

INFERTILITY IN THE BITCH

Infertility in dogs and cats can be due to wrong breeding management, uterine disease, ovarian disease, failure of the male to achieve a complete mount, or poor semen quality. From a practical standpoint, fertility means achieving conception, then establishing a pregnancy through implantation and carrying the pregnancy to term. Although technically the process of delivering the foetus/es through parturition also influences fertility, dystocia is not commonly perceived from owners as a fertility problem, and therefore, it will not be dealt with here.

FACTOR INFLUENCING CONCEPTION AND PREGNANCY IN THE BITCH

Errors in breeding management, anovulatory cycles and ovarian/uterine problems are frequently encountered as a cause of infertility in bitches of all ages, while poor semen quality is often a feature of adult to older male dogs. The most common factors influencing the conception and Pregnancy are:

Breeding Management (breeding early or late)

Reproductive cycle disorders (anestrus, short cycles, and failure to ovulate)

Uterine Disease (deterioration of the uterine lining)

Poor Semen Quality (prostate disease, testicular disease or degeneration)

Failure to Achieve a Normal Mating (lack of experience, no coital lock, poor female receptivity)

Infection of the reproductive tract (Brucella canis, Herpes virus canis, bacterial infections)

Non-infectious causes of embryonic-fetal death (endocrine disease, chromosomal abnormalities, improper use of drugs)

Ovarian Disease (ovarian cysts or tumours)

BREEDING MANAGEMENT(INFERTILITY IN THE BITCH)

As most bitches ovulate on day 12 of their season, there is a widespread tendency of owners to assume that day 12 is the ideal breeding day for all bitches. As a matter of fact, some bitches ovulate early (such as on day 8, or 6 or even 4 from the onset of proestrus) while others may ovulate late such as on day 17, 19 or 22-24. One should never assume that a given bitch will ovulate on day 12 unless proven. Also, incidence of early or late ovulation is probably higher in the those bitches who are taken to the veterinarian with a presenting complaint of infertility with respect to the normal canine population; bitches ovulating on day 12 from the onset of proestrus will always conceive at the first mating and therefore will almost never be taken to the veterinarian because of fertility problems. The following data base should be recorded for all previous seasons for which information is available:

1. Date of onset of proestral bleeding
2. Date of onset of first receptivity
3. Breeding(s): dates, out/inside tie, AI, fresh vs frozen semen
4. Date of first refusal of mating
5. Male fertility, age, semen culture
6. *Brucella canis* antibody status of the bitch and dog
7. Pregnancy status at 28 days
8. Previous normal whelping(s)/litter(s)
9. Previous signs of false pregnancy
10. Previous reproductive disease
11. Previous hormonal therapy

Information collected through history can be used by the clinician to decide whether or not the bitch is cycling normally, whether or not she was bred/inseminated at the appropriate time and whether or not reproductive disease is present. Managing a canine breeding requires the client taking the bitch to the veterinary clinic as soon as the first signs of proestrus are displayed (vulvar discharge, male attractiveness) for a first check, and then coming back every 2-3 days to monitor how quickly the female is progressing towards ovulation through vaginal smears and serum progesterone assays. Vaginoscopy and ovarian ultrasound can be very helpful clinical tools in identifying and monitoring the ovulation process. When the first day of ovulation is identified, there are still a few days to achieve a breeding, thanks to longevity of canine oocytes (4-6 days following ovulation).

Performing vaginal cytology as well as checking the bitch's behaviour to look for onset of male receptivity is the 2 most practical ways of determining the best time for breeding. Owners should be instructed to bring their bitch to a male dog to check her behaviour regularly as soon as possible after proestrus onset as well as to have a vaginal smear taken from the veterinarian every 2-3 days. Breeding should be performed as soon as the bitch stands and/or as soon as her smear is fully cornified, in order not to miss early ovulators.

However, behaviour does not always correlate with vaginal cytology: some bitches will not stand to be mounted even though their smear is fully cornified. Provided that vaginal abnormalities (strictures, bands of tissue, hymen) are ruled out, serum P4 as well as using different male dogs (to rule out male preference) are helpful in such cases, although some bitches become receptive to mating only in mid to late estrus. Ovulation should always be timed using serum P4 assay every 2-3 days and the bitch should be bred when a high P4 value is observed (>5.0 ng/ml). Vaginal cytology should also be used to confirm serum P4 data (serum P4 kits which use a semi-quantitative colorimetric system are only 80% accurate) during and (most importantly) after breeding until the first day of cytological diestrus (D1) is identified, which occurs 6-8 days after ovulation.

