



Tick-borne illness:

The signs and symptoms of Lyme disease, ehrlichiosis, and babesiosis

The following information is based on the most current clinical guidelines and authoritative reviews, including those from the Infectious Diseases Society of America, the American Academy of Neurology, the American College of Rheumatology, and the United States Centers for Disease Control and Prevention.^[1-5]

Lyme Disease

- Expanding red rash at the tick bite site (erythema migrans, often “bull’s-eye”)
- Fever, chills, fatigue, headache, muscle and joint aches
- Later: facial paralysis, meningitis, heart rhythm disturbances, arthritis (especially knees)

Ehrlichiosis

- Sudden high fever, chills, headache, muscle aches
- Malaise, fatigue
- Gastrointestinal symptoms: nausea, vomiting, diarrhea, loss of appetite
- Rash (more common in children, up to 30%)
- Confusion or altered mental status in severe cases

Babesiosis

- Fever, chills, sweats
- Fatigue, malaise, muscle aches, headache
- Dark urine (from hemolysis)
- Less common: cough, sore throat, jaundice, enlarged spleen/liver
- Severe: shortness of breath, low blood pressure, organ failure (especially in immunocompromised or asplenic individuals)

The table below, from The New England Journal of Medicine, provides a side-by-side comparison of these and other tick-borne diseases, highlighting their clinical features, vectors, and comments on coinfection risk.



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Table 2. Selected Zoonotic and Vectorborne Infections That May Cause FUO.*

