KEY POINTS

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

Follow-up

For patients who do not require hospitalization, additional evaluation is only necessary in those who do not respond to empiric therapy within 3 days (of a standard 5-day course) or who develop new symptoms.

In contrast, readmission rates among hospitalized patients approach 20%. This population should have close outpatient follow-up to ensure clinical stability after therapy completion. Radiographic clearance often lags behind clinical response, so repeat imaging should be deferred at initial follow-up unless clinical improvement is slow or new symptoms have developed. Postobstructive pneumonia may be the presenting symptom of bronchial carcinoma, and repeat chest radiography in 2 to 3 months is recommended in patients at high risk (age >50 years or those with a significant smoking history) to document resolution.

KEY POINT

- For patients who do not require hospitalization for community-acquired pneumonia, additional evaluation is only necessary in those who do not respond to empiric therapy within 3 days (of a 5-day course) or who develop new symptoms.

Tick-Borne Diseases

Lyme Disease

Lyme disease is the most common vector-borne infection in the United States. More than 30,000 new infections are reported annually, which likely represent only 10% of actual infections. More than 95% of infections in the United States occur in the northeastern, mid-Atlantic, and upper Midwest regions (**Figure 5**). These areas are endemic for the vector, *Ixodes scapularis* (the black-legged deer tick). The causative spirochete, *Borrelia burgdorferi*, is transmitted intradermally when a tick ingests a blood meal. In Europe, *Borrelia garinii* and *Borellia afzelii* cause Lyme disease, with *Ixodes ricinus* as the tick vector.

After a tick bite by *I. scapularis*, administration of a single dose (200 mg) of doxycycline may decrease the risk of subsequent Lyme disease development but should be considered only if (1) the tick is reliably identified as a black-legged deer tick; (2) attachment lasts 36 hours or longer; (3) antibiotics can be started less than 72 hours after tick removal; (4) prevalence of *B. burgdorferi* infection of ticks in the region exceeds 20%; and (5) doxycycline treatment is not contraindicated. Except for these selected situations, observation is recommended, with treatment given if suggestive symptoms occur.

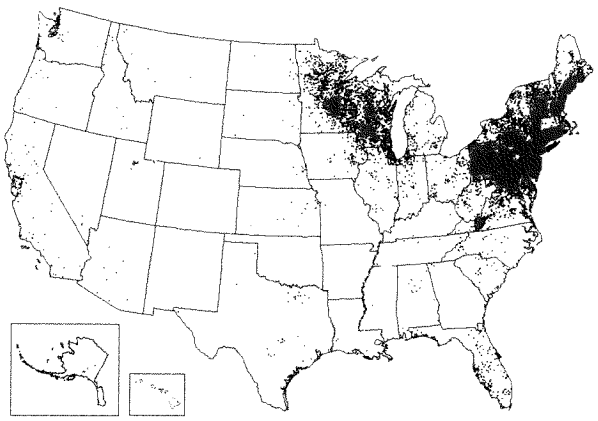

FIGURE 5. Lyme disease cases reported during 2016. Each dot represents the county of residence (not necessarily acquisition) for a confirmed case.

Reprinted with permission from "Reported Cases of Lyme Disease—United States 2016" (Washington, D.C.: Department of Health and Human Services, 2016), https://www.cdc.gov/lyme/resources/reportedcasesoflymedisease_2016.pdf.

The clinical manifestations, diagnostic testing, and treatment of Lyme disease vary according to the stage of infection (**Table 16**).

Early Localized Disease

Early localized disease presents within 4 weeks of infection. Most infected persons (70% to 80%) develop erythema migrans (EM), an annular skin lesion that often presents with central clearing (**Figure 6**). Systemic symptoms are variably present.

EM lesions are typically painless, nonpruritic, and circumferentially enlarging. Atypical presentations of EM, with confluent erythroderma, ulceration, or vesiculation, may confound the diagnosis. Local cutaneous reactions due to 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 onset of an EM lesion. Treatment is with an oral agent. Doxycycline offers the advantage of treating incubating *Anaplasma phagocytophilum*, which also is spread by black-legged ticks and can coinfect patients with Lyme disease.

