

## Tick-Associated Diseases

There are at least eleven recognized human diseases associated with ticks in the United States, seven or eight of which occur in the mid-Atlantic or northeastern states. Each of the diseases is highlighted in this section of the handbook. The greatest attention is given to Lyme disease, ehrlichiosis, and babesiosis. Although each is a zoonotic vector-borne disease, not all are caused by an infectious agent or are exclusively tick transmitted. A toxin causes tick paralysis, tularemia can be transmitted through contaminated animal tissue or other materials, and babesiosis and ehrlichiosis can be transmitted perinatally and through blood transfusion. Tick associations with other pathogens like *Bartonella* or *Mycoplasma* are not yet clearly defined. The causative pathogens transmitted to humans by the tick vector are maintained in a reservoir host. *Ixodes* ticks can be infected with more than one agent and co-transmission and infection can occur. Alternatively, multiple infections can occur from multiple tick bites. In a Connecticut and Minnesota study, 20% of Lyme disease patients also had serological evidence of exposure to another tick-borne agent.

**Table 2.** Tick-associated diseases in the United States.

Disease	Pathogen or causal agent	Tick Vector
Babesiosis	<i>Babesia microti</i> , <i>Babesia</i> spp.	<i>I. scapularis</i> , <i>I. pacificus</i>
Colorado tick fever	CTF virus (Retoviridae)	<i>D. andersoni</i>
Ehrlichiosis, monocytic	<i>Ehrlichia chaffeensis</i>	<i>A. americanum</i>
Ehrlichiosis, granulocytic	<i>Anaplasma phagocytophilum</i>	<i>I. scapularis</i> , <i>I. pacificus</i>
Lyme disease	<i>Borrelia burgdorferi</i>	<i>I. scapularis</i> , <i>I. pacificus</i>
Southern rash illness	<i>Borrelia lonestari</i> (?)	<i>A. americanum</i>
Powassan encephalitis	Powassan virus	<i>I. cookei</i>
Rocky Mountain spotted fever	<i>Rickettsia rickettsia</i>	<i>D. variabilis</i> , <i>D. andersoni</i>
Tick-borne Relapsing Fever	<i>Borrelia</i> species	<i>Ornithodoros</i> species ticks
Tularemia	<i>Franciscella tularensis</i>	<i>D. variabilis</i> , <i>A. americanum</i> , others
Tick paralysis	Toxin	<i>D. variabilis</i> , <i>D. andersoni</i>

Lyme disease, monocytic and granulocytic ehrlichiosis, Rocky Mountain spotted fever, and tularemia are nationally reportable diseases. The amount and quality of surveillance data provided to state health departments and then to CDC is quite variable. Most surveillance is passive, dependent upon physician reporting. Most diseases are greatly underreported. Active surveillance or laboratory-based reporting may also exist in some states or areas. Case reports are based on a standardized surveillance case definition, which is not meant to be the basis for diagnosis. An increase in case reports can represent a true increase in disease or increased awareness of the disease and increased reporting. Conversely, a decrease may represent a change in reporting or a lack of reporting, rather than a true decrease in the incidence of disease. Nevertheless, surveillance case reports generally provide valuable long-term tracking of disease trends and may be useful for targeting intervention strategies.

### Lyme Disease

Lyme disease is the leading arthropod-associated disease in the United States and is caused by the spirochete *Borrelia burgdorferi*, a corkscrew-shaped bacterium. It is associated with the bite of certain *Ixodes* ticks, particularly the blacklegged tick, *I. scapularis*, in the northeastern and north-central United States and the western blacklegged tick, *Ixodes pacificus*, on the Pacific Coast. Other *Ixodes* ticks spread the disease in Europe and Asia. The disease has been reported from 49 states, as well as parts of Canada, and across Europe and Asia.

Lyme disease was first recognized as a distinct clinical entity in a group of arthritis patients from the area of Lyme, Connecticut in 1975. In 1981, Dr. Willy Burgdorfer discovered spirochetes

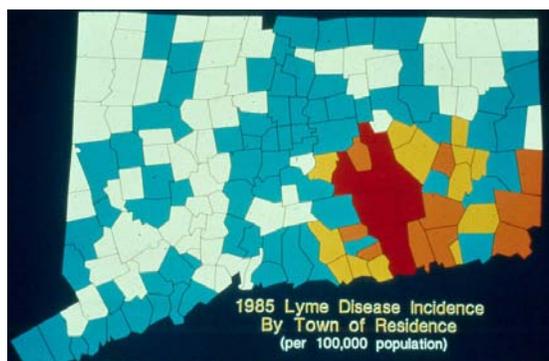
in the mid-gut of some *I. scapularis* ticks from Long Island, New York and the bacteria were later named after him. A Lyme disease testing program by the Connecticut Agricultural Experiment Station and Connecticut Department of Public Health found the greatest prevalence in Connecticut in 1984 and 1985 was in towns east of the Connecticut River (map below right). The distribution of the tick and the risk of disease have since expanded dramatically (see map next page). Nationally, 17,739 human cases were reported in 2000, 17,029 cases were reported in 2001 and 23,763 cases were reported in 2002. Twelve states accounted for 95% of reported cases. In order of incidence in 2002 they were Connecticut, Rhode Island, Pennsylvania, New York, Massachusetts, New Jersey, Delaware, New Hampshire, Wisconsin, Minnesota, Maine, and Maryland. Lyme disease is underreported and these numbers may represent only 10-20% of diagnosed cases.



