Bacterial and protozoal causes of pregnancy loss in the bitch and queen

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Abstract

Several bacterial species have been implicated in canine and feline pregnancy loss. Brucella canis is one of the more important bacterial infectious agents that cause pregnancy loss in the bitch. Brucella has been documented in the queen but in general infectious abortion from bacteria and protozoal agents is uncommon in the species. Protozoal causes of pregnancy loss in the bitch and queen are less common than in other species. Etiology, clinical signs, diagnosis and treatment of bacterial and protozoal causes of pregnancy loss in the bitch and queen are reviewed. Veterinary practitioners should be aware that many of these organisms have zoonotic potential.

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1. Introduction

Pregnancy loss may occur at any stage of gestation in the dog and cat and may be manifested by embryonic or fetal resorption, abortion of a live or dead fetus(es), mummification, or retention of the fetus(es) in the dam’s uterus or peritoneal cavity beyond the expected time of parturition [1].

Both infectious and noninfectious etiologies can result in pregnancy loss in the bitch and queen. Although viral agents comprise some of the causes of pregnancy loss, nonviral causes such as bacterial and protozoal diseases have been reported. The most important bacterial cause of pregnancy loss in the bitch is Brucella canis. A review of bacterial and protozoal causes of pregnancy loss in the bitch and queen is provided.

2. Bacterial causes of pregnancy loss in the bitch and queen

2.1. Brucella canis

Dogs can be infected by four of the six species of Brucella (B. canis, B. abortus, B. melitensis, and B. suis) [2]. The dog is the reservoir host for B. canis, a gram-negative coccobacillus [3]. Infected animals will shed the organism in urine, vaginal discharge, aborted tissue, semen, and to a lesser extent in mammary, salivary, nasal and nonestrus vaginal secretions [4]. Ingestion and inhalation are the primary means of transmission, whereas transplacental and venereal transmission are also possible [4]. Although infrequently reported, this organism has zoonotic potential.

The most important clinical signs seen are late-term abortions in bitches [5] and epididymitis in males, as well as generalized lymphadenitis, discospondylitis, and uveitis in both sexes [3].
Morbidity may be high with *B. canis*, but mortality is low and some dogs may be asymptomatic [2]. Pregnancy loss in bitches from *B. canis* can also result from early embryonic death (EED) or fetal resorption, and may occur as a result of infertility in both sexes [2]. When late-term abortion does occur, the loss typically occurs between 45 and 59 d of gestation [6]. Aborted puppies usually appear partially autolyzed, with characteristic lesions of generalized bacterial infection, including subcutaneous edema and degenerative lesions in the liver, spleen, kidneys, and intestines [3]. After abortion, a brownish or serosanguinous vaginal discharge is common and can last up to 6 wk [6].

The only method that provides a definitive diagnosis of brucellosis in the canine is bacteriological isolation of the organism from blood, lymph node aspirates, or infected tissues or discharges [7]. Blood culture is the most accurate test available in the first 8 wk after infection, but one negative culture alone does not rule out the disease. Although the dog is undergoing a bacteremia by 2 wk after infection, serological methods of diagnosis may be negative during the first 3 to 8 wk of infection [8].

Initial serological screening in veterinary medicine utilizes agglutination tests that identify the presence of antibodies to cell wall antigens to *B. canis*. A rapid slide agglutination test (RSAT, card test) is commercially available and commonly used as an “in-house” test. Negative results with the RSAT are 95% accurate [7,9], making them highly sensitive. Specificity is low with this test, with false positive results of 50–60% reported [10,11]. The low specificity occurs because of cross-reacting organisms including Bordetella, Pseudomonas, Moraxella-type organism, and other gram-negative bacteria [12,13]. Specificity can be enhanced with the addition of 2-mercaptoethanol (2-ME), which inactivates IgM [2]. If the sample is still positive after the addition of 2-ME, another testing method should be used to verify the result. If this reaction is negative, it should be repeated 15–45 d later to ensure that the false positive was due to a cross-reaction and not to an early infection [3].

The most accurate serological test currently available is the agar gel immunodiffusion test (AGID). Because cytoplasmic protein antigens are more unique to Brucella species than are cell wall antigens, the AGID test using cytoplasmic antigens is more specific [14]. A positive result with AGID is considered definitive for a diagnosis of canine brucellosis. The AGID test is positive in infected animals from 12 wk after infection to 36 mo after the animal becomes abacteremic [4,7].

