

AEROMEDICAL FLYER

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The notion that “international” categories are the only crews exposed to yellow fever and malaria is long gone. Airlines are flying narrow-body aircraft, previously used solely for domestic operations, to areas where malaria and yellow fever are a real concern. In this edition of the *Aeromedical Flyer*, IFALPA provides excellent articles about both illnesses.

Even if you consistently practice all the personal protection measures mentioned here, there is still a chance you could contract malaria or yellow fever, so you need to be aware of their symptoms and how to respond to them. The Centers for Disease Control and Prevention (CDC) also has very extensive information covering these diseases, and I highly recommend that you browse its website (www.cdc.gov).

Remember, you should discuss your concerns with your physician. Your physician is the appropriate person to evaluate your medical condition and make treatment recommendations. Talk to him/her about your international travel to areas that may include destinations with intense malaria or yellow fever transmission.

And finally, to maintain possible Workers' Compensation benefits, don't forget to file an on-the-job accident claim as soon as possible if you believe your illness is work-related.

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Fly Safe! Stay Healthy!

Yellow Fever Information for Pilots

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Introduction

Yellow fever has been known for over 400 years, and the name originates from the jaundice that some patients may acquire. The disease is caused by a mosquito-spread virus. The virus is able to infect both humans and monkeys. The virus is endemic in African and American countries close to the equator. Most of those infected remain asymptomatic, but about 15% develop a hemorrhagic infection, and about half of these patients die. The symptoms are fever, muscular pain, headache, chills, loss of appetite, nausea and/or vomiting, and often a low pulse rate despite the fever. There is no specific treatment for the virus. Yellow fever vaccination is effective and one of the rare vaccinations that may be required to enter some countries. It is suggested that all pilots who fly to or over the endemic yellow fever countries take this vaccination. The vaccination is effective for 10 years, after which a booster is required.



Types of transmission for yellow fever:

- *sylvatic*
- *intermediate*
- *urban*

Virus

Yellow fever virus belongs to the flavivirus group. The virus infects both humans and monkeys and is carried from one animal to another by a biting mosquito. Mosquitoes are also able to pass the virus via infected eggs to their offspring, and thus the mosquitoes are the true reservoir of the virus. The mosquitoes bite during daylight hours and at altitudes up to 2,500 meters.

Epidemics

The virus is constantly present with low levels of infection (i.e., endemic) in some tropical areas of Africa and the Americas, but this viral presence can amplify into epidemics. There are 200,000 estimated cases of yellow fever (with 30,000 deaths) per year. However, due to underreporting, only a small percentage of these cases are identified. Small numbers of imported cases also occur in countries free of yellow fever. Although yellow fever has never been reported from Asia, this region is at risk because the appropriate primates and mosquitoes are present.

Transmission

There are three types of transmission cycle for yellow fever: sylvatic, intermediate, and urban. All three cycles exist in Africa, but in South America, only sylvatic and urban yellow fever occur.

Sylvatic (or jungle) yellow fever: In tropical rainforests, yellow fever occurs in monkeys that are infected by wild mosquitoes. The infected monkeys can then pass the virus on to other mosquitoes that feed on them. These infected wild mosquitoes bite humans entering the forest, resulting in sporadic cases of yellow fever. The majority of cases are young men working in the forest (logging, etc.). On occasion, the virus spreads beyond the affected individual.

Intermediate yellow fever: In humid or semi-humid savannahs of Africa, small-scale epidemics occur. These behave differently from urban epidemics; many separate villages in an area suffer cases simultaneously, but fewer people die from infection. Semidomestic mosquitoes infect both monkey and human hosts. This area is often called the "zone of emergence," where increased contact between man and infected mosquito leads to disease. This is the most common type of outbreak seen in recent decades in Africa. It can shift to a more severe urban-type epidemic if the infection is carried into a suitable environment (with the presence of domestic mosquitoes and unvaccinated humans).

Urban yellow fever: Large epidemics can occur when migrants introduce the virus into areas with high human-population density. Domestic mosquitoes (of one species, *Aedes aegypti*) carry the virus from person to person; no monkeys are involved in transmission. These outbreaks tend to spread outwards from one source to cover a wide area.

