Brucellosis: *Brucella canis*

Contagious Abortion, Undulant Fever

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Importance

Brucellosis is a zoonotic bacterial disease caused by several species in the genus *Brucella*. *Brucella canis* is an important cause of reproductive failure in dogs, especially in kennels. Infections can result in abortions and stillbirths in bitches, and epididymitis, prostatitis, orchitis and sperm abnormalities in males. Although spayed or neutered dogs do not have reproductive signs, they occasionally develop other conditions such as ocular disease and discospondylitis. *B. canis* may persist in an animal even after antibiotic treatment. In kennels, infected dogs are often euthanized to prevent them from infecting other dogs or people. Canine brucellosis is sometimes difficult to diagnose with the currently available tests.

The importance of *B. canis* as a cause of human illness is still unclear. Few clinical cases have been reported in people, and most have been mild. However, human infections with this organism may be underdiagnosed, as the symptoms are nonspecific, diagnostic suspicion among physicians is low, and obtaining a definitive diagnosis may be difficult.

Etiology

In dogs, brucellosis is mainly caused by *Brucella canis*, a Gram-negative coccobacillus in the family Brucellaceae (class Alphaproteobacteria). Other *Brucella* species occasionally associated with disease in dogs include *B. abortus*, *B. melitensis* and *B. suis*. More information on the latter organisms is available in the respective factsheets at http://www.cfsph.iastate.edu/DiseaseInfo/factsheets.htm.

Taxonomy note: At one time, the genus *Brucella* was reclassified into a single species, *B. melitensis*, based on the genetic and immunological evidence that all members of this genus are closely related. Under this system, the various species of *Brucella* were considered to be biovars. This proposal was controversial, and has fallen out of favor for practical reasons.

Species Affected

Dogs are thought to be the only significant hosts for *B. canis* among domesticated animals. Antibodies to this organism have been detected in cats in South America, but bacteria were not recovered. After oral inoculation, 3 of 14 experimentally infected cats developed bacteremia, and agglutinating antibodies were not detected. Antibodies to *B canis* have also been reported occasionally in wild canids including foxes, coyotes (*Canis latrans*) and golden jackals (*Canis aureus*), a wild raccoon (*Procyon lotor*), and diverse captive carnivores including hoary foxes (*Lycalopex vetulus*), little spotted cats (*Leopardus tigrinus*), tayras (*Eira barbara*) and possibly coatis (*Nasua nasua*). *B. canis* nucleic acids have been found in captive pumas (*Puma concolor*), ocelots (*Leopardus pardalis*, and a jaguar (*Panthera onca*). Experimental infections have been established in nonhuman primates, laboratory rodents (mice, guinea pigs) and rabbits. Sheep, swine and cattle were found to be highly resistant to infection by oral and conjunctival inoculation; however, rare field infections with *B. canis* have been reported in cattle.

Zoonotic potential

B. canis is zoonotic, but relatively few cases have been reported to date. One clinical case was caused by the M- strain of *B. canis*, a laboratory strain that has reduced virulence and is used as an antigen for serological testing.

Geographic Distribution

B. canis appears to be widely distributed, and has been reported in North, Central and South America, and parts of Asia, Africa and Europe. New Zealand and Australia appear to be free of *B. canis*; however, Australia has reported some *B. suis* infections in dogs, mainly in animals used to hunt feral pigs.

Transmission

B. canis occurs in birth products (e.g., the fetus, placenta, fetal fluids) and vaginal discharges from an infected bitch, and can persist in vaginal discharges for several weeks. It can also be shed in normal vaginal secretions, particularly during estrus, and in milk. In males, semen can contain high concentrations of *B. canis* for weeks or months after infection, and intermittent shedding of smaller quantities may persist for

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years. This organism is also shed in urine, and low concentrations of bacteria have been detected in saliva, nasal and ocular secretions, and feces.

