Bovine Brucellosis: *Brucella abortus*

Undulant Fever,
Contagious Abortion,
Bang's Disease

Last Updated: July 2009

the Center for Food Security & Public Health
IOWA STATE UNIVERSITY®
College of Veterinary Medicine
Iowa State University
Ames, Iowa 50011
Phone: 515.294.7189
Fax: 515.294.8259
cfsph@iastate.edu
www.cfsph.iastate.edu

INSTITUTE FOR INTERNATIONAL COOPERATION IN ANIMAL BIOLOGICS
Iowa State University
College of Veterinary Medicine
www.cfsph.iastate.edu/IICAB/

Importance

Bovine brucellosis, caused by the bacterium *Brucella abortus*, is an economically important cause of abortions in cattle. *B. abortus* also affects other species including bison, buffalo and elk; some species are maintenance hosts for this organism. Infections in wildlife can hinder eradication efforts in cattle. In addition, *B. abortus* is a human pathogen. In humans, brucellosis can be a serious, debilitating and sometimes chronic disease that may affect a variety of organs. Most cases are the result of occupational exposure to infected animals, but infections can also occur from ingesting contaminated dairy products. In addition, *B. abortus* could be used in a bioterrorist attack.

Etiology

In cattle, bison and buffalo, brucellosis is mainly caused by *Brucella abortus*, a Gram-negative coccobacillus or short rod. This organism is a facultative intracellular pathogen. Up to nine *B. abortus* biovars (1-9) have been reported, but some of these biovars differ only slightly and their status is unresolved. Other *Brucella* species uncommonly associated with disease in cattle include *Brucella melitensis* and *B. suis*. (For information on *B. suis* or *B. melitensis*, see the factsheets titled "Porcine Brucellosis" and "Ovine and Caprine Brucellosis," respectively.)

Genetic and immunological evidence suggests that all members of the genus *Brucella* are closely related, and some microbiologists have proposed that this genus be reclassified into a single species (*B. melitensis*), which contains many biovars. This proposal is controversial, and both taxonomic systems are currently in use. The multiple species nomenclature is used in this factsheet.

Species Affected

Most species of *Brucella* are primarily associated with certain hosts; however, infections can also occur in other species, particularly when they are kept in close contact. Maintenance hosts for *Brucella abortus* include cattle, bison (*Bison* spp.) water buffalo (*Bubalus bubalus*), African buffalo (*Syncerus caffer*), elk and camels. A feral pig population has recently been reported to maintain *B. abortus*. A variety of other species can become "spill-over" hosts where this organism is enzootic. *B. abortus* has been reported in horses, sheep, Rocky Mountain bighorn sheep, goats, chamois, pigs, raccoons, opossums, dogs, coyotes, foxes, wolves and other species. Moose and llamas can be infected experimentally.

Geographic Distribution

B. abortus is found worldwide in cattle-raising regions, except in Japan, Canada, some European countries, Australia, New Zealand and Israel, where it has been eradicated. Eradication from domesticated herds is nearly complete in the U.S. *B. abortus* can be found in wildlife hosts in some regions, including the Greater Yellowstone Area of North America.

Transmission

In animals, *B. abortus* is usually transmitted by contact with the placenta, fetus, fetal fluids and vaginal discharges from infected animals. Animals are infectious after either abortion or full-term parturition. *B. abortus* may also be found in the milk, urine, semen, feces and hygroma fluids. Shedding in milk can be prolonged or lifelong, and may be intermittent. Many infected cattle become chronic carriers.

Infection usually occurs by ingestion and through mucous membranes, but *B. abortus* can be transmitted through broken skin. Although the mammary gland is usually colonized during the course of an infection, it can also be infected by direct contact, with subsequent shedding of the organisms in the milk. *In utero* infections also occur. Venereal transmission seems to be uncommon. Transmission by artificial insemination is reported to occur when contaminated semen is deposited in the uterus but not in the midcervix. *B. abortus* can be spread on fomites including feed and water. In conditions of high humidity, low temperatures, and no sunlight, these organisms can remain viable for several months in water, aborted fetuses, manure, wool, hay, equipment and clothes. *Brucella* species can withstand drying, particularly

© 2007

when organic material is present and can survive in dust and soil. Survival is longer when the temperature is low, particularly when it is below freezing.