Other tests utilized to diagnose *B. canis* include the Tube Agglutination Test (TAT), IFA, and PCR [2]. These tests have varying degrees of sensitivity and specificity and most require at least 6–8 wk post infection to become positive.

Treatment for *B. canis* with antibiotics is not encouraging, as this has not been shown to provide a long-term cure [4,15,16]. If antibiotics are employed, use of a single antibiotic regime has not been shown to be successful and is not recommended [11,17]. Some success has come from a combination of antibiotics of the tetracycline family and dihydrostreptomycin [2]. Despite lengthy treatment regimes, resolution of infection is difficult, due to the intracellular location of the Brucella organism [18].

Pet animals that are housed singly may be neutered and antibiotic therapy attempted, but the owners should be aware of the zoonotic potential of this disease, particularly in young and immunosuppressed individuals.

Control of *B. canis* in a kennel includes (i) confirmation of disease; (ii) quarantine of the kennel; (iii) determination of the source of infection; (iv) elimination of the mode of transmission in the kennel; (v) identification and culling of infected animals; and (vi) implementation of practices to prevent further outbreaks [16]. Animals in a kennel should be tested negative for three consecutive months before the kennel can be declared clear of the disease [4].

Bacterial infection in general as a cause of pregnancy loss is rarely reported in cats [19]. There is little information available in the literature regarding Brucella infections in cats. A serological study of cats in animal shelters showed an incidence of 0 to 11.4%, but bacterial isolation was not attempted [20]. An outbreak of brucellosis in a small town was traced to a domestic cat and *B. suis* was isolated after blood culture [21]. However, Brucellosis does not appear to be an important cause of pregnancy loss in queens.

### 2.2. *Campylobacter*

A recent study reported the prevalence of campylobacter from rectal swabs taken from both household and stray dogs as 2.7 and 23.8%, respectively [22]. *Campylobacter jejuni*, a gram-negative bacillus, was the most prevalent species identified. There are few reports of campylobacter abortion in bitches. In one case, premature labor started on Day 45 of gestation, resulting in one live and two dead puppies [23]. The bitch had no systemic signs of illness. In another report of *C. jejuni* abortion from three German Shepherd...
bitches, the main clinical sign was a profuse and odorless hemorrhagic vaginal discharge [24]. Definitive diagnosis of campylobacter abortion includes culturing of the organism from fetal or neonatal tissues, including stomach or stomach contents, as well as from placenta and vaginal swabs from the bitch [23]. Special incubation requirements are necessary to culture this organism, including selective media and an atmosphere of reduced O₂ and increased CO₂ [23]. Antibiotic treatment can be determined based on culture and sensitivity results. Antibiotics that have been reported to be effective include tetracycline and chloramphenicol [14]. Other antibiotics that have been reported to be effective include erythromycin and neomycin [25]. Other antibiotics that have been isolated from apparently healthy cats [28], but to this author’s knowledge, there are no reports of C. jejuni abortion in queens.

2.3. Salmonella

Salmonellae are mobile, non-spore forming, gram-negative bacilli of the family Enterobacteriaceae [14]. Salmonellosis causes mild to severe gastrointestinal disease in humans [29]. A recent survey showed the prevalence of fecal shedding of salmonella in household and stray dogs was 2.1 and 6.3%, respectively with Salmonella duesseldorf the most dominant serotype [22]. Furthermore, S. enteritidis and S. typhimurium have also been isolated from screening studies [30]. Other surveys have shown a prevalence of 20%, with S. typhimurium and S. anatum the most commonly isolated serotypes [31]. S. panama has been isolated from aborted puppies [32].

Nonclinical salmonellosis occurs in most cases, but the severe form of the disease is manifested by diarrhea, vomiting, fever, depression, abortion and death [31]. Definitive diagnosis is accomplished by culture of fetal tissues and membranes. Drugs that have been suggested for treating salmonellosis include chloramphenicol, trimethoprim-sulfonamides and amoxicillin [25]. Salmonellosis can result in severe clinical signs in humans, especially in immunocompromised individuals.

Salmonella abortion in queens is rarely reported. A report on feline stillbirth associated with S. typhimurium described the feeding of raw chicken to the queen during gestation [33].

2.4. Escherichia coli

Escherichia coli is the most common bacterium isolated from the canine vagina and is also commonly cultured from the uteri of bitches with metritis and pyometra [14]. E. coli has been reported in a bitch that aborted on Day 41 of gestation with vaginal hemorrhage and anemia [34]. E. coli produces an endotoxin that has been shown to be an abortifacient in other species and may result in pregnancy loss in the bitch [14]. Diagnosis includes culturing the organism. However, E. coli has been isolated from the genital tract of normal bitches [35] and queens [36], and unless there are pre-existing or unhygienic conditions, incidence of pregnancy loss should be rare.

