Tick-Borne Infections

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Abstract: There are many tick-borne infections that affect children and adolescents in the United States. These illnesses often begin with nonspecific flulike symptoms such as fever, chills, headache, and myalgia, so obtaining a good travel history is important. Most people do not even realize that they were bitten by a tick, so identification of the specific tick is not necessary. Often, treatment should commence before formal illness identification, as delays may cause more severe disease, and rapid laboratory confirmation is difficult. One of the most important issues is prevention of tick bites with insect repellents, accompanied by thorough tick checks after being outdoors in a tick-infested region.

Key Words: anaplasmosis, Colorado tick fever, babesiosis, ehrlichiosis, Lyme disease, Powassan disease, Rocky Mountain spotted fever (RMSF), *Rickettsia parkeri* rickettsiosis, Southern tick–associated rash illness (STARI), tick-borne infections, tularemia

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TARGET AUDIENCE

This CME review is intended for pediatricians, emergency medicine physicians, family medicine physicians, pediatric emergency physicians, pediatric hospitalists, nurse practitioners, physician assistants, emergency medical services personal, and any health care personnel who care for infants, children, and adolescents in the prehospital, office, urgent care, emergency department, or hospital.

LEARNING OBJECTIVES

After completion of this article, the reader should be better able to:

1. Explain common tick-borne diseases in the United States that affect children
2. Describe rickettsial diseases that are tick-borne
3. Distinguish between early- and late-stage Lyme disease and the appropriate treatment

This article will focus on tick-borne infections that may affect children and adolescents in the United States. The diseases covered will include anaplasmosis, babesiosis, Colorado tick fever, ehrlichiosis, Lyme disease, Powassan disease, *Rickettsia Parkeri* rickettsiosis, Rocky Mountain spotted fever (RMSF), Southern tick-associated rash illness (STARI), tick-borne relapsing fever (TBRF), and tularemia.

One of the key issues with tick-borne infections is that many patients and/or parents may not realize a tick bite occurred. Although identification of the various species of ticks is possible when the ticks are recovered, the geographic region (ie, New England) and time of year of the bite, along with signs and symptoms, often provide sufficient information as to which specific illness is likely. There are also several stages of a tick's life: larva, nymph, adult male or adult female. Although all stages may be found on humans, it is usually the nymphs and adult (especially females) that bite humans.[1] The ticks involved are exceptionally small, with adult females 5 to 8 mm (which become larger when engorged) and nymphs 1 to 2 cm (the size of a pinhead) (Fig. 1). Ticks are usually found in wooded or shrub-filled areas. They do not fly or jump, but they can climb grass or shrubs, so when a person rubs against them, they climb onto a new host.[1]

ANAPLASMOSIS

Anaplasmosis also called human granulocytic anaplasmosis (formerly known as human granulocytic ehrlichiosis) is caused by *Anaplasma phagocytophilum*, a rickettsial bacterium.[2] It is most frequently found on the Northeastern and Upper Midwest United States (same locations as Lyme disease and Powassan disease, so there can be coinfection). It is transmitted by the bite of a blacklegged tick (*Ixodes scapularis*) or Western blacklegged tick (*Ixodes pacificus*), usually in spring, summer, or fall.[1] It can also be transmitted by a blood transfusion.[1] It usually results in nonspecific signs, such as fever, chills, headache, malaise, and myalgias. Laboratory findings include anemia, thrombocytopenia, leukopenia (absolute lymphopenia and a left shift), and mild to moderate elevations of liver enzymes.[1,2] The infection can be diagnosed by identification of morulae in neutrophils on a blood smear or polymerase chain reaction (PCR) assay of whole blood or by 4-fold change in immunoglobulin G (IgG)–specific antibody titers (acute [week 1] plus convalescent titers 2–4 weeks later).[1,2] Clinical suspicion is enough to begin treatment.[1] Treatment is doxycycline (Table 1). Because coinfections with *Babesia microti* and *Borrelia burgdorferi* are possible, if the patient does not respond within 48 hours, consider babesiosis.[2]

