BABESIOSIS

Disease Overview

Babesiosis is a tick-borne infection caused by a protozoan parasite that infects red blood cells; several different *Babesia* species can cause disease in humans. These include *Babesia microti* (in Northeastern and Midwestern US, East Asia, Europe, Australia), *Babesia duncani* (in Western US), and *Babesia divergens* (in Europe). *B. microti* is the most common cause of babesiosis in North America: sporadic cases caused by *Babesia duncani* and *Babesia divergens*-like have been reported.

Symptoms

Although cases of tick-borne illness can occur during any month of the year, most cases occur when ticks are most active, in the spring, summer, and fall. Babesiosis infections range in severity from asymptomatic to severe (occasionally fatal) depending on host and parasite factors. Most symptomatic infections caused by *B. microti* are mild and self-limiting.

Babesiosis is characterized by fever and non-specific flu-like illness (fever, malaise, fatigue, chills, sweats, non-productive cough, arthralgias, nausea, vomiting, photophobia, and headache). Because Babesia parasites infect and destroy red blood cells, babesiosis may also cause hemolytic anemia, with additional symptoms of jaundice and dark urine. Severe symptoms can include thrombocytopenia and renal failure.

Chronic infections may last weeks to months.

Reservoir

Blacklegged ticks (*I. scapularis* and *I. pacificus*) are vectors and can transmit the pathogen to people during tick feeding.

Reservoir hosts support the circulation and maintenance of the pathogen. Vertebrate reservoirs are natural hosts for ticks and once infected, remain infected life long and continue to transmit the pathogen to feeding ticks. In North America reservoir hosts for babesiosis are small rodents (i.e., white footed mouse). Humans serve as accidental hosts.

Mode of Transmission

Primarily vector-borne transmission via bites from infected blacklegged ticks. The transmission window or time of tick attachment and pathogen transmission for *B. microti* appears to be 24 hours and can be 36 – 48 hours.

Untreated individuals can have parasites in their blood for long periods following infection. Less commonly, babesia may be transmitted through transfusion of blood products; and rarely via congenital transmission during pregnancy/delivery or solid organ transplantation.

Incubation period

1 - 4 weeks after tick bite

1 - 9 weeks after contaminated blood transfusion but can be as long as six months

Period of Communicability

No evidence of natural transmission from person to person.

Risk Factors

Increased risk for acquiring illness:

- Exposure to blacklegged ticks

Increased risk for acquiring/severe illness:

- High parasites loads (Babesia parasitemia level ≥ 4%) or low hemoglobin levels (< 100 g/L),
- Functional or anatomical asplenia (or hyposplenism), weakened immune system (due to cancer, AIDS, transplantation, or certain medications), advanced age (> 50 years) or underlying serious health conditions (e.g., chronic liver or kidney disease), or neonatal prematurity.

Surveillance Case Definition

Confirmed Case

Confirmatory laboratory evidence of infection with or without clinical evidence criteria (can include transfusion transmission).

Clinical evidence of infection:

- Clinical evidence of infection (fever and at least one of the following: fatigue, chills, sweats, headache, anorexia, hemolytic anemia, or thrombocytopenia)

Confirmatory laboratory evidence of infection:

- Detection of *Babesia* species *(*e.g., *Babesia microti, Babesia duncani* or *Babesia divergens)* DNA in a whole blood specimen by amplification of a specific target Nucleic Acid Amplification Test (NAAT).

Probable Case

Supportive laboratory evidence of infection AND

- Clinical evidence of infection (fever and at least one of the following: fatigue, chills, sweats, headache, anorexia, hemolytic anemia, or thrombocytopenia).

OR

- Blood or solid organ transplant recipient with an epidemiological link to a confirmed or probable babesiosis case. For the purposes of surveillance, epidemiologic linkage between a transfusion recipient and a blood donor is demonstrated if all the following four criteria are met:

    1. Laboratory evidence of *Babesia* infection in the recipient and donor; AND

2. Transfusion recipient received one or more red blood cell (RBC) or platelet unit(s) within one year before the collection date of the recipient's positive specimen; AND
3. Transfused unit(s) was/were plausibly infectious based on assessment of donor infectivity at time of donation of implicated unit(s); AND
4. Transfusion-associated infection in the recipient is considered at least as plausible as tick-borne transmission.

OR

- Neonate from a mother with confirmed or probable babesiosis.