In dogs, *B. canis* primarily enters the body by ingestion and through the genital, oronasal and conjunctival mucosa, but transmission through broken skin may also be possible. Most cases are thought to be acquired venereally (including via artificial insemination) or by contact with the fetus and fetal membranes after abortions and stillbirths. However, this organism may also be transmitted between dogs during close contact, even in the absence of mating or pregnancy. In one study, uninfected, intact male or female dogs acquired *B. canis* within 6 months when they lived with infected, intact animals of the same sex under laboratory conditions. Sexually immature, intact dogs did not readily transmit this organism to each other under the same conditions. Puppies can be infected *in utero*, and may remain persistently infected even if they appear normal. Puppies can also be infected from milk, but the importance of this route is controversial. Potential iatrogenic sources of infection include blood transfusions and contaminated syringes. There is no evidence that arthropods play any role in the epidemiology of brucellosis; however, some species of *Brucella* have been detected in blood-sucking arthropods such as ticks, *B. abortus* has been transmitted to guinea pigs via tick bites in the laboratory, and transovarial transmission of *B. melitensis* was reported in ticks.

Brucella spp. have been reported to survive on fomites for periods ranging from less than a day to > 8 months, depending on factors such as temperature, humidity, exposure to sunlight and the presence of organic matter. Survival is longer when the temperature is low. Under conditions of high humidity, low temperatures and no sunlight, these organisms can remain viable for several months in water, aborted fetuses, feces and other materials. They can withstand drying, particularly when organic material is present, and may survive in dust and soil.

Humans usually become infected with members of the genus *Brucella* by ingesting organisms or via the contamination of mucous membranes (including the conjunctiva and respiratory tract) and abraded skin. In case reports, *B. canis* infections have occurred after close contact with dogs, especially animals that recently aborted or gave birth, or after exposure to large amounts of the organism in laboratories. However, there have also been clinical cases where the source of the organism could not be determined. There are no reports of person-to person transmission of *B. canis*, although this is theoretically possible. For other species of *Brucella*, routes implicated in rare instances of human-to-human transmission include blood transfusion, bone marrow transplantation, exposure to contaminated material while assisting at a delivery, sexual intercourse and nursing (infants). There is no indication that members of the genus *Brucella* are transmitted between people by casual contact under ordinary conditions.

Disinfection

Brucella spp. are readily killed by most commonly available disinfectants including hypochlorite solutions, sodium hydroxide, quaternary ammonium compounds, 70% ethanol, isopropanol, iodophors, phenolic disinfectants, formaldehyde, glutaraldehyde and xylene. A 1% solution of citric acid was reported to be less effective. Brucellae are inactivated fairly quickly by acid pH < 3.5. They can also be destroyed by moist heat of 121°C (250°F) for at least 15 minutes, dry heat of 320-338°F (160-170°C) for at least 1 hour, or gamma irradiation. Boiling for 10 minutes is usually effective for liquids.

Infections in Animals

Incubation Period

The period between infection and reproductive losses is variable. Abortions are most common during the last trimester of gestation, and early embryonic deaths have been seen a few weeks after venereal transmission. The incubation period for epididymitis is reported to be 5 weeks or more in most cases.

Clinical Signs

B. canis can cause abortions and stillbirths in pregnant dogs. Litters may contain both live and dead pups; however, live pups are often weak and frequently die soon after birth. Some congenitally infected animals appear normal, but may later develop brucellosis. Most abortions occur during the last trimester, especially between 45 and 55 days, and typically have no significant premonitory signs. Abortions are usually followed by a mucoid, serosanguinous or gray-green vaginal discharge that persists for several weeks. Early embryonic deaths and resorption have been reported a few weeks after mating, and may be mistaken for failure to conceive. Reproductive losses recur during subsequent pregnancies in some dogs, but not in others. Such recurrences may be intermittent.

Lymphadenitis is common in dogs infected with *B. canis*, and may be regional or generalized. Epididymitis and scrotal edema can occur during the acute stage in infected males, and orchitis may be seen occasionally. Self-trauma (e.g., licking) can result in scrotal dermatitis. Concurrent prostatitis is common, and may lead to pain and difficulty in urinating and defecating. Unilateral or bilateral testicular atrophy can be seen in chronic infections, and some males become infertile. Other male dogs can have abnormal sperm with morphological abnormalities and reduced viability. Occasionally reported clinical signs in dogs include lethargy or fatigue, exercise intolerance, decreased appetite, weight loss and behavioral abnormalities (loss of alertness, poor performance of tasks); however, most animals do not appear seriously ill, and many are asymptomatic. Occasionally, discospondylitis can cause stiffness, lameness or back pain. Chronic uveitis, unilateral endophthalmitis, dermatitis, endocarditis, osteomyelitis and meningoencephalitis/ low grade meningitis have also been reported. Fever is rare. Dogs with brucellosis may recover spontaneously, beginning a

year after infection, but recovery is more common after 2-3 years, and some animals remain chronically infected for years. Deaths are rare except in the fetus or newborn.

