Brucellosis

Signs and Symptoms	• Acute or insidious irregular fevers, sweats, chills, headache, anorexia, arthralgia • Can be hepatic or splenic abscesses, or osteoarticular or genitourinary symptoms • Chronic infections may cause arthritis, osteomyelitis, endocarditis, or neurological complications	
Incubation	Typically 2-4 weeks (range 5 days-5 months)	
Case classification	**Clinical criteria**: fever and one or more of the following: night sweats, fatigue, anorexia, myalgia, weight loss, headache, arthralgia, arthritis/spondylitis, meningitis, or focal organ involvement (heart, testes, liver, spleen)	
	Confirmed: Clinically consistent with positive culture **or** 4-fold rise in titers taken at least 2 weeks apart	**Probable:** Clinically consistent with epi link to human or animal case **or** titer by agglutination ≥ 160 **or** PCR positive
Differential diagnosis	Includes multiple causes of fever including bacterial endocarditis, viral hepatitis, leptospirosis, lymphoma, malaria, rickettsioses, tuberculosis, toxoplasmosis, tularemia, typhoid, vasculitis	
Treatment	Appropriate antibiotic combination (generally dual therapy) for weeks. Rare deaths from endocarditis.	
Duration	Acute illness days to week, chronic infection months to years	
Exposure	Skin or mucosal membrane exposure to infected birth tissues or fluids from cattle, goats, sheep, elk, deer; consuming raw milk from infected animal; inhalational exposure in a laboratory or slaughterhouse; potential agent of bioterrorism; rare transmission sexually or through breast milk	
Laboratory testing	Local Health Jurisdiction (LHJ) and Communicable Disease Epidemiology (CDE) arrange testing for individual cases and environmental testing for suspected outbreaks • Washington State Public Health Laboratories can culture or confirm Brucella • **Best specimens**: **isolate or paired sera (2+ weeks apart)** *Specimen shipping (Section 4):* • **Special shipping** is needed for suspected Brucella isolates • Ship sera or tissues **cold (freeze if arriving >72 hours from collection),** culture at **ambient temperature**, with Bioterrorism (culture) or Serology (serum) according to PHL requirements: https://www.doh.wa.gov/Portals/1/Documents/5230/302-018-BioterrorismSpecimen.pdf https://doh.wa.gov/public-health-provider-resources/public-health-laboratories/lab-test-menu • Specimen Collection and Submission Instructions https://www.doh.wa.gov/Portals/1/Documents/5240/SCSI-Brucella-spp-V2.pdf	
Public health actions **URGENT**	Immediately report to CDE any cases with likely exposure in the United States • Identify exposures (agricultural or wildlife) including during travel • Identify others sharing the exposure and interview for symptoms • Identify potential laboratory or healthcare exposures to specimens and isolates; assess risk; recommend symptom watch and sequential titers for all exposures, plus antibiotic prophylaxis for high risk exposures • Educate about avoiding future exposures *Infection Control:* standard precautions; cultures are a risk for laboratory personnel	

Brucellosis

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To assist in the diagnosis and treatment of cases.
2. To identify potentially exposed healthcare and laboratory personnel and to provide counseling on post-exposure management.
3. To identify sources of transmission (e.g., an infected animal or a contaminated unpasteurized dairy product) and to prevent further transmission from such sources.
4. To raise the index of suspicion of a possible bioterrorism event when no natural exposure source is identified.

B. Legal Laboratory Reporting Requirements

1. Health care providers and Health care facilities: Notifiable to local health jurisdiction within 24 hours.
2. Laboratories: *Brucella* species notifiable to local health jurisdiction within 24 hours; specimen submission required – any positive result excluding IgG notifiable to **local health jurisdiction** within 24 hours; submission required – isolate, excluding confirmed positive *B. melitensis*, *B. abortus*, or *B. suis*, or if no isolate specimen associated with positive result excluding IgG, within 2 business days (see Sections 3 and 4).
3. Veterinarians: animal cases notifiable to Washington State Department of Agriculture https://app.leg.wa.gov/WAC/default.aspx?cite=16-70
4. Local health jurisdictions: Notifiable to 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. Facilitate the transport of specimens to the Washington State Public Health Laboratories for confirmatory testing.
2. Educate potentially exposed persons, including laboratory personnel, about signs and symptoms of disease; recommend antibiotic prophylaxis when needed.
3. Report all *probable* and *confirmed* cases to CDE (see definitions below). Complete the brucellosis report form https://www.doh.wa.gov/Portals/1/Documents/5100/210-019-ReportForm-Brucellosis.pdf and enter the data in the Washington Disease Reporting System (WDRS).

