	Division of Community and Public Health	
	Section: 4.0 Diseases and Conditions	Revised 2/08
	Subsection: Q Fever	Page 1 of 8

Q Fever Table of Contents

[Q Fever](#)


[CDC Fact Sheet](#)

Disease Case Report (CD-1)

[PDF format](#)

[Word format](#)

[Q Fever Case Report” \(CDC 55.1\)](#)

	Division of Community and Public Health	
	Section: 4.0 Diseases and Conditions	Revised 2/08
	Subsection: Q Fever	Page 2 of 8

Q Fever

Overview ^(1,2)


Q Fever is a potential bioterrorism weapon. If you suspect that you are dealing with a bioterrorism situation, contact the [Senior Epidemiology Specialist from your District](#), and consult your emergency procedure manual.

Q fever is caused by the obligate intracellular pathogen *Coxiella burnetii*. Natural infection in humans is rare; when it does occur, it is most often the result of inhaling aerosolized organisms from the tissues, fluids, or excreta of infected animals. *C. burnetii* is considered a Category B bioterrorism agent; the organism would most likely be disseminated via an infectious aerosol. *C. burnetii* is highly infectious; a single organism may cause disease in a susceptible person. The organism is resistant to heat and drying.

The incubation period of Q fever is typically 7-21 days (range 2-41 days). Many cases of naturally-occurring acute Q fever are asymptomatic or very mild, and remain unnoticed. Of those who develop clinically apparent disease, <5% will be ill enough to require hospitalization. In symptomatic patients, onset is typically abrupt, with high fever, fatigue, headache, and chills. Sweats, myalgias, dry cough, and nausea are common. Fever typically increases to a plateau over 2-4 days then ends abruptly after 1-2 weeks; untreated, fever duration ranges from 5-57 days. Weight loss can occur. While a febrile syndrome with headache is probably the most common clinical presentation, atypical pneumonia or acute hepatitis syndromes are also seen. Patients with atypical pneumonia usually have a nonproductive cough, with pneumonitis on X-ray; in severe cases, lobar consolidation and pneumonia may be seen. Because Q fever usually presents as an undifferentiated febrile illness or a primary atypical pneumonia, it can be difficult to distinguish from a number of other viral and bacterial diseases.

While identification of a cluster of acute Q fever infections would raise concerns of possible bioterrorism, chronic infection with naturally-occurring *C. burnetii* can result in serious complications. The most common Q fever complication is endocarditis, generally involving the aortic heart valves. Most patients who develop chronic Q fever have pre-existing valvular heart disease or have 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 may die of the disease.

Reports of naturally-occurring *C. burnetii* infections in Missouri have been linked to contact with livestock such as cattle and sheep. In the United States, Q fever outbreaks have resulted mainly from occupational exposures involving veterinarians, meat processing plant workers, sheep and dairy workers, livestock farmers, and researchers at facilities housing sheep.

	Division of Community and Public Health	
	Section: 4.0 Diseases and Conditions	Revised 2/08
	Subsection: Q Fever	Page 3 of 8

For a complete description of Q Fever, refer to the following texts:

- [Control of Communicable Diseases Manual \(CCDM\)](#).
- [Red Book](#), Report of the Committee on Infectious Diseases.
- [Q Fever, in USAMRIID's Medical Management of Biological Casualties Handbook \(6th Ed\), 2005, 47-53.](#)

Case Definition ⁽³⁾

Clinical presentation:

- **Acute infection**: Acute fever usually accompanied by rigors, myalgia, malaise, and a severe retrobulbar headache. Fatigue, night-sweats, dyspnea, confusion, nausea, diarrhea, abdominal pain, vomiting, non-productive cough, and chest pain have also been reported. Severe disease can include acute hepatitis, atypical pneumonia with abnormal radiograph, and meningoencephalitis. Pregnant women are at risk for fetal death and abortion. Clinical laboratory findings may include elevated liver enzyme levels, leukocytosis, and thrombocytopenia. Asymptomatic infections may also occur.

Note: Serologic profiles of pregnant women infected with acute Q fever during gestation may progress frequently and rapidly to those characteristics of chronic infection.

- **Chronic infection**: Infection that persists for more than 6 months. Potentially fatal endocarditis may evolve months to years after acute infection, particularly in persons with underlying valvular disease. Infections of aneurysms and vascular prostheses have been reported. Immunocompromised individuals are particularly susceptible. Rare cases of chronic hepatitis without endocarditis, osteomyelitis, osteoarthritis, and pneumonitis have been described.