BABESIOSIS

Babesiosis is caused by parasites of the genus *Babesia. Babesia microti*, which is transmitted by the blacklegged tick (*I. scapularis*), is found in the northeast and Upper Midwest, in the late spring, summer, or fall.[1,5] *Babesia duncani* has caused disease along the Pacific Coast.[2] *Babesia* parasites can also be transmitted by blood transfusion, organ transplantation, and perinatally.[6] Signs and symptoms are usually nonspecific and include fever, chills, sweats, headache, myalgias, arthralgias, and gastrointestinal symptoms such as anorexia and nausea.[1,2] There may also be dark urine due to hemolysis.[1] Laboratory findings include hemolytic anemia, thrombocytopenia, elevated blood urea nitrogen and creatinine, and elevation of liver enzymes.[1,2,5] There are several risk factors for severe disease, which includes asplenia, impaired immune function, and older age, and in these cases, thrombocytopenia, disseminated intravascular coagulation, hemodynamic instability, liver failure, altered mental status, acute respiratory distress, and death may occur.[1] Diagnosis requires identification of the parasite by Giemsa- or Wright-stained thin manual blood smear, or

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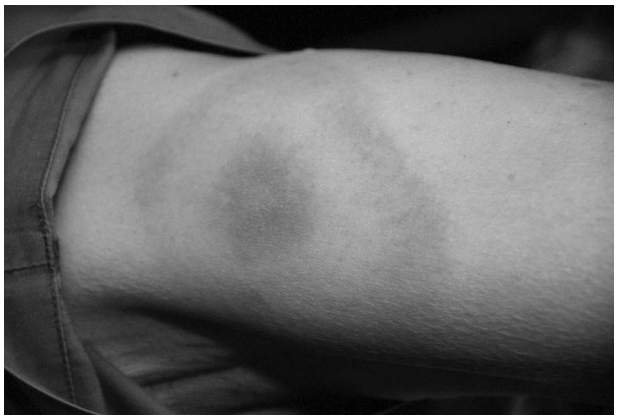

FIGURE 1. Erythema migrans rash of Lyme disease. Photo from the CDC.

PCR for *B. microti*.[2] The observation of a tetrad (Maltese cross) in the blood smear is pathognomonic.[5,6] Serologic testing for a *Babesia*-specific antibody titer by indirect fluorescent antibody (IFA) for IgG can also be performed but does not reliably discriminate between active and past infection.[1] Treatment is reserved for symptomatic and severe patients and includes a combination of atovaquone PLUS azithromycin, OR clindamycin PLUS quinine (Table 2). Partial or complete red blood cell exchange transfusion should be considered for those with parasitemia ≥10%, severe hemolysis, or renal, hepatic, or pulmonary compromise.[2,6] Splenic infarct and rupture are complications of babesiosis.[2] It is also important to note that coinfection with Lyme disease is possible due to the similar endemic regions. In fact, 10% of patients with early Lyme disease have coinfection with babesiosis, whereas 52% of those with babesiosis will have Lyme disease coinfection.[6]

COLORADO TICK FEVER

Colorado tick fever is transmitted by *Dermacentor andersoni*, the Rocky Mountain wood tick in the Western United States. Transmission occurs from March to September.[7] Signs and symptoms include fever, chills, lethargy, headache, and myalgias.[1,7] Some patients develop conjunctival injection, lymphadenopathy and pharyngeal erythema.[1] A maculopapular rash occurs in 15% of patients, and 5% to 10% of children develop meningitis or encephalitis.[7] Approximately 50% of patients have a biphasic illness, with symptoms improving after 2 to 4 days, only to recur 1 to 3 days later.[7] Laboratory finding included leukopenia and thrombocytopenia. Diagnosis is made by reverse transcriptase–PCR and culture.[1,7] Treatment is supportive.

