

## Q fever (*Coxiella burnetii* infection)



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*Coxiella burnetii* is present in extremely high numbers in birth products of infected animals. Once deposited in the environment the bacterium can persist for long periods of time, and bacteria-laden dusts can be inhaled and infect people living in areas where sheep, goats or cattle are present.

### What is Q fever?

Q (query) fever disease is caused by an infection with *Coxiella burnetii*, a Gram-negative bacterium in the Order Legionellales, Family Coxiellaceae. It is an intracellular pathogen that replicates in host monocytes and macrophages. It can infect a wide variety of animal species and is found worldwide except for New Zealand.

This bacterium has two morphotypes. The small-cell variant (SCV) is a dormant, environmentally persistent form of the bacterium that survives outside of host cells. It is often referred to as a spore though it is not. The SCV is also the bacterial form that infects susceptible host animals. The large-cell variant (LCV) is the bacterial form that replicates within

phagolysosomes in host cells. The LCV expresses a different suite of genes than the SCV.

*Coxiella burnetii* undergoes antigenic (also known as phase) variation during infection. Phase variation occurs when the bacterium modifies its lipopolysaccharides (LPS) during infection. When an animal or person is first infected the bacteria is coated with Phase I LPS, or antigen. But as the bacteria replicates in the body and the infection progresses the bacteria express Phase II LPS. High levels of antibody to Phase II LPS are therefore associated with acute infection. A high or increasing antibody response to Phase I LPS is likewise associated with chronic (or persistent) Q fever infections.

## I have a case of Q fever in CEDRS, what should I do?

1. A positive Q fever laboratory test entered into CEDRS triggers a public health investigation to determine if a case of Q fever exists.
2. Obtain the patient's medical case notes from the hospital, healthcare provider, or from an electronic medical records repository.
3. Review the patient's medical case notes to determine if they have a clinically compatible illness.
4. Speak to the healthcare provider if you need additional medical information about the case.
5. If the clinical presentation and laboratory tests indicate the patient is a case, then interview the case patient.
6. Complete the case report form and enter a summary case note in CEDRS

### Interviewing the case patient:

1. Verify the case patient's understanding of their diagnosis and treatment plan
2. Use the case report form to aid in interviewing the patient  
Confirm their date of illness onset and symptomatology
3. Query the case patient about possible exposures, whether other people share those exposures, and if so whether those people are also ill
4. If you feel other people may be at risk call the epidemiologist at CDPHE who handles Q fever to discuss the situation

### How do people get Q fever?

Most people get Q fever by inhaling the bacterium in dusts generated from areas where infected animals such as sheep, goats and cattle have given birth. This is because extremely high numbers of the bacteria can be found in parturition products, and the bacteria

survive for long periods in the environment. *Coxiella burnetii* can also be present in the milk, urine and feces of infected animals. Exposure to a single bacterium is sufficient to produce an infection.

Q fever has historically been seen as an occupational disease of slaughterhouse workers and people working with ruminants. But a number of outbreaks in recent decades have demonstrated that direct contact with these animals or materials derived from these animals is not necessary to acquire the infection.



In Colorado in 2005 a Q fever outbreak occurred at a horse boarding facility whose owners had purchased two goat herds. Persons who lived at or visited the ranch were infected through contacts with the goats. An additional group of people living within 1 mile of the facility (n = 138) were also tested to determine their infection status. Eight of those who tested positive had had no direct contacts with goats at the facility.

Soil samples from the ranch revealed the presence of *C. burnetii* in the environment, and it was suspected that bacteria laden dusts had been dispersed by the wind into the surrounding community. Thus, people in the surrounding community were exposed to the bacterium without ever having direct contact with a goat.

Similarly, a large-scale outbreak of Q fever occurred in the Netherlands between 2007 and 2010. Bacteria laden dusts from dairy goat and sheep farms in the country were dispersed across the landscape by winds, ultimately causing 1000s of infections in susceptible people living in adjacent areas.

Epidemiologically a Q fever case patient may have never had direct contact with an infected animal. Still, direct contact, aerosol exposures to birthing fluids, or spending time in areas where ruminants are present remains a significant risk factor for Q fever. Ranching, farming, practicing veterinary medicine and performing animal research therefore continue to be high risk occupations for the disease.

