

## *Brucella canis* and Public Health Risk

İsfendiyar Darbaz , Osman Ergene 

Department of Obstetrics and Gynaecology, Near East University School of Veterinary Medicine, Nicosia, Cyprus

ORCID IDs of the authors: İ.D. 0000-0001-5141-8165; O.E. 0000-0002-7607-4044.

Cite this article as: Darbaz İ, Ergene O. *Brucella Canis* and Public Health Risk. *Cyprus J Med Sci* 2019; 4(1): 52-6.

Pregnancy losses in dogs are associated with many types of bacteria. *Brucella canis* is reported to be one of the most important bacterial species causing pregnancy loss in dogs. Dogs can be infected by 4 out of 6 *Brucella* species (*B. canis*, *B. abortus*, *B. melitensis*, and *B. suis*). *B. canis* is a Gram-negative coccobacillus first isolated by Leland Carmichael and is a cause of infertility in both genders. It causes late abortions in female dogs and epididymitis in male dogs. Generalized lymphadenitis, discospondylitis, and uveitis are shown as the other major symptoms. *B. canis* infections can easily be formed as a result of the contamination of the oronasal, conjunctival, or vaginal mucosa. Infection can affect all dog breeds and people. While morbidity may be high in infection, mortality has been reported to be low. Most dogs are asymptomatic during infection, and it is difficult to convince their owners that their dogs are sick and should not be used in reproduction. The diagnosis of the disease is quite complex. Serological tests may provide false results or negative results in chronic cases. Therefore, diagnosis should be defined by combining the results of serological studies and bacterial studies to provide the most accurate result. No antibiotic treatment is reported to be 100% effective in *B. canis* infections, and infected animals are recommended to be removed from other animals and not be used for reproduction for a prolonged period.

**Keywords:** *Brucella canis*, humans, pathogen, zoonotic

### INTRODUCTION

*Brucella* infection may form invaginal discharge during abortion or estrous. It may form as a result of the presence of  $>10^{10}$  bacteria/mL in postnatal fetus, placenta, or lochia. It may form as a result of receiving these bacteria from oronasal, conjunctival, or vaginal mucosa contact (1-6). Bacteria are spread with sperm in male dogs (7). The infection may develop after copulation of a non-infected female dog with an infected male dog (8). Bacteria are also spread via urine in both genders. Male dogs can have high levels of bacteria in their urine, and this is the reason why male urination can be dangerous. *Brucella* infection begins to spread via urine after 4-8 weeks of infection (7).

Bacterial concentration in the milk of infected animals is reported to be high (9). The idea of disease spreading with high levels of bacteria in the milk has been a matter of debate (4). While some researchers are defending that milk is insignificant in disease transmission because puppies are infected in the uterus (6), some researchers report that infected milk may be dangerous for environmental contamination (4). Bacterium is isolated in low concentrations from saliva, nose and eye, and feces (10).

The aborted material of dogs infected with *Brucella canis* in dog shelters or in co-cultivated environments is very dangerous for non-infected dogs. Waste placenta tissue and fluids may contain high levels of microorganisms. Infection after contamination in shelters can be spread very quickly (5).

Huts, equipment, and people permanently in contact with infected dogs are also reported as sources of infection (11). Infections in humans are usually reported in laboratory workers and shelter workers exposed to sustained or major exposures. Owners who are in constant contact with infected dogs are also reported to be infected. As a result, animal owners should be informed about the potential risk but not alarmed about this zoonotic disease (12).

### CLINICAL SYMPTOMS

#### Non-Specific Symptoms

*B. canis*-infected dogs may not always show serious clinical symptoms (5). Breeders provide barely or unidentifiable information about the clinical symptoms in *B. canis* infections. These clinical symptoms are weak hair

structure, poor, exhausted, overworked, drowsy movements during exercise, weight loss, lameness, lymphadenitis, and changes in behavior (loss of appetite, poor performance) (2). Death has not yet been reported as a primary cause of death in *B. canis* infections (5).

