CHAPTER
21

Infectious diseases linked to the reproduction of canids and felids

https://doi.org/10.56238/alookdevelopv1-021

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ABSTRACT
The growing demand for companion animals such as dogs and breed cats has mobilized the trade, causing the number of kennels and cats to increase. In these establishments, there are some losses in the production of the reproduction of these animals. There is also a concern to keep some canids and wild felids that can sometimes be at risk of extinction or very close to it, with some in captivity enabling research of pathologies that can intervene in their procreation. Based on studies it is possible to verify that there are infectious diseases capable of harming in some way the reproduction of canids and felids, such as herpesvirus, toxoplasmosis, brucellosis, feline leukemia virus, and feline immunodeficiency virus.

Keywords: canids, felids, infectious diseases, reproduction.

1 INTRODUCTION

Brazil has the second-largest population of dogs, cats, and ornamental songbirds worldwide and is the fourth-largest country in the total pet population (ABINPET, 2014). In this Brazilian scenario of prominence in the population of dogs and cats, there are establishments specialized in reproducing animals for commercial purposes.

The knowledge of the reproduction of canids and wild and domestic felids is of paramount importance for their preservation, trying to curb the extinction of the species, so canids and domestic felids are used as models of study.

Reproductive problems such as miscarriages, low conception rates, underdeveloped puppies, and stillbirths are common situations in companies specializing in animal reproduction. These companies have been increasingly concerned with the improvement of breeds, modernization, and use of biotechnologies available for each species, however, significant losses in the activity have occurred due to dysfunctions in reproduction caused by infectious agents (MAGNABOSCO, C., 2006).

The most common infectious diseases that cause reproductive problems in canids and felids are brucellosis, herpesvirus, toxoplasmosis, erlichiosis, and leptospirosis. *Brucella canis* and canine herpesvirus keep the carrier animal healthy but remain a potential transmitter for susceptible animals (DAHLBOM, et al., 2009).

The objective of this study is to review the main infectious diseases that cause reproductive disorders in domestic and wild canids and felids, given a greater focus on domestic ones, with their clinical signs, the establishment of a diagnosis and treatment.

Infectious diseases linked to the reproduction of canids

Canine herpesvirus type 1 (CaHV-1)

Canine herpesvirus tippo 1 is a double-stranded DNA virus belonging to the subfamily Alphaherpesvirinae (DECARO et al., 2008). This pathogen is widely disseminated worldwide among canine populations, causing infertility, abortions and severe systemic disease in puppies.

The host species of CaHV-1 is restricted to domestic dogs although there are reports of wild canids as carriers of the virus (DECARO; MARTELLA; Buonavoglia, 2008; LEDBETTER et al., 2009).

Transmission occurs by direct contact of dogs with excretions and secretions (ocular, nasal and genital) of infected animals or by fomites and, transmission to puppies can occur during their passage through the birth canal, the transplacental route, or oronasal secretions of the female (GALOSI, 2007; Greene, 2012). A peculiarity of this type of virus is its ability to remain in latency, that is, it can be reactivated in cases of low immunity, in stressful situations, even in the period when the female is pregnant, in concomitant diseases or use of corticosteroids, so in these periods of reactivation can transmit the virus to other animals, collaborating to keep the virus in nature.

Animals may be asymptomatic or show signs and symptoms such as balanoposthitis, abdominal pain, puppies becoming lethargic and stopping nursing, embryonic resorption, infertility, miscarriages, neonatal mortality and vulvovaginitis.

The diagnosis of CaHV-1 infection is established through anamnesis, associated with clinical findings due to the presence of papules and vesicles on the genital and respiratory mucous membranes, necropsy findings, and laboratory techniques (CARMICHAEL; Greene, 2006). Being the "gold standard" for diagnosing viral isolation in cell culture, and since there is no vaccine, serology helps a lot.

There is still no effective treatment, what is commonly done is supportive therapy aimed at decreasing secondary bacterial problems.

Brucellosis

Brucellosis is an infectious disease with a zoonotic character that has been described in the literature since 1966 causing reproductive problems in dogs. Dogs are definitive hosts for *B. canis* infection (NELSON, R. W.; COUTO, G., 2010).

Canids can be infected by 4 species of *Brucella* which are: *B.canis, B.abortus, B.suis, and B. melitensis.* *B. abortus* can infect wild or domestic canids through the ingestion of aborted tissues or fetal remains of infected cattle, transmitting the bacteria through mating and oronasal contact (HOLLET, 2006).

