Brucellosis is a zoonotic bacterial disease caused by *Brucella*. Multiple *Brucella* spp. can infect humans: *B. abortus*, *B. melitensis*, *B. suis*, *B. canis*, *B. ceti* and *B. pinnipedialis*. *Brucella* spp. are designated as Category B agents (i.e., moderate ease of transmission and morbidity with a lower rate of mortality than Category A agents) and 3 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, use or transfer of these organisms requires registration with CDC or USDA.

Mammals are the natural reservoir for *Brucella*. Different *Brucella* 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) and *B. pinnipedialis* (from seals, sea lions, walruses). Infection might 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 include 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 consumed in or imported from brucellosis-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 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, approximately 100 cases were reported annually to CDC between 2011 and 2015. Most (70 to 75%) are caused by *B. melitensis* and *B. abortus* and are associated with consumption of unpasteurized dairy products from endemic countries. A substantial amount of cases reported annually to CDC (approximately 25 to 30%) are caused by *B. suis* and almost all of these are diagnosed in feral swine hunters. In Virginia, the number of reported cases between 2011 and 2015 ranged from zero to three per year, with a five-year average of 1.2 cases per year for 2011–2015. The most common identified risk factors for recent Virginia cases have been the consumption of imported, unpasteurized cheese products and providing assistance during calving.

2. **Clinical Manifestations**

The incubation period for brucellosis is highly variable, usually 5 to 60 days, 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. Patients might present with acute or chronic signs and symptoms. Signs and symptoms include fever that is constant or intermittent, chills, sweats, malaise, anorexia, headache, pain in muscles, joint, or back, fatigue, and weight loss and some patients might develop gastrointestinal symptoms (e.g., nausea, vomiting, abdominal pain). Lymphadenopathy, hepatomegaly, or splenomegaly might be identified upon physical examination. Chronic symptoms could include recurrent fever, chronic fatigue and depression. Localized infections occur in approximately 30% of cases and can affect any organ system, resulting in infections such as arthritis, swelling of the testicle and scrotum area (e.g., epididymo-orchitis), swelling of the vertebrae (e.g., spondylitis), 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. Overall, the case-fatality rate is low (<1%) and fatal outcomes are most commonly associated with endocarditis.

3. **Specimen Collection and Laboratory Testing**

Protocols for sentinel clinical laboratories are no longer posted on the CDC website. The American Society for Microbiology (ASM) has agreed to take the lead in the development and dissemination of sentinel laboratory information. The most current ASM guidelines for specimen collection and laboratory testing (revised March 2016) are available here. For additional laboratory guidance, particularly related to biosafety, refer to the CDC’s Biosafety in Microbiological and Biomedical Laboratories (5th edition) (see References).

Laboratory personnel must be alerted if brucellosis is suspected so that appropriate precautions can be taken. All work on clinical specimens or isolates suspicious of *Brucella* should be performed in a biological safety cabinet and using biosafety level 3 (BSL-3) precautions. Because of the highly infectious nature of some *Brucella* species, consultation with the state public health laboratory, Division of Consolidated Laboratory Services (DCLS), is strongly recommended. The DCLS Emergency Services Officer can be reached 24 hours a day/7 days a week at (804) 335-4617. Sample collection instructions for testing at DCLS are shown in Table 1.
Table 1. Sample Collection and Testing Information for Suspected Brucellosis at DCLS and CDC*

<table>
<thead>
<tr>
<th>Laboratory Test</th>
<th>Acceptable samples</th>
<th>Amount</th>
<th>Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Brucella</em> species identification and genotyping (at CDC)</td>
<td>Blood</td>
<td>10 cc</td>
<td>Use blood isolator tube or aerobic culture bottle. Ship at room temperature. Transport to lab within 16 hours.</td>
</tr>
<tr>
<td><strong>Serum</strong></td>
<td></td>
<td>2–3 mL</td>
<td>Collect acute and convalescent serum (&gt;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.</td>
</tr>
<tr>
<td><strong>Abscess tissue: liver, spleen, or bone (testing conducted at CDC)</strong></td>
<td>1 gram</td>
<td></td>
<td>Place in sterile container; moisten with sterile broth or saline. Ship as soon as possible with cold packs.</td>
</tr>
<tr>
<td><strong>Bone marrow (testing conducted at CDC)</strong></td>
<td></td>
<td>1–2 cc</td>
<td>Ship in syringe with heparin. Remove needle and cap end. Ship at room temperature.</td>
</tr>
<tr>
<td><strong>Joint fluid (testing conducted at CDC)</strong></td>
<td></td>
<td>1 mL</td>
<td>Place in sterile container. Ship as soon as possible with cold packs.</td>
</tr>
<tr>
<td><strong>Culture isolate</strong></td>
<td></td>
<td>N/A</td>
<td>Send culture on an agar slant, not a plate. Agar slants should be shipped at room temperature.</td>
</tr>
<tr>
<td><strong>Serology: <em>Brucella</em> microagglutination test (BMAT)</strong></td>
<td>Serum</td>
<td>2–3 mL</td>
<td>Collect acute and convalescent serum (&gt;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. Note that serology is not available for <em>B. canis</em> or RB51.</td>
</tr>
<tr>
<td><strong>Brucella spp. PCR</strong></td>
<td>Whole blood, serum</td>
<td>0.5 – 1mL</td>
<td>Collect blood in purple top (EDTA). Ship with cold packs. Note that a negative test result does not rule out infection. PCR can detect <em>B. abortus</em>, <em>B. melitensis</em>, <em>B. suis</em> and <em>B. canis</em>; however, actual species identification is accomplished through culture confirmation.</td>
</tr>
</tbody>
</table>

