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# *Brucellosis Backgrounder*

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## Causative agent

Brucellosis is caused by bacteria of the *Brucella* genus. Previously, this genus was considered to include *B. abortus*, *B. melitensis*, *B. ovis*, *B. suis*, *B. canis*, and *B. neotomae*. Within each species, multiple biovars, or strains, were identified. *B. melitensis* was subdivided into 3 biovars, *B. abortus* into 7 biovars, and *B. suis* into 5 biovars. However, DNA hybridization analysis of *Brucella* has led to the proposal that the genus comprises only one organism, *Brucella melitensis*, and that the previously described organisms and their strains are actually biovarieties of *B. melitensis*. The conventional names are still frequently used in current literature, and will be used in this text.

Brucellosis is also known as undulant fever, contagious abortion, Malta fever, or Bangs disease. *Brucella* is a Gram-negative coccobacillus.

## Natural distribution

Brucellosis was first recognized as disease affecting humans on the island of Malta in the 19<sup>th</sup> and early 20<sup>th</sup> centuries. *Brucella* organisms can be found worldwide, but brucellosis is more common in countries having poorly standardized or ineffective animal and public health programs. Biovarieties vary with respect to geographic region. *B. abortus*, *B. ovis*, and *B. canis* are widespread. *B. melitensis* and *B. suis* are irregularly distributed. *B. neotomae* infection of humans or domestic animals has not been reported, and its distribution appears to be limited. In the United States, less than 100 cases of brucellosis in humans are reported each year.

Most laboratory-acquired brucellosis cases are caused by *B. melitensis*, but infection with other strains has also been reported. Most exposures are caused by unsafe laboratory practices.

Domestic and wild animal reservoirs may serve as sources of infection of livestock and humans. Free-ranging bison in Yellowstone National Park and Grand Teton National Park have had positive results of tests for *B. abortus*. More than 50% of the bison populations of Yellowstone National Park are *Brucella*-positive, and present the risk of reintroducing *Brucella abortus* into neighboring cattle herds via migrating animals. Elk populations in the greater Yellowstone area are also infected.

Endemic brucellosis can cause considerable economic losses due to abortion and reduced fertility. In 1954, the United States established the National Brucellosis Eradication Program with the goal of eliminating *Brucella abortus* from domestic cattle and bison herds. Individual states are considered free of brucellosis when no cattle or bison are found to be infected for 12 consecutive months, using an active surveillance program. As of January 2007, only two states (Idaho and Texas) are not free of brucellosis; the two states are designated Class A, with herd infection rates of less than 0.25%.

## Transmission

Brucellosis is generally introduced into herds by infected animals. The organism localizes in the reproductive organs and/or udder. Infected animals may shed high numbers of bacteria in milk, aborted fetuses, vaginal discharges, placental membranes, and birth fluids. Susceptible animals can become infected via ingestion of pasture, feed, or water contaminated with these excretions. Artificial insemination with infected semen can result in infection of the recipient cow. In swine, natural breeding is an important method of transmitting the disease. Horses generally acquire the infection through contact with infected cattle or swine.

Dogs usually become infected by ingesting contaminated fetuses, placentas, or milk. Dog-to-dog transmission is rare.

Most human infections result from physical contact with infected animals or consumption of contaminated, uncooked animal products. Travelers have become infected after eating unpasteurized

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dairy products. Infection can occur via inhalation, direct contact with contaminated animals or their excretions, ingestion, or contact via skin abrasions or mucous membranes. Veterinarians, farmers, slaughterhouse workers, meat inspectors, laboratory technicians, and animal handlers are at higher risk of exposure to *Brucella* organisms. Hunters may become infected during the cleaning of carcasses. Rarely, transmission has occurred via organ transplantation, sexual contact, breastfeeding, or transplacentally. Pus, blood, bone marrow, synovial fluid, cerebrospinal fluid, urine, and genital exudates from infected humans may be infective. Once in the body, the organism localizes in the lungs, spleen, liver, bone marrow, joints, and central nervous system (spinal cord and brain). Because *Brucella* species are highly infectious via aerosols in laboratory environments, biosafety level 3 precautions are recommended. Humans can be infected by aerosol doses of 10 to 500 organisms.

