Lariam often has unpleasant side effects (gastro-intestinal discomfort, dizziness, anxiety and insomnia), that sometimes are very explicitly and cause the already ill person to panic. These side effects would occur less frequent with a reduced dosage. According to us, there are enough reasons not to take Lariam as self-medication, when no adequate medical support is possible.

<b>SCHEME F</b>	<b>HALFAN®</b>
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**HALFAN®** (halofantrine tablets of 250 mg, 6 in 1 box; or in syrup: 100 mg per 5 ml, 45 ml). Only intake by mouth is possible : so only for uncomplicated malaria.

For adults and children weighing more than 40 kg (80 pd.): a total of 6 tablets, given as 2 tablets at 6-hourly intervals. A second course of halofantrine is recommended one week after the first course. For children, a liquid form is available (the instructions mention the correct dose for children).

Adverse reactions : Halfan is generally well tolerated. Abdominal pain, diarrhoea, pruritus and skin rash have been reported.

Recent reports have alerted that the administration of Halfan has been very rarely associated with deadly cardiac rhythm disturbances.

The WHO advises : Halfan can only be used as an emergency presumptive therapy of malaria if an electrocardiogram in the recent past was normal (normal so called "Q-T interval"). Halfan can only be administrated safely if no Lariam (in the last four weeks) nor Quinine (in the last 24 hours) has been taken, as well as a number of other medications such as medications for arrhythmia, anti-depressants, anti-histaminica like Triludan®, certain antibiotics like Erythromycine®, diuretics like Lasix® and other. Therefore it is recommended not to take Halfan® in combination with other medicines, of one is not sure that the combination is safe. On the other hand Halfan is very valuable as a well-tolerated and effective self-treatment of resistant malaria, which permits us to appreciate it for its advantages, even when it involves some risks.

Halofantrine is only used for treatment, not for prevention.

<b>NB. CHLOROQUINE ALONE</b>
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In case you are staying in zone A (only Central America + Mediterranean regions) and you have not taken any preventive drug, you can decide to treat the malaria exclusively with **CHLOROQUINE**. However, it is of utmost importance to do this in a correct manner: 25-mg/kg body weight in three days time, not shorter and not longer.

	Adults		Children
	tablets of 100 mg	tablets of 150 mg (Tanzania)	
day 1	6 tablets at once 3 tablets after 8 hours	4 tablets at once 2 tablets after 8 hours	10 mg/kg
day 2	3 tablets	2 tablets	10 mg/kg
day 3	3 tablets	2 tablets	5 mg/kg

When after 3 days there is no effect of chloroquine, resistance has to be considered. When relapse of the disease symptoms occurs and/or malaria symptoms persist, within 3 to 4 weeks, one has also to consider that the original malaria parasite was not eradicated and that it has developed (partial) resistance against chloroquine (also this is sometimes seen after Fansidar). Sometimes, because of the half-effective chloroquine or Fansidar, the symptoms of malaria are much less clearly recognisable (e.g. low fever, headache, tiredness).

In all these situations it is important not longer to treat with chloroquine, but immediately change to A, B, C, D, E or F.

Once infected with a chloroquine resistant malaria parasite, does not mean that during the next malaria infection again resistance will occur. Resistance against chloroquine or another antimalarial has nothing to do with the infected person, but depends entirely on the malaria parasite present at that moment.

Closing remarks:

The prevention and knowledge on the correct treatment of malaria remains a necessity for every seaman and countryman.

We realise that so far there isn't any scheme offering a 100 % protection against the four parasites.

In many occasions contradicting advice is given about malaria, as well as advice by doctors and malaria specialists as well meant advice in the immediate environment by people who stay already a long time in the tropics.

This information brochure aims to list the current practical knowledge and to offer a logical approach. Do discuss the content of this brochure in any case with your treating doctors, and pass this information to others.

Since the situation continuously changes, there are many unsolved questions. This explains also why during the last 10 years advice had to be updated continuously, and it still will change in the future. In the near future new drugs and new combinations shall have to be taken to protect oneself from malaria.

We hope a vaccine will be available in the future, but there is still a long way to go!

