

Veterinary / Generalized Conditions / Coxiellosis

Overview of Coxiellosis

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Coxiellosis is a zoonotic bacterial infection associated primarily with parturient ruminants, although domestic animals such as cats and a variety of wild animals have been identified as sources of human infection. The zoonotic infection in people associated with *Coxiella burnetii* is widely known as Q fever. *Coxiella* is considered a potential agent of bioterrorism because of its low infectious dose, stability in the environment, and capability for aerosol dispersion.

Etiology, Epidemiology, and Transmission:

Coxiellosis is caused by the gram-negative coccobacillus *C burnetii*. Although classically considered a rickettsial agent, recent phylogenetic analyses suggest that *C burnetii* is more closely related to *Legionella* and *Francisella* than to the genus *Rickettsia*. It resides and reproduces in the acidified phagolysosomes of host monocytes and macrophages. Two forms exist: the large cell variant is a vegetative form found in infected cells, and the small cell variant is the extracellular infectious form shed in milk, urine, and feces and found in high concentration (10^9 ID₅₀/g) in placental tissue and amniotic fluid. The small cell variant is resistant to heat, drying, and many common disinfectants and remains viable for weeks to years in the environment. Once a domestic ruminant is infected, *C burnetii* can localize in mammary glands, supramammary lymph nodes, placenta, and uterus, from which it may be shed in subsequent parturitions and lactations.

The epidemiology of *C burnetii* is complex because there are two major patterns of transmission. In one, the organism circulates between wild animals and their ectoparasites, mainly ticks; the other occurs in domestic ruminants, independent of the wild animal cycle. Ixodid and argasid ticks can act as reservoirs of the organism. Distribution is worldwide (except New Zealand), and the host range includes various wild and domestic mammals, arthropods, and birds. The disease is enzootic in most areas where cattle, sheep, and goats are kept. In the USA, seroprevalence studies have shown significant variability in prevalence of antibodies to *C burnetii* based on difference in test population, test used, and time of year. Evaluation of bulk tank milk sampling of USA cattle dairies has demonstrated prevalence of the organism at the farm level of 77% to >90%. In a comprehensive seroprevalence study conducted in Canada, 48.6% of sheep operations and 63.2% of goat operations had at least one positive animal. Not surprisingly, seroprevalence in veterinarians and small ruminant farmers is also high.

The greatest risk of transmission occurs at parturition by inhalation, ingestion, or direct contact with birth fluids or placenta. The organism is also shed in milk, urine, and feces. High-temperature pasteurization effectively kills the organism. Ticks may transmit the disease among domestic ruminants but are not thought to play an epidemiologically important role in transmission of disease to people.

Clinical Findings and Diagnosis:

Infection in ruminants is usually subclinical but can cause anorexia and late abortion. When infection is subclinical, animals shed much lower bacterial loads of the organism than when abortion occurs. Reports have implicated *C burnetii* as a cause of infertility and sporadic abortion with a necrotizing placentitis in ruminants. New evidence has shown an association of *C burnetii* with subclinical mastitis among dairy cows, although additional work regarding causality is required before this can be considered clinically valid. Experimental infection in cats causes transient fever, dullness, and anorexia lasting several days.

In domestic ruminants, gross lesions are nonspecific, and differential diagnosis should include infectious and noninfectious agents that cause abortion. Immunofluorescence test on paired sera taken ≥ 2 wk apart can be used to detect recent infection; however, shedding of *C burnetii* may occur in the absence of a measurable serum antibody titer in up to 20% of infected animals. Culture, immunohistochemical, and PCR tests may be used to identify *C burnetii* in tissues. Studies conducted in veterinary diagnostic laboratories suggest that *C burnetii* is often found concurrently with other organisms isolated in cases of infectious abortions, so mixed infections may be important. Seasonal variability in shedding of the organism hinders interpretation of a single PCR test. Shedding is highest in the periparturient period and may drop below detectable levels for a significant period during the year despite persistent infection.

Treatment and Control:

Q fever in people is a notifiable disease in the USA, primarily because of its status as a possible bioterrorism agent; reporting requirements for animals vary by state. Vaccines for people and animals have been developed but are not commercially available in the USA. Vaccination has prevented infection when administered to uninfected calves and has improved fertility and reduced shedding in previously infected animals.

There is little evidence-based data to suggest that antibiotic treatment in animals provides significant benefit. Human clinical disease is typically treated with tetracyclines, but significant benefit from tetracycline treatment has not been demonstrated in controlled studies in abortion outbreaks of sheep in Europe. Despite the lack of evidence, some practitioners still advocate the use of parenteral tetracyclines during abortion storms. In known infected herds, the periparturient period represents a significant risk period for transmission because of the large amount of environmental contamination associated with abortion. Standard abortion control measures, including prompt removal of aborted materials (using zoonotic precautions), segregation of animals by pregnancy status, and diagnostic evaluation of abortions, are all warranted.

Zoonotic Risk:

Q fever occurs more frequently in persons who have occupational contact with high-risk species. The clinical presentation in people is highly variable clinically, ranging from a self-limiting, influenza-like illness to pneumonia, hepatitis, and endocarditis. *C burnetii* is highly infectious, and a single organism can reportedly cause infection via the aerosol route in people. Individuals who have artificial heart valves are at particular risk, as well as anyone who is significantly immunocompromised. *C burnetii* has been associated with human abortions, and pregnant women should take precautions to prevent exposure.

The majority of outbreaks in people have been associated with wind dispersion of desiccated reproductive products, contaminated with *C burnetii*, from sites where sheep, goats, or cattle are kept. Farmers and veterinarians are at risk while assisting birthing. Slaughterhouse workers are at risk from contact with infected carcasses, hair, and wool. Transmission may also occur by consumption of unpasteurized milk. Handling of infected tissue poses a threat to laboratory personnel. Q fever has been seen in personnel and human patients in medical institutions where latently infected sheep were used for research. Medical facilities using ruminants in research should attempt to purchase animals from flocks free of coxiellosis or use male animals when possible. In addition, workers should use adequate personal protective equipment to protect against small droplet and aerosol exposure during high-risk medical procedures.



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