Sveriges lantbruksuniversitet
Swedish University of Agricultural Sciences

Fakulteten för veterinärmedicin och husdjursvetenskap
Institutionen för anatomi, fysiologi och biokemi

Reproductive Physiology of the Female Cat

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Honkattens reproduktionsfysiologi

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SUMMARY

The cat is one of our most common pets. Understanding the reproductive physiology of the queen is important, not only for the knowledge of our domestic cats but also for wild undomesticated feline species, many of which have been reported endangered. Understanding the mechanisms behind the estrous cycle, ovulation and pregnancy is also important for handling the feral cat populations that are a problem in several countries. The purpose of this literature study is to look into the hormonal patterns of the reproductive physiology of the female cat, with focus on ovulation, pregnancy and pseudo-pregnancy, and from this information determine in which fields more research would be needed.

The female cat is seasonally polyestrous in Sweden, meaning that she can have several estrous cycles during the breeding season but goes through a long period of reproductive dormancy during the darker months of the year. The queen is considered an induced ovulator, with copulation triggering the release of luteinizing hormone (LH) from the pituitary gland needed for ovulation. However, it has been seen that many queens are capable of spontaneous ovulation in the presence of a tomcat or other female cats in estrus. The estrous cycle in the cat consists of several behavioral phases, defined differently by different authors. In this study, the estrous cycle will be described as consisting of five phases: proestrus, estrus, interestrus, diestrus and anestrus. The induced ovulation in the queen has been shown to be dependent on several factors: the number of matings and the intervals between them, the day of estrus she was mated and individual differences in the LH peak she was able to produce. If the queen ovulates but do not conceive, she will enter into a pseudo-pregnant phase that is similar to pregnancy for the first 40 days. After 40 days, the plasma levels of progesterone produced by the corpora lutea will be back at almost basal level in the pseudo-pregnant cat, due to luteal regression. If the queen is mated and become pregnant, she will go through a longer progesterone dominated phase than during pseudo-pregnancy. Whether the placenta in the cat is responsible for producing the progesterone that maintains pregnancy after the luteal regression has begun is still unclear.

It can be concluded that the reproductive processes of the female cat are not completely mapped out. More research is needed on some subjects, such as the mechanisms of the induced ovulation and the hormonal role of the placenta during pregnancy, for a more complete understanding of the reproductive physiology of the queen.

SAMMANFATTNING

Katten är ett av våra vanligaste husdjur. Att förstå honkattens reproduktionsfysiologi är viktigt, inte bara för våra domesticerade katter, utan även för de vilda icke-domesticerade kattarterna, av vilka många är utrotningshotade. Att förstå mekanismerna bakom löpcykel, ovulation och dräktighet är även viktigt för kontroll av kolonier med hemlösa katter, vilka är ett problem i många länder idag. Syftet med denna litteraturstudie är att beskriva de hormonella mönster som kan observeras vid ovulation, dräktighet och pseudodräktighet, och klargöra inom vilka av dessa områden mer forskning behövs.

Honkatten är i Sverige säsongsmässigt polyöstral, vilket innebär att hon kan ha flera löpcykler efter varandra under parningssäsongen men genomgår en lång period av reproduktiv inaktivitet under de mörkare månaderna på året. Honkatten har en inducerad ovulation, där parning triggar utsöndring av luteiniserande hormon (LH) från hypofysen, vilken krävs för ovulation. Det har dock observerats att många honkatter kan ovulera spontant utan att behöva den mekaniska stimulus som parningen ger. Detta sker ofta vid närvaro av en hankatt eller andra honkatter i östrus. Löpcykeln hos katt består av flera beteendefaser som ofta definieras olika av olika författare. I denna studie beskrivs löpcykeln som bestående av fem faser: proöstrus, östrus, interöstrus, diöstrus och anöstrus. Det har visats att den inducerade ovulationen kan påverkas av flera olika faktorer såsom antalet parningar och intervallet mellan dem, vilken dag under östrus honan paras och individuella skillnader i utsöndringen av LH. Om honkatten ovulerar men ej blir dräktig går hon in i en pseudodräktig fas, som under de första 40 dagarna är mycket lik dräktighet. Efter 40 dagar är dock plasmakoncentrationen av progesteron tillbaka på basal nivå hos den pseudodräktiga katten på grund av tillbakabildning av gulkropparna. Om katten blir dräktig under östrus fortsätter den progesterondominerade perioden längre än om katten varit pseudodräktig. Det är oklart om placentan hos katt är ansvarar för produktion av det progesteron som är nödvändigt för att upprätthålla dräktigheten efter att tillbakabildningen av gulkropparna har börjat.