Post Mortem Lesions

Infected dogs may have regional or generalized lymphadenitis and the spleen and/or liver may be enlarged. Scrotal edema, scrotal dermatitis, epididymitis, prostatitis, orchitis, and testicular atrophy and fibrosis may be detected in males, and metritis and vaginal discharge may be seen in females. Lesions related to localized infections, such as discospondylitis, osteomyelitis, meningitis, focal non-suppurative encephalitis or abscesses in various internal organs may also be observed.

Aborted fetuses are often partially autolyzed and may have evidence of a generalized bacterial infection, such as subcutaneous edema, subcutaneous congestion and hemorrhages in the abdominal region, bronchopneumonia, and degenerative lesions in the liver, spleen, kidneys and intestines. Some fetuses have no gross lesions.

Diagnostic Tests

Canine brucellosis is sometimes difficult to diagnose, and diagnosis is more likely to be successful if more than one technique is used. This disease may be suspected if brucellae are detected by microscopic examination of stained smears from the placenta, reproductive discharges or the contents of the fetal stomach, using modified Ziehl-Neelsen (Stamp) staining. *Brucella* species are not truly acid-fast, but they are resistant to decolorization by weak acids, and stain red. They appear as coccobacilli or short rods, often singly but sometimes in pairs or small groups. Organisms such as *Coxiella burnetii* or *Chlamydia* spp. can resemble *Brucella*.

Serology is often used to diagnose infections with *B. canis*. Some dogs seroconvert as soon as 2-4 weeks after infection, but others may not have detectable titers until 3-4 months. Two commonly used serological tests are the rapid slide agglutination test (RSAT), often used for screening, and the tube agglutination test (TAT). Adding 2-mercaptoethanol (2-ME) to these assays (i.e., the 2-ME RSAT or 2-ME TAT) improves specificity by dissociating IgM, which is more likely to cross-react with other bacteria than IgG. However, this can also decrease sensitivity, especially during the early stage of the immune response when IgM predominates. Positive reactions in screening tests can be confirmed with a more specific assay such as agar gel immunodiffusion (AGID). Other serological tests that have been used either clinically or in research include ELISAs, indirect fluorescent antibody (IFA) tests, complement fixation, immunochromatographic assays and counter-immunoelectrophoresis. False positive reactions can be an issue in some tests, due to cross-reactivity with other Gram-negative bacteria (e.g., *Bordetella*, *Pseudomonas*) or nonspecific agglutination reactions. Chronically infected animals are sometimes seronegative. Antibody titers in chronically infected bitches tend to be higher during estrus or pregnancy, or after an abortion. *B. canis* has "rough" lipopolysaccharide (LPS) in the cell wall, and serological tests for this organism do not detect *Brucella* species that have "smooth" LPS, such as *B. suis*, *B. melitensis* and *B. abortus*.

B. canis may be isolated from the blood, genital tract (e.g., semen, vaginal discharges), placenta, aborted fetuses (gastric contents, liver, spleen), milk, urine, lymph nodes and sites of clinical localization such as infected joints. Samples from the genital tract are particularly valuable in animals with reproductive signs. Bacteremia is prolonged in dogs; however, repeated sampling may be necessary, as it can be intermittent and the number of organisms may be low. *Brucella* spp. can be cultured on a variety of nonselective media, or on selective media such as Farrell's, Thayer-Martin's or CITA medium. Enrichment techniques can also be employed. The use of more than one medium is often recommended, as some isolates may not grow readily on certain media. Some commercial bacterial identification tests can misidentify *Brucella* as another organism. Attempts to isolate *B. canis* are not always successful, especially in chronically infected dogs. Treatment with antibiotics or bacterial overgrowth in nonsterile samples can also interfere with culture.

