09-ID-54

Committee: Infectious

Title: Public Health Reporting and National Notification for Q fever

I. Statement of the Problem

CSTE position statement 07-EC-02 recognized the need to develop an official list of nationally notifiable conditions and a standardized reporting definition for each condition on the official list. The position statement also specified that each definition had to comply with American Health Information Community recommended standards to support "automated case reporting from electronic health records or other clinical care information systems." In July 2008, CSTE identified sixty-eight conditions warranting inclusion on the official list, each of which now requires a standardized reporting definition.

II. Background and Justification

Background[1]

Q fever is a zoonotic disease caused by *Coxiella burnetii*, a species of bacteria that is distributed globally. In 1999, Q fever became a notifiable disease in the United States but reporting is not required in many other countries. Because the disease is underreported, scientists cannot reliably assess how many cases of Q fever have actually occurred worldwide. Many human infections are inapparent.

Cattle, sheep, and goats are the primary reservoirs of *C. burnetii*. Infection has been noted in a wide variety of other animals, including other species of livestock and in domesticated pets. *C. burnetii* does not usually cause clinical disease in these animals, although abortion in goats and sheep has been linked to *C. burnetii* infection. Organisms are excreted in milk, urine, and feces of infected animals. Most importantly, during birthing the organisms are shed in high numbers within the amniotic fluids and the placenta. The organisms are resistant to heat, drying, and many common disinfectants. These features enable the bacteria to survive for long periods in the environment. Infection of humans usually occurs by inhalation of these organisms from air that contains airborne barnyard dust contaminated by dried placental material, birth fluids, and excreta of infected herd animals. Humans are often very susceptible to the disease, and very few organisms may be required to cause infection.

Only about one-half of all people infected with *C. burnetii* show signs of clinical illness. Most acute cases of Q fever begin with sudden onset of one or more of the following: high fevers (up to 104-105° F), severe headache, general malaise, myalgia, confusion, sore throat, chills, sweats, non-productive cough, nausea, vomiting, diarrhea, abdominal pain, and chest pain. Fever usually lasts for 1 to 2 weeks. Weight loss can occur and persist for some time. Thirty to fifty percent of patients with a symptomatic infection will develop pneumonia. Additionally, a majority of

[1] Much of the material in the background is directly quoted from the CDC's Q fever Website. See the References for further information on this source.

patients have abnormal results on liver function tests and some will develop hepatitis. In general, most patients will recover to good health within several months without any treatment. Only 1%-2% of people with acute Q fever die of the disease.

Chronic Q fever, characterized by infection that persists for more than 6 months is uncommon but is a much more serious disease. Patients who have had acute Q fever may develop the chronic form as soon as 1 year or as long as 20 years after initial infection. A serious complication of chronic Q fever is endocarditis, generally involving the aortic heart valves, less commonly the mitral valve. Most patients who develop chronic Q fever have pre-existing valvular heart disease or have a history of 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.

Because the signs and symptoms of Q fever are not specific to this disease, it is difficult to make an accurate diagnosis without appropriate laboratory testing. Results from some types of routine laboratory tests in the appropriate clinical and epidemiologic settings may suggest a diagnosis of Q fever. For example, abnormal liver function tests may support a diagnosis of Q fever. Confirming a diagnosis of Q fever requires serologic testing to detect the presence of antibodies to *C. burnetii* antigens. In most laboratories, the indirect immunofluorescence assay (IFA) is the most dependable and widely used method. *C. burnetii* may also be identified in infected tissues by using immunohistochemical staining, DNA detection methods, or by direct isolation of the agent via culture.

Justification

Q fever meets the following criteria for a nationally notifiable and **standard notification**, as specified in CSTE position statement 08-EC-02:

- A majority of state and territorial jurisdictions—or jurisdictions comprising a majority of the US population—have laws or regulations requiring **standard** reporting of Q fever to public health authorities
- CDC requests **standard** notification of Q fever to federal authorities
- CDC has condition-specific policies and practices concerning the agency's response to, and use of, notifications.

III. Statement of the desired action(s) to be taken

CSTE requests that CDC adopt this standardized reporting definition for Q fever to facilitate more timely, complete, and standardized local and national reporting of this condition.

IV. Goals of Surveillance

To provide information on the temporal, geographic, and demographic occurrence of Q fever to facilitate its prevention and control.

V. Methods for Surveillance

Surveillance for Q fever should use the sources of data and the extent of coverage listed in Table V below.

Table V. Recommended sources of data and extent of coverage for ascertaining cases of Q fever.

