

Brucellosis

(Also Known as Bangs Disease, Undulant Fever, Malta Fever, and Mediterranean Fever)

IMMEDIATELY REPORTABLE DISEASE

Per N.J.A.C. 8:57, healthcare providers and administrators shall immediately report **by telephone** confirmed and suspected cases of brucellosis to the health officer of the jurisdiction where the ill or infected person lives, or if unknown, wherein the diagnosis is made. The health officer (or designee) **must immediately institute the control measures listed below in section 6, “Controlling Further Spread,”** regardless of weekend, holiday, or evening schedules. A directory of local health departments in New Jersey is available at <http://www.state.nj.us/health/lh/directory/lhdselectcounty.shtml>.

If the health officer is unavailable, the healthcare provider or administrator shall make the report to the Department by telephone to 609.826.5964, between 8:00 A.M. and 5:00 P.M. on non-holiday weekdays or to 609.392.2020 during all other days and hours.



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1 THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Brucellosis is caused by infection with *Brucella* bacteria. The species of *Brucella* that infect humans are *B. abortus*, *B. melitensis*, *B. suis*, and, rarely, *B. canis*. Infection with *B. melitensis* occurs more frequently than do infections with the other species in general populations and has the highest prevalence in countries with a high incidence of brucellosis in sheep and goats (Argentina, Mexico, and Peru).

B. Clinical Description

The symptoms of brucellosis may be nonspecific, including sustained or irregular fever of variable duration, headache, weakness, sweats, chills, arthralgias, malaise, weight loss, depression, and generalized aching. Onset of illness may be acute or insidious. Localized infections of organs (including the liver and spleen) and chronic localized infections can occur. The disease may last for days, months, or occasionally longer if inadequately treated. Relapse is not uncommon. Complications affecting the joints are common, as is genitourinary involvement, including orchitis and epididymitis. The case-fatality ratio of untreated brucellosis is $\leq 2\%$. Death often results from endocarditis caused by *B. melitensis*.

C. Reservoirs

Cattle, swine, goats, and sheep are the most common reservoirs. The United States and most European countries are free of bovine brucellosis. 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. Coyotes have also been found to be infected.

D. Modes of Transmission

Brucellosis is spread through direct contact (of mucosal surfaces and cuts and abrasions of the skin) with secretions of living or dead infected animals, including their tissues, blood, urine, vaginal discharges, aborted fetuses, and placentas. 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 *Brucella* vaccine strain used for livestock (strain 19). Person-to-person spread is extremely rare, although it has been reported to occur through breast-feeding, sexual transmission and contaminated tissue transplantation.

E. Incubation Period

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

F. Period of Communicability or Infectious Period

Person-to-person transmission of brucellosis is extremely rare.

G. Epidemiology

Each year about half a million cases of brucellosis occur in humans worldwide. Incidence worldwide may be largely unrecognized and underreported. Humans are accidental hosts. The infection in animal reservoirs provides a key to its occurrence in humans. Argentina, Mexico, and Peru are the Latin American countries with the largest number of recorded cases. The same pattern holds true for Mediterranean countries, Iran, the former Soviet Union, and Mongolia. *B. abortus* and *B. suis* infections usually affect occupational groups; whole *B. melitensis* infections occur more frequently than do other types in the general population. The greatest prevalence of brucellosis is found in countries with a high incidence of *B. melitensis* infection among sheep and goats, where it is commonly seen as an occupational disease in farmers, ranchers, veterinarians, and other people who work directly with animals. It may also be found in people who work in laboratories and slaughterhouses (e.g., meat inspectors). Sporadic cases and outbreaks may occur among consumers of raw (unpasteurized) milk and milk products, especially soft cheeses.

The incidence in the United States is <0.5 cases per 100,000 population, primarily *B. melitensis*. Most cases are reported from California, Florida, Texas, and Virginia. Two confirmed and one probable case were reported in New Jersey residents during 2004 and 2005. Both confirmed cases were attributed to consumption of unpasteurized milk products imported from counties with a high incidence of brucellosis in domestic animals.

H. Bioterrorist Potential

Brucella species are considered potential bioterrorist agents and could cause a serious public health challenge in terms of ability to limit the numbers of casualties and to control other repercussions from such an attack.