*If brucellosis is suspected, notify the local health department immediately to discuss the case and laboratory testing. Specimens should be sent to Division of Consolidated Laboratory Services (DCLS) after the local health department has approved testing. The DCLS Emergency Duty Officer can be reached 24/7 at (804) 335-4617. In addition, the DCLS Blood and Body Fluid Submission Form should be completed with the appropriate test request (i.e., *Brucella* Microagglutination Test).

Presumptive identification criteria include:

- Colony morphology on sheep blood agar: *Brucella* species will 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* species 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 test (Kovac’s modification) positive

• Urease test (Christensen’s method) positive

Additional laboratory guidance is available in the Centers for Disease Control and Prevention (CDC) Brucellosis website available at [http://www.cdc.gov/brucellosis/](http://www.cdc.gov/brucellosis/).

4. Diagnosis

The current CDC case definition for brucellosis is available at [http://wwwn.cdc.gov/nndss/script/casedefDefault.aspx](http://wwwn.cdc.gov/nndss/script/casedefDefault.aspx). Note that a case definition is a 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 should not be used by healthcare providers to determine how to meet an individual patient’s health needs.

5. Treatment

Recommendations for brucellosis treatment 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 will depend on whether a localized infection (e.g., endocarditis, meningitis) or underlying condition that contraindicates certain antibiotics (i.e., pregnant women and children under the age of 8 years for whom tetracyclines are contraindicated) is present.

### Table 2. Brucellosis Treatment Options*

<table>
<thead>
<tr>
<th>Adults, Children ≥ 8 years†</th>
<th>Combination therapy to decrease the incidence of relapse:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Oral doxycycline (2–4 mg/kg per day, maximum 200 mg/day, in 2 divided doses) <strong>or</strong> oral tetracycline (30–40 mg/kg per day, maximum 2 g/day, in 4 divided doses) <strong>and</strong></td>
</tr>
<tr>
<td></td>
<td>• Rifampin (15–20 mg/kg per day, maximum 600–900 mg/day, in 1 or 2 divided doses).</td>
</tr>
<tr>
<td></td>
<td>• Recommended for a <strong>minimum</strong> of 6 weeks.</td>
</tr>
<tr>
<td></td>
<td>• Combination therapy with trimethoprim-sulfamethoxazole (TMP-SMZ) can be used if tetracyclines are contraindicated.</td>
</tr>
</tbody>
</table>

| 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 to 6 weeks. |
|                             | • Combination therapy: consider adding rifampin. Consult physician for dosing or if rifampin is contraindicated. **Tetracyclines (such as doxycycline) should be avoided in children less than 8 years of age.** |

| 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). Streptomycin may not be readily available in the U.S.
- 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.

### References for Treatment Recommendations


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.

### 6. Exposures and Postexposure Prophylaxis

Recommendations for brucellosis post-exposure prophylaxis (PEP) following laboratory exposures are provided in Table 3. Prophylaxis recommendations based on type of exposure (e.g., laboratory exposure, exposure to *B. abortus* RB51 vaccine, clinical and surgical exposures, or intentional exposure) are described below. Prophylaxis can be initiated up to 24 weeks after exposure.

For exposures to *Brucella* in the laboratory, a risk assessment to determine if the exposure was high or low risk based on the activity and location should be conducted (see CDC Brucellosis: Assessing Laboratory Risk Level and PEP, available at [http://www.cdc.gov/brucellosis/laboratories/risk-level.html](http://www.cdc.gov/brucellosis/laboratories/risk-level.html)). PEP should begin immediately in persons/workers with high-risk exposures. Persons with a high-risk exposure should be monitored for the development of signs or symptoms of brucellosis for 24 weeks from the time of last known exposure. In addition, for those with high-risk exposures, serial serum specimens collected at 0, 6, 12, 18 and 24 weeks after exposure is recommended. If brucellosis occurs despite prophylaxis, a treatment regimen based on antimicrobial susceptibility results would need to be selected. PEP is generally not recommended for low-risk exposures, though it may be considered on a case-by-case basis (for example, if the person is immunocompromised or pregnant).

