Malaria and the International Traveler

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Faculty Disclosure
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The division planners and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience
This course is designed for healthcare professionals involved in the care of persons traveling to or from areas where malaria transmission is common.

Accreditations & Approvals

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NetCE designates this continuing education activity for 3 ANCC contact hours.

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AACN Synergy CERP Category A.

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Special Approvals

This activity is designed to comply with the requirements of California Assembly Bill 1195, Cultural and Linguistic Competency, and California Assembly Bill 241, Implicit Bias.

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Course Objective

Malaria poses a particularly serious threat to U.S. travelers to endemic regions, and delayed diagnosis is a leading cause of death among patients with malaria in the United States. The purpose of this course is to provide healthcare professionals with the information necessary to accurately identify, treat, and educate patients regarding the risks of malaria in order to protect those who may be exposed to the disease.

Learning Objectives

Upon completion of this course, you should be able to:

1. Describe the history and natural life cycle of malaria.
2. Identify how and where the transmission of malaria occurs.
3. Differentiate between uncomplicated and severe (complicated) malaria and identify the symptoms of each.
4. Compare the methods used to diagnose malaria and review the importance of prompt diagnosis.
5. Recommend the appropriate treatment for malaria of various origins.
6. Identify the preventive measures against malaria that have been recommended, including presumptive self-treatment, and discuss considerations for non-English-proficient patients.

Pharmacy Technician Learning Objectives

Upon completion of this course, you should be able to:

1. Describe how malaria is transmitted and diagnosed.
2. Identify preventive and treatment measures for malaria.

E B
EVIDENCE-BASED PRACTICE RECOMMENDATION

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

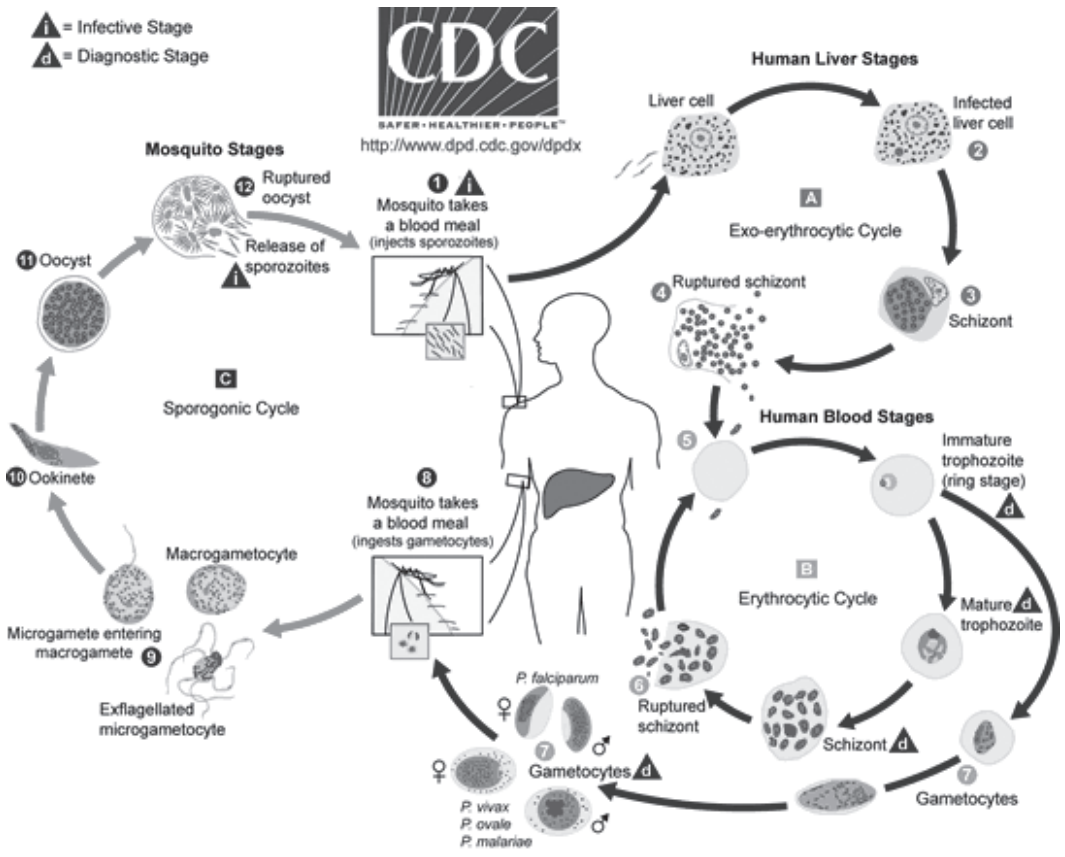
The symptoms of malaria were first described around 2700 B.C.E. in ancient Chinese medical writings, although research indicates it may be thousands of years older [1; 65]. Thousands of years later, malaria continues to be one of the most significant infectious diseases. Approximately 3.2 billion people live in areas of malaria transmission, and an estimated 150 to 300 million cases of malaria are reported each year. Malaria is a leading cause of illness and death in the developing world, killing an average of 600,000 people each year [2; 58]. Young children and pregnant women are the groups most affected [2; 37; 58]. Although the transmission of malaria was successfully interrupted in the United States during the late 1940s, it continues to pose a challenging health threat to individuals who travel to and emigrate from malarious areas [5; 54].

LIFE CYCLE OF MALARIA

Malaria is a mosquito-borne disease caused by a parasite from the genus *Plasmodium*. Although there are more than 100 species of *Plasmodium*, only five are known to infect humans. These include *P. falciparum*, *P. vivax*, *P. malariae*, *P. ovale*, and the more recently discovered *P. knowlesi* (a simian malaria parasite), which has previously been misdiagnosed in humans as *P. malariae* [6; 7; 8; 9; 26]. *P. falciparum* and *P. vivax* cause the most infections worldwide. *P. falciparum* is the agent of severe, potentially fatal malaria due to its unique ability to invade and multiply inside erythrocytes. If treated promptly and effectively, however, it is almost always curable. *P. vivax* is the most geographically widespread of the species. Although it produces symptoms that are less severe, relapses of infection caused by *P. vivax* may occur up to three years after the initial infection. *P. malariae* produces long-lasting infections that have the ability to persist asymptomatically for years. Occurrences of infection from *P. ovale* are rare and generally limited to West Africa [3; 10; 11]. Little is known about the morphology of *P. knowlesi* parasites, but they do appear to have unique characteristics that can be identified through the use of light microscopy [12]. *P. knowlesi* appears to cause less severe clinical disease than *P. falciparum*; however, it may cause more severe and potentially fatal infections than *P. vivax* or *P. malariae* [6]. The severity of infection caused by *P. knowlesi* is the result of its rapid (i.e., 24-hour), targeted erythrocytic cycle. *P. knowlesi* is widespread throughout Malaysia, accounting for approximately 70% of human malaria infections in this area. Cases of infection with *P. knowlesi* have also been reported in Thailand, China, Singapore, and the Philippines [12; 26].

