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Infertility in purebred cats – A review of the potential causes

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ABSTRACT

Although purebred cat breeding is growing in popularity in European countries, most research and publications concern dog reproduction. Infertility in queens has been poorly studied. It may not come as a surprise as common domestic shorthair cats are well known for their excellent fertility. However, even in the latter, the infertility rate is around 20%. Only recently, published articles have analyzed the reproductive performances in different breeds, for example in UK, Sweden, France and Italy, and found similar figures.

In cats, infertility may arise from many factors such as mismating, prolonged anestrus or silent heats, hormonal, nutritional, genetical or chromosomal causes. Also, infectious diseases, probably frequent in breeding facilities, include pathological agents that are well recognized as having a negative effect on pregnancy or other pathogens for which the involvement in fertility problems is unclear. However, analyzing the literature, it appears that the most prevalent causes of infertility in pedigree cats may well be, in females, uterine pathology (sub-clinical endometritis, cystic endometrial hyperplasia, or mucometra), and in males, teratospermia, which may be "permanent" and linked to reduced heterozygosity or "transient" in tomcats that present normal quantitative spermatogenic parameters. The influence of the breed is unknown.

There is an urgent need to study the origin of infertility in purebred cats in order to improve the diagnosis and to develop treatments that may restore normal fertility in subfertile or infertile animals.

1. Introduction

In veterinary medicine and research, the cat remains understudied, and there is still an unbalanced weight of scientific publications in favour of dogs [1]. It is the same for feline reproduction. For example, during the last EVSSAR congress in Berlin (Germany) in June 2019, among 166 submitted presentations that were selected by the scientific committee and which had their abstract printed in the proceedings, only 24 (14.5%) presented some data related to cat reproduction. There is therefore an emergency for specialists to become involved in dedicated research on feline reproduction. Cat breeding is now growing fast all over Europe and the western world, and cat breeders and owners are seeking specific data and dedicated reproductive techniques and treatments. Furthermore, most published studies have been based only on data recovered from domestic shorthair cats, and feline breed reproductive specificities are unclear and not well studied.

2. Is infertility a reality among purebred cats?

Infertility is defined as the inability to conceive and produce viable offspring. In our modern societies, cat over-population is a major concern, and it may appear illogical to enlarge research about fertility problems. However, infertility is a major concern for breeders of purebred cats, as it causes financial and genetic loss, together with personal disappointment and concern for the future.

There are very few published figures about infertility in cats. Swanson et al., in 1994 [2] performed early embryonic collections after natural matings in 48 domestic shorthair ovulating queens, and found that 38 (79.2%) of them produced good-quality embryos or had implantation sites. From the remaining cats, only unfertilized oocytes (n = 5), degenerating embryos (n = 4) or no oocytes/embryos (n = 1) were recovered. Therefore, around 20% of these queens would have remained infertile if the pregnancy had been left to continue. In purebred cats, infertility is still an enigma, with

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very few specific articles [3,4]. The question raised is of course about the reality of infertility. Recent published data about the reproductive performances of pedigree cats in different countries help us quantifying fertility problems in this species: United Kingdom [5], Sweden [6], France [7] and Italy [8]. Ström-Holst and Frössling (2009) analyzing the results of a questionnaire sent to Swedish cat breeders found that 32% of breeders claimed that some of their queens didn't conceive after mating [6]. Furthermore, around 10% of presumably pregnant queens – showing some degree of abdominal development and mammary enlargement around one month of pregnancy – did not produce kittens, which may have been the results of *in utero* embryonic resorption. Fournier et al., in 2017 [7] analyzed the reproductive performances of 5203 French pedigree queens from 45 different breeds, and found that around 15% of mated queens were not pregnant. Furthermore, there was a difference on the pregnancy rate between different breeds, with extremes values varying from 58.1% (117 oestruses) in Oriental queens up to 100% (15 oestruses) in Burmese cats. Subjective reports from cat breeders claimed that 8.2% of apparently pregnant queens (see supra) failed to maintain their pregnancy. These reports lead us to think – as a preliminary conclusion - that infertility and pregnancy losses are a reality among purebred cats, and therefore it appears as an obligation to study the potential causes of this problem.