Early Disseminated Disease

In the absence of 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

TABLE 16. 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, fever, lymphadenopathy, myalgia	Not needed if EM present	Doxycycline, 100 mg PO BID × 10-21 d (first-line therapy) *or* Amoxicillin, 500 mg PO TID × 14-21 d *or* Cefuroxime axetil, 500 mg PO BID × 14-21 d
Early disseminated	2 wk-6 mo	Multiple sites of EM, flu-like syndrome, heart block, myocarditis, facial nerve palsy, meningitis, radiculitis	Not needed if EM is present; otherwise, two-tier serologic testing CSF testing for intrathecal antibody production if CNS involvement is a concern	1. First-degree block with PR interval ≥300 msec, second- or third-degree AV nodal block, myocarditis: IV penicillin or IV ceftriaxone × 28 d 2. First-degree AV block with PR interval <300 msec: oral treatment same as for early localized disease × 14-28 d 3. Meningitis: IV penicillin or IV ceftriaxone × 28 d 4. Other manifestations (including facial palsy): oral treatment the same as for early localized disease × 14-28 d
Late disseminated	≥6 mo	Recurrent large joint 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 × 30 d Recurrent arthritis after initial treatment: IV ceftriaxone Neurologic disease: IV ceftriaxone × 28 d

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.

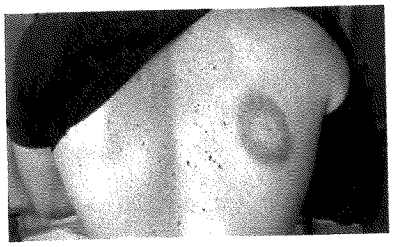

FIGURE 6. Erythema migrans lesion at site of tick attachment.

Figure courtesy of Dr. Karen Bloch.

associated with multiple concurrent EM lesions at sites distant from the original tick attachment.

Infection of cardiac tissue 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 patients with severe cardiac involvement: symptomatic patients with dizziness, syncope, or dyspnea; asymptomatic patients with first-degree AV block and a PR interval of 300 milliseconds or greater; and patients with a higher-degree AV block. Permanent pacemaker placement is not necessary because the heart block is reversible.

Infection of neurologic tissue occurs in approximately 15% of untreated patients. Aseptic meningitis, facial palsy (unilateral or bilateral), and radiculopathy may be present in isolation or associated with skin, musculoskeletal, or cardiac findings. Lumbar puncture is indicated when central nervous system infection (such as neuroborreliosis) is suspected; cerebrospinal fluid lymphocytic pleocytosis supports the diagnosis (see Central Nervous System Infection).

When EM lesions are present, laboratory confirmation is unnecessary. In the absence of diagnostic skin findings, serologic diagnosis should be pursued through a two-tiered approach (**Figure 7**); the initial enzyme-linked immunosorbent assay (ELISA) is highly sensitive but lacks specificity and must be confirmed by a Western blot test. The C6 ELISA test detects antibody against a highly conserved bacterial epitope and may be more sensitive than traditional whole-cell sonicate ELISA, especially for the

