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REVIEW ARTICLE

Babesiosis and blood transfusion: flying under the radar

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Infectious agents of disease continue to plague transfusion medicine as an increasing number of pathogens are described that pose a potential blood safety risk. While the recent focus has been on newly emerged agents, several well-established pathogens provide timely reminders that other agents continue to pose threats, but invariably 'fly under the radar', thereby failing to elicit adequate measures to prevent their transmission by blood transfusion. Perhaps foremost among this group of agents are the *Babesia* spp., which have been known to cause human disease, in the USA, for close to 40 years. *B. microti*, *B. divergens* and several *Babesia*-like agents are responsible for a growing number of human babesiosis infections. Concomitantly, in the USA, there has been a sharp rise in the number of transfusion-transmitted infections of *Babesia* spp., attributable almost exclusively to *B. microti*. Despite the obvious public health issues posed by *Babesia* spp., options for preventing their transmission by blood transfusion remain limited. However, recognition that the *Babesia* spp. are indeed an ongoing and expanding blood safety threat will probably prove instrumental in the development of viable interventions to limit transmission of these agents.

Key words: *Babesia*, emerging, pathogen, red cells, transfusion, transmission.

Introduction

During the last few years, emerging infectious diseases have captured the attention of the transfusion medicine community. Emerging diseases are broadly defined as those whose rates have increased in the last two decades [1]. From a blood safety perspective, current attention has largely focused on those recently emerged agents that may be transmitted by transfusion. In Europe, particularly the UK, measures have been implemented to address concerns regarding potential transmission of prions associated with variant Creutzfeldt–Jakob disease (vCJD) [2,3]. The recent emergence and continued spread of West Nile virus in the USA has led to the rapid implementation of nucleic acid testing (NAT) to reduce the incidence of transfusion transmission [4,5]. Lastly, following the emergence of severe acute respiratory syndrome (SARS), blood collection agencies and test manufacturers rapidly developed measures to address potential transmission of this coronavirus, but as yet these measures have fortunately not required implementation [6].

While transfusion medicine has been focused on recently emerged agents, several agents, first described decades ago, represent ongoing blood safety risks that have not been adequately addressed and in some respects continue to 'fly under the radar'. Perhaps foremost among these agents are several species of *Babesia* known to cause human infections. The first case of human babesiosis, which was also fatal, was reported in 1957 from what was then known as Yugoslavia [7]. In 1966, the first US case was reported on Nantucket Island off the New England coast [8]. Since then, hundreds of cases of human babesiosis have been reported in the USA, and an additional 30 cases have been reported in Europe [9–12]. The known geographical range of the parasite continues to expand owing to environmental and ecological changes, enhanced epidemiological investigations and an overall increase in public health awareness. From a blood safety perspective, transfusion-transmitted infections involving *Babesia* spp. have become increasingly problematic in the USA, with progressively more reported each year [13]. However, despite

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Table 1 Characteristics and transfusion-transmitted cases associated with *Babesia* spp. implicated in human disease

Agent	Geographical distribution	Vector(s)	Reservoir hosts	Reported transfusion-transmitted cases
Babesia microti	USA (northeast, upper Midwest)	*Ixodes scapularis*	Deer mice, shrews	> 50[a]
	Europe	*Ixodes trianguliceps* *Ixodes ricinus*	Voles, field mice	0
	Japan	*Ixodes persulcatus*	Field mice	1
Babesia divergens	Europe	*Ixodes ricinus*	Cattle	0
	USA (KY, MO, WA)	Unknown	Unknown	0
Babesia-like agents				
WA-1, CA-1	USA (Pacific Coast)	*Ixodes pacificus?*	Unknown	2
EU-1	Europe (Austria, Italy)	Unknown	Unknown	0

[a]Includes a transfusion-transmitted infection reported in Canada that was acquired by the implicated donor in the USA.

epidemiological data suggesting that *Babesia* spp. are a growing blood safety concern, particularly in the USA, they continue to be overshadowed by other, often newly emerged, agents. This review will attempt to summarize not only why the *Babesia* spp. remain a neglected blood safety concern, but also why they should be considered as a priority for transfusion medicine.

