

Brucellosis Investigation Guideline

CONTENT:

VERSION DATE:

Investigation Protocol:

- Investigation Guideline 07/2012

Supporting Materials found in attachments:

- Fact Sheet 06/2012
- Case Report Form Exp 06/2013

Revision History:

| Date | Replaced | Comments |
|---------|----------|--|
| 07/2012 | 1/2010 | Added notification section. Updated web-links. |
| 02/2012 | - | Removed references to KS-EDSS |

Brucellosis

Disease Management and Investigative Guidelines

CASE DEFINITION (CDC 2010)

Clinical Description for Public Health Surveillance:

- 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 Case Classification:

- 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
- **Suspect** (Internal KDHE Definition for Data Management Purposes): Lab results only without clinical information. [Follow-up required by local health department or record reason for no clinical information in notes.]

LABORATORY ANALYSIS

The State Public Health Laboratory does not provide testing and sends all specimens to CDC. Specimens sent to CDC must have prior authorization from the State Epidemiology Program (1-877-427-7317) before they are processed.

- Laboratory Kit: Miscellaneous infectious substance.
- Specimen and amount: Call for specific information.
- For additional information concerning collection or sample transport, call (785) 296-1620 or refer to guidance at www.kdheks.gov/labs/lab_ref_guide.htm

Note: [Exposure to RB51 \(vaccine strain of *Brucella abortus*.\)](#) does not induce a measurable antibody response. Monitoring serum specimens in individuals exposed to RB51 will not provide a useful indicator of infection.

EPIDEMIOLOGY

Brucellosis is a zoonotic disease; humans are accidental hosts. It is most often seen in farmers, ranchers, veterinarians, and others who work directly with animals. Employees in certain types of laboratories, slaughterhouses and meat inspectors may also be infected. Sporadic cases and outbreaks occur among consumers of unpasteurized milk and milk products, especially soft cheeses. Brucellosis is not common in the United States; 100 to 200 cases occur each year, but brucellosis can be very common in countries where animal disease control programs have not reduced the amount of disease among animals. Kansas is considered a Brucellosis Class Free State (*B. abortus* in livestock) since July 1, 1999. For the brucellosis status of other states, refer to the USDA-APHIS monthly reports at http://www.aphis.usda.gov/animal_health/animal_diseases/brucellosis/.

DISEASE OVERVIEW

A. Agent:

Brucellosis is caused by the small, nonmotile, gram-negative coccobacillus. Several *Brucella* species infect humans; usually *B. abortus* (cattle, bison, elk), *B. melitensis*, *B. ovis* (sheep, and goats) and *B. suis* (pigs); rarely *B. canis* (dogs).

B. Clinical Description:

Acute or insidious onset with fever, headache, weakness, sweating, chills, arthralgia, depression, weight loss and generalized aching. Relapses are common in untreated persons. Lymphadenia, splenomegaly and hepatomegaly are common but jaundice is rare. Symptoms may last from weeks to years and diagnosis is often difficult. Fatalities are rare.

C. Reservoirs:

Reservoirs include sheep, cattle, swine, and goats. Bison, elk, caribou, and deer may also harbor *Brucella spp.* *B. canis* is an occasional problem associated with laboratories and dog kennels.

D. Mode(s) of Transmission:

Transmission occurs through direct contact with infected animals and/or tissues including: blood, urine, vaginal discharges, aborted fetuses, and placentas. It may also be transmitted through consumption of unpasteurized milk and/or dairy products from infected animals. Airborne transmission may occur through inhalation of aerosols in lab settings and may also occur through accidental self-inoculation of brucellosis vaccine. Human-to-human transmission is rare, but congenital brucellosis has been reported, and infected mothers may transmit to infants through breastfeeding.

E. Incubation Period:

Variable incubation period, ranging from 5-60 days but may be several months; illness most commonly occurs about 1 month after exposure.

F. Period of Communicability:

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

G. Susceptibility and Resistance:

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

H. Treatment:

Administer a combination of rifampin or streptomycin and doxycycline for at least 6 weeks. Corticosteroids may be helpful for severely ill cases.

I. Vaccine:

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

NOTIFICATION TO PUBLIC HEALTH AUTHORITIES

Brucellosis infections shall be designated as infectious or contagious in their nature, and cases or suspect cases shall be reported within seven days:

1. Health care providers and hospitals: report to the local public health jurisdiction or KDHE-BEPHI (see below)
2. Local public health jurisdiction: report to KDHE-BEPHI (see below)
3. Laboratories: report to KDHE-BEPHI (see below)
4. KDHE-BEPHI will contact the local public health jurisdiction by phone within one hour of receiving any suspected brucellosis report.