Fever is rarely seen in *B. canis* infections, which is explained by the lack of endotoxin-producing lipopolysaccharides in the organism (2, 13, 14).

Decrease in pregnancy rate, early embryonic death, fetal resorption, and late-period abortions can be seen in female dogs, whereas painful scrotal growth, testicular atrophy, moist scrotal dermatitis, decrease in ejaculatory volume, loss of libido, reluctance to breed, poor quality sperm with white blood cells, and increase in morphological deformation in sperm can be observed in male dogs in examinations usually during the first 3 months of infection (2, 15). Discospondylitis, meningoencephalitis, or uveitis may also develop as a symptom in both genders (2).

*B. canis* affects the active macrophages (intracellular) during infection, causing the growth of lymph node nodules and reticuloendothelial cell hyperplasia. In addition to lymph nodes, spleen and liver growth can be observed. A hardening and a nodular structure in the spleen have also reported (2).

### Specific Symptoms

Reproductive failure has reported to mean abortion, epididymitis, orchitis, and testicular atrophy. The most obvious clinical symptom that can be seen and reported by patient owners is the spontaneous abortions formed in dogs that are assumed to be healthy. These abortions usually occur between days 45 and 59 of pregnancy. Brucellosis can also result in resorption or early embryonic death after mating. Infants born as a result of pregnancies formed in infected animals may die in 20 days on average. Infected dogs have been reported to be able to give birth normally in the following pregnancy, as well as localized autolyzed fetuses, fetal mortality, or normal fetus that die within a few hours may be born. Puppies that are able to survive are bacteremic for several months (2, 4).

Long-term, viscous, serosanguinous vaginal discharge following abortion may last for 1–6 weeks. This discharge may contain high amounts of bacterial colonies and can be a major problem in infecting patient owners and other dogs. Necessary precautions and warnings must be made against contagion that can occur as a result of contamination with mouth, respiratory tract, or waste material and liquid to protect people and other dogs. Brucellosis does not affect estrus symptoms and mating. Dogs can continue to mate after two or three abortions and then have a normal birth (2, 4).

*B. canis* affects androgen-related organs in male dogs. Acute inflammation associated with pain and swelling can cause orchitis or epididymitis, which can also be determined by hand examination (2, 16, 17). Scrotal dermatitis can be

formed as a result of licking by male dogs for comfort (2, 18). Chronic or prolonged infections can cause unilateral or bilateral testicular atrophy in breeding dogs (17, 19). Atrophy can result in reluctance to mate or loss of libido resulting from pain.

The systems in the body are also affected by bacteria. Discospondylitis in the thoracic vertebrae and lumbar vertebrae can be observed by radiography. Ophthalmologic examinations may result in endophthalmitis and recurrent uveitis (20–22). Non-suppurative meningitis is also reported at low rates (13).

### Clinical Signs in Humans

A small number of studies regarding clinical cases caused by *B. canis* have been published. The consequences of infection with other zoonotic brucellosis range from asymptomatic infections to various syndromes that can appear insidiously or suddenly. Acute brucellosis is a febrile disease with non-specific influenza-like symptoms, such as fever, chills, headache, weakness, backache, muscle aches, and lymphadenopathy (growth in the lymph nodes) and accompanying splenomegaly and/or hepatomegaly. Patients may experience sweating, especially in the evening. Humans acquire *B. canis* infection through direct contact with infected dogs or their reproductive or blood products. Clinical signs and symptoms include undulate fever, chills, malaise, splenomegaly, and peripheral lymphadenomegaly. Diagnosis is often complicated in humans because of the non-specific signs and symptoms coupled with a low index of suspicion by many physicians. If the disease is part of the differential diagnosis, culture is the only test available for diagnosing *B. canis* infection in humans, and confirmation is problematic because of low-level and intermittent bacteremia. Even if physicians suspect brucellosis, diagnoses may be missed because the commercially available serological tests screen for smooth *Brucella* species and will not detect antibodies against *B. canis*. Canine serological tests for *B. canis* infection have been adapted for use in humans, but test results should be interpreted with caution (23–28).