3. Mating problems and ovulation disorders

3.1. Time of mating

In the dog, inappropriate breeding management is often stated as a frequent cause of infertility. Is it also found in cats? Cat breeders declare that 75% of the matings occur during the first 3 days of oestrus [7], which is considered as the ideal time for the breeding. However, many owners remove their queens from the male as soon as some matings have been observed. In domestic shorthair cats, Donoghue et al. (1993) [9] found that follicular oocytes eventually ovulated after matings performed on the first day of oestrus are immature and of poor quality. It may not be recommended to leave queens to be mated only on the first day of oestrus, as more than 85% of queens ovulated in response to three matings on the second or third day of oestrus [2] and even 100% of queens ovulated after multiple copulations on the 3rd day of the heats [10].

3.2. Spontaneous ovulation

Other problems may lead to feline infertility although the mating was performed in apparently good conditions. One of them is the phenomenon of so called "**spontaneous ovulation**", that is an ovulation which appears without any coitus. This is especially frequent in breeding catteries. In domestic shorthair queens living in groups of females, the level of spontaneous ovulations may be as much as 39–87% [11,12], and may be more frequent in queens with a higher bodyweight [12]. This may also represent a real problem in pedigree queens as many of them are living with other females, and may have already ovulated when they are brought to the male for the mating.

3.3. Anovulatory cycles

A queen may fail to ovulate despite mating, if for example the number or frequency of matings are too low, as it is well known that only 50% of the queens ovulate after a single mating [13]. The role of the stimulation of ovulation induced by the penile spines is unclear. In any case, the penis of the tom should be examined to confirm full development of these spicules.

3.4. Stress and inexperience

However, other problems may occur during mating. An aggressive or an abnormally stressed female may not accept the male. Some breeders report that single females lie on their back to avoid being penetrated (personal data). In cats, there is probably a partner preference, as queens accepted to be mated in only 15/38 (39.5%) attempts despite confirmed oestrus [14]. However this has to be further studied. Mating not necessarily occurs, when partners are put into the same room. Failure to mate may happen when partners are too immature or inexperienced, or in breeds, where male with low libido are a problem. We frequently observed this in Persian or Maine Coons (personal data).

3.5. Anatomical and health problems

Anatomical problems in males and females may prevent penetration, such as a preputial hair ring in longhaired cats, preputial or penile problems (phimosis …) in males [15] or vaginal or vulvar atresia in females. Furthermore, lack of teeth or pain in the mouth or jaws because of stomatitis, can render a male incapable to grab the neck of the female during mating; procedure necessary for stabilization [15].

3.6. A practical approach to mating or ovulation disorders

What recommendations could therefore can be made to improve the timing of mating and to recognize spontaneous ovulations? Veterinarians could propose to pedigree cat owners to perform a vaginal smear on the day when they intend to mate a queen, so as to insure that she is in full oestrus, with more than 85% keratinized cells [14]. It may also be interesting – in queens that permit it - to perform an oestrus follow-up of the follicular maturation during the first three days of oestrus by ovarian ultrasonography, or at least, to perform this examination on the day of the mating, as it has been shown that at the pre-ovulatory stage, at least one follicle reaches a diameter greater than 3.0 mm [14]. It may therefore help to see, whether the follicular maturation is clearly at an early stage, or whether the queen has already ovulated, showing a complete follicular collapse under ultrasound examination. Although progesterone blood level begins to increase only after ovulation, it may be interesting to measure the concentration to make sure that it is basal on the day of the mating.