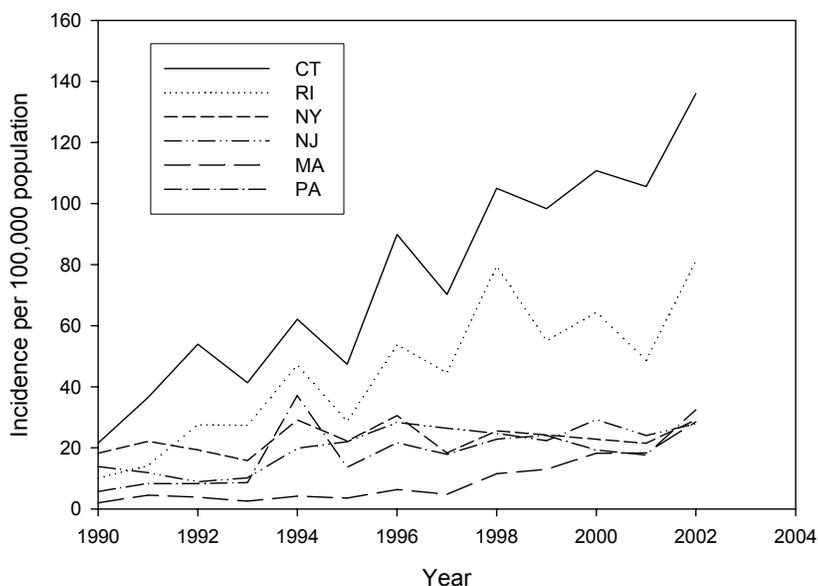
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The spirochete *Borrelia burgdorferi* (CDC)

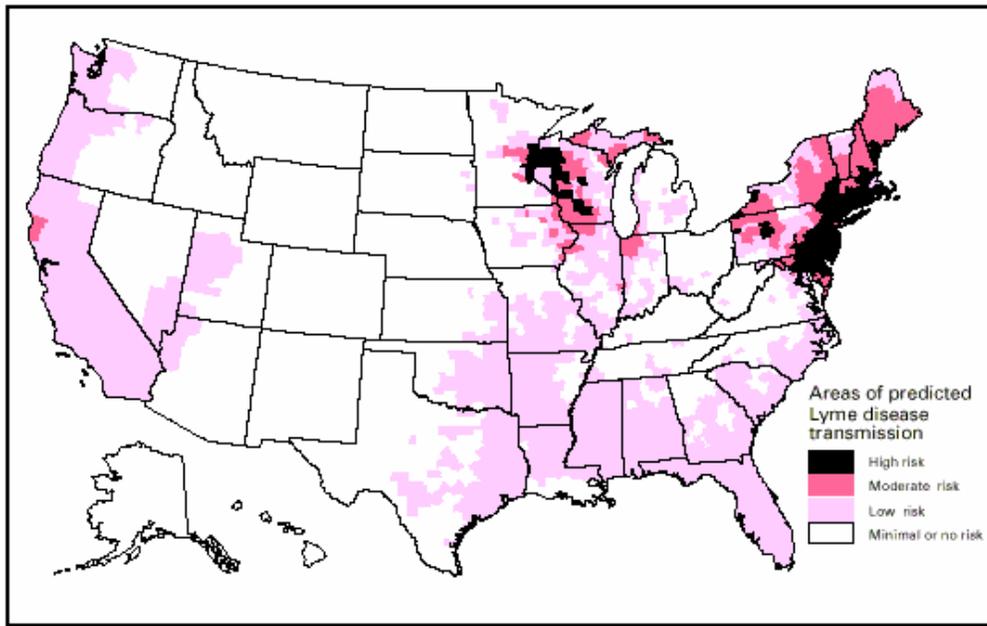
National statistics are available through the CDC website, [www.cdc.gov](http://www.cdc.gov) and local statistics may be available through state public health departments or on their websites. Lyme disease affects all age groups, but the greatest incidence of disease has been in children under 14 and adults over 40 years of age. In most cases, Lyme disease symptom onset occurs during the summer months when the nymphal stage of the blacklegged tick is active (see prevention).



Incidence of Lyme disease per 100,000 population by selected northeastern states, 1990-2002. Connecticut and Rhode Island have had the highest incidence of disease, while New York, Connecticut, Pennsylvania, and New Jersey have had the largest number of reported cases.



### National Lyme disease risk map with four categories of risk



Note: This map demonstrates an approximate distribution of predicted Lyme disease risk in the United States. The true relative risk in any given county compared with other counties might differ from that shown here and might change from year to year. Risk categories are defined in the accompanying text. Information on risk distribution within states and counties is best obtained from state and local public health authorities.