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Brucellosis is the illness caused by gram-negative bacteria in the genus *Brucella*. Species known to cause disease in humans include *Brucella abortus, B. melitensis, B. suis*, and rarely *B. canis*. *Brucella* infection associated with exposure to an infected marine mammal (*B.*

pinnepedalis and *B. ceti)* has also been reported in at least four cases nationally since 2001. Cattle vaccines (attenuated strains of *B. abortus*) used in the United States until the late 1990s also caused human illness. Newer vaccines (e.g., RB51) do not appear to have the same risk of infection, but follow-up on exposure to live culture vaccines should still be conducted.

B. Description of Illness

A systemic bacterial disease with acute or insidious onset, characterized by continued, intermittent, or irregular fever of variable duration; headache; weakness; profuse sweating; chills; arthralgia (joint pains); depression; weight loss; and generalized body aches. Involvement of the liver and spleen, including abscesses, can occur. Acute disease may last from days to weeks but chronic infections lasting months or more may occur if an acute infection is not adequately treated. Osteoarticular complications occur in 20–60% of cases, most commonly sacroiliitis. Genitourinary involvement occurs in 2–20% of cases, orchitis and epididymitis in particular. Involvement of the lymphoreticular, skeletal (arthritis and osteomyelitis), cardiac (endocarditis), and nervous systems are frequently seen in chronic *Brucella* infections. The case-fatality rate of untreated brucellosis is low, with rare deaths due to endocarditis caused by *B. melitensis.*

Subclinical infections can be detected by high levels of antibody even in the absence of symptoms, excepting vaccine-associated strains.

C. Brucellosis in Washington State

Although brucellosis has been eradicated from cattle in Washington since 1988, DOH receives 0 to 3 reports of human brucellosis infections each year usually due to the ingestion of raw milk products in foreign countries. Previously, veterinarians were occasionally exposed to a live vaccine used in animals. Newer vaccines (since 1996) do not pose as great a risk but contact Communicable Disease Epidemiology if a veterinarian reports a live culture Brucella vaccine exposure.

D. Reservoirs

Predominantly cattle, goats, sheep, and swine. Infection may occur in bison, elk, caribou, wild swine, and some species of deer. *B. canis* is an occasional problem in laboratory dog colonies and kennels, stray dogs, pet dogs with outdoor exposures, and coyotes. Human cases occur frequently in certain U.S. regions, particularly states across the southern boundary (Florida to California) https://www.cdc.gov/brucellosis/resources/surveillance.html. CDC recently reported human exposure to marine *Brucella* isolated from a harbor porpoise in Maine; personal protective equipment should be used when handling marine mammal specimens suspected to be infected with *Brucella*.

E. Modes of Transmission

Infection results from contact (through skin breaks or mucous membranes) with infected tissues, blood, urine, vaginal discharges, aborted fetuses and especially placentas, or consuming raw milk or other unpasteurized dairy products from infected dairy animals. Airborne infection can occur in laboratories and abattoirs. Clinical specimens and laboratory isolates are a risk to healthcare or laboratory workers. *Brucella* could be weaponized to create an infectious aerosol which could be used in a bioterrorism event. Cattle vaccines

(e.g., RB51) do not appear to have the same risk of infection, but follow-up on exposure to live culture vaccines should still be conducted.

F. Incubation Period

Highly variable; usually 2-4 weeks; ranges from 5 days to 5 months.

G. Period of Communicability

Direct person-to-person spread of brucellosis is extremely rare. Breast-feeding women may transmit the infection to their infants. Sexual transmission has also been reported.

H. Treatment

In general, persons with brucellosis should be treated with a combination of appropriate antibiotics for a prolonged period of time. Typically, treatment consists of doxycycline in combination with either rifampin or streptomycin for 6 weeks. Note: the RB51 vaccine strain was created through selection on rifampin-enriched media and is therefore resistant to rifampin. Rifampin should not be used in prophylaxis or treatment of persons exposed to or infected with RB51.

3. CASE DEFINITIONS

A. Clinical Case Definition

An illness characterized by acute or insidious onset of fever and one or more of the following: night sweats, fatigue, anorexia, myalgia, weight loss, headache, arthralgia, arthritis/spondylitis, meningitis, or focal organ involvement (endocarditis, orchitis/epididymitis, hepatomegaly, splenomegaly).

