TABLE 12. Complications of Community-Acquired Pneumonia

Organ System	Syndrome	Comments
Pulmonary	Nonresolving pneumonia	Consider resistant infections, noninfectious causes
	Lung abscess	Prolonged course of antimicrobial treatment
	Empyema	Chest tube drainage of infected pleural fluid
	ARDS	Lung protective ventilation strategy indicated; glucocorticoids may decrease this complication
Neurologic	Delirium	May reflect hypoxemia, hypercarbia, or ICU stay
Hematologic	Leukopenia	May be related to sepsis, medication effect
	Thrombocytopenia	May be related to sepsis, medication effect
Cardiac	Acute coronary syndrome	Seen in 5%-10% of hospitalized patients
	Cardiac arrhythmias	Most commonly atrial fibrillation
Kidney	Acute kidney injury	May be related to hypoperfusion or medication effect
Endocrine	Adrenal insufficiency	Waterhouse-Friderichsen syndrome (acute adrenal necrosis), occurring in the setting of overwhelming bacterial infection/septic shock

ARDS = acute respiratory distress syndrome.

KEY POINTS *(continued)*

- Treatment regimens for patients with community-acquired pneumonia requiring ICU care include coadministration of a parenteral β-lactam active against *Streptococcus pneumoniae* and a second agent active against *Legionella* species.

Complications

CAP has a mortality rate of 10% to 12% among hospitalized patients. Survivors may experience significant morbidity, including prolonged hospitalization, protracted convalescence, and high rates of hospital readmission. Related complications include localized lung inflammation, secondary spread of infection, and toxicity related to treatment (**Table 12**).

Lack of response to antimicrobials raises consideration of a resistant or atypical organism, loculated infection (such as empyema), or an infection mimic (tumor, vasculitis, congestive heart failure, pulmonary embolism). Patients with significant pleural fluid collections should undergo diagnostic thoracentesis; chest tube drainage is indicated for empyema.

Glucocorticoids are not routinely recommended and should be reserved for patients without documented adrenal insufficiency or refractory septic shock.

KEY POINTS

- Lack of response to antimicrobials in patients with community-acquired pneumonia raises consideration of a resistant or atypical organism, loculated infection, or an infection mimic.
- Patients hospitalized with community-acquired pneumonia experience significant morbidity and are at high risk for readmission.

Follow-up

In adults with CAP whose symptoms have resolved within 5 to 7 days, routine follow-up chest imaging is typically not necessary.

Readmission rates among hospitalized patients approach 20%. This population should have close outpatient follow-up to ensure clinical stability after therapy completion.

KEY POINT

- In adults with community-acquired pneumonia whose symptoms have resolved within 5 to 7 days, routine follow-up chest imaging is usually not necessary. HVC

Tick-Borne Diseases

Lyme Disease

Lyme disease is the most common tick-borne infection in the United States, with more than 30,000 new infections reported annually. More than 95% of infections in the United States occur in the northeastern, mid-Atlantic, and upper Midwest regions (**Figure 10**). These areas are endemic for the vector, *Ixodes scapularis* (the blacklegged deer tick; **Figure 11**). The causative spirochete, *Borrelia burgdorferi*, is transmitted intradermally when a tick ingests a blood meal.

In highly select situations, prophylaxis with a single dose (200 mg) of doxycycline may decrease the risk of Lyme disease after a tick bite. Prophylactic doxycycline is only recommended if (1) the tick is reliably identified as a blacklegged deer tick; (2) attachment lasts 36 hours or longer; (3) antibiotics can be started less than 72 hours after tick removal; and (4) prevalence of *B. burgdorferi* infection of ticks in the region exceeds 20%. Otherwise, observation is recommended, with treatment given if suggestive symptoms develop.

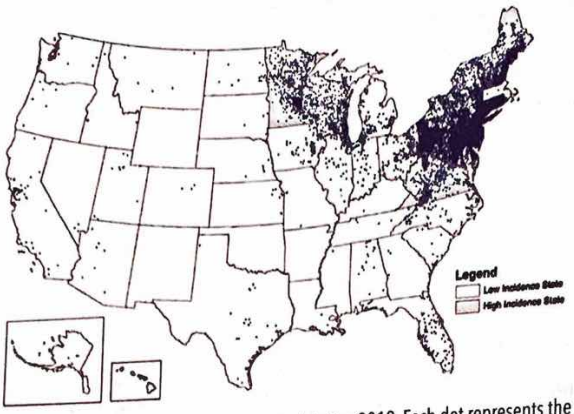

FIGURE 10. Lyme disease cases reported during 2018. Each dot represents the county of residence (not necessarily acquisition) for a confirmed case.

