

New York State Council on Human Blood and Transfusion Services

***BABESIOSIS,
HUMAN EHRLICHIOSIS AND
HUMAN ANAPLASMOSIS:
POTENTIAL TRANSFUSION COMPLICATIONS***

Second Edition
2008

New York State Council on Human Blood and Transfusion Services
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Second Edition 2008, First Edition 1999

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COUNCIL ON HUMAN BLOOD AND TRANSFUSION SERVICES**

**BABESIOSIS, HUMAN EHRLICHIOSIS AND
HUMAN ANAPLASMOSIS:
POTENTIAL TRANSFUSION COMPLICATIONS**

BABESIOSIS

Community Acquisition

Babesiosis is a zoonotic infection in which ticks transmit *Babesia* organisms from a vertebrate reservoir to an incidental human host, where the protozoan parasitizes erythrocytes, causing fever and hemolytic anemia. In New York State, babesiosis is typically caused by *Babesia microti*, which is transmitted to humans primarily by infected nymphal deer ticks (*Ixodes scapularis*), whose bites may not be noticed. The white-footed mouse is the primary enzootic reservoir; after feeding on infected mice, tick larvae become infected and continue to carry parasites as they develop into nymphs. Although mice are responsible for propagation of the parasites, deer nourish and transport adult ticks, spreading them from place to place.

The incidence of community-acquired babesiosis in New York State has increased significantly since 2002, more than doubling from 93 cases in 2002 to 205 in 2007. Nearly 80 percent of the cases have been concentrated in Suffolk, Dutchess and Westchester counties. Another high-incidence area is coastal southern New England, especially Martha's Vineyard and Nantucket Island in Massachusetts and Block Island in Rhode Island. Cases have also been reported from the Midwest and Northwest. Some cases from the Northwest may be due to *B. duncani*, which can be distinguished from *B. microti* by polymerase chain reaction (PCR) and indirect fluorescent antibody (IFA) assay, but not by morphologic criteria. Sporadic cases of babesiosis have also been reported in Europe, Africa, Asia and South America. Serologic surveys in endemic areas have shown fairly high prevalence rates, ranging from 3.7 to 6.9 percent, and suggest that some infections are subclinical and/or are so mild that patients do not seek treatment.

Transfusion Transmission

Transmission of *Babesia* by transfusion of blood or blood components obtained from apparently healthy donors occurs rarely, and usually involves a donor who resides in, or has traveled to, an endemic area and is infected, but asymptomatic. Parasitemia in asymptomatic persons is usually seasonal, but may be protracted (durations exceeding a year), and transfusion transmission may occur year round. New York State has seen multiple cases of transfusion-associated babesiosis in the past several years. Although most of these have occurred in the downstate area, patients throughout the state should be considered to be at risk. The U.S. Food and Drug Administration recently reported a significant increase in fatal transfusion-transmitted babesiosis cases. There have

History of

- exposure to ticks
- splenectomy
- immune suppression
- transfusion

Common Symptoms/Signs

- malaise
- fever
- chills
- myalgias
- anorexia
- abdominal pain
- nausea
- vomiting
- diarrhea

Laboratory Findings

- anemia
- reticulocytosis
- thrombocytopenia
- elevated liver enzymes
- decreased or absent serum haptoglobin
- hemoglobinuria

Laboratory Diagnosis*

- demonstration of parasites in peripheral blood smears
- serology by IFA*
- molecular tests - PCR*

*Available at the New York State Department of Health's Wadsworth Center. See page 8 for specimen submission instructions.

Treatment

- atovaquone plus azithromycin
- exchange transfusion

been nine fatal cases reported in the U.S. since 2005; four of nine implicated donors and six patients lived in areas where *Babesia* infection is not endemic.

