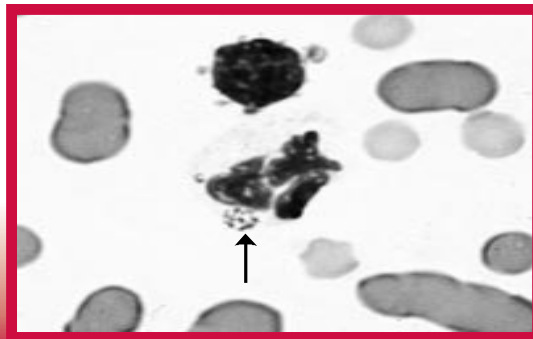


Babesiosis and Ehrlichiosis: Potential Transfusion Complications*



Bacteria that can cause human granulocytic ehrlichiosis are observed in the morulae (cytoplasmic inclusions) of the neutrophils. The bacterial agent has not yet been named, but it closely resembles *Ehrlichia equi* and *Ehrlichia phagocytophila*, the agents of tickborne ehrlichioses in horses and cattle.

(Courtesy of Susan Wong, Ph.D.)

New York State Council on Human Blood and Transfusion Services
New York State Department of Health

February 1999

**This publication is intended to alert physicians that in event of symptoms post-transfusion, these diseases should be considered, as they may result from infection via blood transfusion.*

Requests for technical assistance with diagnosis of babesiosis or ehrlichiosis may be directed to:

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What is babesiosis?

Babesiosis is a tickborne disease caused by a protozoan that parasitizes erythrocytes, and causes fever and hemolytic anemia. In New York State, babesiosis is caused by *Babesia microti*, which is transmitted to humans by infected nymphal and adult *Ixodes scapularis* (also known as *I. dammini*), the deer tick. **More than twenty cases in the U.S. have been reported of the disease transmitted by transfusion of blood or blood components obtained from apparently healthy donors from endemic areas.**

Which blood donors are at risk for babesiosis?

Humans usually acquire babesiosis through the bite of a tick that has fed on an infected mouse. Rodents are reservoirs for *B. microti*. Babesia are parasites of many mammals and are major pathogens of cattle. Deer are important hosts for the ticks. They nourish and transport the ticks, spreading them from place to place, but do not appear to be infected.

Most cases of babesiosis in the U.S. occur in the Northeast, particularly eastern Long Island, Shelter Island and Fire Island in New York; Cape Cod, Nantucket and Martha's Vineyard in Massachusetts; and in mainland Connecticut. Cases have also been reported from the Midwest and Northwest. Some cases from the Northwest may be due to a different species of babesia.

Serologic surveys in endemic areas have shown fairly high prevalence rates, ranging from 3.7% to 6.9%, and suggest that many infections are sub-clinical and/or patients do not seek treatment.

Babesiosis

History

- exposure to *Ixodes* species ticks
- splenectomy
- immune suppression
- **transfusion**

Common Symptoms/Signs

- malaise
- fever
- chills
- myalgia
- anorexia
- abdominal pain
- nausea
- vomiting
- emotional lability
- depression

Laboratory Findings

- anemia
- decreased or absent serum haptoglobin
- reticulocytosis
- hemoglobinuria

Diagnosis*

- demonstration of parasites in thick or thin peripheral blood smears
- serology by immunofluorescence assay*
- molecular tests - PCR*

*Available at New York State Department of Health's Wadsworth Center

Treatment (no controlled trials)

- clindamycin plus quinine
- atovaquone plus azithromycin
- exchange transfusion
- expert consultation advised

Which transfusion recipients are at risk from transfusion-transmitted babesiosis?

Babesiosis should be considered in transfusion recipients with febrile illness if the blood donor may have been at risk for babesiosis. Recipients who are immunologically intact are at risk, but physicians should be aware of the increased risk in elderly, splenectomized and immunocompromised recipients. Because *Ixodes* species ticks carry the agents of Lyme disease and ehrlichiosis, these diagnoses should also be considered in patients in whom babesiosis is suspected.

What are the symptoms of babesiosis?

Most infections are asymptomatic, but in some individuals, especially the elderly, those who have had a splenectomy and the immunocompromised, including patients with AIDS, babesiosis can be severe or even fatal. Symptoms of babesiosis are nonspecific and include malaise, fever, chills, myalgias, anorexia, abdominal pain, nausea, vomiting, and emotional lability and depression.

What is the incubation period?

Reported incubation periods range from 2.5 to 8 weeks among transfusion recipients and 1-6 weeks following tick exposure.

What are the laboratory findings for babesiosis?

Laboratory findings include hemolytic anemia— anemia, decreased or absent serum haptoglobin and/or reticulocytosis.

How is babesiosis diagnosed?

Diagnosis is made by detecting the parasites in Wright or Giemsa stains of thick or thin peripheral blood smears.

The ring-like forms of babesia may be confused with those of *Plasmodium falciparum* malaria. A diagnostic tetrad form may be seen, but may be difficult to detect. Serologic testing by indirect immunofluorescence assay may confirm the diagnosis, but there may be delay in obtaining results.

Physicians and laboratories are required to report confirmed cases of babesiosis to their local county health departments.

Does past infection with babesiosis make a person immune?

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

What is the treatment for babesiosis?

Postexposure prophylaxis is not recommended absent diagnosis. Clindamycin together with quinine for seven to ten days has been used with apparent success to treat babesiosis. In severe cases, exchange transfusion has been used. There are no controlled studies to determine the most effective treatment. Atovaquone with azithromycin may also be effective, and has been administered to patients who did not respond to clindamycin and quinine. Consultation with experts may be helpful.