### Clinical signs and symptoms of Lyme disease

Lyme disease is a multisystem disorder with diverse cutaneous, arthritic, neurologic, cardiac, and occasional ocular manifestations. Symptoms that occur within days or weeks following the tick bite reflect localized or early-disseminated infection. Late manifestations become apparent months or years after infection. The major signs and symptoms provided below do not cover all those associated with infection by *B. burgdorferi*. Those who want additional information can consult the literature provided in the bibliography.

#### Localized infection

- Lyme disease is characterized in the majority of patients (70-90%) by an expanding red rash at the site of the tick bite called erythema migrans (or EM). Therefore, the rash serves as a clinical marker for early disease, although the presence of a rash may go unrecognized.
- Erythema migrans may appear within 3 to 30 days (typically 8 or 9 days) after the tick bite. The rash gradually expands over a period of days to a week or more at a rate of  $\frac{1}{2}$  to  $\frac{3}{4}$  inch per day and should not be confused with the transient reaction to a tick bite.
- Rashes vary in size and shape, and may occur anywhere on the body, although common sites are the thigh, groin, trunk, and axilla. Many rashes reach about 6 inches in diameter, but some can expand to 8-16 inches or more. The CDC surveillance case definition



specifies that an EM rash must be 2.5 inches or greater in diameter (this definition should not be used as diagnostic criteria).

- An EM may be warm to the touch, but it is usually not painful and is rarely itchy. Swelling, blistering, scabbing or central clearing occur occasionally. The "bull's-eye" appearance usually is noted in less than half the cases and is characteristic of older rashes. The EM will resolve spontaneously without treatment.
- Mild nonspecific systemic symptoms may be associated with the rash in about 80% of cases and include fatigue, muscle and joint pain, headache, fever, chills, and stiff neck. These flu-like symptoms may occasionally occur in the absence of an identified rash and be identified as 'summer flu.' Respiratory or gastrointestinal complaints may occur, but are infrequent.



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***Below: Lyme rash (EM) 5 days (left) and 10 days (right) on antibiotic treatment. The rash on the left is the same as above. The rash right is the same EM illustrated on the previous page.***



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### **Early disseminated infection**

Lyme disease spirochetes disseminate from the tick bite site through the skin, lymph, or blood to various organ systems, particularly skin, joint, nervous or cardiac tissue. Signs and symptoms may be intermittent, migratory and changing. Nonspecific viral-like symptoms generally mark early-disseminated infection and up to a fourth of patients may develop multiple secondary rashes. Days or weeks after the bite of an infected tick, migratory joint and muscle pain (also brief, intermittent arthritic attacks), debilitating malaise and fatigue, neurologic or cardiac problems may occur. The symptoms appear to be from an inflammatory response to active infection. Multiple EM, headache, fatigue, and joint pain are the most common clinical manifestations noted in early-disseminated disease in children. Multiple components of the nervous system can be affected by *B. burgdorferi*. Early neurologic symptoms develop in about 15% of untreated patients and these can include Bell's palsy (paralysis of facial muscles), meningitis (fever, stiff neck, and severe headache), and radiculoneuropathy (pain in affected

nerves and nerve roots, can be sharp and jabbing or deep). Children present less often with facial palsy and more commonly with fever, muscle and joint pain, and arthritis (primarily the knee). Carditis (various degrees of heart block) and rhythm abnormalities may occur in 8% or less of patients. Ocular manifestations may include conjunctivitis and other inflammatory eye problems. Antibodies to *B. burgdorferi* are usually detectable in tests during these manifestations.

### Late disseminated infection

A year or more after the bite of an infected tick, symptoms of persistent infection in untreated or inadequately treated individuals may include numbness or tingling of the extremities, sensory loss, weakness, diminished reflexes, disturbances in memory, mood or sleep, cognitive function deficits, and an intermittent chronic arthritis (typically swelling and pain of the large joints, especially the knee). Approximately 50-60% of untreated individuals develop arthritis and about 10% of these will progress to chronic arthritis. Attacks of arthritis may last weeks to months with remissions and relapses over a period of several years.

The course and severity of Lyme disease is variable. Mild symptoms may go unrecognized or undiagnosed and some individuals may be asymptomatic (no early illness). The EM rash or subsequent arthritic, cardiac or nervous system problems may be the first or only sign of Lyme disease. Most symptoms eventually disappear, even without treatment, although resolution may take months to over a year. The



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disease can also be chronic and debilitating with occasional permanent damage to nerves or joints, but is rarely, if ever, fatal. Chronic Lyme disease or post-Lyme disease syndrome is a controversial and unclear constellation of symptoms related to or triggered by infection with *B. burgdorferi*. Disease persistence might be due to a slowly resolving infection, residual tissue damage, inflammation from remains of dead spirochetes, immune-mediated reactions in the absence of the spirochete, co-infection with other tick-borne pathogens, or an alternative disease process that is confused with Lyme disease.