Det kan konstateras att reproduktionsprocesserna hos honkatt ej är helt klarlagda vid denna tidpunkt. Mer forskning inom områden såsom mekanismerna bakom ovulationen och placentans hormonella roll under dräktighet krävs för att få en komplett förståelse för honkattens reproduktionsfysiologi.

INTRODUCTION

There are approximately 1.16 million cats in Sweden (Agria, 2013), making the cat one of our most common pets. Understanding their reproductive physiology grows more and more important as the interest in cat shows and cat breeding increases (Sveriges Kattklubbars Riksförbund, 2014), but also in regard to wild undomesticated felids, as 23 out of the 36 wild cat species in the world have been reported endangered. Breeding wild felids in captivity has turned out to be problematic and increased knowledge about the reproductive mechanisms of the domestic cat is expected to give insights on how to save the endangered species (Brown, 2011). Understanding the mechanisms of the estrous cycle, ovulation and pregnancy can also be of use when trying to control feral cat populations, something that is a problem in several countries. In Sweden for example, the number of feral cats is estimated to be as high as
100 000 (Länsstyrelsen, 2013). Much research on the hormonal regulation of the reproductive system in the queen was conducted during the years 1970-1980 and results gathered from these studies are still relevant today.

The purpose of this literature study was to look into the hormonal patterns of the reproductive physiology of the female cat, with focus on ovulation, pregnancy and pseudo-pregnancy, and determine where more research is needed.

MATERIALS AND METHODS

The databases used to find articles were PubMed, Web of Science and Google Scholar. The keywords used were (cat OR cats OR feline OR felids OR queen) AND (reproduction OR reproductive OR physiology OR endocrin*) AND (progesterone OR progestins OR estradiol OR estrogens OR estrus OR oestrus), which generated multiple relevant articles. More articles were found by going through the references from the studies found in the databases.

The book Fass vet 2014 was used to find the veterinary pharmaceuticals regarding reproduction control currently registered for use in female cats in Sweden, and the book Canine and Feline Endocrinology and Reproduction (Feldman & Nelson, 2004) was used for basic aspects of the reproductive physiology of the queen.

LITERATURE REVIEW

The female cat

The reproductive physiology of the female cat differs from that of many other domesticated species. The queen usually reaches puberty at 4-12 months of age (Brown, 2011), the exact time depending on the current photoperiod, the breed and the weight of the cat (Feldman & Nelson, 2004). The female cat is seasonally polyestrous, meaning that she has several estrous cycles during the breeding season but goes through a long period of anestrus during the darker months of the year. The breeding season usually begins in January or February and continues until late summer or early fall, if ovulation does not occur (Shille *et al.,* 1979). The female cat is considered an induced ovulator, with copulation causing release of luteinizing hormone (LH) that leads to ovulation (Brown, 2006). This is true in most queens, but it has been noted that spontaneous ovulation occurs sporadically in up to 60% of the female cats (Kutzler, 2007).

The estrous cycle

The estrous cycle in the female cat consists of several phases, often defined and used differently by different authors. It is commonly divided into five behavioral phases: proestrus, estrus, interestrus, diestrus and anestrus (Feldman & Nelson, 2004), but four phases where interestrus and anestrus refer to the same period is not unusual (Brown, 2011). In the current study, the estrous cycle is defined as consisting of five phases (Fig. 1).

