

INFERTILITY IN THE QUEEN

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Cat breeding is beginning to be administratively better organized in Europe. Pure bred cats are increasing in popularity and more medical data in this field has been collected in the past few years. Thus, cat breeders having an infertile female will ask veterinarians to be as effective as if faced with canine infertility.

The normal fertility rate in the feline species is difficult to determine with certainty. It probably depends quite a lot on the breed concerned, and so does the number of kittens per litter (average prolificity).

As in the bitch, many different problems can lead to infertility including hormonal problems, infectious diseases, congenital or acquired defects of the genital tract. However, unfortunately, few techniques exist which can be used in the investigation of the reproductive functions in queens.

As in canine specie, 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. Therefore, when investigating a fertility problem, veterinarians must check with precision not only the ovulation period but also the early gestational phase.

The first step in the examination of an infertile queen consists in conducting a very precise survey of her general and reproductive history.

1. ANESTRUS (OR DECREASED FREQUENCY OF ESTRUS)

We have to remember that the queen normally exhibits normal anestrus periods. In Europe, it happens during autumn and early winter. Some queens will not cycle between September and January. Some breeds may suffer from even longer anestrus periods: some female Persians for instance may have only one or two estrus periods each year. At the opposite, some Siamese queens, kept inside, will cycle throughout the year, even if the breeders can notice a decrease of fertility.

Puberty is reached at different ages depending on the breed (long haired queens cycle at a later age than short-haired breeds) and on the date of birth. For instance, if a queen becomes sexually mature at the usual anestrus period, the first estrus is likely to occur only during the next sexual period.

As in bitches, true anestrus has first to be distinguished from false anestrus. **Silent heats** represent a frequent concern for breeders taking care of long haired cats (Persians, Somalis...). Clinical signs of the heat period among the females of these breeds may be so subtle that the breeder does not notice anything. This is more frequent in older queens that frequently do not exhibit clinical signs when in estrus. Vaginal smears (every week in the breeding season) and blood estradiol assays may help diagnosing silent heats. Things can improve if a male is put inside the colony or very near it or if normally cycling queens are housed together with females suffering from silent heats.

Inadequate lighting (or inadequate photoperiod in a big size colony) may prevent the beginning of follicular waves when the breeding season occurs. The light should “provide enough light to read a newspaper 14 hours per day”. **Stress** is another important factor: queens that are stressed during the journey to the male’s house may stop exhibiting estrus. Other **environmental conditions** may play a role. It has been shown that in 75% of the cases, anestrus queens express clinical heats if housed together with normally cycling queens for 3 to 4 months. The bad quality of food or excess food of it, leading to obesity, may create a prolonged anestrus state.

Genetic or congenital defects like pseudohermaphroditism, mosaicism, and testicular feminization have been described in feline species. True hermaphroditism is rare and has always been described in cats that are phenotypically males. Karyotype could be useful if any doubt exists. Congenital hypoplasia or aplasia of the ovaries has been described. It is often unilateral. More frequently, the absence of the ovaries (due to a **previous ovariectomy** or ovariohysterectomy) is the original cause of anestrus. It is often difficult to confirm, as anestrus ovaries are difficult to visualize by ultrasonography. Veterinarians could try either to induce heats with hormones (see later) or, if it does not work, to perform laparotomy.

Some **drugs** are well known to induce abnormally long anestrus in queens. Very often, antifungal treatments of ringworm may induce prolonged anestrus, mainly ketoconazole. It is most of the time reversible spontaneously. Steroids like progestogens or corticosteroids may play a similar role, but induce also cystic endometrial hyperplasia (CEH) of the uterus.

As in bitches, progesterone- **secreting ovarian cysts or ovarian neoplasms** may exist. This is not very frequent. Diagnosis is based on non-basal (> 1.0 ng/ml) serum progesterone concentrations in non pregnant queens that persist for several weeks. Ultrasonography of the ovaries is even more significant than in the bitch. **Hypothyroidism** or **hyperadrenocorticism** have been sometimes described in the queen and may lead to permanent anestrus.

If all these different causes seem appear to be excluded, one can attempt to induce an estrus cycle. Several attempts have been made in order to induce a fertile cycle in the queen.