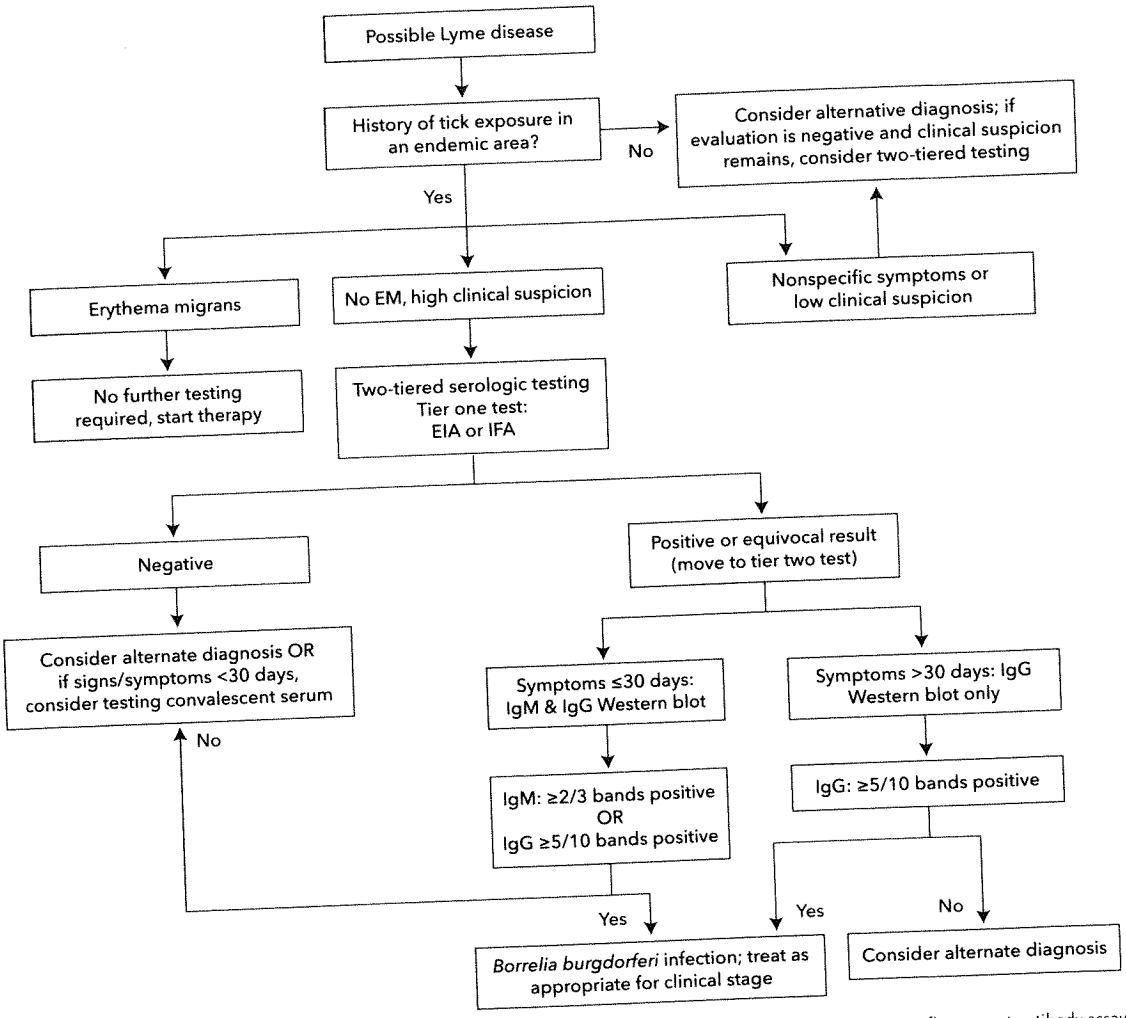

FIGURE 7. Serologic testing for Lyme disease. EIA = enzyme-linked immunosorbent assay; EM = erythema migrans; IFA = immunofluorescent antibody assay.

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

European strains *B. garinii* and *B. afzelii*, but, because of insufficient specificity, confirmatory Western blot testing is still required.

IgM antibody is detectable before IgG antibody in early infection; however, IgG antibody should be detectable after 30 days of symptoms. Because isolated IgM positivity is likely to be a false positive after the first month of symptoms, testing for IgM is not recommended after this time period. Antibodies may remain 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 18 Rheumatology). Late neurologic or skin findings (acrodermatitis chronica atrophicans and borrelial lymphocytoma) are rare in the United States but more frequent in European infections. Diagnosis is made with the two-tier serologic test. Treatment requires prolonged oral antibiotics; parenteral therapy is used when oral therapy is unsuccessful (see Table 16).

Post-Lyme Disease Syndrome

Post-Lyme disease syndrome has been reported in approximately 10% of patients after treatment of EM (**Table 17**). Although often erroneously called "chronic Lyme disease," studies have found no microbiologic evidence of chronic or latent infection after appropriate treatment. Symptoms include fatigue, arthralgia, myalgia, and impairment of memory or cognition that can last for years after treatment of the acute infection. Clinical trials have shown no benefit of prolonged antibiotic treatment for post-Lyme disease syndrome.

TABLE 17. Definition of Post-Lyme Disease Syndrome

Inclusion Criteria
Diagnosis of Lyme disease based on CDC case criteria (EM or positive serologic finding)
Resolution or stabilization of the objective manifestations of Lyme disease after standard treatment
Onset of at least one of the following within 6 months of Lyme disease diagnosis, with persistence for at least 6 months after antibiotic treatment, that is of sufficient severity to result in decreased level of functioning:
1. Fatigue
2. Widespread musculoskeletal pain
3. Cognitive impairment
Exclusion Criteria
An untreated tick-borne coinfection (such as babesiosis)
Ongoing symptoms attributable to Lyme disease (such as antibiotic-refractory Lyme arthritis)
Symptoms of fatigue or musculoskeletal pains or a diagnosis of fibromyalgia or chronic fatigue syndrome predating the onset of Lyme disease
An alternative diagnosis accounting for the symptoms

CDC = Centers for Disease Control and Prevention; EM = erythema migrans.

