

## Prevention of Malaria Infection in Travelers: A Review

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### Mini Review

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### Abstract

Malaria is dangerous if it is not treated as soon as the first peaks of fever appear and deaths are always linked to a delay in the administration of anti malarial drugs. During the transmission season in countries and territories where there is a risk of malaria, all non-immune travelers exposed to mosquito bites, especially between bedtime and sunrise, are at risk of malaria. Although well-managed anti malarial chemoprophylaxis provides about 90-95% protection, personal protective measures remain one of the essential pillars of malaria prevention. Many regions are therefore newly considered as low or moderate risk areas for malaria. The International Congress of Tropical Medicine 2015 in Quebec City has helped revive the debate and oppose three political currents. Preservatives (represented by the Centers for Disease Control in the United States) advocate the need for chemoprophylaxis prevention due to its efficiency. The Liberals (represented by Holland) offer protection against mosquito bites only to avoid the risk of non-severe side effects of chemoprophylaxis. The Swiss offer a reserve treatment to take in case of feverish condition waiting for a medical consultation because chemoprophylaxis in these areas puts the traveler at greater risk of suffering from the side effects of prophylaxis than of malaria itself.

**Keywords:** Malaria; Travelers; Chemoprophylaxis; Personal protective measures; Prevention

### Malaria in the World

Malaria is caused by a protozoan parasite of the genus *Plasmodium*. Human malaria is caused by four different Plasmodium species: *P. falciparum*, *P. malariae*, *P. ovale* and *P. vivax*. Human is occasionally infected with *Plasmodium* species that normally parasitize animals, eg *P. knowlesi*. No case of human-mosquito-human transmission of these "zoonotic" forms of malaria has yet been reported.

Malaria is a major public health challenge. In 2015, there were 214 million cases and 438,000 deaths [1], the

largest burden in the poorest countries, mainly in sub-Saharan Africa (88% of cases). These cases are mainly due to *P. falciparum*, the most prevalent species and associated with the highest mortality rate, and *P. vivax*, the most geographically extensive species. Since the year 2000, a lot of effort has been made to reduce the overall incidence (-37%) and mortality (-60%) of malaria in fifteen years [1]. However, these figures come mainly from the decrease in *P. falciparum*, mobilizing the majority of efforts and funding [2]. Indeed, *P. vivax* does not show the same evolution. Eradication is more difficult because of greater biological complexity [3,4]. The proportion of *P. vivax* cases increases in parallel with the

decrease of those due to *P. falciparum*, and re-emergence is even probably in some areas, such as Ethiopia and Eritrea [1]. Imported *P. vivax* malaria cases are on the rise in some developed countries mainly because of migrants from the Horn of Africa [5].

## Diagnosis and Treatment

Malaria is dangerous if it is not treated as soon as the first peaks of fever appear and deaths are always linked to a delay in the administration of anti malarial drugs. The rapid diagnostic test allows a diagnosis in fifteen minutes. A recent study, conducted in Lausanne, aimed at evaluating a strategy based on rapid diagnostic test coupled with microscopy during working hours, showed that such an attitude allowed a reduction of two hours on average until the result of the first malaria test [6]. An anti malarial treatment, intravenously in the presence of clinical signs of danger or orally, can thus be initiated immediately, guarantee of good evolution. WHO recommends a combination therapy with artemisinin [7].

## Risk for Travelers

During the transmission season in countries and territories where there is a risk of malaria, all non-immune travelers exposed to mosquito bites, especially between bedtime and sunrise, are at risk of malaria. Previously semi-immune travelers, who have lost some or all of their immunity because they have been in safe countries or zones for at least 6 months, are also vulnerable. Children of people who have migrated to safe countries or areas are at particular risk when returning to malarious areas to visit friends or relatives.

Most cases of *P. falciparum* malaria in travelers occur because they do not follow the prophylactic regimen or take appropriate medications or precautions against mosquito bites. Studies of traveler behavior have shown that adherence to chemoprophylaxis can be improved if travelers are informed of the risk of infection and convinced of the benefits of prevention. *P. vivax* or *P. ovale* malaria may occur late despite effective prophylaxis because these parasites cause relapses that cannot be prevented by the currently recommended prophylaxis.

The risk of malaria is unevenly distributed in places where the disease is widespread. Travelers to countries or areas where malaria transmission varies by region should be aware of the risk of infection in the areas they are visiting. If they cannot obtain accurate information before leaving, it is recommended that they take the highest risk precautions listed in the country or territory.

These precautions can be adapted if the traveler gets more information on arrival. This is especially true for people who travel backpacking in remote locations and traveling to areas where health facilities are difficult to access. Travelers who spend the night in rural areas are perhaps the most exposed.