Other species can be infected with *B. abortus* after contact with infected cattle or other maintenance hosts. Carnivores do not seem to be a significant source of infection for other animals. Dogs and coyotes can be infected with *B. abortus*, shed bacteria in reproductive discharges, and can infect cattle if these species are kept in close confinement under experimental conditions. However, no confirmed cases of transmission from dogs to cattle have been reported under natural conditions, and there is no epidemiological evidence that carnivores act as a source of infection for ruminants in *B. abortus* eradication programs. Experimentally infected wolves excrete few organisms in the feces, and the number of organisms is much lower than the reported infective dose for cattle.

Humans usually become infected by ingesting organisms (including contaminated, unpasteurized dairy products) or by the contamination of mucous membranes and abraded skin.

Incubation Period

In cattle, abortions and stillbirths usually occur two weeks to five months after infection. Reproductive losses typically occur during the second half of gestation; thus, the incubation period is longer when animals are infected early in gestation.

Clinical Signs

In cattle, *B. abortus* causes abortions and stillbirths; abortions usually occur during the second half of gestation. Some calves are born alive but weak, and may die soon after birth. The placenta may be retained and secondary metritis can occur. Lactation may be decreased. After the first abortion, subsequent pregnancies are generally normal; however, cows may shed the organism in milk and uterine discharges. Epididymitis, seminal vesiculitis, orchitis or testicular abscesses are sometimes seen in bulls. Infertility occurs occasionally in both sexes, due to metritis or orchitis/epididymitis. Hygromas, particularly on the leg joints, are a common symptom in some tropical countries. Arthritis can develop in some long-term infections. Systemic signs do not usually occur in uncomplicated infections, and deaths are rare except in the fetus or newborn. Infections in nonpregnant females are usually asymptomatic.

In camels, bison, water buffalo, bighorn sheep and other ruminants, the symptoms are similar to cattle. Abortions have also been reported in experimentally infected llamas. Other herbivores may develop more serious disease. Moose die rapidly in experimental infections. Two bighorn sheep rams with no apparent disease other than testicular lesions also died inexplicably, giving rise to speculation that *B. abortus* infections might sometimes be lethal in this species.

Symptomatic infections have been reported in some species of carnivores. Abortions, epididymitis, polyarthritis and other symptoms occur in some *B. abortus*-infected dogs. Experimentally infected wolves remained asymptomatic, although the organism could be recovered from lymphoreticular tissues for at least one year. Infected coyotes and foxes are also reported to be asymptomatic.

In horses, *B. abortus* can cause inflammation of the supraspinous or supra-atlantal bursa; these syndromes are known, respectively, as fistulous withers and poll evil. The bursal sac becomes distended by a clear, viscous, straw-colored exudate and develops a thickened wall. It can rupture, leading to secondary inflammation. In chronic cases, nearby ligaments and the dorsal vertebral spines may become necrotic. *Brucella*-associated abortions are rare in horses

Post Mortem Lesions

Click to view images

At necropsy, granulomatous inflammatory lesions may be present in the reproductive tract, udder, supramammary lymph nodes, other lymphoid tissues, and sometimes in the joints and synovial membranes.

Mild to severe endometritis may be seen after an abortion. The placenta is usually thickened and edematous, and may have exudate on its surface. The intercotyledonary region is typically leathery, with a wet appearance and focal thickening. The regional lymph nodes can be enlarged, and the mammary gland may contain lesions. Some aborted fetuses appear normal; others are autolyzed or have variable amounts of subcutaneous edema and bloodstained fluid in the body cavities. The liver may be enlarged and discolored, and the lungs may exhibit fibrous pleuritis and pneumonia.

In bulls, one or both sacs of the scrotum may be swollen due to orchitis, epididymitis or abscesses. The tunica vaginalis may be thickened and fibrous, and adhesions may be present. Hygromas may be found at slaughter in both sexes on the knees, stifles, hock, angle of the haunch, and between the nuchal ligament and the primary thoracic spines.

These lesions are not pathognomonic for brucellosis.