Risk Factors

Babesiosis should be considered in transfusion recipients with febrile illness in areas, such as all of New York State, where blood donors may be at risk for babesiosis. All recipients are at risk, but physicians should be aware of the increased risk for symptomatic disease in elderly, splenectomized and immunocompromised patients. Because *Ixodes* ticks can carry the agents of Lyme disease and human anaplasmosis, these diagnoses should also be considered in patients in whom babesiosis is suspected. Transfusion transmission of Lyme disease has not been reported. The blood of one donor subsequently found to be co-infected with babesiosis and Lyme disease transmitted babesiosis, but not Lyme disease.

Symptoms

Reported incubation periods generally range from 2.5 to 9 weeks among transfusion recipients, and 1 to 6 weeks following a tick bite in community-acquired cases. About one-quarter of infected adults and one-half of children experience asymptomatic infection or a viral-like illness so mild that infection is only diagnosed incidentally by laboratory testing. The initial clinical features of babesiosis, if they do present, are similar to those of malaria and some viral infections. Symptoms of babesiosis are nonspecific and include fever, chills, pallor, diaphoresis, fatigue, myalgias, anorexia, back and abdominal pain, nausea, vomiting, and diarrhea. Splenomegaly, hepatomegaly and/or jaundice may be observed upon physical examination. Possible complications in severe babesiosis (occurring almost exclusively in immunocompromised patients) can include acute respiratory failure, disseminated intravascular coagulation, congestive heart failure, renal failure, and coma.

Laboratory Findings

Laboratory findings include hemolytic anemia with reticulocytosis; thrombocytopenia; elevated liver enzymes and bilirubin; and decreased or absent haptoglobin. Serum protein electrophoresis usually demonstrates a polyclonal gammopathy, consistent with B-cell hyperactivity in response to T-cell suppression by *Babesia*. Renal dysfunction, demonstrated by proteinuria and elevated BUN and creatinine, can occur in cases of severe hemolysis.

Diagnosis

Babesiosis should be considered in the differential diagnosis of unexplained post-transfusion hemolytic anemia or thrombocytopenia. Diagnosis is based on clinical and laboratory findings. A specific diagnosis of acute babesiosis can generally be made by microscopic identification of the organism on Wright- or Giemsa-stained peripheral blood smears; multiple blood smears should be examined. Pathognomonic tetrad forms of merozoites may be seen, but may be difficult to detect (see Figure 1 on page 3). The ring-like forms of *Babesia* may be confused with those of *Plasmodium falciparum* malaria (see Figure 2 on page 3).

Detection of *B. microti* DNA in blood by PCR or real-time PCR may be more sensitive than peripheral blood smear when parasitemia is below the limit for visual detection. However, a negative PCR result does not rule out infection because PCR is not sufficiently sensitive to detect organisms at very low levels. Detection of antibodies to *Babesia* by IFA is the most sensitive method to indicate infection at some time during the past year regardless of the presence or absence of parasites. Blood donors associated with a reported case of possible transfusion-transmitted babesiosis are tested by IFA. Serologic testing for antibodies to *B.*

microti and PCR testing are available free of charge at the New York State Department of Health's Wadsworth Center. See page 8 for information on specimen submission.

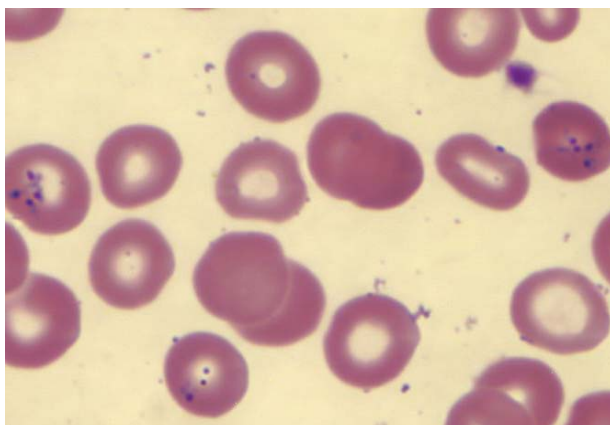


Figure 1. *Babesia microti* in human peripheral blood (courtesy of Janet Keithly, Ph.D.)

