Kansas
Department of Health and Environment
Division of Health

Q Fever (*Coxiella burnetii* Infection) Investigation Guideline

Contents

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05/2018	12/2013	Updated format. Notification Section modified with requirements of new reporting regulations.
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Q Fever (*Coxiella burnetii* Infection)
Disease Management and Investigation Guidelines

CASE DEFINITIONS

Acute (CDC 2009)

Clinical Evidence for Surveillance:

Acute fever **and** one or more of the following:

- rigors,
- severe retrobulbar headache,
- acute hepatitis,
- pneumonia, or
- elevated liver enzyme levels.

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

Laboratory Criteria:

Confirmatory laboratory:

- Serological evidence of a fourfold change in IgG antibody titer to *C. burnetii* phase **II** antigen by IFA between paired serum samples, (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 specific target by PCR assay, or
- Demonstration of *C. burnetii* in a clinical specimen by IHC, or
- Isolation of *C. burnetii* from a clinical specimen by culture.

Supportive laboratory:

- Single supportive IFA IgG titer of ≥1:128 to phase **II** antigen (phase I titers may be elevated as well).
- Serologic evidence of elevated phase II IgG or IgM antibody reactive with *C. burnetii* antigen by ELISA, dot-ELISA, or latex agglutination.

Chronic (CDC 2009)

Clinical Evidence for Surveillance:

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 Criteria:

Confirmatory laboratory:

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

Supportive laboratory:

- An IgG antibody titer to *C. burnetii* phase **I** antigen **≥1:128 and <1:800** by IFA.

Abbreviations:

IgG: immunoglobulin G

IFA: indirect immunofluorescence assay

PCR: polymerase chain reaction

IHC: immunohistochemical methods

IgM: immunoglobulin M

ELISA: enzyme-linked immunosorbent assay

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)

LABORATORY ANALYSIS:

1) The State Public Health Laboratory forwards all specimens and isolates to the CDC. Specimens sent to CDC must have prior authorization from the State Epidemiology Program (1-877-427-7317) before they are processed.
   - For additional information and/or questions call (785) 296-1620.
2) Recommendations from CDC:
   - Paired serum samples: take one sample during the first week of illness and a second sample 3-6 weeks later.
   - For acute testing: The 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.
     - 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.
     - Serologic profiles of pregnant women infected with acute Q fever during gestation may progress frequently and rapidly to those characteristic of chronic infection
   - For chronic 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.
   - Complement fixation (CF) tests and other older test methods are neither readily available nor commonly used.
   - Interpret serologic test results with caution, because baseline antibodies acquired as a result of historical exposure to Q fever may exist, especially in rural and farming areas.
3) Serological testing – Phase I and II antigens:
   - In acute cases, Phase II antibody levels are usually higher than Phase I;

generally detected during the second week of illness.

- In chronic Q fever, Phase I antibody levels usually higher than Phase II.
- Phase I antibodies generally require longer to appear and indicate continued exposure to the bacteria. High levels to Phase I antibodies in later specimens with constant or falling levels of Phase II antibodies and other signs of inflammatory disease suggest chronic Q fever.
- Antibodies to Phase I and II antigens have been known to persist for months or years after initial infection

EPIDEMIOLOGY

A zoonotic disease, Q fever is caused by *C. burnetii*. It is unable to replicate outside a host but the spore-like form of the organism is resistant to heat, dehydration and many antiseptic compounds. *C. burnetii* is very infectious and is usually associated with direct contact to domestic goats, cattle or sheep. The risk is greatest when humans are exposed to these animals during the birthing process when the organism may be aerosolized from the uterus

DISEASE OVERVIEW

A. Agent:

Coxiella burnetii is a pleomorphic intracellular coccobacillus.

B. Clinical Description:

Acute symptoms include 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.

Chronic disease is characterized by an 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. Rare cases of chronic hepatitis without endocarditis, osteomyelitis, osteoarthritis, and pneumonitis have occurred.

C. Reservoirs:

Domestic and wild animals.

D. Mode(s) of Transmission:

Dissemination often occurs by the airborne dissemination of *C. burnetii* in the dust from premises contaminated by placental tissues, birth fluid and excreta of infected animals. Transmission may also occur from direct contact with infected animals and/or other contaminated materials, such as: wool, straw and laundry.

E. Incubation Period:

Usually 14-22 days; range 9-39 days.

