Virginia Department of Health
Brucellosis: Guidance for Healthcare Providers
Key Medical and Public Health Interventions after Identification of a Suspected Case

Table of Contents

1. Epidemiology

Brucellosis is a zoonotic bacterial disease caused by *Brucella*. Multiple *Brucella* spp. can infect humans: *B. abortus, B. canis, B. melitensis, B. suis, B. ceti, B. inopinata, B. neotomae,* and *B. pinnipedialis*. *Brucella* spp. are designated as Category B bioterrorism agents (i.e., moderate ease of transmission and morbidity with a lower rate of mortality than Category A agents). Three species*, B. abortus*, *B. melitensis* and *B. suis*, are specifically designated as select agents, which means that they could be developed as bioterrorism agents and that possession, and use or transfer of these organisms requires registration with the Centers for Disease Control and Prevention (CDC) or the U.S. Department of Agriculture (USDA) through the Federal Select Agent Program.

Mammals are the natural reservoir for *Brucella.* Different *Brucell*a species are associated with different mammal reservoirs, as follows: *B. abortus* (mostly from cattle), *B. melitensis* (mostly from sheep and goats), *B. suis* (mostly from pigs), *B. canis* (mostly from dogs), *B. ceti* (from dolphins, porpoises, whales), *B. pinnipedialis* (from seals, sea lions, walruses), and *B. neotomae* (from wild rodents). Infection can occur in other animals, such as bison, elk, caribou, moose, wild hogs, or deer.

Although brucellosis occurs worldwide, it is more common in countries that do not have effective public health and domestic animal health programs. Areas currently listed as high risk are the following: the Mediterranean Basin (Portugal, Spain, Southern France, Italy, Greece, Turkey, and North Africa), Mexico, South and Central America, Eastern Europe, Asia, Africa, Caribbean, and the Middle East.

The primary sources of brucellosis are consumption of unpasteurized dairy products or undercooked meat, especially those from endemic areas, direct contact through broken skin or mucous membranes with meat or tissues of infected animals (e.g., blood, urine, vaginal discharges, aborted fetuses and placentas) and laboratory exposures to *Brucella* isolates. Auto-inoculation with live,

attenuated animal brucellosis vaccines (e.g., injection or spraying into open wounds or eyes) has also been reported. Brucellosis is primarily an occupational hazard in the United States for slaughterhouse workers, meat-packing plant employees, farm workers, veterinarians, and laboratory workers. Brucellosis is one of the most frequently reported laboratory-acquired infections. Although rare, there have been reported cases of sexual transmission, transplacental transmission, neonatal transmission during delivery or breastfeeding, and transmission through organ donations or blood transfusions.

In the United States, an average of 143 cases (range: 127–165) were reported annually between 2016 and 2019. The majority of cases in children in the United States are associated with consumption of unpasteurized dairy products, often acquired from other countries. In Virginia, the number of reported cases between 2016 and 2019 ranged from zero to five per year, with a five-year average of 2.75 cases per year. Consumption of imported unpasteurized cheese products is a frequently reported risk factor among Virginia cases.

2. Clinical Manifestations

The incubation period for brucellosis is highly variable, ranging from 5 days to 6 months or more, with an average incubation period of 2–4 weeks; but it can be as long as several months or more. The clinical spectrum of brucellosis is wide, ranging from asymptomatic infection to life-threatening disease, and the illness may last days, months, or over a year if not effectively treated. Patients might present with acute, chronic, or relapsing signs and symptoms. Signs and symptoms include fever that is constant or intermittent, chills, sweats, malaise, anorexia, headache, weakness, pain in muscles, joint, or back, fatigue, and weight loss. Some patients might develop gastrointestinal symptoms (e.g., nausea, vomiting, abdominal pain). Abdominal pain and peripheral arthritis are more common in children than adults. Lymphadenopathy, hepatomegaly, or splenomegaly might be identified upon physical examination. Chronic symptoms could include recurrent fever, chronic fatigue and depression. Chronic brucellosis is less common in children than adults.