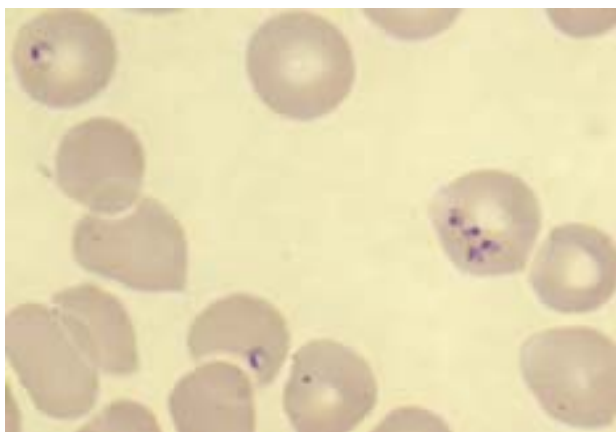


Figure 2. *Babesia microti* in human peripheral blood (courtesy of Janet Keithly, Ph.D.)

Physicians are required to report confirmed cases of babesiosis to the local health department of the patient's county of residence. Laboratories must report cases to the State Department of Health.

Treatment

The preferred treatment for babesiosis is a combination of atovaquone and azithromycin given orally for seven to ten days; this approach is better tolerated than previous regimens. For immunocompromised patients with babesiosis, successful outcomes have been reported with administration of atovaquone combined with higher than usual doses of azithromycin. Clindamycin and quinine are the treatment of choice for patients with severe *Babesia* infections, but often have side effects.

Supplementation with partial or complete red blood cell exchange transfusion is indicated in patients with high-grade parasitemia (>10 percent), significant hemolysis, or renal, hepatic or pulmonary compromise; such treatment may be lifesaving in these situations.

It is not known whether prior exposure, as evidenced by presence of antibody, protects against subsequent infection.

HUMAN EHRLICHIOSIS

Community Acquisition

Human ehrlichiosis (HE), formerly known as human monocytic ehrlichiosis, is caused by rickettsial bacteria, including *Ehrlichia chaffeensis* and *Ehrlichia ewingii*. Like Lyme disease, HE is believed to be spread by ticks, such as the Lone Star tick (*Amblyomma americanum*). Organisms enter the skin by tick bite inoculation and spread through lymphatic and hematogenous routes. The bacteria then invade their target cells – macrophages and monocytes (*E. chaffeensis*) or granulocytes (*E. ewingii*).

People who spend time outdoors in tick-infested areas from April through November are at greatest risk for exposure; peak incidence is from May to July. Three-quarters of HE patients are males whose exposure risk stems from recreational and/or occupational activities. Cases of HE have been reported in 47 states; most have occurred in the southeastern or south central United States. In New York State, most diagnosed cases of HE have occurred on Long Island and in the Hudson Valley. In the Northeast, *E. chaffeensis* is the predominant causative organism.

Transfusion Transmission

Transmission via transfusion of infected human blood and blood components is theoretically possible, but has not been reported.

Symptoms

The incubation period for HE is generally four to ten days after a tick bite, with a mean of seven days. The most common symptoms are fever, myalgias, chills, malaise, anorexia and headache. A rash is present in about half of adult patients with HE. In later stages of the illness, other symptoms, such as nausea, vomiting, arthralgia, and confusion may arise. Severe complications include acute renal insufficiency, central nervous system abnormalities (20 percent) and gastrointestinal hemorrhage. The median duration of the illness is 23 days. HE may occasionally be life-threatening in immunocompromised patients. The fatality rate for diagnosed HE cases is three percent, even despite antibiotic treatment.

Laboratory Findings

Thrombocytopenia (50,000 – 140,000/ μ L) and leukopenia (1,300 – 4,000/ μ L) are common, often striking, laboratory findings. Patients may also exhibit elevated liver enzymes and anemia.

