Q-Fever: A Neglected Zoonosis

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ABSTRACT

Coxiella burnetii is an obligate intracellular pathogen that causes worldwide zoonosis, Q-fever. Infection in animals is mostly persistent. Infection in humans is often asymptomatic but can be manifested as acute or chronic infection. C. burnetii infection in pregnant women may result in abortions, premature deliveries and still births. Infection in nature is maintained and transmitted by ticks as the principal vector and reservoir. Cattle, sheep and goat are the important source of infection to humans. Humans contract infection mostly by aerosol in contact with contaminated environments and wind playing an important role in spreading the infection. Organism exists in two antigenic phases. Host factors such as under-lying disease and cell-mediated immunity play a decisive role in the clinical expression of Coxiella burnetii infection.

INTRODUCTION

Coxiella burnetii is an obligate intracellular gram-negative pathogen. It had been previously identified as a rickettsial agent but has been recently reclassified as Proteobacteria. It replicates in host monocytes and macrophages. It has enormous stability and can achieve high animal concentrations. It is highly immune to environmental conditions and other disinfectants, as it forms unusual spore-like structures. Coxiella burnetii occurs in two antigenic phases which are critical for Q fever diagnosis. Phase I is pathogenic and is present in infected animals, or in nature. Phase II is less pathogenic and is recovered in eggs or cell cultures only after several lab passages. Increased antibodies to the phase II antigens indicate acute infection while chronic infection is indicated by an increase in phase I.

History

Q "Querry" fever was first reported in 1935 by Derrick in Brisbane, Queensland, Australia, who identified febrile disease outbreaks in workers at abattoirs. Burnet and his associate Freeman successfully isolated the organism and studied the disease's epidemiology. In 1938
Coxiella burnetii was named for the organism in honor of Cox and Burnet.

**Transmission**

Aerosolization is the primary mode of transmission in humans, and the most common cause of infection in domestic ruminants. Organisms are commonly found in airborne droplets or dust contaminated with placental tissues, birth fluids or infected animal excreta. Shedding of the organisms into the atmosphere occurs mainly during parturition; at delivery approximately $10^9$ bacteria per gram of the placenta are released. Aerosol or direct transmission can occur while processing infected animals for feed, during necropsies, or while assisting with parturition.

Owing to the persistence of the organism in the atmosphere, dried infectious material can contaminate water, dust, and soil; fomites (i.e., newborn animals, fur, bedding, and clothing) can also be contaminated and may serve as infectious source. Infected mammary glands may shed the organisms in milk, but this organism is destroyed by pasteurization.

*C. Burnetii* has been isolated from several arthropods naturally and experimentally (mainly ticks, but also cockroaches, mosquitoes, flies, fleas, lice, mites). About 40 species of ticks are infected with *C. Burnetii* and transovarial transmission (mother to offspring) and transstadial transmission (between developmental stages) were recorded. Infected arthropod feces may serve as a source of infection with *C. burnetii* and can remain infective for at least 19 months.

Usually animals develop Q fever through exposure to other infected animals, either by direct contact with polluted material or by exposure to aerosols. Transmission from person to person is extremely rare. Transplacental transmission can result in congenital infection. There were also records of transmission from blood transfusions, bone marrow transplants, and intradermal inoculations. Transmission via sexual intercourse has been hypothesized. Sexual transmission of *Coxiella burnetii* has been documented in mice and guinea pigs and hypothesized for a rare number of human cases.

**Epidemiology**

Q fever is a zoonosis which is distributed worldwide. It has been recorded on all continents except New Zealand, and it is common in areas where animals’ reservoirs are found. The reservoir of animals is large and includes many wild and domestic mammals, birds, and arthropods. The main reservoirs, however, are called cattle, pigs, goats, and ticks. Wildlife species recorded as reservoirs include snowshoe hares, moose and white-tailed deer in Nova Scotia, Alaskan wild Dall sheep and Idaho and California black bears. Q fever poses an occupational hazard for people in contact with domestic animals, such as cattle, sheep and goats. People at risk include farmers, livestock producers, veterinarians, slaughterhouse workers and people in contact with dairy products, and culture and diagnostic laboratory staff. Reports of intermittent cases have been growing in people living in urban areas following occasional contact with farm animals or after interaction with infected pets, such as dogs and cats.

**Disease in Humans**

In humans the time of incubation ranges from 2 to 40 days (mean around 20 days). Only as few as one organism can cause illness. Human beings are considered dead end hosts, and they are the only species known to routinely develop disease because of infection. Most Q fever cases are asymptomatic; only around 50 per cent of all infected individuals exhibit clinical signs of illness. The two clinical forms of illness are acute (duration less than 6 months) and chronic (duration longer than 6 months).

Acute disease symptoms can differ in severity and duration; a febrile or flu-like illness often occurs which is self-limiting. Signs include fatigue, chills, "sweats," headache retrobulbar,
tiredness, anorexia, malaise, myalgia, and chest pain. Illness usually lasts from 1-3 weeks. Pneumonia can occur in 30 to 50 per cent of patients with symptomatic disease. In more serious cases, pneumonitis with nonproductive cough may be seen. Radiographs of pneumonic patients mimic those of patients with etiologies of viral pneumonia. Multiple rounded opacities on x-ray of both lungs can be observed, and pleural effusion can also be seen. In addition, many patients who are clinically ill will have irregular liver enzymes and some will develop hepatitis, jaundice which is rare. Exanthema (rash) occurs in about 10% of cases. Acute infection can rarely cause meningoencephalitis or pericarditis. Around 2% of acute infections need hospitalization and mortality results in a similar percentage. Chronic Q fever (duration of infection beyond six months) occurs in 1 to 5 percent of those infected and is relatively rare. It usually occurs in individuals with preexisting heart valve disease. Immunocompromised individuals and pregnant women are also at significant risk for the chronic form. Endocarditis is the main clinical presentation and constitutes 60 to 70 per cent of all cases of chronic Q fever. Infection may also affect the liver which causes hepatitis or cirrhosis in granulomatous form. Kupffer cells are considered to be target cells for Coxiella. There were also records of involvement in bone and arteries. The chronic type can also develop in patients who have had acute Q fever as early as 1 year or as long as 20 years after initial infection.