### Diagnosis and treatment of Lyme disease



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A physician should be consulted if Lyme disease is suspected. In the absence of an EM rash, Lyme disease may be difficult to diagnose because its symptoms and signs vary among individuals and can be similar to those of many other diseases. Conversely, other arthritic or neurologic diseases may be misdiagnosed as Lyme disease. Lyme disease is probably both over-diagnosed and under-diagnosed with some patients without Lyme disease convinced they have it and other patients with the disease

being told they do not have it. A diagnosis of Lyme disease is based primarily on objective clinical findings. A blood test to detect antibodies to Lyme disease spirochetes (serological testing) can aid or support the diagnosis of the disease. Antibodies to *Borrelia* antigens (parts of the bacteria recognized by the immune system) can usually be detected 3-4 weeks after infection. These tests are not reliable enough to be used as the sole criterion for a diagnosis, however, especially during the early stages of the disease. Tests can give false-negative and false-positive results. Newer tests are more specific, greatly reducing false positive reactions. Reliability of the test improves dramatically in the later stages of the disease as serological reactivity increases, although inaccurate results may still occur. Patients with acute or chronic neurologic or arthritic Lyme disease almost always have elevated antibody levels.

Two stage serological testing for Lyme disease is suggested by many public health organizations:

- Stage One: A relatively sensitive first test by enzyme-linked immunosorbent assay (ELISA) or indirect fluorescent antibody (IFA) test. If negative, no further testing is done. Testing at the time of the Lyme disease rash is unnecessary as many will be negative. Antibiotic treatment early in infection may abrogate the antibody response. An ELISA test provides a quantitative measure antibody levels (measurable color reaction) and for rapid testing of large numbers of samples. An ELISA test measures the reaction to all the antigens in disrupted *Borrelia* or to recombinant antigens, but does not allow identification of which antigens are being bound by antibody and can yield false positives from cross-reactive antibodies. ELISA tests using the C6 peptide of the VlsE protein, another protein in *B. burgdorferi* that elicits a strong response by the immune system, may be as sensitive and selective as the two stage testing procedure.
- Stage Two: If the first test is positive or equivocal, a more specific Western immunoblot test is performed to simultaneously demonstrate an antibody response to several *B. burgdorferi* antigens (i.e., proteins recognized by the immune system), which show up as bands on the blot. The Lyme disease spirochete has numerous immunogenic proteins including outer surface proteins (OspA, OspB, and OspC), the 41 kDa antigen on the flagellum, and at least 9 other prominent antigens. The Western blot is labor intensive and requires a subjective interpretation of the results. Although there is an established criterion for a positive blot, there is some disagreement on the number and specific “bands” required for a positive test.

Lyme disease can be treated with one of several antibiotics, including, doxycycline, amoxicillin, cefuroxime axetil, penicillin, ceftriaxone, or cefotaxime. The standard course of treatment is for 14-28 days, depending upon clinical manifestation and drug, though a physician may elect a longer course of treatment. Patients treated in the early stages of the disease usually recover rapidly and completely with no subsequent complications. Oral antibiotics are effective in treating most cases of Lyme disease.

Intravenous antibiotics are indicated for central nervous system involvement and for recurrent arthritis. Full recovery is likely for patients treated in the later stages of the disease but resolution of some symptoms may take weeks even with appropriate treatment. Persistence of some symptoms and inability to determine if the bacteria are eliminated can make decisions on the length of treatment difficult. Courses of antibiotics may have health consequences due to the disruption of the normal intestinal bacteria, allergic reactions, increased sun sensitivity (with doxycycline), gall bladder problems (with ceftriaxone), and infection risks with catheters (extended intravenous antibiotics). Treatment failure may result from incorrect treatment, long delay before treatment, misdiagnosis (not Lyme disease), poor treatment compliance by the patient (did not finish the full course of antibiotics), and infection or co-infection with other tick-borne agents (i.e., *Babesia* or *Anaplasma*). Concurrent babesiosis or ehrlichiosis should be

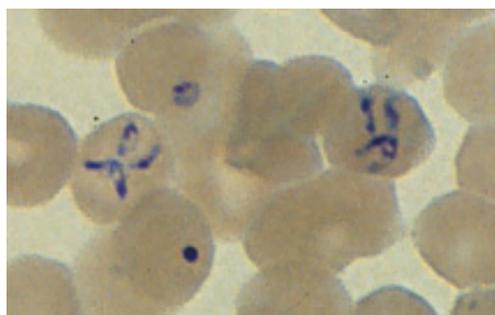
considered in patients with a flu-like illness, particularly fever, chills, and headache, that fails to respond to antibiotic therapy for *Borrelia*. Immunity is insufficient to prevent new infections of Lyme disease with subsequent tick bites that require another course of treatment. Antibody levels generally will decline after treatment, although they may persist for months in some patients after symptoms have resolved.

### Southern Tick-Associated Rash Illness (STARI)

A Lyme-like rash has been noted following the bite of the lone star tick, *A. americanum*, in south central and southeastern states and given the name Southern tick-associated rash illness (STARI). The rash is indistinguishable from the rash caused by *B. burgdorferi*. Little is known about this illness. While spirochetes have been observed in about 1-3% of lone star ticks, the bacteria cannot be cultured in the media used for *B. burgdorferi*. A spirochete named *Borrelia lonestari* has been identified in *A. americanum* by DNA analysis and has recently been cultured in tick cell lines.

