Q Fever

<table>
<tr><td>Signs and Symptoms</td><td colspan="2">• About half of cases are asymptomatic
• Acute onset of febrile illness, may be pneumonia or other organ involvement
• < 5% become chronic infections typically with endocarditis</td></tr>
<tr><td>Incubation</td><td colspan="2">Typically 2-3 weeks (range 3-30 days)</td></tr>
<tr><td rowspan="3">Case classification</td><td colspan="2">Acute clinical criteria: Acute fever and one or more of the following: rigors, severe retrobulbar headache, acute hepatitis, pneumonia, or elevated liver enzyme levels
Chronic clinical criteria: Newly recognized, culture-negative endocarditis, particularly 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</td></tr>
<tr><td>Confirmed acute: Clinically consistent (acute) or epi link to a lab confirmed case with: isolation or fourfold change IgG to phase II antigen by IFA or DNA detected by PCR or positive immunohistochemistry (IHC)</td><td>Probable acute: Clinically consistent (acute) with: single supportive IFA IgG titer ≥1:128 to phase II antigen or elevated phase II IgG or IgM by ELISA, dot-ELISA, or LA</td></tr>
<tr><td>Confirmed chronic: Clinically consistent (chronic) with: isolation or IgG phase I antigen ≥ 1:800 by IFA (phase I titer > phase II titer) or DNA detected by PCR or positive IHC</td><td>Probable chronic: Clinically consistent (chronic) with: phase I IgG antigen ≥1:128 and < 1:800 by IFA</td></tr>
<tr><td>Differential diagnosis</td><td colspan="2">Extensive including: brucellosis, dengue, bacterial endocarditis, influenza, leptospirosis, lupus, lymphoma, meningitis, plague, pneumonia, psittacosis, rickettsioses, sarcoidosis, toxoplasmosis, tuberculosis, tularemia, viral hepatitis</td></tr>
<tr><td>Treatment</td><td colspan="2">Doxycycline for acute Q fever, may relapse, rare deaths. Chronic infection may need multiple antibiotics for extended time and is fatal if untreated.</td></tr>
<tr><td>Duration</td><td colspan="2">Variable; post Q fever syndrome may occur; chronic illness weeks to years later</td></tr>
<tr><td>Exposure</td><td colspan="2">Reservoirs: sheep, cattle, and goats, as well as cats, dogs, and some wild animals. Exposure to aerosolized birth products (e.g., placental tissue and amniotic fluid), urine, feces; raw milk; dust from bedding; direct animal contact; laboratory; rare sexual.</td></tr>
<tr><td>Laboratory testing</td><td colspan="2">Local Health Jurisdiction (LHJ) and Communicable Disease Epidemiology (CDE) arrange testing for individual cases
• Washington State Public Health Laboratories do PCR; other testing is sent to CDC
• Best specimens: whole blood ≤ 4 days of onset for PCR; sera pair ≥ a week of onset and 2-6 weeks apart, tested at same laboratory; tissue (chronic disease)
Specimen shipping (Section 4):
• Keep all specimens cold, ship according to PHL requirements: https://doh.wa.gov/public-health-provider-resources/public-health-laboratories/lab-test-menu</td></tr>
<tr><td>Public health actions

URGENT</td><td colspan="2">Report to CDE any cases, particularly high-risk exposures or suspected bioterrorism
• Identify others potentially exposed: commercial product, shared exposure with case; exposed to case: laboratory, surgery, labor/delivery; veterinary, livestock owner, animal contact
• Educate exposed persons about symptoms
Infection Control: standard precautions; avoid aerosols in medical settings and use PPE for risk medical settings</td></tr>
</table>

Q Fever

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To identify the source of infection (e.g., an outbreak at a rendering plant or farm) and prevent further transmission from that source to others.
2. To educate potentially exposed persons about signs and symptoms of disease, thereby facilitating early diagnosis.
3. To raise the index of suspicion of a possible bioterrorism event if no natural exposure source is identified.