Localized infections can affect any organ system. The most common location is in the bones and joints (e.g., arthritis, spondylitis, sacroiliitis, osteomyelitis, bursitis, and tenosynovitis), which occurs in 20–60% of people with brucellosis. Other localized infections may result in swelling of the testicle and scrotum area (e.g., epididymo-orchitis), tissue abscess, or eye infections (e.g., uveitis). Neurologic involvement (e.g., meningitis) or cardiac involvement (e.g., endocarditis) are less common, but tend to be more severe. In pregnant women, the first and second trimesters carry a heightened risk of spontaneous abortion, and there is an overall risk of preterm delivery, miscarriage, and intrauterine infection leading to fetal demise.

The case-fatality rate is low (<2%) and fatal outcomes are most commonly associated with endocarditis caused by *Brucella melitensis* and infections affecting the brain.

3. Laboratory Testing and Diagnosis

Notification when Brucellosis is Suspected

If brucellosis is suspected, the healthcare provider should **immediately report the case to the local health department** per Virginia's disease reporting regulations. The local health department will discuss options for public health testing. If VDH approves public health testing, specimens may be sent to the Division of Consolidated Laboratory Services (DCLS). The health department will facilitate

notification and shipment to DCLS. Specimens potentially containing *Brucella* should **never** be shipped to DCLS without prior approval.

Laboratory Biosafety

Laboratory personnel **must** be alerted if brucellosis is suspected so that they can take appropriate precautions. All work on clinical specimens or isolates suspicious of containing *Brucella* should be performed in a biological safety cabinet using biosafety level 3 (BSL-3) precautions, which includes PPE (gown, gloves, face/eye protection) and respiratory protection. Because of the highly infectious nature of *Brucella* species, consultation with DCLS, is strongly recommended. The DCLS Emergency Officer can be reached 24 hours a day/7 days a week at 804-335-4617.

Diagnostic Testing

Culture is considered the gold standard for brucellosis testing, but *Brucella* spp. are slow-growing bacteria and culture might require up to 21 days of incubation. Specimens from patients with acute infections are more likely to test positive by culture than those from patients with chronic infections. Although a laboratory in the Laboratory Response Network (LRN) provides confirmatory identification, a clinical laboratory can presumptively identify *Brucella* spp. based on these findings:

- Colony morphology on sheep blood agar: *Brucella* spp. appear as punctate colonies after 48 hours of incubation. Colonies are nonpigmented and nonhemolytic. All suspicious colony types should be examined by Gram stain and urea test.
- Gram stain morphology: *Brucella* spp. have a characteristic Gram stain morphology that is extremely helpful in differentiating them from other gram-negative organisms. *Brucella* cells appear as tiny, faintly stained coccobacilli.
- Oxidase, catalase, and urease positive

Multiple commercial laboratories perform serologic testing for brucellosis. Testing often involves the use of an enzyme-linked immunoassay (EIA) to detect *Brucella* IgM antibodies. The reported sensitivity of IgM detection by EIA has been between 67% and 100%[1,2]; test specificity data are limited, but false-positive IgM test results have been reported.[3] Because the EIA is not considered a confirmatory test, VDH recommends that an abnormal *Brucella* IgM EIA result be verified using a *Brucella*-specific agglutination method, such as a standard tube agglutination test or the *Brucella* microagglutination test (BMAT). The standard tube agglutination test is available at multiple commercial laboratories (e.g., ARUP Laboratories, Mayo Clinic Laboratories, Quest Diagnostics) and is often used as a reflex test if the initial EIA testing is abnormal. A fourfold or greater change in *Brucella* IgM antibody titers between acute- and convalescent-phase serum specimens is considered confirmatory in the context of a clinically compatible illness.

VDH encourages clinicians to use commercial laboratories for brucellosis testing when indicated by clinical presentation and exposure history. Clinicians who suspect brucellosis based on the patient's clinical presentation and exposure history can also contact the local health department to request testing at DCLS. Health department staff will assess the patient's clinical presentation and relevant exposure history (e.g., consumption of unpasteurized dairy products or undercooked meat, contact with infected people or with infected animals through hunting, farming, animal processing or other

[1] Memish ZA, Almuneef M, Mah MW, et al. Comparison of Brucella standard agglutination test with the ELISA IgG and IgM inpatients with Brucella bacteremia. Diag. Microbio. Infect. Dis 2002; 44:129-132.