Morbidity and Mortality

In previously unexposed and unvaccinated cattle, *B. abortus* spreads rapidly and abortion storms are common. The abortion rate varies from 30% to 80%. In herds where this organism has become endemic, only sporadic symptoms occur and cows may abort their first pregnancies. Abortions are less common in water buffalo cows than cattle. Genetic resistance to brucellosis has been reported in both cattle and water buffalo. Deaths are rare in adult animals of most species; however, *B. abortus* can be lethal in experimentally infected moose, and possibly in bighorn sheep.

© 2007

Diagnosis

Clinical

Brucellosis should be considered in all abortions, particularly when there are multiple late-term abortions in the herd.

Differential diagnosis

Other diseases causing abortion or epididymitis and orchitis should be considered. In cattle, the differential diagnosis includes trichomoniasis, vibriosis, leptospirosis, listeriosis, infectious bovine rhinotracheitis and various mycoses.

Laboratory tests

Microscopic examination of smears stained with the Stamp's modification of the Ziehl-Neelsen method can be useful for a presumptive diagnosis, particularly if the direct examination is supported by serology. *Brucell*a species are not truly acid-fast, but they are resistant to decolorization by weak acids, and stain red against a blue background. Brucellae are coccobacilli or short rods, usually arranged singly but sometimes in pairs or small groups. This test is not definitive. Other organisms such as *Chlamydophila abortus* and *Coxiella burnetii* can resemble *Brucella*. Immunostaining is sometimes used to identify *Brucella* in smears.

Serology can be used for a presumptive diagnosis of brucellosis, or to screen herds. Serological tests used to test individual cattle and herds include the buffered *Brucella* antigen tests (rose bengal test and buffered plate agglutination test), complement fixation, indirect or competitive enzyme-linked immunosorbent assays (ELISAs) or the fluorescence polarization assay. Other serological tests include rivanol precipitation, acidified antigen procedures and the serum agglutination test (tube or microtiter test). Supplemental tests such as complement fixation or rivanol precipitation are often used to clarify the results from plate or card agglutination tests. ELISAs or the *Brucella* milk ring test (BRT) can be used to screen herds by detecting antibodies in milk. In vaccinated cattle, the native hapten -based gel precipitation tests (gel diffusion or radial immunodiffusion tests) are sometimes used to distinguish vaccination from infection.

A brucellin allergic skin test can be used to test unvaccinated cattle for *B. abortus*. This test is performed by injecting the allergen intradermally into the caudal fold, the skin of the flank, or the side of the neck.

A definitive diagnosis can be made if *B. abortus* is cultured from an animal. *Brucella* spp. can be isolated on a variety of plain media, or selective media such as Farrell's medium or Thayer-Martin's modified medium. Enrichment techniques can also be used. *Brucella* colonies usually become visible after two days growth. After four days of incubation, the colonies are round and approximately 1-2 mm in diameter with smooth margins. When the plates are viewed in daylight through a transparent medium, the colonies are translucent and a pale honey color. From above, they are convex and pearly white. Smooth (S) *Brucella* cultures can dissociate to rough (R) forms. These colonies are much less transparent and become more granular and dull. In crystal violet staining, rough colonies stain red and smooth colonies stain pale yellow. *B. abortus* can be identified to the species and biovar level by phage typing and cultural, biochemical and serological characteristics. Genetic techniques can also be used for biotyping. The vaccine strains (*B. abortus* strains S19 and RB51) can be distinguished from field strains by their growth characteristics and sensitivity to antibiotics and other additives.

Animal inoculation is rarely used to isolate *B. abortus*, but may be necessary if other techniques fail. Guinea pigs or mice can be used.

Polymerase chain reaction (PCR) techniques and other genetic techniques (restriction fragment length polymorphism or Southern blotting) are available in some laboratories.

Similar tests are used to diagnose *B. abortus* infections in species other than cattle, but each test must be validated in that species.

Samples to Collect

***Brucella abortus* is highly infectious to humans; samples should be collected and handled with all appropriate precautions.**

A variety of samples can be collected for culture and microscopic examination. Milk samples and vaginal swabs are particularly useful for diagnosis in live cows. Milk samples for culture should contain milk from all four quarters. In addition, *B. abortus* can often be isolated from the secretions of nonlactating udders. This organism can also be cultured from aborted fetuses (stomach contents, spleen and lung) or the placenta. The spleen, mammary and genital lymph nodes, udder and late pregnant or early post-parturient uterus are the most reliable samples to collect at necropsy. *B. abortus* can also be cultured from semen, the testis or epididymis, and arthritis or hygroma fluids.