To ensure that penetration has occurred, a vaginal smear or a vaginal wash soon after an observed mating to control the presence of spermatozoa can be performed [16]. Finally, to ensure that ovulation has occurred, blood should be taken one to three weeks after the last observed mating to measure blood progesterone. In case of an anovulatory cycle, the value will remain basal [17]. In case of confirmed anovulatory cycle, induction of ovulation can be tried during the next cycle; even though in cats, there is no standardized protocol for induction of ovulation at the time of natural mating. Preliminary data in our department have shown that a series of 5 vaginal stimulations at 30 min interval on females at the peak of oestrus induced ovulation in 8/11 queens (unpublished results). This is preferable, since hormonal stimulation can cause side effects. In one study, induction of ovulation with hCG lead to disruption of oviductal embryo transport and development, probably due to abnormal endocrine environment [18], although successful ovulation was induced in queens in non-breeding season by administration of eCG and hCG before embryo transfer in the study of the team of Tsutsui [19]. Induction of ovulation can also be performed with GnRH in combination with vaginal stimulations [20].

Finally, veterinarians should advise the cat owners to observe

carefully the post-coital reaction of the queen, as only a frantic rolling on the back is a behaviour that proves in 100% of cases that a penetration by the male has really occurred. Vulvar licking, screaming or chasing the male are not proof that coitus has occurred [21].

4. Uterine pathology: an under-estimated cause of infertility?

In her study on infertile purebred queens belonging to 6 different breeds, Axner et al. (2008) [4] found that in 4/7 cases a uterine pathology was diagnosed: two cases of cystic endometrial hyperplasia (CEH), one case of pyometra with acute endometritis and one case of suspected mild endometritis. The question remains whether uterine problems are a major cause of infertility in cats?

4.1. Endometritis

In dogs, sub-clinical endometritis is a severe problem [22,23]. However, still today the pathogenicity of sub-clinical endometritis is unclear. Above all, the presence and the exact role of bacteria remains unclear. In an observation, among 7 infertile purebred queens, vaginal bacteria were isolated in all cases. Two queens with a profuse bacterial growth were treated with antibiotics became pregnant later [4].

In another study, culture of uterine content was performed in 22 cats suffering from inflammatory uterine diseases or infertility. All isolation attempts yielded growth and E. coli was the organism most commonly isolated [24].

In cats, mild endometritis can be difficult to diagnose. From her study in 2008, Axnér et al. concluded that "low grade endometritis is extremely difficult to diagnose in the queen and its incidence and importance as a cause of infertility are unknown" [4]. Indeed, surgical biopsies preferentially performed in dioestrus at the time of diagnosis by ultrasonography of lack of pregnancy or embryonic resorption, appear as the "gold standard". The procedure allows histological, bacteriological and even molecular examination of samples; the latter for the detection of microbial antigens by means of PCR. However, our experience shows that cat breeders are often reluctant to accept this invasive procedure. *Trans*-cervical uterine flushing with a sterile saline solution has become a potential diagnostic tool since it has been demonstrated that trans-cervical catheterization with endoscopic guidance is possible in the queen [25]. Preliminary unpublished trials in our laboratory with a 1.9 mm diameter rigid endoscope (ref. 67030BA, Karl Storz, Germany) revealed that it is a useful tool and deserves further investigation. In subfertile queens, it is essential to perform an early diagnosis of pregnancy by ultrasound, as early as 10–15 days after the last observed mating, to diagnose an eventual embryonic death; furthermore, the uterine clearance can be observed. In bitches, Freeman et al. (2013) found that the presence of uterine luminal fluid on day + 5 or +14 after a mating was associated with a significantly reduced pregnancy rate, and that no bitches in which fluid was present at day + 14 became pregnant [26]. Indeed, Axnér et al. (2008) observed that 4/7 infertile queens showed intra luminal fluid sonographically at the time of the clinical examination [4].

Furthermore, recent publications have begun to investigate the uterine blood flow in the course of pregnancy. The aim is the early detection of potential anomalies.

Doppler sonography allows examination of maternal and fetal arterial blood flow, and normal parameters are available, helping to recognize abnormalities [27].

