Complications in canine pregnancy and their clinical approach
[Complicações da gestação na cadela - sua abordagem clínica]

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Introduction
In the bitch as in most other species death of conceptus can occur at any stage of pregnancy, resulting in partial or total resorption, partial or total abortion or retention of foetuses which can become mummified or be colonized by bacteria causing a pyometra. The type of outcome depends on what has caused embryonic/fetal death, the stage of pregnancy and fetal/maternal immunocompetence. Abortion is often difficult to diagnose as the bitch rarely show well defined clinical signs (often no signs at all or just a short lasting malaise or anorexia) but it can in rare instance become a life-threatening situation leading to shock. A relevant clinical problem is the lack of an early pregnancy test which would allow to monitor embryonic well-being and diagnose embryonic death. Also, the availability of a histopathological diagnosis on aborted fetuses is frequently hampered by lack of owner collaboration as well as by the fact that bitches often devour or hide dead fetuses. Aborted fetuses and/or placentae (the more the better) should refrigerated at – 4°C and shipped to the diagnostic laboratory within 24 hours of death.

Incidence and clinical signs
Incidence of canine embryonic resorption or spontaneous abortion is not well defined. On laparotomy it has been observed a 5-13% difference between n° of corpora lutea and n° of fetal vesicles. On ultrasound embryonic death is characterized by lack of vesicle growth, reduction of volume of the embryo mass, loss of vesicular roundness, reduction of volume and ecogenicity of embryonic fluids. Death of one or more embryos may not be detrimental to survival of the other embryos even on the same uterine horn. Clinical signs at this stage are frequently absent. Abortion is characterized more frequently than resorption by general clinical signs (from very mild signs to one or more of the followings: anorexia, fever, depression, vomiting, abdominal pain, shock) especially if not all dead fetuses are expelled. Fetal mummification can occur in absence of bacterial contamination, which is - again - often not accompanied by clinical signs, with mummified fetuses often found unexpectedly during a laparotomy or a survey abdominal radiograph.

Causes of prenatal mortality in the bitch
Death of conceptus can be due to developmental defect, maternal endocrine/metabolic imbalance, infectious disease of the reproductive tract, trauma, improper use of drugs.

Developmental defects
Karyotype abnormalities reported in the bitch which may be responsible for death of conceptus include monosomy and trisomy of the X chromosome, translocations and chimeraism. It is generally believed that chromosomal anomalies are very rare as a cause of embryo/fetal death, but there is a paucity of data due to the fact that it is often difficult to find a laboratory which performs karyotyping, and the test in itself can be quite expensive. The true incidence of this phenomenon in the canine could be higher than expected, and most researchers agree that the reduction in fertility observed in highly inbred populations is due to developmental defects. In case of a spontaneous abortion, karyotyping should always be performed. Incidence of congenital anomalies and spontaneous abortion is directly proportional to the degree of inbreeding.
Maternal endocrine imbalance

*Hypothyroidism* – Thyroid insufficiency, a relatively frequent endocrine disease in women, is associated with an increased risk of spontaneous abortion. Hypothyroidism is also relatively common in dogs and a relationship with low fertility in the canine, although still not yet confirmed, is strongly suggested. As in women, canine T3, T4 and thyroid binding globulins are higher during pregnancy. Spontaneous abortion in dogs could be related to hypothyroidism. Hypothyroid bitches should be considered to be at a higher risk of spontaneous abortion and the thyroid function of those undergoing thyroid treatment should be carefully checked during gestation.

*Luteal insufficiency* – In women luteal insufficiency (which is characterized by short cycles, low serum progesterone concentration during the luteal phase and insufficient endometrial development) is reported as a cause of spontaneous abortion. Luteal insufficiency occurs also in otherwise normal women and can be successfully treated with a repositol progesterone treatment. Although never actually demonstrated, luteal insufficiency has been hypothesized as a cause of spontaneous abortion in bitches. However, before a repositol progesterone treatment can be instituted in a bitch, it is necessary to rule out an infectious disease, a maternal health problem or fetal health problem, as a dying fetus should be expelled from the uterus as soon as possible. Administration of progestins such as norethisterone acetate to pregnant bitches have produced anomalies in female fetuses. Regumate has been proposed for supporting progesterone-deficient canine pregnancies.

*Diabetes Mellitus* – In the bitch (as in women and in a few other species) a serum progesterone rise is followed by a rise in serum growth hormone (GH) concentration. GH cause insulin resistance and hyperglycemia. In women, pregnant hyperglycemia is poteniated by a placental insulinase (a mechanism which has not been investigated in the bitch), leading to hypoglycemia which may (especially in diabetic patients) cause intrauterine death. In the pregnant bitch use of a diet with low caloric content is associated with smaller litter size.

*Hypo-Hypercorticalism* – Both disfunctions, although rare in pregnant women (because affected patients have anovulatory cycles), are characterized by a high incidence of fetal death when treatment is not performed during pregnancy. Although no information is available in the dog concerning incidence of fetal death in bitches with hypo- or hypercorticalism (also because these dogs are not generally bred), adrenal pathology should always be ruled out when considering a case of fetal death.