### Human Babesiosis

Human babesiosis is a malaria-like illness that is caused by protozoa found in the red blood cells of many wild and domestic animals. Babesiosis is caused by *Babesia microti* in the northeast and upper mid-west United States. *Babesia microti* is a parasite of white-footed mice, as well as voles, shrews, and chipmunks. Other species or variants of *Babesia* are associated with human disease in other parts of the United States (i.e., California and Missouri), Europe, and Asia. Human babesiosis has been recognized since the early 1970's in parts of Massachusetts (particularly Nantucket Island), Block Island, Rhode Island, and the eastern parts of Long Island, New York. Most cases in Rhode Island are reported from the southern coastal regions. The first Connecticut case of human babesiosis was reported from Stonington in 1988 and the majority of cases continue to be reported from the southeastern portion of that state, although recent evidence indicates that the organism has become more widely distributed in the state. The number of confirmed cases has increased in New Jersey in recent years, which may represent increased risk or increased awareness. The disease is reportable in only a few states. The number of reported cases is probably only a small fraction of clinically diagnosed cases with many other subclinical or mild cases going undetected and unreported. Nevertheless, the distribution and number of cases of babesiosis appears to be increasing.



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*Babesia microti* in red blood cells (CDC).

**Table 3.** Number of reported human cases of babesiosis in select northeastern states, 1997-2001 (compiled from state health department web sites or reports).

State	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
CT	31	45	40	52	56	69				
RI	2	6	18	35	27					
MA	19	66	51	8	18					
NY	26	107	61	72	-					
NJ	3	7	3	15	19					

The white-footed mouse is the primary reservoir for *B. microti*, which is transmitted by *I. scapularis*. While data on the prevalence of infection in *P. leucopus* and particularly in *I. scapularis* is limited to a few studies, babesial parasites have been observed in up to 41% of mice and over 90% can be serologically positive in endemic areas. Infection in mice may be life long. Infections in ticks generally appear to be lower than with *B. burgdorferi*, but in highly endemic areas tick infection by *Babesia* species may be equally prevalent. Maintenance of the parasite seems to require moderate to high tick densities. Most human cases occur during the summer months when nymphs of the blacklegged tick are active. *Babesia* can also be transmitted through blood transfusions from asymptomatic donors.



White-footed mouse with *I. scapularis* ticks.

Both the mouse (or other reservoir competent rodent host such as the meadow vole) and the blacklegged tick are required to complete different aspects of the *Babesia* lifecycle. Larval or nymphal ticks acquire the babesial parasites when feeding on an infected mouse. In the tick gut, male and female gametes unite to form zygotes. Subsequently a stage of the parasite reaches the salivary glands and become dormant until the tick feeds again. The parasite is passed to the next stage of the tick (transstadial transmission). Upon tick attachment, infectious sporozoites are formed and shed in the saliva of the tick. It may require as many as 54 hours of attachment before transmission occurs. Adult *I. scapularis* also can transmit the parasite. During transmission, the sporozoites enter red blood cells, reproduce asexually, and emerge to invade new cells, destroying the infected cells in the process and causing the symptoms associated with babesiosis. Introduction of *B. microti* into another mouse perpetuates the cycle. A female tick does not transmit this parasite to her eggs (transovarial transmission).

The clinical presentation of human infection ranges from subclinical to mild flu-like illness, to severe life-threatening disease. Infection often is accompanied by no symptoms or only mild flu-like symptoms in healthy children and younger adults. The disease can be severe or fatal in the elderly, the immune suppressed (HIV infection or use of immunosuppressive drugs), and people without spleens. The greatest incidence of severe disease occurs in those older than 40 years of age. Symptoms of babesiosis include fever, fatigue, chills, sweats, headache, and muscle pain beginning 1-6 weeks after the tick bite. Gastrointestinal symptoms (nausea, vomiting, diarrhea, abdominal pain), respiratory symptoms (cough, shortness of breath), weight loss, dark urine, and splenomegaly also may occur. Complications such as acute respiratory failure, congestive heart failure and renal failure have been associated with severe anemia and high levels of infected cells (parasitemia). Up to 80% of red blood cells can be infected in a splenectomized patient, although 1-2% parasitemia is typical in those with intact spleens. Illness may last weeks to months and recovery can take many months. Co-infection with *B. microti* and *B. burgdorferi* can result in overlapping clinical symptoms, a more severe illness, and a longer recovery than either disease alone.

