malaria in adults. This drug can be considered for persons who are traveling to areas with or without drug-resistant *P. falciparum* and who are intolerant to other recommended drugs. Abdominal pain and oxidant hemolysis—the principal adverse effects—are not common as long as the drug is taken with food and is not given to G6PD-deficient persons, in whom it can cause serious hemolysis. Travelers must be tested for G6PD deficiency and be shown to have a level in the normal range before receiving primaquine. Primaquine should not be given to pregnant women or neonates. Primaquine, given in a single dose of 0.25 mg/kg as a gametocytocide, together with an ACT is recommended in falciparum malaria treatment regimens in malaria elimination programs.

In the past, the dihydrofolate reductase inhibitors pyrimethamine and proguanil (chloroguanide) were administered widely, but the rapid selection of resistance in both *P. falciparum* and *P. vivax* has limited their use. Whereas antimalarial quinolines such as chloroquine (a 4-aminoquinoline) act on the erythrocyte stage of parasitic development, the dihydrofolate reductase inhibitors also inhibit preerythrocytic growth in the liver (causal prophylaxis) and development in the mosquito (sporontocidal activity). Proguanil is safe and well tolerated, although mouth ulceration occurs in ~8% of persons using this drug; it is considered safe for antimalarial prophylaxis in pregnancy. The prophylactic use of the combination of pyrimethamine and sulfadoxine is not recommended because of an unacceptable incidence of severe toxicity, principally exfoliative dermatitis and other skin rashes, agranulocytosis, hepatitis, and pulmonary eosinophilia (incidence, 1:7000; fatal reactions, 1:18,000). The combination of pyrimethamine with dapsone (0.2/1.5 mg/kg weekly; 12.5/100 mg, adult dose) has been used in some countries. Dapsone may cause methemoglobinemia and allergic reactions and (at higher doses) may pose a significant risk of agranulocytosis. Proguanil and the pyrimethamine-dapsone combination are not available in the United States.

Because of the increasing spread and intensity of antimalarial drug resistance (Figs. 248-2 and 248-10), the CDC recommends that travelers and their providers consider their destination, type of travel, and current medications and health risks when choosing antimalarial chemoprophylaxis. There is an increasingly appreciated problem of counterfeit and substandard antimalarial drugs (and other medicines) on the shelves of pharmacies in Southeast Asia and sub-Saharan Africa; hence, travelers should purchase their preventive drugs from a reputable source before going to a malarious country. Consultation for the evaluation of prophylaxis failures or treatment of malaria can be obtained from state and local health departments and the CDC Malaria Hotline (770-488-7788) or the CDC Emergency Operations Center (770-488-7100).

249 Babesiosis

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Babesiosis is an emerging tick-borne infectious disease caused by protozoan parasites of the genus *Babesia* that invade and eventually lyse red blood cells (RBCs). Most cases are due to *Babesia microti* and occur in the United States, particularly in the Northeast and upper Midwest. The infection typically is mild in young and otherwise healthy individuals but can be severe and sometimes fatal in persons >50 years of age and in immunocompromised patients. Sporadic cases have been reported in Europe and the rest of the world.

ETIOLOGY AND EPIDEMIOLOGY

Geographic Distribution More than 100 *Babesia* species are found in wild and domestic animals; a few of these species cause infection in humans (Fig. 249-1). *B. microti*, a parasite of small rodents, is the most common etiologic agent of human babesiosis and is endemic in the northeastern and upper midwestern United States. Seven states in these two regions (Connecticut, Massachusetts, Minnesota, New Jersey, New York, Rhode Island, and Wisconsin) account for >95% of the reported cases. Other etiologic agents include *Babesia duncani* and *B. duncani*–type organisms on the West Coast and *Babesia divergens*–like organisms in Kentucky, Missouri, and Washington State.

The primary causative agent of human babesiosis in Europe is *B. divergens*, but *Babesia venatorum* and *B. microti* also have been reported. In Asia, cases due to *B. microti*–like organisms have been documented in Japan, Taiwan, and the People's Republic of China. A case caused by *B. venatorum* also has been reported from the People's Republic of China. A case of *B. microti* infection was described in Australia. Sporadic cases due to uncharacterized species have been reported in Colombia, Egypt, India, Mozambique, and South Africa.

Incidence More than 1100 cases were reported in the United States in 2011, the year the disease became nationally notifiable. This figure represents a fivefold increase in incidence over the past decade. The incidence of babesiosis is markedly underestimated because symptoms are nonspecific and because young healthy individuals typically experience a mild or asymptomatic infection and may not seek medical attention. Fewer than 50 cases of *B. divergens, B. divergens*–like, and *B. venatorum* infections have been reported. Babesiosis caused by *B. duncani* and *B. duncani*–type organisms has also been sporadic, with fewer than 10 reported cases.

Modes of Transmission In the United States, *B. microti* is transmitted to humans primarily by the nymphal stage of the deer tick (*Ixodes scapularis*), the same tick that transmits the causative agents of Lyme disease (Chap. 210) and human granulocytotropic anaplasmosis (Chap. 211). Transmission generally occurs from May through October, with three-fourths of cases presenting in July and August. The vectors for transmission of *B. duncani* and *B. divergens*–like organisms are thought to be *Ixodes pacificus* and *Ixodes dentatus*, respectively. In Europe, *Ixodes ricinus* is the vector for *B. divergens* and *B. venatorum*. In Japan, *B. microti*–like organisms have been found in *Ixodes ovatus* ticks.

Babesiosis occasionally is acquired through transfusion of blood or blood products. *B. microti* is the most common transfusion-transmitted pathogen reported to the U.S. Food and Drug Administration, and more than 170 such cases have been identified. Three transfusion-transmitted cases caused by *B. duncani* have been documented. Transfusion-transmitted cases occur year-round, although most cases occur from June through November. More than 80% of cases occur in endemic areas. Transfusion-transmitted babesiosis occurs in nonendemic areas when unrecognized *Babesia*-contaminated blood products are imported from endemic areas: asymptomatically infected residents of endemic areas donate blood in nonendemic areas, or residents of nonendemic areas travel to endemic areas, become infected, and donate blood after they return home. Approximately three-quarters of the transfusion-transmitted babesiosis cases reported between 1979 and 2009 occurred in the last decade of this period, and about one-fifth of patients died.

Seven cases of probable or confirmed congenital *B. microti* infection have been described. Other cases of neonatal babesiosis have been acquired by transfusion or tick bite.

CLINICAL MANIFESTATIONS

Asymptomatic *B. microti* Infection At least 20% of adults and 40% of children do not experience symptoms following *B. microti* infection. Asymptomatic infection, whether treated or not, may persist for >1 year after acute babesial illness. There is no evidence of long-term complications following asymptomatic infection; however, people who are asymptomatically infected may transmit the infection when they donate blood.

Mild to Moderate *B. microti* Illness Symptoms typically develop following an incubation period of 1–4 weeks after tick bite and 1–9 weeks (but as long as 6 months) after transfusion of blood products. Patients experience a gradual onset of malaise, fatigue, and weakness. Fever