

Rickettsiae

Rickettsiae

Rickettsiae

Introduction

Rickettsiae are obligate intracellular bacteria.

They are the agents of
typhus,
spotted fevers
Q fever.

Rickettsiae

Introduction

In USA, there are two rickettsial diseases of significance:

1. Rocky Mountain spotted fever, caused by *Rickettsia rickettsii*,
2. Q fever, caused by *Coxiella burnetii*.

Several other rickettsial diseases are important in developing countries such as:

Epidemic typhus,

Endemic typhus,

Scrub typhus.

Rickettsialpox, caused by *Rickettsia akari*, is a rare disease found in certain densely populated cities in the United States.

Ehrlichia chaffeensis and *Anaplasma equi* other rickettsiae

Rickettsiae

Important Properties

Rickettsiae are very short rods barely visible in the light microscope.

Structurally, their cell wall resembles that of gram-negative rods, but they stain poorly with the standard Gram stain.

Rickettsiae are obligate intracellular parasites because they cannot produce sufficient energy to replicate extracellularly.

Rickettsiae

Important Properties

Therefore, rickettsiae must be grown in cell culture, embryonated eggs, or experimental animals.

Rickettsiae divide by binary fission within the host cell, unlike chlamydiae, which are obligate intracellular parasites but replicate by a distinctive intracellular cycle.

Rickettsiae

Important Properties

Several rickettsiae, such as *Rickettsia prowazekii*, *Rickettsia tsutsugamushi*, & *R. rickettsii*, possess antigens that cross-react with antigens of the OX strains of *Proteus vulgaris*.

The Weil-Felix test, which detects antirickettsial antibodies in a patient's serum by agglutination of the *Proteus* organisms, is based on this cross-reaction.

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Important Properties

C. burnetii has a sporelike stage that is highly resistant to drying, which enhances its ability to cause infection. It also has a very low ID 50, estimated to be approximately one organism.

C. burnetii exists in two phases that differ in their antigenicity & their virulence:

phase I organisms are isolated from the patient, are virulent, & synthesize certain surface antigens, whereas

phase II organisms are produced by repeated passage in culture, are non-virulent, & have lost the ability to synthesize certain surface antigens.

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Important Properties

The clinical importance of phase variation is that patients with chronic Q fever have a much higher antibody titer to phase I antigens than those with acute Q fever.

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Transmission

The most striking aspect of the life cycle of the rickettsiae is that they are maintained in nature in certain arthropods such as ticks, lice, fleas, & mites and, with one exception, are transmitted to humans by the bite of the arthropod.

The rickettsiae circulate widely in the bloodstream (bacteremia), primarily infecting the blood vessel walls' endothelium.

The exception to arthropod transmission is *C. burnetii*, the cause of Q fever, which is transmitted by aerosol & inhaled into the lungs.

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Transmission

Virtually all rickettsial diseases are zoonoses (i.e., they have an animal reservoir), with the prominent exception of epidemic typhus, which occurs only in humans.

It occurs only in humans because the causative organism, *R. prowazekii*, is transmitted by the human body louse.

Table 26–1 Summary of Selected Rickettsial Diseases

Disease	Organism	Arthropod Vector	Mammalian Reservoir	Important in the United States
Spotted fevers				
Rocky Mountain spotted fever	<i>R. rickettsii</i>	Ticks	Dogs, rodents	Yes (especially in southeastern states such as North Carolina)
Rickettsialpox	<i>R. akari</i>	Mites	Mice	No
Typhus group				
Epidemic	<i>R. prowazekii</i>	Lice	Humans	No
Endemic	<i>R. typhi</i>	Fleas	Rodents	No
Scrub	<i>R. tsutsugamushi</i>	Mites	Rodents	No
Others				
Q fever	<i>C. burnetii</i>	None	Cattle, sheep, goats	Yes

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The incidence of the disease depends on
the geographic distribution of the arthropod vector
the risk of exposure, which is enhanced by such things as
poor hygienic conditions & camping in wooded areas.