Geography

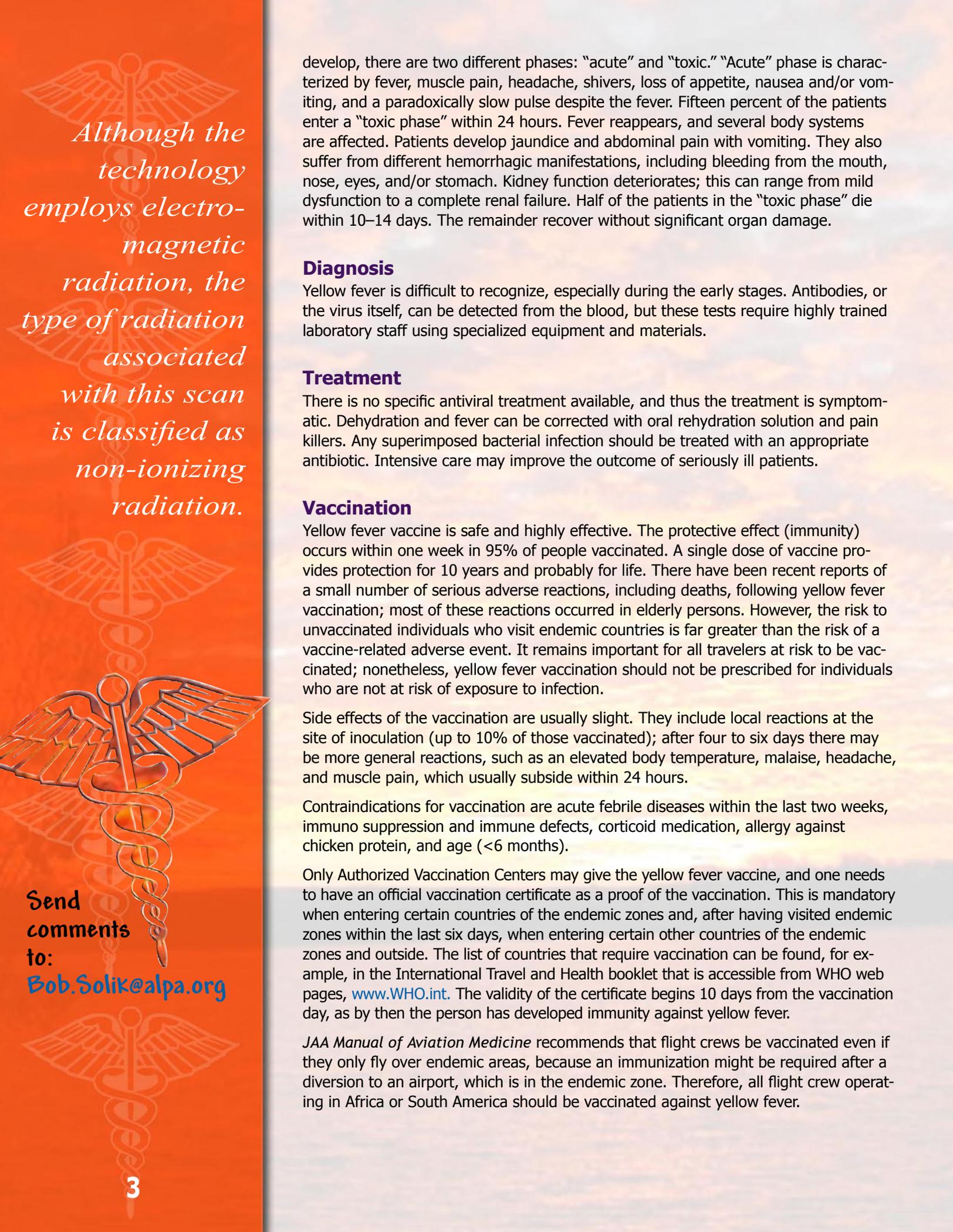
In Africa, yellow fever exists in countries within a band from 15°N to 10°S of the equator. In the Americas, yellow fever is endemic in nine South American countries and in several Caribbean islands. Bolivia, Brazil, Colombia, Ecuador, and Peru are considered at greatest risk. See Fig 1.

