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Brucellosis


Overview^{1, 2, 3, 9, 12}

Brucellosis is a bacterial disease caused by members of the genus *Brucella*. Brucellosis is an important zoonosis and a significant cause of reproductive losses in animals. Brucellosis is usually caused by *Brucella abortus* in cattle, *B. melitensis* or *B. ovis* in small ruminants, *B. suis* in pigs, and *B. canis* in dogs. Some *Brucella* species are also maintained in wildlife populations. Because this pathogen can be easily cultured, aerosolized, stored, and disseminated, it is classified as a potential bioterrorism agent.

In humans, brucellosis can be a serious, debilitating, and sometimes chronic disease that can affect a variety of organs. Naturally-occurring human infection is most often acquired through direct or indirect exposure to aborted fetuses or tissues or fluids of infected animals. Transmission occurs by ingestion of undercooked meat or unpasteurized dairy products; inoculation through mucous membranes or cuts and abrasions in the skin; or inhalation of contaminated aerosols. Person-to-person transmission is unusual; however, rare cases in which sexual transmission was suspected have been reported. In addition, blood transfusions and bone marrow transplants have been sources of infection, indicating a need for screening in endemic areas. People in occupations such as farming, ranching, and veterinary medicine as well as slaughterhouse workers, meat inspectors, and laboratory personnel are at increased risk of acquiring brucellosis.

The incubation period in people varies from 5 to 60 days after exposure (generally beginning 2 to 4 weeks after inoculation). Asymptomatic infections are common. In symptomatic cases, brucellosis has a wide range of symptoms; some of these are similar to the flu and can include: fever, chills, sweats, malaise, anorexia, headache, weight loss, pain in muscles, joints, or back, fatigue, and abdominal pain. Physical findings may include lymphadenopathy, hepatosplenomegaly, and arthritis. Some signs and symptoms may persist for longer periods. Others may never go away or reoccur. These can include: recurrent fevers, arthritis, swelling of the testicle and scrotum area, swelling of the heart (endocarditis), neurologic symptoms (in up to 5% of all cases), chronic fatigue, and depression, swelling of the liver and/or spleen.

Human brucellosis can be prevented by controlling the infection in animals. The incidence of human disease is low in the United States, where 100 to 150 cases occur each year. Brucellosis can be quite common, however, in countries where animal disease control programs have not reduced the prevalence of brucellosis among host species. Areas currently recognized as high risk are the Mediterranean Basin, the Middle East, Mexico, South and Central America, the Caribbean, Eastern Europe, Asia, and Africa. Unpasteurized cheeses, sometimes called "village cheeses" and raw or undercooked animal products (including bone marrow) may pose a particular risk for people visiting or traveling in these areas. Confirmed infections with *B. suis* have occurred among feral swine hunters as a result of their field dressing and butchering activities. Exposure to the organism via unsafe laboratory practices and accidents has led to infections among clinical diagnostic and research laboratorians.

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For a complete description of brucellosis, refer to the following references:

- *Control of Communicable Diseases Manual (CCDM)*, American Public Health Association, 19th ed. 2008.
- American Academy of Pediatrics. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29th ed. 2012.
- *Principles and Practice of Infectious Diseases*, 7th ed., Pennsylvania: Churchill Livingstone Elsevier, 2010.

2010 Case Definition – Brucellosis (*Brucella* spp.)⁴ - (10/13)

Clinical Description

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

Laboratory Criteria for Diagnosis

Definitive

- Culture and identification of *Brucella* spp. from clinical specimens.
- Evidence of a fourfold or greater rise in *Brucella* antibody titer between acute- and convalescent-phase serum specimens obtained greater than or equal to 2 weeks apart.

Presumptive

- *Brucella* total antibody titer of greater than or equal to 160 by standard tube agglutination test (SAT) or *Brucella* microagglutination test (BMAT) in one or more serum specimens obtained after onset of symptoms.
- Detection of *Brucella* DNA in a clinical specimen by PCR assay.

Case Classification


Confirmed

A clinically compatible illness with definitive laboratory evidence of *Brucella* infection.

Probable

A clinically compatible illness 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.