Entity, Pathogens, and Syndromes	Region and Population (Seasonality)	Vector	Reservoir	Manifestations	Treatment	Comments
Rickettsioses						
<i>Rickettsia rickettsii</i> (Rocky Mountain spotted fever), <i>R. africae</i> (African tick bite fever), <i>R. typhi</i> (murine endemic typhus), <i>R. prowazekii</i> (epidemic typhus), <i>Orientia tsutsugamushi</i> (scrub typhus)	All continents except Antarctica (varies)	Ticks, fleas, lice, mites	Small mammals, including rats and flying squirrels (<i>R. prowazekii</i>)	Febrile syndromes with rashes (mild to fatal with DIC and encephalitis); inoculation ulcer uncommon	Tetracyclines	Tropism for vascular endothelial cells results in increased vascular permeability; thus, rash is expected in nearly all cases
Babesiosis						
<i>Babesia</i> species (e.g., <i>B. microti</i> in the U.S., <i>B. divergens</i> in Europe, <i>B. venatorum</i> in China)	Northeastern, southeastern, and upper midwestern U.S.; Europe; northeastern China (usually May–September)	<i>Ixodes scapularis</i> (deer tick); transfusion-related uncommon	White-footed mouse	Constitutional symptoms, hemolysis, ARDS; rash uncommon	Azithromycin plus atovaquone, clindamycin plus quinine	Rash should arouse suspicion of Lyme disease; immunocompromised and asplenic patients at risk for severe disease; coinfection with babesia, anaplasma, borrelia, and Powassan virus in the U.S.
Anaplasmosis						
<i>Anaplasma phagocytophilum</i> (human granulocytic anaplasmosis)	Northeastern and upper midwestern U.S.; central Europe; Asia (mainly spring and summer)	<i>I. scapularis</i>	White-footed mouse	Constitutional symptoms, fever, cytopenias, elevated aminotransferase levels; rash uncommon	Tetracyclines	Rash should arouse suspicion of Lyme disease; coinfection with babesia, anaplasma, borrelia, and Powassan virus in U.S.
Lyme disease						
<i>Borrelia burgdorferi</i> and other borrelia species, <i>B. mayonii</i> in upper midwestern U.S.	Northeastern and upper midwestern U.S.; Europe; Asia (June–August)	<i>I. scapularis</i> in the U.S.	Rodents (e.g., white-footed mouse)	Erythema migrans rash; cardiac, articular, neurologic manifestations; fever uncommon	Tetracyclines, amoxicillin, cefuroxime, ceftriaxone	Coinfection with babesia, anaplasma, borrelia, and Powassan virus in the U.S.; Jarisch–Herxheimer reaction with treatment can present as fever
Ehrlichiosis						
<i>Ehrlichia chaffeensis</i> (human monocytic ehrlichiosis), <i>E. ewingii</i> , <i>E. muris eauclairensis</i> (uncommon)	Southeastern, south-central, and mid-Atlantic U.S.; <i>E. muris</i> and <i>E. muris eauclairensis</i> : Minnesota and Wisconsin (spring and summer)	Lone Star tick (<i>Amblyomma americanum</i>); <i>E. muris</i> and <i>E. muris eauclairensis</i> : <i>I. scapularis</i>	White-tailed deer; <i>E. muris</i> and <i>E. muris eauclairensis</i> : white-footed mouse	Acute febrile illness, systemic symptoms, cytopenia, elevated aminotransferase levels; rash in up to 30% of patients	Tetracyclines	Unexplained fever may last between 17 and 51 days ³¹
Bartonellosis						
<i>Bartonella bacilliformis</i> (Oroya fever); <i>B. quintana</i> , <i>B. henselae</i> (bacteremia, culture-negative endocarditis, bacillary angiomatosis); <i>B. henselae</i> (cat scratch disease)	Oroya fever: valleys of Andes mountains; others: worldwide, homeless populations, persons with HIV infection (year-round)	Varies by organism and syndrome; sandflies, body lice, cat fleas	<i>B. bacilliformis</i> : humans; <i>B. quintana</i> : nonhuman primates; <i>B. henselae</i> : cats	Vary; fevers, constitutional symptoms, culture-negative endocarditis; lymphadenopathy with cat scratch disease; peliosis hepatis with bacillary angiomatosis	Varies by syndrome; tetracycline-based regimens often used; quinolones, rifampin, macrolides used	Survivors of Oroya fever are temporarily at risk for salmonellosis; cat scratch disease can be disseminated in immunocompromised hosts
Leptospirosis						
<i>Leptospira interrogans</i> and other species	Ubiquitous and worldwide (variable; reportedly summer and fall)	Infection typically occurs after exposure to environmental sources (e.g., water/soil contaminated with animal urine)	Multiple mammals (e.g., rodents, cattle, horses)	Protean: fevers, constitutional symptoms, classic conjunctival suffusion; cough, myalgias, aseptic meningitis, pulmonary hemorrhage, jaundice; renal failure (Weil's disease)	Penicillin, tetracyclines	Inoculation into minor breaks in the skin or exposure of mucosal surfaces, occupational exposures (farmers, abattoir workers), adventure tourism
Brucellosis						
<i>Brucella</i> species (e.g., <i>B. melitensis</i> , <i>B. abortus</i> , <i>B. suis</i> , <i>B. canis</i>)	Mediterranean basin, Middle East, Asia, Africa, Mexico, Central and South America (year-round)	Infection occurs after consumption or inhalation of or contact with infected animal products	Various mammals: sheep, goats, cattle, camels, dogs	Malaise, night sweats, arthralgias, back pain, constitutional symptoms; can lead to endocarditis, spondylitis, orchitis or epididymitis	Doxycycline, rifampin, TMP-SMX, ceftriaxone, aminoglycosides	Rare in the U.S. (consumption of imported, unpasteurized dairy products); special handling in microbiology laboratories; postexposure prophylaxis recommended for laboratory exposure
Q fever						
<i>Coxiella burnetii</i>	Worldwide (year-round)	Ticks; animal feces, urine, placentas, or inhalation	Mammals (cattle, other farm animals), birds, arthropods	Fever, influenza-like illness, pneumonia, hepatitis; endocarditis, obstetrical complications	Varies; doxycycline, TMP-SMX, macrolides, hydroxychloroquine	Highest risk in persons in contact with farm animals, laboratory workers, and abattoir workers
Viral zoonoses						
Hantavirus; Powassan virus in Northeastern, West Nile, Zika, dengue, and chikungunya viruses; St. Louis encephalitis; equine encephalitis virus; others	Vary; Powassan virus in northeastern U.S. and Great Lakes region; Canada; Russia (variable seasons)	Sandflies, mosquitoes, ticks (ixodes for Powassan virus)	Primates, birds, rabbits, rodents, cattle, others	Systemic febrile illness; rash, arthralgia, meningoencephalitis, cytopenia, hemorrhage, respiratory failure	Supportive	Illness ranges from self-limited (Zika virus) to potentially chronically debilitating (chikungunya and West Nile viruses) to fatal (hantavirus); consider coinfection with babesia, anaplasma, borrelia, and Powassan virus in U.S.

* Diagnosis of many of these entities can be challenging, and diagnostic testing (including serologic testing, polymerase-chain-reaction assay, and culture) may be insensitive or not readily available (see Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org, for other entities that may cause FUO). ARDS denotes acute respiratory distress syndrome, DIC disseminated intravascular coagulation, and TMP-SMX trimethoprim–sulfamethoxazole.