	Coverage	
Source of data for case ascertainment	Population-wide	Sentinel sites
clinician reporting	x	
laboratory reporting	x	
reporting by other entities (e.g., hospitals, veterinarians, pharmacies)	x	
death certificates	x	
hospital discharge or outpatient records	x	
extracts from electronic medical records	x	
telephone survey		
school-based survey		
other _____		

VI. Criteria for Reporting

Reporting refers to the process of healthcare providers or institutions (e.g., clinicians, clinical laboratories, hospitals) submitting basic information to governmental public health agencies about cases of illness that meet certain reporting requirements or criteria. Cases of illness may also be ascertained by the secondary analysis of administrative health data or clinical data. The purpose of this section is to provide those criteria to determine whether a specific illness should be reported.

A. Narrative description of criteria to determine whether a case should be reported to public health authorities

Report any illness to public health authorities that meets any of the following criteria:

1. Acute Q fever

   One or more of the following laboratory findings:
   - 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
   - Detection of *C. burnetii* DNA in a clinical specimen via amplification of a specific target by polymerase chain reaction (PCR) assay

- Demonstration of *C. burnetii* antigen in a clinical specimen by immunohistochemical methods (IHC)
- Isolation of *C. burnetii* from a clinical specimen by culture
- Single IFA IgG titer of ≥1:128 to phase II antigen
- Serologic evidence of elevated IgG or IgM* antibody reactive with *C. burnetii* antigen by enzyme-linked immunosorbent assay (ELISA)
- Serologic evidence of elevated IgG or IgM* antibody reactive with *C. burnetii* antigen by dot-ELISA
- Serologic evidence of elevated IgG or IgM* antibody reactive with *C. burnetii* antigen by latex agglutination

and either

Fever *and* one or more of the following:

- Rigors
- Severe retrobulbar headache
- Acute hepatitis
- Pneumonia
- Elevated liver enzyme levels

or

(In the instance of a case that does not meet clinical criteria but is otherwise a laboratory confirmed case) an epidemiological link to another laboratory confirmed case of Q fever

2. Chronic Q fever

A person with one of the following clinical presentations in the absence of other known etiology:

- 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
- Chronic hepatitis
- Osteomyelitis,
- Osteoarthritis
- Pneumonitis

and

Infection persists more than 6 months

and

One or more of the following laboratory findings:

- Detection of *C. burnetii* DNA in a clinical specimen via amplification of a Specific target by polymerase chain reaction (PCR) assay
- Demonstration of *C. burnetii* antigen in a clinical specimen by immunohistochemical methods (IHC)
- Isolation of *C. burnetii* from a clinical specimen by culture
- Serological evidence of IgG antibody to *C. burnetii* phase I antigen ≥ 1:800 by IFA and Phase I titer higher than Phase II titer (laboratory confirmed)

- Antibody titer to *C. burnetii* phase I IgG antigen ≥1:128 and < 1:800 by IFA (laboratory probable)

3. A person whose healthcare record contains a diagnosis of Q fever.

4. A person whose death certificate lists Q fever as a cause of death or a significant condition contributing to death.

Other recommended reporting procedures

- All cases of Q fever should be reported.
- Reporting should be on-going and routine.
- Reporting should be immediate.

B. Table of criteria to determine whether a case should be reported to public health authorities

Table VI-B. Table of criteria to determine whether a case should be reported to public health authorities. Requirements for reporting are established under State and Territorial laws and/or regulations and may differ from jurisdiction to jurisdiction. These criteria are suggested as a standard approach to identifying cases of this condition for purposes of reporting, but reporting should follow State and Territorial law/regulation if any conflicts occur between these criteria and those laws/regulations.

Criterion	**Reporting**			
Clinical Evidence				
Fever		N		
Rigors		O		
Severe retrobulbar headache		O		
Acute hepatitis		O		
Pneumonia		O		
Elevated liver enzyme levels		O		
Culture-negative endocarditis (particularly in a patient with previous valvulopathy or compromised immune system)				O
Suspected infection of a vascular aneurysm				O
Suspected infection of a vascular prosthesis				O
Chronic hepatitis				O
Chronic osteomyelitis				O
Chronic osteoarthritis				O
Chronic pneumonitis				O

Infection persists >6 months				N
Absence of other known etiology				N
Healthcare record contains a diagnosis of Q fever	S			
Death certificate lists Q fever as a cause of death or a significant condition contributing to death	S			
Laboratory Evidence†				
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		O	O	
Detection of *C. burnetii* DNA in a clinical specimen via amplification of a specific target by polymerase chain reaction (PCR) assay		O	O	O
Demonstration of *C. burnetii* antigen in a clinical specimen by immunohistochemical methods (IHC)		O	O	O
Isolation of *C. burnetii* from a clinical specimen by culture		O	O	O
Single IFA IgG titer of ≥1:128 to phase II antigen		O	O	
Serologic evidence of elevated IgG or IgM* antibody reactive with *C. burnetii* antigen by enzyme-linked immunosorbent assay (ELISA)		O	O	
Serologic evidence of elevated IgG or IgM* antibody Reactive with *C. burnetii* antigen by dot-ELISA		O	O	
Serologic evidence of elevated IgG or IgM* antibody reactive with *C. burnetii* antigen by latex agglutination		O	O	
Serological evidence of IgG antibody to *C. burnetii* phase I antigen ≥ 1:800 by IFA (laboratory confirmed)				
Antibody titer to *C. burnetii* phase I IgG antigen ≥1:128 and < 1:800 by IFA (laboratory probable)				
Epidemiologic Evidence				
Epidemiological link to a laboratory confirmed case of Q fever			N	

