Transfusion-Associated Babesiosis: Shouldn't We Be Ticked Off?

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Human babesiosis in the United States is attributable almost exclusively to infection with the intraerythrocytic protozoan parasite *Babesia microti*. The primary mechanism of parasite transmission to humans is by the bite of an infected deer/black legged tick, *Ixodes scapularis*, the same tick that serves as the vector for Lyme borreliosis, human granulocytic anaplasmosis, and several other tick-borne diseases (1). Babesiosis is often described as an emerging infectious disease in the United States. The first documented case of clinical disease caused by *B. microti* was reported on Nantucket Island, Massachusetts, in 1969 (2). Since then, hundreds to thousands of babesiosis cases have been described, leading the Council of State and Territorial Epidemiologists to recommend that it be designated as a nationally notifiable disease beginning in January of 2011 (3). Geographically, *B. microti* is limited to endemic areas in the Northeast (Connecticut, Massachusetts, New Jersey, New York, Rhode Island) and Upper Midwest (Minnesota, Wisconsin); another species, *B. duncani*, is reported on rare occasions in California and Washington.

Infections with *B. microti* produce a spectrum of disease, ranging from asymptomatic, self-resolving infections to severe, life-threatening illnesses that are often dictated by the host's immune status. Common signs and symptoms of babesiosis include fever, headache, chills, drenching sweats, myalgia, malaise, and hemolytic anemia. More severe cases frequently occur in immunocompromised populations, including neonates and infants, the elderly, and asplenic patients. Complications of babesiosis may include acute respiratory distress, severe hemolysis, disseminated intravascular coagulation, renal dysfunction, hepatic compromise, myocardial infarction, and death.

Concomitant with the emergence of babesiosis as a public health concern has been a proliferation of cases of transfusion-associated babesiosis. The first documented case of transfusion-transmitted *Babesia* was reported from Boston in 1979 (4). Subsequently, cases of babesiosis associated with blood transfusion have rapidly increased. For many years, based on largely anecdotal information, the number of transfusion-associated cases was estimated to be approximately 70. Determining an accurate tally of cases was deemed difficult because many transfusion cases were not reported in an organized fashion or were not considered novel enough to justify publication. In this issue, Herwaldt and colleagues (5) have compiled an exhaustive list of known cases (n = 162) of transfusion-associated babesiosis from 1979 to 2009, which has important implications for public health and transfusion medicine. In the absence of a feasible and approved method for screening the blood supply, *B. microti* has become the infectious agent most frequently transmitted by blood transfusion in the United States.

Herwaldt and colleagues state that their report probably undercounts transfusion-associated cases. They identified 159 cases of *B. microti* transmission during the 30-year study period (plus 3 additional cases attributed to *B. duncani*), but other, unreported cases have probably occurred. Systematic reporting of transfusion-associated babesiosis remains problematic. That physicians do not recognize babesial infections in blood recipients surely reduces the perceived number of cases. Even severe cases of babesiosis from endemic regions can be misdiagnosed. Among more than 20 index patients in whom intraerythrocytic ring forms were noted, at least 14 were initially treated for malaria. Further, incidental diagnosis of babesiosis also occurred, often unexpectedly, when parasites were detected on blood smears routinely done as part of a complete blood count. Case counts were also limited by the authors selection criteria that required identification of an implicated donor based on laboratory evidence of infection (cases were excluded from consideration if all donors were negative). From my experience, follow-up studies of infected recipients (that is, lookback) frequently do not yield an infected donor (6). Infections in

asymptomatic, immunocompetent donors are often short-lived and resolve spontaneously. By the time donors are evaluated for their potential role in transmission, they are parasitologically and serologically negative. These observations suggest that many more cases of transfusion-associated babesiosis have occurred than the current publication suggests.

Data presented by Herwaldt and colleagues also suggest that the number and frequency of transfusion-associated babesiosis cases are rapidly increasing. Whereas only 7 (4%) cases were reported during the initial 11 years (1979–1989) of study, 122 (77%) cases occurred from 2000–2009. This precipitous increase is corroborated by recently published reports from the U.S. Food and Drug Administration, Rhode Island Blood Center, American Red Cross, and New York City (7–10). The observed rise in cases begs the question of whether the parasite's endemic range is expanding, if prospective donors are becoming infected more frequently, or if physicians and hospitals are more attuned to potential *Babesia* infections in blood recipients. As with many questions regarding emerging infectious agents, this is difficult to answer, but the explanation is probably multifactorial. Studies to define the geographic spread of the parasite are limited but should improve now that babesiosis is a notifiable disease. Although case reporting is still in its infancy, 314 cases of babesiosis have been reported to the Centers for Disease Control and Prevention though the week ending 20 August 2011 (11). Longitudinal seroprevalence studies done by the American Red Cross for more than 10 years in Connecticut blood donors indicate that the prevalence rate has remained near 1% throughout (12). However, where the endemic range of the parasite continues to expand, one can anticipate increased frequency of clinical and transfusion-associated cases. Despite the issues of case recognition discussed earlier, education efforts by the Centers for Disease Control and Prevention, AABB (formerly the American Association of Blood Banks), and state and local health departments during the past decade have led to a better understanding of the public health and transfusion risks posed by *Babesia*. As evidenced by transfusion-associated cases reported in states where *Babesia* is not endemic, physician awareness of babesiosis is becoming more widespread.

Herwaldt and coworkers speculate that increasing recognition of transfusion cases will strengthen the impetus to mitigate transmission risk. Yet, several hurdles prevent implementation of an effective strategy. Presently, a blood screening assay (serologic or nucleic acid) licensed and approved by the U.S. Food and Drug Administration does not exist. In part, manufacturers have shown a reluctance to develop a test for a regionalized agent that may require only a limited number of tests compared with other agents (for example, HIV) that are screened universally. Although *Babesia* transmission risk clearly peaks during the summer months (that is, active tick season), it poses a significant risk year-round that will need to be addressed. Even though transfusion-associated cases of babesiosis attributable to traveling donors or blood products were reported in nonendemic states (for example, Florida and Texas), 87% of the cases compiled by Herwaldt and colleagues were reported in the 7 endemic states, suggesting that any intervention needs to target these regions first. The potential role of pathogen reduction, which has shown feasibility in research studies, also needs to be considered (13, 14). What is not acceptable, however, is the status quo. With reports of 162 transfusion-associated cases of babesiosis probably representing only a fraction of actual cases and a potential causal or contributory role for babesiosis in the deaths of *B. microti*–infected blood recipients, the time to act is now.

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Article and Author Information

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