2.5. Streptococci and other bacteria

Beta hemolytic streptococci and Pasteurella multocida, among other bacteria, have been shown to be common isolates from vaginal swabs of bitches with no evidence of reproductive disease [35]. Similar findings have been reported in queens. Beta hemolytic streptococci have been isolated from a group of bitches with a history of abortion, infertility and neonatal death [37]. Group G Streptococcus canis is a zoonotic pathogen that has been reported to cause reproductive tract infections and abortion in dogs, as well as toxic shock and neonatal sepsis in cats [38–40]. Group G streptococci are considered normal flora of the skin, pharynx, upper respiratory tracts, and genital tracts of cats and infections are rare. Pleuritis and bronchopneumonia were reported in an outbreak of Group G streptococci in a cattery, and the source of the infection could not be determined [41].

Listeria monocytogenes was suggested as a cause for abortion in a 3-y-old beagle bitch that aborted after being presented for lethargy, depression, and a brown vaginal discharge [42].

Abortion, meningitis, and uveitis have been reported in dogs with acute infections of leptospirosis [43]. Dogs are considered to be a maintenance host for infection by serovars icterohaemorrhagiae, canicola, and grippotyphosa. Dogs are an incidental host for infection by serovars autumnalis, australis, tarassovi, ballum, bataviae, and bratislava. Infection in an incidental host is typified by low susceptibility, severe pathogenic effects, and poor transmission. The most common form of leptospirosis in dogs appears clinically as infertility and abortion in breeding colonies and is associated with serovar bratislava infection [44].
Leptospires are typically transmitted though urine and, rarely, venereally. Infection occurs after the organism penetrates mucous membranes or abraded skin. Clinical disease in cats is rare, but serologic surveys suggest that infection does occur in this species. Leptospirosis can affect most mammals and is a zoonotic disease [44]. Humans are an incidental, dead-end host for leptospiiral infections.

*Mycoplasma* and *Ureaplasma* species are the smallest free-living pathogens of animals, and primarily inhabit the mucous membranes of the respiratory and urogenital tracts [45]. The *Mycoplasma* species are gram-negative cell wall-free bacteria, and are frequently associated with diseases of the joints, respiratory tract and urogenital tract. In dogs, mycoplasmas and ureaplasmas have been associated with reproductive disease, including poor conception rates, early embryonic death, fetal resorption, abortion, stillborn pups, weak pups, and neonatal death [46,47]. In utero transmission and infection has been described [48]. These microorganisms are among the recognized normal flora of the vagina [49], and can be recovered from over 60% of clinically normal dogs [47].

The pathogenic *Mycoplasma* species are host-adapted to one or two animal species. *Mycoplasma canis* has been associated in dogs with urogenital tract infections [50]. It has been reported to cause purulent endometritis following intrauterine inoculation [51].

Experimental infection with *T-strain mycoplasm* resulting in abortion and kitten death has been reported [52]. *Mycoplasma* was inoculated into pregnant queens and subsequently recovered from heart blood of kittens that were aborted [53].

*Chlamyphilia felis* is an aerobic gram-negative bacillus and an obligate intracellular pathogen that causes feline pneumonia [45]. *C. felis* primarily infects epithelial cells of the conjunctiva and upper respiratory tract and transmission is via aerosol. Clinical infections are characterized by anorexia, depression, and serous discharges from the eyes and nose, which often becomes mucopurulent due to secondary bacterial infection. Infections in adult cats are often mild and subclinical, and neonatal kittens are more susceptible than adults. Latent infection occurs in some recovered cats, leading to enzootic infection in catteries [54]. There is also weak evidence that chlamydiae may also be capable of causing reproductive tract disease and lameness in cats [55]. Chlamydiae have been experimentally inoculated into the oviducts of cats and this produced acute disease characterized by hyperemia of the tissue and pronounced polymorphonuclear leukocyte infiltration [56]. Although several studies have suggested a role for *C. psittaci* in reproductive disease in cats [57–59], a more recent study suggested an association with FHV-1 infection rather than with *C. psittaci* [60]. The authors found that cats with FHV-1 were much less likely to be positive for feline *C. psittaci* than cats without FHV-1, and cats positive for *C. psittaci* were much less likely to be positive for FHV-1 than those negative for *C. psittaci*. These observations suggest that the presence of *C. psittaci* interferes with the replication or detection of FHV-1, or that FHV-1 infection interferes with the replication or detection of *C. psittaci*.