Reproduced from "Reported Cases of Lyme Disease–United States 2018." Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of Vector-Borne Diseases (DVBD). Last updated November 22, 2019. Available at https://www.cdc.gov/lyme/datasurveillance/maps-recent.html. Accessed August 27, 2020.

The clinical manifestations, diagnostic testing, and treatment of Lyme disease vary according to the stage of infection (**Table 13**).

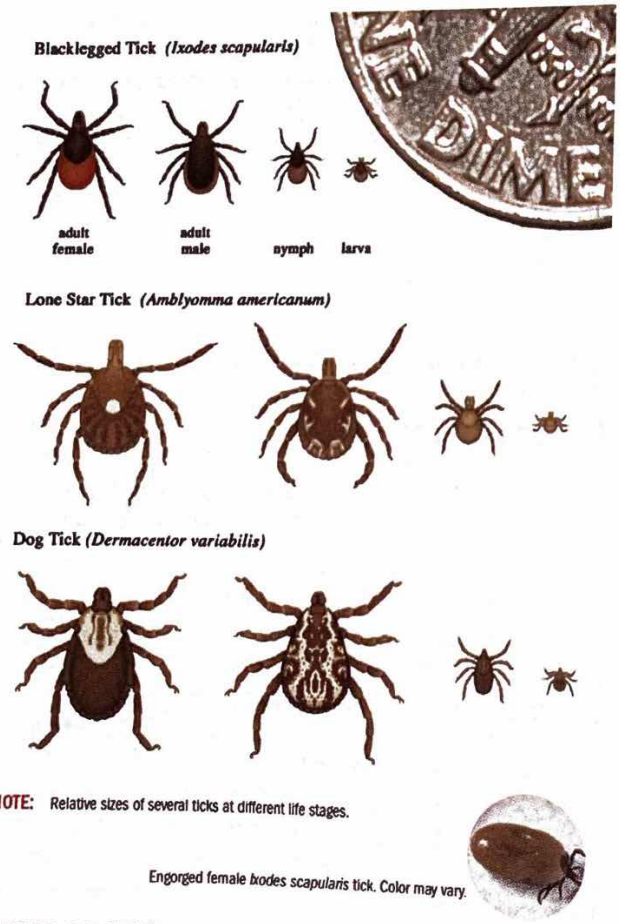

FIGURE 11. The life stages of three hard tick species that spread disease.

Reproduced from Centers for Disease Control and Prevention. Ticks that commonly bite humans. Available at https://www.cdc.gov/ticks/tickbornediseases/tickID.html. Updated January 10, 2019. Accessed January 6, 2020.

Early Localized Disease

Early localized disease typically presents within 4 weeks of infection. Most infected persons (70%-80%) develop erythema migrans (EM), a red, annular skin rash that often has central clearing (**Figure 12**). Systemic symptoms are variably present.

The EM rash is usually painless, nonpruritic, and circumferentially enlarging. Atypical presentations of EM, with confluent erythroderma, ulceration, or vesiculation, may confound the diagnosis. Local cutaneous reactions resulting from hypersensitivity to tick saliva may resemble EM but tend to occur earlier, are pruritic, and do not enlarge significantly after onset.

A patient with EM and a compatible exposure history does not require confirmatory laboratory testing. In fact, antibody testing in early localized disease is insensitive because seroconversion may be delayed for several weeks after appearance of an EM rash. Doxycycline offers the advantage of treating incubating *Anaplasma phagocytophilum*, which is also spread by blacklegged ticks and can coinfect patients with Lyme disease.

Early Disseminated Disease

Without treatment, hematogenous dissemination occurs in up to 60% of patients. Symptoms of early disseminated disease present weeks to months after infection. The most common manifestation is a flu-like illness characterized by fevers, arthralgia, myalgia, and lymphadenopathy and often associated with multiple concurrent EM eruptions at sites distant from the original tick attachment.