**Kansas Department of Health and Environment (KDHE)
Bureau of Epidemiology and Public Health Informatics (BEPHI)**

Phone: 1-877-427-7317

Fax: 1-877-427-7318

- *The local public health jurisdiction will report information requested in the Kansas electronic surveillance system, as soon as possible, ensuring that the electronic form is completed within 7 days of receiving a notification of a report.*

Outbreaks, unusual occurrences of brucellosis, and suspect acts of terrorism should be reported WITHIN 4 HOURS by telephone to 1-877-427-7317.

Further responsibilities of state and local health departments to the CDC:

*As a nationally notifiable condition, **multiple brucellosis cases that are temporally/spatially clustered** require an IMMEDIATE, URGENT report to the Center of Disease Control and Prevention (CDC).*

- KDHE epidemiologist will call the CDC EOC at 770-488-7100 within 24 hours of identifying multiple, probable or confirmed brucellosis cases that are temporally/spatially clustered.
- **Local public health jurisdiction** will report information requested on the disease reporting forms as soon as possible, completing the forms within 7 days of receiving a notification of a report.
- KDHE-BEPHI will file an electronic case report the next regularly scheduled electronic transmission.
(KDHE-BEPHI files electronic reports weekly with CDC.)

INVESTIGATOR RESPONSIBILITIES

- 1) Use current [case definition](#), to confirm diagnosis with the medical provider.
- 2) Conduct a [case investigation](#) to identify potential source of infection.
- 3) Conduct [contact investigation](#) to identify additional cases.
- 4) Identify whether the source of infection is major public health concern.
- 5) Initiate control and prevention measures to prevent spread of disease.
- 6) Complete and report all information requested via the state electronic surveillance system.
- 7) As appropriate, use the disease [fact sheet](#) to educate individuals or groups.

STANDARD CASE INVESTIGATION AND CONTROL METHODS

Case Investigation

- 1) Contact the medical provider who ordered testing of the case and obtain the following information. (This includes medical records for hospitalized patients.)
 - Using the [case report form](#), identify any symptoms of brucellosis:
 - Record onset date (if a reoccurrence – record the earliest onset date)
 - Record the duration of the current illness in weeks
 - Determine if the onset was acute or insidious, recording symptoms
 - Examine the laboratory testing that was done to ensure all testing that could confirm the case has been reported in Epi-Trax.
 - Examine and record the therapy that the case received.
 - Collect case's demographic data and contact information (birth date, county, sex, race/ethnicity, occupation, address, phone number(s))
 - Record hospitalizations: location, admission and discharge dates
 - Record outcomes: recovered or date of death
- 2) Interview the case or proxy to determine source and risk factors; focus on a 6 month incubation period prior to illness onset.
 - Occupation: [Laboratory worker](#), farmer, dairyman, slaughterhouse worker, butcher, persons handling animals and animal by-products
 - Travel to *Brucella* endemic areas (i.e., the Mediterranean Basin, South and Central America, Eastern Europe, Asia, Africa, Caribbean and Middle East)
 - Use of unpasteurized milk, other dairy or imported foods, especially cheese.
 - Contact with potentially infected animals or their tissues, particularly postpartum fluid or tissues;
 - Potential contact with cattle, swine, goats, sheep, horses, and dogs
 - Hunting or other outdoor activities.
 - Parenteral or mucous membrane [Brucella vaccine exposure](#).
- 3) Investigate epi-links among cases (clusters, household, co-workers, etc).
 - For suspected [outbreaks](#) to Managing Special Situations section.

Contact Investigation

- 1) Contacts are those with possible exposure to the source of infection. Contacts are not persons in close proximity to a case only.
- 2) Examine all potential exposures based on possible source and potential modes of transmission, including inoculations, sprays into eyes, nose or mouth, or direct skin contact with substances containing *Brucella spp.*
- 3) Identify persons who participated with the case in any of the at-risk activities and contact them to identify if they are experiencing any symptoms.
- 4) All laboratories handling specimens with confirmed *Brucella* are investigated to identify possible contacts to *Brucella* isolates. Classify based on exposure risk:
 - High-risk exposure: Performing a specifically implicated practice such as sniffing bacteriological cultures, manipulating cultures while on an open bench, or mouth pipetting; being within 5 feet of work with cultures on an open bench, or being present in the lab during an aerosol-generating event.
 - Low-risk exposure: In lab at time of manipulation on an open bench but no other high-risk exposures.

Isolation, Work and Daycare Restrictions

- 1) Hospitals: In addition to standard precautions, contact precautions for patients with draining wounds.
- 2) No restrictions are indicated for outpatient management.

Case Management

None required.