Symptoms

The incubation period (i.e., the time in which the symptoms develop) is three to six days, and most of the infections seem to be asymptomatic. However, if the symptoms



Figure 1: According to World Health Organization data, the countries shaded in yellow are considered to offer the greatest risk of infection.



Although the technology employs electromagnetic radiation, the type of radiation associated with this scan is classified as non-ionizing radiation.

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develop, there are two different phases: "acute" and "toxic." "Acute" phase is characterized by fever, muscle pain, headache, shivers, loss of appetite, nausea and/or vomiting, and a paradoxically slow pulse despite the fever. Fifteen percent of the patients enter a "toxic phase" within 24 hours. Fever reappears, and several body systems are affected. Patients develop jaundice and abdominal pain with vomiting. They also suffer from different hemorrhagic manifestations, including bleeding from the mouth, nose, eyes, and/or stomach. Kidney function deteriorates; this can range from mild dysfunction to a complete renal failure. Half of the patients in the "toxic phase" die within 10–14 days. The remainder recover without significant organ damage.

Diagnosis

Yellow fever is difficult to recognize, especially during the early stages. Antibodies, or the virus itself, can be detected from the blood, but these tests require highly trained laboratory staff using specialized equipment and materials.

Treatment

There is no specific antiviral treatment available, and thus the treatment is symptomatic. Dehydration and fever can be corrected with oral rehydration solution and pain killers. Any superimposed bacterial infection should be treated with an appropriate antibiotic. Intensive care may improve the outcome of seriously ill patients.

Vaccination

Yellow fever vaccine is safe and highly effective. The protective effect (immunity) occurs within one week in 95% of people vaccinated. A single dose of vaccine provides protection for 10 years and probably for life. There have been recent reports of a small number of serious adverse reactions, including deaths, following yellow fever vaccination; most of these reactions occurred in elderly persons. However, the risk to unvaccinated individuals who visit endemic countries is far greater than the risk of a vaccine-related adverse event. It remains important for all travelers at risk to be vaccinated; nonetheless, yellow fever vaccination should not be prescribed for individuals who are not at risk of exposure to infection.

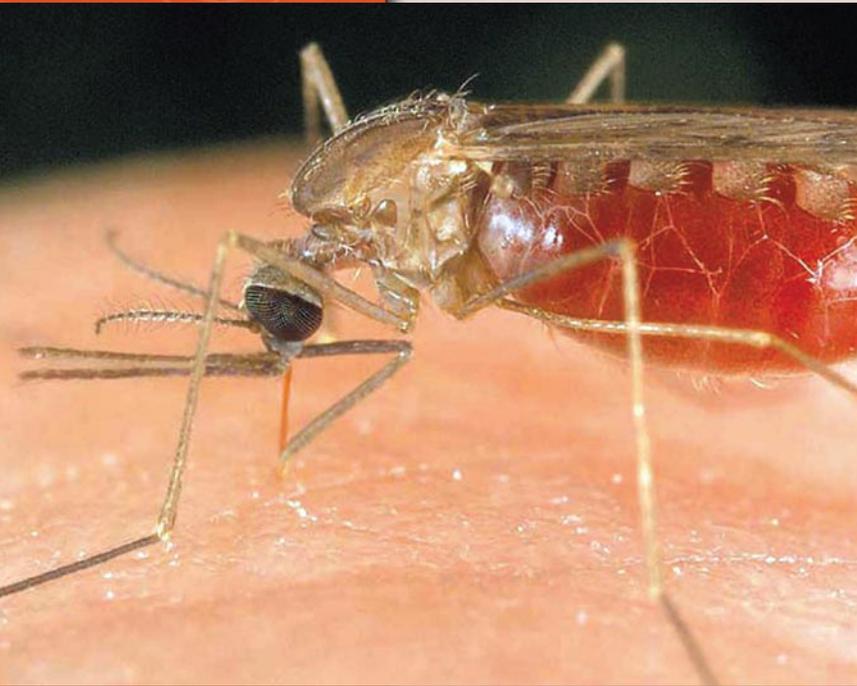
Side effects of the vaccination are usually slight. They include local reactions at the site of inoculation (up to 10% of those vaccinated); after four to six days there may be more general reactions, such as an elevated body temperature, malaise, headache, and muscle pain, which usually subside within 24 hours.

