Babesiosis in immunosuppressed hosts: pathogenesis, diagnosis and management

Howard M. Heller

Purpose of review
This review provides the most recent evidence of the challenges that occur in the management of babesiosis in immunocompromised hosts.

Recent findings
The epidemiology of babesiosis is affected by climate change leading to increasing numbers of cases as well as increasing areas of endemicity. Immunosuppressed hosts, especially with asplenia or B-cell defects, are at high risk of having severe disease as well as persistent and relapsed infection. Resistance to the primary therapies azithromycin and atovaquone can develop leading to further challenges in treating persistent or relapsed disease in the immunocompromised host.

Summary
Babesiosis is likely to become a more frequent infectious complication in immunosuppressed hosts as the areas of endemicity expand. Reduced efficacy of standard therapies is likely to continue emerging so more effort needs to be placed on methods of assessing resistance in vitro and developing more reliable treatments for resistant infections.

Keywords
antibiotic resistance, babesiosis, immunosuppressed

INTRODUCTION

Babesiosis is the disease caused by species of *Babesia*, an intraerythrocytic parasite. Presenting symptoms of infection are usually nonspecific and may include fever, chills, sweats, headache, myalgias, anorexia, nausea and fatigue. Severe cases can progress to adult respiratory distress syndrome, kidney failure and liver inflammation. Immunocompromised hosts are more likely to have severe, sometimes fatal, disease and to have persistent or relapsed disease.

Here we provide an overview of babesiosis with a focus on the changing epidemiology, diagnostics and treatments that are most relevant to the immunocompromised host.

TEXT OF REVIEW

Over a hundred species of *Babesia* exist globally and cause disease in a variety of domestic and wild animals. A few *Babesia* species infect humans. *Babesia microti* is the predominant cause of human babesiosis in North America especially in the Northeast and Upper Midwest United States but other species have been reported in other areas including *B. duncani* on the West Coast of the United States, *B. divergens* in Europe, the United States and China, *B. venaratum* in Europe, *B. bigemina* in South America and *B. crassa*-like pathogen in Northeast Asia and Europe [1▪,2▪,3–5].

B. microti is generally transmitted to humans by the hard bodied tick, Ixodes scapularis, though transfusion associated infection can occur [6▪,7▪]. Transfusion related cases occur and for several years the Food and Drug Administration has required screening of donors in states where Babesia has been reported. Persons who travel to endemic areas and then donate in states that are not required to screen for babesiosis can potentially transmit the infection. Babesiosis has been transmitted through organ donation, but there are no established criteria for screening of organ donors [8].

Harvard Medical School, Massachusetts General Hospital, Infectious Disease Division, Boston, Massachusetts, USA

Correspondence to Howard M. Heller, Harvard Medical School, Massachusetts General Hospital, Infectious Disease Division, 55 Fruit Street, Boston, MA 02114, USA. Tel: +1 617 726 3906; e-mail: HHeller1@mgh.harvard.edu

Curr Opin Infect Dis 2024, 37:327–332
DOI:10.1097/QCO.0000000000001038

KEY POINTS

- Immunosuppressed hosts especially those with asplenia or B cell deficiencies are at high risk of severe disease with babesiosis and for relapse.
- Resistance to atovaquone and azithromycin can occur so should be considered when treating immunosuppressed hosts with babesiosis especially those with severe disease or relapses.
- Clinicians should consider tick-borne diseases when evaluating all febrile patients who might be at risk including immunosuppressed hosts and perform appropriate diagnostics and empiric treatment.
- Immunosuppressed hosts who live/travel in endemic areas for tick-borne diseases need counseling for risk reduction, prevention and early recognition of signs/symptoms.

Climate change has led to changing habitats of tick vectors, as well as the host animals of babesiosis, and as a result there has been and will continue to be increasing geographic areas that are endemic and hyperendemic for babesiosis [9▪,10▪].