Infectious diseases of the reproductive tract

*Brucella canis* - Like all other brucella infections, Brucella canis infection causes endometritis, placentitis and late abortion in the female, epididimitis in the male). Following infection (characterized by mild clinical signs) B. canis proliferates in lymphnodes, spleen, bone marrow and Peyer patches, after which it invades the reproductive tract (uterus, epididymis, prostate). Pregnant bitches will either abort between 30 and 57 days gestation or have a high postnatal mortality. Fertility of breeding kennels may fall from 90% to 30% during the first year after an epidemic. Diagnosis is achieved through isolation of B. canis from the blood (leukocyte fraction) aborted fetuses, vulvar discharge, seminal fluid and various lesions of dogs with clinically evident disease. The Rapid Slide Agglutination Test is sensitive but not very specific, therefore all positive individuals must be rechecked with the Tube Agglutination Test, immunodiffusion, complement fixation or PCR. Treatment consists of associations of antibiotics (tetracycline + streptomicine, minocycline + streptomicine or oxitetracycline and streptomicine) but it is long and efficacy is not 100%. Following complete recovery a dog may become infected again. Because of costs, length and degree of efficacy of treatments, in the US it is recommended that affected dogs of breeding establishments are euthanized. B. canis infection has been reported in France in 1996.
Herpes Virus canis (CHV) - CHV is a DNA-virus whose growth is stimulated at temperature (T) of 35-37 °C, and inhibited at T ≥ 39°C. It generally causes disease only in immunocompromised individuals in which it is responsible for late abortion, neonatal septicemia and urogenital as well as respiratory (kennel cough) diseases. In adults dogs the virus replicates at the point of entry (genital or respiratory system) causing a mild disease (kennel cough or vaginitis) while pregnant bitches may abort showing signs of placentitis and fetal/neonatal infection. Fetuses may contract the infection while passing through the birth canal. The immaturity of the thermoregulatory mechanism of canine neonates creates optimal condition for the development of CHV.

CHV causes a weak and short-lasting immunologic response. T-lymphocytes are very important for the host’s defense mechanism, therefore whenever their function is depressed (i.e. during a parvovirus infection, an immunosuppressive treatment, pregnancy, the perinatal period, or during stress) CHV will become clinically evident.

Diagnosis of CHV has been historically difficult because of problems in isolating techniques and low serum titers during the clinical disease. The use of PCR techniques has solved almost all diagnostic problems, even if some authors believe that a negative PCR response does not mean that the animal does not harbor the virus (while a positive PCR response is unanimously believed to be 100% accurate). PCR is best performed on samples of fresh blood/semen or body fluid (vaginal/bronchial flushings). Samples of semen or vaginal flushings must be shipped to the diagnostic laboratory in liquid nitrogen. There is no specific treatment. Anti-viral drugs used in human medicine have not been tested in small animals. It is very important to keep neonates in a warm environment and have them suckle at least 4 times/day. The highest risk of infection occurs during the 3 weeks prior to and the 3 weeks after parturition. The same female may abort more than once, but generally colostral antibodies will protect puppies as long as they are kept in warm environment. Differential diagnosis of CHV include infectious hepatitis, acute toxoplasmosis, B. canis infection.

Other pathogens - Mycoplasma/Ureaplasma are part of the normal bacteria of the canine reproductive tract but can cause disease following experimental inoculation. Their incidence and role in canine infertility are unknown, also for the difficulties in isolating and culturing techniques. Other pathogens reported as a cause of abortion or found in aborted fetuses include E. coli, T. gondii, Campylobacter, b-haemolitic streptococcus, Chlamydia spp. and salmonella.

Trauma

Death of conceptus can be caused by a direct uterine trauma or indirect trauma to the mother or by an abdominal surgery, all of which may cause death of conceptus either directly (trauma on the conceptus) or indirectly through an early placental detachment. In pregnant women laparotomy may cause abortion especially if surgery is on the uterus or on contiguous organs. Although such a risk is possible in pregnant bitches as well, one should have checked fetal viability prior to the trauma as this may only precipitate an already compromised situation. A surgical procedure is reported in which some canine fetuses are removed and the remaining one are carried normally to term through administration of progesterone IM 2 days prior to surgery (Lowry, 1975).

Drugs

The most delicate period of the canine pregnancy is the first month during which organogenesis takes place. Prior to day 20-22 following ovulation (when implantation occurs and placental development starts) canine embryos are surrounded by “uterine milk”, a protein endometrial secretion which is in homeostatic equilibrium with the blood compartment, i.e. any substance that arrives in the bloodstream reaches the endometrium. Therefore, use of any substance during this time carries the potential risk of harming fetal development even though there is no risk associated for the mother. After placental development fetuses become more resistant to toxic
insults as most substance cannot reach the placental circulation unless they are present in high concentration and for a long time in the bloodstream. However, any drug that reaches the canine fetal circulation must be metabolised by the fetal kidney (in carnivores the fetal liver is not metabolically active) which in itself might threaten fetal survival. Aspirin, dexamethasone, bromocriptine, carbaryl, estradiol benzoate and cypionate, prostaglandin F2α and antiestrogen drugs are widely described as capable of causing embryonic/fetal death in the dog. The effect of various drugs on the canine pregnancy is reported in details by Papich (1989).

References