2 CASE DEFINITION

A. New Jersey Department of Health and Senior Services (NJDHSS) Case Definition

1. Clinical Description

The symptoms of brucellosis may be acute or insidious onset, including sustained or intermittent fever of variable duration, headache, weakness, sweats, chills, arthralgias, malaise, weight loss, depression, and generalized aching. Localized suppurative infections of organs, including the liver, heart, and spleen, can occur. The disease may last for days, months, or occasionally longer if inadequately treated. A relapsing course of illness is not uncommon. Osteoarticular (joint) complications occur in 20% to 60% of cases; sacroiliitis is the most frequent joint manifestation. Genitourinary involvement is seen in 2% to 20% of cases, with orchitis and epididymitis as common manifestations. Part or all of the original syndrome may reappear as relapses.

2. Laboratory Criteria for Diagnosis

Laboratory diagnosis is made by isolation of *Brucella* from blood, bone marrow, and other tissues or patient discharges. Serological tests (enzyme-linked immunosorbent assay [ELISA], agglutination test) are valuable, especially when paired sera show a four-fold rise in antibody titer. Most cases of active infection have agglutination acute serum titers of 1:160 or greater.

The commercial laboratories use PanBio reagents to perform a rapid ELISA test, which reports reactivity in colorimetric (PanBio) units. This ELISA is used for the **qualitative** detection of antibodies to brucellosis; it does not express **quantity** of titer. Therefore, this assay cannot satisfy the case definition requirement of demonstrating significant change in titers between paired sera. This assay is very sensitive, and elevated immunoglobulin M (IgM) results may be seen in healthy asymptomatic individuals with no exposure history. Therefore, equivocal or low positive IgM reactivity without elevated IgG would not be considered a case. If such patients have clinically suspected brucellosis and history of exposure (livestock contact outside North America or Europe, or consumption of unpasteurized milk or cheeses), the treating physician should either repeat the serology to evaluate rising IgM with IgG conversion or consult with the NJDHSS Infectious and Zoonotic Diseases Program (IZDP) about confirming the case with culture or the agglutination serologic assay.

Isolation of *Brucella* species from a clinical specimen is considered a confirmed diagnosis. The New Jersey Public Health and Environmental Laboratories (PHEL) can provide confirmatory testing services for referred isolates of suspected *Brucella* spp from appropriate clinical specimens. PHEL can also facilitate serum agglutination testing for *Brucella* spp in patients with clinically suspected brucellosis and history of exposure, as specified in section 3 below.

3. Case Classification

CONFIRMED

Clinically diagnosed case, AND

Isolation of *Brucella* species from a clinical specimen, OR

Fourfold or greater rise in *Brucella* species agglutination titer between acute and convalescent-phase serum specimens obtained ≥ 2 weeks apart and tested in the same laboratory, OR

Demonstration by immunofluorescence of *Brucella* species in a clinical specimen.

PROBABLE

A clinically compatible case that is epidemiologically linked to a confirmed case, OR

A clinically compatible case that has supportive serology (i.e., *Brucella* species agglutination titer of 1:160 or greater in one or more serum specimens obtained after onset of symptoms).

POSSIBLE

Not used.

3 LABORATORY TESTING AVAILABLE

Two types of tests are primarily performed to diagnosis brucellosis: serology (ELISA or agglutination) or isolation by bacterial culture.

A. PanBio Rapid ELISA Test

- Most commercial laboratories use the PanBio rapid ELISA test, which is labeled “Research Use Only” and is not cleared or approved by the US Food and Drug Administration.
- The PanBio assay will test for *Brucella abortus* IgM and IgG.
- Because the assay reports reactivity in colorimetric (PanBio) units, this test is used for the **qualitative** detection of antibodies to brucellosis; it does not express **quantity** of titer.
- The results of PanBio ELISA assay do not meet the case definition, and reactivity should not be considered diagnostic.

B. Agglutination Assay

- The Centers for Disease Control and Prevention (CDC) recommends that serologic testing for clinically suspected brucellosis, with an exposure history, be done using the agglutination assay. PHEL can forward serum to CDC for agglutination testing for

Brucella species. IZDP at 609.588.3121 must approve submission of serum for agglutination testing to PHEL. All samples must be accompanied by a CDC DASH form, available at http://www.cdc.gov/ncidod/dvbid/misc/CDC50_34.pdf

C. Isolation

- Isolation of *Brucella* species from a clinical specimen is considered a confirmed diagnosis. PHEL can provide testing services for referred isolates of suspected *Brucella* spp from appropriate clinical specimens, with confirmatory testing performed by CDC. IZDP must approve submission of referred isolates of suspected *Brucella* spp to PHEL. All samples must be accompanied by a PHEL Lab-5 form, available at <http://www.state.nj.us/health/forms/lab-5.pdf>, and a CDC DASH form.

4 PURPOSE OF SURVEILLANCE AND REPORTING AND REPORTING REQUIREMENTS

A. Purpose of Surveillance and Reporting

- To help identify the source of infection and prevent further transmission from this source (e.g., an infected animal, a contaminated unpasteurized dairy product).
- To identify cases and clusters of human illness that may be associated with a bioterrorist event.

