# SECTION 10 DISEASES CAUSED BY RICKETTSIAE, MYCOPLASMAS, AND CHLAMYDIAE

## 211 Rickettsial Diseases

David H. Walker, J. Stephen Dumler, Thomas Marrie

The rickettsiae are a heterogeneous group of small, obligately intracellular, gram-negative coccobacilli and short bacilli, most of which are transmitted by a tick, mite, flea, or louse vector. Except in the case of louse-borne typhus, humans are incidental hosts. Among rickettsiae, *Coxiella burnetii*, *Rickettsia prowazekii*, and *R. typhi* have the well-documented ability to survive for an extended period outside the reservoir or vector and to be extremely infectious: inhalation of a single *Coxiella* microorganism can cause pneumonia. High-level infectivity and severe illness after inhalation make *R. prowazekii*, *R. rickettsii*, *R. typhi*, *R. conorii*, and *C. burnetii* bioterrorism threats.

Clinical infections with rickettsiae can be classified according to (1) the taxonomy and diverse microbial characteristics of the agents, which belong to seven genera (*Rickettsia*, *Orientia*, *Ehrlichia*, *Anaplasma*, *Neorickettsia*, *Candidatus* Neoehrlichia, and *Coxiella*); (2) epidemiology; or (3) clinical manifestations. The clinical manifestations of all the acute presentations are similar during the first 5 days: fever, headache, and myalgias with or without nausea, vomiting, and cough. As the course progresses, clinical manifestations—including occurrence of a macular, maculopapular, or vesicular rash; eschar; pneumonitis; and meningoencephalitis—vary from one disease to another. Given the 15 etiologic agents with varied mechanisms of transmission, geographic distributions, and associated disease manifestations, the consideration of rickettsial diseases as a single entity poses complex challenges **(Table 211-1)**.

Establishing the etiologic diagnosis of rickettsioses is very difficult during the acute stage of illness, and definitive diagnosis usually requires the examination of paired serum samples after convalescence. Heightened clinical suspicion is based on epidemiologic data, history of exposure to vectors or reservoir animals, travel to endemic locations, clinical manifestations (sometimes including rash or eschar), and characteristic laboratory findings (including thrombocytopenia, normal or low white blood cell [WBC] counts, elevated hepatic enzyme levels, and hyponatremia). Such suspicion should prompt empirical treatment. Doxycycline is the drug of choice for most of these infections. Only one agent, *C. burnetii*, has been documented to cause chronic illness. One other species, *R. prowazekii*, causes recrudescent illness (Brill-Zinsser disease) when latent infection is reactivated years after resolution of the acute illness.

Rickettsial infections dominated by fever may resolve without further clinical evolution. However, after nonspecific early manifestations, the illnesses can also evolve along one or more of several principal clinical lines: (1) development of a macular or maculopapular rash; (2) development of an eschar at the site of tick or mite feeding; (3) development of a vesicular rash (often in rickettsialpox and African tick-bite fever); (4) development of pneumonitis with chest radiographic opacities and/or rales (Q fever and severe cases of Rocky Mountain spotted fever [RMSF], Mediterranean spotted fever [MSF], louse-borne typhus, human monocytotropic ehrlichiosis [HME], human granulocytotropic anaplasmosis [HGA], scrub typhus, and murine typhus); (5) development of meningoencephalitis (louse-borne typhus and severe cases of RMSF, scrub typhus, HME, murine typhus, MSF, and [rarely] Q fever); and (6) progressive hypotension and multiorgan failure as seen with sepsis or toxic shock syndromes (RMSF, MSF, louse-borne typhus, murine typhus, scrub typhus, HME, HGA, and neoehrlichiosis).

Epidemiologic clues to the transmission of a particular pathogen include (1) environmental exposure to ticks, fleas, or mites during the season of activity of the vector species for the disease in the appropriate geographic region (spotted fever and typhus rickettsioses, scrub typhus, ehrlichioses, anaplasmosis); (2) travel to or residence in an endemic geographic region during the incubation period (Table 211-1); (3) exposure to parturient ruminants, cats, and dogs (Q fever); (4) exposure to flying squirrels (*R. prowazekii* infection); and (5) history of previous louse-borne typhus (recrudescent typhus).

Clinical laboratory findings, such as thrombocytopenia (particularly in spotted fever and typhus rickettsioses, ehrlichioses, anaplasmosis, and scrub typhus), normal or low WBC counts, mild to moderate serum elevations of hepatic aminotransferases, and hyponatremia, suggest some common pathophysiologic mechanisms.

Application of these clinical, epidemiologic, and laboratory principles requires consideration of a rickettsial diagnosis and knowledge of the individual diseases.

### TICK-, MITE-, LOUSE-, AND FLEA-BORNE RICKETTSIOSES

These diseases, caused by organisms of the genera *Rickettsia* and *Orientia* in the family Rickettsiaceae, result from endothelial cell infection and increased vascular permeability. Pathogenic rickettsial species are very closely related, have small genomes (as a result of reductive evolution, which eliminated many genes for biosynthesis of intracellularly available molecules), and are traditionally separated into typhus and spotted fever groups on the basis of lipopolysaccharide antigens. Some diseases and their agents (e.g., *R. africae*, *R. parkeri*, and *R. sibirica*) are too similar to require separate descriptions. Indeed, the similarities among MSF (*R. conorii* [all strains] and *R. massiliae*), North Asian tick typhus (*R. sibirica*), Japanese spotted fever (*R. japonica*), and Flinders Island spotted fever (*R. honei*) far outweigh the minor variations. The Rickettsiaceae that cause life-threatening infections are, in order of decreasing case-fatality rate, *R. rickettsii* (RMSF); *R. prowazekii* (louse-borne typhus); *Orientia tsutsugamushi* (scrub typhus); *R. conorii* (MSF); *R. typhi* (murine typhus); and, in rare cases, other spotted fever–group organisms. Some agents (e.g., *R. parkeri*, *R. africae*, *R. akari*, *R. slovaca*, *R. honei*, *R. felis*, *R. massiliae*, *R. helvetica*, *R. heilongjiangensis*, *R. aeschlimannii*, and *R. monacensis*) have never been documented to cause a fatal illness.

#### ROCKY MOUNTAIN SPOTTED FEVER

**Epidemiology** RMSF occurs in 47 states (with the highest prevalence in the south-central and southeastern states) as well as in Canada, Mexico, and Central and South America. The infection is transmitted by *Dermacentor variabilis*, the American dog tick, in the eastern two-thirds of the United States and California; by *D. andersoni*, the Rocky Mountain wood tick, in the western United States; by *Rhipicephalus sanguineus* in Mexico, Arizona, and probably Brazil; and by *Amblyomma cajennense* and *A. aureolatum* in Central and/or South America. Maintained principally by transovarian transmission from one generation of ticks to the next, *R. rickettsii* can be acquired by uninfected ticks through the ingestion of a blood meal from rickettsemic small mammals.

Humans become infected during tick season (in the Northern Hemisphere, from May to September), although some cases occur in winter. The mortality rate was 20–25% in the preantibiotic era and remains at ~3–5%, principally because of delayed diagnosis and treatment. The case-fatality ratio increases with each decade of life above age 20.

**Pathogenesis** *R. rickettsii* organisms are inoculated into the dermis along with secretions of the tick's salivary glands after ≥6 h of feeding.