These malaria-causing parasites are carried and transmitted by the female *Anopheles* mosquito. As the mosquito takes a human blood meal, it injects the parasites as sporozoites (the invasive form of the parasites) [13]. The sporozoites travel to the liver, where they invade liver cells, grow, divide, and produce successive generations of parasites called merozoites. The merozoites exit the liver cells and continue the cycle by invading other red blood cells, replicating asexually, and releasing newly formed merozoites into the host bloodstream. Some of these infected cells leave the cycle of asexual replication and develop into male or female gametocytes, which continue circulating in the host bloodstream. When the gametocytes are ingested by the mosquito during a blood meal, another cycle of growth and multiplication in the mosquito is begun (***Figure 1***) [3; 10]. The success of this cycle depends on factors such as temperature, humidity, mosquito longevity, and individual host factors [3; 14].

THE LIFE CYCLE OF MALARIA



Source: [52] *Figure 1*

TRANSMISSION

As discussed, malaria is transmitted to humans by the female *Anopheles* mosquito. Only 30 to 40 of the known *Anopheles* species are vectors and spread malaria. The *A. gambiae*, which exists exclusively in Africa, is one of the most efficient vectors and also one of the most difficult to control [3]. Malaria transmission may also occur through exposure to contaminated blood or tissue products or from mother to fetus; however, these instances are rare [10; 15].

Malaria is transmitted in areas that allow the *Anopheles* mosquito to survive and multiply. This occurs mainly in tropical and subtropical areas where the temperature, humidity, and rainfall create an environment that allows malaria parasites to complete their growth cycle in the mosquitoes. Temperature is particularly critical to completion of the life cycle. For example, even within the areas where transmission is most common (i.e., tropical and subtropical regions), it does not occur at high altitudes, during cooler seasons in some areas, and in most desert areas. Transmission is most common in sub-Saharan Africa (85% of cases in 2018), with the highest case

rates (69.9%) occurring among travelers returning from West Africa [15]. Although malaria has been eliminated in western Europe and the United States, the presence of the *Anopheles* mosquito in these regions poses a constant risk of reintroduction of the disease, especially in regions with temperate climates [2; 53].

The Centers for Disease Control and Prevention (CDC) began malaria surveillance in 1957. Since then, 63 outbreaks of locally acquired malaria have occurred [15]. The last outbreak, which consisted of eight cases, occurred in the United States in 2003 and was linked to a strain of the *P. vivax* parasite. Testing by the CDC indicated that the parasite originated in the Americas [17]. There was also one case of congenital malaria in 2004, also linked to the *P. vivax* parasite [59].

SYMPTOMS AND DIAGNOSIS

Following the infective mosquito bite, an incubation period of between 7 and 30 days usually passes before the first symptoms of disease appear. Shorter incubation periods are associated with *P. falciparum*; longer periods are characteristic of *P. malariae*. A string of recurrent attacks is typical and generally includes chills, fever, and sweating. In addition to these symptoms, headache, general malaise, fatigue, muscular pains, nausea, vomiting, and diarrhea are also common [3; 10; 18].

Although infrequently observed, a classical attack of "uncomplicated" malaria lasts from 6 to 10 hours and recurs either every second or third day, depending on the infectious *Plasmodium* species. Additional physical findings may include weakness, an enlarged spleen or liver, mild jaundice, and an increased respiratory rate. Laboratory results may indicate mild anemia, thrombocytopenia, elevated bilirubin, aminotransferases, and albuminuria and the presence of urinary casts [3; 18].

Malaria infections with *P. falciparum* are categorized as severe when complicated by serious organ failure or abnormalities in the patient's blood or metabolism. Severe malaria occurs most frequently in persons either with no immunity or decreased immunity to the disease. The presence of one or more of the following clinical criteria indicates severe malaria [3; 4]:

- Seizures or other neurologic abnormalities
- Impaired consciousness or coma
- Abnormal behavior
- Severe normocytic anemia
- Pulmonary edema
- Acute respiratory distress syndrome
- Circulatory shock
- Disseminated intravascular coagulation
- Spontaneous bleeding
- Acidosis
- Hypoglycemia
- Hemoglobinuria
- Jaundice
- Acute kidney failure
- Repeated generalized convulsions
- Parasitemia greater than 5%

Severe illness is a medical emergency requiring urgent, aggressive treatment [3].

Prompt diagnosis of malaria is important to ensure timely treatment and prevent the spread of infection. Malaria may be suspected based on the patient's symptoms, travel history, and physical findings at examination. Patients with suspected infection should be urgently and thoroughly evaluated. Delayed diagnosis is a leading cause of death among patients with malaria in the United States [3]. It is important, however, that treatment not begin until the diagnosis has been confirmed with specific diagnostic tests (e.g., microscopy or rapid diagnostic tests) that help identify the type of infectious parasite and determine the severity of the infection. Identification of these factors will help the clinician determine the appropriate course of treatment [4; 18].

The criterion standard of microscopic diagnosis involves examination of thick and thin blood smears. (Thick smears are more sensitive but more difficult to read.) The smears are stained, usually with the Giemsa stain, which gives the parasites a distinctive appearance. A negative blood smear usually indicates no presence of infection. However, because nonimmune individuals may be symptomatic at very low parasite densities that are initially undetectable, the CDC has recommended that smears be repeated every 12 to 24 hours for 48 to 72 hours [4; 20].

Alternative methods for laboratory diagnosis include immunologic tests to detect antigens derived from malaria parasites [18; 21]. These rapid diagnostic tests (RDTs) provide results within minutes and may be used where reliable microscopic diagnosis is not available. In 2007, the U.S. Food and Drug Administration (FDA) approved the first RDT for use in the United States. Because RDTs cannot confirm the species of malaria, the CDC has recommended that all RDT results be confirmed with microscopy [4; 22]. Due to recent improvements in quality and cost-effectiveness, RDTs are becoming more common in areas with little access to microscopy services [2; 27]. Polymerase chain reaction (PCR) may be used to detect parasite nucleic acids. Although it is a more sensitive and accurate diagnostic tool than microscopy, PCR is not a useful tool for diagnosing the acutely ill patient, primarily because of the time required to obtain results [4].

Diagnosis of malaria may be difficult, and misdiagnosis is a common problem, particularly in areas where malaria is not endemic, like the United States. In areas where malaria is endemic, diagnosis may be difficult because intense transmission allows some individuals to develop immunity that protects them against illness but not infection. Healthcare providers should obtain a travel history from every febrile patient and should routinely suspect malaria in a patient who has recently traveled to an area with known malaria transmission [4; 5; 15].

Malaria is a reportable disease in the United States and is included in the National Notifiable Diseases Surveillance System [23]. The CDC has recommended that healthcare providers report all cases of laboratory-confirmed malaria to their local or state health departments. These reports are then transmitted to the CDC for surveillance, prevention, and reporting purposes. Information about how to report a case of malaria, as well as reporting forms, are available from the CDC at https://www.cdc.gov/malaria/php/case-reporting [24].

TREATMENT

As previously stated, treatment of malaria should not be initiated until the diagnosis has been confirmed by laboratory analysis. After the diagnosis has been confirmed, treatment should begin immediately and be guided by the infecting *Plasmodium* species, the drug susceptibility of the infecting parasites, the geographical location (if known) of infection, and the patient's clinical status [4; 10].

EVIDENCE-BASED PRACTICE RECOMMENDATION

After the diagnosis of malaria has been made, appropriate antimalarial treatment must be initiated immediately. The Centers for Disease Control and Prevention recommend that treatment be guided by three main factors:

- The infecting *Plasmodium* species
- The clinical status of the patient
- The drug susceptibility of the infecting parasites as determined by the geographic area where the infection was acquired
- Previous use of antimalarials, including those taken for malaria chemoprophylaxis

(https://www.cdc.gov/malaria/hcp/clinical-guidance/general-treatment.html. Last accessed October 14, 2025.)