It should be noted that Q fever infections have also been acquired from animal species other than ruminants. Birds, reptiles, rodents and other pet animals can also be infected and be a source of exposure to people. Infections acquired from contacts with parturient pet cats and dogs have been reported. Ticks can also transmit *C. burnetii* to people through a tick bite though they are rarely identified as a source of infection.

### The clinical picture for Q fever

Asymptomatic infections occur in  $\geq 50\%$  of people. The incubation period for the disease is normally 2 to 3 weeks following an exposure, but may be up to almost 6 weeks. Time to illness onset depends at least in part on the bacterial dose and route of transmission.

Those with symptomatic infections may present with a highly variable clinical picture. Most cases report high fever and some combination of other symptoms such as chills, headache (can be severe), sore throat, malaise, fatigue, weight loss and myalgia. Patients may develop atypical pneumonia with non-productive cough and pneumonitis on X-ray. Hepatitis may appear as a granulomatous

process or accompanied by hepatomegaly, and rarely jaundice. Rash may be present.

Uncommon complications of acute infection have been reported involving the heart, nerves, gut and bone marrow. Laboratory findings for acute infection include thrombocytopenia and many patients will have moderately elevated serum transaminases.

The table below reports the clinical presentations of Colorado's acute Q fever cases from 2013.

Acute Q fever cases, CO

Primary clinical presentation	Age (years)	Sex
Culture negative endocarditis	31	F
Pneumonia	57	M
Pneumonia	78	M
Febrile illness	43	M
Night sweats, weight loss, joint pain	66	M

Chronic Q fever can develop months to years following acute symptomatic or asymptomatic infection. Patients with chronic Q fever will have persistently increased antibody (IgG) to Phase I LPS (antigen). Thrombocytopenia, anemia and hematuria may be present. Immunosuppressed people or those with a pre-existing heart defect are most at risk of developing chronic Q fever.

Recall that  $\geq 50\%$  of Q fever infections will be asymptomatic, and that mild Q fever can resemble a simple flu-like illness. This makes it easily understandable why infection with

this bacterium can go unrecognized leading to adverse outcomes. Risk of pregnancy complications exists for both acute and chronic Q fever. Cases of abortion and premature delivery have been associated with *C. burnetii* infection in pregnant women.

Endocarditis is the condition most commonly associated with chronic Q fever, though osteomyelitis, osteoarthritis, aortic aneurysms, hepatitis, and pulmonary or reproductive organ involvement are also reported. Healthcare providers should do an echocardiogram on patients who present with chronic Q fever to assess for cardiac involvement in the disease process. Patients with endocarditis will commonly have elevated sedimentation rates and C-reactive protein.

The table below reports the clinical presentations of Colorado’s chronic Q fever cases from 2013.

Chronic Q fever cases, CO

Primary clinical presentation	Age (years)	Sex
Endocarditis and hepatitis	29	M
Endocarditis	43	M
Osteomyelitis	46	M
Endocarditis	66	M

### Q fever in children

Reports of Q fever in children are uncommon. Colorado has had six pediatric Q fever cases since 2000. These were reported from Weld, Prowers and Pueblo Counties. The children all had direct exposures to goats, cows and/or sheep. They all presented to healthcare with a

febrile illness, were diagnosed serologically and were treated with doxycycline.

In general children seem to demonstrate a milder course of illness than adults. Duration of fever tends to be shorter, only 7 - 10 days as compared to 14 days in older people. Headaches occur frequently. Gastrointestinal symptoms are reported in 50 - 80% of cases, whereas they are rarely reported in adults. Rash may be present in up to 50% of cases. Pneumonia, hepatitis, and cardiovascular and neurological manifestations seem to occur less commonly than reported in adults. Cases of chronic Q fever in children are also rare. Osteomyelitis and endocarditis are the chronic conditions that have been reported in children.

### Understanding the laboratory tests, and what’s the difference between an acute and a chronic Q fever case?

A variety of laboratory tests are available to assist healthcare providers in diagnosing Q fever. Serology (IFA or ELISA) and PCR of tissue samples including blood and cardiac tissue are the most common assays used. Healthcare providers often also order serological titers on patients diagnosed with Q fever to allow for efficacy monitoring of antibiotic treatment in their patients.

