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Chapter 2
The Pre-Travel Consultation
Malaria

Chapter 2: Varicella (Chickenpox) (/travel/yellowbook/2010/chapter-2/varicella.aspx)

Chapter 2: Malaria Risk Information and Prophylaxis, by Country (/travel/yellowbook/2010/chapter-2/malaria-risk-information-and-prophylaxis.aspx)

MALARIA

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Infectious Agent

Malaria in humans is caused by one of four protozoan species of the genus *Plasmodium*: *P. falciparum*, *P. vivax*, *P. ovale*, or *P. malariae*. Recently, *P. knowlesi*, a parasite of Old World monkeys, has been documented as a cause of human infections and some fatalities in Southeast Asia. Investigations are ongoing to determine the extent of its transmission to humans.

Mode of Transmission

All species are transmitted by the bite of an infected female *Anopheles* mosquito. Occasionally, transmission occurs by blood transfusion, organ transplantation, needle sharing, or congenitally from mother to fetus.

Occurrence

- Each year malaria causes 350–500 million infections worldwide and approximately 1 million deaths.
- Transmission occurs in large areas of Central and South America, parts of the Caribbean, Africa, Asia (including South Asia, Southeast Asia, and the Middle East), Eastern Europe, and the South Pacific (Maps 2-7 and 2-8).
- Information about malaria transmission in specific countries (see the Malaria Risk Information and Prophylaxis, by Country (/travel/yellowbook/2010/chapter-2/malaria-risk-information-and-prophylaxis.aspx) , section later in this chapter) is derived from various sources, including WHO.
- Tools such as the interactive malaria map can assist in locating more unusual destinations and determining if malaria transmission occurs there (see www.cdc.gov/malaria/map/index.html (http://www.cdc.gov/malaria/map/index.html)).

Risk for Travelers

- The risk for a traveler acquiring malaria differs substantially from region to region and from traveler to traveler, even within a single country.
- From 1997 through 2006, 10,745 cases of malaria among U.S. residents were reported to CDC. Of these, 6,376 (59.3%) were acquired in sub-Saharan Africa; 1,498 (13.9%) in Asia; 1,427 (13.3%) in the Caribbean and Central and South America; and 278 (0.03%) in Oceania. During this period, 54 fatal malaria infections occurred among U.S. residents; 46 (85.2%) were caused by *P. falciparum*, of which 33 (71.1%) were acquired in sub-Saharan Africa.
- These absolute numbers of cases should be considered within the context of the volume of travel to these locations. Regions with the highest estimated relative risk for infection for travelers are West Africa and Oceania. Regions with moderate estimated relative risk for infection are the other parts of Africa, South Asia, and South America. Regions with lower estimated relative risk are Central America and other parts of Asia. There is considerable country-by-country variation, as well as variable transmission within countries and sometimes seasonal variation.
- Prevention of malaria involves striking a balance between ensuring that all people who will be at risk for infection use the appropriate

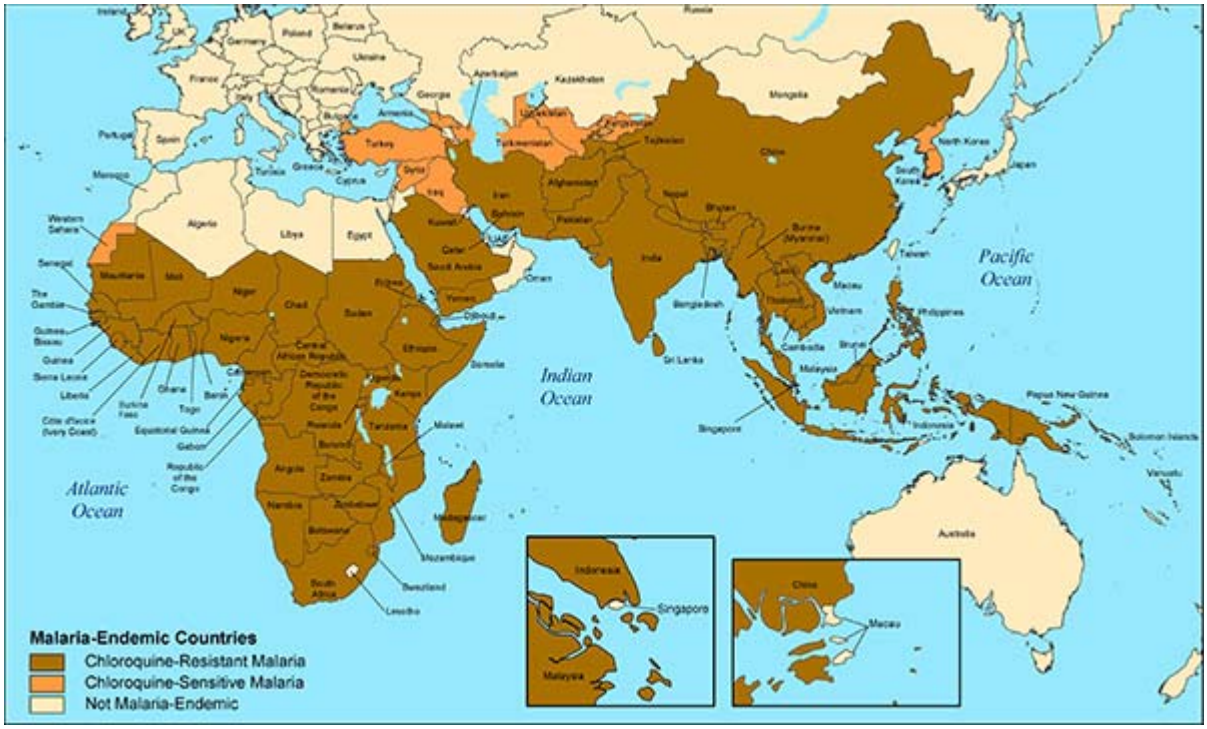
prevention measures, while preventing adverse effects of those interventions among people using them unnecessarily. An individual risk assessment should be conducted for every traveler, taking into account not only the destination country, but also the detailed itinerary, including specific cities, types of accommodation, season, and style of travel. In addition, conditions such as pregnancy or the presence of antimalarial drug resistance at the destination may modify the risk assessment.

