bed-nets (ITNs) has been shown to reduce all-cause mortality in African children by 20%. New drugs have been discovered and developed, and one vaccine candidate (the RTS,S vaccine) will soon be considered for registration. Highly effective drugs, long-lasting ITNs, and insecticides for spraying dwellings are being purchased for endemic countries by the Global Fund to Fight AIDS, Tuberculosis, and Malaria; the President's Malaria Initiative (funded by the U.S. Agency for International Development and managed by the CDC in partnership with endemic countries); UNICEF; and other organizations. Malaria research and control are being strongly supported by the National Institute of Allergy and Infectious Diseases, the CDC, the Wellcome Trust, the Bill & Melinda Gates Foundation, the Multilateral Initiative on Malaria, the Roll Back Malaria Partnership, and the WHO among others. While a laudable goal, the global eradication of malaria is not feasible in the immediate future because of the widespread distribution of *Anopheles* breeding sites; the great number of infected persons; the continued use of ineffective antimalarial drugs; and inadequacies in human and material resources, infrastructure, and control programs. The call for and commitment to ultimate eradication of malaria by the Gates Foundation in 2007—seconded by Margaret Chan, Director General of the WHO—added great impetus to all malaria initiatives, especially those aimed at discovery and implementation of new interventions. Malaria may be contained by judicious use of insecticides to kill the mosquito vector, rapid diagnosis, patient management, and—where effective and feasible—administration of intermittent preventive treatment, seasonal malaria chemoprevention, or chemoprophylaxis to high-risk groups such as pregnant women, young children, and travelers from nonendemic regions. Malaria researchers are intensifying their efforts to gain a better understanding of parasite-human-mosquito interactions and to develop more effective control and prevention interventions. Despite the enormous investment in efforts to develop a malaria vaccine and the 30–60% efficacy in African children of a recombinant protein sporozoite-targeted adjuvanted vaccine (RTS,S) in field trials, no safe, highly effective, long-lasting vaccine is likely to be available for general use in the near future **(Chap. 148)**. Indeed, protection from RTS,S in the very youngest recipients dropped to 16% only 4 years after vaccination. While there is great promise for one or several malaria vaccines on the more distant horizon, prevention and control measures continue to rely on antivector and drug-use strategies. Furthermore, recent gains are threatened by increasing insecticide resistance and behavioral changes (to avoid ITN contact) in anopheline mosquito vectors and by spreading artemisinin resistance in *P. falciparum*.

PERSONAL PROTECTION AGAINST MALARIA

Simple measures to reduce the frequency of infected-mosquito bites in malarious areas are very important. These measures include the avoidance of exposure to mosquitoes at their peak feeding times (usually dusk to dawn) and the use of insect repellents containing 10–35% DEET (or, if DEET is unacceptable, 7% picaridin), suitable clothing, and ITNs or other insecticide-impregnated materials. Widespread use of bed nets treated with residual pyrethroids reduces the incidence of malaria in areas where vectors bite indoors at night.

CHEMOPROPHYLAXIS

(**Table 248-8**; *wwwnc.cdc.gov/travel/yellowbook/2014/chapter-3-infectious-diseases-related-to-travel/malaria*) Recommendations for prophylaxis depend on knowledge of local patterns of *Plasmodium* species drug sensitivity and the likelihood of acquiring malarial infection. When there is uncertainty, drugs effective against resistant *P. falciparum* should be used (atovaquone-proguanil [Malarone], doxycycline, or mefloquine). Chemoprophylaxis is never entirely reliable, and malaria should always be considered in the differential diagnosis of fever in patients who have traveled to endemic areas, even if they are taking prophylactic antimalarial drugs.