B. Legal Reporting Requirements

1. Health care providers and Health care facilities: notifiable to **local health jurisdiction** within 24 hours.
2. Laboratories: notifiable to **local health jurisdiction** within 24 hours; submission required – specimen associated with a presumptive positive result, within 2 business days
3. Veterinarians: animal cases notifiable to Washington State Department of Agriculture. See: https://app.leg.wa.gov/WAC/default.aspx?cite=16-70
4. Local health jurisdictions: notifiable to Department of Health (DOH) Communicable Disease Epidemiology (CDE) within 7 days of case investigation completion or summary information required within 21 days.

C. Local Health Jurisdiction Investigation Responsibilities

1. **If bioterrorism is suspected, notify CDE immediately (24/7): 1-877-539-4344.**
2. Facilitate the transport of specimens to Washington State Public Health Laboratories (PHL) for confirmatory testing.
3. Identify potentially exposed persons and make appropriate recommendations.
4. Report all *confirmed* and *probable* cases (see definitions below) to CDE. Use the Q fever case report form https://www.doh.wa.gov/Portals/1/Documents/5100/210-043-ReportForm-Qfever.pdf and enter the data in the Washington Disease Reporting System (WDRS).

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Q fever is caused by *Coxiella burnetii*, a gram negative bacterium with two antigenic phases. The organism is highly resistant to heat and many disinfectants and can survive long periods under harsh environmental conditions. *C. burnetii* can reach high concentrations in animal tissues, particularly placentas and birthing fluids, and can be spread by wind and stirred up dust. A few organisms can cause infection.

B. Description of Illness

Human infections with *C. burnetii* range from asymptomatic seroconversion (~50%) to severe disease. Acute Q fever is characterized by sudden onset of fever, chills, headache, myalgia, nausea, vomiting, diarrhea, and sometimes non-productive cough and severe sweats. Untreated, the fever can persist for up to 14 days. It is most often a self-limited febrile illness, though atypical pneumonia is a major clinical presentation, occurring in 30% to 50% of patients. Acute hepatitis is also a frequent presentation, though may be mild. Other severe but rare manifestations include meningoencephalitis, pericarditis, myocarditis, or cholecystitis. Clinical laboratory findings commonly include elevated liver enzyme levels. Pregnant women are at risk for miscarriage, stillbirth, and premature birth. Acute Q fever has a low mortality rate (<2%).

Although the majority of people with acute Q fever recover completely, a post-Q fever fatigue syndrome has been reported in up to 20% of acute cases. This syndrome is characterized by constant or recurring fatigue, night sweats, severe headaches, photophobia, myalgia, mood changes, and difficulty sleeping.

Chronic Q fever is rare (<5% of acute cases), occurs weeks to years after acute infection, and manifests primarily as endocarditis. Other manifestations include chronic hepatitis, chronic vascular infections, osteomyelitis, osteoarthritis, or pneumonitis. Pregnant women, immunosuppressed persons, and patients with pre-existing valvulopathy, aneurysm, prosthetic heart valve, vascular prosthesis, or renal insufficiency are at highest risk for chronic Q fever. Untreated it is often fatal; mortality rates may be as high as 65%.

C. Q Fever in Washington State

Typically 0 to 3 cases of Q fever are reported per year. In 2011, an outbreak associated with goats occurred in Washington and Montana, resulting in 21 infected persons; of these 8 symptomatic cases and 4 asymptomatic infections were Washington residents. In 2016, 7 sporadic cases were reported, not linked to common exposures.

D. Reservoirs

The most common reservoirs are sheep, cattle, and goats. Cats, dogs, and some wild animals and birds can also be infected. Infected animals are usually asymptomatic, but fertility issues such as abortion can occur. The organism is shed in urine, feces, milk, and especially birth products (e.g., placental tissue and amniotic fluid).