[2] Fadeel MA, Hoffmaster AR, Shi J, et al. Comparison of four commercial IgM and IgG ELISA kits for diagnosing brucellosis. J Med Microbiol 2011; 60:1-7.

[3] Centers for Disease Control and Prevention. Public Health Consequences of a False-Positive Laboratory Test Result for Brucella --- Florida, Georgia, and Michigan, 2005. MMWR 2008; 57: 603-605.

activities), and recent travel to or residence in an endemic area to determine if public health testing is warranted.

Serologic testing for brucellosis does have limitations. With EIA or agglutination tests, cross-reactions with other gram-negative bacteria (e.g., E. coli O157, *Francisella tularensis*, *Moraxella phenylpyruvica*, *Yersinia enterocolitica*, *V. cholerae* and certain *Salmonella* species) can occur. Serologic testing for *B. abortus* RB51 and *B. canis* cannot be performed with BMAT because of structural differences in the bacterial cell wall component, lipopolysaccharide. BMAT tends to perform better for acute infections than chronic infections. For suspected chronic infections, clinicians might consider testing for *Brucella* IgG antibodies at a commercial laboratory.

Sample Collection

If VDH approves testing at DCLS, the clinician should collect new acute and convalescent serum specimens (collected >14 days apart) for BMAT. DCLS can also perform PCR on whole blood specimens. Instructions for testing at DCLS are shown in Table 1. Because of the highly infectious nature of this organism, consultation with DCLS about specimen collection and handling is strongly recommended. The DCLS Emergency Officer can be reached 24 hours a day/7 days a week at 804-335-4617.

Case Definitions used by Public Health

The current CDC case definition for brucellosis is available at https://ndc.services.cdc.gov/conditions/brucellosis/. Note that a case definition is set of uniform criteria used to define a disease for public health surveillance. Case definitions enable public health to classify and count cases consistently across reporting jurisdictions and they should not be used by healthcare providers to determine how to meet an individual patient's health needs.

Table 1. Sample Collection and Testing Information for Suspected Brucellosis at DCLS and CDC*

Laboratory Test and Turnaround Time	Acceptable Samples	Amount	Instructions
Brucella species identification and genotyping (at CDC) Estimated turnaround time varies	Blood	10 mL	Use blood isolator tube or aerobic culture bottle. Ship at room temperature. Transport to lab within 16 hours.
	Serum	2–3 mL	Collect acute and convalescent serum (>14 days apart) in red top or tiger top tube. Remove serum and place in sterile tube. Acute and convalescent specimens can be shipped together (freeze acute specimen until convalescent specimen has been collected and is ready for shipment; ship both specimens on dry ice); if shipping separately, ship with cold packs.
	Abscess tissue: liver, spleen, or bone (testing conducted at CDC)	1 gram	Place in sterile container; moisten with sterile broth or saline. Ship as soon as possible with cold packs.
	Bone marrow (testing conducted at CDC)	1–2 mL	Ship in syringe with heparin. Remove needle and cap end. Ship at room temperature.
	Joint fluid (testing conducted at CDC)	1 mL	Place in sterile container. Ship as soon as possible with cold packs.
	Culture isolate	N/A	Send culture on an agar slant, not a plate. Agar slants should be shipped at room temperature.
Serology: *Brucella* microagglutination test (BMAT, at DCLS) Estimated turnaround time: 3 business days upon specimen receipt	Serum	2–3 mL	Collect acute and convalescent serum (>14 days apart) in red top or tiger top tube. Centrifuge tube, remove serum and place in sterile tube. Acute and convalescent specimens can be shipped together (freeze acute specimen until convalescent specimen has been collected and is ready for shipment; ship both specimens on dry ice); if shipping separately, ship refrigerated with cold packs. Note that serology is not available for *B. canis* or RB51.
Brucella spp. PCR (at DCLS) Estimated turnaround time: 1 business days upon specimen receipt	Whole blood, serum	0.5–1 mL	Collect blood in purple top tube (EDTA). Ship with cold packs. Note that a negative test result does not rule out infection. PCR can presumptively detect *Brucella* species (e.g., *B. abortus*, *B. melitensis*, *B. suis* and *B. canis);* actual species identification, however, is accomplished through culture confirmation.