Level of Evidence: Expert Opinion/Consensus Statement

Determination of the infecting species is important because *P. falciparum* infections may progress rapidly and lead to severe illness or death. They therefore require urgent initiation of the appropriate therapy. *P. vivax* and *P. ovale* infections require specific, additional treatment because they produce dormant liver-stage parasites that are capable of causing relapses. *P. falciparum* and *P. vivax* species have demonstrated drug resistance patterns that vary by geographic region. Identification of the infecting species as well as knowledge of the geographic area where the infection was acquired can provide information about the drug resistance pattern of the infecting parasite and enable the clinician to choose an appropriate drug regimen and course of treatment [4]. Knowledge of drug resistance patterns is vital to the development and discovery of new antimalarial drugs [25].

The CDC has indicated that oral antimalarial drugs are an effective treatment choice for patients diagnosed with uncomplicated malaria. More severe disease requires aggressive treatment with parenteral antimalarials [4].

TREATMENT OF UNCOMPLICATED MALARIA

An oral antimalarial regimen is an effective choice for uncomplicated malaria; severe illness requires aggressive management and (initially) parenteral therapy. The CDC provides treatment of malaria guidelines for clinicians based on drug options available in the United States [4]. The CDC guidelines may be accessed online at https://www.cdc.gov/malaria/hcp/clinical-guidance/general-treatment.html, with treatment tables available at https://www.cdc.gov/malaria/hcp/clinical-guidance/malaria-treatment-tables.html. The CDC also maintains a malaria hotline at (855) 856-4713 or (770) 488-7788 for after-hours, weekends, and holidays.

Table 1 contains a summary of the CDC treatment recommendations for uncomplicated malaria. For cases in which the diagnosis or the infecting species has not yet been confirmed, treatment against *P. falciparum* should begin immediately and should include continuous monitoring of the patient's clinical status. Blood smears should be made to confirm an adequate response to treatment of infections with *P. falciparum* or suspected chloroquine-resistant *P. vivax* [4].

Relapses may occur in patients in whom either *P. vivax* or *P. ovale* are the infectious agent because, as noted, these agents have dormant liver-stage parasites capable of reactivating. Relapses may occur months to years after the initial infection and may or may not have associated symptoms. Therefore, for infections subsequently diagnosed as *P. vivax* or *P. ovale*, treatment with primaquine should be administered to prevent relapse. The CDC recommends 30 mg primaquine phosphate by mouth once daily for 14 days or one 300-mg dose of tafenoquine [4]. It is important to note that primaquine may cause hemolytic anemia in persons with glucose-6-phosphate-dehydrogenase (G6PD) deficiency; therefore, patients (including pediatric patients) should be screened for G6PD deficiency prior to commencement of treatment. Primaquine is contraindicated during pregnancy [3; 4].

Treatment without the benefit of laboratory confirmation ("presumptive" treatment) should be initiated only in extreme circumstances, such as strong clinical suspicion of infection, indications of severe disease, or the inability to obtain prompt confirmation via laboratory investigations [4]. The CDC has additionally recommended presumptive treatment of *P. falciparum* malaria in persons emigrating from Sub-Saharan Africa prior to their entry into the United States or postarrival, in certain instances [63]. This strategy is designed to decrease the risk of complications or death in a population that might lack access to health care. It is also designed to prevent existing infections from progressing to severe disease and reduce the risk of reintroduction of malaria into the United States [15].

TREATMENT RECOMMENDATIONS FOR UNCOMPLICATED MALARIA			
***Plasmodium* species**	**Drug**	**Dosing**	**Comments**
P. falciparum or "species not identified" in areas **without** chloroquine-resistant strains	Chloroquine phosphate	Initial oral dose: 600 mg base (1,000 mg salt), followed by 300 mg base (500 mg salt) at 6, 24, and 48 hours Maximum dose: 1,500 mg base (2,500 mg salt)	Use adult dosing in pregnancy. Adjust pediatric dosing by patient weight; do not exceed recommended adult dosing. Consider atovaquone-proguanil (preferred) or mefloquine if quinine is unavailable. Quinine and atovaquone-proguanil are recommended for use in children 8 years of age and younger.
	Hydroxychloroquine (Second-line alternative)	Initial oral dose: 620 mg base (800 mg salt), given immediately, followed by 310 mg base (400 mg salt) at 6, 24, and 48 hours Maximum dose: 1,550 mg base (2,000 mg salt)	
P. falciparum or "species not identified" in areas **with** chloroquine-resistant strains (Choose one of the following four options. If later diagnosed as *P. vivax* or *P. ovale*, add antirelapse treatment)	Atovaquone/proguanil	Adults: 1 g/400 mg dose, once daily for three days Available as 250 mg/100 mg adult tablets and 62.5 mg/25 mg pediatric tablets	These are fixed-dose combination medicines that may be used for nonpregnant adult and pediatric patients. Both have been found to be very effective. Adjust pediatric dosing by patient weight.
	Artemether/lumefantrine	Available as 20 mg/120 mg tablets. Three day, four dose course: Initial dose at hour 0 and second dose at hour 8, then one dose on days 2 and 3 5–<15 kg: 1 tablet per dose 15–<25 kg: 2 tablets per dose 25–<35 kg: 3 tablets per dose ≥35 kg (and adults): 4 tablets per dose	
	Quinine sulfate[a] (plus doxycycline, tetracycline, or clindamycin)	Quinine sulfate: 542 mg base (650 mg salt) three times per day for 3 or 7 days Doxycycline: 100 mg twice per day for 7 days Tetracycline: 250 mg four times per day for 7 days Clindamycin: 20 mg/kg/day divided in three daily doses for 7 days	Clindamycin is the preferred option in pregnancy and for children <8 years old
	Mefloquine	Three tablets (750 mg dose) at 0 hours followed by two tablets (500 mg dose) at 6–12 hours	Use only when other options are unavailable. Adjust pediatric dose by patient weight.
P. vivax or *P. ovale* acquired in all areas except Papua New Guinea or Indonesia (choose one of the two acute treatment options AND prescribe antirelapse treatment)	Chloroquine	Same as for *P. falciparum*	If patient is nonresponsive, change treatment to one of the three options listed for treatment of *P. vivax* or *P. ovale* malaria acquired in Papua New Guinea and notify state health department and the CDC.
	Hydroxychloroquine (Second-line alternative)		
	Antirelapse treatment: Primaquine or tafenoquine	Primaquine: 30 mg oral daily for 14 days, OR one oral dose of tafenoquine 300 mg	If regimens other than either chloroquine or hydroxychloroquine used for acute treatment, primaquine is the only option for antirelapse treatment.

Table 1 continues on next page.