Epidemiology

Human infections with *Babesia* spp. are primarily attributed to two species: *B. microti* and *B. divergens* (Table 1). *B. microti* is predominately found in the northeastern and upper midwestern USA, but is also endemic in Europe [10,14,15]. Additionally, *B. microti*-like agents have been identified recently in Europe, Japan and parts of Asia, suggesting a wider dissemination [16–18]. *B. divergens* is mainly limited to Europe [12], but three zoonotic cases in the USA have been attributed to *B. divergens*-like organisms that bear nearly identical 18S ribosomal RNA gene sequences (similarity score: 99·5–99·8%) to the European parasite [19,20]. However, the past decade has also seen the emergence of *Babesia*-like agents, which have been implicated in human disease and at least two transfusion-transmitted infections, but are phylogenetically distinct from *B. microti* and *B. divergens* [21,22]. These agents, often designated by their geographical location, include CA-1 (California), WA-1 (Washington) and EU-1 (Austria and Italy) [23]. Other sporadic cases of human babesiosis have been reported from Egypt, South Africa and Mexico, but the aetiologic agents were not fully characterized [24–26]. Taken together, it seems likely that new agents and a broadened geographical distribution for *Babesia* spp. will continue to be reported.

Babesiosis is a zoonotic disease maintained in nature by a complex interaction of tick vectors, animal reservoirs and maintenance/transport hosts. Worldwide, the primary vectors for *Babesia* spp. are ticks of the genus *Ixodes*. In the USA, the black-legged tick, *I. scapularis* (synonymous with *I. dammini*), serves as the primary vector for *B. microti*, while *I. pacificus* is thought to be the vector of WA-1. The European vector for *B. microti* is *I. trianguliceps*, but this tick does not feed on humans, perhaps explaining why few, if any, human cases of *B. microti* are reported in Europe [15]. The sheep tick, *I. ricinus*, has also been shown to be a competent vector for *B. microti* [27,28], but this tick is primarily recognized as the European vector of *B. divergens* [10]. In each of these locations the implicated *Ixodes* tick vector for *Babesia* is the same vector that locally transmits *Borrelia burgdorferi*, the aetiological agent of Lyme disease. While the tick vector for the *B. microti*-like agent in Japan has not been definitively identified, by analogy it has been described as *I. persulcatus*, which is the Japanese vector of Lyme borreliosis [17]. For each of these ticks, adult and nymphal stages are capable of transmitting the infection; however, in most instances the tick must feed for 48 h or longer to successfully transmit the parasite [29,30].

Also critical to the parasite's life cycle are reservoir and transport hosts. For most *Babesia* that infect humans, a rodent or insectivore acts as the reservoir host critical for maintaining the infection in the wild. The primary US reservoir host for *B. microti* is the white-footed mouse, *Peromyscus leucopus*, which may also serve as the reservoir for WA-1, CA-1 and MO-1. Also playing a critical role in the USA are white-tailed deer, which, while not competent hosts for *B. microti*, do serve as transport hosts for adults of *I. scapularis*. The analogous reservoir host in Japan is probably the field mouse, *Apodemus speciosus*, which was first shown to be infected with *B. microti*-like parasites over 20 years ago [31]. In contrast, throughout the distribution of *B. divergens* in Europe, cattle serve as the reservoir host for human infections, as well as the definitive host of the parasite.

Clinical features

Symptoms

Babesial infections demonstrate a spectrum of disease that ranges from asymptomatic to severe life-threatening illness, which is influenced by the infecting species. The tick vector deposits thousands of infective sporozoites in the dermis during the latter stages of feeding (i.e. after 48 h) [10]. Within the human host, sporozoites infect erythrocytes and become trophozoites that replicate by binary fission, producing the characteristic Maltese cross forms seen in some cases (e.g. WA-1) [32]. Replication, in turn, leads to cell rupture, lysis, and release of merozoites that infect additional erythrocytes. These replicate cycles can produce high levels of parasitemia and haemoglobinuria within the host.

Asymptomatic disease is not uncommon for infections with *B. microti* and often goes undetected. Symptomatic infections with *B. microti* are generally mild and self-limiting, producing flu-like symptoms that appear 1–6 weeks postinfection. Characteristic symptoms include fever, headache, chills, drenching sweats, myalgia and malaise, but these usually abate within a few weeks. More severe disease complications (including haemolytic anaemia, thrombocytopenia, haematuria and renal failure) have been observed in infants, elderly, asplenic and immunocompromised patients. Parasitaemia levels, particularly among asplenic patients, can approach 85% and result in severe, even life-threatening, anaemia [10]. In the USA, the mortality rate for clinically apparent *B. microti* infections is almost 5% [33].