Diagnosis

PCR performed on EDTA-anticoagulated blood is rapidly becoming the test of choice because of the timeliness of its results. Its sensitivity is 60 to 80 percent. The most sensitive finding to confirm a diagnosis of HE is detection of seroconversion or a fourfold increase in antibody titer during the convalescent phase. Serologic testing for antibodies to *E. chaffeensis* and PCR

Acquisition

- exposure to ticks
- residence in or travel to Long Island, the Hudson Valley, or southeast or south central U.S.
- transfusion

Common Symptoms/Signs

- fever
- myalgias
- chills
- malaise
- headache
- rash

Laboratory Findings

- thrombocytopenia
- leukopenia
- elevated liver enzymes
- anemia

Laboratory Diagnosis (NY)

- cytoplasmic inclusions (morulae) in peripheral monocytes
- serology by IFA*
- molecular tests – PCR*

* Available at the New York State Department of Health's Wadsworth Center. See page 8 for specimen submission instructions.

Treatment

- doxycycline

testing are available free of charge at the New York State Department of Health's Wadsworth Center. See page 8 for information on specimen submission. Because *E. ewingii* has not been cultured, antigens are not available for use in serologic testing. Therefore, *E. ewingii* infection is diagnosed by molecular methods (PCR).

In Wright- or Giemsa-stained peripheral blood smears, clusters of *E. chaffeensis* may occasionally (< 7 percent of patients) be observed in cytoplasmic vacuoles of monocytes called morulae because the microcolonies resemble mulberries (see Figure 3). Blood smears or buffy coat smears should be prepared within four hours of collection, preferably at the facility where the patient is receiving care.

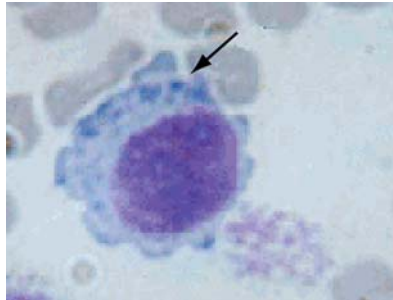


Figure 3. *Ehrlichia chaffeensis* in human peripheral blood smear, buffy-coat preparation. From Martínez MC, Gutiérrez CN, Monger F, et al. *Ehrlichia chaffeensis* in child, Venezuela (letter). *Emerg Infect Dis* [Internet]. 2008 Mar [cited Jan 20, 2009];14:519-20. Available at <http://www.cdc.gov/EID/content/14/3/519.htm>

Physicians are required to report confirmed cases of HE to the local health department of the patient's county of residence. Laboratories must report cases to the State Department of Health.

Treatment

Doxycycline is the treatment of choice and is generally well tolerated. Patients usually recover rapidly. Because of the risk of adverse effects, children under eight years of age and pregnant women should be treated in consultation with an infectious disease expert. Serologic tests can confirm the diagnosis, but patients with symptoms and/or laboratory findings consistent with HE should be treated empirically. However, prophylactic post-exposure treatment following tick bites is not recommended in the absence of symptoms.

HUMAN ANAPLASMOSIS

Community Acquisition

Human anaplasmosis (HA), formerly known as human granulocytic ehrlichiosis and human granulocytic anaplasmosis, is caused by *Anaplasma phagocytophilum*, formerly known as *Ehrlichia phagocytophila*. Humans usually acquire HA through the bite of a tick that has fed on an infected rodent. Major proven reservoir hosts are the white-footed mouse and wood rats. After a tick bite, the bacterium migrates to the bone marrow and spleen, and then invades its target cells – neutrophils.