TREATMENT RECOMMENDATIONS FOR UNCOMPLICATED MALARIA			
P. vivax or *P. ovale* acquired in Papua New Guinea or Indonesia (choose one of the following four options AND prescribe antirelapse treatment) High possibility of chloroquine-resistant strains	Atovaquone/proguanil	Same as for *P. falciparum* in areas with chloroquine-resistant strains	These are fixed-dose combination medications that may be used and are effective for nonpregnant adult and pediatric patients. Use mefloquine only when other options are unavailable.
	Artemether/lumefantrine		
	Mefloquine		
	Quinine sulfate[a] (plus doxycycline, tetracycline, or clindamycin)		Clindamycin should be used in pregnancy and for children <8 years old
P. malariae or *P. knowlesi*	Any of the antimalarial regimens above may be prescribed; antirelapse treatment is not required. Mefloquine should only be used in the absence of other options.	For specific dosing, see above.	There is little evidence comparing various medications for the treatment of *P. knowlesi*.
[a]Pediatric dosing may require compounding.			
Source: [4; 12; 31]			*Table 1*

TREATMENT DURING PREGNANCY

Malaria infection during pregnancy has been associated with high risks to both mother and fetus, including miscarriage, premature delivery, low birth weight, congenital infection, and maternal and perinatal morbidity and mortality. The reasons for these risks are poorly understood but may include a reduced maternal immune response that ineffectively clears the malaria infection. This is compounded by the ability of the malaria parasites to sequester and replicate in the placenta. Pregnant women are three times more likely than nonpregnant women to develop severe malaria [4]. Healthcare providers should counsel nonpregnant women of childbearing age to use contraception and avoid pregnancy during, and for up to three months following, treatment for malaria [4].

TREATMENT OF SEVERE MALARIA

Of the 1,800 cases of malaria diagnosed in the United States each year, approximately 10% are cases of severe malaria that carry an increased risk of death [28]. Because most deaths from severe malaria occur within the first 24 to 48 hours, patients with manifestations of severe malaria (including pregnant women) should be treated aggressively with parenteral antimalarial therapy as soon as possible after the diagnosis has been made [4]. If laboratory diagnosis cannot be immediately made but severe malaria is strongly suspected, blood should be collected for diagnostic testing and empiric treatment started. Oral antimalarial drugs are not recommended for the initial treatment of severe malaria unless the recommended medication, intravenous (IV) artesunate, is not immediately available [3; 4]. The treatment recommendations for patients with severe malaria are summarized in ***Table 2***.

TREATMENT RECOMMENDATIONS FOR SEVERE MALARIA		
The regimen for the treatment of severe malaria in the United States consists of intravenous (IV) artesunate and, if infected with *P. vivax* or *P. ovale*, antirelapse therapy.		
Drug	**Dosing**	**Comments**
Artesunate	IV dose: 2.4 mg/kg Administer at 0, 12, and 24 hours (3 total)	If IV artesunate is not immediately available, patients should be started on oral antimalarials: artemether/lumefantrine (preferred); or atovaquone-proguanil; or quinine sulfate; or mefloquine (only if no other options available). Antirelapse treatment should include one of either primaquine or tafenoquine. Reassess parasite density at least four hours after the third dose. If parasite density ≤1%, migrate to oral follow-on therapy. If parasite density >1%, continue IV artesunate, same dose, up to 6 more days until parasite density ≤1%. Dosing for all oral agents, including antirelapse treatment, is the same as for uncomplicated malaria (***Table 1***).
Source: [4]		*Table 2*

Quinidine gluconate, an antiarrhythmic drug with antimalarial action, was previously the only parenterally administered antimalarial drug available in the United States. However, the marketing of quinidine was discontinued by the manufacturer in March 2019 [60]. In 2020, parenteral artesunate (from the class of medications known as artemisinins) was approved to treat severe malaria in adult and pediatric patients [60]. The CDC and the World Health Organization (WHO) now recommended artesunate for the treatment of severe malaria [4; 28]. Intravenous artesunate is indicated for all patients with severe malaria disease, regardless of infecting species, [4; 28]. If artesunate cannot be obtained commercially within 24 hours, it can be obtained directly from the CDC by calling the malaria hotline [4].

A full course of oral therapy (artemether/lumefantrine is preferred) should follow the initial IV course if parasite density is ≤1% and the patient can tolerate oral medication. If parasite density is >1% after the first three doses of IV artesunate or if the patient cannot tolerate oral medications, they should be given the recommended IV dose once per day until the density is ≤1% (for a maximum of seven days) or until they can tolerate oral medications. Artesunate is safe in infants, children, and in the second and third trimesters of pregnancy. In the first trimester of pregnancy, no harmful effects have been observed (limited clinical data), and the CDC advises that the benefit of IV artesunate outweighs the risk to the patient and fetus [4]. Individuals administered IV artesunate should be monitored weekly for four weeks for evidence of hemolytic anemia.

Previously, the CDC recommended that exchange transfusion (e.g., the removal of infected red blood cells) be strongly considered for persons with a parasite density of more than 10%. It was also considered if the patient has complications, such as cerebral malaria, acute respiratory distress, or renal complications. However, exchange transfusion has not been proven beneficial in an adequately powered randomized controlled trial. In 2013, the CDC conducted an analysis of cases of severe malaria treated with exchange transfusion and was unable to demonstrate a survival benefit of the procedure. As a result, the CDC no longer recommends the use of exchange transfusion as an adjunct procedure for the treatment of severe malaria [4].

Reports of the emergence of parasites that are resistant to artemisinin derivatives are considered a threat to the global effort to control and eliminate malaria, and WHO has taken steps to confirm and contain such strains [2].

PREVENTION

Between 2000 and 2022, more than 35,000 cases of malaria among U.S. residents were reported to the CDC. The vast majority of these cases (86.8%) were acquired as a result of travel outside the United States [35]. In 2022, 1,999 cases were reported in the United States, with 1,870 resulting from international travel or immigration; one case resulted from blood exposure and three cases were cryptic (i.e., unidentified) [3; 15]. Cases have been increasing in the United States since 1970, with an apparent peak in 2017. Travelers to sub-Saharan Africa are at greatest risk of acquiring a fatal malarial infection [15; 29; 32]. Although malaria poses a serious threat to travelers, it is preventable in most cases [33].

Malaria prevention consists of a combination of infection prevention (including personal protection) and chemoprophylaxis among persons at risk. It also includes assessing the risk factors for individual travelers and identifying appropriate preventive measures based upon that assessment. Travelers to malaria-endemic areas who have previously acquired malaria should be reminded that it may be acquired more than once [30; 33].

There is no criterion standard for assessing a traveler's risk of contracting malaria, so it is important that pre-travel guidance be obtained from a healthcare professional experienced in travel medicine. The level of risk and the individual traveler's profile will guide decision making in determining appropriate preventative measures [30; 34].

RISK ASSESSMENT

Factors to consider and include in a traveler's profile include knowledge about the traveler's destination, the season during which travel will occur, how and for how long the individual will travel, and the traveler's basic personal history. It is important to know the traveler's destination because the risk of acquiring malaria is not uniformly distributed throughout all countries; it may be confined to small areas in some countries. The season of travel is also important because temperature and rainfall may affect malaria transmission. The traveler's anticipated accommodations and activities should also be included in the risk assessment. Indoor accommodations, for example, may be less risky to the traveler than outdoor (e.g., camping) accommodations. Additionally, if the traveler expects to participate in outdoor evening activities, this will increase the risk of exposure to the infecting mosquito. The CDC has found that the greatest risk is among first- and second-generation immigrants who live in non-malaria-endemic countries and then return to their countries of origin to visit family and friends. Because many of these individuals incorrectly consider themselves to be immune, they forego pre-travel preventive measures [30; 33; 34].