E. Modes of Transmission

The disease is most commonly acquired by inhalation of aerosols containing *C. burnetii*. This can occur through inhalation of dust from premises contaminated by placental tissues, birth fluids and excreta of infected animals; in establishments processing infected animal products; in necropsy rooms; or during direct contact with infected animals, placentas, or other contaminated materials such as wool, straw, fertilizer, and laundry. Less common routes include ingestion of contaminated raw milk, tick bites, receipt of contaminated blood or bone marrow, and handling of cultures in the laboratory. A recent report from the New York State Department of Health described four cases of Q fever in persons treated with fresh sheep cell injections in Germany. Alternative therapies involving fresh cell injections are controversial and not available in the United States, however, patients may travel overseas to receive fresh cell injections.

F. Incubation Period

The incubation period depends on the size of the infecting dose, but is typically around 2-3 weeks, with a range of 3 to 30 days

G. Period of Communicability

Direct person-to-person transmission occurs rarely, but sexual transmission may occur. Fomites such as contaminated clothing may be a source of infection.

H. Treatment

Doxycycline is the treatment of choice for acute *C. burnetii* infection and should be started promptly; monitor for relapses requiring retreatment. Chronic infections may require extended treatment with multiple antibiotics and may require surgery.

3. CASE DEFINITIONS

A. Acute Q Fever

1. Clinical Evidence

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

2. Laboratory Evidence

Confirmatory:

- Serological evidence of a fourfold change in immunoglobulin G (IgG)-specific 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; phase I 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.

Supportive:

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

Note: Serologic profiles of pregnant women infected during gestation may progress rapidly to those characteristic of chronic infection.

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.

3. Case Classification for Acute Q Fever (2009)

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

Probable: 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.

B. Chronic Q Fever

1. 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.

2. Laboratory Evidence

Confirmed:

- Serological evidence of IgG antibody to *C. burnetii* phase I antigen ≥ 1:800 by IFA (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.

Supportive:

- 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 II) 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 tests are not readily available.

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.

3. Case Classification for Chronic Q Fever (2009)

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

***Probable*:** 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).

C. Exposure

Exposure is usually via aerosol 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.

4. DIAGNOSIS AND LABORATORY SERVICES

A. Laboratory Diagnosis

Laboratory diagnosis is commonly made by demonstration of a rise in specific antibodies in acute and convalescent specimens. High antibody titers to Phase I antigen indicate chronic infection; whereas high Phase II antibody titers occur during acute infection. The diagnosis can also be made by isolation or identification of the organism in blood, sputum or tissue (e.g., liver biopsy or heart valve) by culture, immunohistochemical methods, or polymerase chain reaction (PCR). These latter tests are less convenient than serologic tests because they require processing in a biosafety level 3 laboratory. Note that approximately 5% of people in the US will test phase I IgG positive due to past infection; a low titer may indicate a historical infection.

Confirmatory laboratory testing by a reference laboratory such as Centers for Disease Control and Prevention (CDC) or Washington State Public Health Laboratories is recommended, though may not be necessary when a 4-fold rise in *C. burnetii* titer has been documented. Substantial variability exists between clinical laboratories, so titers should only be compared if specimens are tested at the same laboratory. Acute and convalescent sera should be collected 2-6 weeks apart, ideally, during the first week of illness and 2-4 weeks after. Detectable antibody titers are not typically present until 7-10 days after illness onset; therefore, if Q fever is suspected, a convalescent specimen is necessary for confirmation. Negative or very low titers are expected during the first week of illness and do not rule out Q fever. PCR on blood has highest diagnostic yield in the first week of illness onset, prior to antibiotic administration; but may be performed on tissues for chronic illness. Although a positive PCR result is diagnostic, a negative result does not rule out Q fever, and treatment should not be withheld due to a negative result.

B. Tests Available at the Washington State Public Health Laboratories (PHL)

The PHL perform PCR testing only. Specimens for serology, culture, or immunohistochemistry will be forwarded to the CDC. Contact Communicable Disease Epidemiology for approval prior to submitting specimens.

