Babesiosis

Chapter 232 | Part 5: Infectious Diseases

KEY CLINICAL POINTS

1. Babesiosis is caused by protozoan parasites of the genus Babesia that invade and lyse red blood cells (RBCs).
2. Most U.S. cases are caused by B. microti, reported from the Northeast and upper Midwest during summer months.
3. Transmission occurs via Ixodes scapularis tick bites or blood transfusion (transfusion-transmitted babesiosis).
4. Asplenia and immunosuppression are major risk factors for severe disease.
5. Diagnosis is confirmed by Giemsa-stained thin blood smears showing intraerythrocytic ring forms or tetrads (Maltese cross).
6. First-line treatment for mild to moderate B. microti infection: atovaquone + azithromycin for 7–10 days.
7. Red cell exchange (RCE) is recommended when parasitemia >10% or complications like renal failure occur.
8. Mortality in immunocompetent patients is ~0.6%; higher in immunocompromised (~20%).
9. Tafenoquine is an emerging treatment for relapsing cases but contraindicated in G6PD deficiency.

1. DEFINITION & OVERVIEW

Babesiosis is an emerging infectious disease caused by protozoan parasites of the genus Babesia that invade and lyse red blood cells (RBCs). Most U.S. cases are caused by B. microti, transmitted via Ixodes scapularis ticks or blood transfusion. Symptoms resemble flu-like illness. Mild to moderate infections are treated with atovaquone + azithromycin for 7–10 days. Asplenic and immunocompromised patients require extended treatment. Red cell exchange is indicated for severe cases.

2. EPIDEMIOLOGY

Cases are reported weekly to CDC via the National Notifiable Diseases Surveillance System. In 2023, >3200 cases were reported from 33 states. Incidence increased due to tick density and northward expansion of Ixodes scapularis. B. microti is predominant in the U.S., while B. divergens and other species are reported globally. Risk factors include age ≥50, asplenia, immunosuppression, and transfusion history.

2.1 Geographic Distribution

- **United States**: >95% of cases caused by B. microti in Northeast (Massachusetts, Connecticut) and upper Midwest (Minnesota, Wisconsin). Symptomatic infections with B. duncani reported in Pacific Northwest.

- **Europe**: B. divergens cases linked to cattle farms in France/Ireland; most patients asplenic.
- **Asia**: B. microti recognized in Taiwan; emerging in mainland China with B. venatorum and B. crassa-like organisms.
- **Other Regions**: Cases reported in Canada, Mexico, and South Korea.

2.2 Incidence & Trends

- **CDC Reporting**: 1126 cases reported in 2011 (first nationally notifiable year); >3200 cases reported in 2023.
- **Transfusion-transmitted babesiosis (TTB)**: Increased sharply; ARC began screening blood donations in 2020, reporting no TTB cases during the following 13 months.

2.3 Risk Factors

- **Age**: ~80% of symptomatic patients ≥50 years; hospitalized patients median age 68.
- **Asplenia**: Congenital, functional (celiac disease, hemoglobinopathies), or acquired (splenectomy).
- **Immunosuppression**: Iatrogenic (autoimmune disorders, malignancies, transplantation).
- **Transfusion Risk**: Patients requiring RBC transfusions.

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3. ETIOLOGY & PATHOPHYSIOLOGY

Babesia species use mammals as reservoir hosts, with humans as dead-end hosts. Pathogenesis involves RBC lysis leading to hemolysis, anemia, renal failure, splenic infarction, and systemic inflammation. The spleen is the immunodominant organ; asplenia increases severity.

3.1 Modes of Transmission

- **Tick Bite**: 45% of patients recall tick bite within 8 weeks of onset; nymphs and adults transmit B. microti.
- **Blood Transfusion**: >300 TTB cases reported, primarily via packed RBCs; B. microti remains viable in refrigerated units for up to 42 days.
- **Vertical Transmission**: Rare (<1%); symptoms develop 3–6 weeks postpartum with parasitemia 2–5%.
- **Organ Transplantation**: Single case report of transmission via kidney allograft from donor with prior transfusions.