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Pathogenesis

The typical lesion caused by the rickettsiae is a vasculitis, particularly in the endothelial lining of the vessel wall where the organism is found.

Damage to the vessels of the skin results in the characteristic rash & in edema & hemorrhage caused by increased capillary permeability.

There is some evidence that endotoxin is involved, which is in accord with the nature of some of the lesions such as fever & petechiae, but its role has not been confirmed.

No exotoxins or cytolytic enzymes have been found.

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Clinical Findings & Epidemiology

This section is limited to the two rickettsial diseases that are most common in the United States, i.e.,

Rocky Mountain spotted fever

Q fever, & to the other major rickettsial disease, & Typhus.

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Rocky Mountain Spotted Fever

Caused by *Rickettsia rickettsii*,

The name of the disease is misleading because it occurs primarily along the East Coast of the USA (in the southeastern states of Virginia, North Carolina, & Georgia), where the dog tick, *Dermacentor variabilis*, is located.

The name "Rocky Mountain spotted fever" derives from the region where the disease was first found.

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Rocky Mountain Spotted Fever

This disease is characterized by the acute onset of nonspecific symptoms (fever, severe headache, myalgias, & prostration).

The typical rash, which appears 2 to 6 days later, begins with macules that frequently progress to petechiae.

The rash usually appears first on the hands & feet & then moves inward to the trunk.

In addition to headache, other profound CNS changes such as delirium & coma can occur.

DIC, edema, & circulatory collapse may ensue in severe cases.

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Rocky Mountain Spotted Fever

The diagnosis must be made on clinical grounds & therapy started promptly, because the laboratory diagnosis is delayed until a rise in antibody titer can be observed.

The tick is an important reservoir of *R. rickettsii* as well as the vector;

The organism is passed by the transovarial route from tick to tick, & a lifetime infection results.

Certain mammals, such as dogs & rodents, are also reservoirs of the organism.

Humans are accidental hosts & are not required for the perpetuation of the organism in nature;

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Rocky Mountain Spotted Fever

There is no person-to-person transmission.

Most cases occur in children during spring & early summer when the ticks are active.

Rocky Mountain spotted fever accounts for 95% of the rickettsial disease in the USA; there are about 1000 cases per year.

It can be fatal if untreated, but if it is diagnosed & treated prompt cure results .

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Q Fever

Caused by *Coxiella burnetii*

Unlike other rickettsial diseases, the lungs are the main organ involved in Q fever.

It begins suddenly with fever, severe headache, cough, & other influenza like symptoms.

This is all that occurs in many patients, but pneumonia ensues in about half.

Hepatitis is frequent enough that the combination of pneumonia & hepatitis should suggest Q fever.

Q stands for "Query"; the cause of this disease was a question mark, i.e., was unknown, when the disease was first described in Australia in 1937.

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Q Fever

A rash is rare, unlike in other rickettsial diseases.

In general, Q fever is an acute disease & recovery is expected even in the absence of antibiotic therapy.

Rarely, chronic Q fever characterized by life-threatening endocarditis occurs.

Q fever is the one rickettsial disease not transmitted to humans by an arthropod bite.

The important reservoirs for human infection are cattle, sheep, & goats.

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Q Fever

The agent, *C. burnetii*, which causes an inapparent infection in these reservoir hosts, is found in high concentrations in the urine, feces, placental tissue, & amniotic fluid of the animals.

It is transmitted to humans by inhalation of aerosols of these materials.

The disease occurs worldwide, chiefly in individuals whose occupations expose them to livestock, such as shepherds, abattoir employees, & farm workers.

Cows' milk is usually responsible for subclinical infections rather than disease in humans.

Pasteurization of milk kills the organism.

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Typhus

There are several forms of typhus, namely,

Louse-borne epidemic typhus caused by *R. prowazekii*,

Flea-borne endemic typhus caused by *Rickettsia typhi*,

Chigger-borne scrub typhus caused by *R. tsutsugamushi*,

Several other quite rare forms.

