



**FIGURE 249-2** Giemsa-stained thin blood films showing *Babesia microti* parasites. *B. microti* are obligate parasites of erythrocytes. Trophozoites may appear as ring forms (A) or as ameboid forms (B). Merozoites can be arranged in tetrads and are pathognomonic (C). Extracellular parasites can be noted, particularly when parasitemia is high (D). (Adapted from E Vannier, PJ Krause: *N Engl J Med* 366:2397, 2012.)

Tetrads are characteristic of *B. microti*, *B. duncani*, and *B. divergens*-like organisms in human erythrocytes. Because the number of parasitized RBCs may be low, particularly at the onset of symptoms, identification of the parasite may require multiple blood smears over several days. Parasitemia levels can range from 1% to 20% in immunocompetent hosts and can be as high as 85% in immunocompromised patients. If parasites cannot be identified by microscopy and the disease is still suspected, amplification of the babesial 18S rRNA gene by polymerase chain reaction (PCR) is recommended. Quantitative PCR has greatly lowered the threshold for detection of *B. microti* DNA.

Serology can suggest or confirm the diagnosis of babesiosis. An indirect immunofluorescent antibody test for *B. microti* is most commonly used. IgM titers of  $\geq 1:64$  and IgG titers of  $\geq 1:1024$  suggest active or recent infection. Titers typically decline over 6–12 months. Antibodies to *B. microti* do not cross-react with *B. duncani* or *B. divergens* antigen. In *B. divergens* infection, serology is of limited use because symptoms often appear before antibodies can be detected. Sera from patients infected with *B. divergens*-like organisms or *B. venatorum* are reactive against *B. divergens* antigen.

## TREATMENT BABESIOSIS

### ASYMPTOMATIC *B. MICROTI* INFECTION

People who experience asymptomatic *B. microti* infection often are not diagnosed and treated. Current guidelines recommend antibiotic therapy for asymptomatic carriers only if parasitemia persists for >3 months. Laboratory-based tests are being developed for the purpose of screening the blood supply and will result in the identification of a greater number of asymptomatic *B. microti* carriers, raising the question of whether they should be treated.

### MILD TO MODERATE *B. MICROTI* ILLNESS

Atovaquone plus azithromycin, given orally for 7–10 days, is the recommended antibiotic treatment combination for mild to moderate

**TABLE 249-1** TREATMENT OF HUMAN BABESIOSIS

Adults	Children
<b><i>B. microti</i> Infection (Mild to Moderate Illness<sup>a,b</sup>)</b>	
Atovaquone (750 mg q12h PO)	Atovaquone (20 mg/kg q12h PO; maximum, 750 mg/dose)
<b>plus</b>	<b>plus</b>
Azithromycin (500 mg/d PO on day 1, 250 mg/d PO thereafter)	Azithromycin (10 mg/kg qd PO on day 1 [maximum, 500 mg/dose], 5 mg/kg qd PO thereafter [maximum, 250 mg/dose])
<b><i>B. microti</i> Infection (Severe Illness<sup>c,d</sup>)</b>	
Clindamycin (300–600 mg q6h IV or 600 mg q8h PO)	Clindamycin (7–10 mg/kg q6–8h IV or 7–10 mg/kg q6–8h PO; maximum, 600 mg/dose)
<b>plus</b>	<b>plus</b>
Quinine (650 mg q6–8h PO)	Quinine (8 mg/kg q8h PO; maximum, 650 mg/dose)
<b>plus</b>	<b>plus</b>
Consider exchange transfusion	Consider exchange transfusion
<b><i>B. divergens</i> Infection</b>	
Immediate complete exchange transfusion	Immediate complete exchange transfusion
<b>plus</b>	<b>plus</b>
Clindamycin (600 mg q6–8h IV)	Clindamycin (7–10 mg/kg q6–8h IV; maximum, 600 mg/dose)
<b>plus</b>	<b>plus</b>
Quinine (650 mg q8h PO)	Quinine (8 mg/kg q8h PO; maximum, 650 mg/dose)

<sup>a</sup>Treatment duration, 7–10 days. <sup>b</sup>A high dose of azithromycin (600–1000 mg) combined with atovaquone has been recommended for immunocompromised hosts. <sup>c</sup>Treatment typically is given for 7–10 days, but its duration may vary. In severely immunocompromised patients, therapy should be continued for at least 6 weeks, including 2 weeks after parasites are no longer detected on blood smear. <sup>d</sup>Several alternative regimens have been used in a limited number of cases of *B. microti* infection, and their efficacy is uncertain. These regimens include atovaquone, azithromycin, and clindamycin; atovaquone, azithromycin, and doxycycline; atovaquone, clindamycin, and doxycycline; atovaquone, doxycycline, and artemisinin; atovaquone-proguanil; azithromycin and quinine; and azithromycin, clindamycin, and doxycycline.

**Sources:** (1) ME Falagas, MS Klemperer: *Clin Infect Dis* 22:809, 1996. (2) PJ Krause et al: *N Engl J Med* 343:1454, 2000. (3) PJ Krause et al: *Clin Infect Dis* 46:370, 2008. (4) CM Shih, CC Wang: *Am J Trop Med Hyg* 59:509, 1998. (5) CP Stowell et al: *N Engl J Med* 356:2313, 2007. (6) JM Vyas et al: *Clin Infect Dis* 45:1588, 2007. (7) GP Wormser et al: *Clin Infect Dis* 50:381, 2010.

babesiosis (Table 249-1). Clindamycin plus quinine is a second choice. Symptoms usually begin to resolve within 48 h of therapy initiation, but complete resolution may take weeks to months. An atypical or poor response to therapy should raise concern about the possibility of concurrent Lyme disease (Chap. 210) or human granulocytotropic anaplasmosis (Chap. 211). In the first prospective trial of antibabesial therapy, the combination of atovaquone plus azithromycin was compared with clindamycin plus quinine in adults. These two drug combinations were equally effective in resolving symptoms and clearing parasitemia. Adverse effects were reported in 15% of trial participants who received atovaquone plus azithromycin but in 72% of those who received clindamycin plus quinine. Adverse reactions were so severe that treatment had to be stopped in about one-third of participants taking clindamycin plus quinine but in only 2% of those taking atovaquone plus azithromycin.

### SEVERE *B. MICROTI* ILLNESS

Clindamycin given intravenously plus quinine given orally for 7–10 days constitute the recommended treatment for severe babesiosis. Intravenous quinidine may be used instead of oral quinine but requires cardiac monitoring because of the risk of QT prolongation and polymorphic ventricular tachycardia.

Standard antimicrobial therapy is sometimes insufficient to resolve symptoms and clear parasitemia, especially in patients with