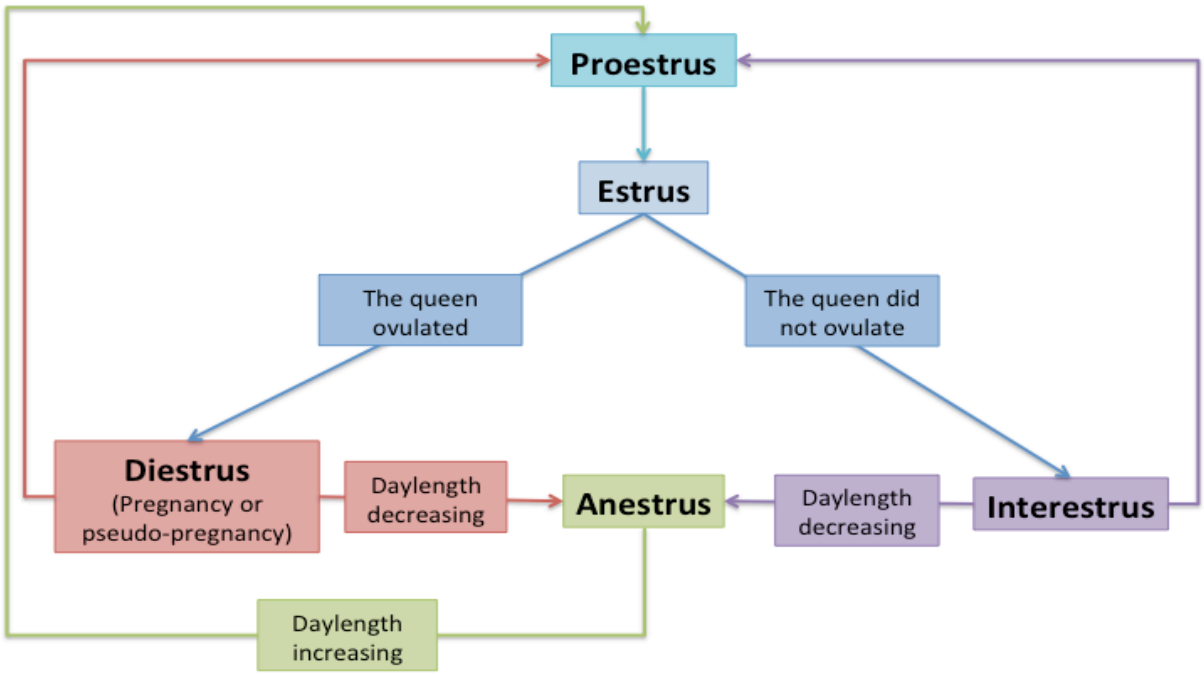

Figure 1. An overview of the behavioral phases of the estrous cycle, as defined in this literature study. Based on Feldman & Nelson (2004).

Proestrus

The proestrus phase lasts for an average of 1.2 days (range between 0.4-2 days) in the female cat and is difficult to notice, due to the short period of time and the lack of signs on external genitalia. In a study done in 1979, proestrus could only be observed in 27 of 168 cycles, and in the remaining 141, the females appeared to proceed directly into estrus from an anestrous or interestrous period. The proestrus phase consists of follicular growth and the synthesis of estrogens that enter the circulation in high concentrations, often twice as high as can be found in a queen during anestrus or interestrus (Shille *et al.,* 1979). The cat starts showing signs of estrus behavior such as vocalizing, rubbing the head and neck against objects and rolling on the ground. A queen in proestrus attracts the male but refuse all advances and does not allow him to mount her. The end of proestrus is marked by her acceptance of the male (Brown, 2011).

Estrus

Estrus is the breeding phase of the cycle and normally lasts for an average of 7.2 days, but periods of 2-19 days has been observed (Shille *et al.,* 1979). The clinical signs of estrus are the same as in proestrus, only intensified, and the female allows the male to mount her. The queen goes into mating position if a tomcat is present, or if she is being petted on the back at the base of the tail (Feldman & Nelson, 2004). The estrus behavior is closely related to the follicular phase, which is defined as the period of time when the follicles produce and secrete high levels of estrogens (Verhage *et al.,* 1976). In a study by Shille *et al.* (1979), it was concluded both that the duration of the follicular phase ranges from 3-16 days with an average of 7.4 days, and that the length of the phase was not altered by copulation or ovulation. Only 8% of the females showed estrus behavior on day 1 of the follicular phase while it could be seen in 100% of the queens on day 5, indicating that the two phases do not perfectly coincide (Shille *et al.,* 1979). The blood levels of estrogens continue to increase up to a peak concentration, on average reached on day 3 of the follicular phase, and then rapidly decline (Banks & Stabenfeldt, 1982), although most queens continue so show estrus behavior for 1-4 days after the follicular phase is ended (Shille *et al.,* 1979). Even if ovulation is induced, leading to the concentrations of plasma progesterone starting to increase, the sexual receptiveness of the queen will continue on to the end of the estrus period (Paape *et al*., 1975). If ovulation is not induced during estrus, the queen will enter an anovulatory phase, often referred to as interestrus, and proceed into proestrus again soon afterwards. If the queen ovulates during estrus, she will become either pregnant or pseudo-pregnant, depending on if she conceives or not (Feldman & Nelson, 2004).