* Adapted from American Society for Microbiology's Sentinel Level Clinical Laboratory Guidelines for Suspected Agents of Bioterrorism and Emerging Infectious Diseases: Brucella species (2016). If brucellosis is suspected, notify the local health department immediately to discuss the case and laboratory testing. If VDH approves public health testing, specimens may be sent to Division of Consolidated Laboratory Services (DCLS) with the DCLS Test Request Form; include the name of the test on the form (e.g., *Brucella* Microagglutination Test). For questions about collecting specimens or for notifying DCLS when submitting specimens, contact the DCLS Emergency Officer available 24/7 at 804-335-4617.

4. Treatment

Treatment recommendations for brucellosis are summarized in Table 2. Key factors to consider for treatment are the following: 1) combination therapy is recommended because monotherapy can be associated with a higher rate of relapse and could potentially lead to drug resistance; 2) treatment regimens depend on whether a localized infection (e.g., endocarditis, meningitis) or underlying condition that contraindicates certain antibiotics is present. Surgical intervention may be necessary for some localized infections. Relapses generally are not associated with development of *Brucella* resistance but rather with premature discontinuation of therapy, localized infection, or monotherapy.

Table 2. Brucellosis Treatment Options*

Population	Treatment Recommendation
Adults, Children ≥8 years†	Combination therapy to decrease the incidence of relapse: • Oral doxycycline (2–4 mg/kg per day, maximum 200 mg/day, in 2 divided doses) OR oral tetracycline (30–40 mg/kg per day, maximum 2 g/day, in 4 divided doses) AND • Rifampin (15–20 mg/kg per day, maximum 600–900 mg/day, in 1 or 2 divided doses) • Recommended for a minimum of 6 weeks Notes: 1) Combination therapy with trimethoprim-sulfamethoxazole (TMP-SMZ) can be used if tetracyclines are contraindicated. 2) Red Book® lists dose for oral doxycycline as 2.2-4.4 mg/kg per day, maximum 200 mg/day, in 2 divided doses.
Children <8 years	• Oral TMP-SMZ (trimethoprim 10 mg/kg per day, maximum 480 mg/day; and sulfamethoxazole 50 mg/kg per day, maximum 2.4 g/day) divided in 2 doses for 4–6 weeks Notes: 1) Combination therapy: Red Book® recommends adding rifampin. 2) Consult physician for dosing or if rifampin is contraindicated. 3) Tetracyclines (such as doxycycline) should be avoided in children less than 8 years of age. 4) Red Book® lists dose for rifampin as 15–20 mg/kg per day, maximum 600 mg/day, in 1 or 2 divided doses.
Pregnancy	Tetracyclines are contraindicated for pregnant patients. Consult obstetrician regarding specific antimicrobial therapy instructions.
Complicated Cases (Endocarditis, Meningitis, Osteomyelitis, etc.)	• Streptomycin§ or gentamicin for the first 14 days of therapy in addition to a tetracycline for 6 weeks (or TMP-SMZ if tetracyclines are contraindicated) • Rifampin can be used in combination with this regimen to decrease the rate of relapse • For life-threatening complications, such as meningitis or endocarditis, duration of therapy often is extended for 4 to 6 months • Case-fatality rate is <1% • Surgical intervention should be considered in patients with complications such as deep tissue abscesses Notes: Red Book® recommends a 3-drug regimen: gentamicin included for the first 7 to 14 days of therapy, in addition to doxycycline (or trimethoprim- sulfamethoxazole, if doxycycline is not used) and rifampin for a minimum of 6 weeks.
References for Treatment Recommendations	• Ariza J et al. 2007. Perspectives for the Treatment of Brucellosis in the 21st Century: The Ioannina Recommendations. PLoS Med. 4(12): e317. http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.0040317 • Al-Tawfiq JA. 2008. Therapeutic options for human brucellosis. Expert Rev Anti Infect Ther. 6(1): 109-120. https://pubmed.ncbi.nlm.nih.gov/18251668/ • Solera J. 2010. Update on brucellosis: therapeutic challenges. Intl J Antimicrob Agent. 36S, S18–S20. http://www.ncbi.nlm.nih.gov/pubmed/20692127