B.canis infection has a compromising role mainly in reproduction, but lymphadenopathy can be observed, the animals do not have fever. Miscarriage after about 45 days is the most commonly reported clinical sign of *B. canis* infection in canid females.

Fetal death occurs at any time during pregnancy and occasionally a litter is born, but they usually die a few days after birth. In males, infectivity, scrotal enlargement, and epididymal enlargement are usually transitorily at the onset of infection. Abnormalities in seminal quality occur within 5 weeks of infection and become pronciada for 8 weeks (NELSON, R. W.; COUTO, G., 2010).

The main mode of transmission is by the venereal route with high propagation by the number of bacteria eliminated in the reproductive secretions. The disease can occur in animals of any age, but a predisposition to this bacterium has been described by young and sexually mature animals (HOLLET, 2006). The other forms of transmission are oronasal, conjunctival, and artificial insemination.

Diagnosing animals with brucellosis is very important because infected animals are a source of infection by eliminating the agent in their secretions. The diagnosis of B. *canis* infection is suggested by the history of miscarriage in females, infertility and seminal abnormalities in the male, and the relative absence of physical abnormalities (NELSON, R. W.; COUTO, G., 2010).

The diagnosis is confirmed by the identification of the *B.canis* microorganism in culture or by PCR. Serological results should be confirmed with direct methods. Materials for diagnosis are blood, post-abortion vaginal discharge, and semen. Blood culture or PCR is the best method for preoce identification of infection (2 to 8 weeks) (NELSON, R. W.; COUTO, G., 2010).

Antimicrobial treatment rarely results in a cure, so prevention is the best way to control it. The use of antibiotic therapy and castration of positive animals is essential to eliminate genital secretions, but not by other routes. The prevention of *B. canis* in dog breeding should always happen because the spread of the disease is fast and because it is the only form of control (KEID, 2006).

Toxoplasmosis

Toxoplasmosis is a zoonosis in which the infectious agent is a protozoan, *Toxoplasma gondii*, very worrisome during pregnancy especially in women, due to the predilection of this protozoan for fetal tissues.

This protozoonoze is widespread throughout the world and affects almost all homeothermic beings, with the felids being its only hosts in definitive, promotes significant economic losses due to reproductive disorders such as fetal resorption, abortions in different gestational phases, fetal mummification and stillbirth (BRESCIANI, 2003).

Dogs can become infected orally, with the ingestion of animal tissues containing protozoan cysts, by the ingestion of oocysts eliminated in the feces of cats and by congenital, transplacental infection, the latter not being very common but the one that can finally bring disorders such as abortions, stillbirths or neonatal mortality. There are also other non-common forms such as organ transplants and blood transfusion. In dogs and cats the infection by ingestion of small mammals and birds is important, especially in semi-domiciled animals, loose and fed with raw meat (DUBEY, 2006).

In dogs the appearance of the disease is marked by fever, lassitude, anorexia, diarrhea, pneumonia and neurological manifestations, infection may occur along with distemper or vaccination against distemper (URQUHART; et al., 1996). In the dog is uncommon the clinical manifestation of the disease.

For diagnostic purposes, the main method is the serological, or parasitological feces is not very reliable and there is still the possibility of detection of tachyzoites in intracellular inclusion corpuscles.

There is still no excellent treatment, but clindamycin is well-used in both dogs and cats and is also an auxiliary therapy in cases that affect the animal's eyes. A combination of the drug pyrimethamine with sulfadiazine has been described as effective against tachyzoites, but not against bradyzoites, but it is quite toxic in cats (URQUHART; et al., 1996). For animals that have a guardian it is possible to prevent, especially by avoiding giving them raw or undercooked meats.

Leptospirosis

Leptospirosis is an infectious disease considered important in public health because it is a zoonosis. Leptospires are filamentous spirochetes, 0.1 to 0.2 μm wide by 6 to 12 μm long, that infect animals and humans (NELSON, R. W.; COUTO, G., 2010).

Water contaminated with urine, sewage and manure are important modes of transmission of leptospirosis. Summer is the season of the year where the incidence of leptospirosis increases, due to rains and flooding of urban areas, being common the occurrence of epidemic outbreaks in times of higher rainfall (COIRO et al., 2011).

Canids are intermediate hosts, reservoirs and sentinel animals of various serovars. In Brazil and most of the world, the serovarieties *Canicola and Icterohaemorrhagiae* have been associated with canine leptospirosis (COIRO et al., 2011).