Interestrus

The queen will enter the interestrus phase once the period of estrus is over. This is a period of reproductive inactivity and is also the period of the estrous cycle that make the queen different from females of most other domesticated species (Feldman & Nelson, 2004). The interestrus period has been observed to last for 1.4-16.6 days, with the average at 9 days, but continues on

for much longer if ovulation was induced during estrus (Kutzler, 2007). The estrogen and progesterone levels in the circulation remain low during the entire interestrus phase, since the ovaries are hormonally inactive. The female returns to normal behavior and does not attract males (Feldman & Nelson, 2004). Interestrous is sometimes referred to as the three different outcomes possible after estrus: an anovulatory phase, pseudo-pregnancy after ovulation or pregnancy. If interestrus is referred to in this way, the term diestrus is usually not used (Paape *et al.,* 1975). In the current study however, interestrus is defined as consisting of the anovulatory phase only.

Diestrus

Diestrus is defined as a period of progesterone dominance, which is the phase after estrus if ovulation was induced. A queen in diestrus can be either pregnant or pseudo-pregnant, the latter meaning that she ovulated but did not conceive. The corpora lutea develops 1-2 days after ovulation and start synthesizing and secreting progesterone, which inhibit secretion of gonadotropin-releasing hormone (GnRH) from hypothalamus and, in turn, LH and follicle stimulating hormone (FSH) from the pituitary gland (Feldman & Nelson, 2004). At the end of diestrus, the queen will proceed into either proestrus or anestrus, depending on the season.

Anestrus

Anestrus is a phase of reproductive dormancy where plasma concentrations of both estrogens and progesterone remain at basal level. Females do not attract males nor express any sexual behavior. In the fertile queen in Sweden, seasonal anestrus usually begins in the late summer or early fall and last until early spring. Since the queen is dependent on photoperiod for her estrous cycling, shorter days can trigger onset of anestrus even in the middle of the breeding season. It has also been suggested that higher temperatures might initiate a period of anestrus, as can be the case during high summer. Therefore, it has been seen that the breeding season is sometimes divided into two periods, one in the spring and one in the early fall, with a period of anestrus during the warmer months of summer (Feldman & Nelson, 2004). Anestrus is hormonally similar to interestrus and they are sometimes referred to as the same phase (Brown, 2011).

Induced ovulation

During copulation, the penis of the tomcat stimulates receptors in the vagina that transmit a signal to the hypothalamus through an afferent spinal pathway. The hypothalamus is stimulated to release GnRH, which in turn causes release of LH and FSH from the pituitary gland (Feldman & Nelson, 2004). Release of FSH is then inhibited by inhibin from large follicles (Bristol & Woodruff, 2004).

Spontaneous ovulation has frequently been observed even though most female cats need mechanical or pharmaceutical stimuli to ovulate (Brown, 2006). It has been seen that these reflex ovulations are more common in some individuals, but housing conditions (such as closeness to owner and other animals in the household) and presence of a tomcat has been concluded to be

important factors as well. In several wild feline species it has been observed that presence of other females in estrus trigger spontaneous ovulation at a higher frequency.