## Prevention of Malaria Infection in Travelers

Although well-managed anti malarial chemoprophylaxis provides about 90-95% protection, personal protective measures remain one of the essential pillars of malaria prevention. In a double-blind study, 85% of travelers reported mild side effects independent of the prescribed antimalarial drug (mefloquine, atovaquone / proguanil, doxycycline and chloroquine / proguanil) [8]. *Anopheles*, mosquitoes responsible for the transmission of malaria, has a nocturnal activity: from dusk until sunrise. For better protection, it is essential to combine several measures of personal protection. The use of impregnated mosquito nets has been largely effective [9]. In order to protect oneself indoors, it is also important to apply mosquito nets to windows and doors. WHO also recommends several insecticides that can be used for residual indoor residual spraying [10]. On the outside, it is proposed to wear loose, long and light clothing, to which it is possible to apply a pyrethroid insecticide to increase its effectiveness. The application of repellents on the skin is also indicated.

Malaria in pregnant women is more often severe and carries a higher risk of death and increased maternal-fetal complications [11]. When it is not possible to shift the stay in endemic areas, it is essential to advise the pregnant woman to protect herself optimally against mosquito bites. Pregnant women would be twice as likely to attract anopheles and leave their bed twice as often during the night as non-pregnant women [12]. The use of impregnated mosquito nets and pyrethroids is safe during pregnancy [13,14]. At present, mefloquine is the only antimalarial drug that can be prescribed for chemoprophylaxis during pregnancy and lactation [15,16]. During breastfeeding, this treatment is recommended as soon as the child has reached a weight of 5 kg [17]. No termination of pregnancy is indicated during the accidental taking of an antimalarial during pregnancy.

Adherence to chemoprophylaxis and personal protection measures during long stays is poor [18,19]. Teaching about preventing malaria improves adherence [20]. The different possible strategies, their advantages and disadvantages must be discussed with the traveler

[19-22]. Personal protective measures are effective with minimal toxicity. Knowing that they are not well followed, the focus should be on using mosquito nets impregnated on the bed and on windows and doors. While the risk of malaria increases linearly over time, the risk of new side effects increases at the beginning of anti malarial use, then remains constant or even decreases thereafter [23]. Long-term chemoprophylaxis is strongly recommended for high malaria risk, as well as for pregnant women, infants and travelers with much comorbidity.

In particular, the traveler must be informed of the symptoms of malaria and be given early diagnosis and treatment in all febrile conditions up to one year after returning from travel. Rapid tests have largely been shown to be effective in the diagnosis of malaria [24,25]. On the other hand, their use by travelers independently cannot be recommended because they do not use them adequately [26-28].

The risk of malaria is proportional to the length of stay. Long-stay travelers in endemic areas need to be aware of the risk they are exposed to as well as effective preventive measures: vector protection and chemoprophylaxis. Special emphasis should be placed on the use of night-treated mosquito nets and doors and windows. When chemoprophylaxis is indicated, it should be prescribed during the first three to six months of stay. Thereafter, advice on chemoprophylaxis can be individualized, while informing the traveler of the advantages and disadvantages of the various possible strategies: continuous chemoprophylaxis, seasonal, emergency treatment.

### Challenges of Malaria Prevention in Low Risk Areas

The number of international travelers surpassed one billion in 2012, and could double by 2030 [29]. At the same time, the global incidence of malaria has decreased by 37% between 2000 and 2015, and there is a decline of more than 75% in more than half of the countries with active transmission [30,31]. Many regions are therefore newly considered as low or moderate risk areas for malaria, mainly in Latin America and Southeast Asia. This decline is the result of a major effort through impregnated mosquito net distribution campaigns, the promotion of rapid diagnostic tests and more effective treatments based on artemisinin derivatives.

In terms of impact for the traveler, these figures call into question certain prevention strategies [32, 33]. While anti malarial chemoprophylaxis, with mosquito-bite

prevention measures in high-endemic areas, remains appropriate, there are various recommendations for areas of low or moderate risk of transmission [34-36].

The International Congress of Tropical Medicine 2015 in Quebec City has helped revive the debate and oppose three political currents. Preservatives (represented by the Centers for Disease Control in the United States) advocate the need for chemoprophylaxis prevention. Their arguments were that offer maximum protection for a life-threatening disease and very effective prevention if taken properly [37]. The Liberals (represented by Holland) offer protection against mosquito bites only. Their arguments were the risk of non-severe side effects of chemoprophylaxis in 80% of cases, severe in 6-11% [38], and a rare use of reserve treatment in practice [39]. The Swiss offer a reserve treatment to take in case of feverish condition waiting for a medical consultation. Their arguments indicated that chemoprophylaxis in these areas puts the traveler at greater risk of suffering from the side effects of prophylaxis than of malaria itself [40,41], adherence to chemoprophylaxis is in practice 30-50% only [42,43].

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