F. Period of Communicability:
Direct transmission from person-to-person rarely, if ever, occurs

G. Susceptibility and Resistance:
Susceptibility is general and immunity following illness is life-long.

H. Treatment:
Q fever usually resolves without treatment within 15 days; however, tetracycline or doxycycline have been shown to shorten the duration of illness and are the drugs of choice; chloramphenicol may be used in children.

NOTIFICATION TO PUBLIC HEALTH AUTHORITIES

Suspected cases of Q fever shall be reported within 24 hours, except if the reporting period ends on a weekend or state-approved holiday, the report shall be made by 5:00 p.m. on the next business day after the 24-hour period:

1. Health care providers and hospitals: report to local public health.
2. Local public health jurisdiction: report to KDHE-BEPHI (see below).
3. Laboratories: report to KDHE-BEPHI (see below).

Kansas Department of Health and Environment (KDHE)
Bureau of Epidemiology and Public Health Informatics (BEPHI)
Phone: 1-877-427-7317
Fax: 1-877-427-7318

Further responsibilities of state and local health departments to the CDC:

As a nationally notifiable condition, confirmed and probable cases require a STANDARD report to the Center of Disease Control and Prevention (CDC).

1. STANDARD reporting requires KDHE-BEPHI to file an electronic report for within the next reporting cycle.
2. **Local public health jurisdiction** will report information requested as soon as possible, ensuring that the electronic form is completed within 3 days.

INVESTIGATOR RESPONSIBILITIES

1) Report all Q fever cases to the KDHE-BEPHI.
   - Initiate the case investigation within 1 days of notification of a report.
   - Complete the investigation within 3 days of the notification.
2) Contact medical provider to collect additional information and confirm diagnosis using current case definition. For all diagnosed cases:
   - Collect all information requested in Step 1 of case investigation.
   - Ensure that case/proxy is aware of the diagnosis.
3) Conduct a case investigation to determine the individual's risks of exposure and potential geographical location of exposure.
4) Identify whether the source of infection is major public health concern.
5) Record data, collected during the investigation, in the KS EpiTrax system under the data's associated [tab] in the case morbidity report (CMR).
6) As appropriate, use the disease fact sheet.

STANDARD CASE INVESTIGATION AND CONTROL METHODS

Case Investigation

Keep in mind that for Q fever, exposure is usually via aerosol and may be unnoticed (especially for chronic infection). Common exposures include the presence of goats, sheep, or other livestock, especially during periods of parturition. Direct contact with animals is not required, and incubation periods may be dose dependent. Infectious particles can be carried downwind a half-mile or more, contributing to sporadic cases.

1) Contact the medical provider who ordered testing of the case and obtain the following information. (This includes medical records for hospitalized patients.)
   - Did the medical provider diagnose Q fever?
     - Yes: Record the diagnosis date [Clinical] and continue the investigation.
     - No, not diagnosed based on other findings: Record the alternative diagnosis in the [Notes] of EpiTrax. No further investigation required. "Complete" and "Approve" the case as directed in Data Management.
   - Determine what information has been released to the patient and identify if needed epidemiologic data can be found in the clinical record.
   - If hospitalized: obtain admission/progress notes and discharge summary.
     - Record hospitalizations: reason, location and duration of stay [Clinical]
   - Obtain information that supports clinical findings, especially:

– Acute o Fever **and** o rigors, severe **retrobulbar** headache, acute hepatitis, pneumonia, or elevated liver enzyme levels
– Chronic: Newly recognized, culture-negative endocarditis or chronic hepatitis, osteomyelitis, osteoarthritis, or pneumonitis in the absence of other known etiology.

   - Obtain information on any laboratory tests performed and fax results to KDHE at 1-877-427-7318, if not previously reported. Including:
     - Results of liver enzyme testing.
     - Results of x-rays or other radiographical testing
     - Results of culture, if done.
   - Record onset date of first symptoms associated to this episode [Clinical]
     - Symptoms: [Investigation – Symptoms].
     - Immunocompromised patient? [Investigation – Symptoms]
     - Complications: [Investigation – Complications]
   - Record treatment: [Clinical]
   - Record hospitalizations: location and duration of stay
   - Record outcomes: survived or date of death [Clinical]
   - Record pregnancy status for women. [Clinical]
   - Collect patient's demographics (address, birth date, gender, race/ethnicity, primary language, and phone number(s)). [Demographic]
2) Establish if the patient's illness is clinically compatible to Q fever based on lab criteria and clinical symptoms.

