

07-ID-04

Committee: Infectious Diseases

Title: Revision of the Surveillance Case Definition for Q fever

Statement of the Problem:

The purpose of the recommended revisions to the surveillance case definition of Q fever, a disease under public health surveillance, is to clarify misleading or poorly defined laboratory statements, and to improve case classification for reporting.

Statement of the desired action to be taken:

Revise the national surveillance case definition for Q Fever.

Goals of surveillance:

The improved case definition will provide the tools to help establish the burden of disease due to this pathogen. This will provide a greater understanding of this disease among physicians, nurses, and public health professionals and allow for appropriate prevention messages to the public.

Methods for surveillance:

Case finding is conducted through clinician and laboratory reporting. Core surveillance data will be reported to the National Notifiable Disease Surveillance System (NNDSS) through the National Electronic Telecommunications System for Surveillance (NETSS) or the National Electronic Disease Surveillance System (NEDSS), as per state protocol.

Case Definition:**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 characteristic 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.

1. Acute Q fever

Laboratory evidence:

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

Laboratory supportive:

- Has a single supportive IFA IgG titer of $\geq 1:128$ to phase II antigen (phase I titers may be elevated as well).
- 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.

1. Chronic Q fever

Laboratory evidence:

Laboratory confirmed:

- 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
- Detection of *C. burnetii* DNA in a clinical specimen via amplification of a specific target by PCR assay, or
- Demonstration of *C. burnetii* antigen in a clinical specimen by IHC, or
- Isolation of *C. burnetii* from a clinical specimen by culture.

Laboratory supportive:

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

Case definition tables:

Suggested codes for case ascertainment

To be developed.

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).

Period of surveillance:

Ongoing. This revision of the surveillance case definition will be effective January 1, 2008.

Background and Justification:

The case definition for Q fever was first developed and posted in 1999 and has not been subsequently modified. While the Laboratory Resource Network (LRN) has assays and protocols for *Coxiella burnetii*, the current case definition is not designed to be used for that purpose. The LRN has different threshold levels which initiate additional testing and authoritative response. The case definition for public health surveillance is designed to better define the burden of disease due to this pathogen in the United States. In the current revision, the acute and chronic forms of the disease and the corresponding laboratory features are better delineated. By separating the acute and chronic forms of the disease, we believe we will be able to gain a better understanding of the Q Fever disease complex as it currently exists in U.S. populations. This should eliminate confusion that has existed in the previous definition. These improvements will also serve to improve Q fever surveillance and consequently will improve surveillance for possible use of this agent in a bioterrorism event.

References:

- **1999 Case Definition**

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