- Depending on level of risk, it may be appropriate to recommend no specific interventions, mosquito avoidance measures only, or mosquito avoidance measures plus chemoprophylaxis.
- For areas of intense transmission, such as West Africa, exposure for even short periods of time can result in transmission, so this area should be considered high risk.
- Malaria risk is not distributed homogeneously throughout all countries. Some destinations have malaria transmission occurring throughout the whole country, while in others it occurs in defined pockets. If travelers are going to the high-risk pockets during peak transmission times, even though the country as a whole may be low risk, this destination for this individual may be high risk.
- Geography is just one part of determining a traveler's risk for infection. Risk can differ substantially for different travelers if their behaviors and circumstances differ. For example, travelers staying in air-conditioned hotels may be at lower risk than backpackers or adventure travelers. Similarly, long-term residents living in screened and air-conditioned housing are less likely to be exposed than are persons living without such amenities.
- The highest risk is associated with first- and second-generation immigrants living in nonendemic countries who return to their countries of origin to visit friends and relatives (VFRs). VFR travelers often consider themselves to be at no risk because they grew up in a malarious country and consider themselves immune. However, acquired immunity is lost very quickly, and VFRs should be considered as having the same risk as otherwise nonimmune travelers.
- Travelers should also be reminded that even if one has had malaria before, one can get it again and preventive measures are still necessary. All travelers going to malaria-endemic countries, even for short periods of time, such as cruise ship passengers, may be at risk for becoming infected with malaria.
- Persons who have been in an area where malaria transmission occurs, either during daytime or nighttime hours, are not permitted to donate blood in the United States for a period of time after returning from the malarious area. Persons who are residents of nonmalarious countries are not permitted to donate blood for 1 year after they have returned from a malarious area. Persons who are residents of malarious countries are not permitted to donate blood for 3 years after leaving a malarious area. Persons who have had malaria are not allowed to donate blood for 3 years after treatment for malaria.
- Risk assessments may differ between travel medicine providers and blood banks. A travel medicine provider advising a traveler going to a relatively low-risk country for a short period of time and engaging in behaviors that place them at lower risk for exposure may choose insect avoidance only and no chemoprophylaxis for the traveler. However, upon the traveler's return, a blood bank may still choose to defer that traveler for 1 year because of the travel to an area where transmission occurs.

Map 2-7. Malaria-endemic countries in the Western Hemisphere.


United States
Atlantic Ocean
The Bahamas
Mexico
Belize
Cuba
Dominican Republic
Jamaica
Honduras
Haiti
Guyana
Guatemala
Panama
Suriname
El Salvador
Venezuela
French Guiana
Nicaragua
Costa Rica
Colombia
Ecuador
Peru
Brazil
Pacific Ocean
Bolivia
Paraguay
Chile
Argentina
Uruguay
Falkland Islands
Malaria-Endemic Countries
Chloroquine-Resistant Malaria
Chloroquine-Sensitive Malaria
Not Malaria Endemic

Map 2-8. Malaria-endemic countries in the Eastern Hemisphere.



(Updated July 2, 2010)

Clinical Presentation

- Malaria is characterized by fever and influenza-like symptoms, including chills, headache, myalgias, and malaise; these symptoms can occur at intervals.
- Uncomplicated disease may be associated with anemia and jaundice. In severe disease, most commonly caused by *P. falciparum*, seizures, mental confusion, kidney failure, acute respiratory disease syndrome (ARDS), coma, and death may occur.
- Malaria symptoms can develop as early as 7 days (usually at least 14 days) after initial exposure in a malaria-endemic area and as late as several months or more after departure.

Diagnosis

- Travelers who have symptoms of malaria should be advised to seek medical evaluation **as soon as possible**.
- Smear microscopy remains the gold standard for malaria diagnosis. Microscopy can also be used to determine the species of malaria parasite and quantify the parasitemia—both of which are necessary pieces of information for providing the most appropriate treatment.
- Various test kits are available to detect antigens derived from malaria parasites. Such immunologic (immunochromatographic) tests most often use a dipstick or cassette format and provide results in 2–15 minutes. These rapid diagnostic tests (RDTs) offer a useful alternative to microscopy in situations where reliable microscopic diagnosis is not available. The U.S. Food and Drug Administration (FDA) has approved one RDT for use in the United States by hospital and commercial laboratories, not by individual clinicians or by patients themselves. This RDT, called BinaxNOW Malaria test, is produced by Inverness Medical Professional Diagnostics, located in Scarborough, Maine.
- Polymerase chain reaction (PCR) tests are also available for detecting malaria parasites; however, none are FDA-approved. Although these tests are slightly more sensitive than routine microscopy, results are not usually available as quickly as microscopy results should be, thus limiting the clinical utility of this test. PCR testing can be used to determine the species of the parasite if the microscopic results are ambiguous.
- In sub-Saharan Africa, the rate of false-positive blood films for malaria may be very high. Travelers to this region should be warned they

may be diagnosed with malaria incorrectly, even though they are taking a reliable antimalarial regimen. In such cases, acutely ill travelers should be advised to seek the best available medical services and follow the treatment offered locally (except the use of halofantrine which is not recommended; see below), but **not** to stop their chemoprophylaxis regimen.