*Adapted from CDC Brucellosis Reference Guide: Exposures, Testing, and Prevention (February 2017) and Red Book: 2021-2024 Report of the Committee on Infectious Diseases. 32nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2021 (Accessed May 22, 2023)
Note: The *B. abortus* strain used in the RB51 vaccine was derived by selection in rifampin-enriched media and is resistant to rifampin in vitro. This strain is also resistant to penicillin. If infection is due to this vaccine strain, treatment should be determined accordingly (example: doxycycline and TMP-SMZ in place of rifampin). Specifics on the regimen and dose should be established in consultation with the person's health care provider in case of contraindications to the aforementioned. For additional information on dosing, please consult with the package inserts.
† VDH modified this category to include children aged 8 years or older based on personal communication with CDC
§ May not be readily available in the United States

5. Exposures and Postexposure Prophylaxis

Prophylaxis recommendations based on type of exposure (e.g., laboratory exposure, exposure to *B. abortus* RB51 vaccine, clinical and surgical exposures, or intentional exposure), as well as symptom surveillance, and serological monitoring are described below. Recommendations for postexposure prophylaxis (PEP) following laboratory exposures are provided in Table 3; if *Brucella* were intentionally released as a biological weapon, these PEP regimens should be followed because the guidelines cover aerosol-generating events. Detailed guidance on PEP following veterinary exposures can be found in CDC's Brucellosis Reference Guide: Exposures, Testing, and Prevention (February 2017).

In general, PEP decisions should be made in consultation with the healthcare provider and PEP can be initiated up to 24 weeks after exposure. Persons who are pregnant, less than 8 years old, or have contraindications to the suggested antimicrobial agents, should consult with their health care provider for alternative PEP. Suitable combinations of agents may be selected from the treatment references listed previously. If clinical symptoms develop at any point while on PEP and brucellosis infection is confirmed by culture and isolation or serology, PEP is no longer appropriate, and treatment and monitoring is required.

For **exposures to *Brucella* in the laboratory**, a risk assessment to determine if the exposure was high, low, or minimal (but not zero) risk based on the activity and location should be conducted (see CDC Brucellosis: Assessing Laboratory Risk Level and PEP). Table 3 (see below, page 10) summarizes recommendations about PEP and follow-up monitoring by exposure risk.

The ***B. abortus* RB51 vaccine**, a modified live vaccine, is currently the only vaccine used in the United States for prevention of brucellosis in cattle herds. Vaccine exposures typically occur through direct contact; therefore, all individuals exposed to RB51 should be considered to have a high-risk exposure. Local adverse events have been reported less than 24 hours after exposure and systemic reactions might begin 1–15 days after exposure. Because RB51 is resistant to rifampin in vitro, this drug should not be used for PEP (or treatment) courses. Upon exposure to RB51 vaccine, PEP should be comprised of doxycycline in addition to another suitable antimicrobial (such as TMP-SMZ) for 21 days (see Table 3). Specifics on the regimen and dose should be established in consultation with the person's healthcare provider in case of contraindications. Persons with RB51 vaccine exposures should monitor for symptoms for 24 weeks after exposure; this is particularly important because serologic monitoring is not available for RB51 exposures. If brucellosis occurs despite prophylaxis, treatment regimens would need to be selected based on antimicrobial susceptibility results.

