

## R – Reproduction

### INFERTILITY IN THE BITCH

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In comparison to the last 10 or 20 years, veterinarians are now frequently requested to solve fertility problems in the dog, mainly due to the increased popularity of purebred dogs as well as for sentimental or financial reasons. In fact, breeders may be concerned about different kinds of problems which include but are not limited to true infertility (their bitches produce no pups after mating or Artificial Insemination), anoestrus or a low prolificity rate.

Many different problems can lead to infertility including hormonal problems, infectious diseases, congenital or acquired defects of the genital tract. We recommend that veterinarians follow a very strict progression, commencing with the most frequent cause to the most uncommon cause. In the bitch, things become even more difficult when we realize that apparent infertility can be due to very different situations which prove difficult to distinguish, such as lack of fertilization (no union between eggs and sperm) and early embryonic death.

#### 1. MISTIMED BREEDING

According to the vast majority of scientific publications, mistimed breeding represents by far the most common cause of infertility in the bitch. The incidence may vary between 40% to 80% of infertile bitches.

Although the following belief has been clearly proved erroneous in approximately 30% of bitches, many breeders are still convinced that a bitch will conceive when mated around the 12<sup>th</sup> day of the heat period. Actually, it has been clearly demonstrated that a bitch may ovulate as early as the 3<sup>rd</sup> or 4<sup>th</sup> day after the onset of pro-oestrus and as late as the 30<sup>th</sup> day of the heat period.

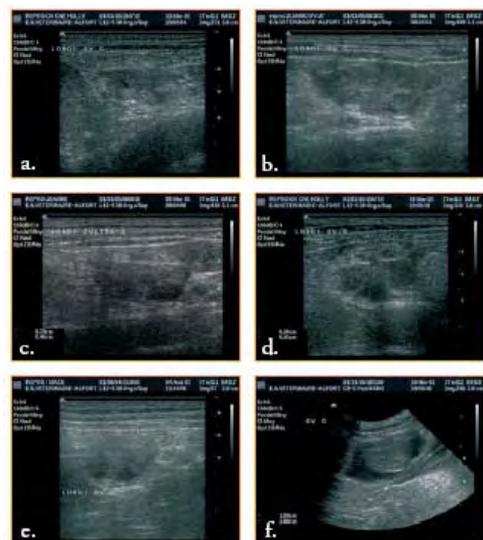
Clinical factors such as the increased swelling of the vulva and the decreasing bleeding of the genital tract at the time of the ovulation period may help veterinarians determine if bitches are obviously mated at a wrong time. But, these criteria are in no way precise enough.

Nowadays, numerous available techniques may be utilized to investigate the “optimal time for breeding”: vaginal cytology, endoscopic appearance of vaginal folds and progesterone assays are the most commonly used methods. Ovarian ultrasonography is especially indicated in infertile bitches, as it represents the most



*Ultrasonographic appearance of the ovaries during the late proestrus (preovulatory) period in the bitch.*

*Due to the large amount of anechoic fluid within the follicles, they become really easy to visualize, the follicular walls become thicker, around 1 mm in width. Depending on the size of breed, the size of the pre-ovulatory follicles varies between 6 to 9 mm.*



*Ultrasonographic appearance of the ovaries of the bitch at the time of ovulation. A complete disappearance of the follicular cavities (“follicular collapses”) can be visualized (photos a and b). However, in 50 % of the cases, some intra-ovarian hypoechoic structures persist (photos c and d). Often non-ovulated round follicles remain in the same ovary (photo e). In around 40% of the cases, some liquid is visualized between the ovary and the ovarian bursa in the hours following ovulation (photo f).*

accurate way to determine the precise date of ovulation (see ultrasound ovarian scanning below). This method also helps quantify the number of growing follicles as well as follicles undergoing ovulation and as such, it helps to evaluate the fertility potential of the bitch.

## 2. MALE INFERTILITY

After mistimed breeding, male infertility is the most common cause of conception failure in bitches presented with infertility. This is developed in the second lecture.

## 3. OTHER CAUSES OF INFERTILITY

As it is often ascertained in large animals, we suggest that veterinarians should first consider if infertile bitches show regular inter-estrus intervals or irregular ovarian cycles.