EHRLICHIOSIS

Ehrlichiosis is caused by *Ehrlichia chaffeensis* or *Ehrlichia ewingii*, which are transmitted by the lone star tick (*Amblyomma americanum*). The adult female tick has a white dot or "lone star" on its back.[1] Cases occur predominantly in the Southeastern, South Central, and Eastern United States, but may be seen as far west as Texas. In addition, *Ehrlichia muris eauclarensis* has recently been found in the Upper Midwest and may cause ehrlichiosis as well. Transmission is in spring, summer, or fall.[3] Signs and symptoms include fever, headache, chills, malaise, and muscle pain. Gastrointestinal symptoms (anorexia, nausea, vomiting, diarrhea), confusion, and a maculopapular rash (more often noted in children), which usually begins 5 days after the onset of fever and involves the extremities, but can affect the palms, soles, or face, can also occur.[1,3,8] Severe disease may result in acute respiratory distress syndrome, shock, coagulopathy, hepatic and renal failure, and rarely in death.[8] Laboratory findings during the first week of clinical disease may include thrombocytopenia, absolute leukopenia, lymphopenia, anemia, and mild elevation in liver enzymes.[3] Diagnosis relies on PCR of whole blood and is most sensitive during the first week if illness. Morulae can be detected in whole-blood smears of 20% of patients. *E. chaffeensis* usually infects monocytes, whereas *E. ewingii* infects granulocytes.[1] A 4-fold change in IgG-specific antibody titer by IFA in acute and convalescent serum can also be used. Treatment is with doxycycline (Table 1) and should begin with clinical suspicion of the illness.[1]

LYME DISEASE

Lyme disease is due to the spirochete *B. burgdorferi*, which is transmitted by the blacklegged tick (*I. scapularis*) and the Western blacklegged tick (*I. pacificus*). *Ixodes scapularis* is found in the Eastern and Southern United States, as well as the Upper Midwest, whereas *I. pacificus* is found along the Pacific Coast. *Borrelia mayonii* has been found in the Upper Midwest and may cause symptoms similar to Lyme disease.[1] Transmission occurs during spring, summer, or fall, with 50% of cases occurring in June or July.[9] Clinical findings of Lyme disease can be divided into 3 stages: localized, disseminated, and late.[9] The localized stage is characterized by erythema migrans (EM), a red ring-like circular or homogenous rash that spreads and is usually at least of 5-cm diameter[1,2] (Fig. 2). It occurs in 70% to 80% of patients within 1 to 2 weeks of the tick bite.[2,10] There may be flulike symptoms such as fever, headache, malaise, myalgias and arthralgias, and lymphadenopathy.[1,10] All patients diagnosed with EM in endemic areas should be presumed to have Lyme disease, as serologic testing is not sensitive early in the course of the illness. Treatment with doxycycline, amoxicillin, or cefuroxime should be initiated, as this shortens the duration of EM and usually prevents later sequelae[10] (Table 3).

It is important to note that prophylaxis with a single dose of doxycycline, if given within 72 hours of a tick bite in an endemic region, is recommended. The dose is 4.4 mg/kg (maximum 200 mg) orally (PO) for children and 200 mg PO for adolecents.[10,11]

If a patient has 1 or more skin lesions suggestive but atypical of EM, antibody testing on acute and convalescent phase serum (if acute was negative) is recommended before treatment.[11]

TABLE 1. Treatment of Anaplasmosis, Ehrlichiosis, and RMSF

Age	Drug	Dosage	Max	Duration
Children	Doxycycline	2.2.mg/kg per dose twice a day (BID) PO, IV	100 mg/dose	10–14 d anaplasmosis; at least 3 d after fever resolves, but minimum 5–7 d for ehrlichiosis and RMSF
Adolescents	Doxycycline	100 mg BID, PO, IV	100 mg/dose	10–14 d anaplasmosis, at least 3 d after fever resolves, but minimum 5–7 d for ehrlichiosis and RMSF

Table developed from References 1–4.

RMSF indicates Rocky Mountain spotted fever.