Contraindications for vaccination are acute febrile diseases within the last two weeks, immuno suppression and immune defects, corticoid medication, allergy against chicken protein, and age (<6 months).

Only Authorized Vaccination Centers may give the yellow fever vaccine, and one needs to have an official vaccination certificate as a proof of the vaccination. This is mandatory when entering certain countries of the endemic zones and, after having visited endemic zones within the last six days, when entering certain other countries of the endemic zones and outside. The list of countries that require vaccination can be found, for example, in the International Travel and Health booklet that is accessible from WHO web pages, www.WHO.int. The validity of the certificate begins 10 days from the vaccination day, as by then the person has developed immunity against yellow fever.

JAA Manual of Aviation Medicine recommends that flight crews be vaccinated even if they only fly over endemic areas, because an immunization might be required after a diversion to an airport, which is in the endemic zone. Therefore, all flight crew operating in Africa or South America should be vaccinated against yellow fever.

Malaria Information for Pilots



In sub-Saharan Africa over 90% of human malaria infections are due to P. falciparum infection.

Executive Summary

Malaria is a common and life-threatening disease in many tropical and subtropical countries. Malaria is transmitted to humans by the bite of an infected female anopheles mosquito. P. falciparum is the only species associated with severe morbidity and mortality. In sub-Saharan Africa over 90% of human malaria infections are due to P. falciparum infection. The other three species cause milder illness; however, infections with P. ovale and P. vivax may relapse months later if appropriate treatment is not provided. Mixed infections involving more than one species may also occur.

Clinical presentation and diagnosis

Symptoms and signs of malaria may present as early as seven days after exposure, with a usual range of 10–21 days elapsing after being bitten by an infected mosquito. Longer incubation periods may occur in patients who have been on chemoprophylaxis or selected antibiotics.

The diagnosis and management of malaria is urgent. Delayed diagnosis and inappropriate treatment are associated with significantly increased morbidity and mortality. Classically, malaria presents with fever, rigors, headache, and body pains, but the clinical features are nonspecific and may be confused with many other diseases, especially influenza. Malaria should be suspected in any person presenting with any of the above symptoms who has a history of travel to, or residence in, a malaria transmission area. It is therefore vitally important to inform your physician about your history of travel.

Malaria – The Disease

Human malaria is an infectious disease caused by four species of Plasmodium parasite:

- Plasmodium falciparum (P. falciparum)
- Plasmodium malariae (P. malariae)
- Plasmodium ovale (P. ovale)
- Plasmodium vivax (P. vivax)

Malaria is transmitted to humans by the bite of an infected female anopheles mosquito. In sub-Saharan Africa over 90% of human malaria infections are due to P. falciparum infection. P. falciparum is the only species associated with severe morbidity and mortality. The other three species cause milder illness; however, infections with P. ovale and P. vivax may relapse months later if appropriate treatment is not provided. Mixed infections involving more than one species may also occur.

Particular high-risk groups for the development of severe P. falciparum malaria include non-immune travelers to malaria areas and residents (of all age groups) in malaria areas.

Life cycle of malaria parasites in humans and mosquitoes

Following infection during a mosquito blood meal, there is an asymptomatic incubation period of approximately 7 to 30 days while the parasites develop in the liver and during initial multiplication in the blood. This can be prolonged in patients taking drug therapy. Reproduction in the blood is extremely rapid, and destruction of red blood cells soon induces disease symp-

toms. Without treatment the illness may deteriorate rapidly. Following appropriate treatment, *P. faciparum* and *P. malariae* infections are normally permanently cured. However, the dormant stage in the liver may be responsible for relapses of *P. vale* and *P. vivax* presenting two to three months or more after the original infection.

The mosquito vector

Mosquitoes are scientifically classified by their appearance into groups. The Anopheline family is one of the species responsible for transmitting malaria. With ideal hot conditions the larval stage may be as short as five to seven days and adults may survive for three to four weeks. Water is essential for larval survival.