- If any of the following situations are present the investigation can be closed as 'Not a Case':
  - The medical provider states it is not a case and gives an alternative diagnosis for the symptoms.
  - For an acute case with no fever (subjective or measured). (Continue the investigation if the presence of fever is unknown.)
  - For an acute case with fever but no symptoms of: rigors, severe **retrobulbar** headache, acute hepatitis, pneumonia, or elevated liver enzyme levels present. (Continue investigation if symptoms unknown).
  - For chronic cases: there was no newly recognized, culture-negative endocarditis or chronic hepatitis, osteomyelitis, osteoarthritis, or pneumonitis in the absence of other known etiology

3) If a continued investigation is needed and the patient charts do not provide information on the following risk factors or travel, interview the case to determine risk factors and transmission. [Investigation – Exposure]

   (Remember to examine lifetime history of exposures or travel for chronic cases and for acute cases consider exposures in the last 2 weeks to 40 days.)

   - Occupation: Laboratory worker, veterinarian, farmer, dairyman, wool-processor or in a packinghouse, stockyard or rendering plant. Also consider rural construction workers, laundry workers and undertakers.
   - Exposure to cattle, sheep and goat byproducts (e.g., wool, fertilizer, birth products, etc.) and dust from contaminated corrals.
   - Use and source of unpasteurized dairy products or imported foods.
   - Travel (location and dates) to areas with large concentrations of cattle, sheep, and goats.
   - Record patient's occupation [Epidemiologic]

4) Examining the epidemiological information, record where the infection was most likely imported from. (Indigenous or out-of-county, state, or U.S.) [Epidemiologic].

Contact Investigation

1) Contacts are defined as those with possible exposure to the source of infection.
2) Symptomatic acquaintances contacts should be strongly urged to contact their physician for a medical evaluation.
3) After identifying potential contacts, evaluate whether a risk of transmission exits. ONLY if a risk of transmission exists, create a line listing of contacts at-risk of developing disease. [Contact]
4) Follow-up with at-risk contacts as instructed in Contact Management.

Isolation, Work and Daycare Restrictions

1) Q fever is not transmissible from person-to-person. No respiratory isolation is needed.
2) No restrictions are indicated for outpatient management.

Case Management

None.

Contact Management

1) If a contact listing was created because of the high possibility of disease transmission, follow-up with the listed contacts. [Contact]
2) If any are ill, inform them (or their physician) of possible exposure, in order to facilitate proper diagnosis and therapy.
3) Persons who are not ill but who were potentially exposed should be educated on the signs and symptoms and incubation period and instructed to inform their medical providers of the potential exposure if symptoms do develop.
4) Report the final disposition of each contact investigated. [Contact]

Environmental Measures

1) Pasteurize all milk and dairy products.
2) Exercise care when handling placenta and fetus from aborted animals.
3) Disinfect contaminated areas with a bleach solution or other commercial disinfectant.

Education

As opportunities allow, the following general messages should be distributed:

1) Discuss availability of medical services for people engaged in activities associated with farm animals, their body wastes and by-products.
2) Educate public on sources of infection and the need to pasteurize milk.
3) Counsel persons at highest risk for developing chronic Q fever, especially persons with pre-existing cardiac valvular disease or individuals with vascular grafts.

MANAGING SPECIAL SITUATIONS

A. Outbreak Investigation:

- There are no formal outbreak definitions; however, the investigator may consider the possibility of an outbreak when there is an unusual clustering of cases in time and/or space.
- Notify KDHE immediately, 1-877-427-7317.

B. Intentional Contamination

Q fever has been proposed as a biological warfare agent. *Coxiella burnetii* is a highly infectious agent that is rather resistant to heat and drying. It can become airborne and inhaled by humans. A single *C. burnetii* organism may cause disease in a susceptible person. Because the laboratory confirmation could be delayed, any findings that suggest the possibility of an intentional release of *C. burnetii* should result in the immediate issue of a health alert.

If suspected:

- Notify local law enforcement and state public health officials.

- Implement "Chain of Custody" procedures for all samples collected, as they will be considered evidence in a criminal investigation.
- Work to define population at risk which is essential to guide response activities. Public health authorities will play the lead role in this effort, but must consult with law enforcement, emergency response and other professionals in the process. The definition may have to be re-evaluated and redefined at various steps in the investigation and response.
- Once the mechanism and scope of delivery has been defined, identify symptomatic and asymptomatic individuals among the exposed and recommend treatment and/or chemoprophylaxis.
- Establish and maintain a detailed line listing of all cases and contacts with accurate identifying and locating information.