### 3.1. INFERTILITY WITH PROLONGED INTERESTROUS INTERVALS

The apparent prolongation of interestrus intervals occurs in dogs with a silent heat, defined as ovarian activity in the absence of overt physical and behavioral changes characteristic of canine estrus.

Among the hormonal causes of anoestrus we find hypothyroidism, hyperadrenocorticism, hyperprolactinemia, or bitches treated with hormonal compounds such as progestagens, androgens (racing dogs) or anabolic steroid compounds.

Ovarian cysts that secrete progesterone may cause prolonged interestrus intervals. The surgical removal of the cyst is often the best solution. Hormonal attempts using prostaglandins are not well documented in bitches.

Bitches housed in very bad environmental conditions (including a high concentration of animals, low luminosity, low quality food) may undergo prolonged interestrus intervals.

### 3.2. INFERTILITY WITH SHORTENED INTERESTROUS INTERVALS

This type of infertility may be divided into two major causes: bitches suffering from ovarian hyperstimulation (mainly follicular cysts or Granulosa cells tumor), and/or bitches showing a premature decline in progesterone during diestrus.

#### 3.2.1. Ovarian cysts or tumors

It is important to diagnose and remove these hormonally active cysts or tumors as quickly as possible for at least two reasons. First, it is necessary to cure them and try to restore fertility. Second, the secretion of high quantity of estrogens may act on the uterus as a potential

factor towards the cystic endometrial hyperplasia – pyometra complex, but also on the bone marrow in creating progressive non regenerative anemia.

**Follicular cysts** may be single or multiple; if multiple cysts are present in one ovary, the cysts do not communicate. The ovarian cysts in the bitch may be present in only one or both ovaries.

Estradiol assays during the pro-estrus period may be useful for practitioners who do not perform ultrasonography. The patterns of estrogen secretion are often modified.

Still, when possible, it is much more valuable to perform ovarian ultrasonography. Follicular cysts appear as focal hypoechoic to anechoic structures. Many authors consider that anechoic structures greater than 1cm are supposed to be cystic structures.

The treatment of choice of ovarian follicular cysts is ovariectomy or ovario-hysterectomy when the uterus is damaged. Some authors recommend induction of luteinization of the cystic follicles, using GnRH or hCG. We personally do not recommend such protocols, as they increase the progesterone plasma level after a prolonged period of estrogen secretion. Based upon our clinical experience, this treatment very often leads to the occurrence of pyometra in the following weeks.

Surgical removal of a cyst, or aspiration of a cyst with a fine sterile needle under laparotomy or ultrasonography may be new alternatives in therapy.

Granulosa cells produce estrogens; and therefore, it is not surprising that **GCTumours** often lead to infertility with prolonged heat periods.

(Note: **Exogenous estrogens** administered to elderly ladies receiving treatment after the end of genital activity with estrogens containing gels can penetrate through the skin of miniature breeds when they are frequently handled on the forearm and cause prolonged estrus signs).

#### Premature decline in progesterone

**Split heats** are defined as successive short proestrus signs, at intervals of 2 weeks to 2 months, associated with short interestrus intervals. This pattern is more often observed in young bitches and leads to no real infertility in the rest of the genital life of the bitch.

**Anovulatory cycles** are not frequent in bitches. In such anovulatory cycles, serum progesterone level never increases above 3.5 to 6 ng/ml. This explains why the following heat period will often occur earlier than usual.

Bitches may also suffer from hypoluteoidism, which is the lack of progesterone secretion

during pregnancy which makes the pregnancy impossible to maintain. Some breeds are well known to express **hypoluteoidism**, like Rottweilers and German Shepherds. Progesterone supply can be given parentally (progesterone in oil: 2 mg/kg every 3 days; ally-trenbolone...). In France, veterinarians often use oral micronised progesterone which is currently given to women.

A "**short anoestrus syndrome**" has also been described in Rottweilers and German Shepherds.

**Early embryonic or fetal death** remains most of the time impossible to detect, as no vulvar swelling occurs in general. Possible causes include endometritis, cystic endometrial hyperplasia, embryonic defects and possibly inbreeding. Our clinical data seem to show that it is often associated with a decline in blood progesterone concentration.