The mode of infection is by ingestion of materials contaminated with the bacteria, and penetration of the agent by skin continuity solutions, via transplacental or venereal route. Dogs of any age, breed or gender can develop leptospirosis if they are not previously immunized (NELSON, R. W.; COUTO, G., 2010).

Clinical manifestations in canids are acute, chronic, and subclinical. The predominant form is acute and febrile, accompanied or not by enteric, renal or hemorrhagic manifestations. (NELSON, R. W.; COUTO, G., 2010).

Leptospirosis is an agent commonly involved in reproductive problems, miscarriages and infertility (GREENE; Carmichael, 2006). The febrile syndromes and jaundice that causes miscarriages, neonatal death and death of newborns. The serovariety associated with reproductive diseases in canids is Bratislava.

The diagnosis is based on a well-conducted anamnesis, whether the animals have been vaccinated or not and laboratory tests that are: PCR, bacterial isolation, and serological ELISA-IgM and SAM. According to NELSON, R. W.; COUTO, G., 2010, the organism is not seen in the urinary sediment by ordinary light microscopy.

Prevention is through vaccination of animals, not coming into contact with the environment that can be a disseminator of the bacteria. Treatment is with antibiotics such as penicillin, streptomycins, and doxycycline. Treatment with doxycycline prevents miscarriages and renal overloads while vaccination, containing specific bacteria, prevents reproductive diseases (GRAHAM; TAYLOR, 2012).

Ehrlichiosis

It is a bacterial disease transmitted by vectors that are *the Rhipicephalus sanguineus,* brown dog tick. The vector concomitantly transmits *Anaplasma platys* and *Babesia canis* which cause co-infection and in domestic canids cause thrombocytopenia. Some species of the genus *Erlichia*, including those that parasitize dogs, were transferred to the genus Anaplasma (FRUET, 2005).

The species that infects felines has not yet been characterized, but the genomic material of E. *canis* has been amplified and sequenced from felines and the vector is not known.

Clinical disease due to ehrlichial infection can occur in any dog, but the severity varies according to the organism, host factors, and presence of co-infection (NELSON, R. W.; COUTO, G., 2010). Clinical signs in dogs are: anorexia, apathy, polyuria, polydipsia, arthritis, pale coloration of

the mucous membranes, hepatomegaly and splenomegaly, and corneal opacity. In reproduction, the clinical importance is the non-reproductive activity due to weakness in females and the interest of males.

Diagnosis is through clinical and hematological changes, but the definitive diagnosis is through IFAT and Western blotting serological tests, molecular tests can be done such as PCR, and bacteriological isolation. In indirect immunofluorescence testing, seropositivity begins between 7 to 21 days after infection and reaches maximum levels 80 days and persists unless treatment is carried out (FRUET, 2005).

Treatment is through antibiotic therapy, those used are tetracycline, oxytetracycline, doxycycline, and antiparasitics such as imidocarb. Corticosteroids can be used to preserve vascular integrity or platelet function in the chronic phase. Quinolones are not effective in the treatment of *E. canis* infection (NELSON, R. W.; COUTO, G., 2010).

Mycoplasmosis

Mycoplasma and Ureaplasma are members of the normal flora in the canine vagina, foreskin and distal urethra (RICHARD W., et al, 2010). In Brazil, there are not many reports of mycoplasmosis in dogs and there is still no differential between the prevalence of *Mycoplasma* isolation from animals considered healthy and normal from that found in animals with reproductive disorders.

It is known that immunocompetent dogs do not show clinical signs, unlike immunosuppressants that may present: fever, weight loss, anorexia, lethargy, pallor of the mucous membranes, severe anemia that is capable of being fatal can occur. The laboratory findings of animals with mycoplasmosis may also present reticulocytosis, polychromasia, hyperbilirubinemia and bilurrubinuria, spherocytosis, and self-agglutination (STOCKHAM & SCOTT, 2011). The diagnosis of canine mycoplasmosis can be made from blood strains of samples collected peripherally in the animal, in addition to molecular tests such as the polymerase chain reaction of whole blood (COSTA, 2011). A therapeutic diagnosis can also be made.

The treatment is done with the use of tetracyclines and fluoroquinolones, and in some cases, enrofloxacin or azithromycin may be used.