Safety Considerations:

- Risks to response personnel are not significant.

Risk Communication Materials:

- Factsheet(s) for Q fever:

Vaccination:

- A vaccine for Q fever has been developed and has successfully protected humans in occupational settings in Australia. However, this vaccine is not commercially available in the United States.
- Persons wishing to be vaccinated should first have a skin test to determine a history of previous exposure. Individuals who have previously been exposed to *C. burnetii* should not receive the vaccine because severe reactions, localized to the area of the injected vaccine, may occur.

Treatment:

- Drug-resistant organisms might be used as a weapon, conduct antimicrobial susceptibility testing quickly and alter treatments as needed.
- Antibiotics for treating patients infected with Q Fever in a bioterrorist event are included in the national pharmaceutical stockpile maintained by CDC, as are ventilators and other emergency equipment.

Postexposure prophylaxis (PEP):

- Not recommended for contacts. However, all exposed should be monitored closely to allow for quick initiation of antibiotics upon onset of symptoms.

Surveillance:

- Arrange for medical monitoring of contacts for 6 weeks to detect sudden onset of: high fevers (104-105° F), severe headache, general malaise, myalgia, confusion, sore throat, chills, sweats, non-productive cough, nausea, vomiting, diarrhea, abdominal pain, and chest pain

DATA MANAGEMENT AND REPORTING TO THE KDHE

A. Accept the case assigned to the LHD and record the date the LHD investigation was started on the [Administrative] tab.

B. Organize and collect data, using appropriate data collection tools including:
- The CDC Q-Fever Case Report Form can be used to collect information.
- Alternatively, investigators can collect and enter all required information directly into EpiTrax [Investigation], [Clinical], [Demographics], [Epidemiological] tabs.
- During outbreak investigations, refer to guidance from a KDHE epidemiologist for appropriate collection tools.

C. Report data collected during the course of the investigation via EpiTrax**.**
- Verify that all data requested on the CDC Q-Fever Case Report Form has been recorded on an appropriate EpiTrax [tab], or that actions are completed for a case lost to follow-up as outlined below.
- Some data that cannot be reported on an EpiTrax [tab] may need to be recorded in [Notes] or scanned and attached to the record.
- Paper report forms do not need to be sent to KDHE after the information is recorded and/or attached in EpiTrax. The forms should be handled as directed by local administrative practices.

D. If a case is lost to follow-up, after the appropriate attempts to contact the case have been made:
- Indicate 'lost to follow-up' on the [Investigation] tab with the number of attempts to contact the case recorded.
- Record at least the information that was collected from the initial reporter.
- Record a reason for 'lost to follow-up' in [Notes].

E. After the requirements listed under Case Investigation have been completed, record the "Date LHD investigation completed" field located on the [Administrative] tab.
- Record the date even if the local investigator's Case or Contact Management for the contact is not "Complete".

F. Once the entire investigation is completed, the LHD investigator will click the "Complete" button on the [Administrative] tab. This will trigger an alert to the LHD Administrator so they can review the case before sending to the state.
- The LHD Administrator will then "Approve" or "Reject" the CMR.
- Once a case is "Approved" by the LHD Administrator, BEPHI staff will review and close the case after ensuring it is complete and that the case is assigned to the correct event, based on the reported symptoms reported.

  (Review the EpiTrax User Guide, Case Routing for further guidance.)

ADDITIONAL INFORMATION / REFERENCES

A. **Treatment / Differential Diagnosis:** Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015.

B. **Epidemiology, Investigation and Control:** Heymann. D., ed., Control of Communicable Diseases Manual (CCDM), 20th Edition. Washington, DC, American Public Health Association, 2015.

C. **Case Definitions:** CDC Division of Public Health Surveillance and Informatics, Available at: wwwn.cdc.gov/nndss/

D. **Kansas Regulations/Statutes Related to Infectious Disease:** www.kdheks.gov/epi/regulations.htm

E. **Animals in Public Places Compendium:** www.kdheks.gov/epi/human_animal_health.htm

F. **Additional Information (CDC):** www.cdc.gov/qfever/info/index.html

ATTACHMENTS

- **Fact Sheet**