Treatment

- Malaria can be treated effectively early in the course of the disease, but delay of appropriate therapy can have serious or even fatal consequences.
- Travelers who have symptoms of malaria should be advised to seek medical evaluation **as soon as possible**.
- Specific treatment options depend on the species of malaria, the likelihood of drug resistance (based on the location of acquisition of infection), the age of the patient, pregnancy status, and the severity of infection. If possible, it is advisable to consult with a provider who has specialized travel/tropical medicine expertise or with an infectious disease physician.
- CDC recommendations for malaria treatment can be found at http://www.cdc.gov/malaria/diagnosis_treatment/treatment.html (http://www.cdc.gov/malaria/diagnosis_treatment/treatment.html) .
- Medications that are not used in the United States for the treatment of malaria, such as halofantrine (Halfan), are widely available overseas. CDC does not recommend halofantrine for treatment because of cardiac adverse events, including deaths, which have been documented following treatment doses. These adverse events have occurred in persons with and without pre-existing cardiac problems and both in the presence and absence of other antimalarial drugs (e.g., mefloquine).

Self-Treatment (Table 2-22)

- Travelers who reject the advice to take prophylaxis, who choose a suboptimal drug regimen (e.g., chloroquine in an area with chloroquine-resistant *P. falciparum*), or who require a less-than-optimal drug regimen for medical reasons are at greater risk for acquiring malaria and needing prompt treatment.
- Travelers who are taking effective prophylaxis but who will be in very remote areas may decide, in consultation with their health-care provider, to take along a full course of an approved malaria treatment regimen for self-treatment. This should occur very rarely.
- Travelers should be advised to take their presumptive self-treatment promptly if they have fever, chills, or other influenza-like illness and if professional medical care is not available within 24 hours. **Travelers should be advised that this self-treatment of a possible malarial infection is only a temporary measure and that prompt medical evaluation is imperative.**
- Atovaquone/proguanil may be used for presumptive self-treatment for travelers NOT taking atovaquone/proguanil for prophylaxis. If taking atovaquone/proguanil for prophylaxis, the use of the same drug at therapeutic doses is not recommended to empirically treat fever (suspected malaria). The CDC Malaria Branch (Malaria Hotline 770-488-7788) can provide consultation to health-care providers on other potential options for self-treatment if atovaquone/proguanil cannot be used.

Malaria Hotline

- Health-care professionals who require assistance with the diagnosis or treatment of malaria should call the CDC Malaria Hotline (770-488-7788) from 8:00 am to 4:30 pm Eastern time. After hours or on weekends and holidays, health-care providers requiring assistance should call the CDC Emergency Operations Center at 770-488-7100 and ask the operator to page the person on call for the Malaria Branch.
- Information on diagnosis and treatment is available at www.cdc.gov/malaria (http://www.cdc.gov/malaria) .

Table 2-22. Presumptive self-treatment of malaria

Drug	Adult Dose	Pedatric Dose	Comments
Atovaquone/proguanil (Malarone). Self-treatment drug to be used if professional medical care is not available within 24 hours.	4 tablets (each dose contains 1,000 mg atovaquone and 400 mg	Daily dose to be taken for 3 consecutive	Contraindicated in persons with severe renal impairment (creatinine clearance <30 mL/min). Not recommended for self-treatment in persons on

Drug	Adult Dose	Pedatric Dose	Comments
Medical care should be sought immediately after treatment.	proguanil) orally as a single daily dose for 3 consecutive days.	days: 5–8 kg: 2 pediatric tablets; 9–10 kg: 3 pediatric tablets; 11–20 kg: 1 adult tablet; 21–30 kg: 2 adult tablets; 31–40 kg: 3 adult tablets; >41 kg: 4 adult tablets	atovaquone/ proguanil prophylaxis. Not currently recommended for children <5 kg, pregnant women, and women breastfeeding infants weighing <5 kg

Preventive Measures for Travelers

Malaria prevention consists of a combination of mosquito avoidance measures and chemoprophylaxis. Although very efficacious, none of the recommended interventions are 100% effective.

Mosquito Avoidance Measures

- Because of the nocturnal feeding habits of *Anopheles* mosquitoes, malaria transmission occurs primarily between dusk and dawn.
- Contact with mosquitoes can be reduced by remaining in well-screened areas, using mosquito bed nets (preferably insecticide-treated nets), using a pyrethroid-containing flying-insect spray in living and sleeping areas during evening and nighttime hours, and wearing clothes that cover most of the body.
- All travelers should use an effective mosquito repellent.
- The most effective repellent against a wide range of vectors is DEET (*N*,*N*-diethylmetatoluamide), an ingredient in many commercially available insect repellents. The actual concentration of DEET varies widely among repellents. DEET formulations as high as 50% are recommended for both adults and children older than 2 months of age (see the Protection Against Mosquitoes, Ticks, and Other Insects and Arthropods section later in this chapter). DEET should be applied to the exposed parts of the skin when mosquitoes are likely to be present.
- In addition to using a topical insect repellent, a permethrin-containing product may be applied to bed nets and clothing for additional protection against mosquitoes.