B. canis can be identified to the species level by phenotypic (phage typing and cultural, biochemical and serological characteristics) or genetic techniques. Species identification is often done at reference laboratories, as it is complicated by the high genetic similarity between brucellae and the possibility of ambiguous phenotypic tests. *B. canis* and *B. suis* are particularly difficult to distinguish with genetic methods. Most PCR tests only identify *Brucella* to the genus level, but a few *B. canis*-specific PCRs have been published. Multiplex PCR assays that can identify more than one species of *Brucella* (e.g., the Bruce-ladder assay) are also used. Other tests that can be employed for species identification, such as single nucleotide polymorphism (SNP) typing and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS), have been described. Techniques such as multiple-locus variable number tandem repeat analysis (MLVA) can be used in epidemiological investigations of outbreaks.

PCR tests for *Brucella* are mainly used to identify organisms in culture; however, some laboratories may use these tests directly on clinical samples. *B. canis*-specific PCR tests have not yet been extensively evaluated in canine populations. A few laboratories used immunohistochemistry to identify *B. canis* antigens in tissue samples (e.g., placenta, fetuses) in clinical case reports; however, these tests are not used routinely for diagnosis.

Treatment

Some dogs have been treated successfully with long-term antibiotics. Treatment is usually with a combination of two different antibiotics, such as tetracyclines or fluoroquinolones combined with aminoglycosides. Enrofloxacin alone appeared to be successful in one trial, but it has not been extensively evaluated. No treatment is certain to eliminate *B. canis*, and recrudescence is possible. Even when this organism seems to have disappeared, it may persist

in tissues such as the lymph nodes, spleen, uterus and prostate. For this reason, euthanasia of infected animals is often recommended in kennels, and this option should also be discussed when *B. canis* is found in a pet. Intact animals should be neutered, and some sources recommend that treated dogs be isolated even after treatment. It should be noted that *B. canis* has been detected in the urine of some castrated males. Periodic serological monitoring might be able to detect rising antibody titers if organisms persist and begin to replicate again in treated animals.

Control

Disease reporting

Veterinarians who encounter or suspect canine brucellosis should follow their national and/or local guidelines for disease reporting. *B. canis* is not nationally notifiable in the U.S.; however, it is reportable in a number of states.

Prevention

Some countries free of *B. canis* require that imported dogs be tested for this organism. Testing animals before they are allowed to breed also helps reduce disease transmission. In endemic areas, brucellosis is usually introduced into a kennel in an infected dog or semen, and new animals should be isolated and tested. A second serological test, performed before the dog is released from isolation, may detect animals that are in the early stage of the infection and seronegative on arrival. The currently available assays can miss some infected animals, and some authors recommend that kennels routinely test all of their dogs, either annually or twice a year. This may reduce losses in the event that *B. canis* is introduced.

In infected kennels, brucellosis can be controlled by sanitation and infection control measures, together with the euthanasia, isolation or removal (e.g., to a research facility) of infected dogs. Housing in individual cages reduces the spread of the organism. Dogs from infected kennels should not be sold or used for breeding. Repeated testing and removal of infected animals, combined with quarantine, has been used to eradicate brucellosis from some kennels. There is no vaccine for *B. canis.*

Morbidity and Mortality

All breeds of dogs are susceptible to brucellosis. *B. canis* can spread rapidly in confined populations, especially during breeding or incidents of abortion, and the prevalence of infection can be high in breeding kennels. Although deaths are rare except in the fetus and neonate, reproductive losses can be significant. Up to 75% fewer puppies may be weaned from some infected kennels.

Outside a kennel environment, *B. canis* can be a significant issue in dog populations where uncontrolled breeding is common. Around the world, most surveys have reported seroprevalence rates ranging from < 1% to approximately 15% in various groups of dogs, with higher rates generally reported in strays than pets. Rates higher than 15% have been reported occasionally, especially among strays or owned dogs in poverty-stricken areas. Many of these serological surveys were done in the 1970s, but a few recent reports are available. In recent years, high seroprevalence has been documented in some impoverished areas of South America (e.g., 30% in one neighborhood in Argentina), and in rural dogs (21%) and urban dogs (13%) in Zimbabwe. A few reports from developed countries suggest that the incidence of canine brucellosis might be rising.

Infections in Humans

Incubation Period

There is little information about the incubation period for brucellosis caused by *B. canis*. Relatively few cases have been documented, and in many cases reported in the literature, exposure was ongoing or the source was unknown. The acute symptoms caused by other species of *Brucella* usually appear within 1-4 weeks, but the onset can be insidious, and some cases have been diagnosed as late as 6 months after exposure.