When evaluating the immunocompromised host for febrile illness initial concerns often focus on opportunistic infections and infections related to indwelling central line catheters. It is critical to assess for risk of tick-borne disease so that the evaluation and empiric treatment can cover tick-borne diseases if necessary. The history of risk for tick bites is more critical than a history of a tick bite itself since most patients with tick-borne diseases do not recall having had a tick bite. Some of the typical laboratory findings of tick-borne diseases (anemia, leukopenia, thrombocytopenia) are common in immunocompromised hosts due to the underlying condition or due to medications. Significant changes from baseline might be inappropriately attributed to the underlying disease. Empiric treatment that covers most bacterial infections will miss coverage for potentially fatal infections including babesiosis, anaplasmosis and ehrlichiosis. Because the tick vector of *B. microti*, *Ixodes scapularis,* is also the vector of Lyme disease and anaplasmosis patients can develop concurrent infection with 2 or all three of these pathogens. Because babesiosis has fairly localized areas of endemicity it is important to obtain domestic travel histories when evaluating immunocompromised patients. Patients who live in area of the United States where babesiosis does not exist may pick up the infection during a brief vacation to a hyperendemic area such as New England.

Immunosenescence results in more severe disease in persons over age 50, but the most severe disease is seen in patients with asplenia or B-cell deficiencies [11▪,12]. Rituximab is the most common B-cell depleting agent associated with severe babesiosis, but it has been reported with others including ocrelizumab [13]. A recent multicenter, retrospective review of immunocompromised patients with babesiosis identified 57 patients, 79% were immunocompromised, 37% were asplenic/hyposplenic and 19% were both [14▪]. 35% were co-infected with Lyme disease. Three cases (5%) experienced relapse, four patients died within 90 days of the babesiosis diagnosis and for one patient babesiosis was the cause of death. A case of hemophagocytic lymphohistiocytosis associated with recurrent *B. microti* and concurrent Lyme disease was reported in a patient treated with ocrelizumab [15]. Severe disease has also been reported in patients with HIV and low $CD4^+$ counts, hemolytic anemia, sickle cell disease, and organ transplants. One patient with myelodysplastic syndrome treated with stem cell transplant and rituximab had prospective evaluation of immune response to *B. microti* in a 4-year period during which he had initial infection and two relapses. He was found to have high levels of *B. microti* specific antibodies despite few circulating B-cells, presence of long-lasting NK cells and T memory stem cells and high levels of IP-10 cytokine that directly correlated with cytokine burden [16▪▪]. It is imperative that the clinician caring for the immunosuppressed host recognizes and diagnoses Babesia in the immunosuppressed individual, as disease can be severe with relapse and even death, in some instances.

Immune response to *Babesia* infection includes both innate and adaptive mechanisms that likely confer some protective immunity in patients who experience reinfection [17▪▪,18].

The most rapid method of diagnosing babesiosis is with examination of a peripheral blood smear [19▪▪]. Most patients with symptomatic disease, especially immunocompromised patients, will have positive smears. Polymerase chain reaction (PCR) is more sensitive than peripheral smear but, laboratory turnaround time is generally longer for PCR. For immunocompromised patients a delay of even 2–3 days can be fatal so if peripheral smear is not available and there are clues suggesting ongoing hemolysis (e.g. hemoglobin/hematocrit lower than baseline, erythrocyte mean cell volume higher than baseline, reticulocytosis, low haptoglobin, elevated LDH or bilirubin) then treatment should be initiated while awaiting PCR results. Another advantage of peripheral smear exam is that it allows quantification of the degree of parasitemia and success/failure of therapy. PCR can remain positive for months even after the infection has resolved. PCR cycle

threshold information might give a clue about degree of parasitemia. Note that PCR tests that are currently commercially available will only detect *B. microti* so if other species are suspected then peripheral smear examination is critical. If PCR for *B. microti* is negative and epidemiologic history is consistent with infection with other species then serology can be helpful in diagnosis [20▪▪].

Antibody testing is generally not helpful in diagnosing active infection since IgG can persist for years and could represent remote prior infection. Presence of *Babesia* immunoglobulin M (IgM) strongly suggests acute infection, but false positive results occur as they do with many other IgM serologies.

Many medical facilities and laboratories offer "tick panels" that generally include Lyme serology, *Anaplasma/Ehrlichia* PCR and *Babesia* PCR. Peripheral smear might not even be offered as an initial option or might have very limited availability. Because the turnaround time of PCR tests generally is 2–5 days clinicians should also check CBC and other laboratory markers to see if there are clues of hemolysis suggesting babesiosis that would warrant immediate initiation of treatment while awaiting the PCR result.

On examination of peripheral smear *Babesia* can be mistaken for *Plasmodium* sp. unless the unique "Maltese cross" form of *Babesia* is seen. Most antimalarial drugs including artemether-lumefantrine and mefloquine do not have demonstrated activity against *Babesia* so it is imperative that if intraerythrocytic parasites are seen on smear and if the patient has geographic risks for both malaria and babesiosis that other more specific tests for malaria, e.g. malaria antigen test be included in the decision about empiric treatment while awaiting PCR results. Rapid nucleic acid amplification diagnostic tests for *Babesia* are under development but are not yet commercially available.