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## APPENDIX

### NAMES OF MALARIA-MEDICATIONS AND SIDE-EFFECTS

What follows is a list of all malaria medication available all over the world. The problem is that most of the sailors are overwhelmed by different names and can not distinguish between prevention and treatment. Most of these medications are not for immediate use on board the ships. The first group is a list with names **for medication and side-effects** for direct use on board. Secondly, there is a list with names that are only for **indirect use**, and should therefore not be ordered immediately to the ship-chandler.

NB.

Beware of the dangerous use of homeopathic drugs, which aren't active and may be the reason of lethal evolution.

#### GROUP 1

##### 1. CHLOROQUINE

**Nivaquine - Resochin - Avlochlor - Aralen - Chloroquine FNA - Chloroquine - Cidanchin - Delagil - Dichinalex - Crokinfosfat - Lagaquin - Malarex - Malarivon - Malatets - Aralis - Savarine** (+ paludrine)

Chloroquine is the most popular medication for malaria prevention and treatment.

Weekly doses of 300 mg., always on the same day of each week.

The tablets are available in 100 mg. or 250 mg.

A dose of 300 mg. weekly cannot cause eye-problems. However, there can be eye-problems if a very high dose is taken over a very long period.

Other side effects can be:

- accommodation problems of the eye
- itching frequent with black skin (then give antihistamine)
- dizziness
- sometimes headache
- gastro- intestinal problems
- nausea
- diarrhoea
- very rare psychotic problems, anxiety, personality change

In selected cases it is used for treatment of rheumatoid arthritis (in high dosage).

Can be taken during pregnancy.

##### 3. SAVARINE®

= 100 mg chloroquine + 200 mg proguanil: once daily. Only prevention!

##### 2. PROGUANIL

**Paludrine**

**Savarine®** (+ chloroquine)

- Very useful for malaria prevention in combination with chloroquine in multi-drug resistance regions (Zone B - C)

- Good resorption.

- Daily doses of 200 mg. = 2 tablets of 100 mg or 1 tablet Savarine ® daily

- In the recommended doses no side effects

- Can be taken during pregnancy; the same for chloroquine

- In combination with chloroquine, Paludrine is a very useful drug in maritime malaria prevention.

### 3. QUININE

**Adaquine - Biquin - Biquinate - Chinine - Dentogel - Grisotets - Kinin- Myoquiun - Quinate - Quinbisal - Quindan - Quinoctal - Quinsana - Quinsul - Quiphile - Quinbisal - Quinbisul - Quine - Quinoforme - Quiphile.**

Quinine is orally used for uncomplicated attacks of *Plasmodium falciparum* due to chloroquine or multidrug resistance strains, and parenterally (Intravenous by infusion) for severe or complicated malaria.

- Normally available in tablets of 500 mg.(see Scheme A,B)
- rapidly acting

Side effects:

- bitter taste
- tinnitus (ears)
- nausea
- vomiting
- gastritis
- mild form of disturbed vision
- abdominal pain
- fever
- itching
- rashes on skin
- hearing loss (temporarily)
- not to associate with digitalis
- some patients are allergic to quinine and have immediate adverse effects symptoms

**Quinimax ®** = equivalent of quinine, but 100 mg Quinimax ® = 70 mg quinine! (see scheme A,B)

### 4. MEFLOQUINE

**Lariam, Mephaquin, Eloquine 250**

Lariam in doses of 250 mg. (tablets) is recommended in most areas of the world where chloroquine-resistance has been noticed. Strongly recommended in Zone C.

- Not to take during the three first months of pregnancy; also avoid pregnancy for three months after stopping Lariam.
- Lariam can no longer be recommended for prophylaxis along the borders of Thailand with Cambodia or Burma, because mefloquine resistant strains of *Plasmodium falciparum* are very common in those areas. In this area daily use of one tablet (= 100 mg. doxycycline) or Malarone™ is recommended.