In one study, pregnancy arrest was induced in queens by using the anti-progestine aglepristone. Authors observed an abnoemal increase in the resistancy index of the uterine artery together with the embryonic death [28]. But to the best of our knowledge no such measures have been published in field pathological conditions. Markers of uterine inflammation, such as C-reactive protein (CRP), prostaglandin 15-ketodihydro-PGF2alpha metabolites (PGFM) or serum amyloid A, may be a promising diagnostic approach, although mostly experimental at the moment and mainly orientated towards the diagnosis of pyometra in dogs [29]. One recent study in cats has been published [30].

4.2. Cystic endometrial hyperplasia

This potentially – but still to be proved – detrimental role of sub-clinical endometritis should not let us forget other uterine diseases as a potential cause of infertility. CEH may occur following the use of progestins [31], or in queens getting older and/or having presented several episodes of spontaneous ovulations, with subsequent progesterone secretion leading to endometrial development without pregnancy [17]. It may of course be a cause of infertility due to the incapacity of embryos to survive in such a hostile environment. Nowadays, the diagnosis of CEH is easily done by ultrasound, but as in bitches, the uterine changings are irreversible; there is no standardized treatment.

4.3. Hydrometra and mucometra

Finally, hydrometra or mucometra is sometimes found in infertile young queens without any clinical sign. Very often, the exact cause is impossible to determine and there is no standardized treatment [32].

5. Infectious diseases: a high risk in breeding facilities?

Infectious diseases caused by viruses or bacteria may lead to pregnancy arrest, neonatal diseases or loss of kittens. Cat shows increase the risk of infections. A study conducted in Sweden has shown that, when coming back from a show, 10.4% of breeders reported conjunctivitis in some of their cats, and 14.6% reported upper respiratory tract diseases [6].

The role of cat shows for the development of reproductive problems in cateries has not been studied but cannot be excluded.

There are few recent reviews about the role of infectious agents towards feline infertility [33–35]. These agents may prevent implantation and/or embryonic development or induce pregnancy loss, which may remain unnoticed if the embryos are resorbed *in utero* and therefore appear as "infertility".

5.1. Viruses

Among viral diseases, only retroviruses (FeLV, FIV) and the parvovirus have been confirmed as "aborting" agents. The role of Feline Herpesvirus (FHV) or Calicivirus remains unclear; more studies should be performed as these two diseases are a major concern in cateries. After an experimental inoculation with FHV a pregnancy loss occurred in one study [36]. However, its exact role effect on fertility in catteries is still unclear and controversial. Resorption or abortion due to Calicivirus may occur in unvaccinated queens, due to fetal contamination [37], and there is no full protection from vaccination. Furthermore, asymptomatic carriers exist. Feline Coronavirus is considered ~~as~~ an uncommon cause of reproductive problems [38].

5.2. Bacteria

Chlamydophila felis was mentioned as possible cause for abortions and was isolated in cases of reproductive disorders concurrent

with upper respiratory tract disease; however, its role as a cause for infertility is still unclear. However, for some authors, there is circumstantial evidence that *C. felis* may cause abortion [39]. One publication reports about the potential role of *Chlamydia psittaci*, stating however that in cats with reproductive disorders and upper respiratory tract disease, FHV was more often isolated than *Chlamydia psittaci* [40]. Further causes of infertility might be *Coxiella burnetii* [41] *Leptospira* sp. or *Bartonella henselae* [42]. In one report, *Brucella* spp. and *Brucella abortus* were mentioned as possible causative organisms for pyometra in queens [43].

As in bitches, the role of the imbalance of the vaginal flora is probably under-estimated, and especially the potential pathogenic role of *E. coli* [24]. As already said earlier, it may be a potential cause of endometritis and pregnancy arrest. But very few studies have been done on the genital flora in cats [44] and pure growth of bacteria within the vagina seems to be a normal finding in many queens without any reproductive failure [45].