Clinical evidence:

- **Acute Q fever**: Acute fever and one or more of the following: rigors, severe retrobulbar headache, acute hepatitis, pneumonia, or elevated liver enzyme levels.
- **Chronic Q fever**: Newly recognized, culture-negative endocarditis, particularly in a patient with previous valvulopathy or compromised immune system, suspected infection of a vascular aneurysm or vascular prosthesis, or chronic hepatitis, osteomyelitis, osteoarthritis, or pneumonitis in the absence of other known etiology.

Laboratory evidence:

- **Acute Q fever**
Laboratory confirmed:
 - Serological evidence of a fourfold change in immunoglobulin G (IgG)-specific antibody titer to *C. burnetii* phase II antigen by indirect immunofluorescence assay (IFA) between paired serum samples, (CDC suggests one taken during the first week of illness and a second 3-6 weeks later, antibody titers to phase I antigen may be



elevated or rise as well), **or**

- o Detection of *C. burnetii* DNA in a clinical specimen via amplification of a specific target by polymerase chain reaction (PCR) assay, **or**
- o Demonstration of *C. burnetii* antigen in a clinical specimen by immunohistochemical methods (IHC), **or**
- o Isolation of *C. burnetii* from a clinical specimen by culture.

Laboratory supportive:

- o Has a single supportive IFA IgG titer of $\geq 1:128$ to phase II antigen (phase I titers may be elevated as well).
- o Has serologic evidence of elevated IgG or IgM antibody reactive with *C. burnetii* antigen by enzyme-linked immunosorbent assay (ELISA), dot-ELISA, or latex agglutination.

• **Chronic Q fever**

Laboratory confirmed:

- o Serological evidence of IgG antibody to *C. burnetii* phase I antigen $\geq 1:800$ by IFA (while phase II IgG titer will be elevated as well; phase I titer is higher than the phase II titer), **or**
- o Detection of *C. burnetii* DNA in a clinical specimen via amplification of a specific target by PCR assay, **or**
- o Demonstration of *C. burnetii* antigen in a clinical specimen by IHC, **or**
- o Isolation of *C. burnetii* from a clinical specimen by culture.


Laboratory supportive:

- o Has an antibody titer to *C. burnetii* phase I IgG antigen $\geq 1:128$ and $< 1:800$ by IFA.

Note: Samples from suspected chronic patients should be evaluated for IgG titers to both phase I and phase II antigens. Current commercially available ELISA tests (which test only for phase 2) are not quantitative, cannot be used to evaluate changes in antibody titer, and hence are not useful for serological confirmation. IgM tests are not strongly supported for use in serodiagnosis of acute disease, as the response may not be specific for the agent (resulting in false positives) and the IgM response may be persistent. Complement fixation (CF) tests and other older test methods are neither readily available nor commonly used. For acute testing, CDC uses in-house IFA IgG testing (cutoff of $\geq 1:128$), preferring simultaneous testing of paired specimens, and does not use IgM results for routine diagnostic testing. ⚠Serologic test results must be interpreted with caution, because baseline antibodies acquired as a result of historical exposure to Q fever may exist, especially in rural and farming areas.

Exposure:

Exposure is usually via aerosol, is broadly interpreted, and may be unknown (especially for chronic infection), but often includes the presence of goats, sheep, or other livestock,

	Division of Community and Public Health	
	Section: 4.0 Diseases and Conditions	Revised 2/08
	Subsection: Q Fever	Page 5 of 8

especially during periods of parturition. Direct contact with animals is not required, and variable incubation periods may be dose dependent.

Detailed definitions for case classification:

Confirmed acute Q Fever: A laboratory confirmed case that either meets clinical case criteria or is epidemiologically linked to a lab confirmed case.

Probable acute Q Fever: A clinically compatible case of acute illness (meets clinical evidence criteria for acute Q fever illness) that has laboratory supportive results for past or present acute disease (antibody to Phase II antigen) but is not laboratory confirmed.

Confirmed chronic Q Fever: A clinically compatible case of chronic illness (meets clinical evidence criteria for chronic Q fever) that is laboratory confirmed for chronic infection.

Probable chronic Q Fever: A clinically compatible case of chronic illness (meets clinical evidence criteria for chronic Q fever) that has laboratory supportive results for past or present chronic infection (antibody to Phase I antigen).

Information Needed for Investigation

Verify the diagnosis. What laboratory tests were conducted and what were the results?

Establish the extent of illness. Determine if household, close contacts or other individuals in the geographic area are, or have been, ill by contacting the health care provider, patient or family members.


Determine the source of the infection by identifying possible exposure to livestock or other animals, especially those that have recently delivered offspring or had spontaneous abortions. Infected livestock may be asymptomatic.