Contact Management

- 1) Symptomatic acquaintances, household members, associates, or co-workers should be strongly urged to contact their physician for a medical evaluation.
- 2) Persons who are not ill but who were potentially exposed should begin a fever watch. From their last exposure, temperature should be actively monitored for fever for four weeks.
- 3) Broader symptoms of brucellosis should be passively monitored for six months from the last exposure. Broader symptoms include:
 - Acute: fever, chills, headache, low back pain, joint pain, malaise, diarrhea
 - Sub-Acute: malaise, muscle pain, headache, neck pain, fever, sweats
 - Chronic: anorexia, weight loss, abdominal pain, joint pain, depression, constipation
- 4) Recommend PEP to those contacts with high-risk exposures to *Brucella*:
 - Doxycycline 100 mg twice daily and rifampin 600 mg once daily for 3 weeks. (Note: High risk contacts to RB-51 in animal vaccine should receive doxycycline only. The spraying of any *Brucella* containing vaccine in the eyes may require 6 weeks of treatment.)
 - Trimethoprim-sulfamethoxazole as an alternative for patients with contraindications to doxycycline.
 - Pregnant contacts with high-risk exposure should consider PEP in consultation with their obstetricians.
- 5) [For laboratory personnel](#) refer to managing special situations.
- 6) [For vaccine exposure](#) refer to managing special situations.

Environmental Measures

- 1) Pasteurize all milk and dairy products.
- 2) Exercise care when handling placenta and fetus from aborted animals.
- 3) Disinfect contaminated areas with a bleach solution or other commercial disinfectant.

Environmental inspection may be necessary through the Kansas Department of Agriculture in the following situations:

- 1) If a commercial dairy is implicated through the distribution of unpasteurized milk or dairy products.
- 2) If a meat packing or distributor is implicated as a source of infection.
- 3) If a restaurant or food distributor is implicated through the distribution of unpasteurized milk or dairy products.

It is very important to verify the location or previous location of the source of the infection (i.e., from what state or country was the meat or dairy was obtained). If

any domestic animal or animals that resides in the state of Kansas is believed to be affected by brucellosis, the Kansas Animal Health Department should be notified immediately (785-296-2326)

Education

- 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.

MANAGING SPECIAL SITUATIONS

A. Outbreak Investigation:

There are no formal outbreak definitions; however, the investigator may consider the possibility of an outbreak when there is an unusual clustering of cases in time and/or space.

- 1) Notify KDHE immediately, 1-877-427-7317.
- 2) Active case finding will be an important part of any investigation.

B. Intentional Contamination

Brucellosis is a potential bioterrorism weapon. If the case has no known exposures or is not employed in an occupation that is prone to exposure, then consider a bioterrorist event. An attack may take the form of dissemination of an aerosol among a large gathering of people or by the contamination of food or water. Because the laboratory confirmation could be delayed, specific epidemiological, clinical, and microbiological findings that suggest an intentional release of brucella should result in the issue of a health alert.

If suspected:

- 1) Notify local law enforcement, the local Health Officer, the on-call epidemiologist (local) and KDHE (1-877-427-7317) immediately.
- 2) Implement "[Chain of Custody](#)" procedures for all samples collected, as they will be considered evidence in a criminal investigation.
- 3) Work to define 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. The definition may have to be re-evaluated and redefined at various steps in the investigation and response.
- 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.

Safety Considerations:

- Risks to public health, health care and emergency response personnel are not significant.

Risk Communication Materials:

- Factsheet for brucellosis: Located in KDHE [Public Information and Communication Standard Operating Guide](#), Supporting Document F – Public Information, Biological Hazards.

Diagnosis:

- Physicians who suspect brucellosis should promptly collect blood or bone marrow for culture. Liver, spleen, joint fluid and abscesses can also be cultured. Serum collected for serologic diagnosis, requires an acute specimen collected as soon as possible after onset and a convalescent-phase specimen should be collected > 14 days after the acute specimen.
- Alert the laboratory to the possibility of *Brucella* and need for special safety procedures. Level A laboratories should consult with state public health laboratory director (or designate) prior to or concurrent with testing if *Brucella* species is suspected by the physician.
- Serology and Rapid Testing: The standard laboratory test for Brucella antibody is the tube agglutination test, but the more rapid simple slide agglutination test is commonly used in commercial and hospital laboratories. The slide agglutination test is 97%--100% sensitive and may be as low as 88% specific. If used in a population with a low prevalence of disease, the risk for a false-positive result is high. Therefore, diagnostic laboratory testing should be integrated with epidemiologic investigation when assessing potential covert biological terrorism events to rule out false-positive laboratory findings. PCR and ELISA testing may also be available.
- Biopsy specimens: *Brucella spp.* can be identified through direct examination of biopsy specimens using direct fluorescent antibody stains.
- Cultures: *Brucella spp.* will grow only in aerobic blood culture bottles after 2-4 days; followed by isolation as typical colonies on BAP and CHOC within 48 hours. Presumptively identified as a small, gram-negative coccobacilli that is oxidase, catalase and urea positive. Confirmatory identification is made by agglutination with specific antiserum in a reference laboratory.