Source: Wormser GP, Dattwyler RJ, Shapiro ED, Halperin JJ, Steere AC, Klempner MS, et al. The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis. 2006;43:1089-134. [PMID: 17029130]

Evaluation for coinfection with another tick-borne pathogen or for a noninfectious cause is indicated; when no alternative diagnosis is found, treatment is symptomatic.

KEY POINTS

- The causative spirochete of Lyme disease may be transmitted when an infected *Ixodes scapularis* tick attaches for at least 36 hours.

HVC

- 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 antibiotic therapy.
- 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 Western blot testing, with presumptive treatment depending on disease severity.
- Post–Lyme disease syndrome (fatigue, arthralgia, myalgia, and impairment of memory or cognition) can last for years, even after treatment of the acute infection; there is no role for prolonged antibiotics for this condition.

Babesiosis

Babesiosis is caused by the intraerythrocytic protozoan *Babesia microti*, which is spread by the black-legged deer tick. Because of the common vector, babesiosis occurs in areas of Lyme endemicity (see Figure 5), most frequently during summer months. In Europe, babesiosis is caused by several different *Babesia* species and is spread by the *I. ricinus* tick. Transfusion of infected blood products and rare congenital transmission also allows for year-round infection, which may occur outside endemic regions.

Clinical findings range from asymptomatic presentations (approximately 20%) to fatal disease (10%). Risk factors for severe disease include age older than 50 years, immunocompromise, or asplenia. Symptoms begin within 1 month after tick bite and within 6 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. With severe disease, thrombocytopenia, elevated liver enzyme levels, and acute kidney injury are possible.

Babesiosis is diagnosed by visualization of the causative organism on thin blood smears, manifesting as intraerythrocytic ring forms similar to those seen in malaria or as tetrads resembling a Maltese cross (**Figure 8**). With low-level parasitemia, multiple smears may need to be examined, and the sensitivity of microscopy is low. Therefore, polymerase chain reaction or serology should be pursued if smear findings are negative but clinical suspicion of babesiosis is high.

Treatment depends on disease severity (**Table 18**). After treatment, patients should be monitored closely for relapse; if relapse occurs, prolonged therapy extending more than 2 weeks after clearance of parasitemia is necessary for cure.

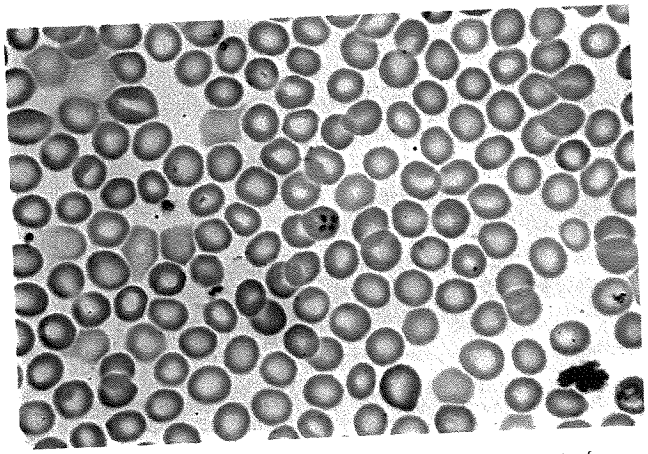

FIGURE 8. Peripheral blood smear showing babesiosis. The diagnosis of babesiosis is typically established by evaluation of a peripheral blood smear showing intraerythrocytic parasites. Occasionally, merozoites are arranged in tetrads, resembling a Maltese cross.

TABLE 18. Treatment for Babesiosis

Severity	Regimen
Asymptomatic, ≤3 months of parasitemia	Monitor for clearance; no treatment indicated
Asymptomatic, >3 months of parasitemia	Atovaquone plus azithromycin
Mild to moderate disease	Atovaquone plus azithromycin
Severe disease requiring ICU admission	Clindamycin plus quinine
Severe disease with >10% parasitemia, hemoglobin level <10 g/dL (100 g/L), ARDS, liver failure or kidney failure	Clindamycin plus quinine *and* Exchange transfusion

ARDS = acute respiratory distress syndrome.