B. Laboratory Reporting Requirements

1. The New Jersey Administrative Code (NJAC 8:57-1.6) stipulates that laboratories **immediately report** (by telephone, confidential fax, or over the Internet using the confidential and secure Communicable Disease Reporting and Surveillance System [CDRSS]) any suspect or confirmed case of brucellosis to the local health officer having jurisdiction over the locality in which the patient lives or, if unknown, to the health officer in whose jurisdiction the healthcare provider requesting the laboratory examination is located. If this is not possible, call IZDP at 609.588.7500 during business hours or 609.392.2020 after business hours or on weekends and holidays.
2. The report shall contain, at a minimum, the reporting laboratory's name, address, and telephone number; the age, date of birth, gender, race, ethnicity, home address, and telephone number of the person tested; the date of testing; the test results; and the healthcare provider's name and address.

C. Healthcare Provider Reporting Requirements

1. NJAC 8:57-1.4 stipulates that healthcare providers **immediately report** (by telephone, confidential fax, or over the Internet using CDRSS) any suspect or confirmed case of brucellosis to the local health officer having jurisdiction over the locality in which the patient lives or, if unknown, to the health officer in whose

jurisdiction the healthcare provider requesting the laboratory examination is located. If this is not possible, call IZDP.

2. The report shall contain, at a minimum, the reporting laboratory's name, address, and telephone number; the age, date of birth, gender, race, ethnicity, home address, and telephone number of the person tested; the date of testing; the test results; and the healthcare provider's name and address.

D. Local Department of Health Reporting Requirements

NJAC 8:57-1.8 stipulates that each local health officer must report the occurrence of any case of brucellosis, as defined by the reporting criteria in section 2A above. Current requirements are that confirmed or probable cases be **immediately reported** to IZDP. A report can be filed electronically using CDRSS.

5 CASE INVESTIGATION

The most important step a local health officer can take upon learning of a suspect or confirmed case of brucellosis, or any suspected bioterrorist event, is to call IZDP immediately.

NJDHSS will direct brucellosis case investigation of New Jersey residents. If a bioterrorist event is suspected, NJDHSS in conjunction with CDC and other response authorities will work closely with local health officer(s) and provide instructions/information on how to proceed.

A. Laboratory Reports

1. If the local health department (LHD) receives the lab or provider report, the LHD should investigate the case by contacting the patient or a family member or the healthcare provider and enter the information into CDRSS as instructed below.
2. If the lab or provider report is received by NJDHSS and includes the patient's address, the report will be entered into CDRSS and not mailed to the LHD.
3. If the lab or provider report received by NJDHSS does not include the patient's address, the report will be returned to the sending laboratory or healthcare provider or they will be telephoned to obtain a complete address. Once it is received, the report will be entered into CDRSS as "PENDING."

B. Entry into CDRSS

The mandatory fields in CDRSS include: disease, last name, county, municipality, gender, race, ethnicity, case status, report status.

The following table can be used as a quick reference guide to determine which CDRSS fields need to be completed for accurate and complete reporting of brucellosis cases. The “Tab” column includes the tabs which appear along the top of the CDRSS screen. The “Required Information” column provides detailed explanations of what data should be entered.

CDRSS Screen	Required Information
Patient Info	Enter the disease name (“BRUCELLOSIS”), patient demographic information, illness onset date, and the date the case was reported to the local health department (LHD). There are no subgroups for this disease.
Addresses	Enter any alternate address (e.g., a second residence outside of the US). Use the Comments section in this screen to record any pertinent information about the alternate address. Entering an alternate address will allow other disease investigators access to the case if the alternate address falls within their jurisdiction.
Clinical Status	Enter any treatment that the patient received and record the names of the medical facilities and physician(s) involved in the patient’s care. If the patient received care from two or more hospitals, be sure that all are entered so the case can be accessed by all infection control professionals (ICPs) covering these facilities. If immunization status is known, it should also be entered here. If the patient died, date of death should be recorded under the Mortality section.
Signs/Symptoms	Check appropriate boxes for signs and symptoms and indicate their onset. Make every effort to get complete information by interviewing the physician, family members, ICP, or others who might have knowledge of the patient’s illness. Also, information regarding the resolution of signs and symptoms should be entered.
Risk Factors	Enter complete information about risk factors to facilitate study of brucellosis in New Jersey, using the approximate incubation period range (five to 60 days) for brucellosis. Ask the case-patient about consumption of raw milk or cheeses made with unpasteurized milk, contact with livestock outside North America, or contact with <i>Brucella</i> vaccine or laboratory cultures.

