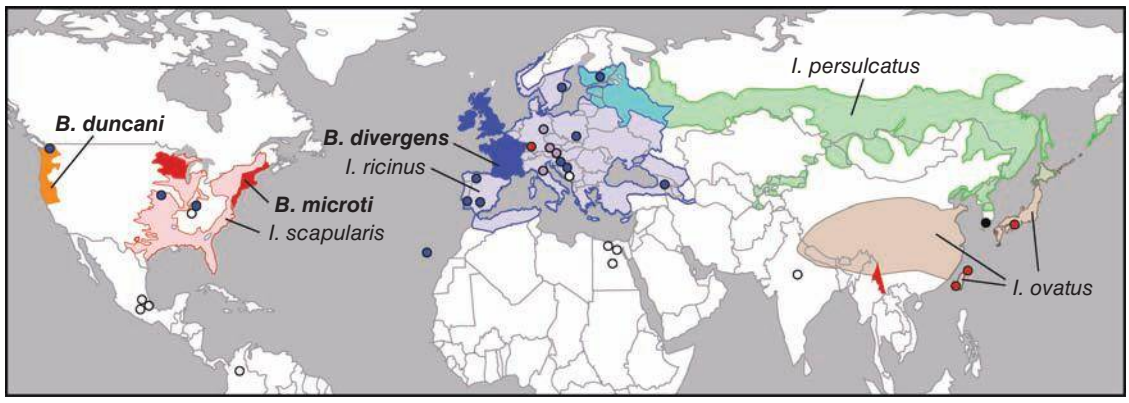

FIGURE 249-1 Worldwide distribution of human babesiosis. *Dark colors* designate areas where human babesiosis is either endemic or sporadic (as defined by more than three tick-borne cases reported in a country or state). Isolated cases of babesiosis are denoted by *circles*. Colors designate causative *Babesia* species: *Babesia microti* and *B. microti*–like organisms in *red*, *Babesia duncani* and *B. duncani*–type organisms in *orange*, *Babesia divergens* and *B. divergens*–like organisms in *blue*, *Babesia venatorum* in *purple*, KO1 in *black*, and unspeciated *Babesia* organisms in *white*. Due to space constraints, the 10 cases reported from Montenegro are denoted by a single *white circle*, and those from Australia, Mozambique, and South Africa are not shown. *Light colors* denote areas that are enzootic for *Ixodes* tick species known to transmit one or several *Babesia* species but where human babesiosis has yet to be documented. *(Adapted from E Vannier, PJ Krause: N Engl J Med 366:2397, 2012.)*

can reach 40.9°C (105.6°F) and is accompanied by one or more of the following: chills, sweats, headache, myalgia, arthralgia, nausea, anorexia, and dry cough. Less common symptoms include sore throat, photophobia, abdominal pain, vomiting, weight loss, shortness of breath, and depression. On physical examination, fever is the salient feature. Ecchymoses and petechiae have been reported. An erythema migrans rash signifies concurrent Lyme disease (Chap. 210). Splenomegaly and hepatomegaly occasionally are noted. Lymphadenopathy is absent. Jaundice, slight pharyngeal erythema, and retinopathy with splinter hemorrhages and retinal infarcts rarely occur. Symptoms typically last 1–2 weeks, but fatigue may persist for several months.

Severe *B. microti* Illness Severe babesiosis requires hospital admission and typically occurs in patients with one or more of the following: age of >50 years, neonatal prematurity, male gender, asplenia, HIV/AIDS, malignancy, hemoglobinopathy, and immunosuppressive therapy. More than one-third of hospitalized patients develop complications, including acute respiratory distress syndrome, disseminated intravascular coagulation, congestive heart failure, renal failure, splenic infarcts, and splenic rupture. Patients who develop complications tend to have severe anemia (hemoglobin, ≤10 g/L). Laboratory prognostic factors for severe outcome—defined by hospitalization for >14 days, an intensive care unit stay of >2 days, or death—include an elevated alkaline phosphatase level (>125 U/L) and parasitemia of >4%. The fatality rate is 5–9% among hospitalized patients but is ~20% among immunocompromised patients and patients with transfusion-transmitted babesiosis.