Features of the Anopheline mosquito

- They are relatively small, about 8mm long with dark-spotted or dappled wings.
- Their posture when resting or feeding is distinctive—head down, body at an angle, and hind legs raised. This is in contrast with the horizontal position maintained by most other mosquito species.
- They fly more quietly and bite more subtly than other mosquitoes.
- They generally prefer clean water for the development of their larval stages.
- They favor resting indoors. This results in residual household spraying being more effective in eradication.
- The adults are carried by the wind, but few are found farther than 1 to 2 km from their larval site. Adults may rest inside motor vehicles, trains, and aircraft.
- The adult female anopheles mosquito requires protein from blood meals for their eggs to mature. They generally only feed between sunset and dawn.
- Anopheles prefer to feed near ground level, often selecting feeding on the lower leg and foot rather than arms or upper body. It is especially important that insect repellent is applied to these parts of the body.

Preventive Measures

The following factors should be taken into consideration prior to entering an area where malaria is prevalent. These factors determine the likelihood of a traveler acquiring malaria and should aid a traveler in determining whether chemoprophylaxis is needed in addition to stringent non-drug measures:

- The malaria risk in the area being visited.
- The length of stay in the area.
- The time of the year or time of the day of the visit.
- The intensity of transmission and the prevalence of drug-resistant malaria in the area.
- Type of accommodation (e.g., air-conditioned rooms, camping).
- Mode of travel (e.g., backpacking, motoring, flying).
- Whether destination is rural or urban.
- Activities (safaris/jungle expeditions), especially between dusk and dawn.
- Access to medical care.

The World Health Organization estimates that each year 300–500 million cases of malaria occur worldwide and more than two million people die of malaria.



Is chemoprophylaxis (drug therapy) necessary?

The decision as to whether chemoprophylaxis is necessary is subjective. It depends on the areas to be visited and the risk that the traveler has of being exposed to mosquitoes and of developing malaria.

When deciding on the need for chemoprophylaxis, it must be remembered that all medicines have adverse effects and that the risk of developing a serious adverse effect must be weighed against the risk of developing malaria. One of the most common prophylactic medicines, mefloquine, is not suitable for pilots because of its central nervous system side effects. Atovaquone plus proguanil and doxycycline are usually suitable for pilots. However, no chemoprophylaxis is 100% effective. Avoiding mosquito bites is more important than using preventive drugs. Malaria mosquitoes feed between dusk and dawn both indoors and outdoors.

Choosing the appropriate chemoprophylaxis

In order to choose a safe and appropriate prophylactic agent, various clinical and drug-related factors need to be taken into account:

- Pregnancy or planning a pregnancy during or shortly after the trip.
- Other medications being taken.
- Activities requiring fine coordination and spatial discrimination.
- Length of visit to the area.

The following should be noted:

- Antimalarials should be taken with food and adequate fluids.
- All antimalarials should be started before entering a malaria area.
- Antimalarials should be taken with unflinching regularity for the duration of exposure and for a further four weeks after leaving the malaria area.
- Antimalarials taken weekly must be taken on the same day each week.
- There is no evidence to support use of homeopathic preparations for the prevention or treatment of malaria.

Adverse Reactions

Mefloquine

Adverse effects associated with mefloquine include insomnia, strange dreams, mood changes, nausea, diarrhea, and headache. Mefloquine may cause spatial disorientation and lack of fine coordination. Mefloquine is not suitable for pilots.

Malarone (Atovaquone plus proguanil)

Atovaquone plus proguanil is usually well tolerated. Side effects include mild nausea, headache, or rash. Malarone is suitable for pilots.

Doxycycline

This drug affects bone formation in the first eight years of life. It should not be given during pregnancy. Adverse effects include gastrointestinal symptoms and candida infection of the gut and vagina. Severe skin sensitivity to sunburn may develop. Other symptoms include dizziness, headache, and blurred vision. Pilots are allowed to use doxycycline.

Chloroquine plus Proguanil

Chloroquine resistance is widespread in Africa. Serious side effects are rare, but may occur with long-term use. Mild reversible side effects include headache, gastrointestinal effects, skin rashes, and mouth ulcers. Pilots are allowed to use chloroquine plus proguanil.