Disseminated infection may also involve the heart and the central nervous system. Lyme myocarditis results in injury to the conduction system and atrioventricular (AV) nodal block. Progression to complete heart block can occur rapidly despite antibiotic treatment, so hospitalization is indicated for close monitoring of symptomatic patients with

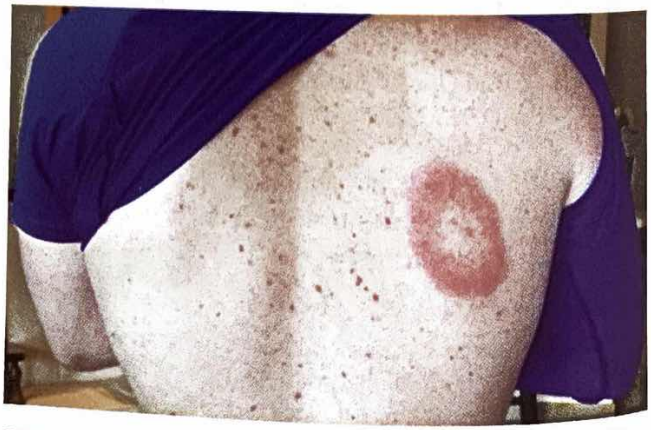

FIGURE 12. The erythema migrans lesion begins as an expanding macule to form a red annular lesion with a partially clearing middle at the site of tick attachment. The center may become indurated, vesicular, or necrotic. Some patients will develop concentric rings.

Figure courtesy of Dr. Karen Bloch.

TABLE 13. Clinical Manifestations, Diagnostic Testing, and Treatment of Lyme Disease by Stage of Infection

Lyme Stage	Onset after Infection	Clinical Findings	Laboratory Confirmation	Treatment[a]
Early localized	≤4 wk	EM at site of tick attachment, variably with fever, lymphadenopathy, myalgia	Not needed if EM present	Doxycycline, 100 mg PO BID × 10 d (first-line therapy) *or* Amoxicillin, 500 mg PO TID × 14 d *or* Cefuroxime axetil, 500 mg PO BID × 14 d
Early disseminated	2 wk-6 mo	Constitutional: Multiple sites of EM, flu-like syndrome Cardiac: heart block, myocarditis Neurologic: cranial neuropathies, meningitis, radiculitis, mononeuritis multiplex, spinal cord or brain parenchymal inflammation	Not needed if EM is present; otherwise, two-tier serologic testing CSF evaluation when CNS involvement is a concern	1. Cardiac Hospitalized patients (first-degree block with PR interval ≥300 msec, higher degree heart block, other arrhythmias, myopericarditis): initial IV ceftriaxone with transition to oral for total of 14-21 days Outpatients (first-degree AV block with PR interval <300 msec): oral treatment same as for early localized disease × 14-21 d 2. Meningoencephalitis: IV penicillin G, IV cefotaxime, or IV ceftriaxone or oral doxycycline × 14-21 d (IV antibiotics preferred for spinal or brain parenchymal involvement) 3. Other manifestations (including facial palsy): oral treatment the same as for early localized disease × 14-21 d
Late disseminated	≥6 mo	Arthritis; neurologic symptoms (peripheral neuropathy, encephalopathy), or dermatologic symptoms (acrodermatitis chronica atrophicans)	Two-tier serologic testing	Initial rheumatologic treatment: same as for early localized but × 28 d Arthritis unresponsive to initial treatment: IV ceftriaxone 2-4 weeks

AV = atrioventricular; BID = twice daily; CSF = cerebrospinal fluid; CNS = central nervous system; EM = erythema migrans; IV = intravenous; PO = by mouth; TID = three times daily.

[a]Doses are for adults with normal kidney function.

cardiac involvement or asymptomatic patients with first-degree (or higher grade) AV block and a PR interval of 300 milliseconds or greater. Permanent pacemaker placement is not necessary because the heart block is reversible with antibiotic therapy.

Neurologic infection occurs in approximately 15% of untreated patients. Aseptic meningitis, facial palsy (unilateral or bilateral), and radiculopathy can present alone or with skin, musculoskeletal, or cardiac findings. Lumbar puncture is indicated when central nervous system involvement is suspected; cerebrospinal fluid lymphocytic pleocytosis supports the diagnosis (see Central Nervous System Infection).