Other infectious diseases can lead to problems in the reproductive system of canids such as distemper, parvovirus, *infestation by Toxocara canis, Ancylostoma caninun and Dirofilaria immitis*. For these cases, emphasis should always be placed on prevention with vaccines and regular deworming of animals, especially those of the company, where the spread can occur devastatingly, culminating in unnecessary and avoidable losses.

Infectious diseases linked to the reproduction of felids

Infectious diseases linked to the reproduction of felids have not been studied as much as those linked to the reproduction of canids, but some have been identified as agents of pregnancy loss, especially viral diseases.

The infectious diseases that can cause pregnancy loss in feline females are divided into viral diseases (feline panleukopenia virus (FPL), feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), and feline herpes virus-1 (HVF-1), bacterial (coliforms, Streptococcus spp., *Staphylococcus* spp., and *Salmonella* spp.), and protozoa (*Toxoplasma*). (LITTLE, 2015)

The loss of pregnancy may be by direct action of the agent or secondary to systemic disease and weakness.

Feline herpesvirus-1 (HVF-1)

HVF-1 is a α-herpesvirus that infects the upper respiratory tract of domestic cats, stimulating a disease known as feline viral rhinotracheitis. FeHV-1 infection is distributed worldwide. In Brazil, the occurrence of infection and disease has been reported in several regions. The virus has already been isolated from cheetahs and lions and positive serology has also been demonstrated among captive-bred wild cats, which are also susceptible to the virus (FRANCO et al, 2017).

The transmission of the agent occurs mainly by direct or indirect contact with nasal discharges. The virus can also be transmitted by aerosols and, less frequently, by contaminated fomites. Cats carrying latent infection are the reservoirs of FeHV-1 and constitute the main source of dissemination of the agent in cattle and animal shelters (FRANCO et al, 2017).

According to HOOVER (1971), FeHV-1 can produce placental lesions, fetal death and fetal infection when introduced experimentally intravenously in pregnant cats.

The feline herpesvirus-1 (FHV-1), known, causes abortion in cats, probably due to weakness and not direct effects on the fetus and placenta (VERSTEGEN et al, 2008). Cats who become acutely ill during pregnancy, especially with fever, anorexia and dehydration, are at greater risk of pregnancy loss (LITTLE, 2015).

Although FHV infection causes miscarriage in pregnant cats, the virus is not normally recovered from the abortion material. Intranuclear inclusions are found in histological samples of the uterus, placenta and aborted fetuses of infected cats (NELSON, R.W; DALANEY, S.J., 2010).

The presumptive diagnosis can be established by history and clinical signs. Isolation of the virus can be performed by inoculation of nasal, conjunctival and pharyngeal secretions. Antibodies to FeHV-1 can be detected in serum, aqueous humor, and cerebrospinal fluid through seroneutralization

assay or ELISA. Treatment is supportive. In addition to vaccination, sanitary control should be emphasized (FRANCO et al, 2017).

Feline immunodeficiency virus (FIV)

The feline immunodeficiency virus is a *Lentivirus* that has a worldwide distribution and has also been isolated from wild cats, in addition to several isolates from domestic cats. The main form of transmission seems to be by direct contact, through saliva, and by bites during fights between animals. The virus can also be transmitted by semen during copulation and by the milk of infected females (oral infection) (RAVAZZOLO, A.P; da COSTA, U.M, 2017).

Pregnant cats with acute FIV infection transmitted the virus to their offspring through prenatal and postnatal routes. Intrauterine transmission has led to several pathogenic consequences, including disrupted fetal development, miscarriage, stillbirth, the birth of underweight puppies, and the birth of viable, virus-infected, asymptomatic but T-cell deficient puppies. 1995).

The clinical symptomatology observed in FIV-infected cats is nonspecific and reflects a general picture of immunosuppression. Pictures suggestive of immunosuppression should be investigated for the presence of antibodies, antigens, or viral nucleic acids. After the identification of the positive animals, the control can be carried out by their separation from the other animals, reducing the possibility of transmission. Limiting domestic cats' access to the streets can reduce their risk of acquiring the infection, but this is not always feasible. (RAVAZZOLO, A.P; da COSTA, U.M, 2017).

Feline leukemia virus (FeLV)

Feline leukemia virus (FeLV) is a single-stranded RNA virus in the family *Retroviridae*, subfamily *Oncovirinae*. The main route of FeLV infection is prolonged contact with the saliva and nasal secretions of infected cats, self-sanitization of cats, and sharing of water and food sources effectively result in infections. Transplacental, lactation, and venereal transmission are less important than casual contact (LAPPIN, 2010).