- **Social interactions:** sometimes, placing a tom cat nearby or together with anestrus queens may stimulate them enough to induce heats;
- **Increasing the length of daily light** given to the breeding queens may greatly help them to come in heat. The optimal photoperiod consists of 14 hours of light per day, during at least 25 days. Some authors have described discontinuous protocols consisting of daily 12 hours light, 1 hour darkness, 1 hour light and 9 hours darkness. Under such protocols, queens may exhibit two estrus periods each month. Continuous lighting, on the contrary, reduces the sexual activity of the queens. Ideally, breeders may associate lighting and social interactions.
- **Medical protocols** may also be used. Repeated injections of eCG (PMSG) are used by some authors. Recommended dosage varies depending on the period of the year. But the fertility results are not very good (mating failures, increased number of non-ovulatory follicles).

Month of the year	Dose of eCG (IU)							
	J1	J2	J3	J4	J5	J6	J7	J8
December and January	100	50	50	50	50	50	50	50
February to august	100	50	50	25	25	25	25	25
September to November	100	100	50	50	50	50	50	50

Dose of PMSG in order to induce estrus in the queen, depending on the period of the year, in New-Hampshire

(Colby.Current therapy in theriogenology. D.Morrow. 1980)

eCG treatments may be used together with light increasing treatments, at a unique dosage of 100 IU. Fertility results seem then to be much better.

Many authors seem to be using **FSH** (2mg daily IM or SC injections until the onset of estrus (3 to 7 days)). The fertility rate could reach 70% or more. Many cystic follicles may happen with this protocol, due to hyper stimulation of the ovaries. If used together with light increase, the dose has to be reduced: 2 mg the first day and 1 mg only the following days.

According to our own experience, dopaminergic compounds, like cabergoline, given orally every day may also induce fertile heats in secondary anestrus queens during the breeding season.

2. INFERTILITY WITH SHORTENED INTERESTROUS PERIODS OR EVEN PERSISTENT ESTRUS.

Several causes may induce prolonged estrus in the queen. Such a clinical state is not always associated with infertility. For example, **overlapping of two successive follicular waves** may occur. It means that, when the serum estradiol level declines at the end of a non-ovulatory cycle, another follicular wave has already started and therefore, the vaginal smears remain full of cornified estrus cells and the serum estradiol concentrations never fall to a basal level. Repeated ultrasound observations of the ovaries (every other day for example), may help following the follicular waves and mate the queen at the proper time, when the serum estradiol level is high. Pregnancy may normally occur in such conditions.

Owners may think that their queen suffers from permanent estrus but it may not be true. In some breeds like Siamese (but it may happen in any breed), the interval between two successive anovulatory cycles may be very short, i.e. one or two days, so that it is hardly noticeable. The veterinarian is advised to perform vaginal smears every two days up to a period of 19 days, in order to visualize the decrease of cornification of the vaginal cells. Estradiol assays may help. Here again, repeated ultrasonography investigations of the ovaries are especially recommended.

Follicular cysts have been reported to be common in feline specie, and their frequency increases with age. Diagnosis is easily done using ultrasonography, when the diameter of the “follicles” exceeds 4.0 mm or if they do not disappear at the time of atresia of the other surrounding follicles. Treatment could involve luteinization with hCG (200 to 500

UI), GnRH (25 mg IM), ultrasonography guided puncture and removal of the intra-cystic fluid, or surgical removal of the cyst or of the ovary.

Ovarian tumors inducing persistent estrus are mainly Granulosa Cells Tumors (GCT). They may secrete estradiol, progesterone, or both. Therefore, these tumors act strongly on the endometrium, leading easily to CEH and pyometra. As in bitches, unilateral ovariectomy in order to restore fertility may be considered only if the state of the uterus is good. Otherwise, bilateral neutering is preferable.

As in bitches, exogenous estrogens administered to elderly ladies receiving treatment after the end of genital activity with estrogens containing gels can penetrate through the skin of pet queens when they are frequently handled on the forearm and cause prolonged estrus signs.