TABLE 2. Treatment of Babesiosis

Age		Drug	Dosage	Maximum	Duration
Children	**Give both**	Atovaquone	20 mg/kg per dose every 12 h PO	750 mg/dose	7–10 d
		Azithromycin	10 mg/kg day 1 then 5 mg/kg once a day IV if hospitalized, PO if ambulatory	500 mg/dose day 1, then 250 mg/dose	7–10 d
		OR			
		Clindamycin	7–10 mg/kg IV if hospitalized, PO if ambulatory every 8 h	600 mg/dose	7–10 d
		Quinine sulfate	6 mg base/kg (8 mg salt/kg) every 6–8 h PO	542 mg base, 650 mg salt	
Adolescents	**Give both**	Atovaquone	750 mg every 12 h PO	N/A	7–10 d
		Azithromycin	Day 1: 500–1000 mg PO, next days: 250–1000 mg/d IV if hospitalized, PO if ambulatory	1000 mg/d	7–10 d
	OR				
Adolescents	**Give both**	Clindamycin	300–600 mg IV every 6 h if hospitalized, if ambulatory 600 mg every 8 h PO	N/A	7–10 d
		Quinine	650 mg every 6–8 h PO	N/A	7–10 d

Table developed from References 1,2,5,6.

One condition that can be confused with Lyme disease is STARI, associated with a bite from the lone star tick (which cannot transmit *B. burgdorferi*).[1,11] Although those in some of the endemic regions do overlap, STARI is uncommon in most Lyme-endemic regions.[2] Because STARI cannot be distinguished from Lyme disease EM in regions endemic for both, antibiotic therapy is recommended.

Disseminated Lyme disease can present with various symptoms, usually within weeks to a few months after the tick bite. Flulike symptoms, lymphadenopathy, and multiple annular rashes can occur. Additional manifestations may include neurologic findings (in 10%–15% of cases), such as Bell palsy or other cranial nerve palsies, meningitis, encephalitis, and motor and sensory radiculopathy; cardiac findings in 1% to 2%, including conduction abnormalities (often heart block), pericarditis, and myocarditis; and rheumatologic symptoms in up to 30%, consisting of transient migratory arthritis in 1 or several large joints; migratory pain in tendons, muscles, bones, or bursae; or Baker cyst, with the latter usually occurring >6 months after the tick bite.[1,2] Additional findings may include conjunctivitis, uveitis, keratitis, mild hepatitis, and splenomegaly.[1] Laboratory testing shows elevated erythrocyte sedimentation rate (ESR), mildly elevated liver enzymes, and/or microscopic hematuria or proteinuria. In Lyme meningitis, there is lymphocytic pleocytosis, elevated protein, and normal glucose.[1] Serologic testing in disseminated Lyme calls for a 2-step test that consists of an enzyme immunoassay or IFA followed, if the enzyme immunoassay is reactive or equivocal, by IgM and IgG Western blot testing if the illness is ≤4 weeks, or IgM Western blot alone if the illness is >4 weeks.[1,2] If the first step is negative, no further testing is needed. Those with infections with *B. mayonii* will also test positive by the 2-step method. If there is central nervous system (CNS) involvement, cerebrospinal fluid (CSF) can be tested for intrathecal IgM or IgG antibody production and/or *Borrelia* DNA.[2] For those with Lyme arthritis, PCR of synovial fluid has a greater than 75% sensitivity in IgG-positive patients.[2] On the other hand, culture of *Borrelia* species from body fluids has poor sensitivity.[2] Treatment for disseminated Lyme disease is based on the system affected and whether the patient is going to be at home or hospitalized (Table 4). Coinfection with human granulocytic anaplasmosis or babesiosis should be considered for those with Lyme disease who have a fever for >48 hours while on antibiotics; those with leukopenia, thrombocytopenia, and/or anemia; and patients who have symptoms that seem severe than those with Lyme alone.[1,2]

Late Lyme disease occurs in patients not treated earlier and usually manifests as Lyme arthritis in children. In Lyme arthritis,