Chemoprophylaxis

- All currently recommended primary chemoprophylaxis regimens involve taking a medicine before travel, during travel, and for a period of time after leaving the malaria endemic area. Beginning the drug before travel allows the antimalarial agent to be in the blood before the traveler is exposed to malaria parasites.
- Presumptive antirelapse therapy (also known as terminal prophylaxis) uses a medication towards the end of the exposure period (or immediately thereafter) to prevent relapses or delayed-onset clinical presentations of malaria caused by hypnozoites (dormant liver stages) of *P. vivax* or *P. ovale*. Because most malarious areas of the world (except the Caribbean) have at least one species of relapsing malaria, travelers to these areas have some risk for acquiring either *P. vivax* or *P. ovale*, although the actual risk for an individual traveler is difficult to define. Presumptive anti-relapse therapy is generally indicated only for persons who have had prolonged exposure in malaria-endemic areas (e.g., missionaries, volunteers).
- In choosing an appropriate chemoprophylactic regimen before travel, the traveler and the health-care provider should consider several factors. The travel itinerary should be reviewed in detail and compared with the information on where malaria transmission occurs within a given country (see the Malaria Risk Information and Prophylaxis, by Country, section later in this chapter) to determine whether the traveler

will actually be traveling in a part of the country where malaria occurs and if significant antimalarial drug resistance has been reported in that location.

- The resistance of *P. falciparum* to chloroquine has been confirmed in all areas with *P. falciparum* malaria except the Caribbean, Central America west of the Panama Canal, and some countries in the Middle East. In addition, resistance to sulfadoxine–pyrimethamine (e.g., Fansidar) is widespread in the Amazon River Basin area of South America, much of Southeast Asia, other parts of Asia, and in large parts of Africa. Resistance to mefloquine has been confirmed on the borders of Thailand with Burma (Myanmar) and Cambodia, in the western provinces of Cambodia, in the eastern states of Burma (Myanmar), on the border between Burma and China, along the borders of Laos and Burma, and the adjacent parts of the Thailand–Cambodia border, as well as in southern Vietnam (Map 2-9).
- Additional factors to consider are the patient's other medical conditions, medications being taken (to assess potential drug–drug interactions), the cost of the medicines, and the potential side effects.
- The medications recommended for chemoprophylaxis of malaria may also be available at overseas destinations. However, combinations of these medications and additional drugs that are not recommended may be commonly prescribed and used in other countries. Travelers should be strongly discouraged from obtaining chemoprophylactic medications while abroad. The quality of these products is not known, and they may not be protective and may be dangerous. These medications may have been produced by substandard manufacturing practices, may be counterfeit, or may contain contaminants. Additional information on this topic can be found in *Perspectives*: Counterfeit Drugs (http://counterfeit-drugs.aspx) later in this chapter and in an FDA document Purchasing Medications Outside the United States (www.fda.gov/ora/import/purchasing_medications.htm (/travel/forward.aspx?t=aHR0cDovL3d3dy5mZGEuZ292L29yYS9pbXBvcnQvcHVyY2hhc2luZ19tZWRpY2F0aW9ucy5odG0%3d-vviamfQJ834%3d)).

Medications Used for Chemoprophylaxis

Atovaquone/Proguanil (Malarone)

- Atovaquone/proguanil is a fixed combination of the two drugs, atovaquone and proguanil.
- Prophylaxis should begin 1–2 days before travel to malarious areas and should be taken daily, at the same time each day, while in the malarious areas, and daily for 7 days after leaving the area (see Table 2-23 for recommended dosages).
- Malarone is very well tolerated, and side effects are rare. The most common adverse effects reported in persons using atovaquone/proguanil for prophylaxis or treatment are abdominal pain, nausea, vomiting, and headache. Malarone should not be used for prophylaxis in children weighing <5 kg, pregnant women, or patients with severe renal impairment (creatinine clearance <30 mL/min). It should be used with caution by patients taking coumadin (warfarin) for anticoagulation.

Chloroquine (Aralen) and Hydroxychloroquine (Plaquenil)

- Chloroquine phosphate or hydroxychloroquine sulfate can be used for prevention of malaria only in destinations where chloroquine resistance is not present (see Maps 2-7 and 2-8 or the next section in this chapter, Malaria Risk Information and Prophylaxis, by Country).
- Prophylaxis should begin 1–2 weeks before travel to malarious areas. It should be continued by taking the drug once a week, on the same day of the week, during travel in malarious areas and for 4 weeks after a traveler leaves these areas (see Table 2-23 for recommended dosages).
- Reported side effects include gastrointestinal disturbance, headache, dizziness, blurred vision, insomnia, and pruritus, but generally these effects do not require that the drug be discontinued. High doses of chloroquine, such as those used to treat rheumatoid arthritis, have been associated with retinopathy; this serious side effect appears to be extremely unlikely when chloroquine is used for routine weekly malaria prophylaxis. Chloroquine and related compounds have been reported to exacerbate psoriasis. Persons who experience uncomfortable side effects after taking chloroquine may tolerate the drug better by taking it with meals. As an alternative, the related compound hydroxychloroquine sulfate may be better tolerated.

Doxycycline (Many Brand Names and Generic)

- Doxycycline prophylaxis should begin 1–2 days before travel to malarious areas. It should be continued once a day, at the same time each day, during travel in malarious areas and daily for 4 weeks after the traveler leaves such areas.
- Insufficient data exist on the antimalarial prophylactic efficacy of related compounds such as minocycline (commonly prescribed for the treatment of acne). Persons on a long-term regimen of minocycline who are in need of malaria prophylaxis should stop taking minocycline 1–2 days before travel and start doxycycline instead. The minocycline can be restarted after the full course of doxycycline is completed. (See Table 2-23 for recommended dosages.)
- Doxycycline can cause photosensitivity, usually manifested as an exaggerated sunburn reaction. The risk for such a reaction can be minimized by avoiding prolonged, direct exposure to the sun and by using sunscreens. In addition, doxycycline use is associated with an increased frequency of vaginal yeast infections. Gastrointestinal side effects (nausea or vomiting) may be minimized by taking the drug with a meal. To reduce the risk for esophagitis, travelers should be advised not to take doxycycline before going to bed. Doxycycline is contraindicated in persons with an allergy to tetracyclines, during pregnancy, and in infants and children <8 years of age.
- Vaccination with the oral typhoid vaccine Ty21a should be delayed for at least 24 hours after taking a dose of doxycycline.