Pregnant women traveling to malarious areas should be warned about the potential risks. All pregnant women at risk in endemic areas should be encouraged to attend regular antenatal clinics. Mefloquine is the only drug advised for pregnant women traveling to areas with drug-resistant malaria; this drug is generally considered safe in the second and third trimesters of pregnancy, and the data on first-trimester exposure, although limited, are reassuring. Chloroquine and proguanil are regarded as safe. The safety of other prophylactic antimalarial agents in pregnancy has not been established. Antimalarial prophylaxis has been shown to reduce mortality rates among children between the ages of 3 months and 4 years in malaria-endemic areas; however, it is not a logistically or economically feasible option in many countries. The alternative—to give intermittent preventive treatment or seasonal malaria chemoprevention—shows promise for more widespread use in infants, young children, and pregnant women. Children born to nonimmune mothers in endemic areas (usually expatriates moving to malaria-endemic areas) should receive prophylaxis from birth.

Travelers should start taking antimalarial drugs 2 days to 2 weeks before departure so that any untoward reactions can be detected and so that therapeutic antimalarial blood concentrations will be present when needed (Table 248-8). Antimalarial prophylaxis should continue for 4 weeks after the traveler has left the endemic area, except if atovaquone-proguanil or primaquine has been taken; these drugs have significant activities against the liver stage of the infection (causal prophylaxis) and can be discontinued 1 week after departure from the endemic area. If suspected malaria develops while a traveler is abroad, obtaining a reliable diagnosis and antimalarial treatment locally is a top priority. Presumptive self-treatment for malaria with atovaquone-proguanil (for 3 consecutive days) or another drug can be considered under special circumstances; medical advice on self-treatment should be sought before departure for malarious areas and as soon as possible after illness begins. Every effort should be made to confirm the diagnosis by parasitologic studies.

Atovaquone-proguanil (Malarone; 3.75/1.5 mg/kg or 250/100 mg, daily adult dose) is a fixed-combination, once-daily prophylactic agent that is very well tolerated by adults and children, with fewer adverse gastrointestinal effects than chloroquine-proguanil and fewer adverse central nervous system effects than mefloquine. It is proguanil itself, rather than the antifolate metabolite cycloguanil, that acts synergistically with atovaquone. This combination is effective against all types of malaria, including multidrug-resistant falciparum malaria. Atovaquone-proguanil is best taken with food or a milky drink to optimize absorption. There are insufficient data on the safety of this regimen in pregnancy.

Mefloquine (250 mg of salt weekly, adult dose) has been widely used for malarial prophylaxis because it is usually effective against multidrug-resistant falciparum malaria and is reasonably well tolerated. The drug has been associated with rare episodes of psychosis and seizures at prophylactic doses; these reactions are more frequent at the higher doses used for treatment. More common side effects with prophylactic doses of mefloquine include mild nausea, dizziness, fuzzy thinking, disturbed sleep patterns, vivid dreams, and malaise. The drug is contraindicated for use by travelers with known hypersensitivity to mefloquine or related compounds (e.g., quinine, quinidine) and by persons with active or recent depression, anxiety disorder, psychosis, schizophrenia, another major psychiatric disorder, or seizures; mefloquine is not recommended for persons with cardiac conduction abnormalities although the evidence that it is cardiotoxic is very weak. Confidence is increasing with regard to the safety of mefloquine prophylaxis during pregnancy; in studies in Africa, mefloquine prophylaxis was found to be effective and safe during pregnancy. However, in one study from Thailand, treatment of malaria with mefloquine was associated with an increased risk of stillbirth; this effect was not seen subsequently.

Daily administration of doxycycline (100 mg daily, adult dose) is an effective alternative to atovaquone-proguanil or mefloquine. Doxycycline is generally well tolerated but may cause vulvovaginal thrush, diarrhea, and photosensitivity and cannot be used by children <8 years old or by pregnant women.

Chloroquine can no longer be relied upon to prevent *P. falciparum* infections in most areas but is used to prevent and treat malaria due to the other human *Plasmodium* species and for *P. falciparum* malaria in Central American countries west and north of the Panama