KEY POINTS

- Babesiosis, an infection caused by an intraerythrocytic protozoan, presents with clinical findings ranging from asymptomatic infection to fatal disease; symptoms are usually nonspecific, but hemolytic anemia is a hallmark of disease.
- Diagnosis of babesiosis is by visualization of the organism on blood smear, serology, or polymerase chain reaction.
- Treatment of babesiosis depends on disease severity; atovaquone plus azithromycin are most appropriate for mild disease, whereas clindamycin plus quinine remains the regimen of choice for severe disease.

Southern Tick-Associated Rash Illness

Southern tick-associated rash illness (STARI) presents with EM lesions identical to those seen in Lyme disease but without clinical progression or complications. STARI is associated with *Amblyomma americanum*, also known as the Lone Star tick, and occurs in the southeastern, south-central, and eastern United States. No infectious cause has been confirmed. Therefore, diagnosis is based on clinical and geographic features. Because STARI and early-stage Lyme disease may be clinically indistinguishable, treatment with doxycycline is recommended.

KEY POINT

- Southern tick-associated rash illness may be clinically indistinguishable from early-stage Lyme disease, and thus treatment with doxycycline is recommended.

Human Monocytic Ehrlichiosis and Granulocytic Anaplasmosis

Human monocytic ehrlichiosis (HME) and human granulocytic anaplasmosis (HGA) are clinically similar illnesses spread by different tick vectors and caused by distinct bacterial pathogens. HME is caused by *Ehrlichia chaffeensis*, which is transmitted by the Lone Star tick, and occurs most commonly in the southeastern and south-central United States. HGA is caused by *Anaplasma phagocytophilum*, which is transmitted by *Ixodes* ticks, and occurs in areas of Lyme endemicity (see Figure 5).

These syndromes typically begin with a nonspecific febrile illness 1 to 2 weeks after a tick bite (**Table 19**). Rash is uncommon in contrast to Rocky Mountain spotted fever. Laboratory study abnormalities, including leukopenia, thrombocytopenia, and increased serum aminotransferase levels, are nonspecific.

The organisms causing HME and HGA replicate inside leukocytes and cause hallmark basophilic inclusion bodies called morulae (**Figure 9**). Serologic findings often are negative in acute illness; testing of a convalescent specimen 2 to 4 weeks after onset of symptoms is usually confirmatory. Polymerase chain reaction of whole blood at the time of acute illness may be diagnostic, particularly if performed before therapy. Doxycycline is the recommended treatment for both HME and HGA. Because delay in treatment is associated with increased mortality, empiric therapy should be started even in the absence of confirmatory testing.

KEY POINTS

- Human monocytic ehrlichiosis and human granulocytic anaplasmosis cause a nonspecific febrile illness beginning 1 to 2 weeks after a tick bite.
- Acute serologic findings are often negative in both human monocytic ehrlichiosis and human granulocytic anaplasmosis; polymerase chain reaction of whole blood at the time of acute illness may be diagnostic.
- Doxycycline is recommended for both human monocytic ehrlichiosis and human granulocytic anaplasmosis; empiric therapy should be started without awaiting results of confirmatory testing.

Rocky Mountain Spotted Fever

Rocky Mountain spotted fever (RMSF) is caused by *Rickettsia rickettsii* and transmitted by multiple tick vectors. It has been reported throughout the continental United States but occurs most frequently in the "RMSF belt" extending from North Carolina to Oklahoma.

Clinically, RMSF presents with nonspecific symptoms similar to those of HME and HGA (Table 19) but can progress to aseptic meningoencephalitis. The hallmark feature is a macular eruption around the ankles or wrists, with central spread and progression to petechiae or purpura (**Figure 10**). 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. Although skin findings are ultimately noted in greater than 90% of patients with RMSF, the earliest macular rash occurs a median of 3 days after onset

TABLE 19. Comparison of Epidemiologic and Clinical Features of Human Monocytic Ehrlichiosis, Human Granulocytic Anaplasmosis, and Rocky Mountain Spotted Fever