The WHO has compiled a convenient ABCDE memory aid for travelers [55]:

- Be **aware** of the risk, the incubation period, and the main symptoms.
- Avoid being **bitten** by mosquitoes, especially between dusk and dawn.
- Take antimalarial drugs **(chemoprophylaxis)** to suppress infection where appropriate.
- Immediately seek **diagnosis** and treatment if a fever develops one week or more after entering an area where there is a malaria risk and up to three months after departure.
- Avoid outdoor activities in **environments** that are mosquito breeding places, such as swamps or marshy areas, especially in late evenings and at night.

PERSONAL PROTECTIVE MEASURES

The CDC and the Infectious Diseases Society of America have recommended that individuals traveling outside the United States be aware of and employ the following personal protective measures [30; 33]:

- Avoid travel to known malaria-endemic areas, when possible. Check https://wwwnc.cdc.gov/travel for updates on regional disease transmission patterns and outbreaks.
- Be aware of peak exposure times and places, usually outdoors at dawn and dusk.
- Wear clothing that minimizes skin exposure (e.g., long sleeves, pants, hats, boots).
- Use bed nets and ensure that they completely cover the sleeping area (e.g., down to the floor or tucked under the mattress). Nets pretreated with pyrethroid insecticides or repellents may be purchased prior to travel. Nets may also be treated after purchase.
- Use insecticides (with caution and as directed). *N*,*N*-diethyl-meta-toluamide (DEET) is an ingredient in many commercially available products and has historically been the most effective repellent; however, any EPA-registered repellant will be equally effective if used correctly. Metofluthrin and allethrin insecticides and spatial repellants (e.g., aerosol sprays, coils, vaporizing mats) are also recommended by the CDC to clear rooms of mosquitoes.

CHEMOPROPHYLAXIS

According to the WHO, more than 10,000 travelers become ill with malaria each year, despite the fact that malaria in travelers is usually preventable [29]. Most cases of malaria acquired due to travel occur because of "poor adherence to, or complete failure to use medicines, or use of inappropriate prophylactic malaria drug regimens, combined with failure to take adequate precautions against mosquito bites" [29]. A CDC surveillance summary of cases of malaria in patients with onset of illness in 2018 found that only 5% of these patients had adhered to or took a region-appropriate regimen of chemoprophylaxis [15].

In addition to the personal protective measures previously discussed, malaria prophylaxis is an important prevention component [15]. All travelers to malaria-endemic areas should take an antimalarial drug. Drug recommendations depend upon the country of travel. Up-to-date recommendations may be found on the CDC Traveler's Health website at https://wwwnc.cdc.gov/travel.

Travelers should be reminded that no antimalarial drug regimen is 100% protective and that it should always be combined with the personal protective measures, as discussed. The CDC has compiled a list of drugs for consideration in those instances when more than one drug has been recommended for a specific area (***Table 3***). Travelers should also be cautioned to be alert for counterfeit antimalarial drugs, which may contain either none or less than the required amount of the active ingredient(s).

CHOOSING A MALARIA PROPHYLAXIS REGIMEN FOR TRAVELERS		
Drug Option	**Benefits**	**Risks/Contraindications**
Atovaquone/ proguanil	May be started one to two days before traveling to a malaria-endemic area Must only be continued for seven days after traveling, rather than four weeks Very well tolerated medicine Pediatric tablets are available and may be more convenient	Contraindicated in women who are pregnant or breastfeeding a child who weighs less than 5 kg Contraindicated in patients with severe renal impairment Tends to be more expensive than some of the other options Some patients would rather not take a daily medication
Chloroquine	Taken only weekly Some patients (e.g., those with chronic rheumatologic conditions) may already be taking hydroxychloroquine Can be used in all trimesters of pregnancy	Cannot be used in areas with chloroquine or mefloquine resistance May exacerbate psoriasis Must continue taking medication for four weeks after travel Must be started one to two weeks prior to travel
Doxycycline	May be started one to two days before traveling to a malaria-endemic area Tends to be the least expensive antimalarial Patients may already be taking doxycycline chronically for prevention of acne Doxycycline can also prevent some additional travel-related infections (e.g., *Rickettsia* and leptospirosis), particularly if patients plan to hike, camp, or swim in fresh water	Contraindicated for pregnant women and children younger than 8 years of age Some patients would rather not take a daily medication Must continue taking medication for four weeks after travel Long-term antibiotic use can increase the risk of fungal overgrowth Increased risk of sun sensitivity and gastrointestinal side effects
Mefloquine	Taken only weekly Can be used in the second and third trimester of pregnancy and in the first trimester if there is no other option (e.g., postpone travel)	Contraindicated for travel to areas with mefloquine resistance and in patients with seizure disorders and certain psychiatric conditions Not recommended for patients with cardiac conduction abnormalities Must be started at least two weeks prior to travel and continued for four weeks after return
Primaquine	One of the most effective medications for preventing *P. vivax* May be started one to two days before traveling to a malaria-endemic area Must only be continued for seven days after traveling, rather than four weeks	Contraindicated in patients with glucose-6-phosphatase dehydrogenase (G6PD) deficiency or whose G6PD deficiency status is unknown Contraindicated in pregnant women and women who are breastfeeding, unless the infant has also been tested for G6PD deficiency Increased risk for gastrointestinal side effects
Tafenoquine	One of the most effective drugs for prevention of *P. vivax* malaria, but also prevents *P. falciparum* May be appropriate for shorter trips (taken once, one week after traveling) or for last-minute travel (started three days before traveling to an endemic area)	Contraindicated in patients with glucose-6-phosphatase dehydrogenase (G6PD) deficiency, nor those who have not been tested for G6PD deficiency Contraindicated in children and women who are pregnant or breastfeeding Not recommended for those with psychotic disorders
Source: [47]		*Table 3*

PRESUMPTIVE SELF-TREATMENT[a] OF MALARIA		
Patient	**Dose**	**Comments**
Atovaquone/Proguanil		
Adult	Four tablets (250 mg atovaquone and 100 mg proguanil each) orally as a single daily dose for three consecutive days	Not currently recommended for pregnant women and women breastfeeding infants weighing less than 5 kg Contraindicated in persons with severe renal impairment
Child 5–≤8 kg	Two pediatric tablets (62.5 mg atovaquone and 25 mg proguanil each)	Not currently recommended for children <5 kg
Child 8–≤10 kg	Three pediatric tablets	
Child 10–≤20 kg	One adult tablet	
Child 20–≤30 kg	Two adult tablets	
Child 30–≤40 kg	Three adult tablets	
Child ≥40 kg	Four adult tablets	
Artemether/Lumefantrine		
5 to <15 kg	1 tablet (artemether 20 mg / lumefantrine 120 mg)	Patients should take an initial dose, followed by a second dose 8 hours later, then 1 dose twice a day for the next 2 days (total of 6 oral doses over 3 days). Not for people taking mefloquine chemoprophylaxis Not recommended for children weighing <5 kgb or women breastfeeding infants weighing <5 kg Absorption improved when taken with a fatty meal
15 to <25 kg	2 tablets	
25 to <35 kg	3 tablets	
≥35 kg	4 tablets	

[a]Self-treatment should be initiated if professional medical care is not available within 24 hours. Medical care should be sought immediately after treatment.
[b]In 2025, artemether/lumefantrine was approved for treatment of neonates and infants 2–5 kg by Swissmedic (Marketing Authorization for Global Health Products), but this was not reflected in the CDC guidelines as of October 2025.