Infections with *B. divergens* are generally more severe and often produce fulminant, life-threatening infections. To date, ≈ 30 cases of human babesiosis caused by *B. divergens* have been reported in Europe, and in most cases the patient was asplenic [11,12]. Symptoms appear rapidly, 1–3 weeks postinfection, and can be characterized by haemoglobinuria followed by jaundice as a result of severe haemolysis. The severity of infection coupled with asplenia contributes to a mortality rate for *B. divergens* of 42% [10]. WA-1 also appears to be more virulent than *B. microti*, producing severe disease, even in immunocompetent patients [34].

Unlike infections with *B. divergens*, those with *B. microti* also can demonstrate chronicity. In one study, parasitaemia was shown to persist for 18 months, based on positive polymerase chain reaction (PCR) results [35]. More recent studies have corroborated the presence of parasitaemia among blood donors with antibodies to *B. microti*, which in some cases persists for months [13,36]. However, this latter study also demonstrated that some patients infected with *B. microti* produce long-term elevated antibody titres in the absence of measurable parasitaemia. This suggests that some patients maintain chronic babesial infections that are below the limit of detection by PCR: parasites may only circulate in the peripheral blood at extremely low numbers, on an intermittent basis or they may be restricted to sequestered tissue or organ sites. Indeed, recrudescence of measurable parasitaemia among serologically positive patients has been reported in several instances, in the absence of obvious re-exposure to infected vectors, thus possibly indicating underlying, silent infections [35,36]. These observations support earlier contentions by Gorenflot *et al.*, who suggested that immunocompetent, spleen-intact people may act as asymptomatic carriers of babesiosis [37]. Alternatively, it has been suggested that chronic infections associated with *Babesia* spp. may be linked to the parasite's ability to undergo antigenic variation, which is expressed on the cell surface of the infected erythrocyte [38]. While antigenic variation has not been implicated as an evasion strategy for *B. microti*, this parasite's considerable allelic polymorphism may allow for frequent recombinant events leading to mixed infections, thereby allowing some parasites to evade recognition by the immune response.

Diagnosis

Diagnosis of babesiosis, in part, relies upon the symptomatology described above, but the non-specific nature of the symptoms often makes an accurate clinical diagnosis difficult. Additional diagnostic information can be obtained from an assessment of risk factors, including details of travel to *Babesia*-endemic areas, recent blood transfusion, splenectomy or exposure to ticks [10]. Unfortunately, most people infected with a tick-borne disease do not recall an associated tick bite [9,39,40]. Thus, diagnostic assay play a crucial role in identifying infections with *Babesia* spp.

In some cases, direct detection of infection is possible by examination of thin and thick blood smears, stained with Wrights or Giemsa stains, for red cells containing merozoites. However, for most infections the parasitaemia levels fall well below the limits of visual detection. Detection by smear is also labour intensive, subjective in nature and easily misinterpreted owing to similarities with ring forms of *Plasmodium falciparum*. Direct detection can be enhanced by inoculating susceptible rodents, hamsters or mice for *B. microti* and by inoculating gerbils for *B. divergens*, with patient blood. *Babesia* spp. readily replicate in appropriate rodent hosts and thus the amplified infection can be identified in smears of rodent blood; however, these animals must be checked periodically over a 6–8-week period, making this technique impractical for rapid diagnosis.

Serological assays that detect immunoglobulin M (IgM) or immunoglobulin G (IgG) provide a reliable alternative to direct detection for most non-*B. divergens* infections [41,42]. The rapid onset of symptoms (e.g. haemoglobinuria) associated with *B. divergens* makes serological detection impractical in many patients, because the infection may

prove fatal before detectable antibodies are present. The gold standard for serological detection of *B. microti* infection is the immunofluorescence assay (IFA), which uses infected rodent red cells as the antigen source. The presence of IgM is indicative of a recent or acute infection, but the failure to demonstrate IgG on a subsequent sample may suggest a false-positive result [41,43]. While IgM is present only during the acute phase of disease, IgG persists for months, sometimes years. Critical for successful identification of babesial infection is the use of appropriate antigen sources for each agent. For example, sera from a patient, in Washington State, with a recent *B. divergens*-like infection did not react with *B. microti* or WA-1 antigens, but showed marked IFA reactivity to antigens of *B. divergens* [20]. More recently, enzyme-linked immunosorbent assay (ELISA)-based methods that use antigens derived from infected hamster cells or synthetic peptide antigens have been developed [44,45]. This format has the advantage of potential automation and high throughput, but remains primarily a research tool.