Impact of single and multiple copulations

Even though the female cat is considered to be an induced ovulator, a single copulation is not always enough to cause the LH peak needed for ovulation. In a study done by Concannon *et al.* (1980), only 50% of the queens ovulated after a single mating with a fertile male, indicating a significant variability between individuals in regulation of the LH peak. This interindividual variation was suggested to be the major factor deciding whether ovulation occurred or not. After four copulations, 100% of the queens had ovulated. In the same study, it was shown that plasma levels of LH in the queens that ovulated were higher and lasted longer after multiple copulations compared to after a single mating. The release of LH following a single copulation occurred only minutes after mating and had a peak concentration 10 minutes to 1 hour later, and was still elevated 8 hours afterwards in the females that ovulated. In comparison, the LH peak after four copulations was observed at 1 hour in 13 of the females, and after 4 hours in the remaining 10. The exact duration of the elevated levels of LH in plasma following multiple copulations was not documented in this study, although the circulating concentration at 8 hours after the first copulation was considerably higher compared to the levels in the single-mated females. In the females that did not ovulate after a single mating, the plasma concentration was at basal level after 4 hours, and the peak concentration was considerably lower compared to the ones that ovulated. The relation between multiple copulations and LH concentrations can be seen in figure 2. The significant difference between plasma concentrations in single-mated females and those mated multiple times is believed to be the result of repeated release of GnRH. This also indicates that the interval between multiple copulations might have an effect on ovulation (Concannon *et al*., 1980). In a study by Shille *et al.* (1983), it could be concluded that elevated levels of LH for 2-4 hours could induce ovulation in the queen, and that a prolonged LH surge was not needed. The release of LH after copulation in female cats has been observed to be continuous, while the release during the rest of the estrus cycle has been shown to be pulsatile. This is not seen in species with spontaneous ovulation, where the pulsatile release is intensified only shortly before ovulation (Shille *et al.,* 1983).

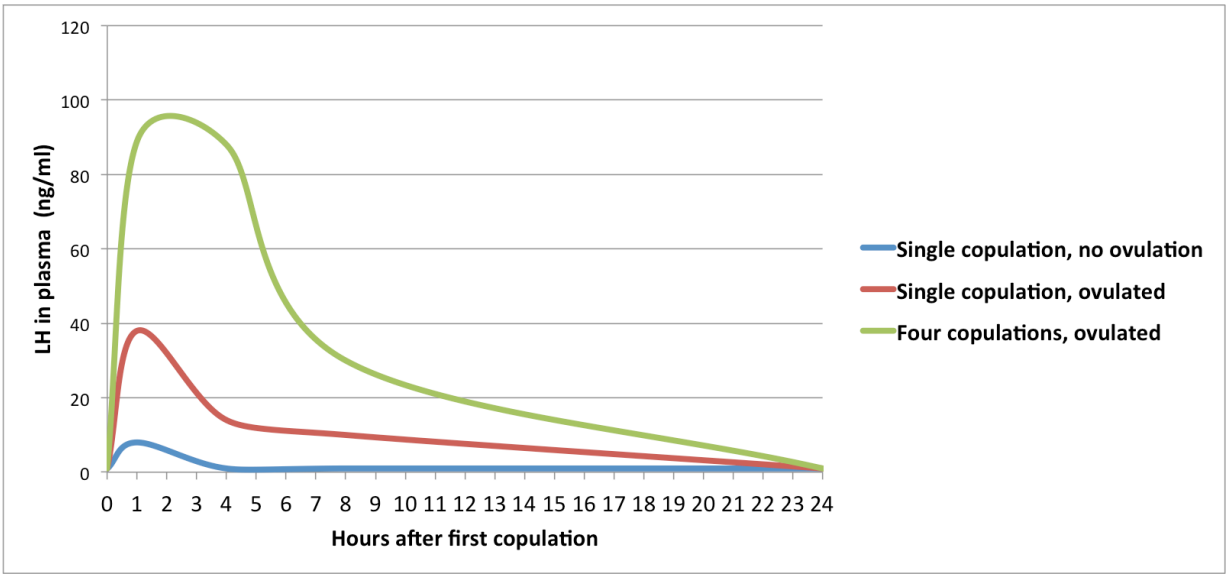

Figure 2. The concentrations of LH in plasma after single and multiple copulations. Data from Concannon et al. (1980).