Side effects:

- Normally about 70-90 % percent well tolerated at normal doses of one tablet of 250 mg. weekly.
- in about 30 percent adverse effects (mostly mild) with:
  - nausea
  - dizziness
  - vertigo
  - diarrhoea
  - vomiting
  - abdominal pain
  - not to be given to patients with a psychiatric past or depression
  - skin rashes
  - very rare bradycardia without symptoms (slow rhythm of the heart)

- Patients with kidney - renal or liver dysfunction should not take Lariam.
- Patients who take medication:
  - quinine
  - beta blockers
  - digitalis
 should not take LARIAM in combination with these medication, especially if used for cardiac arrhythmia's.

**- Fansimef**

Isa multi-ingredient preparation containing mefloquine and Fansidar.  
Fansidar forms a combination of pyrimethamine with sulfadoxine.

**5. DOXYCYCLINE**

**Dagramycine, Doxy-100, Doxyfim, Doxilets, Doxymycine, Doxytab, Logamycil, Roxyne, Unidox, Vibramycin, Vibratab.**

- Doxycycline is an effective drug for adequate protection of chloroquine resistance falciparum malaria
- 100 mg. = 1 tablet daily
- not during pregnancy or early childhood
- Doxycycline must be taken when seated in combination with a large quantity of liquid or during the meals.
- side-effect:
  - photosensitivity, just like other tetracyclines
  - Doxycycline may be the cause of fototoxicity and fungal infections in the mouth or genitals.
  - very rarely nausea: vomiting diarrhoea
- The combination of doxycycline with quinine is very useful on board for treatment of acute malaria crisis.

**OTHER ANTIBIOTICS**

- Tetracyclines: also effective against multi drug resistant strains of Plasmodium falciparum

**6. HALOFANTRINE**

**Halfan**

- antimalaria drug useful for treatment of symptoms of acute malaria crisis in areas with resistance of Plasmodium falciparum to chloroquine, paludrine and possibly Lariam prophylaxis
- very quick medical result without any side-effects
- normal 500 mg, repeat after 6 or 12 hours
- not to be taken use together with meals
- most effective on empty stomach
- many times used as "stand by" treatment for travellers in tropical countries
- people with heartproblems should not take Halfan, therefore it is recommended to ask for electrocardiogram before using Halfan, to detect heart problems
- using mefloquine or quinine tablets in combination with Halfan is not allowed.
- when breakthrough malaria under mefloquine prophylaxis (once a week lariam) treatment with Halfan treatment is not allowed due to cross-resistance.
- Halfan is not used as a preventive drug for malaria.
- Halfan can be very useful for treatment of maritime malaria when the patient has no heart problems.

## **7. ARTEMISININ (QING HAO SU) + PALUTHER®**

- originating from a plant (Asia - China)
- very useful in treatment for cerebral malaria, active against chloroquine resistant and chloroquine sensitive of Plasmodium falciparum and Plasmodium vivax
- at present only used in tropical hospitals for treatment; not for prevention on board
- there is a semisynthetic derivation of artemisinin: **Artemether, Paluther, Arteminth.**  
It is more effective than quinine in quinine resistant regions, but no MARITIME PORTS in Thailand = no danger of malaria. It is easy to take without side effects
- can be bought in different doses on the Asiatic markets: China, Thailand, Vietnam
- it is recommended to use artemisinin only for treatment and not for prevention of malaria, for correct treatment of acute malaria see the above mentioned notes on quinine and doxycycline.
- a very important advantage is the rapid effect on the symptoms of malaria but in monotherapy (only artemisinin) frequent recidives.
- probably the first choice for the treatment of cerebral malaria. On board, however, it is better to use quinine with doxycycline or tetracycline.
- at the moment on the market in tablets suppositories and ampuls for intramuscular injections (**PALUTHER®**)
- the combination of artemether with mefloquine is probably more effective.

## **8. MALARONE Ô**

Atovaquone 250 mg + Paludrine 100 mg in one tablet

Dose for treatment : 4 tablets a day in one gift, for 3 days

Dose for prevention: 1 tablet daily, start 1 day before arrival in endemic malaria area, continue during stay in malaria endemic zone, and after leaving malaria zone till 7 days; not for pregnant women or patients with insufficient kidney function. Sometimes patients with light symptoms of headache, abdominal pain or vomiting. The normal period of taking this tablet is about 36 days, but in the future this period will be longer without any problem.