More than 1,300 cases in the U.S. have been reported to the Centers for Disease Control and Prevention since 1994. People who spend time outdoors in tick-infested areas between April and November are at risk for exposure. HA peaks in July and again in November, coinciding with the nymphal and adult stages of the *Ixodes scapularis* tick in the eastern U.S. Endemic areas in the U.S. (northeastern, mid-Atlantic, upper midwest and Pacific northwest states), Europe (Slovenia, Czech Republic, Sweden, Norway, Switzerland) and Asia all correspond to the territory of *Ixodes scapularis* ticks. Male HA patients outnumber female patients by two to one. HA is infrequently diagnosed in children. In New York State, most diagnosed cases of HA have occurred on Long Island and in the Hudson Valley. Because *Ixodes* ticks can carry the agents of Lyme disease and babesiosis, these diagnoses should also be considered in patients in whom HA is suspected.

Transfusion Transmission

In December 1998, a case of probable transfusion-transmitted HA was reported, linked to an asymptomatic donor who had a history of Lyme disease in 1997 and extensive deer tick bites in the fall of 1998. In November 2007, a case of probable transfusion-transmitted HA in Minnesota was reported, linked to an asymptomatic donor. The donor, who resided in an endemic area, had no known tick bites, but recalled various outdoor activities in wooded areas before the donation. The implicated red blood cell unit was donated 15 days prior to transfusion. Twenty days after the red cell transfusion, the patient began experiencing symptoms, and a peripheral blood smear demonstrated cytoplasmic inclusions of *A. phagocytophilum* morulae in the patient's neutrophils. Whole blood specimens collected from the patient at this time were positive for *A. phagocytophilum* infection by PCR and IFA. Retained segments from the implicated red blood cell unit were positive for evidence of *A. phagocytophilum* infection by both PCR and IFA.

Symptoms

The incubation period for HA is generally four to ten days after a tick bite, with a mean of seven days. Common symptoms include fever, myalgias, severe headache, malaise, and arthralgias. More than one-third of patients complain of nausea and some have a nonproductive cough or stiff neck. A rash is rare – present in < 10 percent of patients with HA. Central nervous system

Acquisition

- exposure to ticks
- residence in or travel to Long Island or the Hudson Valley
- transfusion

Common Symptoms/Signs

- fever
- myalgias
- headache
- malaise
- arthralgias

Laboratory Findings

- thrombocytopenia
- leukopenia
- elevated liver enzymes
- anemia

Laboratory Diagnosis

- cytoplasmic inclusions (morulae) in peripheral neutrophils
- serology by IFA*
- molecular tests - PCR*

* Available at the New York State Department of Health's Wadsworth Center. See page 8 for specimen submission instructions.

Treatment

- doxycycline

infections are also rare in HA, but severe complications can arise, such as respiratory insufficiency, septic shock-like illness, hemorrhage, and multiorgan failure. In most patients, clinical symptoms resolve within 30 days; however, nearly half of recognized cases require hospitalization, and up to 17 percent require intensive care. HA is rarely fatal (< 1 percent of cases), but it is associated with opportunistic pathogens, such as fungi and viruses.

Laboratory Findings

Laboratory features include thrombocytopenia, leukopenia, mild anemia and elevated liver enzymes in the first seven days of illness. Serum creatinine may also be elevated.

Diagnosis

Diagnosis should be attempted during the active phase of disease to facilitate early treatment that can prevent complications. Observation of characteristic cytoplasmic inclusions (morulae) in neutrophils may assist in diagnosis (see Figure 4). However, they may be few in number or may be absent, especially after the first week. PCR performed on EDTA-anticoagulated blood is rapidly becoming the test of choice because of the timeliness of its results and its sensitivity (67 to 90 percent). Serologic testing for antibodies to *A. phagocytophilum* and PCR testing are available free of charge at the New York State Department of Health's Wadsworth Center. See page 8 for information on specimen submission.