3. ABNORMAL SEXUAL BEHAVIOR.

Many factors may prevent a normal mating to occur. Stress has to be avoided. Some queens that lack socialization may refuse to be mounted. Some females refuse certain males and will accept others. Breeders have to make sure that the **post coital yowl of the queen** has occurred, stating that the queen has been penetrated by the penis of the male.

4. INFERTILITY WITH NORMAL BEHAVIOR AND NORMAL CYCLES.

4.1. MALE INFERTILITY

Male infertility is a common cause of conception failure in queens presented with infertility. If a normally cycling queen accepting to be mated has remained infertile, it is important to check the **quality of the semen** of the male.

Very young males or, on the contrary, old cats may have a reduced fertility capacity. If a male is overused (when more than 4 daily coitus occur), the quality of semen may decrease.

But male cats may be infertile because of other factors than the bad quality of semen. **Libido** may be reduced due to psychological problems. **Gingivitis** may prevent the male from biting the neck of the female during coitus, thus preventing immobilization and penetration. In long-haired breeds, **strangulation of the penis** by the hair located in the genital is frequently noticed. A pain of the pelvis or lumbar vertebra may compromise intromission.

4.2. HORMONAL PROBLEMS.

Anovulatory cycles happen in mated queens. The number of coitus may be insufficient to induce LH peak leading to ovulation. Also, if the queen is mated during the first two days of the estrous period, ovulation may not occur. Some sedative drugs used by breeders in order to calm the queens at the mating period may counteract ovulation. Because ovulation is induced by coitus in the queen, lack of ovulation is easily detected by assaying progesterone blood level 5 days after the mating period.

Spontaneous ovulation may occur in some females, thus being mated too late.

Queens may also suffer from **hypoluteoidism**, which is the lack of progesterone secretion during pregnancy which makes the pregnancy impossible to maintain. It can be diagnosed by assaying progesterone blood levels before 30 days, because after this time, the level of progesterone drops when the queen is expressing pseudo-pregnancy. Therefore, it will be impossible to know if a real hypoluteoidism has occurred. Progesterone replacement therapy may be given to the queen (daily 1 to 2 mg IM injections); it may induce prolongation of pregnancy over the usual time. A cesarean section will therefore sometimes be necessary.

Premature atresia of the ovaries has also been described in some queens.

4.3. INFECTIOUS DISEASES

FeLV is the most important viral cause of infertility in the queen. Excretion of the virus in the blood during pregnancy may induce early embryonic or fetal death, abortion or stillbirths or neonatal death. **Panleucopenia** may also sometimes play the same role. Attenuated vaccines given to pregnant queens may be dangerous. Coronavirus has not clearly been demonstrated to cause reproductive problems in the queen.

Bacterial causes of infertility may be quite common. It is often due to lack of hygiene in the cattery. Frequently, *E.coli*, *Streptococcus sp.*, *Staphylococcus sp.* or *Salmonella sp.* are identified as potential causes of abortion. Genital infection with *Chlamydia sp.* is often suspected in queens suffering from infertility. Its role is however still unclear.

4.4. DRUGS INDUCED INFERTILITY

In practice, many breeding cats may be treated with drugs that may contribute to the decline of fertility. Steroid hormones and anti-fungic compounds (mainly ketoconazole) may create hormonal defects in pre-pubertal or adult queens. Abortive drugs such as prostaglandins, antiprogestins and antiprolactinic substances have to be avoided during pregnancy.

4.5. ANATOMICAL ABNORMALITY OF THE VULVA, VESTIBULE OR VAGINA

Congenital defects like persistence of the hymen have been described in the queen.

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

4.6. UTERINE PATHOLOGY

Queens with **cystic endometrial hyperplasia** (CEH) are often infertile due to implantation failure after conception. Often, no abnormality is noticed during the heat period and ovulation. Somehow, ultrasonography usually permits the visualization of the glandular endometrium. CEH often leads to pyometra.

Hydrometra, leading to infertility, is often seen in breeder's queen. But congenital or acquired uterine abnormalities are not well documented.

4.7. MISCELLANEOUS CAUSES

Nutritional deficiencies (vitamin A, linoleic or arachidonic acids...) or excess food-intake may lead to decrease of libido.

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