Serological tests also suffer from the inability to differentiate between active and past infections. Despite low parasitaemia levels routinely observed during the early acute phase, reliable and extremely sensitive PCR assays designed to amplify highly conserved sequences of the small-subunit rRNA (ss-rDNA) gene *Babesia* spp. are available [46]. PCR assays can thus be used to identify patients in the acute phase, as well as those who remain persistently or chronically infected [13,35]. That said, PCR assays are limited somewhat by the initial sample volume, thus a negative PCR assay alone does not preclude the presence of an ongoing *Babesia* infection.

Treatment

As already discussed, most infections with *B. microti* are self-limiting and do not require drug treatment. In those cases in which symptomatic disease is persistent or more severe, drug treatment may be necessary. Since 1982, the preferred therapy has been a 7-day course of clindamycin and quinine [47]. While generally successful, drug-related side-effects, including tinnitus and gastroenteritis, occur frequently, and infections may persist, despite treatment. An alternative therapy (atovaquone and azithromycin), has been shown to be equally effective with reduced adverse consequences [48]. In those rare instances in which drug treatment is ineffective, high levels of parasitaemia persist, or signs of haemodynamic instability exist, an exchange transfusion may be prescribed [20,49,50]. Exchange transfusion for babesiosis, like that for malaria, is designed to rapidly reduce overall parasitaemia levels and related haemolysis. While rare, this procedure has been shown to be effective for some cases of babesiosis, especially in splenectomized patients.

Seroprevalence

The frequency of *Babesia* spp. infections in human populations is difficult to determine precisely. As mentioned previously, many infections are not recognized, and babesiosis is not a notifiable disease in the USA. Moreover, there have been few systematic seroprevalence studies published for the *Babesia* spp., and determinations of their prevalence in blood donors are rare, except for a few studies from the USA and Europe.

In the northeast USA, the seroprevalence of *B. microti* has been reported to range from 0·3% in Connecticut to 9·5% in patients with Lyme disease [51–53]. Several reports of *B. microti* in blood donors have been published, with rates as high as 4·3% (5 of 115 positive) on Shelter Island, New York [52,54,55]. A recent Connecticut study reported that 30 of 3490 (0·9%) blood donors were seropositive for *B. microti* [13]. Perhaps more importantly, 10 of 19 (53%) seropositive donors from this study were demonstrably parasitemic when tested by PCR, indicating an obvious transmission risk. Several studies have reported the seroprevalence of WA-1 in residents of northern California and Washington, ranging from 0·9% (1 of 115) to 17·8% (39 of 219), with 25 of 124 (20·8%) Sacramento (California) blood donors showing evidence of antibodies to WA-1 [32,34,56]. These relatively high rates, particularly in areas where the parasite is not endemic, have led some to suggest that serological tests employed in these studies may have lacked specificity [10]. Indeed, accurate seroprevalence measurements of emerging agents, such as WA-1, require reliable and well-characterized assays, but these are not always readily available.

European studies have focused on *B. divergens* and *B. microti*, but the absence of more extensive studies is probably attributable to the misconception that *Babesia* infection is not common in Europe. The observed seroprevalence rate for *B. divergens* among a group of Swedish Lyme borreliosis patients was 13% [57], while a small study of healthy German blood donors identified 8 of 100 (8%) with antibodies to *B. microti* [58]. In contrast, a more recent German study identified seroprevalence rates for *B. microti* and *B. divergens* of 5·4% (25 of 467) and 3·6% (17 of 467), respectively [59]. A subpopulation of healthy blood donors within this latter German study included two (1·7%) donors with antibodies to *B. microti* and one (0·8%) donor with antibodies to *B. divergens*.

Transfusion transmission

Babesia spp. exhibit several characteristics that favour their successful transmission by blood transfusion. Once introduced into a human host by an infected tick, the parasite invades and replicates within human red blood cells, thereby providing a suitable vehicle for transmission to transfusion

recipients via an infected blood unit. The intra-erythrocytic location of *Babesia* spp. suggests that in addition to red cell units, platelet units contaminated with red cells pose a risk for transmitting the parasite by transfusion. As most infections are asymptomatic and parasitaemia can persist for many months, an infected donor may be at risk for transmitting *Babesia* spp. for extended periods of time. Lastly, the parasite is well adapted to survival under standard blood storage conditions, remaining viable for 21 days under empirical conditions and for 35 days based on a reported transfusion-transmitted infection [60,61].