3.2 Pathogenesis

- **Anemia & Renal Failure**: RBC debris accumulates in kidneys, causing failure; free hemoglobin scavenges nitric oxide, promoting thrombosis.
- **Splenic Complications**: RBC lysis in splenic capillaries triggers infarction and splenomegaly.
- **Immune Response**: CD4+ T cells are critical for immunity; B cells/antibodies may be essential in some patients.

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4. CLINICAL FEATURES

Symptoms appear 1–4 weeks post-tick bite or 3–7 weeks post-transfusion. Fever (up to 40.9°C), fatigue, chills, myalgia, and anorexia are common. Severe cases present with dark urine, jaundice, renal failure (20%), respiratory failure (7%), and splenic complications.

4.1 Physical Examination Findings

- **Fever**: Primary symptom.
- **Jaundice/Scleral Icterus**: Indicates severe hemolysis.
- **Abdominal Tenderness**: Suggests splenomegaly or infarction.
- **Hypotension/Tachycardia**: May indicate splenic rupture.

4.2 Severity & Complications

- **Severe Disease Predictors**: Total bilirubin >1.9 mg/dL, WBC ≥10 imes 10^3/µL, creatinine >1.2 mg/dL.
- **Mortality**: ~0.6% in immunocompetent patients; ~20% in immunocompromised.
- **Relapsing Infection**: Common in rituximab-treated patients.

4.3 Other Babesia Infections

- **B. duncani**: 8 U.S. cases reported; one fatality.
- **B. divergens**: All 7 cases in splenectomized patients; 3 deaths.
- **B. venatorum**: Mild to severe in splenectomized Europeans; no deaths in Chinese patients.
- **B. crassa**: Mild illness in Chinese patients; no hospitalizations.

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5. DIFFERENTIAL DIAGNOSIS

Distinguish from malaria (BinaxNOW test), Lyme disease (coinfection common), other tick-borne pathogens (Anaplasma phagocytophilum, Borrelia miyamotoi), and HELLP syndrome in pregnant patients.

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6. INVESTIGATIONS & DIAGNOSIS

Diagnosis confirmed by Giemsa-stained blood smears showing ring forms or tetrads (Maltese cross). PCR detects 1–10 parasites/µL. Serology may persist >1 year; IgM ≥1:20 and IgG ≥1:64 for B. microti. Parasitemia >4% predicts severe disease.

6.1 Routine Laboratory Testing

- **CBC**: Anemia, elevated reticulocytes.
- **Hemolysis Markers**: Low haptoglobin, elevated LDH.
- **Thrombocytopenia**: Often precedes severe anemia.
- **Liver Enzymes**: Elevated ALP, AST, ALT.
- **Renal Function**: Elevated BUN, creatinine.

6.2 Specific Testing

- **Microscopy**: Giemsa-stained thin smears confirm diagnosis (ring forms or tetrads).
- **PCR**: Detects 1–10 parasites/µL; speciation via fluorescent probe.
- **Serology**: IgM ≥1:20, IgG ≥1:64 for B. microti.

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7. MANAGEMENT & TREATMENT

Treatment depends on severity and species. Atovaquone + azithromycin is the standard for mild/moderate cases. Severe cases or B. divergens require more aggressive management including clindamycin and quinine, and potentially red cell exchange (RCE).

7.1 Drug Therapy: Mild to Moderate Infection

- **Adults**: Atovaquone 750 mg q12h PO + Azithromycin 500 mg/d PO (day 1) then 250 mg/d.
- **Children**: Atovaquone 20 mg/kg q12h PO (max 750 mg/dose) + Azithromycin 10 mg/kg qd PO (day 1) then 5 mg/kg qd PO (max 250 mg).