**Risk to Pregnant Women**

Pregnant women who are diagnosed with C. burnetii appear to be asymptomatic. The organism may be transmitted transplacentally. There may be neonatal death, premature birth, low birth weight, or placentitis, depending on the timing of the infection abortion. The greatest risk is that of the first trimester. Pregnant women also have an increased chance of developing chronic infection with Q-fever. Pregnant women with Q fever may pose a degree of risk to medical staff.

**Prognosis**

Q fever is typically a self-limiting illness and most cases resolve within two days to two weeks. Approximately 50 to 60 per cent of cases are considered asymptomatic, and complications from the acute disease type are rare. About 2 percent of Coxiella burnetii-infected people experience serious disease and need hospitalisation. Overall, if treated, the mortality rate is 1 per cent or less. Chronic Infectious Disease is usually fatal if untreated. In patients with endocarditis, the fatality rate can range from 45 to 65%; additionally, 50 to 60% need valve replacement surgery. Because severe disease is rare the overall case-fatality rate for Q fever ranges from <1 to 2.4%.

**Diagnosis**

In humans, Q fever is usually diagnosed with serology (increase in the amount of antibody titer) that can be achieved as early as the second week of illness. Q-fever serological tests include IFA (immunofluorescence assay), CF (complement fixation), ELISA (enzyme-linked immunosorbent assay), and microagglutination. The most accurate and commonly used approach is Indirect IFA. C. burnetii may also be identified in infected tissue by IHC (immunohistochemistry) and DNA detection methods (PCR-polymerase chain reaction). Isolation of the organism is rarely done due to the risk C. burnetii poses for laboratory personnel. Clinical signs and patient history can also aid in diagnosis.

**Treatment**

Doxycycline is the antibiotic medication of choice. Treatment with antibiotics is most successful if started within the first three days of illness. For chronic disease, treatment may be necessary for 2 to 3 years. Doxycycline and quinolones are contraindicated in pregnant women but in some cases, long-term cotrimoxazole treatment (the combination of trimethoprim/sulfamethoxazole) has prevented fetal death. People recovering from Q fever are
thought to develop long-term (maybe lifelong) immunity.

Animal Disease

The most common reservoirs of Q fever are sheep, cattle, and goats. For animals, the incubation time is variable. The infected animals may be asymptomatic; reproductive failure is typically the only symptom seen when clinical illness occurs. This can include abortions, stillbirths, retention of placentas, infertility, frail newborns and milk cattle mastitis. Lambs that are born after abortions by *Coxiella* may be carried to term. However, ewes can remain infected chronically, and tend to shed organisms. After parturition, organisms can be shed several days in milk and feces. The dogs, cats, horses, pigs, and most species of mammals and fowls may carry *Coxiella burnetii*. Animals can get infected with tick bite, placenta or milk consumption from infected ruminants, or by the aerosol route. Most infections are asymptomatic; however, the most symptoms are related to reproductive failure. Still births and weak offspring are commonly reported.

PM Lesions

Placentitis is the most characteristic lesion in ruminants. The placenta is typically leathery and thickened. It may contain large amounts of creamy, white-yellow exudates at the edges of cotyledons and in the intercotyledonary area. Lesions are usually non-specific in aborted fetuses.

Diagnosis and Treatment

*C. burnetii* can be detected in Vaginal secretions, placenta or its fluids, aborted fetuses, milk, urine, and feces. Identification of the organism can be achieved with Modified Ziehl-Neelson or Gimenez stains but is not normally detected by Gram stain. IHC can also confirm bacterial identity. PCR techniques are also available in some laboratories. Several serological tests are also available (i.e., immunofluorescence (IFA), enzyme-linked immunosorbent assays (ELISA) and complement fixation (CF). The complement fixation test is done most. Although organism isolation can be achieved in a variety of methods, it is hazardous for laboratory staff, and must be performed in a Laboratory at Biosafety level 3. So, it is seldom used.

Little is known about the effectiveness of antibiotic treatment in animals. In the weeks preceding parturition in enzootic herds tetracycline was administered in water. This is thought to help minimize shedding in birthing materials. Antimicrobial therapy may not eradicate carrier state of infection with *C. burnetii* but can suppress abortion numbers.

Prevention and Control

Effective husbandry plays a large part in preventing and managing this disease. Tick avoidance should be used to help prevent the disease from spreading. Animals about to give birth should be separated from the rest of the herd. Fetal membranes and the aborted fetuses should be disposed of either by burying or burning immediately. New or sick animals should be isolated from the rest of the herd until it can be determined that the animals are not contagious or do not pose risk of infection. Vaccinations for humans and animals have been developed for this disease. However, they are not currently licensed for use in the United States.

Pasteurization of milk from cows, sheep, and goats is important in stopping the spread of Q fever by contaminated milk sources. The amount of *C. burnetii* in the environment can be greatly reduced by thorough cleaning. A 10% bleach solution should be used to disinfect areas after cleaning where animals give birth. Eradication is impossible because of environmental stability, infectivity for wild animals, asymptomatic and carrier state in animals and people, and arthropods.
REFERENCES