## **GROUP 2**

### **1. PRIMAQUINE - QUINOCIDE**

This medication is not for prevention or treatment, but it is only used to prevent relapse of Plasmodium ovale and Plasmodium vivax malaria. It can only be taken by prescription from a doctor.

### **2. MEPACRINE**

#### **Atebrine, Quinacrine**

- was formally used for suppression and treatment of malaria (100 mg daily)
- no more useful for prevention and treatment of malaria.
- but it still used for treatment of Giardia lamblia.

### **3. PYRIMETHAMINE**

#### **Daraprim, Erbapreline (Italy), Pirimecidan (Spain), Tindurin (Hungary)**

- anti-malaria drug
- tablets of 25 mg, normal doses at weekly bases
- at present there is resistance of Plasmodium falciparum against Daraprim.
- no more useful for maritime malaria prevention
- multi drug combinations containing pyrimethamine

**Fansidar:** pyrimethamine 25 mg + sulfadoxine 500 mg

**Maloprim:** pyrimethamine 12,5 mg + dapsone 100 mg

**Fansimef:** fansidar + mefloquine.

### **4. PYRIMETHAMINE + SULFADOXINE**

#### **Fansidar**

- normal doses are once a week
- multi resistance strains of Plasmodium malaria for fansidar
- long acting Sulfamide with serious skin and mucosa lesions (Stevens - Johnsons; Lyell syndrome) to people who are allergic to Sulfamides.
- be very careful with patients who are allergic to Sulfamides
- combination of pyrimethamine 25 mg + sulfadoxine 500 mg
- curative doses: 3 tablets at once

### **5. PYRIMETHAMINE + DAPSONE**

#### **Maloprim**

- combination of pyrimethamine 12,5 mg + dapsone 100 mg
- is -and was- used for prophylaxis of malaria
- one a week
- not very effective anymore, and therefore not recommended in malaria prophylaxis

### **6. PYRIMETHAMINE + SULFADOXINE**

#### **Dapsone**

- combination of pyrimethamine + sulfadoxine
- sometimes very serious side-effects, even death, due to allergy to Sulfamides

## **7. HYDROXYCHLOROQUINE SULPHATE**

### **Plaquenil**

- antimalaria prevention effect similar to chloroquine
- tablets 200 mg
- is mainly used in the treatment of
  - rheumatoid arthritis
  - lupus erythematosus (immunology diseases)
- not useful for maritime malaria prevention

## **8. CHLORPROGUANIL HYDROCHLORIDE**

### **Lapudrine**

- antimalaria drug similar to proguanil (paludrine)

## **9. CYCLOGUANIL EMBOLAT**

### **Camolar**

- similar actions and use as proguanil (paludrine)
- only available in injections