Note that PHL require all clinical specimens have two patient identifiers, a name **and** a second identifier (e.g., date of birth) both on the specimen label and on the submission form. Due to laboratory accreditation standards, specimens will be rejected for testing if not properly identified. Also include specimen source and collection date. For details see: https://www.doh.wa.gov/Portals/1/Documents/5240/SCSI-Coxiella-burnetii-V1.pdf

C. Specimen Collection

Clinical laboratories should call PHL prior to shipping specimens (206-418-5400) for shipping instructions. Ship serology or microbiology specimens according to PHL requirements: https://doh.wa.gov/public-health-provider-resources/public-health-laboratories/lab-test-menu

5. ROUTINE CASE INVESTIGATION

Since Q fever is an uncommon disease, call DOH Communicable Disease Epidemiology (CDE) to discuss the case investigation. Interview the case and others who may be able to provide pertinent information.

A. Evaluate the Diagnosis

Collect copies of laboratory results. Confirmatory laboratory testing by a reference laboratory is recommended, unless a 4-fold titer rise was documented (see Section 4). Single serum positives must be interpreted with caution. IgM antibodies may persist for months or longer and IgM has a much lower specificity for *C. burnetii* than IgG. Cross reactions with *Legionella* and *Bartonella* species have been reported. Facilitate collection of additional specimens and/or facilitate submission to PHL as needed. Proceed with investigation upon receipt of preliminary lab results for sporadic cases. During an outbreak or potential bioterrorism situation, start investigation before results are available.

B. Manage the Case

Hospitalized patients should be cared for in accordance with standard precautions. No special precautions are necessary for routine care. However, if surgeries or autopsies for Q fever patients are planned, advise staff to wear extra respiratory protection (e.g., N95 masks) and use negative pressure rooms *if* performing any aerosol-generating procedures (e.g., bone saw use). During obstetrical procedures on infected women, contact and droplet precautions should be used; aerosolization of birth fluids should be avoided.

Chronic Q fever patients should be referred to an infectious disease specialist for management. These patients require long-term antibiotic therapy, periodic diagnostics, and long-term monitoring.

Patients diagnosed with acute Q fever with valvular disease, blood vessel abnormalities, immunosuppression, and pregnancy women should be clinically evaluated and serologically tested at 3, 6, 12, 18, and 24 months following acute infection to ensure rapid diagnosis and treatment of chronic Q fever.

C. Identify Potential Sources of Infection

Investigate possible exposures during the 2 to 3 weeks prior to onset of acute disease. For chronic disease, inquire about previous diagnosis of or illness consistent with acute Q fever. Ask about history of:

- Travel;
- Contact with potentially infected animals or their tissues, particularly postpartum fluid or tissues;
- Consumption of unpasteurized milk products;
- Work with sheep, goats, cattle;
- Work in a laboratory (especially animal necropsy); and
- Possible exposure to dust or other aerosols associated with livestock.
- Medical procedures or alternative therapies conducted outside of the US

D. Identify Contacts/Others Potentially Exposed

1. Identify and contact persons who participated with the case in any of the activities above.
2. Identify laboratory workers who handled infected tissue or laboratory isolates. (Note that culture requires special methods and facilities so exposure to isolates is unlikely at most hospital and diagnostic laboratories; for instance, there is no risk for standard blood cultures handled using normal precautions).
3. Identify surgeons, pathologists, and other staff present in surgical or autopsy rooms during aerosol-generating procedures, e.g., use of bone saws.
4. Identify delivery room personnel if aerosolization of birth fluids occurred from a woman with active Q fever.
5. Identify veterinarians, veterinary pathologists, and livestock owners who handled infected animal specimens (especially placentas or stillborn animals) or who were present during the delivery of infected animals.
6. Inform all identified persons of their possible exposure and symptoms of Q fever. See "Management of Other Exposed Persons" below.
7. Determine if the case donated blood or tissue and notify the appropriate agency.
8. Consider alerting healthcare providers in the surrounding area if widespread exposure is suspected

E. Management of Other Exposed Persons

Persons potentially exposed should be educated regarding symptoms to facilitate early diagnosis. In general, no specific management is recommended for asymptomatic people who have been exposed. For high-risk exposures, call Communicable Disease Epidemiology to discuss circumstances.

