UTAH DEPARTMENT OF HEALTH

Brucellosis

Disease Plan

Quick Links

Last updated: January 16, 2018 by Dallin Peterson.

Questions about this disease plan?

Contact the Utah Department of Health Bureau of Epidemiology: 801-538-6191.

✓ CRITICAL CLINICIAN INFORMATION

Clinical Evidence

Signs/Symptoms

- Fever
- Night sweats
- Arthralgia
- Headache
- Fatigue
- Anorexia
- Myalgia
- Weight loss
- Endocarditis
- Orchitis
- Meningitis

Incubation Period

- Highly variable ranging from 5-60 days, most common about one month after exposure

Mode of Transmission

- Person-to-person is rare but has been reported to be sexually transmitted. Most commonly transmitted by direct contact with living or dead animal carcasses and secretions. It may also be spread by ingestion of raw or unpasteurized dairy products. Airborne transmission may occur in laboratory settings.

Laboratory Testing

Type of Lab Test

- Culture
- Serology (Brucella microagglutination test (BMAT)) – serum and convalescent obtained 2 weeks or grater apart.
- Nucleic Acid Test (PCR or NAT)

Type of Specimens

- Whole blood in vacutainer tube at least 3 mL (Culture)
- Serum in serum separator tube at least 3 mL at 4˚C (Serology)
- Blood in EDTA tube at least 1 mL at 4˚C (PCR)

Treatment Recommendations

Type of Treatment

- Combination of doxycycline and rifampin or streptomycin for at least 6 weeks

Prophylaxis

- Doxycycline 100 mg twice daily and rifampin 600 mg once daily for 3 weeks

Contact Management

Isolation of Case

- None

Quarantine of Contacts

- None

Infection Control Procedures

- Standard body substance precautions
- Laboratory workers should be compliant with biosafety regulations

✓ WHY IS BRUCELLOSIS IMPORTANT TO PUBLIC HEALTH?

Brucellosis is a zoonotic disease of wild and domestic animals. Human infections are transmitted by contact with fluids from infected animals, or derived food products, such as unpasteurized milk and cheese. In the United States, 100 to 200 cases of brucellosis are reported annually, and 3-10% of cases occur in people younger than 19 years of age. Brucellosis may be used as a biological weapon because of the protracted illness associated with it. Confirmed *Brucella* cases are rare in Utah but have been seen among lab workers.

✓ DISEASE AND EPIDEMIOLOGY

Clinical Description

Brucellosis is a systemic disease with acute or insidious onset characterized by sustained, intermittent, or irregular fever of variable duration. Symptoms may include fever, night sweats, weakness, malaise, anorexia, weight loss, arthralgias, myalgias, abdominal pain, and headache. Localized and chronic localized infections of organs (including the liver and spleen) can occur. Complications affecting the bones and joints are common (they occur in 20-60% of cases). Involvement of the genitourinary system, including orchitis and epididymitis, occurs in up to 20% of cases in males. Neurologic symptoms can occur in up to 5% of cases. The disease may last for days, months, or occasionally longer if inadequately treated. Most cases recover, but some individuals develop significant disabilities. The rate of relapse following treatment is about 5-15%, and it usually occurs within the first six months following completion of treatment. Asymptomatic infections can occur.

Causative Agent

Brucellosis is caused by bacteria of the genus *Brucella.* The species of *Brucella* that may infect humans are *B. abortus, B. melitensis, B. suis*, and rarely, *B. canis.* Three recently identified species, *B. ceti, B. pinnipedialis,* and *B. inopinata*, are potential human pathogens.

Differential Diagnosis

Symptoms are non-specific and diagnosis can be difficult. This disease can be mistaken for other chronic febrile illnesses.

Laboratory Identification

Clinicians can send cultures for *Brucella* to most large reference labs and is the most common for the diagnosis of brucellosis. Appropriate specimens for isolation include blood (best), CSF, bone marrow, spleen, liver, body fluids and abscess aspirates. It is important to indicate on the test request slip that *Brucella* is suspected, as different media and/or incubation times will be used. Most strains require complex media for growth, bone marrow is the gold standard for culture diagnosis.