Precautions regarding the use of insecticides

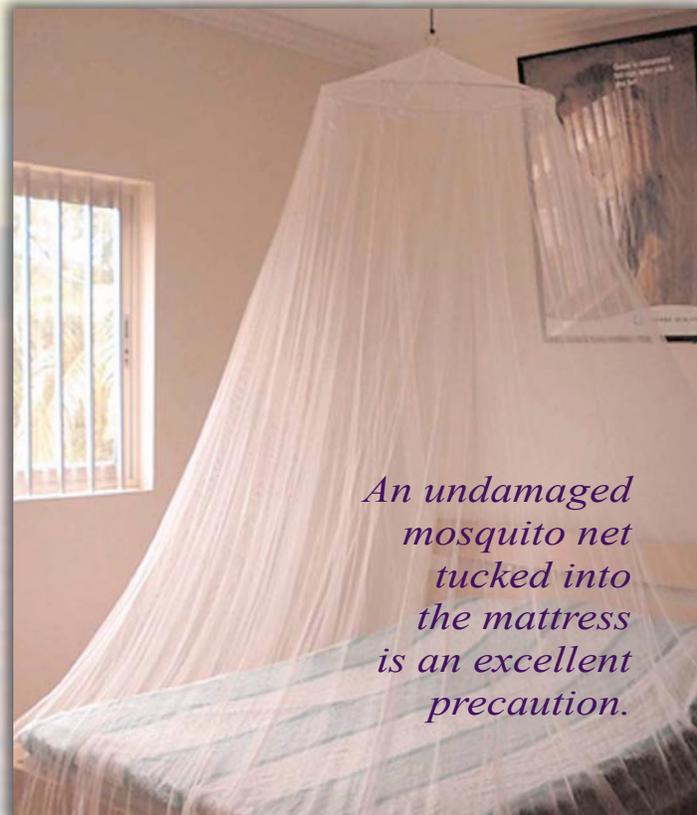
- Apply repellent sparingly to exposed skin or clothing.
- Repeat applications at intervals of four to six hours according to the manufacturer's instructions.
- Reapply more frequently after bathing, showering, sweating, etc.
- Avoid contact with eyes, mucous membranes, and broken skin. Do not inhale or ingest.
- Avoid applying high concentrations of the products to the skin.
- People who are prone to allergy should avoid using plant extracts.
- People with sensitive skin should avoid using gels and lotions, as these often contain alcohol.
- If a suspected reaction to the insect repellent occurs, wash treated skin and seek medical attention.
- DEET (N,N-diethyl-3-methylbenzamide) can opacify spectacles, binoculars, and other plastics.
- **STOP using DEET if a change in the individual's behavior is noticed, and obtain immediate medical advice.**
- Read the entire repellent label before use, and use only as directed.

Personal protection measures

Avoiding mosquito bites is more important than using preventive drugs. Malaria mosquitoes feed between dusk and dawn both indoors and outdoors.

The following is advised:

- Remain indoors between dusk and dawn.
- Wear long-sleeved clothing (preferably light-colored), long trousers, and socks.
- Stay in well-constructed and well-maintained buildings in the best developed part of town.
- Cover doorways and windows with screens, but if not available, windows and doors should be closed at night.
- Ceiling fans and air conditioners are very effective.
- Use a mosquito-proof bed net over the bed, with edges tucked in under the mattress. Ensure that the net is not torn and that there are no mosquitoes inside. Protection will be increased by periodically treating the net with an insecticide registered for this purpose, e.g., a pyrethroid.
- Spray inside the room with an aerosol insecticide at dusk after closing the windows.
- Use mosquito mats, impregnated with an insecticide, or burn mosquito coils in living and sleeping areas during the night.
- Treat clothes with an insecticide registered for this purpose, e.g., a pyrethroid.



An undamaged mosquito net tucked into the mattress is an excellent precaution.

Guidelines for the Treatment of Malaria

Objectives

The objectives of malaria treatment are:

- To prevent mortality.
- To prevent disease progression and development of severe malaria.
- To reduce morbidity.
- To eliminate parasitaemia to minimize transmission.
- To limit the emergence and spread of drug resistance.