5.3. Parasites

Cat reproduction may also be impaired by parasitic infection. There is a special concern about *Toxoplama gondii*, because cats are both definitive and intermediate hosts, although the reproductive tract is not commonly affected [46]. Experimentally induced transplacental contamination and even abortion may occur [47]. If a pregnant queen is seronegative, it may therefore be recommended to avoid her hunting and eating raw meat. *Cytauxzoon felis*, a tick-transmitted protozoal parasite has also been mentioned in a case report [48].

6. Bad semen quality in purebred male cats?

Pet animal males, opposed to farm animals, are selected for breeding mostly on the basis of their appearance and behaviour, not reproductive traits. This may lead to various fertility problems and lower semen quality in pedigree individuals. Although there are numerous studies describing semen quality and sperm characteristics in cats, they were performed mostly on Domestic Shorthair cats and data regarding semen quality in purebred cats are very scarce.

There are very few data regarding the relation between breeds and fertility. Axner et al., 1996 described 10 cases of infertile tomcats of different breeds (Cornish Rex, Burmese, Siamese, Persian, Ragdoll, domestic shorthair) and in 4/10 cases the cause of infertility was bad semen quality - azoospermia and teratozoospermia [49]. The department of Reproduction in Wrocław (Poland) has registered nine tomcats presented for infertility (unpublished data). They were of different breeds (Sphynx, Main coon, Bengal, Ragdoll, Siberian Forest Cat) and from different catteries. In three cases the diagnosis was severe oligospermia and teratozoospermia, in two cases - teratozoospermia with normal total sperm count, in three cases - sperm DNA damage. Regarding these data, it seems that azoospermia/oligospermia and teratozoospermia often cause fertility problems in pedigree cats.

6.1. Teratozoospermia

Teratozoospermia is a common phenomenon in felids (both wild and domestic cat) [50]. The threshold for teratozoospermia in cats has been established at less than 40% of normal spermatozoa in the sample [51].

One study showed that teratozoospermic spermatozoa possessed worse motility parameters, compromised ability to capacitate and undergo the acrosome reaction, abnormal chromatin integrity and lower expression of phospholipase C Zeta [52]. Importantly, even apparently normal spermatozoa from teratozoospermic males were impaired [51].

In none of these studies *in vivo* fertility was evaluated and it is known that teratozoospermic tomcats can be fertile. In one study [53], 11 teratozoospermic cats with known breeding records were all fertile. Unpublished data from our laboratory showed that 6 out of 20 ejaculates from ten fertile pedigree cats (four cats collected more than once) were classified as teratozoospermic.

When considering teratozoospermia in cats, one important fact has to be emphasized: in cats there are two different types of teratozoospermia, of different origins and differently affecting spermatogenic parameters [54], although no cut-off value has been established so far. The first type, which can be named 'persistent', is a permanent feature of a particular tomcat – such male consistently produces spermatozoa of poor morphology. This type is connected to several alterations of spermatogenesis: fewer Sertoli cells per tubule with increased number of round spermatids (increased Sertoli cell efficiency [55], accompanied by reduced germ cell apoptosis [56], which leads to higher sperm output - a phenomenon called "quantity rather than quality" [55]. This type of teratozoospermia is linked to reduced heterozygosity and can be found in highly inbred rare wild felids (e.g. Florida panthers, clouded leopards and cheetahs) and can be established experimentally via incestuous breeding [50].

The other type of teratozoospermia, which can be named 'random', is found in tomcats that present normal quantitative spermatogenic parameters and may be a transient worsening of semen quality. The etiology of this type of teratozoospermia is unknown. Some studies comparing normo- and teratozoospermic cats suggest that potential factors may include: hormonal imbalance in the testes [57], diet and stress [58], age and season [53]. This list remains open and more studies are required to understand the causes of 'random' teratozoospermia and its connection to fertility.

