



Malaria Prophylaxis:

A WORTHWHILE HEALTH INVESTMENT

Malaria Prophylaxis:

A WORTHWHILE HEALTH INVESTMENT

Malaria is a significant global health concern as over 200 million new infections occur each year, and malaria has been a health issue for millennia. The disease gets its name from the medieval Italian “mala aria,” or bad air, and human cases have been documented for nearly 5,000 years. Malaria is an infectious, insect-borne disease spread to people through the bite of the female *Anopheles* mosquito. The mosquitoes themselves are infected with a parasitic protozoan from the *Plasmodium* genus, which passes into the person during the biting process. Infection with one of the five species of *Plasmodium* protozoans results in development of symptoms that, although often mild, can become severe and lead to death. Malaria primarily occurs in the tropics, but it is also endemic in subtropical areas, which makes it a major concern to anyone traveling to equatorial regions. There are many preventive measures that people can take to protect themselves against infection, and it is crucial that travelers prepare themselves so they do not become another statistic.

However, the question remains: **Why is it worth it to bite back against this life-threatening disease?**



What is Malaria?

Infection with the parasites that cause malaria produces a wide range of symptoms, explains the Centers for Disease Control and Prevention¹. Some people infected with the parasites might not experience any symptoms at all, while others develop mild or moderate symptoms. In some cases, the clinical symptoms are severe, resulting in severe illness or even death. In most cases, however, when malaria is diagnosed in its earliest stages by a physician or a travel health specialist, an infected person will make a full and prompt recovery.

The most common symptoms of malaria begin seven to 30 days after the infectious bite from the mosquito. During this time, the parasites infect erythrocytes, which are blood cells. The waste materials created by the parasites cause the body's immune

system to release macrophages to kill the infected cells. In turn, the body responds with symptoms including the classic malarial fever, chills, headaches, sweating, body aches and vomiting. In rare cases, the parasites cause severe symptoms that can include severe anemia, hypoglycemia, blood clotting disorders, respiratory distress, kidney failure, low blood pressure, metabolic acidosis, seizures, coma, or death.

As noted previously, malaria has been a global scourge for much of human history, and symptoms of malaria or a similar infection have been reported from around the world for thousands of years. For example, around 2700 BC, the infection was described in the Nei Ching, or The Canon of Medicine that was edited by Emperor Huang Ti of China. According to the CDC², reports of the infection had spread as widely as

Greece by the 4th century BCE. Famous early physicians such as Hippocrates, the father of modern medicine, described the most common and important symptoms of the disease. In India, the Susruta, a Sanskrit medical treatise, explained that the symptoms were caused by insect bites. Ancient Roman writers reported that the disease was common in swampy areas in which mosquitoes are prevalent. By the second century BCE, Chinese physicians related in the text of 52 Remedies that the Qinghao plant (*Artemisia annua*) could lessen malarial symptoms. Interestingly, in 1971, this very plant's active chemical, artemisinin, was found to have potent effects against malaria. The artemisinins are used today in combination with other medications to treat the symptoms of malaria.

Although anyone can be infected with the parasites that cause malaria, certain groups are at an increased risk of infection. These high risk groups include:

- Young children who have not yet developed full immunity
- Pregnant women
- People who are HIV-positive or have developed AIDS
- International travelers from non-endemic areas
- Emigrants from endemic areas who return to those areas after their immunity has waned