The *B. abortus* RB51 vaccine, a modified live vaccine, is currently the only vaccine used in the US 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 may begin one to 15 days after exposure. RB51 is resistant to rifampin in vitro, and therefore 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 health care provider in case of contraindications to the aforementioned. 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 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 (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.

For a Brucella exposure in which the organism was intentionally released as a biological weapon, prophylaxis regimens outlined in Table 3 for laboratory exposures should be followed because these guidelines cover aerosol-generating events.
### Table 3. Laboratory Risk Assessment and Post-Exposure Prophylaxis*

<table>
<thead>
<tr>
<th>Risk</th>
<th>Specimen handling</th>
<th>Exposure scenario</th>
<th>PEP</th>
<th>Follow-up/monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Minimal (but not zero) Risk</strong></td>
<td>Routine clinical specimen (e.g., blood, serum, cerebrospinal fluid)</td>
<td>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).</td>
<td>None</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>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).</td>
<td></td>
<td>May consider symptom watch for following scenarios:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Enriched material (e.g., a <em>Brucella</em> isolate, positive blood bottle) or reproductive clinical specimen (e.g., amniotic fluid, placental products)</td>
<td>Person who manipulates enriched material (e.g., a <em>Brucella</em> 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).</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Person present in the lab while someone manipulates enriched material (e.g., a <em>Brucella</em> isolate, positive blood bottle) or reproductive clinical specimen (e.g., amniotic fluid, placental products) in a certified Class II biosafety cabinet.</td>
<td></td>
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<tr>
<td><strong>Low Risk</strong></td>
<td>Enriched material (e.g., a <em>Brucella</em> isolate, positive blood bottle) or reproductive clinical specimen (e.g., amniotic fluid, placental products)</td>
<td>Person present in the lab at a distance of greater than 5 feet from someone manipulating enriched material (e.g., a <em>Brucella</em> 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).</td>
<td>• May consider if immunocompromised or pregnant.</td>
<td>• Regular symptom watch (e.g., weekly) and daily self-fever checks through 24 weeks post-exposure, after last known exposure.</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• Discuss with health care provider.</td>
<td>• Sequential serological monitoring at 0 (baseline), 6, 12, 18, and 24 weeks post-exposure, after last known exposure.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• <strong>Note:</strong> RB51 is resistant to rifampin in vitro, and therefore this drug</td>
<td>• <strong>Note:</strong> no serological monitoring currently available for RB51 and <em>B. canis</em> exposures in humans.</td>
</tr>
</tbody>
</table>
| 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 courses.  
• 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. |
<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Enriched material (e.g., a <em>Brucella</em> isolate, positive blood bottle) or reproductive clinical specimen (e.g., amniotic fluid, placental products)</td>
<td>Person who manipulates (or is ≤ 5 feet from someone manipulating) enriched material (e.g., a <em>Brucella</em> isolate, positive blood bottle) or reproductive clinical specimen (e.g., amniotic fluid, placental products), outside of a certified Class II biosafety cabinet.</td>
<td>Person who manipulates enriched material (e.g., a <em>Brucella</em> 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).</td>
<td>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 <em>Brucella</em> isolate, positive blood bottle) or reproductive clinical specimen (e.g., amniotic fluid, placental products) on an open bench.</td>
</tr>
</tbody>
</table>

7. Vaccination

No vaccine is available for humans. A vaccine is used for cattle in areas heavily affected by brucellosis (not Virginia); however, the control strategy for cattle focuses on testing animals for infection and isolating and euthanizing infected herds.

8. Infection Control

In addition to standard precautions, contact precautions are indicated for patients with draining wounds.

9. Decontamination

*Brucella* is sensitive to exposure 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.

10. Postmortem Practices

If brucellosis is suspected as a cause of death, the district Office of the Chief Medical Examiner should be immediately notified (see [http://www.vdh.virginia.gov/medExam/ContactUs.htm](http://www.vdh.virginia.gov/medExam/ContactUs.htm)). Consultation should occur regarding whether an autopsy should be conducted, parties responsible for conducting the autopsy, and proper personal protective procedures to follow.

11. Public Health Measures

- Suspected or confirmed brucellosis cases should be reported immediately to the local health department. See [http://www.vdh.virginia.gov/LHD/index.htm](http://www.vdh.virginia.gov/LHD/index.htm).
- Laboratory specimens should 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 Services 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 or exposure to infected animals).
  - Investigate contacts of the patient for compatible illness to investigate a potential common exposure.
  - 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.
VDH will work with the CDC, Federal Bureau of Investigation (FBI) and other state or federal agencies as necessary.

12. References and Resources