Standard treatment for babesiosis is atovaquone plus azithromycin. An alternative option is clindamycin plus quinine. (Table 1)) Atovaquone absorption can be 20 times higher when taken with a fatty meal than when taken with no fat meal or without food [21]. It is therefore critical that patients be instructed about this requirement lest they have inadequate absorption and essentially end up on inadequate azithromycin monotherapy. Treatment duration is 7–10 days in immunocompetent patients. For highly immunocompromised patients treatment is initiated with oral atovaquone and intravenous azithromycin with transition to oral azithromycin once there has been clinical improvement. Duration of treatment for highly immunocompromised patients is 6 weeks. If parasites are seen on smear during the final 2 weeks then treatment duration should be prolonged further.

For some patients who are severely ill or if there are concerns about atovaquone absorption or atovaquone resistance then more aggressive initial regimens should be considered including atovaquone + azithromycin + clindamycin or atovaquone + azithromycin + clindamycin + quinine. Atovaquone/proguanil + azithromycin can be considered as an alternative if oral atovaquone suspension is unavailable or not tolerated by the patient [22▪].

Acquired atovaquone resistance has been reported. This may be a particular problem in immunocompromised patients who acquire babesiosis while taking atovaquone for *Pneumocystis jiroveci* prophylaxis [23▪▪]. Mutations associated with atovaquone resistance as well as resistance or diminished susceptibility to azithromycin have been identified [24,25].

Exchange transfusion is no longer recommended as adjunctive treatment for malaria because the currently used antimalarials have high and rapid activity against the parasite. However for babesiosis, exchange transfusion should still be considered for

Table 1. Treatment of *Babesia microti* infection

	Treatment regimen	Alternative treatment regimen
Ambulatory patients: mild-moderate disease (Immunocompetent, mild-moderate symptoms, parasitemia <4%, do not require hospitalization)	Atovaquone oral plus azithromycin oral for 7–10 days	Clindamycin oral plus quinine oral
Hospitalized patients: acute severe disease	Atovaquone oral plus azithromycin IV until symptoms abate then convert to oral "step down"	Clindamycin i.v. plus oral quinine sulfate oral
Hospitalized patients: step down therapy (switch to oral)	Atovaquone oral plus azithromycin oral for 7–10 days	Clindamycin oral plus oral quinine sulfate oral
Highly immunocompromised patients	Same regimen as for hospitalized patients but for 6-week duration	

See IDSA guidelines for dosing details (Krause 2020).

patients with severe disease (parasitemia >10%), those with severe hemolytic anemia or pulmonary, renal or hepatic complications [3]. A lower threshold for exchange transfusion should also be considered for those with severe immunosuppression or if there is increased concern for drug resistance, e.g. patients who acquire babesiosis while taking atovaquone monotherapy for *Pneumocystis* prophylaxis.

For immunocompetent hosts parasitemia should be monitored while on treatment but not after symptoms have resolved. For immunocompromised hosts parasitemia should be monitored even after becoming asymptomatic and until smears are negative. If smears are negative but symptoms persist and if there is continued evidence of hemolysis than PCR testing should be done [3].

In immunocompromised hosts, the duration of therapy appears more important than the treatment regimen. Relapses in immunocompromised patients generally occurs within weeks so if recurrence occurs several weeks after the infection appears to have resolved then re-infection should be considered if the patient has continued to be at risk for tick-borne disease.

Low grade asymptomatic parasitemia may persist for weeks after infection in immunocompetent hosts [26]. In immunocompromised hosts babesiosis may persist even longer so longer courses of therapy are recommended. Since relapses can occur it is imperative that immunocompromised hosts continue to be monitored after completing therapy with symptom review and/or monitoring of hemoglobin/hematocrit.

For patients who have responded to treatment but who then relapse it is appropriate to retreat with the same agents but to develop strategies for more aggressive treatment and monitoring if there is not a rapid response to the standard therapy. This might include extending treatment to 6 weeks or using PCR negativity and a measure of cure before stopping treatment.