Mefloquine

- Mefloquine prophylaxis should begin at least 2 weeks before travel to malarious areas. It should be continued once a week, on the same day of the week, during travel in malarious areas and for 4 weeks after a traveler leaves such areas (See Table 2-23 for recommended dosages). (Updated April 20, 2010)
- Mefloquine has been associated with rare serious adverse reactions (e.g., psychoses, seizures) at prophylactic doses; these reactions are more frequent with the higher doses used for treatment. Other side effects that have occurred in chemoprophylaxis studies include gastrointestinal disturbance, headache, insomnia, abnormal dreams, visual disturbances, depression, anxiety disorder, and dizziness. Other more severe neuropsychiatric disorders occasionally reported during postmarketing surveillance include sensory and motor neuropathies (including paresthesia, tremor, and ataxia), agitation or restlessness, mood changes, panic attacks, forgetfulness, confusion, hallucinations, aggression, paranoia, and encephalopathy. On occasion, psychiatric symptoms have been reported to continue long after mefloquine has been stopped. Mefloquine is contraindicated for use by travelers with a known hypersensitivity to mefloquine or related compounds (e.g., quinine, quinidine) and in persons with active depression, a recent history of depression, generalized anxiety disorder, psychosis, schizophrenia, other major psychiatric disorders, or seizures. It should be used with caution in persons with psychiatric disturbances or a previous history of depression. A review of available data suggests that mefloquine may be used in persons concurrently on beta blockers, if they have no underlying arrhythmia. However, mefloquine is not recommended for persons with cardiac conduction abnormalities.
- Any traveler receiving a prescription for mefloquine must also receive a copy of the FDA Medication Guide, which can be found at the following website: www.fda.gov/cder/foi/label/2003/19591s19lbl_Lariam.pdf (/travel/forward.aspx?t=aHR0cDovL3d3dy5mZGEuZ292L2Rvd25sb2Fkcy9EcnVncy9EcnVnU2FmZXR5L3VjbTA4ODYxNi5wZGY%3d-uHnONogFUdg%3d) (PDF).

Primaquine

- Primaquine phosphate has two distinct uses for malaria prevention: primary prophylaxis and presumptive antirelapse therapy (also called terminal prophylaxis).
- When taken for primary prophylaxis, primaquine should be taken 1–2 days before travel to malarious areas, daily, at the same time each day, while in the malarious areas, and daily for 7 days after leaving the areas (see Table 2-23 for recommended dosages). Primary prophylaxis with primaquine obviates the need for presumptive antirelapse therapy.
- When used for presumptive antirelapse therapy, primaquine is administered for 14 days after the traveler has left a malarious area. When chloroquine, doxycycline, or mefloquine is used for primary prophylaxis, primaquine is usually taken during the last 2 weeks of postexposure prophylaxis. When atovaquone/proguanil is used for prophylaxis, primaquine may be taken during the final 7 days of atovaquone/proguanil, and then for an additional 7 days. It is preferable that primaquine be given concurrently with the primary prophylaxis medication. However, if that is not feasible, the primaquine course should still be administered after the primary prophylaxis medication has been completed.
- The most common adverse event in glucose-6-phosphate dehydrogenase (G6PD) in normal persons is gastrointestinal upset if primaquine is taken on an empty stomach. This problem is minimized or eliminated if primaquine is taken with food.
- In G6PD-deficient persons, primaquine can cause hemolysis that can be fatal. **Before primaquine is used, G6PD deficiency MUST be ruled out by appropriate laboratory testing**.

Travel to Areas with Limited Malaria Transmission

For destinations (see the next section in this chapter, Malaria Risk Information and Prophylaxis, by Country) where malaria cases occur sporadically and risk for infection to travelers is assessed as being very low, it is recommended that travelers use mosquito avoidance measures only, and no chemoprophylaxis should be prescribed.

Travel to Areas with Mainly P. vivax Malaria

- For destinations where the main species of malaria present is *P. vivax*, in addition to mosquito avoidance measures, primaquine is a good choice for primary prophylaxis for travelers who are not G6PD-deficient. Its use for this indication is considered off-label use in the United States.
- The predominant species of malaria and the recommended chemoprohylaxis medicines are listed in the following section in this chapter, Malaria Risk Information and Prophylaxis, by Country.
- For persons unable to take primaquine, other drugs can be used as described below, depending on the presence of antimalarial drug resistance.

Travel to Areas with Chloroquine-Sensitive Malaria

- For destinations where chloroquine-sensitive malaria is present, in addition to mosquito avoidance measures, the many effective chemoprophylaxis alternatives include chloroquine, atovaquone/proguanil, doxycycline, mefloquine, and in some instances primaquine for travelers who are not G6PD-deficient.
- Longer-term travelers may prefer the convenience of weekly chloroquine, while shorter-term travelers may prefer the shorter course of atovaquone/proguanil or primaquine.

Travel to Areas with Chloroquine-Resistant Malaria

For destinations where chloroquine-resistant malaria is present, in addition to mosquito avoidance measures, chemoprophylaxis options are limited to atovaquone/proguanil, doxycycline, and mefloquine.