Transfusion-transmitted cases

Establishing an accurate estimate for the number of transfusion-transmitted cases of infection with *Babesia* spp. is difficult. While case numbers in excess of 40–50 are routinely reported [62], exact numbers are increasingly difficult to determine. In many instances, new transfusion-transmitted cases are no longer reported or published on a consistent basis because they are not considered novel or noteworthy. Indeed, to my knowledge, at least 10 transfusion-transmitted cases involving *B. microti* occurred in the USA during 2004, but specific information concerning these cases has not been widely disseminated. The creation of a centralized reporting centre for *Babesia* spp. transfusion-transmitted cases should perhaps be considered as a way to monitor the extent of this blood safety threat.

The large majority of transfusion-transmitted cases, however, are probably either asymptomatic or are not recognized owing to the non-specific nature of symptoms or the unfamiliarity of physicians with clinical babesiosis. Published transfusion-transmitted cases have involved blood recipients ranging in age from neonates to 79 years and, with the exception of two cases implicating WA-1, all have been attributed to *B. microti* [21,22,63]. In most instances, the recipients were immunocompromised and in several cases asplenic, perhaps allowing these cases to be more easily recognized. Observed incubation periods for these cases ranged from 1 to 9 weeks. For reported transfusion-transmitted cases, all have occurred in the USA with the exception of one case in Canada and another in Japan [64,65]. The Japanese case implicated a geographical variant of *B. microti* (99·2% homology) that was acquired locally and thought to be maintained in native field mice populations. In contrast, the Canadian case involved a donor who apparently became infected with *B. microti* while in the USA, and later donated an infectious unit of blood upon returning to Canada. This case highlights the potential for donors to become infected while on vacation or during travel to *Babesia*-endemic areas.

While transfusion-transmitted cases of infection are becoming increasingly common, few estimates of transmission risk are available. A Connecticut study published in 1994 determined the risk of transmitting *B. microti* through blood transfusion by prospectively measuring seroconversion in cardiothoracic surgery patients [66]. The risk of acquiring *B. microti* from a unit of red cells was reported to be 1 in 601, or 0·17% [95% confidence interval (CI): 0·004–0·9%), but the rate for platelet units was 0 in 371, or 0% (95% CI: 0–0·8%). A more recent Connecticut study estimated the risk of acquiring *B. microti* from a transfused red cell unit as being 1 in 1800 [67]. This estimate was based, in part, on observed seroprevalence rates of 1·2% in *Babesia*-endemic and 0·3% in non-endemic areas of Connecticut, a 56% rate of demonstrable parasitemia among seropositive donors, and 26% of lookback investigations yielding a blood recipient infected with *B. microti*.

Blood safety interventions

From a blood safety perspective, available options to prevent or reduce transmission of *Babesia* by transfusion are limited at this time (summarized in Table 2). The primary risk factor for acquiring *Babesia* spp. is exposure to infected ticks. Published studies have described the ability of blood donors to recall recent tick exposure. However, a clear correlation between a donor's ability to recall a tick exposure and demonstrable *Babesia* infection could not be made, largely because the sensitivity of such questions is low [52]. Indeed, as previously mentioned, most people infected with a tick-borne disease do not recall an associated tick bite.

In contrast, serological assays capable of detecting *Babesia* spp. antibodies would appear to offer a reasonable means of identifying infected donors and interdicting potentially infectious blood products. Although most people infected with *B. divergens* will be too ill to donate blood, those infected with *B. microti*, while often asymptomatic, demonstrate a strong and measurable antibody response that can last for months or years following initial infection. As already discussed, IFA and ELISA formats for *Babesia* exist, but the former is not automated and the latter are largely developmental in nature. Despite these issues, the development of a serological test for *B. microti* is both practical and feasible given the host's robust immune response. Several manufacturers offer diagnostic assays capable of detecting IgG to *B. microti*; however, no tests have been submitted to, much less licensed and approved by, the US Food and Drug Administration for *B. microti* blood screening applications in the USA.