Patients who continue to relapse or who are not responding despite aggressive standard therapy may need to be treated with alternate regimens. Clofazamine in combination with atovaquone has been shown to be effective in mouse models but human clinical data is lacking [27,28]. Tafenoquine, an 8-aminoquinoline used for treatment and prophylaxis of malaria and for cure of *Plasmodium vivax* infection has been shown to be effective in mouse models of *B. duncani* infection including atovaquone-resistant strains [29]. There are limited case reports of tafenoquine successfully used to treat relapsing babesiosis in immunocompromised patients with atovaquone and azithromycin resistant strains [30▪▪,31▪▪,32]. A case report of tafenoquine failure with relapse after a 6-week course has also been reported [33]. Tafenoquine remains a promising option for relapsing Babesiosis in patients with multidrug resistant infection who are not G6PD deficient. A randomized clinical trial of atovaquone/azithromycin with or without tafenoquine has been proposed [34▪]. However since G6PD levels must be checked before administering tafenoquine and this would likely result in delays in treatment some have felt that tafenoquine is not appropriate as a first line drug for babesiosis [35▪].

Optimal treatment regimens for non-*B. microti* species have not been determined but current recommendations generally include clindamycin with quinine depending on species and severity of disease (Table 2) [36].

All immunocompromised patients who live in areas endemic for tick borne disease should receive counseling for reducing risks of tick-borne diseases. This includes: personal risk reduction with use of acaricides/insecticide such as DEET when outdoors and wearing long sleeved shirt and long trousers. Reducing tick population in backyards with the use of "tick tubes" or spraying with insecticides. Daily thorough "tick checks" with prompt removal of attached ticks. Use of tick repellants/acaricides for pets. Symptom recognition and need for rapid evaluation for tick-borne diseases. Use of doxycycline for Lyme postexposure prophylaxis while emphasizing that this will not prevent babesiosis. Counseling and reminders should occur periodically either at the time of review of immunizations or before and during "tick season."

Table 2. Antimicrobial agents used to treat non-Babesia microti species (Smith 2020)

	Mild disease	Severe disease	Adjunctive/alternative therapy in severe cases
Babesia divergens	Clindamycin	Clindamycin plus quinine	Exchange transfusion, hemodialysis.
Babesia divergens-like *Babesia duncani*	Clindamycin plus quinine	Clindamycin plus quinine	Exchange transfusion, hemodialysis.
Babesia veneratum	Clindamycin	Clindamycin plus quinine	Exchange transfusion, consider alternative treatment with atovaquone plus azithromycin

CONCLUSION

Babesiosis is an increasingly common tick-borne disease that causes severe disease in immunocompromised hosts especially those with asplenia and B-cell disorders. Rapid diagnosis is essential so the diagnosis should be considered in symptomatic patients who have been at risk for tick-borne infections in endemic areas. Persistent and relapsed infection are common in immunocompromised hosts. Drug resistance especially to atovaquone can occur so alternative regimens may be needed in patients who do not respond to standard treatment or who relapse. Further research is needed for the development of rapid diagnostic tools and for treatments of resistant infection.

Acknowledgements

The author would like to thank colleagues who have discussed complex Babesia cases over the years and provided invaluable insight especially Drs Jeffrey Gelfand and Jacob Lemieux.

Financial support and sponsorship

This work was supported by the Division of Infectious Diseases, Massachusetts General Hospital, Boston MA.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

1. Hildebrandt A, Gray J, Montero E. Characteristics of human babesiosis in ■ Europe. Pathogens 2023; 12:323.

Epidemiology of non*microti* Babesia human pathogens in Europe.

2. Calvopiña M, Montesdeoca-Andrade M, Bastisdas-Caldes C, *et al.* Case ■ report: first report on human infection by tick-borne *Babesia bigemina* in the Amazon region of Ecuador. Front Public Health 2023; 11:1079042.

Describes the most recently discovered human Babesia pathogen, *B. bigemina* in South America.

3. Krause PJ, Auwaerter PG, Bannaru RR, *et al.* Clinical practice guidelines by the Infectious Disease Society of America (IDSA): guideline on diagnosis and management of babesiosis. Clin Infect Dis 2020; 72:e49–e64.
4. Doderer-Lang C, Filisetti D, Badin J, *et al. Babesia crass*-like human infection indicating need for adapted PCR diagnosis of Babesiosis, France. Emerging Infect Dis 2022; 28:449–452.
5. Jia N, Zheng Y-C, Jiang J-F, *et al.* Human babesiosis caused by a *Babesia crassa*-like pathogen: a case series. Clin Infect Dis 2018;67:1110–9.
6. Eder AF, O'Callaghan. Kumar S. Reduced risk of transfusion-transmitted ■ babesiosis with donor blood testing. Clin Infect Dis 2024; 78:228–230.