Source: [19; 30; 35] *Table 4*

Some of these counterfeits have reportedly led to deaths [36]. Precautions that all travelers should employ when buying antimalarial drugs include [36]:

- Buying them in their home country before travel begins
- Carrying the manufacturer's name and the drug names (generic and brand) with them in case an additional supply is needed
- Inspecting the drug's packaging carefully and ensuring that it is intact
- Being suspicious of drugs that have a peculiar odor, taste, or color. Additional information about counterfeit drugs may be found on the FDA website.

PRESUMPTIVE SELF-TREATMENT

Malaria may be effectively treated early in the course of the disease; however, delay of appropriate treatment may have serious, even fatal, consequences. Travelers who choose not to take an antimalarial drug, who are on a less than effective regimen (e.g., chloroquine in a chloroquine-resistant risk area), whose medical history dictates a suboptimal drug, or who may be traveling to very remote areas may be prescribed a presumptive self-treatment course (***Table 4***). Travelers should be advised to take the treatment promptly if fever, chills, or other influenza-like illness occurs. This is particularly important if the traveler is unable to access professional medical care within 24 hours. Travelers should also be advised to seek medical care as soon as possible after self-treatment [15; 35].

INFECTION AND DISEASE PREVENTION

Infection may be prevented when the offending mosquitoes are prevented from biting humans. The three most common methods of prevention include insecticide-treated bed nets, intermittent preventive treatment of malaria in pregnant women, and indoor residual spraying [37].

Insecticide-Treated Bed Nets

Insecticide-treated bed nets have been shown to effectively reduce illness, disease, and death caused by malaria. They can reduce overall child mortality by as much as 20% and have additionally been shown to reduce the intensity of transmission [38; 39]. Because mosquitoes are able to feed through nontreated nets and those with even the tiniest holes or tears, the application of insecticides to bed nets improves protection significantly by repelling mosquitoes. Additionally, in communities where insecticide-treated nets are widely used, an overall reduction in the mosquito population has been found to occur.

Long-lasting insecticide-treated nets have also been developed. They offer significant maintenance and use advantages over the older nets, which had to be retreated frequently. The long-lasting insecticide-treated nets offer protection for up to three years. The WHO has recommended several long-lasting insecticide-treated nets [40]:

- Interceptor G2 (BASF)
- Olyset Plus (Sumitomo Chemical)
- PermaNet 3.0 (Vestergaard-Frandsen)
- Royal Guard (Disease Control Technologies)
- Tsara Boost (NRS Moon Netting)
- Tsara Plus (NRS Moon Netting)
- Veeralin (VKA Polymers Private Limited)

Infection and Disease Prevention During Pregnancy

As previously discussed, malaria can have severe, even fatal consequences for a pregnant woman and her fetus. Women who are having their first or second pregnancy and women who are HIV-positive are at an increased risk. The effects of malaria infection on the pregnant woman and her fetus have been found to vary according to the area of transmission. These effects range from maternal anemia, acute respiratory distress, and low-birth-weight infants (generally in areas of high transmission) to severe disease, premature delivery, and even fetal loss (generally in areas of low transmission) [41]. Intermittent preventive treatment involves administration of a full course of an antimalarial at specified intervals (generally two doses for pregnant women), regardless of the confirmed presence of infection. Intermittent preventive treatment has been recommended for pregnant women in areas of high transmission [37]. The antimalarial sulfadoxine-pyrimethamine has been found to reduce the burden of malaria in this population [42; 43].

Indoor Residual Spraying

Indoor residual spraying involves the application of long-acting chemicals to the walls and other surfaces of a house. The goals of indoor residual spraying are to reduce both the population density and the life span of infecting mosquitoes. Indoor residual spraying was part of a global eradication effort conducted from 1955 to 1969, which was successful in Europe, the Soviet Republic, parts of Asia, and the Caribbean. The effort did not include the African continent [44].

VACCINE

For years, research has focused on the development of an effective vaccine to prevent malaria in endemic areas [16; 48; 49; 50; 51; 56; 57]. In 2021, the first vaccine to prevent malaria, RTS,S/AS01 (RTS,S), was approved and recommended by the WHO for children in sub-Saharan Africa and in other regions with moderate-to-high malaria transmission [61].

The vaccine is provided in a schedule of 4 doses in children from 5 months of age [62]. More than 2 million doses of the vaccine were administered prior to the WHO's recommendation, with good safety and efficacy [62]. Along with continued infection prevention strategies, the vaccine is expected to drastically reduce the burden of malaria in effected areas. Research continues into additional vaccines, including those that may be appropriate in adults or for travelers.

In 2023, the WHO approved and recommended a second-in-class vaccine, R21/Matrix-M, for children 5 months of age and older [64]. This additional approval is expected to result in sufficient vaccine supply to benefit all children living in malaria-endemic areas.

CONSIDERATIONS FOR NON-ENGLISH-PROFICIENT PATIENTS

Because patient education is such a vital aspect of preventing the spread of malaria, it is each practitioner's responsibility to ensure that information and instructions are explained in such a way that allows for patient understanding. When there is an obvious disconnect in the communication process between the practitioner and patient due to the patient's lack of proficiency in the English language, an interpreter is required.

In this multicultural landscape, interpreters are a valuable resource to help bridge the communication and cultural gap between clients/patients and practitioners. Interpreters are more than passive agents who translate and transmit information back and forth from party to party. When they are enlisted and treated as part of the interdisciplinary clinical team, they serve as cultural brokers, who ultimately enhance the clinical encounter.

CONCLUSION

Malaria is one of the most significant infectious diseases in the world. It affects between 150 and 300 million people each year worldwide and is a leading cause of illness and death in the developing world. Malaria imposes significant costs to individuals and governments. Such costs can add substantially to the economic burden of malaria on endemic countries and impede their economic growth [2; 18].

Malaria poses a particularly serious threat to U.S. travelers who lack immunity. Although the transmission of malaria was successfully interrupted in the United States during the late 1940s, it continues to pose a challenging health threat to individuals who travel to and emigrate from malarious areas. Because malaria cases are rare in the United States, misdiagnosis is a common problem [4; 5]. Malaria may be suspected based on the patient's symptoms, travel history, and physical findings at examination. Patients with suspected infection should be urgently and thoroughly evaluated. Delayed diagnosis is a leading cause of death among malaria patients in the United States [3].

Patients suspected of having malaria infection should be urgently evaluated, and the diagnosis should be confirmed by laboratory investigations before treatment begins. Presumptive treatment, without the benefit of laboratory confirmation, should be reserved for extreme circumstances [4; 5].