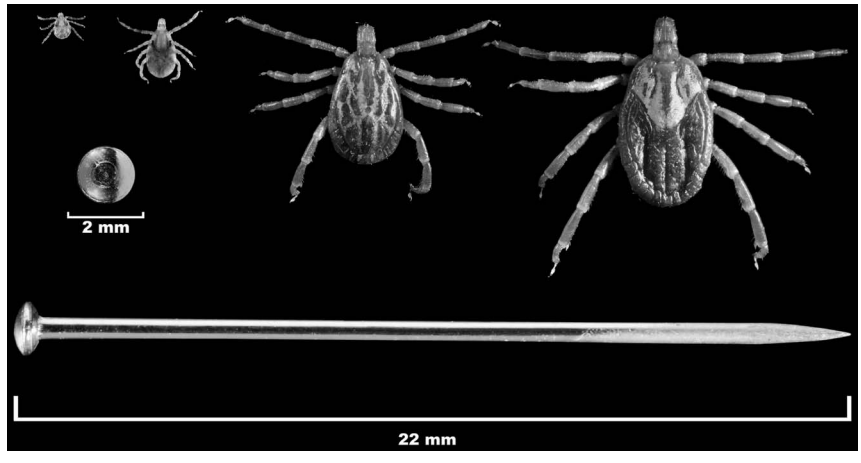

FIGURE 2. Tick life stages and size. From left: larval stage, nymph, adult male, adult female. Photo from the CDC: Dr. Chrisopher Paddock.

TABLE 3. Treatment of Lyme Disease–EM, Arthritis

Age	Drug	Dosage	Maximum	Duration
Children	Amoxicillin	50 mg/kg per day PO, divided into 3 doses	500 mg/dose	14 d EM, 28 d arthritis
	Doxycycline	4.4 mg/kg per day PO divided into 2 doses	100 mg/dose	10 d EM, 28 arthritis if ≥8 y (if <8 y, use amoxicillin)
	Cefuroxime axetil	30 mg/kg per day, PO divided into 2 doses	500 mg/dose	14 d EM, 28 d arthritis
	Ceftriaxone	50–75 mg/kg IV	2 g/dose	Arthritis 28 d
Adolescents	Doxycycline	100 mg BID PO	N/A	10 EM, 28 arthritis
	Cefuroxime axetil	500 mg BID PO	N/A	14 EM, 28 arthritis
	Amoxicillin	500 mg thrice a day PO	N/A	14–21 EM, 28 arthritis

Table developed from References 1,2,9–11.

the joint swelling/effusion is often out of proportion to the degree of pain or disability. The neutrophil count and ESR are usually lower than with septic arthritis, and white blood cells are seen in the synovial fluid (but also usually at a lower level than septic arthritis (generally 60,000 in Lyme vs >70,000 in septic joints).[9,11] The 2-step serum antibody test has the best sensitivity for diagnosis.[11] Encephalopathy, encephalitis, and polyneuropathy are rare late manifestations.[9] Treatment for late disease is doxycycline but for a longer time course (Table 3). Those who have responded incompletely or who relapse shortly after stopping treatment can be given a second course of therapy.[9] Unfortunately, 10% to 15% of those with Lyme arthritis can have persistent synovitis that can last for months to years.[9]

Risk factors for developing Lyme disease (and likelihood %) include an identified *Ixodes* species, a bite in an endemic geographic region of the country (5%–10%), and an engorged tick that has been present for >72 hours (25%). If all 3 are satisfied, prophylaxis with a single dose of doxycycline is recommended.[11] If not, observation is recommended.[11]