Details the reduction in transfusion-related babesiosis since adoption of mandatory testing of donated blood in states where babesiosis in endemic. Cases still do rarely occur when blood is collected in nonendemic states from donors who have recently traveled to endemic areas.

7. Drews SJ, Kjenmtrup AM, Krause PJ, *et al.* Transfusion-transmitted *Babesia* ■ sp.: a changing landscape of epidemiology, regulation and risk mitigation. J Clin Microbio 2023; 61:e0126822.

Data showing the effect of blood screening on reducing the incidence of transfusion associated babesiosis.

8. Brennan MB, Herwaldt BL, Kazmierczak JJ, *et al.* Transmission of *Babesia microti* parasites by solid organ transplantation. Emerging Infect Dis 2016; 22:1869–1876.
9. Drews SJ, Wendel S, Leiby DA, *et al.* Climate change and risk to the blood ■ supply. Transfusion 2023; 61:638–645.

Description of how climate change and the effect on the geographic spread of tick-borne disease will continue to have effects on the blood supply requiring continuing monitoring and updating of screening regulations.

10. Edelson PJ, Harold R, Ackelsberg J, *et al.* Climate change and the epidemiol- ■ ogy of infectious diseases in the United States. Clin Infect Dis 2023; 76:950–956.

Description of how climate change and the effect on the geographic spread of tick-borne disease will continue to have effects on the blood supply requiring continuing monitoring and updating of screening regulations.

11. Foerst E, Shankar K, Zhou J, Ghaneie A. A presentation of babesiosis in the ■ setting of low grade follicular lymphoma. Cureus 2024; 16:e52585.

A case report reminder than even in patients with B cell malignancies fever and other symptoms may be due to babesiosis and not the underlying malignancy.

12. Raffalli J, Wormser GP. Persistence of bebasiosis for >2 years in a patient on rituximab for rheumatoid arthritis. Diagn Microbiol Infect Did 2016; 85:231–232.
13. Haberli N, Coban H, Padam C, *et al. Babesia microti* infection in a patient with multiple sclerosis treated with ocrelizumab. Mult Scler Relat Disord 2021; 48:102731.
14. Harris CE, Kakoullis L, Aleissa MM, *et al.* Complications of Babesiosis in ■ immunocompromised and asplenic/hyposplenic patients. Open Forum Infect Dis 2023; 10(Suppl 2):S1187.

An abstract that provides data on complications in immunocompromised hosts.

15. Zahra A, Marcos LA. Hemophagocytic lymphohistiocytosis associated with recurrent babesiosis with Lyme disease co-infection in an immunocompromised host on anti-CD20 monoclonal antibody therapy: a case report. IDCases 2022; 29:e01570.
16. Little JS, Oakley MS, Thorner AR, *et al.* Immune control in repeated *Babesia* ■■ *microti* infection in a patient with B-cell deficiency. Open Form Infect Dis 2023; 11:ofad568.

A thorough examination of the immune response to babesia in an immunosuppressed patient that demonstrates the combination of innate and adaptive immune response.

17. Conti J, Gagliardi T, Arnaboldi PM, *et al.* Immune mediators important for a ■■ protective secondary response to *Babesia microti*. Pathogens 2024; 13:123.

A mouse study that elucidates the innate and adaptive immune response to Plasmodium and Babesia.

18. Djokic V, Rocha SC, Parveen N. Lessons learned for pathogenesis, immunology, and disease of erythrocytic parasites: Plasmodium and Babesia. Front Cell Infect Microbiol 2021; 11:685239.
19. Miller JM, Binnicker MJ, Campbell S, *et al.* Guide to the utilization of the ■■ microbiology laboratory for diagnosis of infectious diseases: 2024 update by the Infectious Disease Society of America (IDSA) and the American Society for Microbiology (ASM). Clin Infect DIs 2024; ciae104.

Updated guidelines for diagnosis of babesiosis recommends peripheral smear as test of choice though many hospitals and labs only off PCR as first option for *Babesia* diagnosis.

20. Tijani MK, Svensson J, Adlerborn P, *et al.* How to detect antibodies against ■■ *Babesia* divergens in human blood samples. Open Forum Infect Dis 2024; 11:ofae028.