Published clinical cases associated with *B. canis* contain various representations suitable for this description. They vary from fatigue, nausea, tremor, night sweats, and fever with headaches to one symptom, such as mild tiredness or fatigue and intermittent fever. There is sometimes a long-standing syndrome of unknown fever in some people. Spleen and/or liver enlargement and increased liver enzymes have been reported in various cases. Weight loss, anemia, enlarged lymph nodes/ovaries, and abdominal pain have also been documented. Nausea, vomiting, and diarrhea have been described especially in children, and constant cough, sore throat, and conjunctival burning, in addition to night sweats, headache, numbness, and muscle pain, have been reported in one person. Serious complications have been reported, including endocarditis in a few cases. *B. canis* was associated with aortic valve and lower extremity aneurysm in one child and associated with calvarial osteomyelitis, epidural abscess, pleural effusion, and

pulmonary nodules in another child. *B. canis* bacteremia and peritonitis were observed in an adult with concurrent hepatitis C infection and cirrhosis. Liver disease is also a predisposing factor in rare cases of peritonitis associated with other *Brucella* species. Very few *B. canis* infections have been described in immunosuppressed individuals; however, this organism causes non-specific febrile syndromes in two individuals who are simultaneously infected with human immunodeficiency virus-1 (28-32).

A laboratory worker exposed to a less virulent M-strain of *B. canis* developed symptoms similar to the symptoms caused by *Brucella's* wild-type strains (24, 33).

### Incubation Period

There is less information about the incubation period of brucellosis caused by *B. canis*. Acute symptoms caused by other *Brucella* species usually occur within 1-4 weeks. However, it may be insidious at first, and some cases are diagnosed 6 months after exposure (28, 31).

### Diagnosis

Infertility, abortion, enlarged lymph nodes, swollen scrotum, and testicular atrophy are reported as clinical symptoms in *B. canis* infections; however, no clinical symptoms have been reported in some cases (34).

Bacterial isolation has been reported to be required from the tissue, discharge, blood, sperm, vertebra, or eye for a definitive diagnosis of *B. canis* cases. The results obtained should also be supported by positive serological agglutination tests, other serological titers, and hemoculture results. The variable amount and duration of bacteria in dogs make diagnosis difficult (35). Owing to this, a single negative blood culture does not show that there is no *B. canis* infection.

### Diagnostic Tests

It can be difficult to diagnose brucellosis, which is caused by *B. canis*, in humans. The serological tests used to diagnose infections of the most commonly isolated zoonotic species (*Brucella abortus*, *Brucella suis*, and *Brucella melitensis*) do not detect antibodies against *B. canis*, and the tests used to detect *B. canis* antibodies are not usually available in diagnostic laboratories. In some studies, antibody reactions have been identified with the tests developed for this purpose or identified from analyses of dogs in the institute. These tests include microagglutination, tube agglutination, rapid slide agglutination test, and enzyme-linked immunosorbent assay (28, 36, 37).

### Morbidity and Mortality

There is very less information about *B. canis* infections in humans. Since relatively few clinical cases have been documented (<100 since 2018) and most reported cases are mild, the virulence of this organism for humans may be low. However, the diagnosis of this disease is also insufficient given the low clinical suspicion and the difficulties of making a definite diagnosis among physicians. In a limited number of disease studies, some individuals who have been exposed

to infected dogs have developed clinical findings or have had subclinical infection findings, such as laboratory abnormalities in liver function tests, whereas no evidence of disease was observed in others despite antibody detection. Nowadays, no deaths have been reported resulting from *B. canis* infections. The case mortality rate for untreated diseases caused by other *Brucella* species, including the highly virulent organism *B. melitensis*, is generally estimated to be 1%-2% or less. In serological studies, mostly conducted during the 1970s and early 1980s, <2% of the studied populations were reported to have antibodies against *B. canis*, and the seroprevalence of 68% in dogs, 73% in veterinarians, and 57% in male blood donors was observed in people who are in contact with dogs at average levels in a study conducted at the Oklahoma Health Sciences Center in 1975. A previous study in the 1970s reported that 13% of the hospitalized patients due to various diseases in Mexico are seropositive. During the last decade, two studies, one of which was published in the United States and the other in Turkey, found seroprevalence rates of  $\leq 4\%$  even during regular exposure to dogs. However, some studies indicate that *B. canis* infections may occur in some weakened/impooverished areas where dogs roam freely. In a previous study of a child with dog brucellosis in Argentina, 19% of the people in the neighborhood were seropositive (31, 38-43).