Clinical presentation and diagnosis

Symptoms and signs of malaria may present as early as seven days after exposure, with a usual range of 10–21 days elapsing after being bitten by an infected mosquito. Longer incubation periods may occur in patients who have been on chemoprophylaxis or selected antibiotics, e.g., cotrimoxazole, tetracycline, macrolides, chloramphenicol, and quinolones. Malaria due to infections with *P. vivax*, *P. ovale*, or *P. malariae* can take up to 12 months to first manifest clinically.

As signs and symptoms of malaria are very nonspecific, a high index of suspicion is critical.

Uncomplicated malaria

Symptoms

- Fever
- Sore throat
- Headache
- Diarrhea
- Rigors (cold shivers and hot sweats)
- Nausea and vomiting
- Loss of appetite
- Muscular pain
- Weakness
- Abdominal pain
- Dizziness

Malaria should be suspected in any person presenting with any of the above symptoms who has a history of travel to, or residence in, a malaria transmission area.

Clinical Signs

Fever, enlarged spleen and/or liver

Severe malaria

Severe malaria is a medical emergency.

Presentation of *P. falciparum* malaria is very variable and may mimic many other diseases (and vice versa), including influenza, viral hepatitis, meningitis, septicemia, typhoid, tick bite fever, gastroenteritis, viral hemorrhagic fever (Ebola fever), trypanosomiasis (sleeping sickness), HIV seroconversion illness, urinary tract infection, and relapsing fever. Non-immune patients with uncomplicated malaria are at increased risk of disease progression to severe *P. falciparum* malaria. Life-threatening complications can develop rapidly in these patients. Unless *P. falciparum* malaria is promptly diagnosed and treated, the clinical picture may deteriorate rapidly. Severe malaria carries a significant morbidity and mortality.

Symptoms

- Fever
- Confusion
- Severe prostration
- Impaired consciousness
- Persistent vomiting
- Convulsions
- Pallor
- Extreme weakness
- Abnormal bleeding

Clinical Signs

- Severe anemia
- Pulmonary edema
- Impaired consciousness
- Hemoglobinuria (blood in urine)
- Multiple convulsions
- Increased respiratory rate
- Respiratory distress
- Jaundice
- Circulatory collapse
- Enlarged spleen and/or liver
- Shock
- Decreased urine output

Complications

- Anemia
- Metabolic acidosis
- Hypoglycemia
- Respiratory complications
- Cerebral malaria
- Hepatic dysfunction
- Renal failure
- Secondary infections
- Circulatory collapse
- Shock

Laboratory diagnosis

A diagnosis of malaria cannot be confirmed or excluded clinically. Since the clinical presentation is nonspecific and may mimic many other diseases, the patient's blood should be examined immediately to confirm or exclude the diagnosis. A blood test for parasites should be done irrespective of the time of the year or whether the patient has or has not taken chemoprophylaxis. In the majority of malaria cases, examination of correctly stained blood smears will reveal malaria parasites. However, a negative smear does not exclude the diagnosis; repeat specimens should be examined regularly and urgently without waiting for fever peaks, until the diagnosis is confirmed, the patient has recovered, or another definitive diagnosis is made. Examination of the peripheral blood smear will give an indication of the species of parasite as well as the parasite density.

A number of commercial rapid diagnostic tests (RDTs) are available for early diagnosis in health facilities where microscopy is not immediately available. The majority of the tests will only detect *P. falciparum*, while some will detect the other malaria species but are less sensitive for these. The rapid tests for *P. falciparum* are generally highly sensitive.

Performance is, however, dependent on the correct storage, usage, and interpretation of results and the quality of the particular test used. These tests should be used only for diagnosis of acute malaria infections, and not for follow-up, as they may remain positive for several weeks even after successful treatment. The test may be negative early in the disease, and false positives may be encountered rarely.

If the diagnosis of malaria cannot be confirmed (unavailability of laboratory tests, or negative tests), the decision to commence malaria therapy should be made on clinical grounds based on whether exposure to malaria parasites was possible and the severity of the clinical features. In cases of severe malaria, a blood smear or rapid malaria test is likely to be positive.

IFALPA provides this data for information only. In all cases pilots should follow their company's guidance and procedures.

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