RESOURCES

CDC Malaria Hotline
855-856-4713 (Monday through Friday, 9 a.m. to 5 p.m., Eastern)
770-488-7788 (for emergency consultation after hours and holidays)

CDC Travelers' Health
This site contains general traveler's health precautions and malaria-specific information. The current *CDC Health Information for International Travel* (the Yellow Book) may also be viewed.
https://wwwnc.cdc.gov/travel

Partnership to End Malaria
https://endmalaria.org

CDC Malaria
Clinical Guidance: Malaria Diagnosis and Treatment in the U.S.
https://www.cdc.gov/malaria/hcp/clinical-guidance

PATH Center for Vaccine Innovation and Access (CVIA)
This site contains information about the research into and development of a vaccine for malaria.
https://www.malariavaccine.org

U.S. Food and Drug Administration: Counterfeit Medicine
The site contains information for consumers about counterfeit medications.
https://www.fda.gov/drugs/buying-using-medicine-safely/counterfeit-medicine

Implicit Bias in Health Care

The role of implicit biases on healthcare outcomes has become a concern, as there is some evidence that implicit biases contribute to health disparities, professionals' attitudes toward and interactions with patients, quality of care, diagnoses, and treatment decisions. This may produce differences in help-seeking, diagnoses, and ultimately treatments and interventions. Implicit biases may also unwittingly produce professional behaviors, attitudes, and interactions that reduce patients' trust and comfort with their provider, leading to earlier termination of visits and/or reduced adherence and follow-up. Disadvantaged groups are marginalized in the healthcare system and vulnerable on multiple levels; health professionals' implicit biases can further exacerbate these existing disadvantages.

Interventions or strategies designed to reduce implicit bias may be categorized as change-based or control-based. Change-based interventions focus on reducing or changing cognitive associations underlying implicit biases. These interventions might include challenging stereotypes. Conversely, control-based interventions involve reducing the effects of the implicit bias on the individual's behaviors. These strategies include increasing awareness of biased thoughts and responses. The two types of interventions are not mutually exclusive and may be used synergistically.

Works Cited

1. Centers for Disease Control and Prevention. The History of Malaria: An Ancient Disease. Available at https://stacks.cdc.gov/view/cdc/135582. Last accessed October 13, 2025.
2. World Health Organization. *World Malaria Report: 2024*. Geneva: WHO Press; 2025. Available at https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2024. Last accessed October 13, 2025.
3. Centers for Disease Control and Prevention. Malaria. Available at https://www.cdc.gov/malaria. Last accessed October 13, 2025.
4. Centers for Disease Control and Prevention. Clinical Guidance: Malaria Diagnosis and Treatment in the U.S. Available at https://www.cdc.gov/malaria/hcp/clinical-guidance. Last accessed October 13, 2025.
5. Griffith KS, Lewis LS, Mali S, Parise ME. Treatment of malaria in the United States: a systematic review. *JAMA*. 2007;297(20):2264-2277.
6. Kantele A, Jokiranta S. *Plasmodium knowlesi: the fifth species causing human malaria*. *Duodecim*. 2010;126(4):427-434.
7. Wilairatanal P, Krudsood S, Tangpukdee N. Management of Plasmodium knowlesi malaria without PCR confirmation. *Southeast Asian J Trop Med Public Health*. 2010;41(1):19-21.
8. Lee KS, Cox-Singh J, Singh B. Morphological features and differential counts of Plasmodium knowlesi parasites in naturally acquired human infections. *Malar J*. 2009;8:73.
9. Cox-Singh J, Davis TM, Lee KS, et al. *Plasmodium knowlesi* malaria in humans is widely distributed and potentially life threatening. *Clin Infect Dis*. 2008;46(2):165-171.
10. National Institute of Allergy and Infectious Diseases. Malaria. Available at https://www.niaid.nih.gov/diseases-conditions/malaria. Last accessed October 13, 2025.
11. Spadafora C, Awandare GA, Kopydlowski KM, et al. Complement receptor 1 is a sialic acid-independent erythrocyte receptor of *Plasmodium falciparum*. *PloS Pathog*. 2010;6(6):e1000968.
12. Figtree M, Lee R, Bain L, et al. *Plasmodium knowlesi* in human, Indonesian Borneo. *Emerg Infect Dis*. 2010;16(4):672-674.
13. Zhang M, Fennell C, Ranford-Cartwright L, et al. The *Plasmodium* eukaryotic initiation factor-2{alpha} kinase IK2 controls the latency of sporozoites in the mosquito salivary glands. *J Exp Med*. 2010;207(7):1465-1474.
14. Sullivan D. Uncertainty in mapping malaria epidemiology: implications for control. *Epidemiol Rev*. 2010;32(1):175-187.
15. Mace KE, Lucchi NW, Tan KR. Malaria surveillance—United States, 2018. *MMWR*. 2022;71(SS8):1-29.
16. Kappe SH, Vaughan AM, Boddey JA, Cowman AF. That was then but this is now: malaria research in the time of an eradication agenda. *Science*. 2010;328(5980):862-866.
17. Filler SJ, MacArthur JR, Parise M, et al. Locally acquired mosquito-transmitted malaria: a guide for investigations in the United States. *MMWR*. 2006;55(RR13):1-9.
18. World Health Organization. Malaria. Available at https://www.who.int/news-room/fact-sheets/detail/malaria. Last accessed October 13, 2025.
19. Medicines for Malaria Venture. First Malaria Medicine for Newborn Babies and Young Infants 2–5 kg Receives Approval. Available at https://www.mmv.org/newsroom/news-resources-search/first-malaria-medicine-newborn-babies-and-young-infants-2-5-kg. Last accessed October 13, 2025.
20. Thwing J, Skarbinski J, Newman RD, et al. Appendix: microscopic procedures for diagnosing malaria. *MMWR*. 2007;56(SS6):39-40.
21. Maltha J, Gillet P, Bottieau E, Cnops L, van Esbroeck M, Jacobs J. Evaluation of a rapid diagnostic test (CareStartTM Malaria HRP-2/pLDH (Pf/pan) Combo Test) for the diagnosis of malaria in a reference setting. *Malar J*. 2010;9:171.
22. Centers for Disease Control and Prevention. Malaria Diagnostic Tests. Available at https://www.cdc.gov/malaria/hcp/diagnosis-testing/malaria-diagnostic-tests.html. Last accessed October 13, 2025.
23. Centers for Disease Control and Prevention. National Notifiable Disease Surveillance System Malaria (*Plasmodium* spp.) 2014 Case Definition. Available at https://ndc.services.cdc.gov/case-definitions/malaria-2014/. Last accessed October 13, 2025.
24. Centers for Disease Control and Prevention. How to Report a Case of Malaria. Available at https://www.cdc.gov/malaria/php/case-reporting. Last accessed October 13, 2025.
25. Lucumi E, Darling C, Jo H, et al. Discovery of potent small molecule inhibitors of multi-drug resistant *P. falciparum* using a novel miniaturized high-throughput luciferase-based assay. *Antimicrob Agents Chemother*. 2010;54(9):3597-3604.
26. Singh B. *Plasmodium knowlesi*: an update. *Microbiology Australia*. 2016;1:39-42.
27. World Health Organization. Malaria: Rapid Diagnostic Tests. Available at https://www.who.int/teams/global-malaria-programme/case-management/diagnosis/rapid-diagnostic-tests. Last accessed October 13, 2025.
28. Centers for Disease Control and Prevention. Appendix C: How to Acquire IV Artesunate in the United States. Available at https://www.cdc.gov/malaria/hcp/clinical-guidance/iv-artesunate-us.html. Last accessed October 13, 2025.
29. World Health Organization. International Travel and Health: Malaria. Available at https://cdn.who.int/media/docs/default-source/travel-and-health/9789241580472-eng-chapter-7.pdf?sfvrsn=8be7067_13. Last accessed October 13, 2025.