As with early localized disease, when classic EM is present, laboratory confirmation is unnecessary. Without diagnostic skin findings, serologic testing should be pursued through a two-tiered approach (**Figure 13**); the initial enzyme-linked immunosorbent assay (ELISA) is highly sensitive but lacks specificity, and positive or equivocal tests must be confirmed. Until recently, Western blot was the recommended confirmatory test; however, an alternative option using a second sequential enzyme immunoassay has been approved for this purpose.

IgM antibody is detectable before IgG antibody in early infection; therefore, both antibodies should be tested in patients presenting within 30 days of symptom onset. After this time, the recommendation is to test only IgG antibody because, after the first month of symptoms, an isolated IgM antibody is likely to be a false positive. Antibodies may remain detectable for years despite treatment; therefore, serial titers are not useful.

Late Disseminated Disease

Approximately 60% of untreated patients with Lyme disease develop a monoarticular or oligoarticular inflammatory arthritis as a late complication. The knee and other large joints are disproportionally affected. Even without antibiotic treatment, inflammation typically resolves over weeks to months but can have a relapsing-remitting pattern. In approximately 10% of untreated patients, arthritis persists (see MKSAP 19 Rheumatology). Late neurologic or skin findings (acrodermatitis chronica atrophicans and borrelial lymphocytoma) are