CDRSS Screen	Required Information
Laboratory Eval	<p>Enter appropriate lab and diagnostic tests. Select microorganism identified if a culture was performed. Record specimen type as appropriate. Antimicrobial susceptibility testing results should be documented in the Comments section. Select <i>Brucella</i> antibody if a serology test was performed. Record titer in “Value” field. NOTE: Review case definition in section 2 for a discussion on the rapid ELISA test offered by commercial laboratories that is an unverified screening test. Serologic reactivity with this assay is not expressed as a titer and would not meet case definition.</p>
Contact Tracing	<p>Confirm that the laboratory where the culture was identified exercised the proper precaution when working with the bacteria. Infectious aerosols can occur when manipulation of the isolate is done outside of a biosafety hood. Information regarding contacts with the case patient is not required for this disease.</p>
Case Comments	<p>Enter general comments (i.e., information that is not discretely captured by a specific topic screen or drop-down menu) in the Comments section. NOTE: Select pieces of information entered in the Comments section CANNOT be automatically exported when generating reports. Therefore, whenever possible, record information about the case in the fields that have been designated to capture this information; information included in these fields CAN be automatically exported when generating reports.</p>
Epidemiology	<p>Under the Other Control Measures section, indicate if the patient falls into any of the categories listed under Patient Role(s)/Function(s). Record name of and contact information for case investigators from other agencies (e.g., CDC, out-of-state health departments). Document communication between investigators in the Comments section.</p>
Case Classification Report Status	<p>Case status options are: “REPORT UNDER INVESTIGATION (RUI),” “CONFIRMED,” “PROBABLE,” “POSSIBLE,” and “NOT A CASE.”</p> <ul style="list-style-type: none"> • All cases entered by laboratories (including LabCorp electronic submissions) should be assigned a case status of “REPORT UNDER INVESTIGATION (RUI).” • Cases still under investigation by the LHD should be assigned a case status of “REPORT UNDER INVESTIGATION (RUI).”

CDRSS Screen	Required Information
	<ul style="list-style-type: none"> • Upon completion of the investigation, the LHD should assign a case status on the basis of the case definition. “CONFIRMED” “PROBABLE”, and “NOT A CASE” are the only appropriate for options for classifying a case of brucellosis (see section 2). <p>Report status options are: “Pending,” “LHD open,” “LHD review,” “LHD closed,” “Delete,” “Reopened,” “DHSS open,” “DHSS review,” and “DHSS approved.”</p> <ul style="list-style-type: none"> • Cases reported by laboratories (including LabCorp electronic submissions) should be assigned a report status of “PENDING.” • Once the LHD begins investigating a case, the report status should be changed to “LHD OPEN.” • The “LHD REVIEW” option can be used if the LHD has a person who reviews the case before it is closed (e.g., health officer or director of nursing). • Once the LHD investigation is complete and all the data are entered into CDRSS, the LHD should change the report status to “LHD CLOSED.” • “LHD CLOSED” cases will be reviewed by DHSS and be assigned one of the DHSS-specific report status categories. If additional information is needed on a particular case, the report status will be changed to “REOPENED” and the LHD will be notified by e-mail. Cases that are “DHSS APPROVED” cannot be edited by LHD staff (see section C below). <p>If a case is inappropriately entered the case should be assigned a report status of “DELETE.” A report status of “DELETE” should NOT be used if a reported case of brucellosis simply does not meet case definition. Rather, it should be assigned the appropriate case status, as described above.</p>

C. Other Reporting/Investigation Issues

1. It is not always possible to obtain all the information necessary to determine the case status of a patient. A minimum of three attempts (not necessarily to the same person, not at the same time during the day, and only one attempt through a letter/form by mail) should be made to obtain necessary information. If at this time information is not acquired, the case should be entered into CDRSS with as much information as is known, with attempts (dates and results of attempts) documented in the “COMMENTS” section and the case status changed to “NOT A CASE” and report status to “LHD CLOSED.”