B. Laboratory Criteria for Diagnosis

Definitive:

1. Culture and identification of *Brucella* spp. from a clinical specimen; or
2. Evidence of a fourfold or greater rise in *Brucella* antibody titer between acute- and convalescent-phase serum specimens obtained two or more weeks apart.

Presumptive:

1. *Brucella* total antibody titer ≥160 by standard tube agglutination test (SAT) or *Brucella* microagglutination test (BMAT) in one or more serum specimens obtained after onset of symptoms; or
2. Detection of *Brucella* DNA in a clinical specimen by PCR assay.

C. Case Classification (2010)

Probable: a clinically compatible case with at least one of the following:

- Epidemiologically linked to a confirmed human or animal brucellosis case
- Presumptive laboratory evidence, but without definitive laboratory evidence of *Brucella* infection.

Confirmed: a clinically compatible illness with definitive laboratory evidence of *Brucella* infection.

4. DIAGNOSIS AND LABORATORY SERVICES

A. Laboratory Diagnosis

Brucella can be isolated from blood, bone marrow, and other tissues/fluids. Brucellosis can also be diagnosed through acute and convalescent serological studies. A single convalescent specimen can be tested, but results may be inconclusive. Specific serologic techniques are needed for *B. canis* antibodies, which do not cross-react with other *Brucella* species; however these serologic assays are not currently available in the United States.

Confirmatory laboratory testing must be performed by a reference laboratory such as the Washington State Public Health Laboratories (PHL).

The organism is highly infectious and presents a risk to laboratory workers. **Alert laboratory personnel when specimens are sent from a suspect brucellosis case.** Laboratories should hold cultures for 30 days, as *Brucella* grows slowly, and use great caution to avoid exposure within the laboratory by aerosol. If bacterial growth is suspicious for *Brucella,* contact PHL immediately to arrange for confirmatory testing.

B. Services Available at PHL

PHL Microbiology identifies *Brucella* species from pure isolates as well as culturing clinical specimens. PHL Microbiology also performs rapid diagnostic testing using nucleic acid amplification methods (e.g., polymerase chain reaction), and can provide immediate testing in suspected bioterrorism situations.

PHL does not perform serologic tests; serum samples will be forwarded to Centers for Disease Control and Prevention (CDC) for testing. Call Communicable Disease Epidemiology at 206-418-5500 for approval before collecting and shipping specimens. Also see: https://www.doh.wa.gov/Portals/1/Documents/5240/SCSI-Brucella-spp-V2.pdf

Note that PHL requires 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.

C. Specimen Collection

1. **Isolates:** Submit isolates or clinical specimens with a completed PHL Bioterrorism form https://www.doh.wa.gov/Portals/1/Documents/5230/302-018-BioterrorismSpecimen.pdf For additional questions regarding shipping and handling, laboratories should contact PHL at 206-418-5400.
2. **Serology:** For serology collect 1–2 ml of both acute and convalescent sera (collected at least two weeks apart). If the specimen is freshly collected or still refrigerated, then ship cold, not frozen, on regular cold packs. If the specimen is already frozen, keep it frozen during transport by shipping on dry ice. Serum specimens should be submitted according to PHL requirements: https://doh.wa.gov/public-health-provider-resources/public-health-laboratories/lab-test-menu.

5. ROUTINE CASE INVESTIGATION

Interview the case and others who might be able to provide pertinent information.

A. Evaluate the Diagnosis

Review the clinical presentation and laboratory results. **Confirmatory laboratory testing should be performed by a reference laboratory such as Washington State Public Health Laboratories (PHL).** Facilitate submission of laboratory specimens to PHL for confirmation. Proceed with investigation after preliminary or confirmatory laboratory results are available for sporadic cases. During an outbreak or a potential bioterrorism event, start the investigation before laboratory results are available.

B. Identify Potential Sources of Infection

Reservoirs are cattle, goats, sheep, swine, bison, elk, caribou, some deer, and marine mammals. Investigate possible exposures during the period 5 to 60 days before illness onset, including:

1. Travel to *Brucella*-endemic areas including the Mediterranean Basin, South and Central America, Eastern Europe, Asia, Africa, the Caribbean, and the Middle East;
2. Consumption of unpasteurized dairy products from reservoir animals;
3. Contact with potentially infected animals such as livestock in risk countries or wild grazing game animals (including via skinning, slaughtering, assisting with birthing, etc.) or their tissues, particularly postpartum fluid or tissues;
4. Parenteral or mucous membrane exposure to *Brucella* vaccine;
5. Work in a microbiology laboratory or as a healthcare worker.