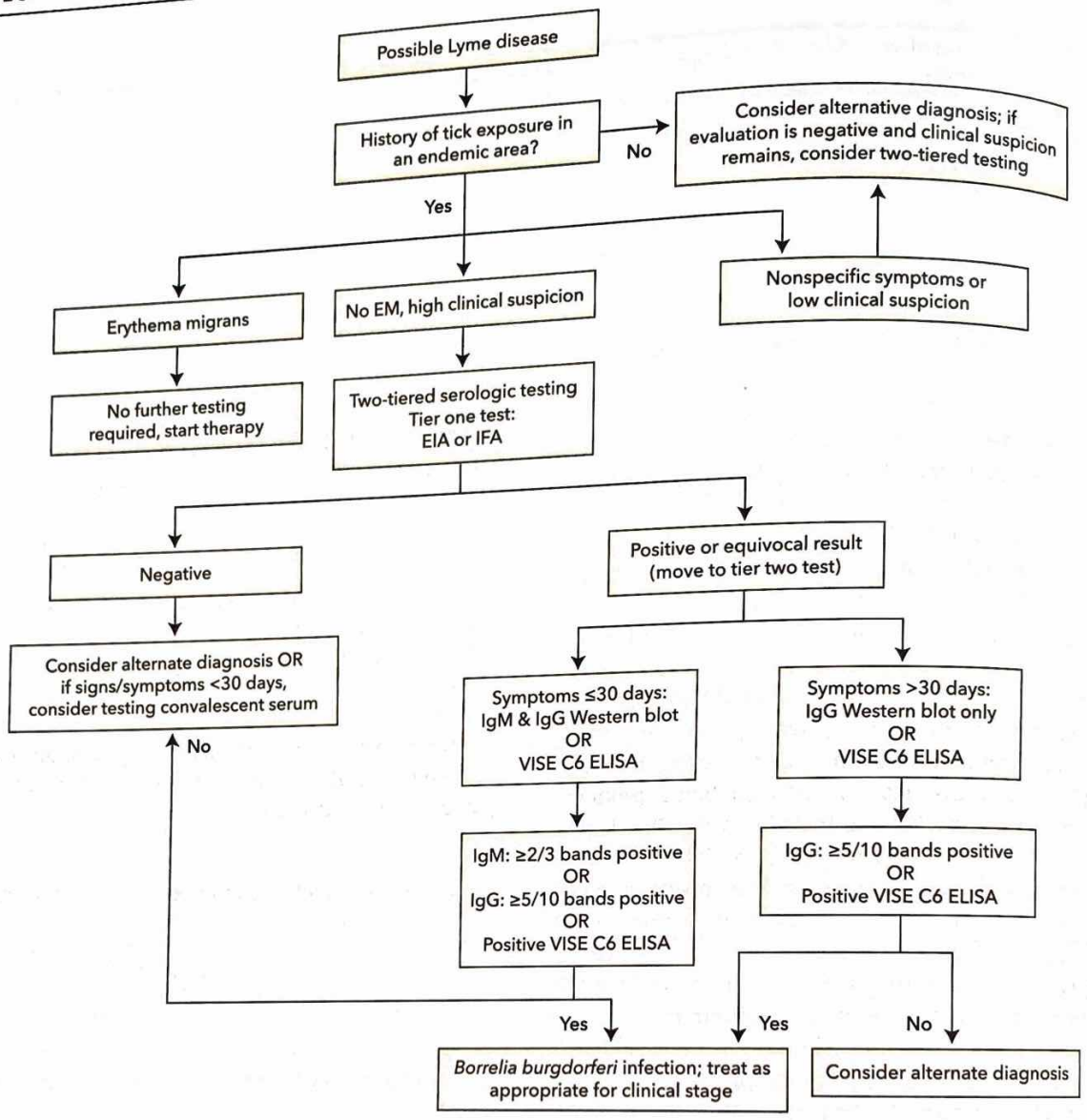

FIGURE 13. Serologic testing for Lyme disease. EIA/ELISA = enzyme-linked immunosorbent assay; EM = erythema migrans; IFA = immunofluorescent antibody assay.

Adapted with permission from Moore A, Nelson C, Molins C, Mead P, Schriefer M. Current guidelines, common clinical pitfalls, and future directions for laboratory diagnosis of Lyme disease, United States. Emerg Infect Dis. 2016;22:1169. [PMID: 27314832] doi:10.3201/eid2207.151694

rare in the United States but more frequent in European infections. Laboratory confirmation at this stage is necessary for diagnosis. Treatment requires prolonged oral antibiotics; parenteral therapy is used when oral therapy is unsuccessful (see Table 13).

Post-Lyme Disease Syndrome

Post-Lyme disease syndrome has been reported in approximately 10% of patients after treatment of EM. Although often erroneously called "chronic Lyme disease," no microbiologic evidence of chronic or latent infection is found after appropriate treatment. Symptoms include fatigue, arthralgia, myalgia, and impairment of memory or cognition that can last for years despite treatment. Clinical trials have shown no benefit to prolonged antibiotic treatment for post-Lyme disease syndrome. Evaluation for coinfection with another tick-borne pathogen or for a noninfectious cause is indicated.

KEY POINTS

- The causative spirochete of Lyme disease may be transmitted when an infected *Ixodes scapularis* tick attaches for at least 36 hours.
- Early localized Lyme disease usually presents within 4 weeks of infection and is characterized by erythema migrans (EM) at the site of tick attachment; patients with EM and a compatible exposure history do not require confirmatory laboratory testing and should receive oral doxycycline.

(Continued)

KEY POINTS *(continued)*

- Early disseminated Lyme disease can affect the cardiovascular and neurologic systems; the diagnosis should be confirmed through an enzyme-linked immunosorbent assay followed by confirmatory testing, with parenteral antibiotic treatment indicated depending on disease severity.
- Post–Lyme disease syndrome (fatigue, arthralgia, myalgia, and impairment of memory or cognition) can last for years, even after appropriate treatment; prolonged antibiotics are not effective in treating this condition.

HVC

Babesiosis

Babesiosis is caused by the intraerythrocytic protozoan *Babesia microti*, which is spread by the blacklegged deer tick and, therefore, occurs in areas of Lyme endemicity (see Figure 10). Transmission through transfusion of infected blood products may result in infections outside of endemic regions.

Approximately 20% of infections are asymptomatic, with the remainder ranging from mild illness to fatal disease (10%). Risk factors for severe disease include age older than 50 years, immunocompromise, or asplenia. Symptoms typically begin within 1 month after tick bite and within 2 months after transfusion of infected blood products. Symptoms are nonspecific and include fever (89%), fatigue (82%), chills (67%), headache (47%), myalgia (43%), and cough (28%). Physical examination may reveal jaundice, hepatomegaly, and splenomegaly, which rarely progresses to splenic rupture. The hallmark of babesiosis is hemolysis, with anemia almost invariably present. Severe disease may include thrombocytopenia, elevated serum aminotransferase levels, and acute kidney injury.

Visualization of *B. microti*, manifesting as intraerythrocytic ring forms similar to those seen in malaria or as tetrads resembling a Maltese cross (**Figure 14**), on thin blood smears is diagnostic. With low-level parasitemia, the sensitivity of microscopy is poor. Therefore, polymerase chain reaction should be pursued if the clinical suspicion of babesiosis is high. Antibody testing does not differentiate acute from previous infection and is not recommended for diagnosis.