As purebred cats may present higher homozygosity, higher incidence of teratozoospermia can be expected. Indeed, in one study [53] Pedigree cats had a lower mean percentage of normal spermatozoa than did household cats.

6.2. Azoospermia

Azoospermia is defined as a lack of spermatozoa in the semen sample. In the case of azoospermia it is crucial to exclude 'false' azoospermia, which means unsuccessful collection of spermatozoa - spermatozoa are produced in the testes but for some reasons they were not expelled into the ejaculate. The potential causes include: retrograde ejaculation [49], blockage or abnormalities of ductus deference (obstructive azoospermia), or failure of the collection method. The two most commonly used methods (electroejaculation and urethral catheterization) are characterised by high efficacy (more than 90% success), nevertheless, in the case of no spermatozoa in the sample the authors always recommend a second attempt of collection after several days to avoid a false diagnosis. Sometimes the changing of a collection method is helpful (personal observations).

True azoospermia can be observed e.g. in cases of chromosomal abnormalities or testicular hypoplasia and degeneration [59]. As spermatogenesis is directed by testosterone, hormonal background of azoospermia/oligozoospermia may be considered.

To differentiate 'true' and 'false' azoospermia, alkaline phosphatase (AP) can be measured in the sample. It is an enzyme produced in the testis and epididymis [59], therefore in a normal ejaculate its concentration in seminal plasma is high (>20 000 UI/l [60], or even 160 000 UI/l [59]. To the best of our knowledge, no cut off value has been determined for tomcats. In the case of an unsuccessful collection, its concentration is low.

In human medicine testicular biopsy is a common diagnostic procedure, helpful in differentiating different disturbances of spermatogenesis (e.g. Sertoli cell only syndrome, maturation arrest, hypospermatogenesis [61]. There are some publications describing this procedure in cats [62].

7. Endocrine disturbances

Endocrine disturbances are also often stated as a potential cause of infertility. Hyperoestrogenism may exert a negative effect on reproduction. It may happen in the case of follicular cysts, reported to be common in the cat [16] or granulosa cell tumours. Some queens, frequently Orientals or Siameses (personal observations), show abnormally frequent oestruses, so close to each other that the successive follicular waves overlap, creating prolonged heats [17]. Such abnormal cycles have to be diagnosed and treated without delay, as they may lead to further development of a pyometra or a non-regenerative anaemia due to bone marrow toxicity of oestrogens (personal observations). Hypoluteoidism or lack of progesterone to maintain the pregnancy has been suspected to occur occasionally in the queen [63], although not confirmed. In a survey, Maine Coon was the most frequent breed to be cited by veterinarians as potentially suspected to suffer from hypoluteoidism [64].

8. Nutrition

Nutrition may have an effect on reproductive performances. Essential nutrients such as taurine, arachidonic acid and the supply of poly-unsaturated fatty acids (PUFAs) and copper have to be provided in the cat food. Some studies have demonstrated the impact of nutrition on semen quality in Felids [65,66]**.** Due to the growing interest of purebred cat breeders for raw-food diets, attention is drawn to the microbiological content of it, as bacteria exerting potential bad effects on reproduction and general health (*Salmonella* spp., *Campylobacter* spp., *Listeria* spp., *E. coli* …) may sometimes be isolated if the conservation of the food has not be done correctly [67]. A recent publication [68] found also a high content of mycotoxins in pelleted cat food in South Africa. An evaluation of diseases, including reproductive problems, affecting dogs and cats and their relationship to pet food mycotoxin contamination was reported in Brazil [69].

9. Chromosomical or genetical problems

Chromosomical or genetical problems are not uncommon in cats. Abnormal chromosomic formulas may be found, such as a monosomy 37X0, trisomies (39 XXY, 39XXX, 39XYY) chimerism or mosaicism [70]. This may lead to primary anoestrus or to infertility in females that seem to cycle normally, or to abortion of foetuses with an abnormal karyotype. In male cats, attention has to be drawn to the special case of tortoiseshell male cats who often suffer from the Klinefelter syndrome (39 XXY) and present azoospermia [71].