Serum samples and milk samples can be collected for serology.

Recommended actions if brucellosis is suspected

Notification of authorities

Brucellosis caused by *B. abortus* is a notifiable disease in the U.S. All cases should be reported immediately to state or federal authorities.

Federal: Area Veterinarians in Charge (AVIC):

www.aphis.usda.gov/animal_health/area_offices/

State Veterinarians:

www.usaha.org/Portals/6/StateAnimalHealthOfficials.pdf

© 2007

Control

Bovine brucellosis is usually introduced into a herd in an infected animal, but it can also enter in semen from infected bulls and on fomites. In endemic areas, vaccinated calves or nonpregnant heifers are the best herd additions in uninfected herds. Any pregnant or fresh cows should come from brucellosis-free areas or herds, and should be seronegative. Herd additions should be isolated for approximately a month and retested for *B. abortus* before they are added to the herd. Selective breeding for disease-resistant genotypes may also be feasible as a control strategy in water buffalo.

B. abortus can be eradicated from a herd by test and removal procedures, or by depopulation. Many countries, including the U.S., have eradication programs for this organism. Eradication can be accomplished by quarantine of infected herds, vaccination, test-and-slaughter techniques, various forms of surveillance and tracebacks. Any area exposed to infected animals and their discharges should be thoroughly cleaned and disinfected. Infections in other species are generally prevented by controlling *B. abortus* in its maintenance hosts.

Two *B. abortus* vaccines, Strain 19 and RB51, can be used to control this disease in endemic areas, or used as part of an eradication program. Routine vaccination is often done in calves to minimize the production of persistent antibodies that can interfere with serological tests. In the U.S., RB51 has largely replaced Strain 19. RB51 is less likely to induce persistent antibodies, and it is safer for humans. Both vaccines are live and can cause abortions in pregnant cattle and adverse effects in humans.

B. abortus can become endemic in some wild populations, and may occasionally be transmitted from these animals to domesticated ruminants. In the U.S., this organism is endemic in some wild bison and elk herds in the Greater Yellowstone Area. It has recently been found in a feral swine herd in South Carolina. Various control methods are being directed at these herds.

Brucella species are readily killed by most commonly available disinfectants including hypochlorite solutions, 70% ethanol, isopropanol, iodophores, phenolic disinfectants, formaldehyde, glutaraldehyde and xylene; however, organic matter and low temperatures decrease the efficacy of disinfectants. Disinfectants reported to destroy *Brucella* on contaminated surfaces include 2.5% sodium hypochlorite, quaternary ammonium compounds, 2-3% caustic soda, 20% freshly slaked lime suspension, or 2% formaldehyde solution (all tested for one hour). Ethanol, isopropanol, iodophores, substituted phenols or diluted hypochlorite solutions can be used on contaminated skin; alkyl quaternary ammonium compounds are not recommended for this purpose. Autoclaving (moist heat of 121°C for at least 15 minutes) can be used to destroy *Brucella* species on contaminated equipment. These organisms can also be inactivated by dry heat [320-338° F (160-170°C) for at least 1 hour]. Boiling for 10 minutes is usually effective for liquids. Xylene (1ml/liter) and calcium cyanamide (20 kg/m3) are reported to decontaminate liquid manure after 2 to 4 weeks. *Brucella* species can also be inactivated by gamma irradiation (e.g. in colostrum) and pasteurization. Their persistence in unpasteurized cheese is influenced by the type of fermentation and ripening time. The fermentation time necessary to ensure safety in ripened, fermented cheeses in unknown, but is estimated to be approximately three months. *Brucella* survives for very short periods in meat, unless it is frozen; in frozen meat, survival times of years have been reported.