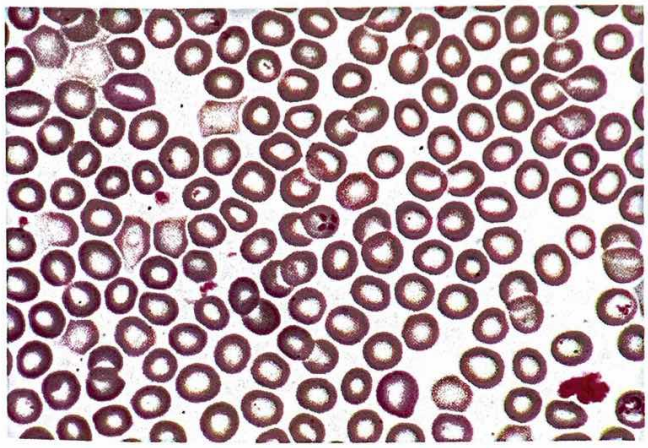

FIGURE 14. Peripheral blood smear showing babesiosis. The diagnosis of babesiosis is typically established by evaluation of a peripheral blood smear showing intraerythrocytic parasites. Occasionally, merozoites are arranged in tetrads, resembling a Maltese cross, as seen in the center of this image.

TABLE 14. Treatment for Babesiosis

Severity	Regimen
Mild to moderate disease	Atovaquone plus oral azithromycin for 7-10 days
Severe disease requiring ICU admission	Atovaquone plus IV azithromycin for 7-10 days[a]
Highly immunocompromised patients	Atovaquone plus high-dose azithromycin (500-1000 mg) for at least 6 weeks

IV = intravenous.

[a]Can transition to oral treatment as step-down therapy following improvement.

The first-line treatment for babesiosis is atovaquone plus azithromycin (**Table 14**). In patients intolerant of this regimen, clindamycin plus quinine is an alternative. Exchange transfusion may be indicated in patients with severe infection and high-grade (>10%) parasitemia. Immunocompromised patients require a longer treatment duration, typically 2 weeks after documented clearance of parasites on blood smear.

KEY POINTS

- Babesiosis, an infection caused by an intraerythrocytic protozoan parasite, presents with clinical findings ranging from a mild febrile illness to fatal infection; symptoms are usually nonspecific, but hemolytic anemia is a hallmark of disease.
- Babesiosis is diagnosed by direct visualization of the organism on blood smear or polymerase chain reaction.
- The first-line treatment for babesiosis is atovaquone plus azithromycin, with extended treatment duration recommended for severely immunocompromised patients.

Southern Tick-Associated Rash Illness

Southern tick-associated rash illness (STARI) presents with EM identical to that seen in Lyme disease but without clinical progression or complications. STARI is associated with *Amblyomma americanum*, also known as the Lone Star tick, which is endemic to the southeastern, south-central, and eastern United States (see Figure 11). No infectious cause has been confirmed. Therefore, diagnosis is based on clinical and geographic features. Because skin findings for STARI and early-stage Lyme disease are indistinguishable, treatment with doxycycline is often offered; however, it is uncertain if treatment for STARI is necessary or beneficial.

KEY POINT

- Southern tick-associated rash illness may be clinically indistinguishable from early-stage Lyme disease, so treatment with doxycycline is often offered.

Ehrlichiosis and Anaplasmosis

Ehrlichiosis and anaplasmosis are clinically similar illnesses spread by different tick vectors and caused by distinct bacterial pathogens. Ehrlichiosis is usually caused by *Ehrlichia chaffeensis*, which is transmitted by the Lone Star tick. Anaplasmosis is caused by *Anaplasma phagocytophilum*, which is transmitted by *Ixodes* ticks, and occurs in areas of Lyme endemicity (see Figure 10).

These syndromes typically begin with a nonspecific febrile illness 1 to 2 weeks after a tick bite (**Table 15**). Rash is uncommon in adults. Leukopenia, thrombocytopenia, and increased serum aminotransferase levels are often present.