C. Infection Control Recommendations/Case Management

Hospitalized patients should be cared for using standard precautions. However, if surgeries or autopsies for *Brucella*-infected 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 or drill use). During obstetrical procedures on infected women, contact and droplet precautions should be used; aerosolization of birth fluids should be avoided.

Alert laboratories that might receive specimens from a brucellosis case.

D. Identify Potentially Exposed Persons

1. Identify and interview persons who participated with the case in any risk activities as well as any acquaintance or household member with similar illness. Inform ill persons (or their physician) of possible exposure, in order to facilitate proper diagnosis and treatment.
2. Identify laboratory workers who handled specimens or laboratory isolates. If cultures are still pending, laboratory workers should be reminded of appropriate handling of suspected *Brucella* cultures, i.e. do not work with cultures on an open bench.
3. Identify healthcare workers who performed aerosolizing procedures on the infected patient, including drilling, use of bone saws, or suction.

See below for recommended antibiotic prophylaxis of exposed persons.

E. Management of Exposed Persons

See CDC's Brucellosis Reference Guide for additional details and resources for post-exposure monitoring: https://www.cdc.gov/brucellosis/pdf/brucellosi-reference-guide.pdf

All laboratory staff handling specimens with confirmed *Brucella* should undergo a risk assessment to determine their needs for post-exposure prophylaxis and follow-up. Similarly, persons with reported exposure to an animal known to be infected with *Brucella* or exposure to live culture vaccine should undergo a risk assessment to determine their needs for post-exposure prophylaxis and follow-up. Additionally, healthcare workers who performed aerosolizing procedures should be assessed.

High-risk exposures include: handling infected tissue without respiratory protection, direct contact with infected blood and body fluids through breaks in the skin, mucosal exposure to aerosolized *Brucella* organisms after an aerosol-generating procedure, handling specimens on an open bench (i.e., not under a hood) or being within 5 feet of this manipulation; having direct skin contact with a culture; having exposure to a culture through sniffing, mouth pipetting, inoculation, or spraying it into the eyes, nose, or mouth; or being present in the laboratory room during any procedure that might result in widespread aerosolization of an isolate, e.g. centrifuging without sealed tubes, vortexing, sonicating, catalase testing, accidents resulting in spillage or splashes from a tube/bottle, etc. Low-risk exposures include being present in the operating or laboratory room but without activities qualifying as a high risk exposure. All exposed persons should be educated about the symptoms of illness and told to seek care if fever develops.

Persons with high risk exposures should begin post-exposure prophylaxis (PEP) and serial serum titers should be assessed at baseline (as soon as possible following exposure) and at 6, 12, 18, and 24 weeks following the exposure for all high-risk exposed persons. The live culture *Brucella* vaccine does not produce an antibody response, so serological follow-up is not necessary in the case of vaccine exposure. Similarly, no serologic monitoring is available for *B. canis* exposures. Persons with high-risk exposures should also conduct regular symptom watch for 24 weeks, including daily fever checks. PEP should include doxycycline 100 mg orally twice daily and rifampin 600 mg once daily for at least 21 days. Trimethoprim-sulfamethoxazole is an alternative for those with contraindications to doxycycline. Note: the RB51 vaccine strain was created through selection on rifampin-enriched media and is therefore resistant to rifampin. Rifampin should not be used in prophylaxis or treatment of persons exposed to or infected with RB51; trimethoprim-sulfamethoxazole, ciprofloxacin, or streptomycin should be substituted.

PEP and serial titers should be offered to persons who had low-risk exposures. These persons should also be counseled to conduct symptom watch for 24 weeks.

Call Communicable Disease Epidemiology to discuss the need for PEP for other persons exposed and to request serologic testing via *Brucella* microagglutination test (BMAT). Please provide a summary report of the number of persons exposed, their exposure categories (high vs. low risk), initiation and completion of PEP, and any pregnant or otherwise immunocompromised persons.

Note that *Brucella abortus, B. meletensis,* and *B. suis* are considered select agents; though *B. canis* is not. Any laboratory exposure will require the laboratory to complete forms

documenting an "accidental release" of a select agent. This is coordinated by the CDC Select Agent Program. See:

https://www.cdc.gov/brucellosis/laboratories/risks.html

https://www.cdc.gov/brucellosis/laboratories/risk-level.html

F. Environmental Evaluation

CDE can assist in notifying other state agencies when necessary for environmental investigations.