Travel to Areas with Mefloquine-Resistant Malaria

For destinations where mefloquine-resistant malaria is present, in addition to mosquito avoidance measures, chemoprophylaxis options are reduced to either atovaquone/proguanil or doxycycline.

Chemoprophylaxis for Infants, Children, and Adolescents

- Infants of any age or weight or children and adolescents of any age can contract malaria. Therefore, all children traveling to malaria-risk areas should take an antimalarial drug.
- In the United States, antimalarial drugs are available only in tablet form and may taste quite bitter. Pediatric dosages should be carefully calculated according to body weight but should never exceed adult dosage. Pharmacists can pulverize tablets and prepare gelatin capsules for each measured dose. If the child is unable to swallow the capsules or tablets, parents should prepare the child’s dose of medication by

breaking open the gelatin capsule and mixing the drug with a small amount of something sweet, such as applesauce, chocolate syrup, or jelly, to ensure the entire dose is delivered to the child. Giving the dose on a full stomach may minimize stomach upset and vomiting.

- Chloroquine and mefloquine are options for use in infants and children of all ages and weights, depending on the presence of drug resistance at their destination.
- Primaquine can be used for children who are not G6PD-deficient traveling to areas with principally *P. vivax*.
- Doxycycline may be used for children who are at least 8 years of age.
- Atovaquone/proguanil may be used for prophylaxis for infants and children weighing at least 5 kg (11 lbs). Providers should note that this prophylactic dosing for children weighing <11 kg constitutes off-label use in the United States.
- Pediatric dosing regimens are contained in Table 2-23.

Chemoprophylaxis during Pregnancy and Breastfeeding

- Malaria infection in pregnant women can be more severe than in nonpregnant women. Malaria can increase the risk for adverse pregnancy outcomes, including prematurity, abortion, and stillbirth. For these reasons, and because no chemoprophylactic regimen is completely effective, women who are pregnant or likely to become pregnant should be advised to avoid travel to areas with malaria transmission if possible (see the Traveling while Pregnant section in Chapter 8). If travel to a malarious area cannot be deferred, use of an effective chemoprophylaxis regimen is essential.
- Pregnant women traveling to areas where chloroquine-resistant *P. falciparum* has not been reported may take chloroquine prophylaxis. Chloroquine has not been found to have any harmful effects on the fetus when used in the recommended doses for malaria prophylaxis; therefore, pregnancy is not a contraindication for malaria prophylaxis with chloroquine phosphate or hydroxychloroquine sulfate.
- For travel to areas where chloroquine resistance is present, mefloquine is currently the only medication recommended for malaria chemoprophylaxis during pregnancy. A review of mefloquine use in pregnancy from clinical trials and reports of inadvertent use of mefloquine during pregnancy suggests that its use at prophylactic doses during the second and third trimesters of pregnancy is not associated with adverse fetal or pregnancy outcomes. More limited data suggest it is also safe to use during the first trimester.
- Because of insufficient data regarding the use during pregnancy, atovaquone/proguanil is not currently recommended for the prevention of malaria in pregnant women.
- Doxycycline is contraindicated for malaria prophylaxis during pregnancy because of the risk for adverse effects seen with tetracycline, a related drug, on the fetus, which include discoloration and dysplasia of the teeth and inhibition of bone growth.
- Primaquine should not be used during pregnancy because the drug may be passed transplacentally to a G6PD-deficient fetus and cause hemolytic anemia in utero.
- Health-care professionals who require additional assistance with the management of pregnant travelers who are unable to take mefloquine chemoprophylaxis should call the CDC Malaria Hotline (770-488-7788).
- Very small amounts of antimalarial drugs are excreted in the breast milk of lactating women. Because the quantity of antimalarial drugs transferred in breast milk is insufficient to provide adequate protection against malaria, infants who require chemoprophylaxis must receive the recommended dosages of antimalarial drugs listed in Table 2-23.
- Because chloroquine and mefloquine may be safely prescribed to infants, it is also safe for infants to be exposed to the small amounts excreted in breast milk.
- Although data are very limited about the use of doxycycline in lactating women, most experts consider the theoretical possibility of adverse events to the infant to be remote.
- Although no information is available on the amount of primaquine that enters human breast milk, the mother and infant should be tested for G6PD deficiency before primaquine is given to a woman who is breastfeeding.
- Because data are not yet available on the safety of atovaquone/proguanil prophylaxis in infants weighing <5 kg (<11 lbs), CDC does not currently recommend it for the prevention of malaria in women breastfeeding infants weighing <5 kg. However, it can be used for treatment of women who are breastfeeding infants of any weight when the potential benefit outweighs the potential risk to the infant (e.g., treating a breastfeeding woman who has acquired *P. falciparum* malaria in an area of multidrug-resistant strains and who cannot tolerate other treatment options).

Changing Medications during Chemoprophylaxis as a Result of Side Effects

- Medications recommended for prophylaxis against malaria have different modes of action that affect the parasites at different stages of the life cycle. Thus, if the medication needs to be changed because of side effects before a full course has been completed, there are some special considerations.
- If a traveler starts prophylaxis with a medication such as mefloquine or doxycycline and then changes to atovaquone/proguanil during or after travel, the standard duration of prophylaxis for atovaquone/proguanil would be insufficient.
- If the switch occurs 3 weeks or more before departure from the risk area, atovaquone/proguanil should be taken for the remainder of the stay in the risk area and for 1 week thereafter.
- If the switch occurs <3 weeks before departure from the risk area, atovaquone/proguanil should be taken for 4 weeks after the switch.
- If the switch occurs following departure from the risk area, atovaquone/proguanil should be continued until 4 weeks after the date of departure from the risk area.
- Due to their pharmacokinetics, switching from a daily medicine such as doxycycline to a weekly medicine such as mefloquine should be avoided.
- Health-care professionals who require additional assistance with the management of travelers who need to change medications during prophylaxis should call the CDC Malaria Hotline (770-488-7788).