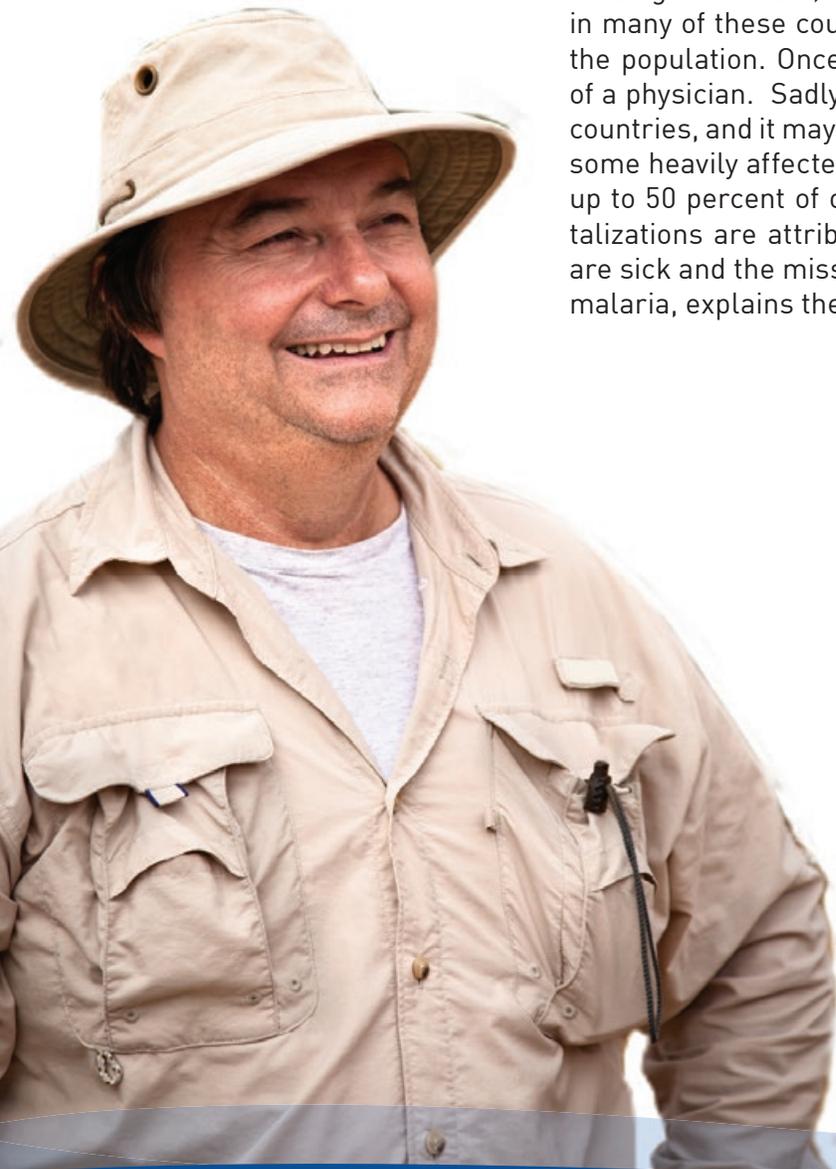


Where Does Malaria Occur?

Malaria occurs where the Anopheles mosquitoes thrive. In general, this means climates that are consistently warm and humid. Indeed, the Plasmodium falciparum, one of the four varieties of Plasmodium that causes malaria, is not able to complete its lifecycle if the temperature drops below 68 degrees Fahrenheit [3]. The other species of Plasmodium parasites that cause malaria include Plasmodium vivax, Plasmodium malariae, and Plasmodium ovale, and all thrive in warm temperatures [4].

The mosquitoes that transmit the parasites that cause malaria also need humid conditions and consistent weather. Tropical and subtropical areas where malaria infections occur year round include sub-Saharan Africa, Papua New Guinea and much of Oceania, India, and the parts of South America that include the Amazon rain forest. Some parts of Latin America and the Middle East also experience seasonal transmission [4].

Because malaria primarily occurs in the world's poorest countries, it has an especially devastating and well-documented impact on their populations. According to the CDC, lack of resources for prevention and treatment of malaria in many of these countries further exacerbates the effect the disease has on the population. Once infected, an individual needs medications and the care of a physician. Sadly, such care is prohibitively expensive in many developing countries, and it may also simply be impossible to obtain care in rural areas. In some heavily affected nations, up to 40 percent of public health expenditures, up to 50 percent of outpatient visits, and 30 to 50 percent of inpatient hospitalizations are attributed to malaria disease. The lost earnings while adults are sick and the missed opportunities for ill children further add to the cost of malaria, explains the World Health Organization [5].



Is Malaria an Issue for Travelers?

Worldwide, there were an estimated 216 to 219 million malaria infections in 2010. Of those infected, an estimated 655,000 to 660,000 people died. More than 90 percent of the deaths from malaria occurred in sub-Saharan Africa[6]. Of those who died, 86 percent were children. Malaria take an unequivocal toll on developing regions, but travelers to these regions are by no means immune to risk, simply because they are staying in the country for a short time. In fact, when someone from a non-endemic area visits a country in which Anopheles mosquitoes carrying Plasmodium are present, he or she is actually at a higher risk of infection. People who reside in malarious regions can acquire immunity to malaria parasites through natural exposure and the natural defense mechanisms of the human body. However, international travelers are highly unlikely to have developed such a response, and this lack of immunity makes international travelers highly vulnerable to malaria.