1. If the exposure source appears to be domestic animals, including livestock, the Washington State Department of Agriculture will be notified for an animal disease investigation and testing if needed.
2. If the source of infection appears to be wild animals, the Washington Department of Fish and Wildlife will be notified.

6. MANAGING SPECIAL SITUATIONS

A. Bioterrorist Event

Brucella has been classified as a "category B" agent for bioterrorism; it is moderately easy to disseminate by aerosol and can cause severe illness but has low mortality rates. An intentional release (bioterrorist event) should be suspected if unusual clusters are seen in otherwise healthy individuals or in people in buildings with common ventilation systems. **Call Communicable Disease Epidemiology immediately at 206-418-5500 if brucellosis is suspected in an unusual cluster.**

B. Animal diagnosed with *Brucella* infection

Brucella infections in animals are reportable to the Washington State Department of Agriculture (WSDA). WSDA reports positive laboratory findings to DOH, which notifies the LHJ of animal residence. Recently, DOH has received higher numbers of reports of canines diagnosed with *B. canis*; it is unknown whether this is due to truly increased prevalence, increased diagnosis by veterinarians, or improved surveillance and cross-agency reporting.

Clinicians, pet/kennel/farm owners, veterinary staff, and others in contact with infected animals should be provided information and assessed as described in section 5; high-risk activities may also include specimen draws during clinical examination, surgical procedures, or disinfection and cleaning of contaminated environments. Inhalation of aerosolized *Brucella* organisms and contamination of the conjunctiva or broken skin are common routes of exposure during the aforementioned high-risk procedures. See the Brucellosis Reference Guide for additional details: https://www.cdc.gov/brucellosis/pdf/brucellosi-reference-guide.pdf.

The NASPHV also maintains guidance for public health follow-up of *B. canis*:

http://www.nasphv.org/Documents/BrucellaCanisInHumans.pdf

7. ROUTINE PREVENTION

A. Prevention Recommendations

1. **Avoid raw dairy foods.** Do not consume unpasteurized milk, or products such as cheese or ice cream made from unpasteurized milk, especially during travel. If you are not sure

that a dairy product is pasteurized, do not eat it. Even in brucellosis-free regions, these products can contain other pathogens.

2. **Avoid contact with sick or dead animals.** If you hunt, wear gloves when handling dead animals. When skinning wild game keep gloves away from eyes and other mucous membranes. Thoroughly wash hands after handling wild game carcasses. Wild game meat should be cooked "well done" (to at least 74°C/165°F).
3. **Wear gloves.** Veterinarians, farmers, and hunters should wear gloves when handling sick or dead animals or when assisting an animal giving birth. In the case of aerosol-generating procedures such as necropsy, respiratory protection should be worn.
4. **Take safety precautions.** Laboratory workers should handle all specimens under appropriate biosafety conditions.
5. **Immunize domestic animals.** Although brucellosis vaccination is not mandatory, many farmers and ranchers vaccinate their herds, and milk is tested two to four times a year for signs of the bacteria.
6. **Neuter and spay pets** to reduce risk of *B. canis* transmission to pets.
7. For more information, see: https://www.cdc.gov/brucellosis/laboratories/risk-level.html

ACKNOWLEDGEMENTS

This document is a revision of the Washington State Guidelines for Notifiable Condition Reporting and Surveillance published in 2002 which were originally 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

June 2009: Treatment recommendations and laboratory forms updated.

January 2010: The clinical description was expanded in Section 3A.

January 2011: The Legal Reporting Requirements section has been revised to reflect the 2011 Notifiable Conditions Rule revision. The reporting form link was corrected (Section 1). Additional details were added regarding alerting labs about suspected cases (Section 4A), specimen collection and shipping procedures (Section 4C), and managing lab exposures (Sections 5C and 6C).

May 2012: Section 6 was revised to reflect new guidance from CDC on managing laboratory exposures. Minor changes were also made in descriptions of available tests in Section 4.

January 2015: Former Section 6 (Controlling Further Spread) was merged into Section 5 (Routine Case Investigation). Sections 2A,C, and 5E were updated to include risk of transmission from marine mammals and live culture vaccine exposure.

March 2017: Front page added, general updates.

December 2019: Section 5C-E updated, Section 6B added, Section 7 updated, routine review.

December 2022: For 2023 WAC revision combined provider and facility reporting requirement (Section 1B1-2), updated laboratory submission (Section 1B3)

December 2023: For 2024 WAC revision updated laboratory submission process.

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