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# *Q Fever Backgrounder*

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## Causative agent

Q Fever is caused by *Coxiella burnetii*, a Gram-negative, pleomorphic coccobacillus. It is an obligate intracellular organism (it cannot survive or grow independently outside of host cells). The bacterium exists in several forms. The small cell variant and small dense cells, which are sporelike forms, are very stable in the environment. The large cell variant is the growing, metabolically active form.

*C. burnetii* has historically been classified as a member of the Rickettsiaceae family of bacteria; however, scientific investigations have shown that it is genetically more comparable to *Francisella* and *Legionella* bacterial families; therefore, it has been placed in the Coxiellaceae family of bacteria.

## Natural distribution

Q Fever was first reported in Australia in 1935, after slaughterhouse workers developed febrile disease. The organism could not be identified at that time, and the disease was named Q (for query) Fever. The bacterium was simultaneously discovered in the United States as the cause of a laboratory-acquired infection following isolation of a tick-borne agent; at the time, it was called “Nine Mile agent” due to the proximity of the tick vectors to Nine Mile creek. The two agents were proven to be identical, and the name *Coxiella burnetii* was chosen to honor Cox and Burnet, the two scientists who independently isolated the bacterium. It has been reported worldwide, with the exception of New Zealand.

*C. burnetii* normally cycles between ticks and small ground mammals. Natural hosts include 35 species of tick and 8 species of small mammals. Cattle, sheep, and goats are the primary reservoirs of *C. burnetii*, but cats, dogs, some wild mammals, birds, and ticks are also natural reservoirs.

Q Fever is a zoonotic disease, and the bacterium is considered to be endemic (established) in the United States. Most Q Fever outbreaks in people result from occupational exposure of veterinarians, sheep and dairy handlers, livestock farmers, meat processing plant employees, and researchers working with high-risk species.

## Transmission

*C. burnetii* are shed in high numbers from the birth-related tissues (e.g., amniotic fluid, placenta and uterus) of infected animals and in lower numbers from their milk, urine, vaginal mucus, semen, and feces. The bacteria are very resistant to drying and therefore are easily transmitted by aerosols. Placentas of infected sheep may contain up to  $10^9$  bacteria per gram of tissue, and infected milk may contain up to  $10^5$  bacteria per gram.

Animals are generally infected with *C. burnetii* through direct exposure to contaminated body fluids or aerosolized bacteria. Sexual transmission of *C. burnetii* may occur, and females can pass infection to their offspring. Ticks may also transmit the bacteria among animals, and may play important roles in maintaining *C. burnetii* in the environment. *C. burnetii* infection may persist in ruminants for years, and may be lifelong.

Unlike most other rickettsial diseases, which are spread by tick vectors, human infection most commonly results from inhalation of airborne bacteria. The greatest risk of transmission occurs at parturition (giving birth) by inhalation, ingestion, or direct contact with birth fluids or placenta. The bacteria can persist in dust from contaminated premises, posing a continued risk of infection for weeks to months. Outbreaks have also occurred in establishments processing infected animals or their byproducts. Infection can also develop following ingestion of contaminated, unpasteurized dairy products. Vector transmission to humans via ticks and human-to-human transmission is rare. Domestic dogs and cats may

be infected by exposure (ingestion or aerosol) to contaminated excretions or birth products and shed the bacteria in milk and urine, serving as potential sources of human infection.

In susceptible people, a single *C. burnetii* bacterium may result in infection and induce disease; therefore, its use as a potential bioterrorism agent has been acknowledged. Currently, Q Fever is classified as a Category B agent. Due to the potential for transmission of infection from animals to people, the World Organization for Animal Health (OIE) has classified Q Fever as a notifiable animal disease.

The incubation period is variable, and is affected by the extent of exposure; the more bacteria infecting the patient, the shorter the incubation period. Most people who become infected develop clinical signs within 1 to 3 weeks of exposure.

### Clinical Signs

*Cattle, sheep, and goats*—*C. burnetii* produces inapparent or mild illness in domestic animals, but it can induce abortion in sheep, goats, and cattle. Cattle may also exhibit dead or weak calves, retained placentas, metritis (uterine infection), and infertility. Abortion is more common in smaller ruminants (sheep and goats) than in cattle. Up to 50% of pregnant animals in a single flock of sheep or herd of goats may abort. Other signs of disease in small ruminants include premature births, dead or weak lambs or kids, uterine infection, and fertility. Sporadic abortions and necrotic placentitis in horses caused by *C. burnetii* have been reported in South Africa.

*Humans*—Clinical disease develops in approximately 50% of people infected. Fever (up to 105° F for 1 to 2 weeks), severe headache, myalgia (muscle pain), pharyngitis (sore throat), disorientation, chills, sweating, coughing, nausea, vomiting, diarrhea, abdominal pain, chest pain, and weight loss are typical of acute infections. Pneumonia develops in 30-50% of infected people, and some develop granulomatous hepatitis (inflammation of the liver).