Brucella can also be diagnosed through acute and convalescent serologies collected 2-4 weeks apart. A fourfold rise in antibodies indicates infection of Brucella. IgM antibodies are elevated during acute infection however decline within weeks. See figure 1 for antibody response in untreated Brucellosis. Serology testing for laboratory workers should be drawn at 0, 6, 12, 18 and weeks post exposure.

PCR is primarily used for suspect bioterror agent. Environmental samples can include swabs, powders, whole blood, sera, tissues, etc.

The Utah Public Health Laboratory (UPHL) will provide confirmation of clinical isolates.

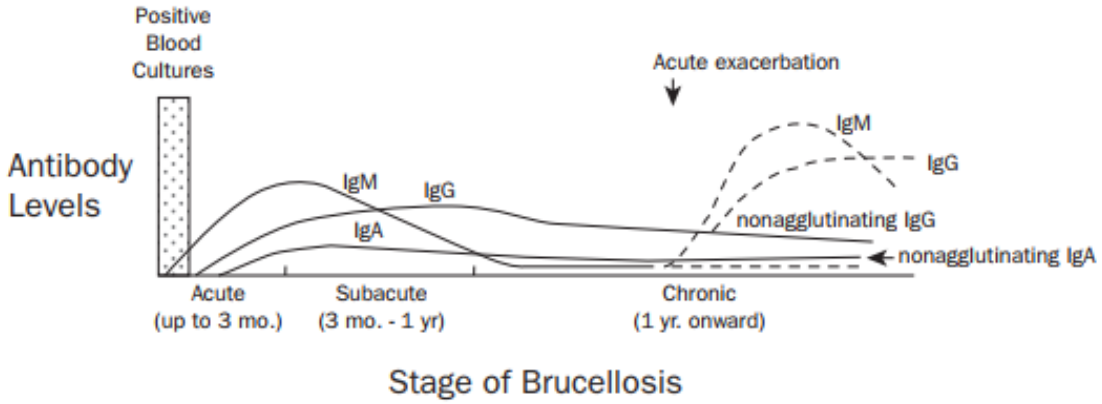

Figure 1: Antibody response in untreated Brucellosis.

Treatment

The Table 1 below provides a summary of recommended treatment options.

Subject	Summary
Adults, Children > 8 years of age	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. Combination therapy with trimethoprim-sulfamethoxazole (TMP-SMZ) can be sued if tetracyclines are contraindicated.
Children < 8 years of age	• 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	Tetracylcines 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 interventions should be considered in patients with complications such as deep tissue abscesses.

Table 1: Brucellosis Treatment Options

Case Fatality

The case-fatality rate of untreated brucellosis is less than 1%; however, death may result from complications associated with brucellosis infections.

Reservoir

Cattle, swine, goats, and sheep are the most common reservoirs. Bison, elk, caribou, and some species of deer may also harbor *Brucella* species. *B. canis* is an occasional problem in laboratory dog colonies and kennels. A small percentage of pet dogs and a higher proportion of stray dogs have *B. canis* antibody titers, and coyotes have been found to be infected as well.

Transmission

Brucellosis is spread to humans by direct contact with living or dead infected animals and their carcasses or secretions (including their tissues, blood, urine, vaginal discharges, aborted fetuses, and especially, placentas). Infection is transmitted by inoculation through non-intact skin or through direct contact with mucosal surfaces. It may also be spread through ingestion of raw milk and dairy products (e.g., unpasteurized cheese) from infected animals. Airborne transmission may occur through inhalation of contaminated aerosols (e.g., in laboratory settings). Persons may also be infected through accidental inoculation with live vaccine-strain *Brucella* used for livestock. Person-to-person spread is extremely rare, although it has been reported to be sexually transmitted. Breastfeeding women may transmit infection to their infants.

Susceptibility

Most people are susceptible; duration of acquired immunity is uncertain.

Incubation Period

The incubation period for brucellosis is highly variable, ranging from 5-60 days; illness most commonly occurs about one month after exposure.

Period of Communicability

Person-to-person transmission of brucellosis is extremely rare. Animals may be infectious for years.