Feature	HME	HGA	RMSF
Vector	Lone Star tick	Black-legged deer tick	American dog tick, brown dog tick, Rocky Mountain wood tick
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 or Heartland virus because of common vector	Lyme disease, babesiosis, Powassan virus, *Borrelia miyamotoi*	None
Incubation period	5-14 days	5-14 days	3-12 days
Presenting signs and symptoms	Fever, headache, myalgias, nausea, vomiting, diarrhea, conjunctival injection	Fever, headache, myalgias, chills	Fever, headache, chills, mylagia, nausea, abdominal pain, photophobia, aseptic meningitis
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, edema; onset, median of 3 days after fever
Laboratory study abnormalities	Leukopenia, thrombocytopenia, increased serum aminotransferase levels, mild anemia	Leukopenia, thrombocytopenia, increased serum aminotransferase levels, mild anemia	Thrombocytopenia, increased serum aminotransferase levels, normal or slightly increased leukocyte count, 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
Treatment	Doxycycline	Doxycycline	Doxycycline
Fatality	3%	<1%	5%-10%

HGA = human granulocytic anaplasmosis; HME = human monocytic ehrlichiosis; PCR = polymerase chain reaction; RMSF = Rocky Mountain spotted fever; STARI = Southern tick-associated rash illness.

[a]Two thirds of all patients with RMSF are infected in Arkansas, Missouri, North Carolina, Oklahoma, and Tennessee.

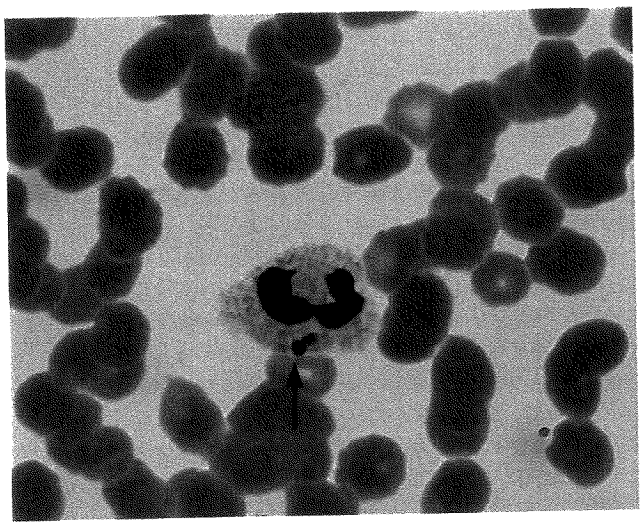

FIGURE 9. Morulae (*arrow*) appearing as basophilic inclusion bodies in leukocytes of a patient with ehrlichiosis.

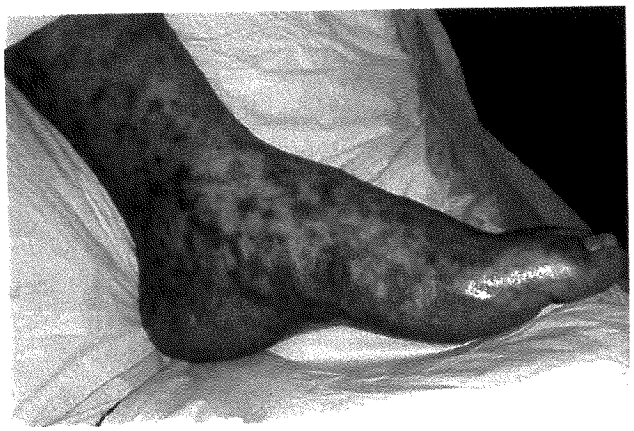

FIGURE 10. Petechial and purpuric skin eruption in a patient with late-stage Rocky Mountain spotted fever.

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

of fever and thus may not be found at the first clinical presentation.

Immunohistochemical analysis of skin biopsy samples may be diagnostic. As with HME and HGA, acute serology is not sensitive, although testing convalescent serum may provide a retrospective diagnosis. Doxycycline should be given empirically when RMSF is clinically suspected because treatment delay is associated with more severe disease and increased mortality.

KEY POINTS

- Rocky Mountain spotted fever (RMSF) presents similarly to both human monocytic ehrlichiosis and human granulocytic anaplasmosis; the major differentiating feature of RMSF is the presence of a rash, but the rash may not appear until 3 days after onset of fever.
- Doxycycline should be given empirically when Rocky Mountain spotted fever is clinically suspected.