F. Environmental Evaluation/Measures

Surgical/autopsy areas can be decontaminated with 70% ethanol, MicroChem-Plus®, or quaternary ammonia solution. Contact time should be 30 minutes.

If the suspected source is farm animals or unpasteurized dairy products, contact CDE who will contact the Washington State Department of Agriculture.

6. MANAGING SPECIAL SITUATIONS

A. Bioterrorist Event

C. burnetii has been classified as a potential bioterrorism agent because of its very low infectious dose, its ability to survive in the environment, and the fact that it can potentially be disseminated by aerosol. One should suspect bioterrorist spread of Q fever if there is a cluster of patients with a non-specific febrile illness and in about one quarter of the cases pulmonary symptoms. Chemoprophylaxis with tetracycline or doxycycline may be appropriate for people exposed in a bioterrorism event. ***If bioterrorism is suspected, call Communicable Disease Epidemiology immediately (24/7) at 1-877-539-4344 or 206-418-5500.***

7. ROUTINE PREVENTION

A. Immunization Recommendations

There is currently no licensed vaccine against Q fever in the United States.

B. Prevention Recommendations https://www.cdc.gov/qfever/#prevention

1. Educate the public on sources of infection.
2. Recommend use of personal protective equipment (PPE) while assisting with birthing or handling aborted fetuses, placentas, and other birth products, or while conducting surgical or pathological procedures. PPE may include a properly fitted respirator mask (N95 or higher rated), eye protection, disposable gloves, protective clothing, and rubber boots.
3. Appropriately dispose of placenta, birth products, fetal membranes, and aborted fetuses at facilities housing livestock, particularly sheep and goats. For additional details, see: https://agr.wa.gov/FoodAnimal/AnimalHealth/Diseases/QFeverManagementPractices.pdf
4. Follow good hygiene practices after animal contact, including washing hands and arms and removing coveralls and footwear used during farm work prior to entering homes.
5. Restrict access to barns and laboratories used in housing potentially infected animals.
6. Consume only pasteurized milk and milk products.
7. Use appropriate procedures for bagging, autoclaving, and washing of laboratory clothing.
8. Quarantine imported animals.
9. Ensure that holding facilities for sheep are located away from populated areas. Research animals should be routinely tested for antibodies to *C. burnetii,* and measures should be implemented to prevent airflow to other occupied areas.
10. Counsel exposed persons at highest risk for developing chronic Q fever, especially pregnant women, persons with pre-existing cardiac valvular disease or vascular grafts, or immunocompromised individuals.

ACKNOWLEDGEMENTS

This is a revision of the guideline originally published in 2002, which was based on the Control of Communicable Diseases Manual (CCDM), 17th Edition; James Chin, Ed. APHA 2000. We would like to acknowledge the Oregon Department of Human Services for developing the format and select content of this document.

UPDATES

December 2008: Minor wording changes were made to the case definition (Section 3). The link to the PHL microbiology form was updated (Section 4).

January 2011: The Legal Reporting Requirements section has been revised to reflect the 2011 Notifiable Conditions Rule revision. Section 4 was updated to reflect current lab submission requirements.

December 2012: Illness description and occurrence in Washington (Sections 2 B & C) were revised. Additional laboratory detail was added in Section 4. The Routine Case Investigation and Controlling Further Spread sections were combined into a single Section 5, with additional detail added to parts B, D and F.

January 2015: Sections 2, 4, 5, and 7 were updated in accordance with the 2013 NASPHV guidelines for prevention and control of *Coxiella burnetii* infection and updated CDC guidelines.

March 2017: Front page added.

December 2019: Routine review

December 2022: For 2023 WAC revision combined provider and facility reporting requirement, updated laboratory

submission (Section 1B)

December 2023: For 2024 WAC revision updated laboratory submission.

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