The incubation period is usually two to four weeks, but can range from less than one week to several months.

Although *B. canis* has been transmitted to humans, human infection by infected dogs is uncommon. Veterinarians may be at higher risk of infection because of increased contact with infected excretions and body fluids. Immunocompromised humans are more susceptible to the disease.

Because of the potential for human infection and the rapidity of spread of the organisms, the World Organisation for Animal Health (OIE) has classified brucellosis as a listed animal disease that requires notification of OIE. In recognition of the potential for use in bioterrorism, *Brucella* species are classified as Category B agents.

### Clinical Signs

The most common signs of infection in cattle, bison, and yaks are abortion and epididymitis. Affected animals exhibit reduced milk production, weight loss, abortion, calf weakness, retained placentas, infertility, and lameness. Abortions are most common between the 5<sup>th</sup> and 7<sup>th</sup> months of gestation. In bulls, primary clinical signs are enlarged testes, decreased libido, infertility, seminal vesiculitis, and ampullitis. The most common clinical sign of infection in elk is abortion; retained placentas are less common in this species.

Clinical signs observed in swine and goats are similar to those observed in cattle. Swine may also develop bone, joint, and tendon sheath infections. Sheep appear to be more resistant to infection, and abortion is less common. *B. ovis* produces a clinical syndrome called ram epididymitis. The infection may result in testicular atrophy and sterility. Camelids can be infected by *Brucella*, resulting in abortion and neonatal mortality.

Infection of the supraspinatus bursa, also known as fistulous withers, is the most common manifestation of brucellosis in horses. The withers are swollen and painful, and purulent discharge may occur. Osteomyelitis (bone infection) of the spinous processes of the thoracic vertebrae may occur, requiring removal of infected bone and tissue. Infection of the supraatlantal bursa, also called poll evil, is a less common syndrome of brucellosis. *Brucella* has also been reported as a cause of recurrent uveitis, abortion, and orchitis (inflammation of the testes), but horses appear to be more resistant to infection than cattle, swine, and goats.

Cats are resistant to *Brucella*. Dogs infected with *B. canis* exhibit prolonged bacteremia (bacteria circulating in the bloodstream), embryonic death, abortions, prostatitis, epididymitis, lymphadenitis (inflammation of the lymph nodes), and inflammation of the spleen.

Clinical signs of acute (less than eight weeks from onset) human brucellosis are generally nonspecific and flu-like, and include fever, headache, depression, malaise, chills, night sweats, sexual impotence, constipation, fatigue, and joint pain. Patients are frequently bacteremic during the early phases of the disease, facilitating detection by bacteriologic culture of blood. The undulant phase of the disease develops within one year of onset, and symptoms include recurrent fever, arthritis, and inflammation of the epididymis and/or testes in males. Hepatitis (inflammation of the liver), enlarged lymph nodes, eye problems, breast abscesses, pneumonitis (inflammation of the lung), clots in deep veins, endocarditis (infection or inflammation of the heart valves), or meningitis (inflammation of the surface of the brain and/or spinal cord) may also develop. Bone and joint infections occur in 20 to 60% of human brucellosis cases, and infection and inflammation develops in the male reproductive organs in 2 to 20% of cases.

Humans infected for one year or more are considered chronic cases; clinical signs include chronic fatigue syndrome, depression, and arthritis.

### Diagnosis

Bacteriologic culture of blood or bone marrow samples may reveal the presence of *Brucella* organisms, especially during the acute phase of disease. Demonstration of serologic conversion (four-fold rise in antibody titer) from samples collected two to three weeks apart is diagnostic for brucellosis.

Tests accepted by the USDA-APHIS for brucellosis detection and/or confirmation for cattle and bison include the concentration immunoassay technology (CITE) test, complement fixation (CF) test, enzyme-linked immunosorbent assay (ELISA), and fluorescence polarization (FP) assay. *Brucella* infection of sheep can be diagnosed by microscopic observation of organisms in semen or by ELISA, RBT, CF test, and FP assay.

