



The long road to *Babesia* blood screening

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Testing for *Babesia*, a parasitic agent involved in over 200 cases of transfusion-transmission, is now part of routine blood screening in endemic areas of the United States. The editorial commentary paper “Blood screening for *Babesia* in the blood supply” by Dr. Bloch and Dr. Krause, does an excellent job in summarizing the *Babesia* screening data obtained before the test was broadly implemented. However, it is important to remember that, while this sounds like a success story, the history of the implementation of *Babesia* screening is long and complicated. After a handful of cases of transfusion-transmitted babesiosis (TTB) were reported in the literature between 1980 and 1986, the first data about antibody prevalence in blood donors were published (1,2). Although these studies were small and the samples collected in highly endemic areas, the positive rates were alarmingly high (between 3.7% to 4.7%). Nevertheless, TTB was still considered a relatively rare event, and the only recommendation was for physicians to include babesiosis in the differential diagnosis of a blood recipient’s febrile illness. As naturally-acquired human babesiosis caused by *B. microti*, the species responsible for most of the human infections in the US, started emerging as a public health issue, so did the recognition of TTB, and beginning in 2000, the number of reported cases increased dramatically. A report published in 2011 described 159 US cases of TTB occurring between 1979 and 2009, 122 of which were reported between 2000 and 2009 (3). At the same time, several publications reported on *B. microti* seroprevalence in blood donors residing in endemic areas of the Northeastern United States with rates between 0.9% and 1.4% in Connecticut and on the offshore islands of Massachusetts (4,5).

By 2010 it was clear that an intervention was needed to reduce transmission of *B. microti* to US blood recipients. So, why did it take so long for a screening test to be

implemented? Several factors have contributed to this “perfect storm,” starting with the geographically restricted distribution of the parasite. The endemicity of *B. microti*, although expanding, has been largely confined to specific territories, mostly in the Northeast and the upper Midwest. Testing blood donors residing in non-endemic states was deemed costly and unnecessary, and the prospect of developing a blood screening assay that would not be used nationwide seemed less than appealing for most test-manufacturers. However, this was an urgent matter for blood establishments, who shortly after 2010, started working with companies having research screening tests used under FDA approved investigational new drug (IND) protocols. Although *B. microti* blood donation screening under IND had focused only on a limited geographic area, the impact was significant (6). The concomitant reduction of TTB cases from donors resident in endemic areas demonstrated that testing is a successful strategy. However, without a better option available, the initial investigational screening relied heavily, if not exclusively, on antibody testing. A nucleic acid test (NAT) was performed by PCR, but the limited sensitivity of the assay would not allow it to be the only screening tool. Many positive donors identified during the IND studies were positive only for antibodies, as expected, considering that antibody to *B. microti* can be detected years after the infection is resolved. Without a donor re-entry policy in place, donors who tested positive by any test (antibody or DNA) were permanently deferred, a costly price to pay for the blood establishments. Some of the tests used under IND were abandoned along the way, but the combination of antibody and PCR tests developed by IMUGEN received FDA licensure in July 2018, and in the same year, the FDA released draft guidance with recommendations for reducing the risk of TTB by using the licensed two-test systems. However,

shortly after, for financial reasons, IMUGEN discontinued *B. microti* blood donation screening. By then, a new generation of NAT-only, more sensitivity assays, due to the ability to amplify ribosomal RNA templates versus only DNA templates, were available and in use under IND protocols (7). These new tests are used on existing blood screening platforms, and the testing is performed in pools, providing a significant advantage for the screening of a larger number of samples. Also, these new tests detect the four strains of *Babesia* known to infect humans. As the new assays received FDA licensure in 2019, new recommendations for reducing the risk of TTB were released. The new guidance includes *Babesia* screening for all donation types collected in endemic areas and areas contiguous to endemic areas (i.e., 14 states plus District of Columbia), unless pathogen inactivation is performed. The deferral for reactive donors was reduced to two years.

With the implementation of *Babesia* screening, the expectation is that the number of TTB cases will be reduced almost to zero. Travelers to endemic areas from non-endemic, non-screened states may still offer a risk, but these cases represent less than 2% of the total reported TTB cases. We are finally on the right path but should always remember to check for ticks.

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Footnote

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