Cases of flea-borne endemic typhus, also called murine typhus, occur in small numbers in the southern regions of California & Texas.

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epidemic Typhus

Typhus begins with the sudden onset of chills, fever, headache, & other influenza-like symptoms approximately 1 to 3 weeks after the louse bite occurs.

Between the 5th & 6th days after the onset of symptoms, a maculopapular rash begins on the trunk & spreads peripherally.

The rash becomes petechial & spreads over the entire body but spares the face, palms, & soles.

Signs of severe meningoencephalitis, including delirium & coma, begin with the rash & continue into the second & third weeks.

In untreated cases, death occurs from peripheral vascular collapse or from bacterial pneumonia.

Rickettsiae

epidemic Typhus

Epidemic typhus is transmitted from person to person by the human body louse, *Pediculus*.

When a bacteremic patient is bitten, the organism is ingested by the louse & multiplies in the gut epithelium.

It is excreted in the feces of the louse while biting the next person & autoinoculated by the person while scratching the bite.

The infected louse dies after a few weeks, & there is no louse-to-louse transmission; therefore, human infection is an obligatory stage in the cycle.

Epidemic typhus is associated with wars & poverty

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Brill-Zinsser disease

A recurrent form of epidemic typhus is called Brill-Zinsser disease

The signs & symptoms are similar to those of epidemic typhus but are less severe, of shorter duration, & rarely fatal.

Recurrences can appear as long as 50 years later & can be precipitated by another intercurrent disease.

In the USA, the disease is seen in older people who had epidemic typhus during World War II in Europe.

Brill-Zinsser disease is epidemiologically interesting; persistently infected patients can serve as a source of the organism should a louse bite occur.

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Laboratory Diagnosis

Laboratory diagnosis of rickettsial diseases is based on serologic analysis rather than organism isolation.

Although rickettsiae can be grown in cell culture or embryonated eggs, this is a hazardous procedure that is not available in the standard clinical laboratory.

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Laboratory Diagnosis

Of the serologic tests, the indirect immunofluorescence & ELISA tests are most often used.

A fourfold or greater rise in titer between the acute & convalescent serum samples is the most common way the laboratory diagnosis is made.

This is usually a retrospective diagnosis, because the convalescent sample is obtained 2 weeks after the acute sample.

If the clinical picture is typical, a single acute-phase titer of 1:128 or greater is accepted as presumptive evidence.

If the test is available, a diagnosis can be made during the acute phase of the disease by immunofluorescence assay on tissue obtained from the site of the petechial rash.

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Laboratory Diagnosis

The Weil-Felix test is based on the cross-reaction of an antigen in many rickettsiae with the O antigen polysaccharide found in *P. vulgaris* OX-2, OX-19, & OX-K.

The test measures the presence of anti rickettsial antibodies in the patient's serum by their ability to agglutinate *Proteus* bacteria.

The specific rickettsial organism can be identified by the agglutination observed with one or another of these three different strains of *P. vulgaris*.

However, as mentioned above, this test is no longer used in the United States.

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Treatment

The treatment of choice for all rickettsial diseases is **tetracycline**, with chloramphenicol as the second choice.

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Prevention

Prevention of many of these diseases is based on reducing exposure to the arthropod vector by wearing protective clothing & using insect repellent.

Frequent examination of the skin for ticks is important in preventing Rocky Mountain spotted fever; the tick must be attached for several hours to transmit the disease.

There is no vaccine against Rocky Mountain spotted fever.

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Prevention

Prevention of typhus is based on personal hygiene & "delousing" with DDT.

A typhus vaccine containing formalin-killed *R. prowazekii* organisms is effective & useful in the military during wartime but is not available to civilians in the USA

Persons at high risk of contracting Q fever, such as veterinarians, shepherds, abattoir workers, & laboratory personnel exposed to *C. burnetii*, should receive the vaccine that consists of the killed organism.