Ovulation on different days of estrus

In a study conducted by Banks & Stabenfeldt (1982), it could be observed that the day of estrus when the queen was mated had an impact on the LH surge she could produce. A release of LH sufficient to induce ovulation was seen after two matings on day 1 of estrus in only six out of 14 queens, while nine out of 14 were able to produce an ovulatory surge on day 2. One theory of the authors was that either the pituitary gland or hypothalamus needs the elevated levels of plasma estrogens that occur during the follicular phase to be prepared to release a sufficient amount of GnRH and, in response, LH. The researchers also commented that this might be a result of the follicular phase not seamlessly coinciding with the estrus behavior, as observed by Shille *et al.* (1979). However, Wildt *et al.,* (1981) found that three copulations within a period of 3 hours induced ovulation in 10 out of 12 females on the first day of estrus, indicating that the two matings per queen in the first study might not have been enough. Another theory for the different result, as suggested by Banks & Stabenfeldt (1982), might be the interval between copulations, as the two matings in their study occurred 6 hours apart. It was also seen in this study that during one estrus phase, the female cat is capable of one-two LH surges sufficient enough to induce ovulation. This is in agreement with the study done by Wildt *et al.* (1982), which showed that LH concentrations peaked on day 1 and 2 of estrus when the queen was being mated several times, but continued copulation after that did not cause any significant hormonal surge.

Time from copulation to ovulation

In a study by Shille *et al.,* (1983), the first signs of ovulation were detected 23 hours after copulation, with a completed ovulation at 25 hours. Average time for ovulation to occur was concluded to be 23-32 hours after mating and the number of copulations did not seem to alter the

length of that period. However, in an earlier study conducted by Wildt *et al.,* (1981), the time from copulation to ovulation was shown to be 48-64 hours. It is to be noted that in the first study mentioned, the queens were mated on day 3-4 of estrus, and in the one conducted by Wildt *et al.,* (1981), the females were mated on the first day of estrus and then repeatedly on following days throughout the cycle. According to Banks & Stabenfeldt (1982), an earlier study (Shille, 1979) found that the time from copulation to ovulation ranged between 25-30 hours, but no full text could be found at present time.

Pseudo-pregnancy

If the queen ovulates but fails to conceive, she goes into a pseudo-pregnant phase. This can be the result of a spontaneous ovulation, mating with an infertile male or induced by the owner to get a longer period without estrus (Shille & Stabenfeldt, 1979; Brown, 2006). To artificially induce ovulation, both pharmacological substances (often GnRH-agonists) and mechanical stimulation with a cotton swab of the vaginal mucosa can be used (Goericke-Pesch, 2010). There are currently no pharmaceuticals registered in Sweden for inducing ovulation in cats (Läkemedelsindustriföreningen, 2014).

In a study done by Paape *et al.,* (1975), the feline corpora lutea could be seen to develop quickly after ovulation and remain functional for an average of 36.5 days, but an additional time period passed before the queens entered proestrus again, making the average duration for pseudo-pregnancy 40.7 days (normal range between 30-44 days, and lasting 73 days in one queen). These results are in agreement with other studies on the subject (Verhage *et al.*, 1976; Wildt *et al.*, 1981). It is to be noted that the duration of pseudo-pregnancy gathered from these studies is close to half the duration of pregnancy (see below), making the queen different from females of several other species. For example, the pseudo-pregnancy in the bitch lasts for at least the same duration as the real gestation. This gives her a disadvantage compared to the queen in terms of reproducing quickly, since the queen can re-enter proestrus and be ready to breed again much sooner (Paape *et al.,* 1975).

Estradiol and progesterone levels during pseudo-pregnancy

Verhage *et al.,* (1976), showed that estradiol levels in plasma had a peak immediately after copulation but decreased shortly afterwards and stayed at basal level until the queen once again reached estrus. The levels of progesterone stayed at basal concentration for the first 2-3 days after copulation and then rapidly increased to have a peak at day 21, then declined until the concentration was back at basal level, which was observed at day 40. These conclusions about the pattern of progesterone secretion are in agreement with the concentrations and time intervals found in several other studies (Wildt *et al.,* 1981; Paape *et al.,* 1975; Shille & Stabenfeldt, 1979). An overview of the estradiol and progesterone levels during pseudo-pregnancy can be seen in figures 3 and 4.