Basophilic inclusion bodies called morulae visualized in the cytoplasm of leukocytes (**Figure 15**) suggest the diagnosis but are present in few cases. Antibody tests are often negative in acute illness; a convalescent specimen 2 to 4 weeks after onset of symptoms showing a four-fold rise in titer is confirmatory. Polymerase chain reaction of whole blood at the time of acute illness is highly sensitive, particularly if performed before therapy. Doxycycline is the recommended treatment for ehrlichiosis and anaplasmosis. Because delay in

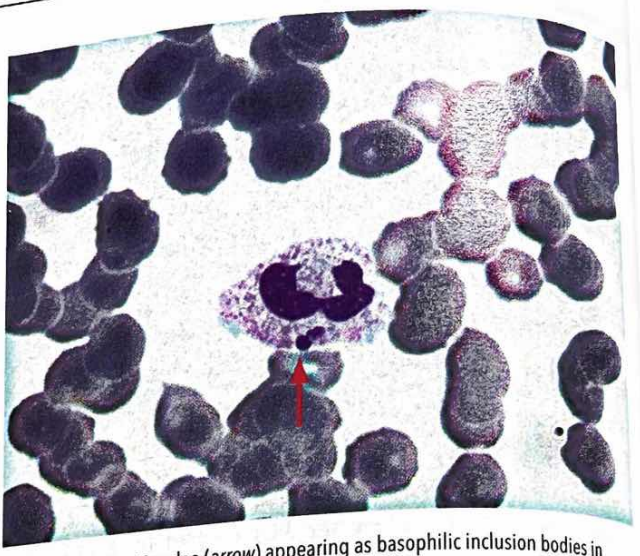

FIGURE 15. Morulae (*arrow*) appearing as basophilic inclusion bodies in leukocytes of a patient with ehrlichiosis.

TABLE 15. Comparison of Epidemiologic and Clinical Features of Ehrlichiosis, Anaplasmosis, and Spotted Fever Rickettsioses

Feature	Ehrlichiosis	Anaplasmosis	Spotted Fever Rickettsioses
Vector	Lone Star tick	Blacklegged deer tick	American dog tick, brown dog tick, Rocky Mountain wood tick, and others
Geography	Southeastern, mid-Atlantic, and south-central United States	Northeastern and upper Midwest United States	Throughout the United States[a]
Coinfection	Not reported; potential for coinfection with STARI, Heartland virus, or Bourbon virus because of common vector	Lyme disease, babesiosis; potential for coinfection with Powassan virus, *Borrelia miyamotoi*, or *Ehrlichia muris eauclairensis* because of common vector	Not reported
Incubation period	5-14 days	5-14 days	3-12 days
Presenting signs and symptoms	Fever, headache, myalgias	Fever, headache, myalgias, chills	Fever, headache, chills, myalgias, abdominal pain, meningismus
Cutaneous signs	Nonspecific rash in <30% of adults, with median onset 5 days after fever	Rash rare (<10%)	Maculopapular eruption in >90% of patients, progressing to petechia with involvement of palms and soles; onset, median of 3 days after fever
Laboratory study abnormalities	Leukopenia, thrombocytopenia, increased serum aminotransferase levels	Leukopenia, thrombocytopenia, increased serum aminotransferase levels	Thrombocytopenia, increased serum aminotransferase levels, hyponatremia
Diagnosis	Morulae in monocytes (<30%), acute and convalescent serologies, whole-blood PCR	Morulae in neutrophils (~50%), acute and convalescent serologies, whole-blood PCR	Acute and convalescent serologies, biopsy of skin with immunohistochemical analysis or skin PCR
Treatment	Doxycycline	Doxycycline	Doxycycline
Fatality	3%	<1%	5%-10%

PCR = polymerase chain reaction; STARI = Southern tick-associated rash illness.

[a]Two thirds of all spotted fever rickettsial infections occur in Arkansas, Missouri, North Carolina, Oklahoma, and Tennessee.

treatment is associated with increased mortality, empiric therapy should be started even in the absence of confirmatory testing.

KEY POINTS

- Ehrlichiosis and anaplasmosis cause a nonspecific febrile illness beginning 1 to 2 weeks after a tick bite.
- Antibody levels are often negative at the time of presentation in ehrlichiosis and anaplasmosis but usually become positive within 4 weeks of illness; polymerase chain reaction of whole blood at the time of acute illness may be diagnostic.
- Doxycycline is recommended for ehrlichiosis and anaplasmosis; empiric therapy should be started without awaiting results of confirmatory testing.