In Colorado epidemiologists often receive serological test results for IgG against both phase I and II LPS (antigens). It can take a week or more from illness onset for an IgG response to develop, and if a sample is drawn too early in the course of infection the test result may be negative, or what we consider non-informative. Some laboratories can also perform IgM testing of patient serum but the IgM test is not commonly requested. Samples that test positive on a screening assay will be reflexed to titers, so expect titers to be

reported out for these serological assays.

Blood, cardiac valve or other tissues can be evaluated for the presence of the bacterium by PCR. Culture of this fastidious bacterium can only be done by certain laboratories under specific culture conditions and therefore culture results are seen infrequently. Immunohistochemistry demonstrating the presence of bacterial antigen can also be performed on tissue samples to yield a diagnosis.

During infection *C. burnetii* undergoes phase variation, essentially switching between two differently structured LPS. The LPS is a part of the bacterium that the body can 'see' and produce antibodies against. These modifications of bacterial LPS produce changes in the body's immune response over the course of infection. Thus serological (antibody) profiles tend to differ between patients with acute and chronic infections, as shown in the table below.

Type of Infection	Antibody response profile	Ratio rule of thumb
Acute	Phase II > Phase I (IgG and IgM)	PII : PI > 1
Chronic	Phase II < Phase I (IgG)	PII : PI < 1
Unclear	Phase II ≈ Phase I (IgG)	PII : PI ≈ 1

## Diagnosis of Q fever

Diagnosis of acute Q fever is based on clinical symptoms and results of laboratory tests. Antibody to *C. burnetii* usually begins to develop 7 to 10 days following acute symptom onset. Serology performed during the first week of illness may be negative, but a

subsequent sample should demonstrate a rise in serum antibodies. Blood taken very early in infection before antibiotic treatment is started may test positive by PCR or grow the bacterium in culture.

Diagnosis of chronic Q fever is more difficult because the clinical presentation is non-specific and the bacterium can infect bone, organs, lungs or reproductive tissues. Culture negative endocarditis is commonly associated with chronic Q fever. In such cases PCR of heart valve tissue may be necessary to confirm the etiologic agent. Serological tests are very helpful in making a diagnosis, and typically demonstrate a greater antibody response to Phase I LPS than to Phase II.

The table below shows a comparison between the antibody response profiles for acute and chronic Q fever.

Type of Infection	Antibody response	Example
Acute	Phase II > Phase I (IgG and IgM)	4096 > 1024
Chronic	Phase II < Phase I (IgG)	4096 < 32,768
Unclear	Phase II ≈ Phase I (IgG and IgM)	4096 = 4096

## What's the treatment for Q fever?

Q fever is a bacterial infection and can be successfully treated with antibiotics. The drug of choice for acute illness in adults is doxycycline. Doxycycline is also recommended for children who are severely ill with Q fever. Children with a mild infection and pregnant women who present with acute Q fever may be

treated with co-trimoxazole. The duration of antibiotic treatment depends on the type of patient and severity of illness, but is generally 2 to 3 weeks.

Chronic Q fever is commonly treated with a combination of doxycycline and hydroxychloroquine. The length of treatment depends on the patient's response to therapy, but is generally at least 18 months. If a patient has Q fever endocarditis then cardiac valve replacement surgery may be indicated.

### Do you have a cluster of cases, or an outbreak?

It is possible that you may identify additional suspect cases of Q fever during your interview with your case patient. If the exposures and illnesses you hear about seem compatible with such a scenario it may be warranted to investigate further.

Please call CDPHE to discuss your suspect case(s) with an epidemiologist who handles Q fever. This person can assist you in evaluating the exposure scenario, in arranging and conducting an environmental health investigation, and can facilitate testing of suspect cases if it seems indicated.

### The Q fever bacterium, *Coxiella burnetii*, is a select agent.

When investigating a case of Q fever the illness and circumstances surrounding the exposure should be evaluated to determine if an act of bioterrorism is suspected.

Immediately notify CDPHE if you suspect in any way that an infection might be related to bioterrorism.

Public health resources for Q fever are available at CDPHE's [Q fever webpage](#), or at [www.colorado.gov/pacific/cdphe/Q-fever](http://www.colorado.gov/pacific/cdphe/Q-fever).

## Resources