Box 2-2. Clinical pearls

- Overdose of antimalarial drugs, particularly chloroquine, can be fatal. Medication should be stored in childproof containers out of the reach of infants and children.
- Chemoprophylaxis can be started earlier if there are particular concerns about tolerating one of the medications. For example, mefloquine can be started 3–4 weeks in advance to allow potential adverse events to occur before travel. If unacceptable side effects develop, there would be time to change the medication before the traveler's departure.
- The drugs used for antimalarial chemoprophylaxis are generally well tolerated. However, side effects can occur. Minor side effects usually do not require stopping the drug. Travelers who have serious side effects should see a health-care provider who can determine if their symptoms are related to the medicine and make an appropriate medication change.
- In comparison with drugs with short half-lives, which are taken daily, drugs with longer half-lives, which are taken weekly, offer the advantage of a wider margin of error if the traveler is late with a dose. For example, if a traveler is 1–2 days late with a weekly drug, prophylactic blood levels can remain adequate; if the traveler is 1–2 days late with a daily drug, protective blood levels are less likely to be maintained.
- In those who are G6PD deficient, primaquine can cause hemolysis, which can be fatal. Be sure to document a normal G6PD level before prescribing primaquine.
- Travelers should be informed that malaria can be fatal if treatment is delayed. Medical help should be sought promptly if malaria is suspected, and a blood sample should be taken and examined for malaria parasites on one or more occasions.
- Malaria smear results or an RDT test must be available immediately. Sending specimens to offsite laboratories where results are not available for extended periods of time (days) is not acceptable. If a patient has an illness suggestive of severe malaria and a compatible travel history in an area where malaria transmission occurs, it is advisable to start treatment as soon as possible, even before the diagnosis is established. CDC recommendations for malaria treatment can be found at www.cdc.gov/malaria/diagnosis_treatment/index.html (http://www.cdc.gov/malaria/diagnosis_treatment/index.html) .

Map 2-9. Geographic distribution of mefloquine-resistant malaria

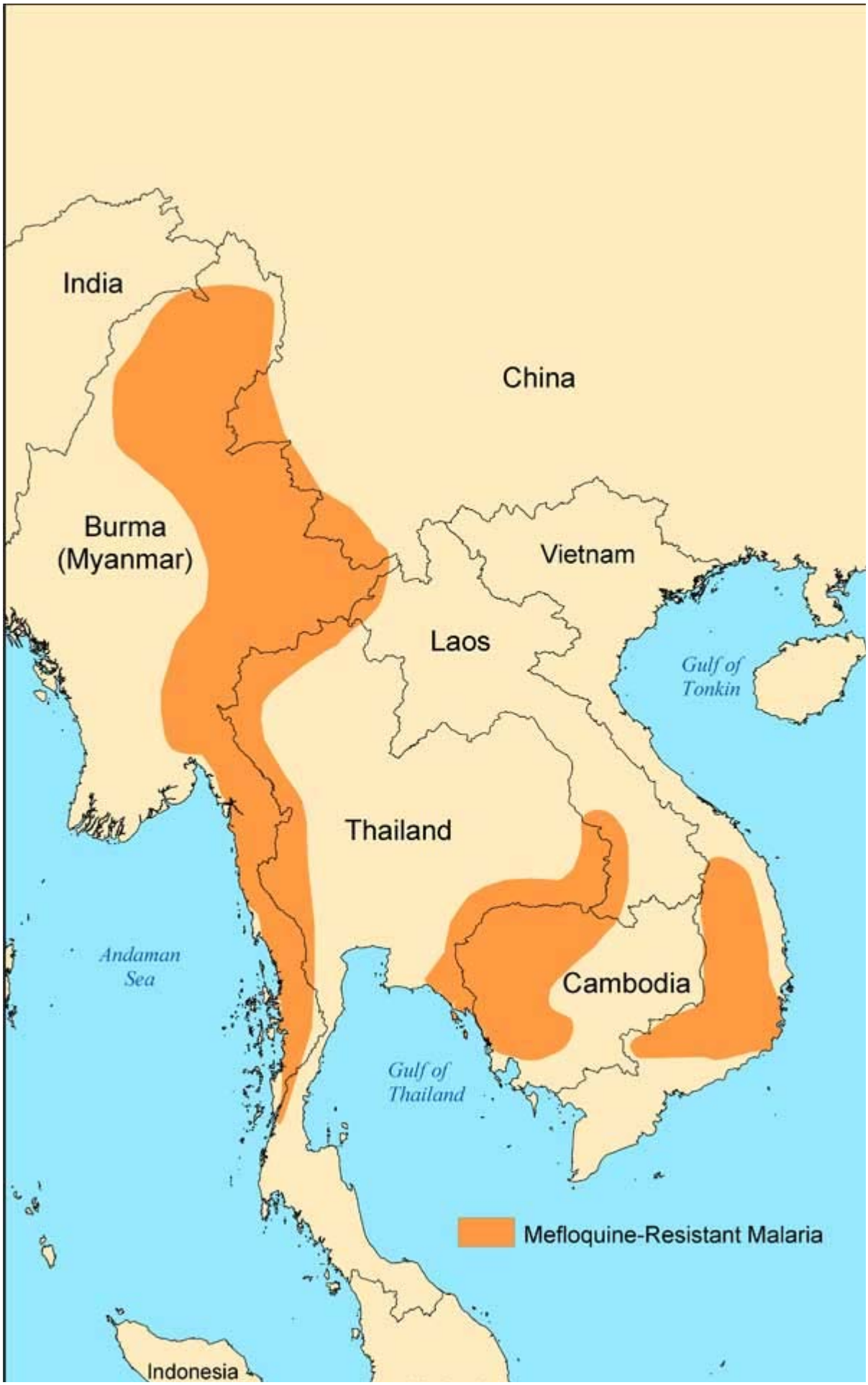

India
China
Burma
(Myanmar)
Vietnam
Laos
Gulf of
Tonkin
Thailand
Andaman
Sea
Cambodia
Gulf of
Thailand
Mefloquine-Resistant Malaria
Indonesia