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The Human Ehrlichioses

What is ehrlichiosis?

Ehrlichiosis is a tickborne disease caused by *Ehrlichia* species of bacteria (*Rickettsia*). Human monocytic ehrlichiosis, caused by *Ehrlichia chaffeensis*, was first recognized in 1986, and human granulocytic ehrlichiosis, caused by an *E. phagocytophila* group bacterium, was first reported in 1994.

Transmission via transfusion of infected human blood or blood products is theoretically possible.

Which blood donors are at risk for ehrlichiosis?

People who spend time outdoors in tick-infested areas from April until October are at greatest risk for exposure.

As in Lyme disease, ehrlichiosis is believed to be spread by ticks such as the deer tick, the dog tick, and the lone star tick. Transmission takes place after a bite from an infected tick.

Most cases of human monocytic ehrlichiosis have been reported from the southeastern and south central United States, and human granulocytic ehrlichiosis cases, from the Northeastern, upper Midwest, and Pacific Coastal regions.

In recent years, several Westchester County physicians reported treating patients for suspected ehrlichiosis. It was determined that some of these patients were suffering from human granulocytic ehrlichiosis, which has been strongly associated with bites from the deer tick, *Ixodes scapularis*.

In New York State, most diagnosed cases of human granulocytic ehrlichiosis have occurred in the lower Hudson Valley. Human monocytic ehrlichiosis cases have also been found on Long Island and the coastal islands, such as Fire Island.

History

- known or possible exposure to ticks
- travel to southeastern and south central U.S., Hudson Valley, Long Island (Shelter Island)

Common Symptoms/Signs

- fever
- myalgia
- headache
- chills
- malaise

Other Symptoms

- cough
- joint pain
- confusion
- nausea
- vomiting
- rash (macular or papular)
- respiratory distress

Laboratory Findings

- thrombocytopenia
- leukopenia
- elevated liver enzymes
- anemia

Diagnosis

- cytoplasmic inclusions (morulae) in peripheral granulocytes or human granulocytic ehrlichiosis-not very sensitive
- serology by immunofluorescence assay*
- molecular tests - PCR*

*Available at New York State Department of Health's Wadsworth Center

Treatment

- doxycycline
- tetracycline

What are the symptoms of ehrlichiosis?

Infection usually produces mild to moderately severe illness, with fever and headache, but may occasionally be life-threatening or even fatal.

The most common symptoms of ehrlichiosis are fever, myalgia, chills, malaise and headache. Other symptoms include nausea, vomiting, arthralgia and confusion. Rash is less common, and the clinical presentation of the disease has been described as "spotless Rocky Mountain spotted fever."

What is the incubation period?

The incubation period is usually four to ten days after a tick bite (acute onset).

What are the laboratory findings for ehrlichiosis?

Thrombocytopenia and leukopenia are common and striking laboratory findings. Patients may also exhibit elevated liver enzymes and anemia.

How is ehrlichiosis diagnosed?

Serology for antibodies to *E. chaffeensis* and human granulocytic ehrlichiosis agent and polymerase chain reaction (PCR) testing are available free of charge at the New York State Department of Health's Wadsworth Center.

- Each sample should be submitted in individual New York State laboratory mailers, available through local county health departments. The Wadsworth Center can supply lists of acceptable specimens and mail containers with all required documentation forms.
- Submit acute specimens, drawn prior to treatment, 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 below) for shipping address.
- For questions about submission of specimens, contact the Wadsworth Center at **(518)474-8566**, by FAX to its diagnostic immunology laboratory at **(518)486-7971**, or write: **Diagnostic Immunology, Wadsworth Center, New York State Department of Health, Empire State Plaza, P.O. Box 509, Albany, New York 12201-0509.**

Physicians and laboratories are required to report confirmed cases of ehrlichiosis to their local county health departments.

Laboratory Testing

The Wadsworth Center provides testing for patients with suspected ehrlichiosis who meet the following criteria:

- fever $\geq 100.4^{\circ}\text{F}$;
- thrombocytopenia ($<150,000/\mu\text{L}$) or leukopenia ($<5,000/\mu\text{L}$); and
- malaise or headache.

In Wright or Giemsa stain smears, the etiologic agent of human granulocytic ehrlichiosis may occasionally be observed in peripheral granulocytes, so-called "morulae." These blood smears or buffy coat smears should be prepared within four hours of drawing from the patient, and preferably at the facility where the patient is cared for.

Although serologic tests can confirm the diagnosis, patients with symptoms and/or laboratory findings consistent with ehrlichiosis should be treated empirically.

What is the treatment for ehrlichiosis?

Treatment should not be delayed until laboratory confirmation is obtained. However, prophylactic post-exposure treatment following tick bites is not recommended in the absence of symptoms.

Tetracycline antibiotics for seven days are usually rapidly effective for ehrlichiosis. Because these antibiotics can cause dental staining in children, physicians should consult a pediatric infectious disease expert when treating children. Doxycycline may be better tolerated by patients.

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The text of this publication was developed by the Transfusion Safety Committee and endorsed by the New York State Council on Human Blood and Transfusion Services on November 10, 1998. A listing of the Council's membership follows.

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The Council gratefully acknowledges the assistance of Murray Wittner, M.D., Ph.D., Albert Einstein College of Medicine, New York, NY, and the special efforts of Committee members Drs. Gold and McKittrick, in preparation of the text on ehrlichiosis.



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