Identify possible exposure to facilities where livestock are kept or processed, such as feedlots, slaughterhouses etc. Bear in mind that the major mode of transmission is airborne spread of dust and other particles that have become contaminated with the organism. Airborne spread of over one-half mile from the source has been documented.⁽⁴⁾

Identify possible exposure to potentially contaminated livestock products, such as raw milk, wool, hides, etc. Also, consider such indirect exposure as laundering clothes that may have been contaminated with birth tissues or fluids.

Notification and Control Measures

- Contact the [District Communicable Disease Coordinator](#) for assistance, if needed. The Department of Health and Senior Services’ Situation Room (DSR) is available (24/7) for assistance at (800)-392-0272.

	Division of Community and Public Health	
	Section: 4.0 Diseases and Conditions	Revised 2/08
	Subsection: Q Fever	Page 6 of 8

Control Measures

General:

Although most cases resolve spontaneously, antibiotics are often recommended due to the risk of serious sequelae. Persons with suspected Q fever should be encouraged to consult a physician.

Isolation of the Hospital Patient:

None. Direct person-to-person transmission occurs rarely, if ever. However, contaminated clothing may be a source of infection. Use **Standard Precautions** during patient care.

Concurrent disinfection using .05% hypochlorite, 5% peroxide or a 1:100 solution of Lysol for sputum, blood, or articles contaminated with sputum or blood.

See the Control of Communicable Diseases Manual, Q Fever, “Methods of control.”

See the Red Book, Q Fever, “Control Measures.”

Laboratory Procedures


Specimens:

Serum: The serologic tests (IgG and IgM) are available from major commercial laboratories and generally require a minimum of 1-2 ml of serum. The State Public Health Laboratory (SPHL) does not test for *C. burnetii*, but can submit specimens to CDC for testing. CDC performs indirect immunofluorescence serology.

Coxiella burnetii exists in two antigenic phases called phase I and phase II. This antigenic difference is important in diagnosis. In acute cases of Q fever, 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. Thus, 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 antigens and II have been known to persist for months or years after initial infection.

Recent studies have shown that greater accuracy in the diagnosis of Q fever can be achieved by looking at specific levels of classes of antibodies other than IgG, namely IgA and IgM. Combined detection of IgM and IgA in addition to IgG improves the specificity of the assays and provides better accuracy in diagnosis. IgM levels are helpful in the determination of a recent infection. In acute Q fever, patients will have IgG antibodies to phase II and IgM antibodies to phases I and II. Increased IgG and IgA antibodies to phase I are often indicative of Q fever endocarditis.

Generally, bacterial isolation is not recommended due to risk to the technicians.

	Division of Community and Public Health	
	Section: 4.0 Diseases and Conditions	Revised 2/08
	Subsection: Q Fever	Page 7 of 8

Additional information on laboratory procedures can be obtained from the District Communicable Disease Coordinator or from staff at the SPHL. The SPHL telephone number is 573-751-3334 and the web site is: <http://www.dhss.mo.gov/Lab/index.html> (2/08).

Reporting Requirements


Q fever is a Category I(B) disease and shall be reported to the local health authority or to the Missouri Department of Health and Senior Services (DHSS) within 24 hours of first knowledge or suspicion by telephone (800) 392-0272, facsimile or other rapid communication.

1. For all reported cases complete a “[Disease Case Report](#)” (CD-1) (2/08).
2. For confirmed and probable cases, complete a “[Q Fever Case Report](#)” (CDC 55.1) (2/08).
3. Entry of the complete CD-1 into MOHSIS negates the need for the paper CD-1 to be forwarded to the District Health Office.
4. Send the completed secondary investigation form to the District Health Office.
5. All outbreaks or “suspected” outbreaks must be reported as soon as possible (by phone, fax or e-mail) to the District Communicable Disease Coordinator. This can be accomplished by completing the [Missouri Outbreak Surveillance Report \(CD-51\)](#) (2/08).
6. Within 90 days from the conclusion of an outbreak, submit the final outbreak report to the District Communicable Disease Coordinator.

NOTE: Q Fever is a potential bioterrorism weapon. All cases of Q Fever reported in Missouri to date have been from naturally occurring causes. **If the case has no remarkable travel history and is not employed in an occupation that is prone to exposure (working with livestock or other animals), a bioterrorism event should be considered.** If you suspect that you are dealing with a bioterrorism situation, contact the [Senior Epidemiology Specialist for your District](#), or the Missouri Department of Health and Senior Services Situation Room (800) 392-0272 immediately.

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	Division of Community and Public Health	
	Section: 4.0 Diseases and Conditions	Revised 2/08
	Subsection: Q Fever	Page 8 of 8

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