Clinical Signs

Relatively few descriptions of clinical cases caused by *B. canis* have been published. The consequences of infection with other zoonotic brucellae range from asymptomatic infections to diverse syndromes that may appear insidiously or abruptly. Acute brucellosis is usually a febrile illness with nonspecific flu-like signs such as fever, chills, headache, malaise, back pain, myalgia and lymphadenopathy, which may be accompanied by splenomegaly and/ or hepatomegaly. Patients may experience drenching sweats, particularly at night. Nonspecific gastrointestinal signs including anorexia, vomiting, diarrhea and constipation may also be seen. Some people recover spontaneously, while others develop persistent nonspecific symptoms (e.g., fever, weakness) that typically wax and wane. Localized infections in various organs and tissues can result in a wide variety of syndromes. Fever may be absent or mild in these cases. Infections in bones and joints, the most common sites of localization, can manifest as arthritis, spondylitis, sacroiliitis, osteomyelitis, bursitis and tenosynovitis. Other syndromes have included neurological involvement (e.g., meningitis, meningoencephalitis, brain abscesses), ocular signs (uveitis, optic neuritis, endophthalmitis and other signs), anemia, thrombocytopenia, nephritis, cardiovascular complications (e.g., vasculitis, aneurisms, endocarditis), respiratory involvement (e.g., bronchopneumonia or pulmonary abscesses), peritonitis, pancreatitis, myelitis, and cutaneous rashes, ulcers or abscesses. Elevations in the liver enzyme alanine aminotransferase (ALT), with no unusual liver pathology, were reported to be common in some people infected with *B. suis*. Epididymo-orchitis, prostatitis and seminal vesiculitis can be seen in males, and pregnant women may abort or give birth prematurely. Sepsis, pneumonia and other syndromes have been reported in congenitally infected infants, but some infected newborns are asymptomatic. Deaths are uncommon except in infants, and are usually caused by endocarditis or infections affecting the brain. After treatment, recovery may take a few weeks to months.

Published clinical cases associated with *B. canis* have included a variety of presentations consistent with this description. They range from mild fatigue, or fatigue and intermittent fever as the only symptoms, to a febrile illness with fatigue, malaise, nausea, chills, night sweats and headache. Fever of unknown origin, sometimes prolonged, was the presenting syndrome in some individuals. Enlargement of the spleen and/or liver and elevated liver enzymes were reported in several cases. Weight loss, anemia, enlarged lymph nodes and abdominal pain have also been documented. Nausea, vomiting and diarrhea have been described, especially in children, and one individual reported a persistent cough, sore throat and conjunctival burning (in addition to night sweats, headache, lethargy and myalgia). Serious complications including endocarditis have been reported in a few cases. *B canis* was associated with aortic valve vegetations and lower extremity aneurysms in one boy, and calvarial osteomyelitis, epidural abscess, pleural effusion and pulmonary nodules in another child. Peritonitis with *B. canis* bacteremia was seen in an adult with concurrent hepatitis C infection and cirrhosis. Liver disease also appears to be a predisposing factor in rare incidents of peritonitis associated with other species of *Brucella*. Very few *B. canis* infections have been described in people who were immunocompromised; however, this organism caused nonspecific febrile syndromes in two people concurrently infected with HIV-1.

Occasionally, *B. canis* has been detected in clinical cases where its role, if any, in the presenting signs is unclear. For instance, this organism was found in blood cultures from an adult with Guillain Barré syndrome and suspected ventilator-associated pneumonia. In another case, it appeared to be responsible for a persistent elevation in liver enzymes discovered after an acute respiratory illness in a child; however, the respiratory signs resolved very shortly after admission to the hospital and might have been unrelated. In one case, oral lesions were found in a child concurrently infected with *B. canis* and cytomegalovirus, and resolved with antibiotic treatment for brucellosis. Some conditions caused by other brucellae, such as epididymo-orchitis and neurological signs, have not been attributed to *B. canis* as of 2018. This might be because so few clinical cases have been described, or because this species has relatively low virulence for humans.

A laboratory worker exposed to the less virulent M-strain of *B. canis* developed symptoms similar to those caused by wild-type strains of *Brucella*.