Clinical or surgical exposures to *Brucella* spp. can occur and there are several publications of occupationally acquired brucellosis. When standard precautions are followed, most clinical procedures are considered to be low-risk activities. Higher-risk activities may include handling of tissues with potentially high concentrations of *Brucella* organisms (e.g., placental tissues), direct contact with infected blood and body fluids through breaks in the skin, or mucosal exposure to aerosolized *Brucella* organisms during or after an aerosol-generating procedure. Aerosol-generating procedures may include cardiopulmonary resuscitation, disturbance of fluids from an abscess, the use of saws or other electrical devices, and high-pressure irrigation. If there is a *Brucella* exposure during a surgical procedure, the potential exposure should be evaluated for all personnel who pass through the surgical unit. Assessments should be based on adherence to personal protective equipment (PPE) requirements, types of surgical devices utilized, risk of aerosolization and duration of the surgical procedures. High-risk exposures within surgical settings include being within an

operating room during an aerosol-generating procedure and cleaning the operating room after an aerosol-generating procedure.

When performing surgery on a patient with brucellosis, there are pre-operative and post-operative recommendations. Pre-operative recommendations include starting antibiotic therapy to decrease bacterial load. During the operation, aerosol-generating procedures should be minimized, personnel should be limited to those who are essential to the procedure, and all staff in the operating room should wear appropriate PPE, including gloves, masks, eyewear, and respiratory protection to include an N95 respirator (if there is a potential for aerosol-generating procedures). Post-operative recommendations include reviewing appropriate PPE use and any possible breaches in PPE; symptom and serological monitoring (if applicable) are recommended for all personnel for whom a breach of PPE is identified. PEP may be considered for all who were present during or after a potential aerosol-generating procedure was done. Serological monitoring (if applicable) and PEP can be considered for staff who are pregnant or immunocompromised.

Symptom Surveillance
An occupational health provider should arrange for regular (at least weekly) monitoring for febrile illness or symptoms consistent with brucellosis for all exposed workers. In addition, daily self-administered temperature checks are recommended for 24 weeks post-exposure, from the last known date of exposure. Exposed persons should be informed of common brucellosis symptoms and are encouraged to seek immediate medical treatment if illness develops within 6 months of the exposure, regardless of whether or not the patient has already undergone PEP. It is important for workers to notify their healthcare provider of their recent *Brucella* exposure so that receiving diagnostic laboratories may be notified and take precautions. Individuals who have risk factors for relapse of brucellosis may require a follow-up time that extends beyond 24 weeks. CDC's Brucellosis Reference Guide: Exposures, Testing, and Prevention (February 2017) has symptom monitoring tools for exposed individuals and health care professionals conducting the surveillance. These can be found in Appendix 2 (page 28) of the CDC Reference Guide.

Serological Monitoring
All exposed workers should undergo quantitative serological testing in order to detect an immune response to Brucella spp. Evidence suggests that seroconversion can occur shortly before symptoms appear, and therefore may be an earlier indicator of infection. It is recommended that sera be drawn and submitted to the same laboratory at 0 (baseline), 6, 12, 18, and 24 weeks following the exposure event.

CDC's Zoonotic and Select Agent Laboratory (ZSAL) is able to perform serial serological monitoring at no cost. If monitoring is conducted by other laboratories, it is recommended that an agglutination assay is used to quantify seroconversion. Instructions for serology submission to ZSAL are available in Appendix 1 of CDC's Brucellosis Reference Guide: Exposures, Testing, and Prevention (February 2017).

***B. canis* and *B. abortus* RB51:** Serological testing is currently not available for *Brucella canis* and *Brucella abortus* RB51 vaccine. Serological monitoring following exposure to these strains is not recommended, except to collect a baseline serum sample in order to rule out infection with other *Brucella* spp.