### Treatment

Brucellosis is usually treated with long-standing antibiotics, and usually two or more drugs are combined in some part or all of the treatment in humans. Different antibiotics may be recommended depending on the patient's age, gestational status, and syndrome. Monotherapy has reported high levels of recurrence. If treatment is inadequate, recurrence may occur. Most recurrence often occurs within 3-6 months. Surgery may sometimes be required for localized focus. It has limited experimentation with *B. canis* in particular. However, standard antibiotic treatments for brucellosis appear to be effective in the cases reported. Several patients relapse as result of poor treatment (24, 25, 28, 31).

Future study is required to improve diagnostic assays for humans and animals and to generate policies to prevent the spread of disease (23, 28, 44-46).

### CONCLUSION

Brucellosis in dogs remains endemic to many areas worldwide and without stronger intervention measures will probably remain an under-recognized threat to human health and animal welfare. Potential hazards for humans should be discussed when a dog is diagnosed with brucellosis because antibiotics do not eliminate *B. canis* safely, and the level of risk in humans is now uncertain. Euthanasia in infected animals is often recommended in shelters and is also a choice in pets. Some authors suggest follow-up for periodic serological testing of pets starting treatment.

**Peer-review:** Externally peer-reviewed.

**Author contributions:** Concept - İ.D., O.E.; Design - İ.D., O.E.; Supervision - İ.D., O.E.; Resource - İ.D., O.E.; Materials - İ.D., O.E.; Concept - İ.D., O.E.; De-

sign - i.D., O.E.; Supervision - i.D., O.E.; Resource - i.D., O.E.; Materials - i.D., O.E.; Data Collection and/or Processing - i.D., O.E.; Analysis and/or Interpretation - i.D., O.E.; Literature Search - i.D., O.E.; Writing - i.D., O.E.; Critical Reviews - i.D., O.E. Collection and/or Processing - i.D., O.E.; Analysis and/or Interpretation - i.D., O.E.; Literature Search - i.D., O.E.; Writing - i.D., O.E.; Critical Reviews - i.D., O.E.