Malaria's effect on travelers to endemic regions is profound, as the following cases show. Indeed, even a full prescription of malaria medications does not fully prevent the disease. Kelly Granger, a study abroad student, visited Ghana in the summer of 2010 for six weeks. Her student health physician prescribed a course of malaria prophylaxis, which she took during her trip. Upon returning home, however, she soon began to experience troubling symptoms that included fever and headaches. Her chills and fatigue increased, and two days after her first visit to her physician, her fever spiked and her symptoms worsened to include hallucinations, abnormal behavior, and jaundice. She was quickly admitted to the intensive care unit and began intravenous treatment for severe malaria disease. Her complications from infection with Plasmodium falciparum included severe anemia and loss of consciousness. Her condition quickly deteriorated despite aggressive treatment.

Eventually, a red blood cell transfusion led to a decrease in the load of parasites in her body. With physical therapy and continued treatment, she was able to return home a few days later. As this example shows, even in people who have taken malaria prophylaxis, the disease should always be considered as a cause for illness upon returning from travel in an endemic country [7].

In 2000, Fatai and Hanifat Adisa and their first child moved to the United States from Nigeria and settled in Indiana, where Mr. Adisa began work as a physical therapist. In 2005, the family had grown to include four more children, and they all had the opportunity to visit family and friends in Nigeria. Mrs. Adisa took the children to their family pediatrician to receive antibiotics and pain relievers should any of them become ill during their travels. She also took the family to their local health department to inquire about a malaria vaccine. The personnel at the health de-



Is Malaria an Issue for Travelers? *(CONT.)*

partment advised her that there is no vaccine against malaria. However, they did tell her that there were pills that could be taken for protection against malaria disease. However, Mrs. Adisa did not fully understand what malaria prophylaxis meant. She thought that the pills were to be taken only in the event of illness, not as a preventive measure.

The family had an enjoyable trip and returned to Indiana in January 2006. Within two weeks of their return, the four oldest children began to have symptoms that included mood changes, aches, and fever. School administrators

contacted Mrs. Adisa when her oldest child developed severe headaches at school. She took all of her children to the local health clinic. Doctors diagnosed the four children with influenza and said that the oldest also had strep throat. Within days of taking antibiotics and pain relievers, three of the Adisa children developed jaundice and worsening illness. Mrs. Adisa took them to the local hospital, where doctors examined them and sent them to the University of Chicago Hospitals for specialty treatment. Pediatricians at the University of Chicago Hospitals diagnosed the youngsters with malaria caused by the

parasite *Plasmodium falciparum*. The ten-year-old child was severely ill and required a breathing machine and intravenous medication to correct anemia, low blood pressure, and low blood sugar and required extensive blood transfusions. The two other children in the family were also found to be infected with *Plasmodium falciparum* and were treated with oral medication. Fortunately, all five of the children recovered from their illnesses within a week of hospitalization and were able to return home to Indiana [8].

When traveling to areas of the world where malaria is endemic, there are many activities that can put travelers at risk or make them more susceptible to malaria transmission.

Some of these activities include:

- Sleeping out in the open without mosquito nets.
- Not using mosquito repellent.
- Exploring areas with standing water, even small pools of water that collect in old tires, planters, and puddles.
- Spending time outdoors from dusk to dawn, when the *Anopheles* mosquitoes are more active.
- Taking part in activities in areas infested with mosquitoes. These types of activities could include hiking, climbing, swimming, fishing, or boating.
- Returning to a malaria-endemic area after spending a long period of time away.

In short, malaria is a huge concern for travelers, and it can have devastating, costly, and deadly impact.



How to Prevent Malaria

Many infections of malaria disease are completely preventable by taking some basic precautions before and during travel. Some action steps that travelers can take include:

- Using mosquito repellents at all times while abroad.
- Sleeping under mosquito nets impregnated with insecticide. These might be hard to come by in some areas of the world, but you can acquire these and other travel supplies for high risk malaria regions by consulting with a travel health specialist before your trip.
- Taking malaria prophylaxis before and during your trip to areas of the world with a high level of malaria activity.
- Obtaining your malaria medications at home by visiting a travel health specialist. Note that it is generally not advisable to get these prescriptions abroad as medications available internationally can be counterfeit.



How to Prevent Malaria (CONT.)