Treatment:

- Drug-resistant organisms might be used as a weapon, conduct antimicrobial susceptibility testing quickly and alter treatments as needed.
- Antibiotics for treating patients infected with brucellosis in a bioterrorist event are included in the national pharmaceutical stockpile maintained by CDC, as are ventilators and other emergency equipment.

Postexposure prophylaxis (PEP):

- In most brucellosis threat situations post exposure prophylaxis is not recommended. However, if the level of suspicion is high, exposed individuals may begin antimicrobial therapy if a definitive determination cannot be made within 5 days.
- The recommended treatment is: rifampin (600 mg/day) and doxycycline (100 mg twice daily) for 6 weeks.
- PEP of close contacts of brucellosis patients is not recommended because person-to-person transmission is not known to occur.

Surveillance:

- Arrange for active surveillance for 4 weeks for the development of febrile illness and 6 months of passive monitoring for other signs and symptoms of brucellosis among all individuals exposed.

C. Exposure to Brucella containing Vaccine:

- 1) Exposure is defined as a needle stick, splash of vaccine onto broken skin or in the eyes.
- 2) Determine strain of vaccine (RB-51; strain 19; REV-1).
- 3) Instruct contact to seek care of medical provider.
- 4) Recommend the collection of a baseline blood sample to test for antibodies; recheck a second blood sample at 2-3 weeks.
 - Note: Exposure to RB51 (vaccine strain of *B. abortus*) does not induce a measurable antibody response. Monitoring serum specimens in those exposed to RB51 will not provide a useful indicator of infection.
- 5) Recommend PEP based on type of vaccine and exposure. (RB-51 requires PEP with doxycycline only; splashes in the eyes may require 6 week treatment)

D. Laboratory Exposure to *Brucella* isolates:

- 1) Determine number of workers exposed to *Brucella* isolates and classify exposures into high- and low-risk.
- 2) Recommend PEP for workers with high-risk exposures to *Brucella*.
- 3) Discuss PEP with workers with only low-risk exposures.
- 4) Obtain baseline serum samples from all workers as soon as possible after potential *Brucella* exposure is recognized. (If available, obtain pre-exposure stored specimens.)
- 5) Arrange for serologic testing on all workers exposed at 2, 4, 6, and 24 weeks post exposure using agglutination test at the CDC.
 - Note: Exposure to RB51 (vaccine strain of *B. abortus*) does not induce a measurable antibody response. Monitoring serum specimens in those exposed to RB51 will not provide a useful indicator of infection.
- 6) Arrange for regular active surveillance for the development of febrile illness (for 4 weeks) or other signs and symptoms of brucellosis (for 6 months).

DATA MANAGEMENT AND REPORTING TO THE KDHE

A. Organize and collect data.

B. Report data via the Kansas electronic surveillance system.

- All essential data that was collected during the investigation, especially data that helps to confirm or classify a case.

ADDITIONAL INFORMATION / REFERENCES

- A. Treatment / Differential Diagnosis:** Red Book: 2009 Report of the Committee on Infectious Diseases. 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009:237-239.
- B. Epidemiology, Investigation and Control:** Heymann. D., ed., Control of Communicable Diseases Manual, 18th Edition. Washington, DC, American Public Health Association, 2009.
- C. Case Definitions:** CDC Division of Public Health Surveillance and Informatics, Available at: www.cdc.gov/osels/ph_surveillance/nndss/casedef/case_definitions.htm
- D. Chain of Custody:** KDHE Chain of Custody Standard Operating Guide, www.kdheks.gov/cphp/operating_guides.htm#coc
- E. Laboratory Exposures to Brucella:**
- CDC. Laboratory-Acquired Brucellosis --- Indiana and Minnesota, 2006. MMWR 2008 / 57(02); 39-42. Available from www.cdc.gov/mmwr/preview/mmwrhtml/mm5702a3.htm
 - Yagupsky P, Baron EJ. Laboratory exposures to brucellae and implications for bioterrorism. Emerg Infect Dis. [serial on the Internet]. 2005 Aug (date cited). Available from www.cdc.gov/ncidod/EID/vol11no08/04-1197.htm
- F. Additional Information (CDC):** www.cdc.gov/health/default.htm

ATTACHMENTS

- Fact Sheet
- Case Report Form w/ Instructions

To view attachments in the electronic version:

1. Go to <View>; <Navigation Pane>; <Attachments> – OR – Click on the “Paper Clip”  icon at the left.
2. Double click on the document to open.