30. Centers for Disease Control and Prevention. Travelers' Health: Yellow Book Homepage. Available at https://www.cdc.gov/yellow-book/index.html. Last accessed October 13, 2025.
31. LexiDrug. Available at https://online.lexi.com. Last accessed October 13, 2025.
32. Centers for Disease Control and Prevention. Preventing Malaria while Traveling. Available at https://www.cdc.gov/malaria/prevention/index.html. Last accessed October 13, 2025.
33. Bell DJ, Lalloo DG. Malaria and travelers. In: Zuckerman JN (ed). *Principles and Practice of Travel Medicine*. 2nd ed. Oxford: Wiley-Blackwell; 2013: 126-132.
34. Centers for Disease Control and Prevention. Malaria Risk Assessment for Travelers. Available at https://www.cdc.gov/malaria/hcp/risk-assessment. Last accessed October 13, 2025.
35. Brunette GW, Nemhauser JB, Kozarsky PE, et al. (eds). *CDC Health Information for International Travel 2020*. New York, NY: Oxford University Press; 2020.
36. Centers for Disease Control and Prevention. Counterfeit Medicines. Available at https://wwwnc.cdc.gov/travel/page/counterfeit-medicine. Last accessed October 13, 2025.
37. Centers for Disease Control and Prevention. Strategies for Reducing Malaria's Global Impact. Available at https://www.cdc.gov/malaria/php/public-health-strategy/index.html. Last accessed October 13, 2025.
38. UNICEF. Childhood Diseases. Available at https://www.unicef.org/health/childhood-diseases. Last accessed October 13, 2025.
39. Russell TL, Lwetoijera DW, Maliti D, et al. Impact of promoting longer-lasting insecticide treatment of bed nets upon malaria transmission in a rural Tanzanian setting with pre-existing high coverage of untreated nets. *Malar J*. 2010;9(1):187.
40. World Health Organization. WHO Publishes Recommendations on Two New Types of Insecticide-Treated Nets. Available at https://www.who.int/news/item/14-03-2023-who-publishes-recommendations-on-two-new-types-of-insecticide-treated-nets. Last accessed October 13, 2025.
41. Smereck J. Malaria in pregnancy: update on emergency management. *J Emerg Med*. 2011;40(4):393-396.
42. Centers for Disease Control and Prevention. Core Drug-based Malaria Prevention Strategies. Available at https://www.cdc.gov/malaria/php/public-health-strategy/drug-strategies.html. Last accessed October 13, 2025.
43. Kayentao K, Garner P, van Eijk AM, et al. Intermittent preventive therapy for malaria during pregnancy using 2 vs 3 or more doses of sulfadoxine-pyrimethamine and risk of low birth weight in Africa: systematic review and meta-analysis. JAMA. 2013;309(6):594-604.
44. Global Malaria Programme. *Indoor Residual Spraying: Use of Indoor Residual Spraying for Scaling Up Global Malaria Control and Elimination*. Geneva: World Health Organization; 2006. Available at https://apps.who.int/iris/bitstream/handle/10665/69386/WHO_HTM_MAL_2006.1112_eng.pdf. Last accessed October 13, 2025.
45. Alonso PL, Sacarial J, Aponte JJ, et al. Efficacy of the RTS,S/AS02A vaccine against *Plasmodium falciparum* infection and disease in young African children: randomised controlled trial. *Lancet*. 2004;364(9443):1411-1420.
46. Fauci AS, Touchette NA, Folkers GK. Emerging infectious diseases: a 10-year perspective from the National Institute of Allergy and Infectious Diseases. *Emerging Infect Dis*. 2005;11(4):519-525.
47. Centers for Disease Control and Prevention. Choosing a Drug to Prevent Malaria. Available at https://www.cdc.gov/malaria/hcp/drug-malaria. Last accessed October 13, 2025.
48. Olotu A, Fegan G, Wambua J, et al. Seven-year efficacy of RTS,S/AS01 malarial vaccine among young African children. *New Eng J Med*. 2016;374:2519-2529.
49. Malaria Vaccine Initiative. Vaccines. Available at https://www.malariavaccine.org/rd/vaccines. Last accessed October 13, 2025.
50. Clemens J, Moorthy V. Implementation of RTS,S/AS01 malaria vaccine: the need for further evidence. *New Eng J Med*. 2016;374:2596-2597.
51. Malaria Vaccine Initiative. Research and Development. Available at https://www.malariavaccine.org/rd. Last accessed October 13, 2025.
52. Centers for Disease Control and Prevention. DPDx: Malaria. Available at https://www.cdc.gov/dpdx/malaria/index.html. Last accessed October 13, 2025.
53. Centers for Disease Control and Prevention. Where Malaria Occurs. Available at https://www.cdc.gov/malaria/data-research. Last accessed October 13, 2025.
54. Centers for Disease Control and Prevention. CDC and Malaria. Available at https://www.cdc.gov/malaria/cdc-malaria. Last accessed October 13, 2025.
55. World Health Organization. *International Travel and Health: Malaria: 2015 update*. Geneva: World Health Organization; 2015.
56. Malaria Vaccine Initiative. First-Generation Vaccine: RTS,S. Available at https://www.malariavaccine.org/existing-vaccines/rtss. Last accessed October 13, 2025.
57. RTS,S Clinical Trials Partnership. Efficacy and safety of RTS,S/AS01 malaria vaccine with or without a booster dose in infants and children in Africa: final results of a phase 3, individually randomised, controlled trial. *Lancet*. 2015;386(9988):31-45.
58. World Health Organization. World Malaria Report 2018. Available at https://apps.who.int/iris/bitstream/handle/10665/275867/9789241565653-eng.pdf?ua=1. Last accessed October 13, 2025.

59. Centers for Disease Control and Prevention. Congenital malaria—Nassau County, New York, 2004. *MMWR*. 2005;54(15):383-384.
60. U.S. Food and Drug Administration. CDC and FDA Continue Efforts to Ensure Timely Access to Front-Line Treatments for Severe Malaria. Available at https://www.fda.gov/media/130925/download. Last accessed October 13, 2025.
61. World Health Organization. WHO Recommends Groundbreaking Malaria Vaccine for Children at Risk. Available at https://www.who.int/news/item/06-10-2021-who-recommends-groundbreaking-malaria-vaccine-for-children-at-risk. Last accessed October 13, 2025.
62. World Health Organization. Malaria Vaccines (RTS,S and R21). Available at https://www.who.int/news-room/questions-and-answers/item/q-a-on-rts-s-malaria-vaccine. Last accessed October 13, 2025.
63. Centers for Disease Control and Prevention. Immigrant and Refugee Health: Malaria Guidance. Available at https://www.cdc.gov/immigrant-refugee-health/hcp/overseas-guidance/malaria-guidance.html. Last accessed October 13, 2025.
64. Centers for Disease Control and Prevention. Malaria Vaccines. Available at https://www.cdc.gov/malaria/php/public-health-strategy/malaria-vaccines.html. Last accessed October 13, 2025.
65. Michel M, Skourtanioti E, Pierini F, et al. Ancient *Plasmodium* genomes shed light on the history of human malaria. *Nature*. 2024;631(8019):125-133.

Evidence-Based Practice Recommendation Citation

Centers for Disease Control and Prevention. Clinical Guidance: Malaria Diagnosis & Treatment in the U.S. Available at https://www.cdc.gov/malaria/hcp/clinical-guidance/general-treatment.html. Last accessed October 14, 2025.