REPRODUCTIVE CYCLE DISORDERS

Prolonged lack of heat or anestrus is sometimes observed especially in older bitches. Frequent cycling (3-4 heats/year) is also observed in bitches of all ages, and has been associated with infertility, although the mechanism involved is not yet clear. Anovulatory cycles occur fairly frequently (although there are no reported figures on their incidence) both at puberty as well as in the adult bitch. When a bitch experiences an anovulatory cycle, her reproductive behaviour is generally absolutely normal, i.e., she attracts male dogs, has a normal vulvar discharge and accepts breeding. Failure to ovulate can only be diagnosed by finding a low serum progesterone concentration after breeding.

UTERINE DISEASE

Uterine pathology is a common cause of failure to conceive both in bitches and queens. The bitch experiences 2 estrous cycles/year, with spontaneous ovulation, development of corpus luteum and progesterone secretion for about 2 months. The progesterone stimulation on the uterine lining (the endometrium) causes accumulation of secretion of endometrial glands with formation of cystic structures (cystic endometrial hyperplasia = CEH). Such cystic structures are very important for feeding the embryos, and if the female is not pregnant they normally regress towards the end the luteal phase (also called progestational phase or diestrus), leaving the endometrium free to regenerate and be ready for the next chance for a pregnancy. If the female is rarely if ever mated, these cystic structures will eventually persist, thereby making large sections of the endometrium unsuitable for the establishment of pregnancy. Uterine disease is not believed to be a problem in breeding establishments where bitches are bred and conceive on a regular basis, as pregnancy may have a protective effect on the endometrium. Unlike breeding bitches, the average intact bitch kept as a pet may experience problems in becoming pregnant if bred only as an adult dog, due to the deterioration of her uterine lining.

Canine pyometra is a disease characterized by presence of CEH and high serum P4 concentration. CEH is often characterized by prolonged and/or abnormal vulvar discharge at the end of estrus due to excessive bleeding from a hyperplastic endometrium. Presence of excess blood within the uterus facilitates bacterial contamination, which may lead to pyometra. Open cervix pyometra should be treated with specific antibiotics (as indicated by culture and sensitivity test on material obtained from a cervical swab) and PGF2a (100-150 mcg/kg) BID to be continued until the uterus is fluid filled and/or serum progesterone is > 2.0 ng/ml. Table n° 2 shows dosages of prostaglandins commonly used in bitches and queens. Pyometra has a higher incidence of occurrence in bitches not whelping regularly if compared to those who breed regularly, as well as a higher incidence of recurrence in the non pregnant bitch. Therefore, once the bitch has recovered from a pyometra she should be treated aggressively at the onset of the following proestrus with specific antibiotics for about 15 days or until after ovulation, bred with good management to a proven stud, and then spayed as soon as reproductive life ends.

Dosages of the most commonly used prostaglandins in bitches and queens:

Prostaglandin F2a	Daily dosage in the bitch/queen	N° treatments/day
Natural PGF2α or Dinoprost	Bitch--100 µg/kg (0.1 mg/kg) Queen--500 µg/kg (0.5 mg/kg)	2 2
Cloprostenol	Bitch--1-5 µg/kg (0.001-0.005 mg/kg) Queen--5 µg/kg (0.005 mg/kg)	1 1
Alfaprostol	Bitch-- 20 µg/kg (0.02 mg/kg)	2

Antiprolactinic drugs can also induce luteolysis if administered during the second half of diestrus. Below shows dosages of antiprolactinics commonly used in bitches and queens.

Dosages of the 3 antiprolactinic most commonly used in small animals. (*) There is no scientific information available for the queen.

Antiprolactinic	Daily dosage in the bitch/queen	N° treatments/day
Cabergoline	5 µg/kg	1
Bromocriptine	10-30 µg/kg (*)	2
Metergoline	500 µg/kg (*)	2

Progesterone antagonists act by blocking progesterone receptors, causing opening of the cervix and in most cases a resumption of miometrial contractility. They are reported to be very efficacious for closed-cervix pyometra.

POOR SEMEN QUALITY

Dogs ejaculate 500-2000 million spermatozoa diluted in 2-50 cc of seminal plasma. Quantity of spermatozoa as well as of seminal plasma varies according to body weight and testicular size, with Yorkshire terriers and Great Danes producing an average of 2-3 and 20-30 cc of ejaculate, respectively. Semen quality depends on quantity of spermatozoa present, their motility and morphology. Assessing semen quality is an easy task which can be performed in any veterinary clinic, provided that the male dog is accustomed to the technique or a bitch in heat is available to help him concentrate on ejaculation. Semen collection is generally performed through manual stimulation of the dog's penis through an artificial vagina (a latex cone connected to a plastic tube) or just wearing a latex glove in one hand and a smooth glass or plastic container in the other hand. Once collected, the semen must be kept in a warm environment (holding the tube in one's hands is enough) while it is being checked for motility (under a light microscope at 100X), morphology (under light microscope at 200-400X following staining with any cytological stain such as Diff Quick, haematoxylin-eosin or Leishman blue) and number of spermatozoa (using a haemocytometer such as a Neubauer chamber, Thomas chamber or Makler chamber). Poor semen quality can be found in adult to older male dogs, especially if suffering from prostate disease or following orchitis/epididymitis or scrotal trauma. Poor semen quality can be due to also to inbreeding causing early testicular degeneration.