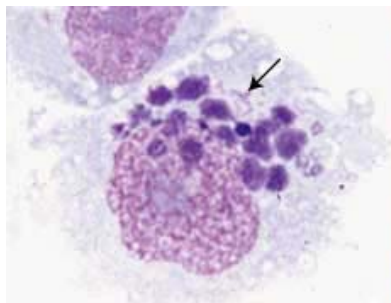


Figure 4. *Anaplasma phagocytophilum* in myelomonocytic cell culture, LeukoStat stain. From Dumler JS, Choi KS, Garcia-Garcia JC, et al. Human granulocytic anaplasmosis and *Anaplasma phagocytophilum*. Emerg Infect Dis [Internet]. 2005 Dec [cited Jan 20, 2009];11:1828-34. Available at <http://www.cdc.gov/ncidod/EID/vol11no12/05-0898.htm>

Physicians are required to report confirmed cases of HA to the local health department of the patient's county of residence. Laboratories must report cases to the State Department of Health.

Treatment

Doxycycline is the treatment of choice and is generally well tolerated. Patients usually recover rapidly. Because of the risk of adverse effects, children under eight years of age and pregnant women should be treated in consultation with an infectious disease expert. Serologic tests can confirm the diagnosis, but patients with symptoms and/or laboratory findings consistent with HA should be treated empirically. However, prophylactic post-exposure treatment following tick bites is not recommended in the absence of symptoms.

SEROLOGIC AND MOLECULAR TESTING AT THE NEW YORK STATE DEPARTMENT OF HEALTH'S WADSWORTH CENTER

Serologic testing for antibodies to *B. microti*, *E. chaffeensis* and *A. phagocytophilum*, as well as PCR testing, are available free of charge at the New York State Department of Health's Wadsworth Center.

- Each specimen should be submitted in an individual New York State laboratory mailer available through local county health departments. The Wadsworth Center also can supply lists of acceptable specimens and mailing containers with all required documentation forms.
- Acute specimens, drawn prior to treatment, should be submitted in one red-top and one purple-top tube, and convalescent specimens, drawn at least three weeks after an acute or another convalescent specimen, in a red-top tube. Acute specimens should be sent to the Wadsworth Center immediately. Please contact the Wadsworth Center (see information below) for shipping address.
- For questions about specimen submission, contact the Wadsworth Center Diagnostic Immunology Laboratory at (518) 486-3845 for serology and/or Tick Borne Disease Laboratory at (518) 474-7983 for PCR.

PERTINENT LITERATURE

- Aguero-Rosenfeld ME, Horowitz HW, Wormser GP, et al. Human granulocytic ehrlichiosis: A case series from a medical center in New York State. *Ann Intern Med* 1996;125:904-8.
- Assi MA, Yao JD, Walker RC. Lyme disease followed by human granulocytic anaplasmosis in a kidney transplant recipient. *Transpl Infect Dis* 2007;9(1):66-72.
- Bakken JS, Dumler JS. Clinical diagnosis and treatment of human granulocytotropic anaplasmosis. *Ann N Y Acad Sci* 2006;1078:236-47.
- Bakken JS, Dumler JS. Human granulocytic anaplasmosis. *Infect Dis Clin North Am* 2008;22:433-48.
- Centers for Disease Control and Prevention. *Anaplasma phagocytophilum* infection acquired through blood transfusion – Minnesota 2007. *MMWR* 2008;57(42):1145-8.
- Centers for Disease Control and Prevention. Statewide surveillance for ehrlichiosis – Connecticut and New York, 1994 - 1997. *MMWR* 1998;47(23):476-80.
- Conrad PA, Kjemtrup AM, Carreno RA, et al. Description of *Babesia duncani* n. sp. (Apicomplexa: Babesiidae) from humans and its differentiation from other piroplasms. *Intern J Parasitol* 2006;36:779-89.
- Dobroszycki J, Herwaldt BL, Bockor F, et al. A cluster of transfusion-associated babesiosis cases traced to a single asymptomatic donor. *JAMA* 1999;281:927-30.
- Dumler JS. *Anaplasma* and *ehrlichia* infection. *Ann N Y Acad Sci* 2005;1063:361-73.
- Dumler JS, Bakken JS. Ehrlichial diseases of humans: Emerging tick-borne infections. *Clin Infect Dis* 1995;20:1102-10.
- Dumler JS, Brouqui P. Molecular diagnosis of human granulocytic anaplasmosis. *Expert Rev Mol Diagn* 2004;4:559-69.
- Dumler JS, Choi KS, Garcia-Garcia JC, et al. Human granulocytic anaplasmosis and *Anaplasma phagocytophilum*. *Emerg Infect Dis* 2005;11:1828-34.
- Dumler JS, Madigan JE, Pusterla N, Bakken JS. Ehrlichioses in humans: Epidemiology, clinical presentation, diagnosis, and treatment. *Clin Infect Dis* 2007;45(Suppl 1):45-51.
- Eastlund T, Persing D, Mathiesen D, et al. Human granulocytic ehrlichiosis after red cell transfusion (abstract). *Transfusion* 1999;39(Suppl):S117.
- Gubernot DM, Lucey CT, Lee KC, et al. *Babesia* infection through blood transfusions: Reports received by the US Food and Drug Administration, 1997-2007. *Clin Infect Dis* 2009;48:25-30.
- Herwaldt BL, Caccio S, Gherlinzoni F, et al. Molecular characterization of a non-*Babesia divergens* organism causing zoonotic babesiosis in Europe. *Emerg Infect Dis* 2003;9:942-8.