Spotted Fever Rickettsioses (including Rocky Mountain Spotted Fever)

Spotted fever group rickettsioses (SFR) are a group of closely related tick-borne infections that are serologically indistinguishable. The most common and most serious of the SFR in the United States is Rocky Mountain spotted fever (RMSF), caused by *Rickettsia rickettsii* and transmitted by the dog tick and other vectors (see Figure 11). RMSF has been reported throughout the continental United States but occurs most frequently in a linear distribution extending from North Carolina to Oklahoma.

Clinically, RMSF presents with nonspecific symptoms similar to those of ehrlichiosis and anaplasmosis (see Table 15). The hallmark feature is a rash; however, skin findings are typically delayed by several days after fever onset and may not be apparent at the initial clinical presentation. The rash evolves from a macular eruption localized to the ankles or wrists, with central spread and progression to petechiae or purpura (**Figure 16**). Lesions are found on the palms and soles in as many as 50% of patients; the face is generally spared. Purpura fulminans may occur and result in loss of digits or limbs. Up to 30% of patients present with meningoencephalitis.

Immunohistochemical analysis of skin biopsy samples may be diagnostic. Serology is insensitive during acute illness, and testing convalescent serum is often needed to confirm the diagnosis. Doxycycline should be given empirically when SFR is suspected because treatment delay is associated with more severe disease and increased mortality.

KEY POINTS

- Spotted fever rickettsiosis, including Rocky Mountain spotted fever, presents with nonspecific signs and symptoms such as fever, headache, malaise, myalgia, arthralgia, with a rash developing 3 to 5 days after presentation.
- Doxycycline should be given empirically when spotted fever rickettsiosis is clinically suspected.

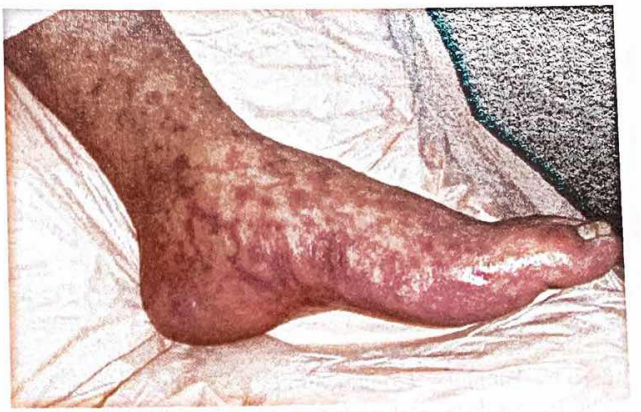

FIGURE 16. Petechial and purpuric skin eruption in a patient with late-stage Rocky Mountain spotted fever. The rash typically begins on the ankles and wrists and spreads toward the trunk.

Reprinted with permission from Biggs HM, Behravesh CB, Bradley KK, Dahlgren FS, Drexler NA, Dumler JS, et al. Diagnosis and management of tickborne rickettsial diseases: Rocky Mountain spotted fever and other spotted fever group rickettsioses, ehrlichioses, and anaplasmosis—United States. MMWR Recomm Rep. 2016;65:1-44. [PMID: 27172113] doi:10.15585/mmwr.rr6502a1

Powassan Virus

Powassan virus is an emerging tick-borne infection (**Table 16**) spread by *Ixodes* ticks. Most reported infections have presented with meningoencephalitis, with a high mortality rate. Diagnostic testing is not commercially available but can be performed through coordination with state health departments. No antiviral therapy is available, and treatment is supportive.

Urinary Tract Infections

Epidemiology and Microbiology

Community-acquired urinary tract infections (UTIs) account for approximately 9 million ambulatory visits and 2 million hospitalizations annually in the United States, making them one of the most common infections for which an antibiotic is prescribed. Another 1 million nosocomial UTIs are diagnosed annually, primarily urinary catheter associated, accounting for approximately 40% of health care–associated infections (see Health Care–Associated Infections). Approximately half of all women experience a UTI by age 30 years; sexual activity is a major risk factor. Other risk factors include structural and functional abnormalities, use of spermicidal agents and diaphragms, pregnancy, diabetes mellitus, obesity, urethral catheterization (or other urinary tract instrumentation), incontinence, immunosuppression, and genetic factors (female relative with history of UTIs).

UTIs are classified based on anatomic location as lower (cystitis), upper (pyelonephritis, perinephric abscess), or prostatitis. The term *uncomplicated* UTI refers to infections in nonpregnant women without structural or neurologic abnormalities or comorbidities. UTIs in men, pregnant women,