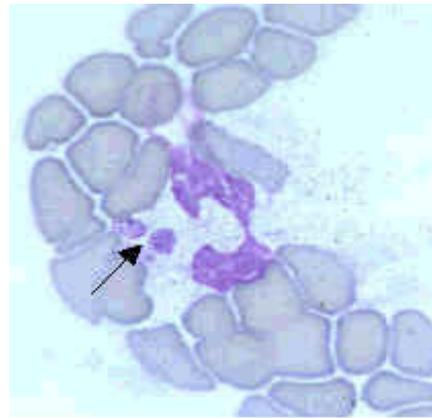
A specific diagnosis of babesiosis can be made by detection of the parasites in Giemsa-stained blood smears and confirmed serologically by an indirect fluorescent antibody (IFA) test. A complete blood count (CBC) is useful in detecting the hemolytic anemia and/or thrombocytopenia (decrease in blood platelets) suggestive of babesiosis. Elevated liver function

tests may be present. The parasite can also be detected by polymerase chain reaction (PCR) assay. The drugs of choice in the treatment of babesiosis are oral clindamycin plus quinine sulfate or a combination of oral azithromycin and atovaquone. Adverse effects (i.e., tinnitus, vertigo, lower blood pressure, gastrointestinal upset) are commonly associated with clindamycin and quinine use and some patients cannot tolerate the treatment. The combination of azithromycin and atovaquone is better tolerated. Severely ill patients should be given intravenous clindamycin and quinine and an exchange blood transfusion. Following drug treatment, the parasites usually are eliminated and there is no recurrence of disease. In immunocompromised individuals, parasitemia may persist for months and possibly years following recovery from illness and relapse may occur. Currently, individuals who have ever been diagnosed with babesiosis are excluded from donating blood.

## Human Ehrlichiosis

The Ehrlichiae are a group of bacteria with several genera and species known to cause disease in dogs, cattle, sheep, goats, horses and humans. These bacteria invade different types of white blood cells (leucocytes) and the disease is often named from the primary type of infected blood cell, including granulocytes or monocytes. Veterinarians have known about canine ehrlichiosis, caused by *E. canis* and transmitted by the Brown dog tick since 1935. Two principal forms of ehrlichiosis in humans currently are recognized in the United States. Human monocytic ehrlichiosis (HME) is caused by *Ehrlichia chaffeensis*. Human granulocytic ehrlichiosis (HGE) is caused by *Anaplasma phagocytophilum* (some cases by *Ehrlichia ewingii*) and accounts for about two-thirds of all ehrlichiosis cases in the U.S. Surveillance for ehrlichiosis in most states is sparse. Ehrlichiosis was added to the national list of reportable diseases in 1999. In Connecticut, there were 544 confirmed cases of HGE reported from 1995-2002. Cases were distributed across all eight Connecticut counties. In New York, both HGE and HME have been reported mainly from the lower Hudson River Valley and eastern Long Island.

Human granulocytic ehrlichiosis was first described from patients in Wisconsin and Minnesota in 1994. The blacklegged tick is the principal vector for HGE (or technically Anaplasmosis) in the northeastern and upper mid-western states. Therefore, most cases of HGE have been reported from states where Lyme disease is highly endemic, particularly Connecticut, New York, and parts of Minnesota and Wisconsin. The western blacklegged tick is the vector in northern California. Laboratory studies indicate transmission can occur within 24 hours of tick attachment and possibly within 8 hours. A single tick has been demonstrated to simultaneously transmit both *B. burgdorferi* and *A. phagocytophilum*.



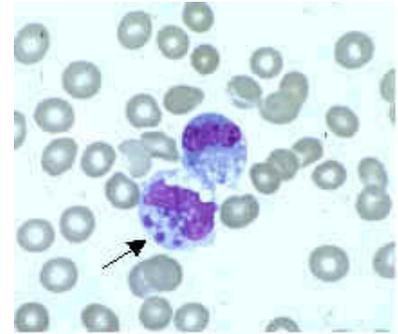
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Morulae of *A. phagocytophilum* in cytoplasm of neutrophil (CDC).

Human monocytic ehrlichiosis, caused by *E. chaffeensis*, was first recognized in the United States in 1986 in a patient who was bitten by a tick in Arkansas. Lone star ticks are the vector for *E. chaffeensis* in south central and southeastern regions of the country where most cases of HME occur. The DNA of *E. chaffeensis* has been detected in lone star ticks from Connecticut and Rhode Island, so cases of HME may occur in southern New England.

Most cases of ehrlichiosis occur in May, June, or July with 80-90% of cases occurring between April and September. This corresponds to the activity of nymphal *I. scapularis* and adult lone star ticks. Symptoms for both types of ehrlichiosis are non-specific and include fever,

headache, muscle pain, nausea, vomiting, and malaise. Initial symptoms appear 5-10 days after the tick bite. Illness may be mild, moderate or severe. Some cases require hospitalization and there have been fatalities. A rash is uncommon in adults, but a rash has been observed in many HME cases in children. Most patients show a decrease in their white blood cell (leukopenia) and blood platelet (thrombocytopenia) counts and an increase in liver enzymes. The number of clinical cases increases with age. The highest rates have been observed for patients 50 years of age or older. Severe cases and fatalities have been reported across all age groups. HME has been confused with Rocky Mountain spotted fever (RMSF). There are no absolute clinical criteria to distinguish Human monocytic ehrlichiosis from RMSF although patients with HME are much less likely to have a rash (10-15 percent) and are more likely to be leukopenic. A diagnosis of ehrlichiosis should be considered for patients with a flu-like febrile illness and possible exposure to *I. scapularis*. Co-infections by the agents of HGE and Lyme disease have been reported and may result in more severe disease. A diagnosis of ehrlichiosis can be confirmed by a serological test, observing the organism in white-blood cells, culturing the organism, or amplification of the DNA of the ehrlichia organism by polymerase chain reaction (PCR). Tests may be negative in the early stages of disease and are more reliable in specimens obtained during the 3<sup>rd</sup> week of illness. The drug of choice for the treatment of ehrlichiosis is doxycycline (tetracycline may also be used) and should be started upon suspicion or clinical diagnosis of ehrlichiosis. Response to antibiotic therapy is rapid with fever subsiding in 24-72 hours. The use of doxycycline in children under 8 years of age is generally not recommended because it may stain the permanent teeth, but could be used in severe cases. Rifampin has been used successfully when doxycycline cannot be used.