There are several different types of malaria drugs that can be taken for protection against infection. Before initiating prophylaxis, however, you should schedule a travel health consultation with a travel health specialist so that you receive the specific malaria pills most appropriate to your situation and avoid adverse drug interactions. Some of the malaria drugs that travelers can take as prophylaxis include:

- **Atovaquone/Proguanil.** This medication is ideal for those taking short trips to affected regions. It is taken daily and can be started just a day or two before you depart on your trip. There is a pediatric version of the medication available. The drug is generally well tolerated with few side effects, explains the CDC [9]. However, the drug should not be taken by pregnant women, women breastfeeding a baby that weighs less than 5 kilograms, or people with kidney disease. This drug is more expensive than some other drugs used for malaria prophylaxis.
 - **Chloroquine.** This medicine is taken weekly. It is good for people taking long trips. Pregnant women can typically safely take this drug. However, some mosquitoes carry Plasmodium parasites with resistance to Chloroquine, so the medication may not be effective in some places. It is generally not a good choice for people taking a last minute trip, and the drug may worsen psoriasis symptoms.
 - **Doxycycline.** This drug can be started at the last minute before travel. It is taken daily. This drug is the least expensive option for malaria prophylaxis. It may also confer protection against other infections that can be transmitted during outdoor activities such as hiking or swimming. The drug is not recommended for use in pregnant women or children under the age of 8. It may increase sensitivity to sunlight, even if sunscreen is used, and it may increase the risk of yeast infections in women. The drug may also cause upset stomachs.
 - **Primaquine.** This drug is highly effective at preventing malaria caused by Plasmodium vivax. This drug is taken daily. It is ideal for people taking short trips of a week or less. It can be started at the last minute before travel to affected regions. The drug cannot be used in anyone with glucose-6-phosphatase dehydrogenase deficiency or who has not been tested for glucose-6-phosphatase dehydrogenase deficiency. It cannot be taken by pregnant women. It could cause an upset stomach.
- 

How to Prevent Malaria *(CONT.)*

Another key anti-malaria drug is Lariam, or mefloquine. It is taken weekly and is safe for use in pregnant women. However, there is significant controversy surrounding use of Lariam. It is not recommended for use in people with seizure disorders or certain psychiatric disorders. It is also not recommended for use by people with heart abnormalities. A small number of people who take the drug for malaria prophylaxis have developed unusual neurological effects, including hallucinations, amnesia, aggression, loss of balance, ringing of the ears, and dizziness. Up to 67 percent of patients taking Lariam have reported such side effects, and about 6 percent had severe side effects, reports the New York Times [10].

In addition to malaria prophylaxis drugs, there is currently a malaria vaccine under development by Sanaria Inc. Clinical trials have been performed on 57 patients, and further testing is being done by the National Institute of Allergy and Infectious Diseases, the Walter Reed Army Institute of Research and the Naval Medical Research Center, as members of the U.S. Armed Forces throughout the world are at a particularly high risk of malaria disease.

Vaccine development is a long process, so it could take 8 to 10 years until the vaccination is fully tested and approved by the Food and Drug Administration, reports CNN[11], if it even gets to this stage in testing. The vaccine works against malaria caused by *Plasmodium falciparum*, which does not cause all malaria infections. In the trials completed so far, several subjects required five shots to attain immunity to malaria. About half of patients receiving four doses still became infected with the disease. However, of the research subjects receiving just a placebo injection, 11 of 12 became infected with malaria. Vaccination is thus a promising option for the future, especially as it requires less patient compliance and may be effective on its own without the need for combining it with other preventive measures such as repellents and netting.



Is Malaria Prophylaxis a Worthwhile Investment?

The question remains: are the preventative measures described above worth the time and cost for travelers to endemic regions. Benjamin Franklin is famous for saying that an ounce of prevention is worth a pound of cure, and this statement holds true especially in the case of malaria prophylaxis. For example, a study published on 18 July 1994 found that the cost of chemoprophylaxis for malaria is highly worthwhile when one considers the economic cost of treating the disease once it occurs. In the study, researchers investigated the cost of providing malaria prophylaxis to residents of the United Kingdom traveling to regions with high levels of malaria activity. The researchers found that imported malaria occurred at an incidence rate of 0.70 percent, and the cost effectiveness of providing anti-malarial drugs was 0.19 for chloroquine and proguanil and 0.57 for a regimen containing mefloquine. In other words, the cost of providing preventive drugs was 19 to 57 percent of the cost of treating travelers returning home with malaria disease[12]. It was much cheaper to pay for and take the prescriptions, instead of having to pay for the costs of treatment. Given the examples of the extensive treatment that a case of malaria can require, it is no wonder a prescription medication is a worthwhile investment.