Supportive laboratory evidence of infection:

- Serological evidence of elevated IgG antibodies to *B. microti* in a single sample by indirect immunofluorescence assay (IFA) where the endpoint titre is ≥ 1:64

OR

- Identification of intraerythrocytic *Babesia* organisms by light microscopy in a Giemsa, Wright, or Wright-Giemsa–stained blood smear

OR

- Demonstration of a positive *B. microti* IgG immunoblot result by Centers for Disease Control and Prevention (CDC)

OR

- Demonstration of a *B. divergens* total immunoglobulin (Ig) or IgG antibody titre of ≥ 1:256 in an IFA

OR

- Demonstration of a *B. duncani* total immunoglobulin (Ig) or IgG antibody titre of ≥ 1:512 in an IFA.

Diagnosis and Laboratory Guidelines

The diagnosis is based on an assessment of exposure risk, clinical signs and symptoms, in addition to laboratory testing.

Microscopy. Identification of intraerythrocytic *Babesia* parasites by light-microscopic examination of peripheral blood smear. In symptomatic patients with acute infection, Babesia parasites typically can be detected by light-microscopic examination of blood smears. However, microscopy may be negative very early in infection due to low parasitemia, therefore a single negative microscopic examination is not sufficient to rule out infection and repeat testing may be needed if no alternate diagnosis is established. Microscopic morphology may occasionally be difficult to differentiate from other blood pathogens such as *Plasmodium* (especially *P. falciparum*). Confirmation by a reference laboratory may be required if a patient's travel history and area of residence indicate exposure to *Babesia* is unlikely.

Molecular detection of *Babesia* species. PCR testing is performed at NML using a laboratory-developed real-time PCR assay. If positive, further species-specific PCR assays and sequencing is performed at NML to identify the organism at the species level. Nucleic Acid Amplification Testing (NAAT) can also be done.

Serology (antibody) testing. *Babesia microti* serology testing is performed by immunofluorescence assay (IFA). Serological antibody titres may be negative early in infection, in patients with severe immunosuppression, or in patients with asplenia. False positive reactions may occur in patients with autoimmune disorders (e.g., rheumatoid arthritis). Antibody titres remain elevated for years following clearance of infection. Antibody titres ≥ 1:1024, or a four-fold increase in titres between acute and convalescent sera, may be useful to distinguish acute from chronic/remote infection. Cross-reactivity may occur with *Plasmodium* spp. at lower antibody titre levels for IFA. Cross-reactivity is not usually reported between *Babesia* species-specific IFAs, therefore a negative *Babesia microti* IFA does not rule out infection with other *Babesia* species. Validated commercial IFAs and/or immunoblots specific for *B. divergens* and *B. duncani* are not currently available but samples may be submitted to reference centres such as the CDC who have validated assays for these rare pathogens.

Public Health staff should discuss the findings with the Medical Officer of Health before initiating an investigation.

Reporting

Per Policy 2.2 Disease and Event notification to OCMOHE and Disease and Event Reporting section

- Enhanced surveillance. For all confirmed and probable cases, an enhanced surveillance form should be completed and sent to OCMOHE within 5 days of completing the interview.
- Routine surveillance (RDSS) for all confirmed cases.

For probable or confirmed cases who have history of donation or transfusion (blood/blood products) within one year of the infection, a Disclosure of Information to Canadian Blood Services Transfusion Transmissible Infections (TTI) must be completed and sent to Canadian Blood Services.

Case Management

Education

Case or relevant caregiver should be informed about:

- Nature of infection, length of communicable period, mode of transmission and disease ecology
- Tick bite prevention

Investigation

Obtain travel history, outdoor activity, and tick exposure to determine if source of infection occurred within a recognized endemic focus or not.

Obtain history on receiving transfusion of blood products or solid organ transplant within one year before collection date of positive specimen for case.

Obtain history on blood donation for previous twelve weeks.

Obtain history of pregnant/peri-natal status.

Exclusion/Social Distancing

Not applicable.

Treatment

Treatment regimens may need to be adjusted depending on a person's age, medical history, underlying health conditions, pregnancy status, or allergies. Consultation with an infectious disease specialist may be considered regarding individual patient treatment decisions.

Immunization

Not applicable.

Contact Management

Education

Not applicable

Investigation

Contacts of cases are not at risk as there is not usually person-to-person transmission except for blood transfusion; and rarely via transplacental, perinatal and solid organ transplantation.

Exclusion/Social Distancing

Not applicable.

Prophylaxis

Not applicable.

Outbreak Management

Activate the local outbreak plan when an outbreak is declared.