Epidemiology

There is worldwide distribution of brucellosis, especially in Mediterranean countries, the Middle East, Africa, central Asia, India, Central and South America, and Mexico. There are approximately 100 to 200 cases of human brucellosis reported annually in the United States, and most of them are due to *B. melitensis.* Brucellosis may be used as a biological weapon because of the protracted illness associated with it. Confirmed *Brucella* cases are rare in Utah but have been seen among lab workers. There were four (4) cases reported in Utah during the period 2010-2015.

Certain occupations are at increased risk of contracting brucellosis, including farmers, ranchers, veterinarians, and other people who work directly with animals. It can also be found in people who work in laboratories and slaughterhouses, or as meat inspectors.

Sporadic cases and outbreaks may occur among consumers of raw (unpasteurized) milk and milk products, especially soft cheeses.

✓ PUBLIC HEALTH CONTROL MEASURES

Public Health Responsibility

- Identify the source of infection and prevent further transmission.
- Rule out the possibility of bioterrorism; *Brucella* is a category B agent.
- Check laboratory workers to assure that there was no exposure to the isolate, or to ensure that exposed laboratory personnel are appropriately treated.
- Notify the Utah Department of Agriculture and Food if case was acquired in Utah.
- Ensure treatment of suspected cases
- Ensure the proper labs are done and specimen is forwarded to the Utah Public Health Lab for testing

Prevention

- Do not consume raw milk or milk products (including imported cheese).
- Workers at occupational risk (e.g., farmers, slaughterhouse workers, meat processors, or butchers) should know the symptoms of the disease, the modes of transmission, and the risks of handling infected animal carcasses and products. They should know the proper way to reduce exposure, such as ventilating slaughterhouses and handling carcasses carefully.
- Hunters should use barrier protection (e.g., gloves or clothing) when dressing wild pigs and burying the remains.
- Anyone who handles or disposes of placentas, fetuses, and/or discharges from an animal should use care and should disinfect potentially contaminated areas.
- Local officials and farmers should search for infection among livestock and should eliminate infected animals. In areas of high prevalence, immunization of livestock may be appropriate. Ultimate control of human brucellosis relies on eliminating the disease in domestic animal populations.

Preventing Laboratory Exposures

Brucellosis is the most commonly reported laboratory-associated bacterial infection; recommendations for safe laboratory practices include:

- Use primary barriers: use safety centrifuge cups, personal protective equipment, and class II or higher Biological Safety Cabinets (BSCs) for procedures with a high likelihood of producing droplet splashes or aerosols.
- Use secondary barriers: restrict access to the laboratory when work is being performed and maintain the integrity of the laboratory's air handling system by keeping external doors and windows closed.
- Perform all procedures on unidentified isolates carefully to minimize the creation of splashes or aerosols.
- Prohibit sniffing of opened culture plates to assist in the identification of isolates. Manipulate isolates of small gram-negative or gram-variable rods within a BSC.

Chemoprophylaxis

Exposed laboratory workers should be referred to an infectious disease physician for appropriate antibiotic treatment, and sequential serological monitoring should be done at 0, 6, 12, 18, and 24 weeks post-exposure from the last known date of exposure.
http://www.cdc.gov/brucellosis/laboratories/risk-level.html

Vaccine

No human vaccine is available. Vaccines are available for cattle and bison.

Isolation and Quarantine Requirements

Isolation: None.
Quarantine: None.

Infection Control

Hospital and clinical settings should take necessary precautions when working with Brucella species. Organisms are easily killed by common disinfectants and heat. Standard hospital approved disinfectants are adequate for cleaning patient rooms. Sine person-person transmission is rare, patients do not have to be held in isolation rooms. Healthcare workers should exercise standard precautions.