The issues surrounding the development of tests for *B. microti* are not technical or scientific in nature, but appear to be associated with manufacturers' perceptions of market size, return on research and development investments, and ongoing concerns of whether screening will actually be implemented. Indeed, because *B. microti* remains regionalized,

Table 2 Potential blood safety interventions for *Babesia* spp.

Intervention	Advantage	Disadvantage
Risk-factor questions	Simple to implement	Lacks sensitivity
Serological testing	Specific and sensitive	Licensed, automated tests unavailable
Regional	Enhanced cost effectiveness	Difficult to define testing region
		Donor travel issues
		Logistically complicated
Universal	Ease of implementation	Reduced cost effectiveness
CMV model	Targets at-risk recipients	Logistically complicated
NAT	Identifies window period	Negative test does not preclude infection
Selective blood collection	Ease of implementation	Impacts blood availability
Leucoreduction	Widely used	Agent intra-erythrocytic, hence ineffective for babesia
Filtration	Simple approach	Need to differentiate infected from non-infected cells, hence ineffective for babesia
Pathogen inactivation/reduction	Feasibility demonstrated	No licensed method currently available for red cells

CMV, cytomegalovirus; NAT, nucleic acid testing.

selective geographical testing has been suggested as a cost-effective intervention [51]. Unfortunately, a regionalized approach is not only problematic from a manufacturer's perspective, but raises logistic issues for blood collection organizations. Perhaps the larger issue is how the transfusion medicine community can persuade assay manufacturers to develop tests for agents that may have limited markets. As economics clearly play a role, a simple solution to this problem is not readily available. Similarly, while NAT would be feasible and invaluable for identifying window-period infections, the cost of developing an assay for what is perceived to be a limited market may likewise preclude its implementation.

While blood screening awaits the development of suitable tests, alternative approaches to managing potentially infectious donors have been proposed. One approach is to avoid blood collection in highly endemic areas during the periods of peak transmission (i.e. June to September) [51]. However, reports of persistent, year-round infections in some blood donors suggest that selective blood collection would only partially reduce the risk of transmission, while negatively impacting local blood availability. Other approaches include leucoreduction, filtration and pathogen reduction, but each poses their own set of technical barriers. Leucoreduction would appear to be ill suited for *Babesia* spp. because the agent is intra-erythrocytic. In contrast, filtration technology would need to differentiate between infected and non-infected red cells. This approach, however, may have some merit as infected red cells will probably present different surface antigens from uninfected cells. Feasibility of pathogen-reduction technology for reducing or inactivating *Babesia* spp. has already been demonstrated [68,69]. Regrettably, host responses to pathogen-reduction technologies, specifically involving red cells, have recently proven to be problematic, leading to the withdrawal of the system from the market. It remains to be seen if these technological hurdles can be overcome.

An alternative approach, sometimes suggested for *Babesia* spp., is one patterned after that used to limit transmission of cytomegalovirus. Blood recipients at greatest risk for developing severe babesiosis (e.g. the elderly or asplenic individuals) would be transfused with units of blood identified as negative for *Babesia* spp. Indeed, most immunocompetent blood recipients tolerate *Babesia* infections with few complications, but the elderly and asplenic can develop severe, even life-threatening, disease. This approach, however, is predicated on the availability of approved tests, which are currently not available.

Conclusions and future directions

Newly emergent agents continue to capture the attention of transfusion medicine, but other, long-known agents, such as *Babesia* spp., pose ongoing and seemingly increasing threats to blood safety that perhaps have received inadequate attention. In part, the lack of attention may be caused by the parasite's limited geographical distribution and the mild, self-limiting disease experienced by most patients. However, the distribution of *Babesia* spp. appears to be greater than originally thought, and the parasite is increasingly implicated in transfusion-transmitted cases, particularly among patients who receive large amounts of blood and are highly susceptible to babesial infection (e.g. elderly, asplenic and immunocompromised). The lack of a consensus approach in preventing transmission of *Babesia* spp. remains problematic and may not be easily resolved in the absence of licensed blood screening tests. One of the greatest hurdles in addressing *Babesia* spp. is persuading manufacturers to develop

approaches, particularly screening assays, for what is perceived to be a limited market. To overcome this obstacle, a concerted effort among government agencies, blood collection organizations and the public health community is needed to encourage the development of suitable interventions for *Babesia* spp. In summary, now that the *Babesia* spp. are clearly visible on our radar screen, appropriate interventions should be considered in order to reduce the blood safety risks posed by this agent.

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