POWASSAN DISEASE

Powassan virus is an arbovirus spread by the bite of a groundhog (*Ixodes cookei*), squirrel (*Ixodes marxi*), or blacklegged or deer tick (*I. scapularis*). Although the first 2 rarely bite people, the latter, which feeds mainly on white-footed mice and deer, does bite people. The ticks may become infected when they feed on groundhogs, squirrels, mice, or other rodents that have the virus in their blood.[12] Powassan disease is found in the Eastern United States and Upper Midwest. Although many people infected with this virus do not have symptoms, there can also be severe disease characterized by meningitis and encephalitis.[1,12] Initial signs and symptoms may include fever, headache, vomiting, and generalized weakness. There may be progression of severe disease, which may produce altered mental status, encephalitis, aseptic meningitis, aphasia, seizures, hemiplegia, cranial nerve palsies, or movement disorders.[1,7,12] The mortality rate for severe disease is 10%. Diagnosis is based on signs and symptoms, history of exposure, and CSF findings of normal or mildly elevated protein, normal glucose, and neutrophils (early in the course). Measurement of virus-specific IgM antibodies in serum or CSF by enzyme-linked immunosorbent assay can be done, but there is cross-reaction with other viruses; therefore, confirmation using a neutralizing antibody testing by a state laboratory or the Centers for Disease Control and Prevention is required for definitive diagnosis.[12] There is no specific treatment, but supportive care including respiratory support, intravenous (IV) fluids, and increased intracranial pressure management may be necessary.

ROCKY MOUNTAIN SPOTTED FEVER

Rickettsia rickettsii, an obligate, intracellular, gram-negative bacillus, is the causative agent of RMSF.[4] It targets endothelial cells lining the small blood vessels of all major organs and tissues, resulting in diffuse small vessel vasculitis.[4] This bacillus is transmitted to humans by an Ixodidae tick—the American dog tick (*Dermacentor variabilis*) in Eastern, Central, and Pacific Coastal United States; the Rocky Mountain wood tick (*D. andersoni*) in Rocky Mountain states; and the brown dog tick (*Rhipicephalus sanguineus*) in the Southwestern United States.[1] Despite its name, it is not most common in the Rocky Mountain area, but instead in the South Central and Southeastern United States. Transmission is usually during spring, summer, or fall.[1,4,8] The hallmark sign is a maculopapular rash that occurs within 2 to 5 days after the onset of fever. It begins on the wrists and ankles, spreading within hours to the trunk, and palms and soles. A petechial rash occurs later and implies more severe disease. Approximately 10% of infected patients never develop the rash.[1,13] Early (days 1–4) signs and

TABLE 4. Treatment of Lyme Disease—Meningitis and Cardiac and Cranial Neuropathy

Age	Drug	Dosage	Maximum	Duration
Children ambulatory	Doxycycline	4.4 mg/kg divided twice a day	100 mg/dose	14 d meningitis, 14–21 d carditis
	Amoxicillin	50 mg/kg per day divided 3 times a day	500 mg/dose	14 d meningitis, 14–21 d carditis
	Cefuroxime axetil	30 mg/kg per day divided 3 times a day	500 mg/dose	14 d meningitis, 14–21 d carditis
Children hospitalized	Doxycycline	50–75 mg/kg IV once daily	2 g/dose	14 d meningitis, 14–21 d carditis
	Cefotaxime	250–200 mg/kg IV divided 3–4 times a day	6 g daily	14 d meningitis, 14–21 d carditis
Adolescents ambulatory	Doxycycline	100 mg PO BID or 200 mg once a day	N/A	14 d meningitis, 14–21 d carditis
Adolescents hospitalized	Ceftriaxone	2 g/d	N/A	14 d meningitis, 14–21 d carditis

Table developed from References 1,2,9–11.

symptoms may include fever, myalgias, severe headache, photophobia, and/or gastrointestinal symptoms such as vomiting, anorexia, diarrhea, and abdominal pain. Late signs (>5 days) may include meningeal irritation, altered mental status, respiratory distress, and multiorgan failure.[1] Laboratory findings may include thrombocytopenia, hyponatremia (<130 mg/dL), and elevated hepatic transaminase levels.[1,4] Because this illness can result in disseminated intravascular coagulation, shock, or even fatality, those with a suggestive clinical presentation should be treated with antibiotics before laboratory confirmation of the diagnosis. Delays in antibiotic treatment particularly beyond the fifth day of symptoms are associated with poor outcomes.[1,4] Diagnosis relies in most cases on indirect immunofluorescence antibody (IFA) test a with a 4-fold increase in IgG-specific antibody titer in samples obtained 2 to 4 weeks after presentation. Detection of DNA in a skin biopsy specimen of a rash lesion, as well as acute whole blood and serum by PCR, is now available in specialized laboratories. Diagnosis can be confirmed by immunohistochemical staining of the organism from skin or tissues. Treatment is doxycycline for all ages and should be started as soon as RMSF is suspected. It is continued until the patient is afebrile for at least 3 days, with minimum course of treatment being 5 to 7 days[1,4] (Table 1).