Ocular infections in humans have been caused by *C. felis* [45], and although the zoonotic potential of these organisms appears low, some precaution is warranted when handling affected cats.

Other bacteria have been associated with abortion in dogs, but implicating a bacterial isolate as a cause of pregnancy loss can be difficult, since many bacteria are normal flora from the cranial or caudal vagina.

### 3. Protozoal causes of pregnancy loss in the bitch and queen

#### 3.1. Toxoplasma gondii

*Toxoplasma gondii* is a protozoan parasite that is capable of infecting all warm-blooded animals via congenital infection, ingestion of infected tissues and ingestion of oocyst-contaminated food [14]. Cats are the definitive hosts and shed non-sporulated oocysts in feces. Dogs may play a role in mechanical transmission of the parasite.

*T. gondii* has been demonstrated experimentally to infect puppies in utero following intravenous or intraperitoneal administration of the gravid bitch with a suspension of tachyzoites [61]. Infected live puppies were delivered 4–6 d after inoculation of the dams; this coincided with signs of systemic illness in the bitch, including depression, anorexia, diarrhea, and ocular and nasal discharge. The pups died soon after birth.

In the queen, experimental trials have failed to demonstrate transplacental infection of kittens following oral infection of queens before or during pregnancy [62,63]. Subsequent trials have suggested transplacental transmission may be possible [64–66].

Abortion in queens from *T. gondii* has been reported following maternal signs of emaciation, lymphadenopathy, dyspnea, lethargy, diarrhea and central nervous system disturbance [53]. Toxoplasmosis does not appear to be an important cause of fetal death in cats, except through debilitating systemic illness in the pregnant queen [1].
Definitive diagnosis of toxoplasmosis involves demonstrating *T. gondii* cysts histologically in fetal tissues. Prevention of exposure to toxoplasmosis is preferred to treatment [19] and involves not allowing dogs and cats access to raw meat in which *T. gondii* cysts may be present.

3.2. *Neospora caninum*

The dog is the definitive host of the protozoan parasite *Neospora caninum*, and in many parts of the world, infection in dogs is relatively common, as determined by serology [67]. Seroprevalences in dogs range from 0 to 20%, however reports of clinically affected dogs are infrequent [67]. Although it is unknown whether *N. caninum* is an important cause of naturally occurring canine abortion, transplacental transmission of this parasite has been demonstrated [68,69]. Live infected puppies have been born and these puppies had slight deficits in proproception, increased muscle tone and spasticity in both pelvic limbs [70]. Antemortem diagnosis is difficult. The diagnosis of *N. caninum* can be confirmed by histology, immunohistochemistry, the use of molecular techniques, on biopsy material or on post mortem examination [71]. Feeding raw meat is a potential risk factor for infection of dogs. Reported treatments include clindamycin and potentiated sulfonamides [71]. Although antibodies to *N. caninum* have been reported, the parasite has not been detected in human tissues [71]. Thus, the zoonotic potential of this parasite is uncertain.

The author is unaware of any reports of *N. caninum* abortion in queens.

3.3. Other protozoa

Leishmaniasis has been reported in a case of abortion in a 1.5-y-old Coonhound [72]. No clinical signs were noted prior to the abortion and physical examination at presentation was normal except for a green and red vaginal discharge. Severe lesions were evident in the placenta from trophoblast necrosis, which were heavily parasitized with protozoa. *Leishmania infantum* was diagnosed based on the finding of amastigotes in placental trophoblasts and the detection of serum antibodies against *L. infantum*.

4. Conclusions

Due to the zoonotic potential of many organisms that may cause pregnancy loss in the queen and bitch, diligence is required to investigate any cause of pregnancy loss to determine if bacteria or protozoa may be the underlying etiology. *B. canis* appears to be the most important bacterial cause of canine pregnancy loss, and should be ruled out in all cases in which this occurs. The most accurate test available for diagnosis of *B. canis* is the AGID. Antibiotic treatment is not recommended. Other bacterial agents may cause maternal illness and are diagnosed by culturing the organism from fetal tissues and fluids. Although cats are the definitive hosts of *Toxoplasma gondii* and this organism is a common cause of pregnancy loss in other species, abortion has only been reported in queens after infection results in material signs of emaciation and debilitation. Transplacental transmission of *N. caninum* has been demonstrated, but it is unknown whether this organism is an important cause of pregnancy loss in the bitch.

References