Public Health

B. abortus is pathogenic for humans. Occupational exposure is seen in laboratory workers, farmers, veterinarians and others who contact infected animals or tissues. Brucellosis is one of the most easily acquired laboratory infections. People who do not work with animals or tissues usually become infected by ingesting unpasteurized dairy products. The Strain 19 *B. abortus* vaccine is also pathogenic for humans and must be handled with caution to avoid accidental injection or contamination of mucous membranes or abraded skin. Adverse events are also reported with the RB51 vaccine, although it appears to be safer than Strain 19.

Asymptomatic infections can occur in humans. In symptomatic cases, the disease is extremely variable and the clinical signs may appear insidiously or abruptly. Typically, brucellosis begins as an acute febrile illness with nonspecific flu-like signs such as fever, headache, malaise, back pain, myalgia and generalized aches. Drenching sweats can occur, particularly at night. Some patients recover spontaneously, while others develop persistent symptoms that typically wax and wane. Occasionally seen complications include arthritis, spondylitis, chronic fatigue, and epididymoorchitis. Neurologic signs (including personality changes, meningitis, uveitis and optic neuritis), anemia, internal abscesses, nephritis, endocarditis and dermatitis can also occur. Other organs and tissues can also be affected, resulting in a wide variety of syndromes. Treatment is with antibiotics; however, relapses can be seen months after the initial symptoms, even in successfully treated cases. The mortality rate is low; in untreated persons, estimates of the case fatality rate vary from less than 2% to 5%. Deaths are usually caused by endocarditis or meningitis.

Internet Resources

Centers for Disease Control and Prevention (CDC). Brucellosis. http://www.cdc.gov/brucellosis/

Food and Agriculture Organization of the United Nations. Manual for the Recognition of Exotic Diseases of Livestock, A Reference Guide for Animal Health Staff. http://www.spc.int/rahs/**

© 2007

Public Health Agency of Canada. Material Safety Data Sheets
http://www.phac-aspc.gc.ca/msds-ftss/index.html

The Merck Manual
http://www.merck.com/pubs/mmanual/

The Merck Veterinary Manual
http://www.merckvetmanual.com/mvm/index.jsp

World Organization for Animal Health (OIE)
http://www.oie.int

OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals
http://www.oie.int/international-standard-setting/terrestrial-manual/access-online/

References

Alton GG, Forsyth JRL. *Brucella* [online]. In Baron S, editor. Medical microbiology. 4th ed. New York: Churchill Livingstone; 1996. Available at: http://www.gsbs.utmb.edu/microbook/ch028.htm.** Accessed 4 Jun 2007.

Borriello G, Capparelli R, Bianco M, Fenizia D, Alfano F, Capuano F, Ercolini D, Parisi A, Roperto S, Iannelli D. Genetic resistance to *Brucella abortus* in the water buffalo (*Bubalus bubalis*). Infect Immun. 2006;74:2115-20.

Centers for Disease Control and Prevention [CDC]. Brucellosis (*Brucella melitensis, abortus, suis*, and *canis*). CDC; 2005 Oct. Available at: http://www.cdc.gov/ncidod/dbmd/diseaseinfo/brucellosis_t.htm.** Accessed 4 Jun 2007.

Cutler SJ, Whatmore AM, Commander NJ. Brucellosis--new aspects of an old disease. J Appl Microbiol. 2005;98:1270-1281.

Forbes LB, Tessaro SV, Lees W. Experimental studies on *Brucella abortus* in moose (*Alces alces*). J Wildl Dis. 1996;32:94-104.

Garner G, Saville P, Fediaevsky A. Manual for the recognition of exotic diseases of livestock: A reference guide for animal health staff [online]. Food and Agriculture Organization of the United Nations [FAO]; 2003. Brucellosis (bovine). Available at: http://www.spc.int/rahs/Manual/BOVINE/BRUCELLOSISE.HTM.** Accessed 4 Jun 2007.

Gidlewski T, Cheville NF, Rhyan JC, Miller LD, Gilsdorf MJ. Experimental *Brucella abortus* induced abortion in a llama: pathologic effects. Vet Pathol. 2000;37:77-82.

Godfroid J, Cloeckaert A, Liautard JP, Kohler S, Fretin D, Walravens K, Garin-Bastuji B, Letesson JJ. From the discovery of the Malta fever's agent to the discovery of a marine mammal reservoir, brucellosis has continuously been a re-emerging zoonosis. Vet Res. 2005;36:313-326.