RICKETTSIA PARKERI RICKETTSIOSIS

It is important to note that *Rickettsia parkeri* rickettsiosis presents in a similar fashion to RMSF and is transmitted by Gulf Coast ticks (*Amblyomma maculatum*) in the Southeastern and mid-Atlantic states and Arizona. It is usually less severe than RMSF and is always associated with an inoculation eschar at the site of the tick bite. It is also treated with doxycycline.[1,8]

SOUTHERN TICK–ASSOCIATED RASH ILLNESS

Southern tick–associated rash illness results from the bite of the lone star tick (*A. americanum)*. It presents with an EM-like rash and flulike symptoms. It has not resulted in long-term sequelae, the cause is unknown, and there is no confirmatory test, but because it resembles Lyme disease, the same antibiotics should be prescribed.[1,11]

TICK-BORNE RELAPSING FEVER

Borrelia hermsii, Borrelia miyamoti and other *Borrelia* species transmit TBRF. *Borrelia hermsii* is transmitted by a soft-bodied tick, whereas *Borrelia miyamotoi* is transmitted by a hard-bodied tick. Soft-bodied ticks often live within rodent nests and bite at night for a short period (15–90 minutes), so the bite is often unnoticed.[14] Sleeping in rodent-infested rustic cabins in Western states is the common source, but cases occur in rodent-infested caves as well.[14] The hard-bodies ticks *I. scapularis* and *I. pacificus* transmit *B. miyamotoi* and are common in the Atlantic region, the Upper Midwest, and the Pacific Coast. Transmission usually occurs in May through September.[14] Symptoms may include sudden onset of high fever, shaking chills, sweats, headache, myalgias and arthralgias, nausea, vomiting, and diarrhea. A fleeting macular rash of the trunk and petechiae of the skin and mucous membranes may occur.[1,14] Laboratory findings may include normal to increased white blood cell count with left shift, increased bilirubin, thrombocytopenia, elevated ESR, and slightly prolonged prothrombin time and partial thromboplastin time. Mortality ranges from 4% to 10% in untreated TBRF, but mainly occurs in those with underlying illnesses and those at the extremes of age.[1] If untreated, the fever usually lasts from 2 to 7 days and then ends, only to recur in several days to weeks, and can relapse again, although subsequent relapses are shorter and milder. Diagnosis is made by observing spirochetes in Wright- or Giemsa-stained blood smears or in CSF.[1,14]*Borrelia miyamoti* can also be diagnosed using PCR and antibody-based tests.[1] Treatment is doxycycline, erythromycin, or tetracycline (adolescents) (Table 5), but before being discharged, the patients should be observed for 4 hours because of the risk of a Jarisch-Herxheimer reaction (an acute febrile reaction with headache, myalgia, hypotension, and even respiratory distress following administration of antibiotic therapy).[1,14]