Q Fever in its chronic form may persist for 6 or more months, and may develop 1 to 20 years after initial exposure and infection. Endocarditis (infection or inflammation of the heart valves) may develop in conjunction with chronic infection. The associated risk is higher in patients with valvular heart disease or vascular grafts, and the aortic valve is most commonly affected. Meningitis or encephalitis develops in approximately 1% of chronic cases. Immunocompromised patients, such as transplant recipients, cancer patients, and patients with chronic renal (kidney) disease, are at greater risk of developing Q Fever in its chronic form.

### Diagnosis

Clinical signs of Q Fever are nonspecific; therefore, a diagnosis based on clinical presentation is not possible. Serologic testing is required for definitive diagnosis. The indirect immunofluorescence assay (IFA) is the most commonly used approach. DNA probes, enzyme-linked immunosorbent assays (ELISA), and complement fixation (CF) analyses are also available.

Two antigenic phases, phase I and phase II, are exhibited by *C. burnetii*. These phases are important to distinguishing between acute and chronic forms of Q Fever. In the acute form, antibodies to phase II antigens are present in greater numbers. In the chronic form, antibodies to phase I antigens predominate.

Immunoelectrophoresis can also provide additional information. Increased concentrations of IgM indicate recent infection. Patients with acute Q Fever have IgG antibodies to phase II antigens and IgM antibodies to both phases. Q Fever-induced endocarditis is often accompanied by increased concentrations of IgG and IgA antibodies to phase I antigens.

### Treatment

In the United States, **Q FEVER is a reportable disease**. State or Federal health officials should be notified immediately if Q Fever is suspected.

Information on the treatment of infected animals is limited; this may be due in part to the number of animals that become infected without developing clinical signs of disease. Prophylactic treatment of

endemic herds (herds in which infection is established) with tetracycline may minimize the shedding of the bacteria in the birth fluids.

Without treatment, most humans with acute Q Fever recover within several months; medical treatment appears to shorten the clinical course of the illness. Full recovery from Q Fever results in lifelong immunity against re-infection. Doxycycline is administered for a minimum of 15 days to those suffering from the acute form of the disease, and optimal results are obtained when treatment is initiated within the first 3 days of clinical illness. Treatment of endocarditis associated with the chronic form of Q Fever is challenging, and may include administration of a doxycycline/quinolone combination for a minimum of 4 years or a doxycycline/hydroxychloroquine combination for 1.5 to 3 years. Refractory cases may require surgical removal and replacement of affected heart valves.

#### Morbidity and Mortality

Animal deaths from *C. burnetii* infection are extremely rare. Without treatment, approximately 1 to 2% of people affected by Q Fever die of the acute form of the disease. The case-fatality rate (the number of people affected who die from the disease) is negligible in treated cases, except for individuals who develop endocarditis. The case fatality rate may approach 65% for chronic cases of Q Fever in people.

#### Prevention and Control

*C. burnetii* is resistant to heat, drying, osmotic shock, ultraviolet light, and many commonly used disinfectants. The bacteria are able to survive in the environment for long periods of time.

To reduce exposure, appropriate disposal methods should be instituted for all sheep and goat placentas, birth fluids, fetal membranes, and aborted fetuses. Those handling fetal membranes, fluids, placentas, and aborted fetuses should maintain good hygiene. Access to potentially infected animals should be restricted, and newly acquired animals should be quarantined. Consumption of pasteurized milk and milk products is recommended. Humans who are immunocompromised or who have valvular heart disease or valve implants should avoid exposure to potentially infected animals.

A vaccine against Q Fever for use in humans has been produced and used successfully for high-risk individuals in Australia, but will no longer be produced after March 2007. Similarly, a vaccine for use in animals has been developed but is not commercially available.

*C. burnetii* is resistant to disinfection with dilute ethanol, 5% bleach, 1% phenol, 1% formalin, 5% alkyl(C12-16)dimethylbenzylammonium chloride, 2% didecyl dimethyl ammonium chloride/alkyl dimethyl benzyl ammonium chloride solutions, and quaternary ammonium compounds. Solutions of 70% ethyl alcohol, 5% chloroform, or 5% N-alkyl dimethyl benzyl, ethylbenzal, and ammonium chloride combinations inactivate *C. burnetii* within 30 minutes. Sterilization, using ethylene oxide, is effective against *C. burnetii* only under conditions of high humidity. Effective disinfection is more difficult when organic material is present.

#### Use of *Coxiella burnetii* as a biological weapon

*C. burnetii* is classified as a Category B agent of bioterrorism. The bacterium is highly infective and is moderately easy to disseminate (spread). The organism can produce moderate morbidity (sickness) and mortality (death) rates. Possible mechanisms for spreading the bacteria include contamination of food or water and aerosolization.