FAILURE TO ACHIEVE A NORMAL MATING

Young stud dogs at their first attempts at breeding may sometime apparently look not capable of mounting properly, e.g., they may approach the female from her flank or from her head, or may spend a considerable amount of time pelvic thrusting without achieving an intromission. Although this should be considered part of the normal process of learning reproductive behaviour in young animals, it is considered abnormal when displayed by adult male dogs. Sometimes a male dog may achieve an incomplete intromission in which the bulbus glandis will engorge outside of the vulva. When this occurs, ejaculation may take place more caudally in the vestibule instead of in the most cranial aspect of the vagina, with a consequent loss of semen due to a retrograde flow of spermatozoa outside the vulva or to a higher degeneration rate of spermatozoa due to the acidic pH of the vagina. Not achieving an inside tie in the dog may be due to lack of experience, disease of the penis or lack of libido. When collecting history for a case of infertility it is important to check whether or not a "coital lock" or an "inside tie" (penis engorged and temporarily blocked into the vagina) occurred. Although outside-tie breedings may be fertile, an outside tie should always be ruled out when investigating causes of canine infertility. Partial or complete failure to accept breeding can also prevent normal mating to occur. If the bitch does not accept to be bred she might not be at the proper time for breeding, might have a vaginal septum or persistent hymen which causes her to feel pain at penetration or might have a behavioural problem (mate preference).

INFECTION OF THE REPRODUCTIVE TRACT

Infectious diseases of the canine reproductive tract which can be responsible for infertility include bacterial infection such as brucellosis due to *Brucella canis* (rarely *Brucella abortus* or *suis*), infection due to salmonella species, streptococci and *E. coli*; viral diseases such as herpes virus, distemper, parvovirus 1 and 2, and to the parasites *Toxoplasma gondii* and *Neospora caninum*. Incidence may vary depending on the country and the area/s within each country. *Brucella canis* and herpes virus are highly contagious. Other bacterial infections (salmonella, streptococcus, *E. coli*) and toxoplasmosis are less contagious and tend to be a feature of the individual bitch. Not much is known about the role of *Neospora caninum* in canine abortion. Herpes virus has always been known as a cause of abortion. A herpes virus vaccine has recently been introduced in Europe, to be used in pregnant bitches. The vaccine is supposed to be used repeatedly in pregnant bitches, initially during early pregnancy followed by a booster injection during the last third of pregnancy. The company claims that such a use is improving fertility in bitches which, if confirmed, would further substantiate the role of canine herpes virus as a cause of failure to conceive.

NON-INFECTIOUS CAUSES OF EMBRYONIC-FETAL DEATH

Endocrine diseases such as inadequate production of progesterone or thyroid hormones during pregnancy may cause abortion. Also, diabetes, adrenal insufficiency and other endocrine diseases may affect foetal viability. The improper use of drugs may also have an adverse effect on pregnancy. Chromosomal abnormalities are widely described as a cause of embryonic/fetal death in the dog. Collecting a whole blood sample and submitting it to a laboratory for karyotype should never be overlooked when dealing with an abortion case.

OVARIAN DISEASE

Ovarian disease (ovarian cysts or ovarian tumors) is a rare cause of infertility in bitches due to the fact that incidence of ovarian cysts or tumors is higher in adult to older bitches (the older the bitch the less likely she is to be used for reproduction). The most common presenting complaint of ovarian cyst or tumor is prolonged heat due to a high estrogen production. Ovarian cysts and tumors have occasionally been reported in bitches as young as 2-3 years of age

NORMAL OVARIAN FUNCTION IN THE DOG

The bitch exhibits estrus every 5 to 8 months, with no significant seasonal influence in most breeds. The puberal estrus occurs between 6 and 24 months of age, with average onset at 10-12 months. Stages of the estrus cycle include proestrus (3-17 days), characterized by ovarian follicular growth and sanguinous vulvar discharge; estrus (3-21 days), characterized by ovulation and receptivity to mating; diestrus (~60 days) characterized by luteal progesterone secretion in the pregnant and nonpregnant female; and anestrus (~4.5 months) which is a time of reproductive quiescence. The bitch is a spontaneous ovulator, ovulating primary oocytes, on average, 24-72 hours after a burst of luteinizing hormone (LH) secretion from the anterior pituitary, which burst coincides, on average, with onset of behavioural estrus. Both onset of proestrus and onset of estrus, however, are not precise indicators of ovulation in the bitch.

The bitch exhibits preovulatory luteinization, with elevation of serum progesterone to concentrations exceeding 1.0 ng/ml occurring as early as two days before ovulation.