TULAREMIA

Francisella tularensis is a small gram-negative pleomorphic coccobacillus.[15] There are two subspecies (A and B) and several genotypes (A1a, A1B, A2a, A2b), with A1b producing more serious disease in humans.[15] There are also several presentations based on routes of inoculation. Tularemia occurs throughout the United States (except Hawaii), usually during May through September.[1,15,16] Although *F. tularensis* can infect many animal species (rabbits, beavers, hamsters, prairie dogs, squirrels, rats, mice, and other rodents), most cases result from the bite of a tick (dog tick, wood tick, or lone star tick) or a deer fly. The tick or deer fly bite usually results in ulceroglandular or glandular tularemia. Handling-infected animals, ingestion of contaminated water, inadequately cooked meat, or inhalation of aerosol (lawn mowing and farming activities) may result in oropharyngeal, intestinal, pneumonic, or typhoidal presentations.[1,15,16] General signs and symptoms include fever, chills, malaise, anorexia, headache, and myalgias. Ulceroglandular cases develop a cutaneous ulcer at the infection site and tender, localized lymphadenopathy and represent the most common form in adults. The affected nodes often suppurate, even with antibiotic therapy.[17] Glandular tularemia, which is the most common form in children, presents with tender regional lymphadenopathy without an identifiable skin lesion.[15,17] Oculoglandular cases manifest with photophobia, conjunctivitis, and preauricular

TABLE 5. Treatment of Tick-Borne Relapsing Fever

Age	Drug	Dosage	Maximum	Duration	
Children	Doxycycline	4.4 mg/kg per day PO divided into 2 doses	100 mg/dose	10 d	Watch for first 4 h after antibiotics for Jarisch-Herxheimer reaction
	Erythromycin	12.5 mg/kg 4 times a day PO	2 g/d	10 d	
	Ceftriaxone (for CNS involvement)	50–75 mg/kg IV	2 g/d	10 d	
Adolescents	Doxycycline	100 mg PO BID	N/A	10	
	Tetracycline	500 mg every 6 h PO	N/A	10 d	
	Erythromycin	500 mg every 6 h PO	N/A	10 d	
	Ceftriaxone (for CNS involvement)	2 g/d IV	N/A	10–14 d	

Table developed from References 1,14.

TABLE 6. Treatment of Tularemia

Age	Drug	Dosage	Maximum	Duration
Children	Gentamicin	5 mg/kg intramuscularly (IM), IV divided 2–3 times a day	Monitor serum drug levels, consults pediatric infectious disease specialist	Minimum 10 d
	Streptomycin	15–20 mg/kg IM BID	2 g/d	Minimum 10 d
	Ciprofloxacin*	15 mg/kg IV, PO BID	500 mg/dose	10–14 d
Adolescents	Streptomycin	1 g IM BID	2 g/d	Minimum 10 d
	Gentamicin	5 mg/kg IM, IV divided 3 times a day	Monitor serum drug levels (min 5 μg/mL)	Minimum 10 d
	Ciprofloxacin*	400 mg IV, 500 mg PO BID	N/A	10–14 d
	Doxycycline	100 mg IV, PO BID	N/A	14–21 d

*Not FDA approved for this indication, but has been used successfully.
Table developed from References 1,15–17.

adenopathy. Oropharyngeal disease, from ingestion of contaminated meat or water, presents with a severe sore throat, stomatitis, exudative pharyngitis, and cervical lymphadenopathy; intestinal infections cause vomiting, diarrhea, and abdominal pain; pneumonic cases result in cough, pleuritic chest pain, and hilar adenopathy. Typhoidal tularemia presents with general symptoms, along with high fever, hepatomegaly, splenomegaly, septicemia, pneumonia, and/or meningitis.[1,15,17] Laboratory findings may include normal or elevated white blood cell count, elevated ESR, thrombocytopenia, hyponatremia, elevated hepatic transaminases, and elevated CPK. Myoglobinuria and sterile pyuria may occur.[1] Diagnosis relies on a 4-fold rise in antibody titer obtained 2 to 4 weeks after onset. A single serum antibody titer of ≥1:128 by microagglutination or >1:160 by tube agglutination can provide a presumptive diagnosis, as can detection of *F. tularensis* by direct fluorescent antibody or PCR.[1,15,17] It is important to notify the laboratory technicians when *F. tularensis* is suspected, as there have been laboratory-acquired infections (it is a biosafety level 3 organism). Identification from ulcer exudate or aspirate can be done by PCR or direct fluorescent antibody.[15] Treatment is with gentamicin, streptomycin, or ciprofloxacin and should begin when tularemia is suspected[1,15,17] (Table 6).

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