The cost of treating malaria infections results in a considerable burden to the public health and medical system of countries around the world. The morbidity and mortality of malaria infections in travelers compared to the low

cost of taking prophylactic medications makes prevention a highly cost effective measure. In addition, the drugs used to prevent malaria are generally inexpensive, easy to obtain from a travel health specialist, and generally well tolerated by most people within a population.

The British researchers found that the prophylactic measures given to travelers are highly effective against malaria infections. The data showed that anti-malarial regimens had a protective efficacy of 72 percent for a combination treatment of chloroquine and proguanil and 92 percent for mefloquine alone. This means that 72 to 92 percent of malaria infections were prevented by following the prescribed malaria prophylaxis regimen.

For an individual receiving malaria prophylaxis, the cost savings of preventive treatment is high. The individual has considerably less risk of missed days from work (and lost wages) upon returning home from travel. The individual would also have less out of pocket expenses for office visits, hospitalization, and procedures related to treatment of malaria infection. For children, in whom

malaria infection can be especially devastating, making sure they receive malaria prophylaxis could save their lives. Malaria prophylaxis benefits society in the aggregate as well. Preventing malaria infections reduces the burden on the healthcare system, protects workers' abilities to be productive, and reduces the years of life lost prematurely due to severe malaria disease.

International travel is an aspiration and pleasure enjoyed by many. By scheduling a pre-travel health consultation with a travel health specialist, travelers can ensure that they are in good health before departing on a trip and receive the type of malaria prophylaxis that is best given their medical history and specific destination. Indeed, travelers do not have to let malaria get in the way of visiting some of the world's most beautiful and culturally rich regions. Prophylactic measures will help ensure continued good health abroad and upon return. With assistance from travel health specialists, you can protect yourself, your family, and employees against infection and complications that can result from malaria infection. Is malaria prophylaxis a worthwhile health investment? Absolutely.



Resources

1. Malaria Disease. Centers for Disease Control and Prevention. 2013. Web. Accessed on 23 August 2013. <http://www.cdc.gov/malaria/about/disease.html>
 2. Malaria History. Centers for Disease Control and Prevention. 2013. Web. Accessed on 23 August 2013. <http://www.cdc.gov/malaria/about/history/>
 3. Where Malaria Occurs. Centers for Disease Control and Prevention. 2013. Web. Accessed on 24 August 2013. <http://www.cdc.gov/malaria/about/distribution.html>
 4. Malaria Fact Sheet. World Health Organization. 2013. Web. Accessed on 24 August 2013. <http://www.who.int/mediacentre/factsheets/fs094/en/>
 5. Economic Costs of Malaria. World Health Organization. 2002. Web. Accessed on 24 August 2013. <https://apps.who.int/inf-fs/en/InformationSheet10.pdf>
 6. Malaria Worldwide Impact. Centers for Disease Control and Prevention. 2013. Web. Accessed on 24 August 2013. http://www.cdc.gov/malaria/malaria_worldwide/impact.html
 7. More Than Just 'Jet Lag'. Centers for Disease Control and Prevention. 2013. Web. Accessed on 24 August 2013. <http://www.cdc.gov/malaria/stories/morethanjetlag.html>
 8. A Cautionary Tale: A Family's Ordeal with Malaria. Centers for Disease Control and Prevention. 2010. Web. Accessed on 24 August 2013. http://www.cdc.gov/malaria/stories/malaria_traveling_family.html
 9. Choosing a Drug to Prevent Malaria. Centers for Disease Control and Prevention. 2011. Web. Accessed on 25 August 2013. <http://www.cdc.gov/malaria/travelers/drugs.html>
 10. Crazy Pills. New York Times. 7 August 2013. Web. Accessed on 25 August 2013. http://www.nytimes.com/2013/08/08/opinion/crazy-pills.html?_r=1&
 11. U.S. Reports a Breakthrough in Malaria Vaccine. CNN. 9 August 2013. Web. Accessed on 25 August 2013. <http://www.cnn.com/2013/08/08/health/malaria-vaccine>
 12. Is travel prophylaxis worth while? Economic appraisal of prophylactic measures against malaria, hepatitis A, and typhoid in travellers. *BMJ* 8 October 1994: 309:918. Web. Accessed on 25 August 2013. <http://www.bmj.com/content/309/6959/918>
- 