Godfroid J. Brucellosis in wildlife. Rev Sci Tech. 2002;21:277-286.

Herenda D, Chambers PG, Ettriqui A, Seneviratna P, da Silva TJP. Manual on meat inspection for developing countries [online]. FAO animal production and health paper 119. Publishing and Multimedia Service, Information Division, FAO; 1994 (reprinted 2000). Brucellosis. Available at: http://www.fao.org/docrep/003/t0756e/T0756E03.htm#ch3.3.7. Accessed 4 Jun 2007.

Kahn CM, Line S, editors. The Merck veterinary manual [online]. Whitehouse Station, NJ: Merck and Co; 2003. Brucellosis in cattle (Contagious abortion, Bang's disease). Available at: http://www.merckvetmanual.com/mvm/index.jsp?cfile=htm/bc/110502.htm. Accessed 4 Jun 2007.

Kahn CM, Line S, editors. The Merck veterinary manual [online]. Whitehouse Station, NJ: Merck and Co; 2003. Brucellosis in horses. Available at: http://www.merckvetmanual.com/mvm/index.jsp?cfile=htm/bc/110504.htm. Accessed 4 Jun 2007.

Kahn CM, Line S, editors. The Merck veterinary manual [online]. Whitehouse Station, NJ: Merck and Co; 2003. Brucellosis in large animals: Introduction. Available at: http://www.merckvetmanual.com/mvm/index.jsp?cfile=htm/bc/110500.htm. Accessed 4 Jun 2007.

Kortepeter M, Christopher G, Cieslak T, Culpepper R, Darling R, Pavlin J, Rowe J, McKee K, Eitzen E, editors. Medical management of biological casualties handbook [online]. 4th ed. United States Department of Defense; 2001. Brucellosis. Available at: http://www.vnh.org/BIOCASU/7.html.* Accessed 16 Dec 2002.

Kreeger TJ, Cook WE, Edwards WH, Cornish T. Brucellosis in captive Rocky Mountain bighorn sheep (*Ovis canadensis*) caused by *Brucella abortus* biovar 4. J Wildl Dis. 2004;40:311-315.

Nicoletti P. Diagnosis and treatment of canine brucellosis. In Kirk RW, Bonagura JD, editors. Current veterinary therapy X. Small animal practice. Philadelphia, PA: WB Saunders; 1989. p. 1317-1320.

Public Health Agency of Canada. Material Safety Data Sheet – *Brucella* spp. Office of Laboratory Security; 2000 Jan. Available at: http://www.hc-sc.gc.ca/pphb-dgspsp/msds-ftss/msds23e.html. Accessed 4 Jun 2007.

Sauret JM, Vilissova N. Human brucellosis. J Am Board Fam Pract. 2002;15:401-406.

Schnurrenberger PR, Brown RR, Hill EP, Scanlan CM, Altiere JA, Wykoff JT. *Brucella abortus* in wildlife on selected cattle farms in Alabama. J Wildl Dis. 1985;21:132-136.

Stoffregen WC, Olsen SC, Jack Wheeler C, Bricker BJ, Palmer MV, Jensen AE, Halling SM, Alt DP. Diagnostic characterization of a feral swine herd enzootically infected with *Brucella*. J Vet Diagn Invest. 2007;19:227-237.

Tessaro SV, Forbes LB. Experimental *Brucella abortus* infection in wolves. J Wildl Dis. 2004;40:60-5.

Tibary A, Fite C, Anouassi A, Sghiri A. Infectious causes of reproductive loss in camelids. Theriogenology. 2006;66:633-647.

Whatmore AM, Perrett LL, MacMillan AP. Characterisation of the genetic diversity of *Brucella* by multilocus sequencing. BMC Microbiol 2007;7:34.

World Organization for Animal Health (OIE). Manual of diagnostic tests and vaccines 2004 [online]. Paris: OIE; 2004. Bovine brucellosis. Available at: http://www.oie.int/eng/normes/mmanual/A_00052.htm.** Accessed 4 Jun 2007.

*Link defunct as of 2007

** Link defunct as of 2012

© 2007