Brucellosis testing in swine herds can be performed using the buffered plate agglutination test (BPAT), rose bengal test (RBT), FP assay, ELISA, and competitive ELISA (CELISA). The allergic skin test can be used to identify infected herds. Serologic testing is not reliable for diagnosis of brucellosis in individual pigs, but is effective for herd testing.

### Treatment

**Brucellosis is a reportable disease.** State or Federal animal health officials should be notified immediately if brucellosis is suspected.

There is no effective treatment for brucellosis in infected animals. Clinical signs may resolve with time, but the animal generally remains infected and a potential source of infection for other animals and humans. Livestock that are confirmed to be infected are usually quarantined until sent to slaughter.

Supportive treatment is often instituted in equine cases. Surgical intervention may be necessary for animals that develop bone or joint infection.

Human brucellosis cases are treated with doxycycline and rifampin for a minimum of three to six weeks. Several months may be required for recovery. Relapses occur in approximately 5% of cases. Veterinarians or other animal healthcare workers that are inadvertently inoculated with the Rev-1 *B. melitensis*, S19 *B. abortus*, or RB51 *B. abortus* strain vaccines should seek medical attention, and postexposure treatment with doxycycline with or without the addition of rifampin is recommended.

### Morbidity and Mortality

Animal deaths from brucellosis, other than aborted fetuses, are rare. The human case fatality rate (the number of affected humans that die from the disease) is less than 5%.

### Prevention and Control

To reduce exposure, appropriate disposal methods should be instituted for all placentas, birth fluids, fetal membranes, and aborted fetuses. Those handling fetal membranes, fluids, placentas, and aborted fetuses should use appropriate hygienic practices. Access to potentially infected animals should be restricted, and newly acquired animals should be quarantined. Consumption of unpasteurized (raw) milk and milk products should be avoided, unless the milk products have been aged for more than 60 days and have low moisture content. Masks, gloves, and protective eyewear should be worn when handling infected animals.

Dairy surveillance programs include bulk tank sampling two to four times per year. Herds that are not used for milk production are monitored by blood tests of animals at market or slaughter. Some states require blood testing of bison and cattle when ownership is changed.

*Brucella* species are susceptible to heat, sunlight, and commonly used disinfectants. *Brucella* organisms may survive for up to six weeks in dust and up to ten weeks in water and soil.

Currently available vaccines are approximately 65% effective. Three vaccines have been manufactured for prevention of *Brucella abortus* infection in livestock. The first vaccine produced used the S19 strain. Although S19 is an attenuated strain of *Brucella*, it does retain a mild degree of virulence and is capable of inducing disease.

The Rev-1 *B. melitensis* vaccine is similar to the strain 19 vaccine, but is used more commonly in small ruminants. The vaccine is administered to three- to six-month-old females or in much lower doses to older females. This vaccine is not currently licensed in the United States. [

In 1996, the USDA approved the use of the strain RB51 vaccine in place of S19. The RB51 strain of *B. abortus* is a genetically stable mutant that lacks the polysaccharide O-side chain. As a result, the vaccine is less virulent and abortigenic than the strain S19 vaccine, but equally capable of producing an effective immune reaction. Unlike the strain S19, the RB51 vaccine does not induce production of antibodies that interfere with diagnostic testing. The vaccine must be administered by an accredited veterinarian or animal health official. Calves should be vaccinated between four and 12 months of age. Vaccination of animals more than 12 months old should only be performed in high risk areas. Following vaccination, animals are tattooed and a metal ear tag is placed. Field safety trials of RB51 vaccine use in bison are currently underway.

A *B. suis* strain 2 vaccine has been developed and used to vaccinate swine in the People's Republic of China, but further studies are necessary before its use is approved by the USDA. The Rev-1 and RB51 strain vaccines have been shown to be effective, but have not yet gained general acceptance and approval for use in swine.

There is no vaccine approved for use in horses. The S19 vaccine has reportedly been used for horses, but efficacy data is lacking and death may result from its administration.

Control measures for ram epididymitis include elimination of clinically affected rams and seropositive rams in addition to separation of young rams from older rams. In dog kennels, serologic monitoring and elimination of seropositive animals is important. Owners of dogs with brucellosis should be thoroughly informed of the risks of zoonotic disease.