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Information Needed for Investigation


Verify the diagnosis. Obtain demographic, clinical, laboratory information, and other epidemiological information necessary to complete the [Disease Case Report \(CD-1\)](#) and the [Brucellosis Case Report Form](#) from the attending physician, hospital, and/or laboratory and patient or a knowledgeable family member. **COMMENTS:** *Brucella* microagglutination test (BMAT), a modified version of the serum (tube) agglutination test (SAT) can detect antibodies to *Brucella* species - *abortus*, *melitensis*, or *suis*. Currently there is no serological test available to detect antibodies to *B. canis*.¹² Some commercial laboratories include a brucellosis screening test in a “febrile antibodies panel; the physician’s office should be asked whether follow-up assays have been ordered.

Establish the extent of illness. Determine if household or other close contacts are, or have been ill by contacting the health care provider, patient, or family member. Identify symptomatic household members, associates, or co-workers and strongly urge them to contact their physician for a medical evaluation. Infections caused by *B. melitensis* may produce endocarditis if left untreated. Although human-to-human transmission is rare, congenital brucellosis has been reported, and infected mothers may transmit *Brucella* spp. to their infants through breastfeeding.²

Identifying the source of infection. Determine the occupation of the index case since this information may help narrow the search for the route of exposure. Information to obtain:

- Do you work in a laboratory? If so, does the lab handle unidentified isolates or *Brucella* specimens?
- Do you work in a slaughterhouse or meat-packing environment?
- Have you assisted animals giving birth? Determine if the case was exposed to abortive livestock or animal fetuses.
- Determine if the case was exposed to brucellosis vaccine.
- Do you hunt? If so, have you come into contact with moose, elk, caribou, bison or wild hogs (feral swine)? **COMMENT:** *B. melitensis* has become the major cause of human brucellosis in Latin America. Although it is normally associated with goats and their dairy products, it can infect cattle and sheep as well. Other sources of *B. melitensis* include bison, elk, caribou, deer, and swine.
- Determine if the case had a history of foreign travel. If so, where? Collect the dates of travel. **COMMENT:** Brucellosis is common in most Latin American countries, around the Mediterranean, Africa, Central Asia, India and the Middle East.
- While traveling, did you consume any undercooked meat or unpasteurized dairy products? **COMMENT:** *Brucellosis is rarely contracted through milk in the United States, but the case or their household contacts should be questioned about consumption of raw milk, particularly in rural areas. Imported cheeses can be a potential source for Hispanic immigrants if they obtain soft or unpasteurized cheeses from Mexico.*³

NOTE: Contact the [District Communicable Disease Coordinator](#) if the case appears to have acquired the disease in the state of Missouri. The District Communicable Disease

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Coordinator will alert the State Public Health Veterinarian who will alert the Missouri Department of Agriculture, if needed. Additional information may need to be collected (e.g. job duties, food histories, and unusual risk factors).


Provide information about brucellosis to persons at risk for infection and the general public. Efforts should be made to promote brucellosis awareness and provide prevention information to the public to reduce the risk of infection. 1) Educate on potential hazards of drinking or eating unpasteurized milk products. 2) Educate high-risk workers (i.e., farmers, slaughterhouse workers, etc.) about the risk of brucellosis and stress methods to reduce occupational exposure such as proper ventilation, appropriate carcass disposal and barrier precautions. Information on brucellosis prevention can be found on CDC's website at: <http://www.cdc.gov/brucellosis/prevention/index.html>.

Brucella Surveillance. Review WebSurv to determine whether there have been other cases in the same geographic area. When cases are related by person, place, or time, efforts should be made to identify a common source. Information obtained through the [Brucellosis Case Report Form](#) is used to identify a possible source of infection and to characterize persons or geographic areas in which additional efforts may be needed to raise awareness and reduce disease incidence.

Brucella species are a potential Class B Bioterrorism Agent. If brucellosis is the result of a terrorist act or the intentional or deliberate release, *Brucella* would most likely be disseminated via an infectious aerosol and is an inhalation threat to humans and wild and domestic animals. It is estimated that inhalation of only 10-100 bacteria is sufficient to cause disease in humans. Aerosolization of *Brucella* in biological weapons could result in a shorter incubation period, lead to higher clinical attack rates, and result in more prolonged, incapacitating and disabling disease than in its natural form.⁷ Infection is possible through abraded skin and is possible by eating/drinking contaminated products. *Brucella* spp. are persistent in the soil for 125 days and the bacteria are stable in water for 20-72 days.⁸

None of the following clues alone constitute proof of intentional use of a biological agent, but together they can assist greatly in determining if further investigation is warranted.¹¹

1. The presence of a large epidemic, with greater case loads than expected, especially in a discrete population.
2. More severe disease than expected for a given pathogen, as well as unusual routes of exposure.
3. A disease that is unusual for a given geographic area, is found outside the normal transmission season, or is impossible to transmit naturally in the absence of the normal vector for transmission.
4. Multiple simultaneous epidemics of different diseases.
5. A disease outbreak with zoonotic as well as human consequences, as many of the potential threat agents are pathogenic to animals (death or illness among animals that precedes or accompanies illness or death in humans).
6. Unusual strains or variants of organisms or antimicrobial resistance patterns disparate from those circulating.