✓ CASE INVESTIGATION

Reporting

Report any illness to public health authorities that meets any of the following criteria:

1. A person with one or more of the following laboratory findings:
    a. Culture and identification of *Brucella* spp. from clinical specimens.

   b. Evidence of a fourfold or greater rise in *Brucella* antibody titer between acute and convalescent-phase serum specimens obtained greater than or equal to two weeks apart.
2. A person with fever and one or more of the clinical findings listed in Table VI-B; AND the following laboratory finding:
   a. 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.
   b. Detection of Brucella DNA in a clinical specimen by PCR assay.
3. A person with fever and two or more of the clinical findings listed in Table VI-B AND one or more of the epidemiological risk factors listed in Table VI-B.
4. A person whose healthcare record contains a diagnosis of brucellosis.
5. A person whose death certificate lists brucellosis as a cause of death or a significant condition contributing to death.

Other recommended reporting procedures

- All cases of brucellosis should be reported.
- Reporting should be on-going and routine.
- Timeliness of reporting should follow the state health department's routine schedule; in Utah, cases should be reported within three business days after identification, unless bioterrorism is suspected. In this situation, cases should be reported immediately.

Table VI-B of criteria to determine whether a *Brucella* case should be reported to public health authorities.

Criterion	**Reporting**		
	1	2	3
Clinical Evidence			
Fever		N	N
Night Sweats		O	O†
Arthralgia		O	O†
Headache		O	O†
Fatigue		O	O†
Anorexia		O	O†
Myalgia		O	O†
Weight loss		O	O†
Endocarditis		O	O†
Orchitis		O	O†
Epididymitis		O	O†
Hepatomegaly		O	O†
Splenomegaly		O	O†
Arthritis		O	O†
Meningitis		O	O†
Spondylitis		O	O†
Healthcare record contains a diagnosis of brucellosis	S		

Death certificate lists brucellosis as a cause of death or a significant condition contributing to death	S		
Laboratory Evidence			
Culture and identification of Brucella spp. from clinical specimens	S		
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	S		
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		O	
Detection of Brucella DNA in a clinical specimen by PCR assay		O	
Epidemiologic Evidence			
Working in a clinical or microbiological laboratory processing samples that could potentially contain Brucella			O
Consumption of unpasteurized dairy products or undercooked meat contaminated with Brucella			O
Involvement with slaughtering, dressing, or butchering of potentially infected animals			O
Epidemiologic link to a confirmed human or animal case of brucellosis			O
Direct or indirect exposure to an environment or food products that were linked to a confirmed case of brucellosis			O
Travel to a Brucella-endemic country			O

Notes:

S = This criterion alone is Sufficient to identify a case for reporting.

N = All —N‖ criteria in the same column are Necessary to identify a case for reporting.

O = At least one of these —O‖ (Optional) criteria in each category (i.e., clinical evidence and laboratory evidence) in the same column—in conjunction with all —N‖ criteria in the same column—is required to identify a case for reporting. (These optional criteria are alternatives, which mean that a single column will have either no O criteria or multiple O criteria; no column should have only one O.)

O† =At least two of any —O‖ criteria in each category (e.g., clinical presentation and laboratory findings) in the same column—in conjunction with all other —N‖ criteria in the same column—is required to report a case.

Case Definition
Brucellosis (*Brucella* spp., 2010)

Clinical Criteria

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 two 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.

Classification Table

Criterion	Case Definition		
	Confirmed	Probable	
Clinical Presentation			
Fever	N	N	N
Night sweats	O	O	O
Arthralgia	O	O	O
Headache	O	O	O
Fatigue	O	O	O
Anorexia	O	O	O
Myalgia	O	O	O
Weight loss	O	O	O
Endocarditis	O	O	O
Orchitis	O	O	O

Epididymitis	O	O	O
Hepatomegaly	O	O	O
Splenomegaly	O	O	O
Arthritis	O	O	O
Meningitis	O	O	O
Spondylitis	O	O	O
Laboratory Findings			
Culture and identification of *Brucella* spp. from clinical specimens	O		
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	O		
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			O
Detection of *Brucella* DNA in a clinical specimen by PCR assay			O
Epidemiological Risk Factors			
Epidemiologically linked to a confirmed human or animal brucellosis case		N	

Notes:
N = All —N‖ criteria in the same column are Necessary to classify a case.
O = At least one of these —O‖ (Optional) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column—in conjunction with all —N‖ criteria in the same column—is required to classify a case.