2. Every effort should be made to complete the investigation within three months of opening a case. Cases that remain open for three months or more and have no investigation or update notes will be closed by NJDHSS and marked as “NOT A CASE.”
3. Once an LHD completes its investigation and assigns a report status of “LHD CLOSED,” NJDHSS will review the case, and when it is complete will change the report status to “DHSS APPROVED.” At this time, the case will be locked for editing. If additional information is received after a case has been placed in “DHSS APPROVED,” an LHD will need to contact NJDHSS to reopen the case. This should be done only if the additional information changes the case status of the report.
4. An epidemiologic investigation to identify the source of infection should be initiated by the local health officer. Specifically, focus on the period beginning about five days before onset of disease date back to approximately 12 weeks before onset for the following exposures:
 - Animal contact: Ask the patient about potential direct or indirect residential, occupational, or recreational exposure to cattle, swine, sheep and goats outside of North America.
 - Food consumption: Ask the patient about the consumption of raw milk and unpasteurized soft cheeses.
 - Travel history: Determine the date(s) and geographic area(s) outside North America visited by the patient.Include any additional comments regarding the case in the “COMMENTS” section.
5. Institution of disease control measures is an integral part of case investigation. It is the responsibility of the local health officer to understand and, if necessary, institute the control guidelines listed below in section 6.

6 CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements

None. Person-to-person transmission of brucellosis is extremely rare.

B. Protection of Contacts of a Case

There is no immunization or prophylaxis for contacts of cases. Follow drainage or secretion precautions if the case has draining lesions, followed by disinfection of surfaces contaminated by purulent discharges.

C. Managing Special Situations

1. Exposure of a Laboratory Worker

Brucellosis is one of the most common laboratory-acquired infections, mostly because aerosolization is a mechanism of transmission in this setting. Consult with IZDP at 609.588.3121 if laboratory workers may have been exposed to brucellosis. Laboratory workers exposed to *Brucella* (e.g., did not use the protection of a laminar air flow/biosafety hood) are categorized as high-risk or low-risk exposures. IZDP staff will assist in identification and evaluation of laboratory workers exposed to *Brucella*.

All *Brucella*-exposed workers shall be handled following this protocol:

1. Obtain baseline serum samples.
2. Arrange for sequential serologic testing (e.g., six, 12, and 24 weeks postexposure).
3. Arrange for weekly active surveillance for development of febrile illness or other signs and symptoms of brucellosis.
4. In addition, postexposure prophylaxis (PEP) is recommended for *Brucella*-exposed workers with **high-risk exposures**:
 - Doxycycline 100 mg twice daily and rifampin 600 mg once daily for three weeks.
 - Consider trimethoprim-sulfamethoxazole for contraindications to doxycycline.
 - Pregnant workers with high-risk exposures should consider PEP in consultation with their obstetricians.

D. Preventive Measures

1. Contaminated Food or Milk

If a patient is suspected to have been infected through the consumption of milk or other food products, the NJDHSS Food and Drug Safety Program will work with IZDP to identify the implicated food item(s) and remove it from the environment.

2. Preventive Measures/Education

To prevent future exposures, advise the following:

- Restrict consumption of milk products made from raw milk (e.g., imported cheeses).
- Workers at occupational risk (such as farmers, slaughterhouse workers, meat processors, or butchers) should know symptoms of the disease, how it is spread, 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. For more information, refer to the US Department of Agriculture, Animal and Plant Health Inspection Service (APHIS) Web site at <http://www.aphis.usda.gov/>.

- Hunters should use barrier protection (gloves or clothing) when dressing wild pigs and burying the remains.
- Animal placentas, fetuses, and/or discharges from an animal should be carefully handled and properly disposed. Contaminated areas should be properly disinfected.
- In the event domestic livestock are implicated as a source of exposure, IZDP will consult with the New Jersey Department of Agriculture to identify and control exposure to any potentially infected animals.

7 OUTBREAK SITUATIONS

If the number of reported cases in an institutional setting or jurisdiction is higher than usual for the time of year, an outbreak might be occurring. In accordance with NJAC 8:57, IZDP should be contacted immediately at 609.588.7500. This situation may warrant an investigation of clustered cases to determine a course of action to prevent further cases. In contrast to what routinely occurs at the local level, IZDP staff can perform surveillance for clusters of illness that may cross several jurisdictions and thereby be better able to assess the extent of an outbreak during its infancy.

If more than one case of brucellosis is reported or suspected in a city or town, or if an outbreak is suspected, investigate to determine the source of infection and mode of transmission. A common vehicle, such as unpasteurized milk products or infected animals, should be sought, and applicable preventive or control measures should be instituted (e.g., removing an implicated food item from the environment). A decision about culturing and testing implicated food items will be made by IZDP in consultation with the NJDHSS Food and Drug Safety Program.

NOTE: If a bioterrorist event is suspected, NJDHSS and other response authorities will work closely with local health officers and provide instructions/information on how to proceed.

Additional Information

A Brucellosis Fact Sheet is available at the NJDHSS Web site at <http://www.state.nj.us/health/cd/index.html>. Click on the “Topics A to Z” and scroll down to the subject “Brucellosis.”

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