Rickettsiae

General Concepts

The rickettsiae are a diverse collection of obligately intracellular Gram-negative bacteria found in ticks, lice, fleas, mites, chiggers, and mammals. They include the genera *Rickettsiae, Ehrlichia, Orientia*, and *Coxiella*. These zoonotic pathogens cause infections that disseminate in the blood to many organs.

Clinical Manifestations

Rickettsia species cause Rocky Mountain spotted fever, rickettsialpox, other spotted fevers, epidemic typhus, and murine typhus. *Orientia* (formerly *Rickettsia*) *tsutsugamushi* causes scrub typhus. Patients present with febrile exanthems and visceral involvement; symptoms may include nausea, vomiting, abdominal pain, encephalitis, hypotension, acute renal failure, and respiratory distress.

Structure, Classification, and Antigenic Types

Rickettsia species are small, Gram-negative bacilli that are obligate intracellular parasites of eukaryotic cells. This genus consists of two antigenically defined groups: spotted fever group and typhus group, which are related; scrub typhus rickettsiae differ in lacking lipopolysaccharide, peptidoglycan, and a slime layer, and belong in the separate, although related, genus *Orientia*.

Pathogenesis

Rickettsia and *Orientia* species are transmitted by the bite of infected ticks or mites or by the feces of infected lice or fleas. From the portal of entry in the skin, rickettsiae spread via the bloodstream to infect the endothelium and sometimes the vascular smooth muscle cells. *Rickettsia* species enter their target cells, multiply by binary fission in the cytosol, and damage heavily parasitized cells directly.

Host Defenses

T-lymphocyte-mediated immune mechanisms and cytokines, including gamma interferon and tumor necrosis factor alpha, play a more important role than antibodies.

Epidemiology

The geographic distribution of these zoonoses is determined by that of the infected arthropod, which for most rickettsial species is the reservoir host.

Diagnosis

Rickettsioses are difficult to diagnose both clinically and in the laboratory. Cultivation requires viable eukaryotic host cells, such as antibiotic-free cell cultures, embryonated eggs, and susceptible animals. Confirmation of the diagnosis requires comparison of acute- and convalescent-phase serum antibody titers.

Control

Rickettsia species are susceptible to the broad-spectrum antibiotics, doxycycline, tetracycline, and chloramphenicol. Prevention of exposure to infected arthropods offers some protection. A vaccine exists for epidemic typhus but is not readily available.

Ehrlichia

Clinical Manifestations

Ehrlichia species cause ehrlichioses that vary in severity from a life-threatening febrile disease that resembles Rocky Mountain spotted fever, except for less frequent rash, to an infectious mononucleosis-like syndrome.

Classification and Antigenic Types

Ehrlichia sennetsu, E chaffeensis, and the human granulocytic ehrlichia are genetically distinct and are easily distinguished antigenically.

Pathogenesis

A reservoir of *E chaffeensis* is deer, and for both human monocytic and granulocytic ehrlichiosis are transmitted when ticks bite human skin and inoculate organisms, which then spread by the bloodstream. Macrophages or neutrophils have cytoplasmic vacuoles that contain ehrlichiae dividing by binary fission in each of these ehrlichioses.

Host Defenses

Host defenses against *E chaffeensis* include cytokine-mediated restriction of iron supplies to the ehrlichiae.

Epidemiology

Sennetsu ehrlichiosis has been documented in Japan and Malaysia. Human infections with *E chaffeensis*- and *E phagocytophila*- like organisms have been found recently. Human monocytic ehrlichiosis originates in most of the Atlantic, southeastern, and south central states from New Jersey to Texas. Human granulocytic ehrlichiosis has been identified in the upper midwest and New England thus far.

Diagnosis

Clinical and laboratory clues must be confirmed serologically or by polymerase chain reaction detection of specific ehrlichial DNA.

Coxiella

Clinical Manifestations

Coxiella burnetii causes Q fever, which may present as an acute febrile illness with pneumonia or as a chronic infection with endocarditis.

Structure, Classification, and Antigenic Types

Coxiella burnetii varies in size and has an endospore-like form. This species has lipopolysaccharide and phage type diversity.

Pathogenesis

Coxiella burnetii organisms are transmitted to the human lungs by aerosol from heavily infected placentas of sheep and other mammals and disseminate in the bloodstream to the liver and bone marrow, where they are phagocytosed by macrophages. Growth within phagolysosomes is followed by formation of T-lymphocyte-mediated granulomas. In the few patients who develop serious chronic Q fever, heart valves contain organisms within macrophages.

Host Defenses

Host defense depends on T lymphocytes and gamma interferon.

Epidemiology

Q fever is found worldwide. It is associated mainly with exposure to infected placentas and birth fluids of sheep and other mammals.

Diagnosis

The disease is difficult to diagnose clinically, and cultivation poses a biohazard. Therefore, serology is the mainstay of laboratory diagnosis.

Control

Antibiotics are effective against acute Q fever. A vaccine containing killed phase I organism shows promise in protecting against infection.