Case Investigation Process

- Fill out morbidity form and disease investigation form.
- Verify case status.
    - Note: a case's clinical sample must be confirmed by UPHL or the CDC in order to confirm the case**.**
- Determine whether patient had travel/exposure history consistent with acquisition of disease in Utah or elsewhere.
- If patient acquired disease in Utah, identify the source of transmission and eliminate it.

Outbreaks

An outbreak will constitute one case of disease without a consistent travel history that indicates infection was obtained in an endemic area such as Central/South America. The investigator may also consider the possibility of an outbreak when there is an unusual clustering of cases in time and/or space.

Identifying Case Contacts

Person-person transmission is rare-possibly sexually transmitted. However, laboratory workers may become exposed during the culture and identification process. Public health should contact the testing laboratory(s) to see whether any personnel were exposed in order to ensure appropriate management of these individuals.

Case Contact Management

All exposed laboratory workers should be referred to an infectious disease physician for appropriate antibiotic management. Sequential serological monitoring should be done at 0, 6, 12, 18, and 24 weeks post-exposure from the last known exposure date.

✓ REFERENCES

American Academy of Pediatrics. [*Brucellosis*]. In: Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. Red Book: 2012 Report of the Committee on Infectious Diseases. Elk Grove Village, IL: American Academy of Pediatrics; 2012.

Bosilkovski, M., MD. (2007). Clinical manifestations, diagnosis, and treatment of brucellosis. Retrieved March 23, 2016, from http://www.uptodate.com/contents/clinical-manifestations-diagnosis-and-treatment-of-brucellosis?source=search_result.

Brucellosis (*Brucella* spp.). National Notifiable Disease Surveillance System (NNDSS). Centers for Disease Control and Prevention. Updated: 07,2015. Accessed: 11, 2015.

Brucellosis. Centers for Disease Control and Prevention. Website: http://www.cdc.gov/brucellosis/ Updated: 11, 2012. Accessed: 11,2015.

Case Definitions for infectious Conditions under Public Health Surweillance. Centers for Disease Control and Prevention. MMWR 46 (RR-10), 1997.

CDC. (2012, December 04). Brucellosis-Clinicians. Retrieved March 23, 2016, from http://www.cdc.gov/brucellosis/clinicians/suspected-infection.html.

Control of Communicable Diseases Manual (20th Edition), Heymann, D.L., Ed; 2015.

✓ VERSION CONTROL

V.03.23: Updated treatment paragraph, epidemiology section, and public health responsibility section, fixed tables to meet CSTE case definition, added hyperlink under chemoprophylaxis, updated references and created infection control paragraph.

V.11.15: Added “Why is Brucellosis Important to Public Health” section. Updated “Disease and Epidemiology” section. Updated “Public Health Control Measures” section. Updated “Case Investigation” section. Added “Version Control” section. Added “UT-NEDSS Minimum/Required Fields by Tab” section. Updated “Case Contact Management” section.

V.01.16: Updated tables to meet CSTE case definition

✓ UT-NEDSS Minimum/Required Fields by Tab

Demographic

- ☑ Patient's name
- ☑ Patients street address
- ☑ City
- ☑ State
- ☑ Zip
- ☑ Phone number
- ☑ Sex
- ☑ Date of birth
- ☑ Ethnicity
- ☑ Race

Clinical

- ☑ Date diagnosed
- ☑ Date of death
- ☑ Died
- ☑ Disease
- ☑ Onset date

Laboratory

- ☑ Lab test date
- ☑ Specimen source
- ☑ Test result
- ☑ Test status
- ☑ Test type

Epidemiological

- ☑ Occupation
- ☑ Imported from
- ☑ Date of exposure
- ☑ Exposure city
- ☑ Exposure county
- ☑ Exposure name
- ☑ Exposure place type
- ☑ Exposure state
- ☑ Exposure street
- ☑ Exposure unit number
- ☑ Exposure zip code

Reporting

- ☑ Date first reported to public health

Administrative

- ☑ LHD case status
- ☑ Outbreak name
- ☑ State case status
- ☑ Outbreak associated