The feline leukemia virus (FeLV) can also be transmitted from the infected mother to her offspring in *utero* or the postnatal period (HARTMANN K, 2006, apud LITTLE, E.S, 2015, p.1732).

The most common clinical signs are those observed in cases of immunodeficiency and are due to opportunistic and repeated infections: chronic stomatitis and gingivitis, skin lesions and subcutaneous abscesses, chronic respiratory diseases and higher incidence of feline infectious peritonitis. (RAVAZZOLO, A.P; da COSTA, U.M, 2017).

Isolation of the virus is not widely used as a diagnostic method, although viral antigens can be detected in peripheral blood cells. Consequently, the most used technique in diagnosis is API, in blood

smears, using specific antibodies to capsid proteins. There are ELISA kits and immunochromatographic tests available for the detection of viral antigens. (RAVAZZOLO, A.P; da COSTA, U.M, 2017).

Infection control can be carried out from the correct diagnosis and necessarily involves the isolation of positive animals, preventing them from transmitting the agent to other animals. Vaccines prepared with the complete inactivated virus obtained from cell cultures are commercially available, as well as recombinant vaccines containing viral proteins expressed in heterologous systems (RAVAZZOLO, A.P; da COSTA, U.M, 2017).

Feline panleukopenia virus (FPL)

Feline panleukopenia is an infectious-contagious disease of worldwide distribution, which affects domestic and wild felids. Transmission occurs through direct or indirect contact of susceptible animals with infected animals or their secretions. The oro-fecal route is the main form of transmission (MORAES, M.P et al, 2017).

The cat may not show the classic signs of gastrointestinal disease, but the virus can infect rapidly dividing fetal cells. If infection occurs early in pregnancy, fetal death and resorption may occur. If the infection occurs in the middle of pregnancy, miscarriage may occur. Late pregnancy infections can cause neural damage, such as cerebellar hypoplasia in native puppies. All cats should be properly vaccinated against FPL before breeding. The use of vaccines against FPL with the modified live virus should be avoided during pregnancy and in the first month of life because the effects of vaccination on developing fetuses or newborn puppies may be similar to those of natural infection (LITLE, E.S, 2015).

The finding of intense leukopenia in cats with a history and clinical signs compatible with FPL is sufficient to establish a presumptive diagnosis. However, the definitive diagnosis depends on the performance of other tests, such as stool electron microscopy (EM), viral isolation, serology and immunofluorescence (API). In fatal cases, intestinal histopathological changes are considered pathognomonic. The treatment of FPL is typically supportive, as there are no specific antiviral drugs (MORAES, M.P et al, 2017).

Toxoplasmosis

Toxoplasma gondii is one of the most prevalent parasites among those infecting warm-blooded vertebrates. Only cats complete the life cycle of the coccid and pass the oocysts to the environment in the feces (LAPPIN, 2010).

Extraintestinal fatal toxoplasmosis can develop from overwhelming intracellular replication of tachyzoites after primary infection; the tissues often involved are hepatic, pulmonary, CNS, and pancreatic tissue. Puppies infected by the transplacental and trans mammary pathways develop the most severe signs of extraintestinal toxoplasmosis and usually die of lung or liver disease. They usually also develop eye disease (LAPPIN, 2010).

Although toxoplasmosis is not a major cause of pregnancy loss in cats, infected females may suffer miscarriage secondary to systemic disease and weakness (LITTLE, 2015).

The diagnosis is made by combining the following topics: demonstration of antibodies in serum, demonstration of IgM titers above 1:64 or a fourfold or greater increase in IgG titer, clinical signs related to toxoplasmosis, exclusion of other common causes for the clinical syndrome and positive response to appropriate treatment (LAPPIN, 2010).

Supportive treatment should be instituted if necessary. Cats with systemic signs of toxoplasmosis, such as fever or muscle pain, combined with uveitis, should be treated with anti-toxoplasma drugs in combination with corticosteroids to prevent secondary lens dislocation and glaucoma (LAPPIN, 2010).

Streptococcus, Staphylococcus and E.coli

Although the loss of pregnancy due to bacterial infection is uncommon in the cat, several species of bacteria that ascend to the interior of the uterus originating in the vagina have been associated, occasionally, with pregnancy loss, such as *Streptococcus, Staphylococcus and E.coli* (LITTLE, 2015).

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