Table 3. Laboratory Risk Assessment and Postexposure Prophylaxis (PEP)*

Risk	Specimen	Exposure Scenario	PEP	Follow-up and Monitoring
Minimal (but not zero) Risk	Routine clinical specimen (e.g., blood, serum, cerebrospinal fluid)	Person who manipulates a routine clinical specimen (e.g., blood, serum, cerebrospinal fluid) in a certified Class II biosafety cabinet, with appropriate personal protective equipment (i.e., gloves, gown, eye protection)	None	N/A
	Routine clinical specimen (e.g., blood, serum, cerebrospinal fluid)	Person present in the lab while someone manipulates a routine clinical specimen (e.g., blood, serum, cerebrospinal fluid) in a certified Class II biosafety cabinet, or on an open bench where manipulation did not involve occurrence of aerosol-generating events† (e.g., centrifuging without sealed carriers, vortexing, sonicating, spillage/splashes)	None	May consider symptom watch for following scenarios: • Person who manipulates a routine clinical specimen (e.g., blood, serum, cerebrospinal fluid) on an open bench with or without appropriate personal protective equipment (i.e., gloves, gown, eye protection), or in a certified Class II biosafety cabinet without appropriate personal protective equipment • Person present in the lab while someone manipulates a routine clinical specimen (e.g., blood, serum, cerebrospinal fluid) on an open bench, resulting in occurrence of aerosol- generating events† (e.g., centrifuging without sealed carriers, vortexing, sonicating, spillage/splashes)
	Enriched material (e.g., a *Brucella* isolate, positive blood bottle) or reproductive clinical specimen (e.g., amniotic fluid, placental products)	Person who manipulates enriched material (e.g., a *Brucella* isolate, positive blood bottle) or reproductive clinical specimen (e.g., amniotic fluid, placental products) in a certified Class II biosafety cabinet, with appropriate personal protective equipment (i.e., gloves, gown, eye protection)		
		Person present in the lab while someone manipulates enriched material (e.g., a *Brucella* isolate, positive blood bottle) or reproductive clinical specimen (e.g., amniotic fluid, placental products) in a certified Class II biosafety cabinet		
Low Risk	Enriched material (e.g., a *Brucella* isolate, positive blood bottle) or reproductive clinical specimen (e.g., amniotic fluid, placental products)	Person present in the lab at a distance of greater than 5 feet from someone manipulating enriched material (e.g., a *Brucella* isolate, positive blood bottle) or reproductive clinical specimen (e.g., amniotic fluid, placental products), on an open bench, with no occurrence of aerosol-generating events† (e.g., centrifuging without sealed carriers, vortexing, sonicating, spillage/splashes)	• May consider if immunocompromised or pregnant. Discuss with health care provider. • Note: RB51 is resistant to rifampin in vitro, and therefore this drug should not be used for PEP or treatment	• Regular symptom watch (e.g., weekly) and daily self-fever checks through 24 weeks post-exposure, after last known exposure • Sequential serological monitoring at 0 (baseline), 6-, 12-, 18-, and 24-weeks post-exposure, after last known exposure • Note: no serological monitoring currently available for RB51 and *B. canis* exposures in humans

Risk	Specimen	Exposure Scenario	PEP	Follow-up and Monitoring
High Risk	Routine clinical specimen (e.g., blood, serum, cerebrospinal fluid)	Person who manipulates a routine clinical specimen (e.g., blood, serum, cerebrospinal fluid), resulting in contact with broken skin or mucous membranes, regardless of working in a certified Class II biosafety cabinet, with or without appropriate personal protective equipment (i.e., gloves, gown, eye protection)	• Doxycycline 100mg twice daily, and rifampin 600 mg once daily, for three weeks. • For patients with contraindications to doxycycline or rifampin: TMP-SMZ, in addition to another appropriate antimicrobial, should be considered. Two antimicrobials effective against *Brucella* should be given. • Pregnant women should consult their obstetrician • Note: RB51 is resistant to rifampin in vitro, and therefore this drug should not be used for PEP or treatment	• Regular symptom watch (e.g., weekly) and daily self-fever checks through 24 weeks post-exposure, after last known exposure • Sequential serological monitoring at 0 (baseline), 6-, 12-, 18-, and 24-weeks post-exposure, after last known exposure • Note: no serological monitoring currently available for RB51 and B. canis exposures in humans
	Enriched material (e.g., a *Brucella* isolate, positive blood bottle) or reproductive clinical specimen (e.g., amniotic fluid, placental products)	Person who manipulates (or is ≤ 5 feet from someone manipulating) enriched material (e.g., a *Brucella* isolate, positive blood bottle) or reproductive clinical specimen (e.g., amniotic fluid, placental products), outside of a certified Class II biosafety cabinet		
		Person who manipulates enriched material (e.g., a *Brucella* isolate, positive blood bottle) or reproductive clinical specimen (e.g., amniotic fluid, placental products), within a certified Class II biosafety cabinet, without appropriate personal protective equipment (i.e., gloves, gown, eye protection)		
		All persons present during the occurrence of aerosol-generating events† (e.g., centrifuging without sealed carriers, vortexing, sonicating, spillage/splashes) with manipulation of enriched material (e.g., a *Brucella* isolate, positive blood bottle) or reproductive clinical specimen (e.g., amniotic fluid, placental products) on an open bench		