Diagnostic Tests

Brucellosis caused by *B. canis* can be difficult to diagnose in humans. The symptoms are often nonspecific, and few diagnostic tests for this organism are available. It can sometimes be found in blood or sites of localization (e.g., bones), and some cases have been detected when it was unexpectedly isolated during routine blood culture. However, *B. canis* grows slowly, and it may not appear within the time that blood cultures are routinely held.

The serological tests used to diagnose infections with the more commonly isolated zoonotic species (*B. abortus*, *B. suis* and *B. melitensis*) do not detect antibodies to *B. canis*, and tests for *B. canis* antibodies are not usually available at diagnostic laboratories. In some reports in the literature, antibody reactions were detected with tests developed for this purpose or adapted from canine assays at the institution. They included microagglutination, tube agglutination, RSAT and ELISAs. A universal indirect ELISA that can recognize antibodies to both smooth and rough *Brucella* was recently published. Some case reports suggest that clinical resolution is associated with declining antibody titers to *B. canis*.

Relying on a single type of test (i.e., either culture or serology) may miss some infections. In the literature, *B canis* was not always found in the blood of some patients identified by serology, and conversely, serology did not always detect antibodies in people who had *B. canis* in the blood.

Treatment

Brucellosis in people is usually treated with a prolonged course of antibiotics, generally combining two or more drugs for part or all of the course. Different antibiotics may be recommended, depending on the patient's age, pregnancy status and syndrome(s). Monotherapy is reported to have a high relapse rate. Relapses can be seen (most often within 3-6 months) if the treatment was inadequate. Surgical intervention may occasionally be required for localized foci. There is only limited experience specifically with *B. canis*; however, standard antibiotic treatments for brucellosis appeared to be effective in published cases. A few patients relapsed with inadequate treatment.

Prevention

Potential hazards to people should be discussed when brucellosis is diagnosed in a dog, as antibiotics do not reliably eliminate *B. canis*, and the level of risk to human companions is currently uncertain. Euthanasia of infected animals is usually recommended in kennels, and it is also an option in pets. Some authors recommend periodic serological monitoring of treated pets, which may detect rising immune responses from recrudescence. Good hygiene, together with personal protective equipment (e.g., gloves, face protection) as appropriate, is likely to decrease human exposure, especially during births and abortions, but also during contact with urine, vaginal secretions and other potential sources of *B. canis*.

Prophylactic antibiotics or serological monitoring may be offered to laboratory workers in some situations.

Morbidity and Mortality

There is little information about *B. canis* infections in humans. The virulence of this organism for humans may be low, as relatively few clinical cases have been documented (< 100 as of 2018), and most reported cases were mild. However, it is also possible this disease is underdiagnosed, given the low clinical suspicion among physicians and the difficulties in making a definitive diagnosis. In a limited number of disease investigations, some individuals exposed

to infected dogs developed overt clinical signs or had subclinical evidence of infection, such as laboratory abnormalities in liver function tests, while others had antibodies but no signs of disease. There are currently no reports of deaths caused by *B. canis*. Estimates of the case fatality rate for untreated illnesses caused by other species of *Brucella*, including the highly virulent organism *B. melitensis*, are usually in the range of 1-2% or less.

Serological surveys, mostly conducted in the 1970s and early 1980s, have generally reported that less than 2% of their study populations had antibodies to *B. canis*, although a 1975 study from the Oklahoma Health Sciences Center found an unusually high seroprevalence of 68% in people "with an average exposure to dogs," 73% in veterinarians and 57% in male blood donors. Another study from the 1970s reported that 13% of hospitalized patients with various illnesses in Mexico were seropositive. Two studies published within the last 10 years, one in the U.S. and the other in Turkey, found seroprevalence rates ≤ 4%, even in people who were regularly exposed to dogs. However, some reports suggest that *B. canis i*nfections may be an emerging issue in certain impoverished areas where dogs are allowed to roam. During an investigation into a child with canine brucellosis in Argentina, 19% of the people living in the same poverty-stricken neighborhood were seropositive.

Internet Resources

Centers for Disease Control and Prevention (CDC). Brucellosis.

CDC. Brucellosis reference guide. Exposures, testing and prevention

European Centre for Disease Prevention and Control. Brucellosis

Public Health Agency of Canada. Pathogen Safety Data Sheets

The Merck Manual

The Merck Veterinary Manual

World Health Organization. Brucellosis

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