**Conflict of Interest:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

## REFERENCES

- Pretzer SD. Bacterial and protozoal causes of pregnancy loss in the bitch and queen. *Theriogenology* 2008; 70: 320-6. [\[CrossRef\]](#)
- Hollett RB. Canine brucellosis: outbreaks and compliance. *Theriogenology* 2006; 66: 575-87. [\[CrossRef\]](#)
- Carmichael LE. Abortion in 200 Beagles. *J Am Vet Med Assoc* 1966; 149: 1126.
- Wanke MM. Canine brucellosis. *Animal Reproduction Science* 2004; 82-83: 195-207. [\[CrossRef\]](#)
- Feldman Nelson. Sección 7. Reproduccion En La Hembra Canina. *Endocrinología Y Reproduccion Canina Y Felina*. 2007
- Carmichael LE, Green EG. Canine brucellosis. In: Greene CE editor. *Infectious Diseases of the Dog and Cat*. WB Saunders Co: Philadelphia; 1990. pp. 573.
- Carmichael LE, Joubert JC. Transmission of *Brucella canis* by contact exposure. *Cornell Vet* 1988; 78: 63-73.
- Greene CE and George LW. Canine brucellosis. In *Clinical Microbiology and Infectious Diseases of the Dog and Cat* (ed. C. E. Greene), W. B. Saunders, Philadelphia, 1984; pp. 646-51.
- Zoha SJ, Walsh R. Effect of a two-stage antibiotic treatment regimen on dogs naturally infected with *Brucella canis*. *J Am Vet Med Assoc* 1982; 180: 1474-5.
- Weber A, Christoph H. Untersuchungen zur natürlichen Übertragung von *Brucella canis* bei Hunden. *Fortschr Veterinarmed* 1982; 35: 351-5.
- Johnson CA, Walker RD. Clinical signs and diagnosis of *Brucella canis* infection. *Compend Cont Educ Pract Vet* 1992; 14: 770-2.
- Meyer ME. The genus *Brucella* In: Shaw MP, Stulp H, Truper HG, Balous A, and Schlegel HG, editors. *The prokaryotes*. Springer-Verlag: New York; 1981. pp. 1063-74. [\[CrossRef\]](#)
- Serikawa T, Muraguchi T, Nakao N, Irie Y. Significance of urine culture for detecting infection with *Brucella canis* in dogs. *Jpn J Vet Sci* 1978; 40: 353. [\[CrossRef\]](#)
- Myer ME. *Brucella* organisms isolated from dogs: comparison of characteristics of members of the genus *brucella*. *Am J Vet Res* 1969; 30: 1751.
- Ergene O, Celebi B, Kucukaslan I. Seroprevalance of Canine Brucellosis and Toxoplasmosis in Female and Male Dogs and Relationship to Various Factors as Parity, Abortion and Pyometra. *Indian J Anim Res* 2017; 1-5. [\[CrossRef\]](#)
- Moore JA, Bennett M. A previously undescribed organism associated with canine abortion. *Vet Rec* 1967; 80: 604-5. [\[CrossRef\]](#)
- George LW, Duncan JR, Carmichael LE. Semen examination in dogs with canine brucellosis. *Am J Vet Res* 1979; 40: 1589-95.
- Schoeb TR, Morton R. Scrotal and testicular changes in canine brucellosis: a case report. *J Am Vet Med Assoc* 1978; 172: 598-600.
- Greene CE, Carmichael LE. Canine brucellosis. In: Greene CE, editor. *Infectious diseases of the dog and cat*. Philadelphia: WB Saunders, Co; 2006. pp. 369-81.
- Gwin RM, Kolwalski JJ, Wyman M, Winston S. Ocular lesions associated with *Brucella canis* infection in a dog. *J Am Anim Hosp Assoc* 1980; 16: 607-10.
- Saegusa J, Ueda K, Got Y, Fujiwara K. Ocular lesions in experimental canine brucellosis. *Jpn J Vet Sci* 1977; 39: 181-5. [\[CrossRef\]](#)
- Riecke JA, Rhoades HE. *Brucella canis* isolated from the eye of a dog. *J Am Vet Med Assoc* 1975; 166: 583-4.
- Hensel ME, Negron M, Arenas-Gamboa AM. Brucellosis in Dogs and Public Health Risk. *Emerg Infect Dis* 2018; 24: 1401-6. [\[CrossRef\]](#)
- Marzetti S, Carranza C, Roncallo M, Escobar GI, Lucero NE. Recent trends in human *Brucella canis* infection. *Comp Immunol Microbiol Infect Dis* 2013; 36: 55-61. [\[CrossRef\]](#)
- Javeri H, Jamieson S, Sehgal R, Cadena J. *Brucella canis* peritonitis. *Infection* 2014; 42: 195-7. [\[CrossRef\]](#)