Urinary Tract Infections

Epidemiology and Microbiology

Community-acquired urinary tract infections (UTIs) account for approximately 8 million ambulatory visits and 1 million hospitalizations each year in the United States, making them one of the most common infections for which an antibiotic is prescribed in clinical practice. Another 1 million nosocomial UTIs are diagnosed annually, primarily indwelling urinary catheter-associated UTIs, accounting for an estimated 40% of all 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. Approximately 5% of otherwise healthy women who experience a UTI are at greater risk of developing future infections. Other UTI risk factors include structural and functional abnormalities, use of spermicidal agents and diaphragms, pregnancy, diabetes mellitus, obesity, urethral catheterization (or other urinary tract instrumentation), immunosuppression, and genetic factors.

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, and persons with foreign bodies (for example, indwelling catheters, calculi), kidney disease, immunocompromise, obstruction, urinary retention from neurologic disorders, health care-associated infections, or recent antibiotic use are considered to be *complicated*. Advanced age in the presence of other major comorbidities or with significant frailty may be considered a complicating factor in UTI, although age alone does not define a complicated versus uncomplicated infection. Designating an infection as complicated influences the choice and duration of antimicrobial therapy and extent of investigation. Nevertheless, the potential for uncomplicated UTIs to evolve into clinically severe disease should not be underestimated, nor should the urgency or seriousness of complicated UTIs be overstated.

Most infections occur by the ascending route. In 95% of these cases, UTIs are caused by a single bacterial species, mainly gram-negative aerobic bacilli originating from the bowel. Uropathogenic *Escherichia coli* accounts for 75% to 95% of UTIs in women. Less common urinary pathogens include other members of the Enterobacteriaceae family, streptococci (in particular *Streptococcus agalactiae*), enterococci, and staphylococci (most often *Staphylococcus saprophyticus*). UTIs occurring in hospitals and long-term care facilities frequently involve a more varied group of organisms (such as *Enterobacter*, *Providencia*, *Morganella*, *Citrobacter*, *Serratia*, and *Pseudomonas*). Isolation of *Staphylococcus aureus* from the urine may be related to instrumentation but should suggest the possibility of a hematogenous infection from a source outside the urinary tract. H

KEY POINTS

- The term *uncomplicated* urinary tract infection refers to infections in nonpregnant women without structural or neurologic abnormalities or comorbidities.
- Designating an infection as complicated influences the choice and duration of antimicrobial therapy and extent of investigation.
- Urinary tract infections in men, pregnant women, and persons with foreign bodies, kidney disease, immunocompromise, obstruction, urinary retention from neurologic disorders, health care-associated infections, or recent antibiotic use are considered to be *complicated*.

Diagnosis H

In persons with symptoms of UTI, diagnosis in the outpatient setting is based on a combination of clinical features, determining if the presumed infectious process is in the lower or upper urinary tract, and the findings of significant pyuria (≥10 leukocytes/μL) and bacteriuria (bacteria in the urine). Pyuria can be detected by urine dipstick, which relies on the presence of leukocyte esterase. Although the sensitivity and specificity of dipstick testing are high (about 75% and 85%, respectively), pyuria may result from urinary tract disorders other than infection. The presence of leukocyte casts supports a diagnosis of pyelonephritis. Microscopic or gross hematuria may be present with a UTI but may also be encountered with nephrolithiasis and tumors. A positive nitrite test result signifies the presence of gram-negative bacteria capable of converting nitrates into nitrites but is negative in UTI caused by nonconverting organisms (*Enterococcus*, *Staphylococcus*, or *Streptococcus* species).

Quantitative cultures of a midstream, clean-void urine sample are the most accurate way to demonstrate bacteriuria in patients with suspected UTI. Because the microbiology is predictable and treatment courses are short, culture is not recommended in women with uncomplicated cystitis. Urine cultures are indicated in pyelonephritis, complicated cystitis, and recurrent UTIs; additionally, they are recommended in patients with histories of multiple antibiotic allergies and in those in whom the presence of a resistant organism is suspected (such as recent antibiotic treatment, health care-associated infection, previous multidrug-resistant UTI). The growth of 10^5 colony-forming units (CFU)/mL of urine is considered significant bacteriuria; however, lower CFU counts support a diagnosis in those with UTI symptoms.