

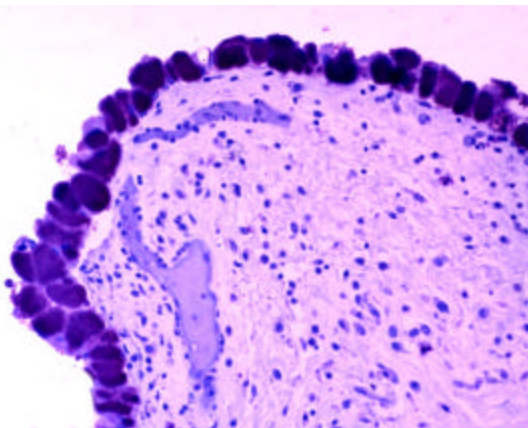


Q FEVER IN GOATS, SHEEP, AND PEOPLE

Wyoming has had three episodes of laboratory confirmed Q fever in animals since 2000. Cases occurred in the towns of Hulett, Powell and Wright. In each case, goats were infected and people were exposed. In the Wright episode, people were infected and developed clinical illness.

The causative agent: Q-fever is a disease caused by the intracellular bacterium *Coxiella burnetii*. The agent is highly infectious. One to ten organisms can establish infection. The agent is resistant to heat and drying, and due to its potential as a bioterrorism agent all laboratory isolates are controlled by the USDA and CDC as a “Select Agent.” It is resistant to many physical and chemical agents, and survives weeks to years in the environment. It spreads to other animals and people through aerosolization of infected particles, by direct contact, or by ingestion of placentas or other reproductive discharges, or of milk, urine and feces. Ticks may transmit the disease among domestic ruminants and, occasionally, people. **The most important mode of transmission from domestic ruminants to people is airborne from reproductive fluids.** Raw milk can be a source of infection, although high-temperature pasteurization kills the organism.

Q fever in animals: Infection is usually subclinical, but it can also cause anorexia and abortion in goats and, less commonly, sheep. *C burnetii* is a cause of sporadic abortion in cattle in the United States, but we have not recognized it in Wyoming cattle. A recent serological survey reported that goats had a higher average seroprevalence (41.6%) than sheep (16.5%) or cattle (3.4%). A survey over 8 years (1991 – 1998) of 221 cases of caprine abortion in southern California reported that *Coxiella burnetii* was the second most commonly diagnosed cause (9%) of reproductive wastage after *Chlamydophila abortus* (14%). The principal lesion is a necrotizing placentitis with large numbers of organisms in trophoblasts. Lesions in aborted fetuses are rare (10%) and modest, consisting of inflammation in liver, lung and kidney. Goats that were infected experimentally at 90 days of gestation with as few as 1,000 organisms had a 100% abortion rate, occurring 25 – 48 days later. Affected kids generally die within 24 hours of birth/abortion. Once a



domestic ruminant is infected, *C burnetii* localizes in mammary glands, supramammary lymph nodes, placenta, and uterus, from which it may be shed in subsequent parturitions and lactations. Abortion in individual goats generally occurs over just one or two successive gestations. Infected placental tissues contain enormous numbers of organisms. Exposure to infected tissues and fluids (from either cases of abortion or from apparently normal reproductive tracts) is a major source of human disease. Goats that abort shed the agent in vaginal discharges up to 14 days and in milk for up to 52 days. Feces contain the organism for days to weeks after abortion, as well as for several weeks before abortion.

Figure: Numerous intracellular *Coxiella burnetii* organisms (dark purple) in placental trophoblasts from a goat that aborted. Immunohistochemistry preparation.

Q fever in people: Only about one-half of all people infected with *C. burnetii* show signs of clinical illness. Most cases of **acute Q fever** begin with sudden onset of one or more of: high fever (up to 104-105° F), headache, malaise, myalgia, confusion, sore throat, chills, sweats, non-productive cough, nausea, vomiting, diarrhea, abdominal pain, and chest pain. Fever usually lasts 1 - 2 weeks. Weight loss can occur and persist for some time. Thirty to fifty percent of patients with symptomatic infection develop pneumonia. Additionally, a majority of patients have abnormal results on liver function tests, due to hepatitis. In general, most patients return to good health within several months without treatment. Only 1% - 2% of people with acute Q fever die of the disease. **Chronic Q fever** is characterized by infection that persists for more than 6 months. Although uncommon, it is a more serious disease. Patients with acute Q fever may develop the chronic form from 1 - 20 years after initial infection. A serious complication of chronic Q fever is endocarditis, generally involving the aortic heart valves and less commonly the mitral valve. Most patients who develop chronic Q fever have preexisting valvular heart disease or a history of a vascular graft. Transplant recipients, patients with cancer, and those with chronic kidney disease are also at risk of developing chronic Q fever. As many as 65% of persons with chronic Q fever can die of the disease. The risk of infection in man is greatly increased in occupations involving direct or indirect contact with infected animals, especially goats and sheep. Veterinarians, stockowners and packing plant employees are at particular risk. Several cases of Q-fever have occurred in personnel and human patients in medical institutions where latently infected sheep were used for research. *Coxiella burnetii* is the second most commonly diagnosed laboratory-acquired infection in the United States. The disease has been officially reportable to health authorities since 1999. Human to human transmission is rare, but it may occur in cases of human pneumonia. Q fever does not cause a clinically distinct illness. The atypical pneumonia it causes resembles viral illness and needs to be differentiated from pneumonia due to *Mycoplasma pneumoniae*, *Legionella pneumophila*, *Chlamydia psittaci*, and *Chlamydia pneumoniae*. Rapidly progressing pneumonia mimics bacterial pneumonias due to atypical agents such as *Yersinia pestis* and *Francisella tularensis*.