Table 2-23. Drugs used in the prophylaxis of malaria

Drug	Usage	Adult Dose	Pediatric Dose	Comments
Atovaquone/proguanil (Malarone)	Prophylaxis in all areas	Adult tablets contain 250 mg atovaquone and 100 mg proguanil hydrochloride. 1 adult tablet orally, daily	Pediatric tablets contain 62.5 mg atovaquone and 25 mg proguanil hydrochloride. 5–8 kg: 1/2 pediatric tablet daily; >8–10 kg: 3/4 pediatric tablet daily; >10–20 kg: 1 pediatric tablet daily; >20–30 kg: 2 pediatric tablets daily; >30–40 kg: 3 pediatric tablets daily; >40 kg: 1 adult tablet daily	Begin 1–2 days before travel to malarious areas. Take daily at the same time each day while in the malarious area and for 7 days after leaving such areas. Contraindicated in persons with severe renal impairment (creatinine clearance <30 mL/min). Atovaquone/proguanil should be taken with food or a milky drink. Not recommended for prophylaxis for children <5 kg, pregnant women, and women breastfeeding infants weighing <5 kg. Partial tablet dosages may need to be prepared by a pharmacist and dispensed in individual capsules, as described in the text.
Chloroquine phosphate (Aralen and generic)	Prophylaxis only in areas with chloroquine-sensitive malaria	300 mg base (500 mg salt) orally, once/week	5 mg/kg base (8.3 mg/ kg salt) orally, once/week, up to maximum adult dose of 300 mg base	Begin 1–2 weeks before travel to malarious areas. Take weekly on the same day of the week while in the malarious area and for 4 weeks after leaving such areas. May exacerbate psoriasis.
Doxycycline (many brand names and generic)	Prophylaxis in all areas	100 mg orally, daily	≥8 years of age: 2 mg/ kg up to adult dose of 100 mg/day	Begin 1–2 days before travel to malarious areas. Take daily at the same time each day while in the malarious area and for 4 weeks after leaving such areas. Contraindicated in children <8 years of age and pregnant women.
Hydroxychloroquine sulfate (Plaquenil)	An alternative to chloroquine for prophylaxis only in areas with chloroquine-sensitive malaria	310 mg base (400 mg salt) orally, once/week	5 mg/kg base (6.5 mg/ kg salt) orally, once/week, up to maximum adult dose of 310 mg base	Begin 1–2 weeks before travel to malarious areas. Take weekly on the same day of the week while in the malarious area and for 4 weeks after leaving such areas.
Mefloquine	Prophylaxis in areas with mefloquine-sensitive malaria	228 mg base (250 mg salt) orally, once/week	≤9 kg: 4.6 mg/kg base (5 mg/kg salt) orally, once/week; >9–19 kg: 1/4 tablet once/week; >19–30 kg: 1/2 tablet once/week; >31–45 kg: 3/4 tablet once/week; ≥45 kg: 1 tablet once/ week	Begin at least 2 weeks before travel to malarious areas. Take weekly on the same day of the week while in the malarious area and for 4 weeks after leaving such areas. Contraindicated in persons allergic to mefloquine or related compounds (e.g., quinine, quinidine) and in persons with active depression, a recent history of depression, generalized anxiety disorder, psychosis, schizophrenia, other major psychiatric disorders, or seizures. Use with caution in persons with psychiatric disturbances or a previous history of depression. Not recommended for persons with cardiac conduction abnormalities. *(Updated April 20, 2010)*
Primaquine	Prophylaxis for short-duration travel to areas with principally *P.vivax*	30 mg base (52.6 mg salt) orally, daily	0.5 mg/kg base (0.8 mg/kg salt) up to adult dose orally, daily	Begin 1–2 days before travel to malarious areas. Take daily at the same time each day while in the malarious area and for 7 days after leaving such areas. Contraindicated in persons with G6PD[1] deficiency. Also contraindicated during pregnancy and lactation unless the infant being breastfed has a documented normal G6PD level.
Primaquine	Used for presumptive antirelapse therapy (terminal prophylaxis) to decrease the risk for relapses of *P. vivax* and *P. ovale*	30 mg base (52.6 mg salt) orally, once/day for 14 days after departure from the malarious area.	0.5 mg/kg base (0.8 mg/kg salt) up to adult dose orally, once/day for 14 days after departure from the malarious area	Indicated for persons who have had prolonged exposure to *P. vivax* and *P. ovale* or both. Contraindicated in persons with G6PD[1] deficiency. Also contraindicated during pregnancy and lactation unless the infant being breastfed has a documented normal G6PD level.

[1] Glucose-6-phosphate dehydrogenase. All persons who take primaquine should have a documented normal G6PD level before starting the medication.

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Chapter 2: Varicella (Chickenpox) (/travel/yellowbook/2010/chapter-2/varicella.aspx)

Chapter 2: Malaria Risk Information and Prophylaxis, by Country (/travel/yellowbook/2010/chapter-2/malaria-risk-information-and-prophylaxis.aspx)

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