## **10. AMODIAQUINE HYDROCHLORIDE**

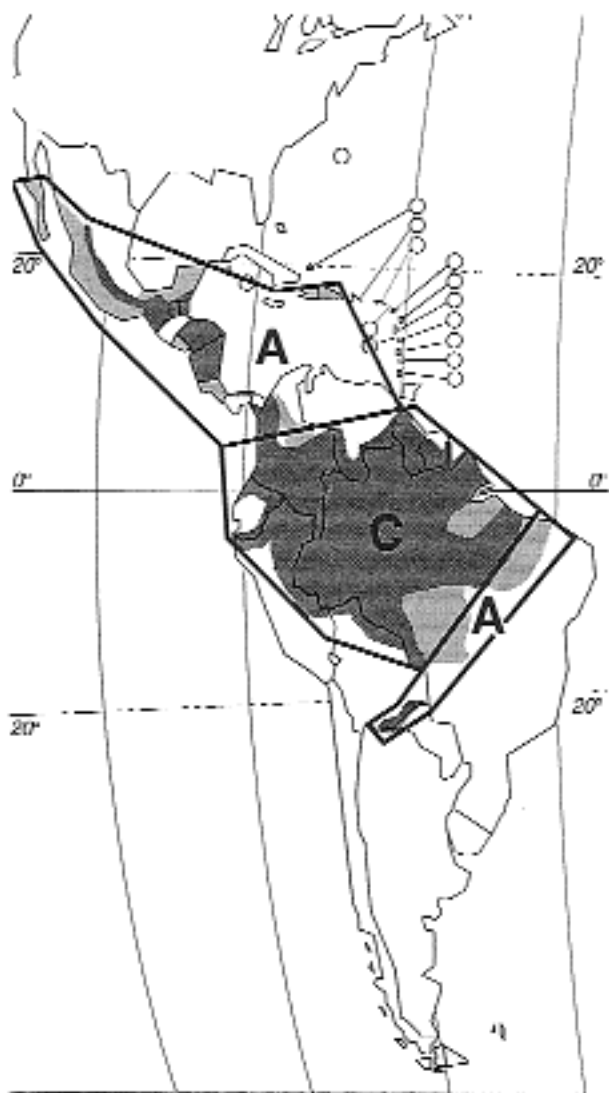
### **Camoquin, Basoquin, Flavoquine**

- antimalarial drug similar to chloroquine
- but due to serious side-effects on blood composition (agranulocytosis) and on the liver function (hepatitis) it is recommended to take chloroquine (Nivaquine)
- tablets of 200 mg.

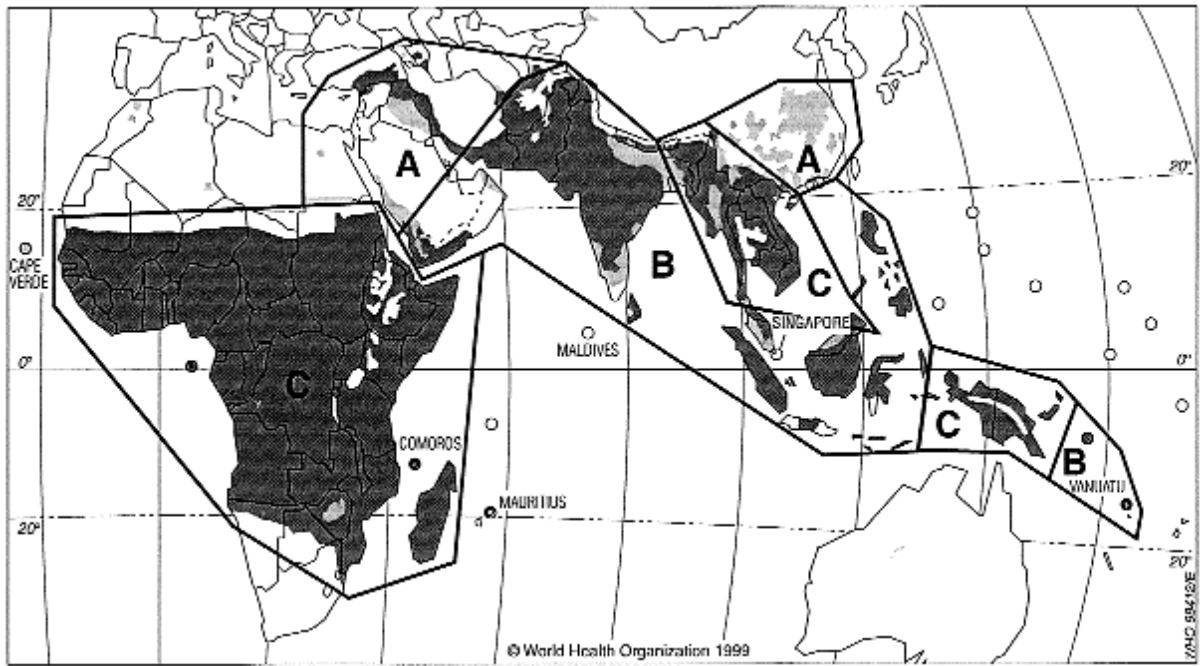
## **11. QUINOCIDE HYDROCHLORIDE**

### **Totaquine**

- same effect on malaria as primaquine.
- not useful for maritime malaria treatment and prevention



- Areas in which malaria has disappeared, been eradicated or never existed
- Areas with limited risk
- Areas where malaria transmission occurs



- Areas in which malaria has disappeared, been eradicated or never existed
- Areas with limited risk
- Areas where malaria transmission occurs

*courtesy of*  GlaxoSmithKline