*Source: CDC. Brucellosis Reference Guide: Exposures, Testing, and Prevention (February 2017).

†Examples of aerosol generating procedures include but are not limited to centrifuging without sealed carriers, vortexing, sonicating, accidents resulting in spillage or splashes (e.g., breakage of tube containing specimen). Other manipulations may require further investigation. These may include automated pipetting of a suspension containing the organism, grinding the specimen blending the specimen, shaking the specimen, other procedures for suspension in liquid to produce standard concentration for identification (i.e., inclusion of steps that could be considered major aerosol generating activities).

6. Vaccination

No vaccine is available for humans. A vaccine is used to effectively control the disease in cattle in areas heavily affected by brucellosis (not Virginia); however, to achieve eradication of the disease in a herd, repeat testing at regular intervals is required with culling of all positive animals.

7. Infection Control

Standard Precautions are recommended for patients with brucellosis; isolation rooms are not necessary. If an airborne generating procedure is done, all healthcare providers should wear appropriate PPE to include gloves, masks, eyewear, and respiratory protection, to include an N95 respirator.

8. Decontamination

Brucella is sensitive to heat and most disinfectants but can survive in the environment for several months under optimum conditions, particularly those with high humidity, low temperatures and no sunlight. Standard hospital approved disinfectants are adequate for cleaning patient rooms.

9. Postmortem Practices

If brucellosis is suspected as a cause of death, the local district Office of the Chief Medical Examiner should be immediately notified. Consultation should occur regarding whether an autopsy should be conducted, parties responsible for conducting the autopsy, and proper personal protective procedures to follow.

10. Public Health Measures

- Suspected or confirmed brucellosis cases should be reported immediately to the local health department
- Laboratory specimens may be sent to the state public health laboratory (DCLS) for confirmation of agent and other studies after consultation and approval by the local health department. For questions about specimen collection, the DCLS Emergency Officer can be reached 24 hours a day/7 days a week at 804-335-4617.
- Designated public health authority should begin an epidemiologic investigation:
    - Collect detailed information from the patient to attempt to identify the source of the exposure (e.g., consumption of unpasteurized dairy products, exposure to infected animals, international travel, high-risk occupation or recreational activity such as hunting; evaluate potential exposures for any suspicion of bioterrorism)
    - Determine if contacts of the patient have compatible illness and investigate if a potential common exposure is suspected
    - Collect suspected food items (e.g., unpasteurized milk, soft cheeses, etc.) for possible testing. VDH's Office of Epidemiology will work with the Virginia Department of Agriculture and Consumer Services (VDACS) if commercially prepared food is implicated.
    - Notify VDACS if animal exposures are identified
    - Implement control measures to prevent disease and additional exposures. For laboratorians or others potentially exposed who might have worked with the agent before identification

as *Brucella* spp., postexposure prophylaxis and monitoring might be recommended based on a risk assessment. Mothers infected with untreated brucellosis should temporarily not breastfeed and not feed expressed breast milk to their infants.

- VDH will work with the CDC, Federal Bureau of Investigation (FBI) and other state or federal agencies as necessary

11. References

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