Epidemiology: *Coxiella burnetii* is distributed worldwide. It is found in various wild and domestic mammals, arthropods, and birds. Domestic goats, sheep, cattle, dogs, and cats are susceptible. The disease is found in most areas where goats, sheep and cattle are kept. Ixodid and argasid ticks can be reservoirs of the organism. All of the Wyoming cases have been associated with goats, in two instances Boar goats originating from Texas. The epidemiology is complex because there are two major patterns of transmission; in one, the organism circulates between free-ranging animals and ectoparasites, primarily ticks; the other occurs in domestic ruminants, independent of the wild animal cycle.

Diagnosis:

- **In animals:** Diagnosis can be made by direct isolation of the organism from tissues such as placenta, by detection of DNA specific for *C. burnetii* using one of several PCR protocols, or by immunohistochemical staining for the rickettsial antigens (see Figure 1). The WSVL has an IHC method for *C. burnetii*. To screen large numbers of animals in a herd or flock, the most effective method is serology. Two tests are commonly used: a complement fixation test (CF) and an immunofluorescent test for phase I and II antigens. The IFA test allows distinction between acute and chronic forms of the disease. In acute cases, the antibody level to phase II is usually higher than that to phase I, often by several orders of magnitude, and generally is first detected during the second week of illness. In chronic Q fever, the reverse situation is true. Antibodies to phase I antigens of *C. burnetii* generally require longer to appear and indicate continued exposure to the bacteria. High levels of antibody to phase I in later specimens in combination with constant or falling levels of phase II antibodies and other signs of inflammatory disease suggest chronic Q fever. Antibodies to phase I and II antigens can persist for months or years after initial infection.
- **In people:** This is generally done with a blood test, to detect antibodies specific for *Coxiella burnetii* antigens. In most laboratories an IFA is the most dependable and widely used method. This can be done through your local physician or the Wyoming Department of Health. In addition to an IFA, enzyme linked immunosorbant assay (ELISA) and complement fixation tests may be used. A fourfold rise in titer between acute and convalescent samples is diagnostic for Q fever.

Treatment and control:

- **Animals:** Effective animal vaccines available in other countries (e.g., Coxevac, CEVA Santé Animale, France), but none is currently licensed by the USDA due to the small market and limited awareness of about the disease. For treatment, tetracycline is the drug of choice, but it is less effective in treatment than for other rickettsioses. Chloramphenicol is also effective. Segregation of pregnant animals and burning or burying reproductive offal greatly reduce spread of the organism.
- **People:** Tetracycline, 500 mg q6h po x 5-7 days or doxycycline 100 mg q12h x 5-7 days are the treatments of choice. A combination of erythromycin 500 mg q6h and rifampin 600 mg qd is also effective. Chronic infection, especially involving endocarditis, often requires extended treatment and should involve appropriate specialists. An investigational Phase I Q fever vaccine available from USAMRIID is recommended for those at high risk (i.e., laboratorians who work with live *C. burnetii* in the laboratory). Chronic Q fever endocarditis is difficult to treat effectively and often requires the use of multiple drugs. Two different treatment protocols have been evaluated: 1) doxycycline in combination with quinolones for at least 4 years and 2) doxycycline in combination with hydroxychloroquine for 1.5 to 3 years. The second therapy leads to fewer relapses, but requires routine eye exams to detect accumulation of chloroquine. Surgery to remove damaged valves may be required for some cases of *C. burnetii* endocarditis.

Disinfection

Coxiella burnetii is susceptible to ethanol, glutaraldehyde and gaseous formaldehyde

The following measures should be used in the prevention and control of Q fever:

- Ensure that the placenta and fetus from goats and sheep that abort are submitted for examination to an accredited veterinary diagnostic laboratory in order to test for *Coxiella burnetii*. The PLACENTA is the key sample to submit – the organism may not be detectable in the fetus.
- Appropriately dispose of placenta, birth products, fetal membranes, and aborted fetuses at facilities housing sheep and goats.
- When considering introducing new animals into a flock or herd, enquire if abortion has occurred on the source property in the recent past – do not purchase from flocks or herds where abortion was known to occur.
- If you can maintain a closed, Q-fever negative flock or herd, discuss with your veterinarian the cost-benefit of testing all animals and eliminating any animals that are serologically positive, as well as quarantining and testing incoming stock.
- Restrict access to barns and laboratories used to house potentially infected animals.
- Use only pasteurized milk and milk products.
- Use appropriate procedures for bagging, autoclaving, and washing of laboratory clothing.
- Vaccinate (where possible) individuals engaged in research with pregnant sheep or live *C. burnetii*.
- Quarantine imported animals.
- Ensure that holding facilities for sheep are located away from populated areas. Animals should be routinely tested for antibodies to *C. burnetii*. Measures should be implemented to prevent airflow to other occupied areas.
- Counsel persons at highest risk for developing chronic Q fever, especially persons with pre-existing cardiac valvular disease or individuals with vascular grafts.

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