Inbreeding – an often cited cause of low reproductive performances - appears uncommon in Pedigree cats. A study among Polish purebred cats [72] evaluated the degree of inbreeding at around 3%. Only Siberian cats were slightly more inbred (more than 5%). In France, Leroy et al. (2014) [73] found an average degree of inbreeding of 5% (except in Devon Rex in which it was higher). The rather low degree of inbreeding may be due to the fact the large majority of breeders are occasional ones and use their reproducers with moderation. In Sweden 58% of purebred cats breeders use their own male [6]. It is even more frequent in France where 93.3% of breeders use their own tom cat [7].

10. Miscellaneous

10.1. Delayed puberty

also called primary anoestrus, may be due to different causes. Lack of social contact with other cats, low luminosity within the breeding facility, a body weight below 2.3 kg (except in giant breeds) or excessive stress may play a role in postponing puberty. Romagnoli et al. (2019) [8] found that, in Italy, the season in which a queen was born, did not influence the age of her puberty; even though females reaching full body weight in winter often show delayed puberty [16]. There may be differences linked with the latitude of the country, southern cats living under stronger light stimulations, or to the fact that nowadays, most breeding facilities occur in better lit facilities. Anatomical malformations or intersexual state, often linked with a chromosomical defect, may be diagnosed during a clinical examination. In such a case, it may be interesting to ask for a karyotype in a competent laboratory. Veterinarians should also ask the owners if the young queen has not been treated with progestins or antifungic drugs – often used to treat ringworm in catteries - that may interfere with the normal hormonal balance at puberty. They should also be aware of queens which have already been spayed, as early neutering is more and more frequently performed before the sale of kittens, to avoid further reproduction. Luteinizing hormone (LH) [74] and/or Anti-Müllerian hormone (AMH) assays [75] may help diagnosing the absence of ovaries in a queen presenting a delayed puberty. In the near future, assaying AMH may also help to detect if a queen is still at a pre-pubertal stage [76].

10.2. Secondary anoestrus or abnormally prolonged interoestrus

in a queen that was cycled before, may be due to several factors, including the season of the year. Romagnoli et al. (2019) studied the distribution of the oestrus cycles in 128 queens from 4 different breeds and found important differences, only 20% of the queens being cycled in November versus more than 70% in March or April [8]. There are also differences in relation to the breed, as a study in UK found that a non-breeding season existed for 90% of long-haired cats (Persians, other long-haired) versus 39.2% of short-haired cats [77]. Vaginal smears are the first step to confirm an anoestrus state, and to differentiate it from cases where the queen is cycled but not presenting any clinical oestrus. In such a case the smear will contain some degree of keratinized superficial cells. This may happen in case of "silent heats" – oestruses without any clinical signs such as crying, lordosis or searching for the male - which seem to be more frequent in Maine Coons and Persians [64]. It may also be due to progesterone secretion down-regulating the hypothalamo-pituitary axis, in case of a pseudo-pregnancy, or ovarian luteinized cysts or ovarian tumours. Progesterone assays, together with ovarian and uterine ultrasonography, may help the diagnostic. An induction of oestrus may be tempted only in a confirmed anoestrus state, with basal progesteronemia or inactive ovaries under ultrasound.

10.3. Environmental pollutants

such as bisphenol A, should also be mentioned, as they are more and more often cited as negative agents on reproductive processes in humans. Bisphenol A has been recently demonstrated to have a suppressive effect on uterine contractions in queens that may lead to infertility [78].

In conclusion, although there is much less published data about cat infertility than there is for dogs, it appears that some potentially predominant causes deserve some dedicated research. Among

them, uterine problems in females and teratospermia in males have to be more deeply studied, in order to understand these factors, to better diagnose them and to develop treatments that may restore a normal fertility in subfertile or infertile purebred cats.

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