### 3.3. INFERTILITY WITH NORMAL INTERESTROUS INTERVALS

#### 3.3.1. HORMONAL PROBLEMS

Hormonal defects may be suspected also in bitches with regular interestrous intervals, and veterinarians should control the hormonal status of the bitch during the heat period and also during pregnancy.

#### 3.3.2. INFECTIOUS DISEASES

Many infectious agents have been suspected to induce infertility in bitches. However, a paucity of studies has been conducted in this field.

Several **viruses** have been shown to play a potential role in canine infertility. **Canine Herpes Virus (CHV)** is well known to have a pathogenic action on neonate pups. Several elements suggest however that CHV may well act on infertility in the bitch.

Transplacental infection by **Canine Distemper Virus** has been shown in experimental conditions. Recently, some papers have pointed out the potential incidence of a parvovirus **Minute Virus of Canines (CPV1)** on resorption during the first half of pregnancy.

The incidence of **bacterial infections** on canine infertility is better documented. **Canine Brucellosis**, which is well known as an abortive agent during late pregnancy, could also generate early embryonic or fetal death through endometritis.

Other **specific bacterial diseases** have been suspected to act on canine infertility. However, **usual genital bacteria** may play a real role on infertility. **Canine Mycoplasmas and Ureaplasmas** are commonly isolated in the

genital tract of fertile and infertile bitches. But it has been shown that there is a higher incidence of these agents in the vagina of infertile bitches. Many bacteria are commonly isolated from the uterus and the vagina of normal fertile bitches. Several studies barely demonstrate any difference in the composition of the vaginal flora between fertile and infertile bitches. But it has been shown that in case of vaginitis, there are significant qualitative and quantitative variations. Strong evidence exists that bacteria causing vaginitis may lead to infertility. It may well have been underestimated due to lack of specific clinical signs and due to the difficulty of the clinical examination of the vagina of the bitch.

The role of **parasitic infections** on infertility is better documented. Recent experimental data suggest that *Neospora caninum* could cause early fetal death in the bitch.

#### 3.3.3. DRUGS INDUCED INFERTILITY

In practice, many breeding bitches may be treated with drugs that may contribute to the decline of fertility. Steroid hormones and anti-fungal compounds may create hormonal defects in pre-puberal or adult bitches. Abortive drugs such as prostaglandins, antiprogestins and antiprolactinic substances have to be avoided during pregnancy.

#### 3.3.4. ANATOMICAL ABNORMALITY OF THE VULVA, VESTIBULE OR VAGINA

Some bitches do not manage to mate because of **congenital abnormalities** of the posterior genital tract (vulva, vestibule or vagina).

**Acquired diseases** or abnormalities of the posterior genital tract (scars after a bad parturition, episiotomy, violent mating...) may also lead to the lack of copulation.

#### 3.3.5. UTERINE PATHOLOGY

**Endometritis** is a common cause of infertility in mares. In bitches, however, it is hard to diagnose. Endometrial smears, eventually performed after endoscopic canulation of the cervix, may be valuable.

Bitches with **cystic endometrial hyperplasia (CEH)** are often infertile due to implantation failure after conception. Somehow, ultrasonography usually permits the visualization of the glandular endometrium. One successful therapy has been described with mibolerone oral administration, 30 microgrammes per 25 lb body weight daily during 6 months.

CEH often leads to pyometra, which may be treated in many cases by a mixed treatment using prostaglandins and antiprogestins

(aglepristone). A healing of the endometrium seems to occur, as many bitches may have successful pregnancies at their next heat period.

### 3.3.6. ABNORMAL SEXUAL BEHAVIOR

Many psychological factors may influence sexual receptivity in bitches. Some authors think that psychology may influence factors like ovulation or early embryonic death in the bitch.

### 3.3.7. MISCELLANEOUS CAUSES

Bitches with systemic diseases like diabetes mellitus, hyperadrenocorticism or renal insufficiency may likely be infertile.

Finally, breeders stress nutrition when their breeding kennel suffers from decreased reproductive results. Little is known in this regard.

### FURTHER READING

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