Notes:
S = This criterion alone is Sufficient to identify a case for reporting.
N = All "N" criteria in the same column are Necessary to identify a case for reporting.
O = At least one of these "O" (Optional) criteria in each category (i.e., clinical evidence and laboratory evidence) in the same column—in conjunction with all "N" criteria in the same column—is required to identify a case for reporting. (These optional criteria are alternatives, which means that a single column will have either no O criteria or multiple O criteria; no column should have only one O.)

* 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.
† 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. 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.

C. Disease Specific Data Elements:

Disease-specific data elements to be included in the initial report are listed below.

II. Case Definition for Case Classification:

A. Narrative description of criteria to determine whether a case should be classified as confirmed or probable (presumptive) is provided in table 3:

Acute Q Fever

Clinical presentation

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.

Clinical evidence

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

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* 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 ≥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.

Note: 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.

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.

Chronic Q Fever

Clinical presentation

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

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

Laboratory confirmed:

- 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.

Laboratory supportive:

- 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.

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.

Case Classification

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).

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.

B. Classification Tables

Table VII-B lists the criteria that must be met for a case to be classified as confirmed or probable (presumptive).

Table VII-B. Table of criteria to determine whether a case is classified.

Criterion	**Acute Q fever**			**Chronic Q fever**	
	Case Definition			**Case Definition**	
	Confirmed		**Probable**	**Confirmed**	**Probable**
Clinical Evidence					
Fever	N		N		
Rigors	O		O		
Severe retrobulbar headache	O		O		
Acute hepatitis	O		O		
Pneumonia	O		O		
Elevated liver enzyme levels	O		O		
Culture-negative endocarditis (particularly in a patient with previous valvulopathy or compromised immune system)				O	O
Suspected infection of a vascular aneurysm				O	O
Suspected infection of a vascular prosthesis				O	O
Chronic hepatitis				O	O
Chronic osteomyelitis				O	O
Chronic osteoarthritis				O	O
Chronic pneumonitis				O	O
Absence of other known etiology				N	N
Laboratory Evidence†					
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	O	O			
Detection of *C. burnetii* DNA in a clinical specimen via amplification of a specific target by polymerase chain reaction (PCR) assay	O	O		O	
Demonstration of *C. burnetii* antigen in a clinical specimen by immunohistochemical	O	O		O	

Criterion	Acute Q fever			Chronic Q fever	
	Case Definition			Case Definition	
	Confirmed		Probable	Confirmed	Probable
methods (IHC)					
Isolation of *C. burnetii* from a clinical specimen by culture	O	O		O	
Single IFA IgG titer of ≥1:128 to phase II antigen			O		
Serologic evidence of elevated IgG or IgM* antibody reactive with *C. burnetii* antigen by enzyme-linked immunosorbent assay (ELISA)			O		
Serologic evidence of elevated IgG or IgM* antibody reactive with *C. burnetii* antigen by dot-ELISA			O		
Serologic evidence of elevated IgG or IgM* antibody reactive with *C. burnetii* antigen by latex agglutination			O		
Serological evidence of IgG antibody to *C. burnetii* phase I antigen ≥ 1:800 by IFA				N	
C. burnetii phase I titer > *C. burnetii* phase II titer				N	
Antibody titer to *C. burnetii* phase I IgG antigen ≥1:128 and < 1:800 by IFA					N
Epidemiological link to a laboratory confirmed case of Q fever		N			

Notes:
N = All "N" criteria in the same column are Necessary to classify a case.
O = At least one of these "O" (Optional) criteria in each category (i.e., clinical evidence and laboratory evidence) in the same column—in conjunction with all "N" criteria in the same column—is required to classify a case.
* 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.
† 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. 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.

VIII. Period of Surveillance

Surveillance should be on-going.

IX. Data sharing/release and print criteria

Notification to CDC for all confirmed and probable cases of Q fever is recommended.

- All confirmed and probable cases should be sent via standard notification to CDC. Summaries and analyses of reported cases of Q fever are compiled and published periodically dependent upon accumulation of data and changes in disease activity and regional incidence.
- Annual state case totals and national incidence rates are available via MMWR.
- Final verification of case counts with state health departments is usually completed by August of the year following the surveillance year and reported annually in the National Summary of Notifiable Diseases - United States published in March or April of the subsequent year.
- Aggregate numbers of cases the United States are available to WHO via MMWR.

X. References

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