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7. Higher attack rates in those exposed in certain areas, such as inside a building if the agent was released indoors, or lower rates in those inside a sealed building if an aerosol was released outdoors.
8. Intelligence that an adversary has access to a particular agent or agents.
9. Claims by a terrorist of the release of a biologic agent.
10. Direct evidence of the release of an agent, with findings of equipment, munitions, or tampering.


Even with the presence of more than one of the above indicators, it may not be easy to determine that an attack occurred through nefarious means.

***NOTE:** If brucellosis is suspected to be the result of a terrorist act or the intentional or deliberate release thereof; the LPHA should:*

1. **Notify local law enforcement** and the [Senior Epidemiology Specialist](#) for the District, or the Missouri Department of Health and Senior Service’s Emergency Response Center (ERC) at (800) 392-0272 (24/7) immediately.
2. Work with law enforcement and implement “Chain of Custody” procedures for all laboratory samples, as they will be considered evidence in a criminal investigation.
3. Work to define the 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.
4. Once the mechanism and scope of delivery has been defined, identify symptomatic and asymptomatic individuals among the exposed and recommend treatment and/or chemoprophylaxis.
5. Establish and maintain a detailed line listing of all cases and contacts with accurate identifying and locating information.

Notification

- Contact the [District Communicable Disease Coordinator](#), the [Senior Epidemiology Specialist](#) for the District, or the Missouri Department of Health and Senior Services (MDHSS) - BCDCP, phone (573) 751-6113, Fax (573) 526-0235, or for afterhours notification contact the MDHSS/ERC at (800) 392-0272 (24/7) immediately if brucellosis is suspected.
- If a case(s) is associated with a childcare center, BCDCP or the LPHA will contact the BEHS, phone (573) 751-6095, Fax (573) 526-7377 and the Section for Child Care Regulation, phone (573) 751-2450, Fax (573) 526-5345.
- If a case(s) is associated with a food handler, BCDCP or the LPHA will contact BEHS, phone (573) 751-6095, Fax (573) 526-7377.
- If a case(s) is associated with a long-term care facility, BCDCP or the LPHA will contact the Section for Long Term Care Regulation, phone (573) 526-8524, Fax (573) 751-8493.
- If a case is associated with a hospital, hospital-based long-term care facility, or ambulatory surgical center BCDCP or the LPHA will contact the Bureau of Health Services Regulation phone (573) 751-6303, Fax (573) 526-3621.

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- If a case(s) is associated with animal or animal product exposure within Missouri, OVPH will contact Missouri Department of Agriculture, Animal Health Division, phone (573) 751-3377, Fax (573) 751-6919.
- Contact the Department of Natural Resources, Public Drinking Water Branch, at (573) 751-1187, Fax (573) 751-3110 if cases are associated with a public water supply, or BEHS, phone (573) 751-6095, Fax (573) 526-7377, if cases are associated with a private water supply.

Control Measures

Brucellosis presenting as endemic disease.

The control of human brucellosis depends on eradication of *Brucella* spp. from cattle, goats, swine, and other animals.² The best way to prevent brucellosis infection is to avoid consuming undercooked meat and unpasteurized dairy products, including: milk, cheese, and ice cream.¹²

*Pasteurization of dairy products for human consumption is important to prevent disease, especially in children.*² People who handle animal tissues (such as hunters and animal herdsman) should protect themselves by using: good hygiene, rubber gloves, goggles, and gowns or aprons. This will help ensure that bacteria from potentially infected animals do not get into eyes or inside a cut or abrasion on the skin.¹²

If possible, obtain copies of the laboratory reports. If the *Brucella* species is available on the laboratory reports, this may help with identifying the source of infection. See the “Humans and *Brucella* Species” table on the CDC’s website at:


<http://www.cdc.gov/brucellosis/clinicians/brucella-species.html>.