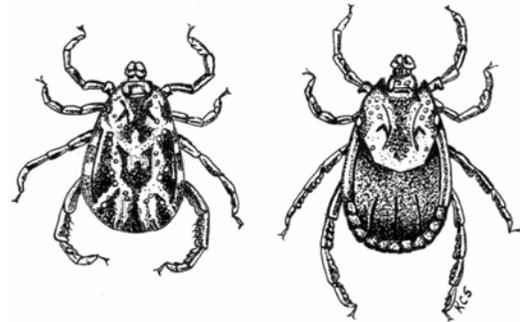


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Morulae of *E. chaffeensis* in cytoplasm of monocyte (CDC).

## Rocky Mountain Spotted Fever

Rocky Mountain spotted fever (RMSF) is caused by *Rickettsia rickettsii*, a type of bacterium that occurs throughout the continental United States, southern Canada, Mexico and Central America and parts of South America. Although the disease was first recognized in 1896 from virulent cases in Idaho and Montana, the name is somewhat misleading as only a small proportion of current cases are reported from the Rocky Mountain region. In the U.S., most cases of RMSF occur in the South Atlantic and West Central states. North Carolina and Oklahoma have the highest rates of RMSF accounting for 35% of the total cases reported to the CDC during 1993-1996. The majority of RMSF cases are associated with the American dog tick. In the western U.S., the vector is the Rocky Mountain wood tick, *D. andersoni*.



RMSF is relatively uncommon in New England. Between 1997 and 2002, based on figures in the CDC's Morbidity and Mortality Weekly Report (MMWR), approximately 3,520 human cases were reported in the United States, of which 28 (less than one percent) were from New England. More cases of RMSF are reported from the mid-Atlantic states, but these still accounted for only 6.7% of the total. Few ticks are infected. Scientists at the Connecticut Agricultural Experiment

Station found that less than 1% of 3,000 American dog ticks examined in Connecticut had spotted fever-group organisms, and not all spotted fever group rickettsiae are infectious to humans.

**Table 4.** Number of reported human cases of Rocky Mountain spotted fever in northeastern states, 1997-2002. (Data compiled from MMWR and/or state health department web sites; 2002 numbers provisional. One case was reported from New Hampshire in 2001).

State	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
CT	3	2	0	0	0	0	3			
RI	1	0	4	0	0	4				
MA	1	0	2	2	2	6				
NY	14	13	14	9	4	18				
NJ	9	12	7	12	9	2				
PA	16	13	18	25	20	20				
US total	409	365	579	495	695	961				

Children are particularly at risk for RMSF with two-thirds of the cases in patients under 15 years of age. Like Lyme disease, the highest rate in children is in the 5 to 9 year old age group. Symptoms usually appear within 2 to 9 days after a tick bite. Patients experience a variety of symptoms including sudden fever (90%), severe headache (89%), muscle pain (83%), and rash (78%). The rash may begin as small, pink, non-itchy spots (macules) and then develop into the spotted (petechial) rash characteristic of RMSF. The rash may include the palms (50%) and soles of the feet. The rash may not be present or faint when a physician initially examines a patient. Some patients (10-15%) never develop a rash. The classic spotted rash of RMSF appears after about six days or later. Prompt antibiotic treatment with doxycycline, tetracycline, or chloramphenicol for suspected cases is important because RMSF is fatal in 15-20% of untreated cases. Delays in diagnosis because of the absence of the rash or no knowledge of a tick bite could be dangerous. RMSF is made more severe with inadvertent use of sulfonamides. In recent years, about 1-4% of cases in the U.S. have been fatal. A clinical diagnosis may be confirmed serologically or by PCR, but antibodies may not yet be present when a patient is seen by a physician early in the illness.

*Below: Examples of spotted fever rash (CDC). Left to right: early (macular) rash on sole of foot, late (petechial) rash on palm and forearm, and rash on hand of a child.*



### Tick Paralysis

A toxin produced by certain *Dermacentor* ticks during feeding can cause a progressive, ascending paralysis, which is reversed upon removal of the tick. Recovery is usually complete. Paralysis begins in the extremities of the body with a loss of coordination and inability to walk. It progresses to the face with corresponding slurred speech, and finally shallow, irregular breathing. Failure to remove the tick can result in death by respiratory failure. Cases appear more frequently in young girls with long hair where the tick is more easily overlooked. Most cases of tick paralysis are caused by the Rocky Mountain wood tick (*Dermacentor andersoni*) in northwestern states. The American dog tick has also been known to cause tick paralysis.