TABLE 232-1

: Treatment of Human Babesiosis

Condition	Adults	Children
Mild to Moderate B. microti Infection	Atovaquone (750 mg q12h PO) + Azithromycin (500 mg/d PO on day 1 followed by 250 mg/d)	Atovaquone (20 mg/kg q12h PO; max 750 mg/dose) + Azithromycin (10 mg/kg qd PO on day 1 [max 500 mg], 5 mg/kg qd thereafter [max 250 mg])
Severe B. microti Infection	Preferred: Atovaquone (750 mg q12h PO) + Azithromycin (500 mg qd IV followed by 250–500 mg qd PO). Alternative: Clindamycin (600 mg q6h IV) + Quinine (650 mg q6–8h PO). Consider exchange transfusion.	Preferred: Atovaquone (20 mg/kg q12h PO; max 750 mg/dose) + Azithromycin (10 mg/kg qd IV followed by 10 mg/kg qd PO [max 500 mg]). Alternative: Clindamycin (7–10 mg/kg q6–8h IV) + Quinine (8 mg/kg q8h PO; max 650 mg/dose). Consider exchange transfusion.
B. divergens Infection	Immediate complete exchange transfusion + Clindamycin (600 mg q6–8h IV) + Quinine (650 mg q8h PO)	Immediate complete exchange transfusion + Clindamycin (7–10 mg/kg q6–8h IV; max 600 mg/dose) + Quinine (8 mg/kg q8h PO; max 650 mg/dose)

7.2 Drug Therapy: Severe Infection

- **Preferred Regimen**: Atovaquone + IV azithromycin.
- **Duration**: 7–10 days; extend if symptoms persist.
- **Immunocompromised Patients**: 6 weeks of therapy, including 2 weeks post-parasitemia clearance.
- **Alternative Regimens**: Clindamycin + quinine (Note: Quinine carries risk of QTc prolongation).

7.3 Exchange Transfusion

- **Indications**: Parasitemia >10% or complications like renal failure.
- **Purpose**: Reduces parasite burden and corrects anemia.

8. PROGNOSIS & COMPLICATIONS

Mortality in immunocompetent patients is ~0.6%. Severe complications include renal failure (20%), respiratory failure (7%), splenic rupture, and DIC.

9. SPECIAL CONSIDERATIONS

- **Asplenic Patients**: Require extended treatment.
- **Tafenoquine**: Emerging option for relapsing infections; contraindicated in G6PD deficiency.
- **Splenic Rupture Management**:
- Hemodynamically unstable → emergent splenectomy.
- Stable patients → embolization.

10. KEY PEARLS & CLINICAL TRAPS

- **Pearl 1**: Asplenia is a major risk factor for severe disease.
- **Pearl 2**: Tafenoquine is effective for relapsing infections but contraindicated in G6PD deficiency.
- **Trap 1**: Do not rely on serology alone; antibodies persist >1 year post-infection.
- **Trap 2**: Clindamycin + quinine has higher toxicity (QTc prolongation, cinchonism).

REFERENCE TABLES

TABLE 232-1

Treatment of Human Babesiosis ADULTS Mild to Moderate B. microti Infection a Atovaquone (750 mg q12h PO) plus...

ADULTS	CHILDREN
Mild to Moderate B. microti Infectiona	
Atovaquone (750 mg q12h PO) **plus** **Azithromycin (500 mg/d PO on day 1 followed by 250 mg/d PO on subsequent days)**	Atovaquone (20 mg/kg q12h PO; maximum, 750 mg/dose) plus Azithromycin (10 mg/kg qd PO on day 1 [maximum, 500 mg], 5 mg/kg qd PO thereafter [maximum, 250 mg])
Severe B. microti Infectionb,c	
Preferredd **Atovaquone (750 mg q12h PO)** **plus** **Azithromycin (500 mg qd IV followed by 250–500 mg qd PO)** **Alternativee,f** **Clindamycin (600 mg q6h IV followed by 600 mg q8h PO)** **plus** **Quinine (650 mg q6–8h PO)** **Consider exchange transfusion**	Preferred Atovaquone (20 mg/kg q12h PO; maximum, 750 mg/dose) plus Azithromycin (10 mg/kg qd IV followed by 10 mg/kg qd PO [maximum, 500 mg]) Alternative Clindamycin (7–10 mg/kg q6–8h IV followed by 7–10 mg/kg q6–8h PO [maximum, 600 mg/dose]) plus Quinine (8 mg/kg q8h PO; maximum, 650 mg/dose) Consider exchange transfusion
B. divergens Infectiong	
Immediate complete exchange transfusion **plus** **Clindamycin (600 mg q6–8h IV)** **plus** **Quinine (650 mg q8h PO)**	Immediate complete exchange transfusion plus Clindamycin (7–10 mg/kg q6–8h IV; maximum, 600 mg/dose) plus Quinine (8 mg/kg q8h PO; maximum, 650 mg/dose)