B. abortus RB51 is a strain of *Brucella* developed specifically for immunization of cattle against brucellosis to allow serological differentiation between naturally infected and vaccinated animals. Accidental human exposure to RB51, though uncommon, has resulted in development of symptoms consistent with brucellosis. Exposures have included needle sticks, eye and wound splashes, and contact with infected material. Other vaccines, such as *B. abortus* S19 for cattle and *B. melitensis* Rev-1 for sheep and goats, can also cause infection in humans. Information on how to reduce the risk of infection from exposure to RB51 can be found on CDC’s website at: <http://www.cdc.gov/brucellosis/veterinarians/cattle.html>.

Brucellosis is the most commonly reported laboratory-associated bacterial infection. For information on: 1) Laboratory Risks, 2) Recommendations for Safe Laboratory Practices, or 3) Assessing Laboratory Risk Level and Post-Exposure Prophylaxis (PEP) see the following CDC website: <http://www.cdc.gov/brucellosis/laboratories/index.html>.

NOTE: *Women who are pregnant and have been exposed to brucellosis should consult with their obstetricians/healthcare provider for evaluation. Laboratory tests and PEP may be recommended.*¹²

Tourists seeking information for vaccination or travel recommendations should be advised there is a high prevalence of this disease in underdeveloped countries. Travelers should avoid any dairy product unless they can be absolutely certain it has been pasteurized.

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Foreign travel recommendations may be found via the Internet using CDC's Travel Health site at: <http://wwwn.cdc.gov/travel/default.aspx>.

PEP is not generally recommended after possible exposure to endemic disease. A three to six week course of oral antibiotics should be considered for high-risk exposure in the following situations:⁷

1. Inadvertent wound or mucous membrane exposure to infected livestock tissues and body fluids and to livestock vaccines.
2. Exposure to laboratory aerosols or to secondary aerosols generated from contaminated soil particles in calving and lambing areas.
3. Confirmed bioterrorism exposure.

For information on the medical management (treatment and chemoprophylaxis) see the [U.S. Army Medical Research Institute of Infectious Diseases. Medical Management of Biologic Causalities Handbook. 7th Ed. Sep. 2011](#), the American Academy of Pediatrics. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29th ed. 2012, *Principles and Practice of Infectious Diseases*, 7th ed., Pennsylvania: Churchill Livingstone Elsevier, 2010 or other suitable reference; several such references are listed at the end of this document.


Brucellosis suspected to be the result of a terrorist act or intentional / deliberate release.

If the source of infection cannot be determined and cases are presenting as multiple cases, temporally/spatially clustered; and/or the [epidemiologic clues](#) discussed above suggest an intentional or deliberate use of a biological agent – **law enforcement must** be involved in the investigation. Even if no conclusive answer can be derived quickly, the means employed in determining the cause of an attack will still provide medical personnel with information that may prevent illness and death.¹¹ Because the laboratory confirmation could be delayed, specific epidemiological, clinical, and microbiological findings that suggest an intentional release of *Brucella* spp. should result in the issue of a health alert.

Laboratory Procedures¹²

Testing for brucellosis is available through commercial clinical laboratories. The isolation and identification of *Brucella* can confirm a diagnosis of brucellosis. *Brucella* is most commonly isolated from blood cultures. It can also, however, be isolated from: bone marrow, cerebrospinal fluid, wounds, purulent discharge, and joint fluid. In addition to bacterial isolation, serological tests can be performed. CDC utilizes a test called BMAT, which is a modified version of the serum (tube) agglutination test (SAT), that can detect antibodies to *Brucella* species - *abortus*, *melitensis*, or *suis*. There is no serological test available to detect antibodies to *B. canis*. For a diagnosis to be made using serology, two serum samples are required. The first serum sample should be taken when a person is acutely ill (≤ 7 days after symptom onset); the second serum sample should be drawn 2 to 4 weeks later to check for a rise in antibodies (a fourfold or greater rise in antibodies would mean an individual is positive for brucellosis). **NOTE:** *When sending specimens to any laboratory for culture and isolation, please be sure the laboratory is aware of the suspected diagnosis.*



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For information on the collection or shipment of specimens to the Missouri State Public Health Laboratory (MSPHL), refer to their website at:

- <http://health.mo.gov/lab/pdf/BrucellosisFactSheet.pdf>, and
- <http://health.mo.gov/lab/specialbacteriology.php>.

COMMENT: *Brucella* spp. grows very slowly and raw clinical specimens will have to be held up to 10 days before the MSPHL reports a negative result. If colonies appear, a presumptive positive using the real-time PCR test could be reported in 4-6 hours, with confirmation within an additional 48 hours.