Other *Babesia* Infections Cases of *B. duncani* infection range in severity from asymptomatic to fatal. Clinical manifestations are similar to those reported for *B. microti* infection. All three patients infected with *B. divergens*–like organisms in the United States required hospitalization; one died. Most cases of *B. divergens* infection in Europe have occurred in people lacking a spleen. The incubation period is 1–3 weeks. Symptoms appear suddenly and consist of fever (>41°C or 105.8°F), shaking chills, drenching sweats, headache, myalgia, and lumbar and abdominal pain. Hemoglobinuria and jaundice are commonly noted, and mild hepatomegaly may occur. If the infection is not treated, patients often develop pulmonary edema and renal failure. All four patients infected with *B. venatorum* in Europe had been splenectomized; their illness ranged from mild to severe, and none died. A child in China who developed *B. venatorum* illness had an intact spleen and survived the infection.

PATHOGENESIS

Anemia is a key feature of the pathogenesis of babesiosis. Hemolytic anemia caused by rupture of infected RBCs generates cell debris that may accumulate in the kidney and cause renal failure. Anemia also results from the clearance of intact RBCs as they pass through the splenic red pulp and encounter resident macrophages. *Babesia* antigens expressed at the RBC membrane promote opsonization and facilitate uptake by splenic macrophages. In addition, RBCs are poorly deformable as a result of oxidation generated by the parasite and the host immune response and are filtered out as they attempt to squeeze across the venous vasculature. Bone marrow suppression due to cytokine production may also contribute to anemia.

An appropriate immune response is necessary for the control and clearance of *Babesia*. However, several lines of evidence suggest that an excessive response contributes to pathogenesis. Studies using laboratory mice have clearly established that CD4+ T cells are critical for resistance to and resolution of *B. microti* infection. CD4+ T cells are a major source of interferon γ (IFN-γ), and lack of this cytokine causes resistant mice to become highly susceptible to *B. microti*. IFN-γ is central to host resistance in *B. duncani* infection, but natural killer cells are its main source. *B. duncani* infection is more severe than *B. microti* infection in rodents and is characterized by pulmonary inflammation. Tumor necrosis factor α is expressed around alveolar septa, whereas IFN-γ is detected around pulmonary vessels. Blockade of either cytokine promotes the survival of mice infected with *B. duncani*.

DIAGNOSIS

A diagnosis of babesiosis should be considered for any patient who lives or travels in a *Babesia*-endemic area and presents with a febrile illness in the late spring, summer, or early autumn or within 6 months after a blood transfusion. Co-infection with *Babesia* should be considered in cases of Lyme disease or human granulocytotropic anaplasmosis when symptoms are more severe or prolonged than usual.

Screening laboratory tests can help support the diagnosis of babesiosis. A complete blood count often shows anemia and thrombocytopenia. Low hematocrit, hemoglobin, and haptoglobin levels and elevated reticulocyte counts and lactate dehydrogenase levels are consistent with hemolytic anemia. Liver enzyme tests often reveal elevated levels of alkaline phosphatase, aspartate and alanine aminotransferases, and bilirubin. Urinalysis may show hemoglobinuria, excess urobilinogen, and proteinuria. Elevated levels of blood urea nitrogen and serum creatinine indicate renal compromise.

A specific diagnosis usually is established by microscopic examination of Giemsa-stained thin blood smears (Fig. 249-2). *Babesia* trophozoites appear round, pear-shaped, or ameboid. The ring form is most common and lacks the central brownish deposit (hemozoin) typical of *Plasmodium falciparum* trophozoites (see Fig. 250e-1*C*). Other distinguishing features are the absence of schizonts and gametocytes and the occasional presence of tetrads ("Maltese cross").