Describes a new enzyme immunoassay that is superior to the previously available immune fluorescent assay for *B. divergens.*

21. Nixon GL, Moss DM, Shone AE, *et al.* Antimalarial pharmacology and therapeutics of atovaquone. J Antimicrob Chemother 2013; 68:977–985.
22. Shahid M, Wechsler B, Parameswaran V, Diaz MA. Atovaquone-proguanil: a ■ promising therapy for persistent relapsing babesiosis. Case Rep Infect Dis 2024; 2024:7168928.

A case report of relapsed babesiosis in a patient with B-cell disorder treated successful with atovaquone-proguanil plus azithromycin and clindamycin.

23. Holbrook NR, Klontz EH, Adams GC, *et al. Babesia microti* variant with ■■ multiple resistance mutations detected in an immunocompromised patient receiving atovaquone prophylaxis. Open Forum Infect Dis 2023; 10:ofad097.

Illustrative case of how atovaquone resistance may develop in patients receiving it for *Pneumocystis* prophylaxis while they acquire babesiosis.

24. Lemieux JE, Tran AD, Freimark L, *et al.* A global map of genetic diversity in *Babesia microti* reveals strong population structure and identifies variants associated with clinical relapse. Nat Microbiol 2016; 1:16079.
25. Simon MS, Westblade LF, Dziedziech, *et al.* Clinical and molecular evidence of atovaquone and azithromycin resistance in relapsed *Babesia microti* infection associated with rituximab and chronic lymphocytic leukemia. Clin Infect DIs 2017; 65:1222–1225.
26. Bloch EM, Kumar S, Krause PJ. Persistence of *Babesia microti* infections in humans. Pathogens 2019; 8:102.
27. Tuvshintulga B, Sivakumar T, Nugraha, *et al.* Combination of clofazimine and atovaquone as potent therapeutic regimen for the radical cure of *Babesia microti* infection in immunocompromised hosts. J Infect Dis 2022; 225:238–242.
28. Vannier E, Gelfand J. Clofazamine for babesiosis: preclinical data support for a clinical trial. J Infect Dis 2022; 225:187–189.
29. Vydyam P, Pal AC, Renard I, *et al.* Tafenoquine-atovaquone combination achieves radical cure and confers sterile immunity in experimental models of human babesiosis. J Infect Dis 2024; 229:161–172.

Strong evidence for activity of tafenoquine+atovaquone albeit in an animal model.

30. Krause PJ, Rogers R, Shah MK, *et al.* Tafenoquine for relapsing babesiosis: a ■■ case series. Clin Infect Dis 2024; 79:130–137.
A series of 5 immunocompromised patients with relapsing babesiosis (1 previously reported), 1 treated unsuccessfully with tafenoquine monotherapy and 4 treated successfully with tafenoquine in combination with other agents.
31. Rogers R, Krause PJ, Norris AM, *et al.* Broad antimicrobial resistance in a case ■■ of relapsing Babesiosis successfully treated with tafenoquine. Clin Infect Dis 2023; 76:741–744.
Case report of successful use of tafenoquine in a patient with B-cell immunosuppression. (This case in included in the case series in Krause PJ 2024.)
32. Marcos LA, Leung A, Kirkman L, Wormser GP. Use of tafenoquine to treat a patient with relapsing babesiosis with clinical and molecular evidence of resistance to azithromycin and atovaquone. IDCases 2022; 27:e01460.
33. Prasad PJ, Wormser GP. Failure of an approximately six week course of tafenoquine to completely eradicate *Babesia microti* infection in an immunocompromised patient. Pathogens 2022; 11:1051.
34. Dow G, Smith B. Trial planned to evaluate safety and efficacy of tafenoquine + ■ atovaquone/azithromycin in hospitalized *Babesiosis* patients. J Infect Dis 2024; 230:271–272.
Proposed trial of tafenoquine as a first line agent for babesiosis. Although it does pose challenges because of the need for G6PD screening prior to initiation there is a need for further clinical trials of new agents.
35. Mamoun CB, Wormser GP. Response to Geoffrey Dow and Bryan Smith on a ■ proposed tafenoquine treatment trial for Babesiosis. J Infect Dis 2024; 230:273.
36. Smith RP, Hunfeld. Krause PJ. Management strategies for human babesiosis. Expert Rev Antiinfective Ther 2020; 18:625–636.