Additional information may be found on CDC's website at:

- http://www.cdc.gov/ncezid/dhcpp/bacterial_special/zoonoses_lab.html, or
- <http://www.cdc.gov/brucellosis/clinicians/brucella-species.html>.

The [CDC SPECIMEN SUBMISSION FORM: SPECIMENS OF HUMAN ORIGIN](#) is used for confirmation testing.

NOTE: Reliance should not be placed on gallery type rapid identification systems as these have misidentified *Brucella* as *Moraxella phenylpyruvica*, with serious consequences for laboratory staff.¹³


Reporting Requirements

Instances of brucellosis that appear to be the result of a terrorist act or the intentional or deliberate release of a biological agent is a Category 1(B) disease and shall be reported to the local health authority or to the Missouri Department of Health and Senior Services (MDHSS) **immediately** upon of first knowledge or suspicion by telephone, facsimile or other rapid communication. The MDHSS may be contacted afterhours through the MDHSS/ERC by calling (800) 392-0272 (24/7).

As a Nationally Notifiable Condition, **confirmed** and **probable** brucellosis cases; *presenting as multiple cases, temporally/spatially clustered* are an **IMMEDIATE, URGENT** report to the Centers of Disease Control and Prevention (CDC). **IMMEDIATE, URGENT** reporting requires MDHSS to call the CDC EOC at 770-488-7100 within 24 hours of cases meeting the notification criteria; followed by submission of an electronic case notification via (WebSurv) in the next regularly scheduled electronic transmission.

Brucellosis also occurs naturally and is a Category 2 (A) disease and shall be reported to the local health authority or to MDHSS within one (1) day of first knowledge or suspicion by telephone, facsimile or other rapid communication. The MDHSS may be contacted afterhours through the MDHSS/ERC by calling (800) 392-0272 (24/7).

As a Nationally Notifiable Condition, **confirmed** and **probable** brucellosis cases; *not temporally/spatially clustered* are a **STANDARD** report to the Centers of Disease Control and Prevention (CDC). **STANDARD** reporting requires the Missouri Department of Health and Senior Services (MDHSS) to report to CDC by electronic transmission via WebSurv within the next normal reporting cycle.


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Reporting Requirements (continued)

1. For confirmed and probable cases, complete a “[Disease Case Report](#)” (CD-1) and [Brucellosis Case Report Form](#)” and send the completed forms to the [DHSS District Health Office](#).
2. Entry of the completed CD-1 into the MOHSIS database negates the need for the paper CD-1 to be forwarded to the District Health Office.
3. MDHSS will report to CDC following the above reporting criteria (see boxes).
4. All outbreaks or “suspected” outbreaks must be reported as soon as possible (by phone, fax or e-mail) to the District Communicable Disease Coordinator. This can be accomplished by completing the [Missouri Outbreak Surveillance Report \(CD-51\)](#).
5. If an outbreak is associated with food, a CDC 52.13 form ([National Outbreak Reporting System – Foodborne Disease Transmission](#)) is to be completed and submitted to the District Communicable Disease Coordinator at the conclusion of the outbreak.
6. If an outbreak is associated with the consumption or use of water for drinking, or with ingestion, contact, or inhalation of recreational water, a CDC 52.12 form ([National Outbreak Reporting System - Waterborne Disease Transmission](#)) is to be completed and submitted to the District Communicable Disease Coordinator at the conclusion of the outbreak.
7. Within 90 days from the conclusion of an outbreak, submit the final outbreak report to the District Communicable Disease Coordinator.

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8. Biological Quick Reference Guides (NRT)
<http://nrt.org/Production/NRT/NRTWeb.nsf/PagesByLevelCat/Level3BiologicalHazards?OpenDocument>. (10/13)
9. Brucellosis Fact Sheet (Center for Food Security and Public Health)
<http://www.cfsph.iastate.edu/Factsheets/pdfs/brucellosis.pdf>. (10/13)
10. Biological Threats - Medical Professionals (DHSS)
<http://health.mo.gov/emergencies/ert/biomed.php>. (10/13)
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Other Sources of Information

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3. Gerald E Maloney, Jr., DO. "Brucellosis" *eMedicine Journal*. May 10 2006, Volume 7, Number 5. Available from: <http://www.emedicine.com/emerg/topic883.htm>. (10/13)