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.

Q fever (*Coxiella burnetii*) case definition

The case definition for Q fever was first developed and posted in 1999 and has not been subsequently modified. While the Laboratory Resource Network 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.

Statement of desired action to be taken:

CSTE recommends that CDC promptly adopt the new surveillance case definition for Q fever, as presented in the Appendix.

CDC should revise the case report form for Q fever to reflect the changes made in this revision.

CDC should partner with local, state, and territorial health departments to transfer technology for molecular testing to the public health laboratories. This will enhance jurisdictions' ability to better determine the burden of disease due to this pathogen.

CDC should partner with local, state, and territorial health departments to improve physician awareness of this disease and methods for diagnosis.

Public health impact:

The benefit of these changes is to reduce the number of cases that are inappropriately categorized, and to improve surveillance reporting by simplifying case categorization.

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.

The changes proposed will require CDC to revise the existing case report form for Q fever. Because the changes are not complex, and will serve to improve surveillance efforts, we anticipate that this task will not be too difficult to complete rapidly.

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APPENDIX

Q Fever *(Coxiella burnetii)*

2007 Case Definition (*proposed*)

Clinical description

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 have been described.

1. Acute Q fever

Clinical criteria

Acute fever and one or more of the following: rigors, severe retrobulbar headache, acute hepatitis, pneumonia, or elevated liver enzyme levels.

Laboratory criteria

- 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.

Case classification

Confirmed: A person with clinical criteria for acute disease or one who is epidemiologically linked to a confirmed case, **either of whom also** meet at least one of the acute Q fever laboratory criteria.

Probable: A person with clinical criteria for acute disease, who does not meet any of the laboratory criteria for for acute Q fever, **but** has a single supportive IFA IgG titer of ≥1:128 to phase II antigen (phase I titers may be elevated as well).

2. Chronic Q fever

Clinical criteria

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 in the absence of other known etiology.

Laboratory criteria

- Serological evidence of IgG antibody to *C. burnetii* phase I antigen ≥ 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.

Case classification

Confirmed: A person who meets chronic Q fever clinical criteria **who also** meets at least one of the chronic Q fever laboratory criteria.

Probable: A person who meets chronic Q fever clinical criteria, who does not meet the criteria for a confirmed case, **but** has an antibody titer to *C. burnetii* phase I IgG antigen ≥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 ≥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.

See also:

- **1999 Case Definition**