## Tularemia

The bacterium, *Francisella tularensis*, that causes tularemia (Rabbit Fever or Deer Fly Fever) is transmitted by the bite of several species of ticks or bites from deer flies. Ticks associated with tularemia include the American dog tick, *D. variabilis*; lone star tick, *A. americanum*; and Rocky Mountain wood tick, *D. andersoni*. Most cases occur during the summer (May-August), when arthropod transmission is common. The disease also may be contracted while handling infected dead animals (particularly while skinning rabbits), eating under cooked infected meat, or by an animal bite, drinking contaminated water, inhaling contaminated dust, or having contact with contaminated materials. Natural reservoirs of infection include rabbits, hares, voles, mice, water rats, and squirrels. Tularemia was removed from the list of reportable diseases after 1994, but was reinstated in January 2000 because of its potential as a bioterrorism agent.

Tularemia occurs throughout the United States. There have been fewer than 200 cases reported each year during the first half of the 1990s and again in 2000 and 2001. Most cases have been reported from the central states of Missouri, Arkansas, and Oklahoma. With the exception of outbreaks of pneumonic tularemia on Martha's Vineyard that appear related to gardening, landscaping or mowing activities that may have stirred up contaminated dust, reports of this disease are not common in New England, although sporadic cases and outbreaks may occur. There have been pneumonic cases resulting from accidentally running over a rabbit with a lawnmower.

All persons are susceptible to tularemia. The clinical symptoms of tularemia depend upon the route of infection. With infection by a tick, an indolent ulcer often occurs at the site of the bite with occasional swelling of the regional lymph nodes. Fever is the most commonly reported symptom. Diagnosis usually is made clinically and confirmed by an antibody test.

Antimicrobials with demonstrable clinical activity against *F. tularensis* include the fluorinated quinolones such as ciprofloxacin as well as streptomycin and gentamicin. While tetracycline or chloramphenicol also may be used, they are less effective and relapses occur more frequently.



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## Powassan Encephalitis

Powassan virus, a *Flavivirus*, is the sole member of the tick-borne encephalitis (TBE) group present in North America. The disease is named after a town in Ontario, Canada where it was first isolated and described from a fatal case of encephalitis in 1958. Documented cases of Powassan encephalitis (POW) are rare, but the disease may be more common than previously realized. While there were only 27 known cases in North America between 1958-1998 (mainly in Canada and New York state), four additional cases were identified in Maine and Vermont from 1999-2001 as a result of increased testing for West Nile virus. The ages of these recent New England cases ranged from 25 to 70 years. Previously, the latest recognized symptomatic cases occurred in New York in 1978 and Massachusetts in 1994. POW presents as meningitis or meningoencephalitis progressing to encephalitis with fever, convulsions, headache, disorientation, lethargy, with partial coma and paralysis in some patients. The disease has a fatality rate of 10-15% and may result in severe long-term disability in the survivors. The principal tick vector appears to be *Ixodes cookei* with cases occurring from May through October.

Patients generally have a history of tick bite, or a history of exposure to tick habitat or exposure to hosts such as squirrels, skunks, or woodchucks. The blacklegged tick is a competent vector of Powassan virus in the laboratory. A virus very closely related to and apparently a separate subtype of the Powassan virus has been isolated from *I. scapularis*, but the prevalence and public health significance of this virus is unknown.

### **Tick-borne Relapsing Fever**

Soft ticks of the genus *Ornithodoros* transmit relapsing fever, caused by *Borrelia hermsi*, or a group of tick-adapted species of the spirochete. Disease is characterized by cycles of high fever and is treated with antibiotics. Relapsing fever ticks are found in rodent burrows, nests, and caves through the western United States. They can live for many years without feeding. Human cases are often associated with people staying in shelters or cabins infested with these ticks. Relapsing fever may be a risk for northeastern residents vacationing or visiting the western U.S..

### **Colorado Tick Fever**

Colorado tick fever, caused by a virus, occurs in mountainous areas of the western United States and Canada. There are 200-400 cases each year. Scientists believe cases are underreported. The virus is transmitted by female Rocky Mountain wood ticks. Symptoms begin with an acute high fever, often followed by a brief remission, and another bout of fever lasting 2-3 days. Other symptoms included severe headache, chills, fatigue, and muscle pain. Illness may be mild to severe, but is self-limited and is not fatal. Treatment is symptomatic. Recovery occurs over several weeks but occasionally may take months.

### ***Bartonella* Infection**

The genus *Bartonella* includes at least 16 species of vector-associated, blood-borne bacteria that infect a wide variety of domestic and wild animals, including rodents. Several are known human pathogens. For example, *Bartonella henselae*, the agent of cat scratch disease, is transmitted to cats by fleas and generally to humans by bites or scratches from infected cats. The DNA of various *Bartonella* have been found in ticks, including *I. scapularis* and *I. pacificus*, clearly ingested during feeding, but the ability of ticks to transmit these bacteria in the laboratory or field still needs to be determined.