- Alton GG, Forsyth JRL. *Brucella* [online]. In Baron S, editor. *Medical microbiology*. 4th ed. New York: Churchill Livingstone; 1996. Available from: URL: <http://www.ncbi.nlm.nih.gov/books/NBK8572/> (Accessed 4 Jun 2007).
- Centers for Disease Control and Prevention (CDC). Brucellosis [website online]. CDC; 2017 Sept. Available from: URL: <https://www.cdc.gov/brucellosis/> (Accessed 3 Mar 2018).
- Cosford KL. *Brucella canis*: An update on research and clinical management. *Can Vet J* 2018; 59: 74-81.
- Lawaczek E, Toporek J, Cwikla J, Mathison BA. *Brucella canis* in a HIV-infected patient. *Zoonoses Public Health* 2011; 58: 150-2. [\[CrossRef\]](#)
- Lucero NE, Maldonado PI, Kaufman S, Escobar GI, Boeri E, Jacob NR. *Brucella canis* causing infection in an HIV-infected patient. *Vector Borne Zoonotic Dis* 2010; 10: 527-9. [\[CrossRef\]](#)
- Olsen SC, Palmer MV. Advancement of knowledge of *Brucella* over the past 50 years. *Vet Pathol* 2014; 51: 1076-89. [\[CrossRef\]](#)
- Piampiano P, McLeary M, Young LW, Janner D. Brucellosis: unusual presentations in two adolescent boys. *Pediatr Radiol* 2000; 30: 355-7. [\[CrossRef\]](#)
- Traxler RM, Lehman MW, Bosserman EA, Guerra MA, Smith TL. A literature review of laboratory-acquired brucellosis. *J Clin Microbiol* 2013; 51: 3055-62. [\[CrossRef\]](#)
- Flores-Castro R, Carmichael LE. Canine brucellosis: current status of methods for diagnosis and treatment. In: 27th gaines veterinary symposium. 1977. pp. 17-24.
- Taul LK, Powell HS, Baker OE. Canine abortion due to an unclassified Gram-negative bacterium. *Vet Med Small Anim Clin* 1967; 73: 543-4.
- Ayala SM, Hasan DB, Celestino CA, Escobar GI, Zhao DM, Lucero NE. Validation of a simple universal IELISA for the diagnosis of human brucellosis. *Eur J Clin Microbiol Infect Dis* 2014; 33: 1239-46. [\[CrossRef\]](#)
- Nomura A, Imaoka K, Imanishi H, Shimizu H, Nagura F, Maeda K, et al. Human *Brucella canis* infections diagnosed by blood culture. *Emerg Infect Dis* 2010; 16: 1183-5. [\[CrossRef\]](#)
- Tuon FF, Gondolfo RB, Cerchiari N. Human-to-human transmission of *Brucella* - a systematic review. *Trop Med Int Health* 2017; 22: 539-46. [\[CrossRef\]](#)
- Monroe PW, Silberg SL, Morgan PM, Adess M. Seroepidemiological investigation of *Brucella canis* antibodies in different human population groups. *J Clin Microbiol* 1975; 2: 382-6.
- Munford RS, Weaver RE, Patton C, Feeley JC, Feldman RA. Human disease caused by *Brucella canis*. A clinical and epidemiologic study of two cases. *JAMA* 1975; 231: 1267-9. [\[CrossRef\]](#)
- Strom Holst B, Lofqvist K, Ernholm L, Eld K, Cedersmyg M, Hallgren G. The first case of *Brucella canis* in Sweden: background, case report and recommendations from a Northern European perspective. *Acta Vet Scand* 2012; 54: 18. [\[CrossRef\]](#)
- Sayan M, Erdenlig S, Stack J, Kilic S, Guducuoglu H, Aksoy Y, et al. A serological diagnostic survey for *Brucella canis* infection in Turkish patients with brucellosislike symptoms. *Jpn J Infect Dis* 2011; 64: 516-9.

43. Weber A, Brunner H. Seroepidemiological investigations on the incidence of *Brucella canis* antibodies in man. *Zentralbl Bakteriolog Orig A* 1977; 238: 237-43.
44. Atluri VL, Xavier MN, de Jong MF, den Hartigh AB, Tsolis RM. Interactions of the human pathogenic *Brucella* species with their hosts. *Annu Rev Microbiol* 2011; 65: 523-41. [\[CrossRef\]](#)
45. Lucero NE, Corazza R, Almuzara MN, Reynes E, Escobar GI, Boreri E, et al. Human *Brucella canis* outbreak linked to infection in dogs. *Epidemiol Infect* 2010; 138: 280-5. [\[CrossRef\]](#)
46. The Center for Food Security and Public Health. *Brucellosis: Brucella canis*. May 2018; 1-10.