Herwaldt BL, de Bruyn G, Pieniazek NJ, et al. *Babesia divergens*-like infection, Washington State. *Emerg Infect Dis* 2004;10:622-9.

Herwaldt BL, McGovern PC, Gerwel MP, et al. Endemic babesiosis in another eastern state: New Jersey. *Emerg Infect Dis* 2003;9:184-8.

Herwaldt BL, Neitzel DF, Gorlin JB, et al. Transmission of *Babesia microti* in Minnesota through four blood donations from the same blood donor over a 6-month period. *Transfusion* 2002;42:1154-8.

Herwaldt BL, Persing DH, Précigout EA, et al. A fatal case of babesiosis in Missouri: Identification of another piroplasm that infects humans. *Ann Intern Med* 1996;124:643-50.

Krause PJ, Daily J, Telford SR, et al. Shared features in the pathobiology of babesiosis and malaria. *Trends Parasitol* 2007;23:605-10.

Krause PJ, Gerwurz BE, Hill D, et al. Persistent and relapsing babesiosis in immunocompromised patients. *Clin Infect Dis* 2008;46:370-6.

Leiby DA, Chung AP, Gill JE, et al. Demonstrable parasitemia among Connecticut blood donors with antibodies to *Babesia microti*. *Transfusion* 2005;45:1804-10.

Linden JV, Wong SJ, Chu FK, et al. Transfusion-associated transmission of babesiosis in New York State. *Transfusion* 2000;40:285-9.

Martínez MC, Gutiérrez CN, Monger F, et al. *Ehrlichia chaffeensis* in child, Venezuela (letter). *Emerg Infect Dis* 2008;14:519-20.

Paddock CD, Yabsley MJ. Ecological havoc, the rise of white-tailed deer, and the emergence of *Amblyomma americanum*-associated zoonoses in the United States. *Curr Top Microbiol Immunol* 2007;315:289-324.

Wallace BJ, Brady G, Ackman DM, et al. Human granulocytic ehrlichiosis in New York. *Arch Intern Med* 1998;158:769-73.

Walker DH, Dumler JS. Human monocytic and granulocytic ehrlichioses. Discovery and diagnosis of emerging tick-borne infections and the critical role of the pathologist. *Arch Pathol Lab Med* 1997;121:785-91.

Wong SJ, Brady GS, Dumler JS. Serological responses to *Ehrlichia equi*, *Ehrlichia chaffeensis*, and *Borrelia burgdorferi* in patients from New York State. *J Clin Microbiol* 1997;35:2198-205.

Wormser GP, Dattwyler RJ, Shapiro ED, et al. The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: Clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis* 2006;43:1089-134.