Pregnancy

If the queen is successfully mated during estrus and get pregnant, the corpora lutea will be active for 40-50 days before starting luteal regression, which is a longer period than observed during pseudo-pregnancy (Feldman & Nelson, 2004). A normal gestation period in the queen lasts 61-69 days (Verhage *et al.,* 1976) and the return to estrus usually takes 2-8 weeks following normal lactation and weaning. However, if the kittens were removed from the queen at an earlier stage, she might enter estrus only 6-8 days after the separation (Feldman & Nelson, 2004).

Estradiol and progesterone levels during pregnancy

In the study already mentioned by Verhage *et al.,* (1976), it was seen that for the first 40 days of pregnancy, the levels of estradiol in plasma were similar to those observed during pseudo-pregnancy, only a little higher on average. However, during pregnancy the concentrations stayed low until day 58-62, elevating slightly again before parturition. Similarly, the levels of progesterone in plasma followed the same pattern as in the pseudo-pregnant queen but had both a higher peak and mean levels, and did not decline as rapidly. The plasma levels were detected at almost basal level right before parturition and dropped further as parturition was over (Fig. 3 and 4). This is in agreement with a study done by Brown *et al.* (1994), in which the same patterns of estradiol and progesterone levels in the pregnant respectively pseudo-pregnant queen were observed.

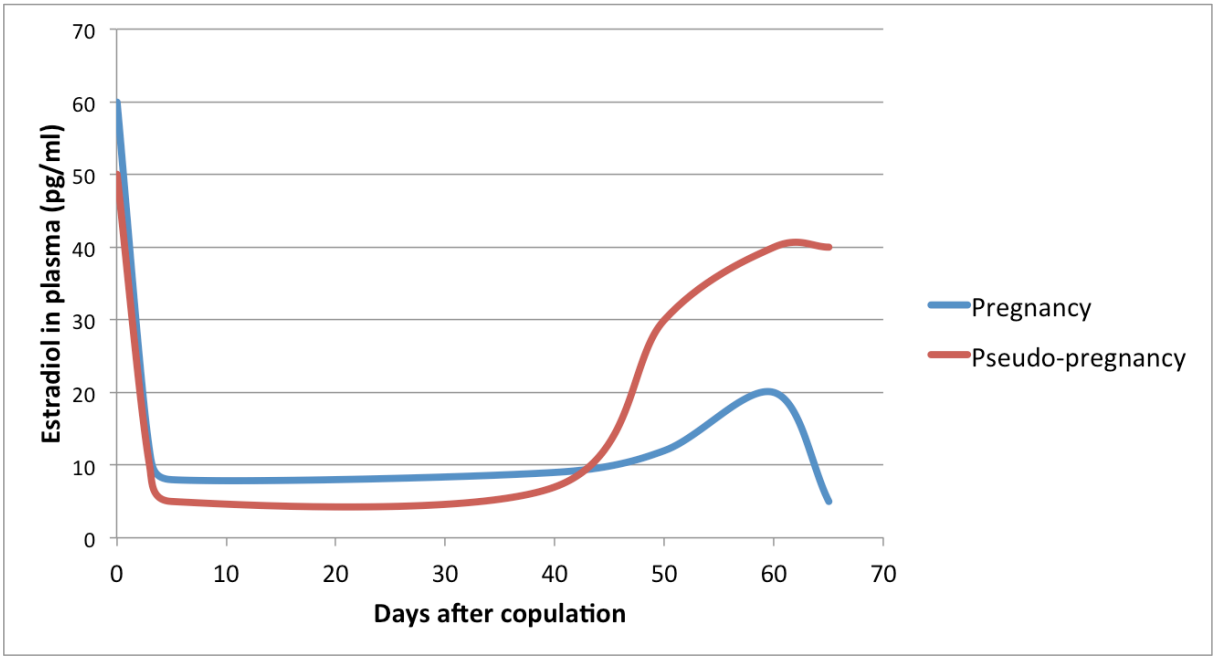

Figure 3. The concentrations of estradiol in plasma during pregnancy and pseudo-pregnancy. Data from Verhage et al. (1976).

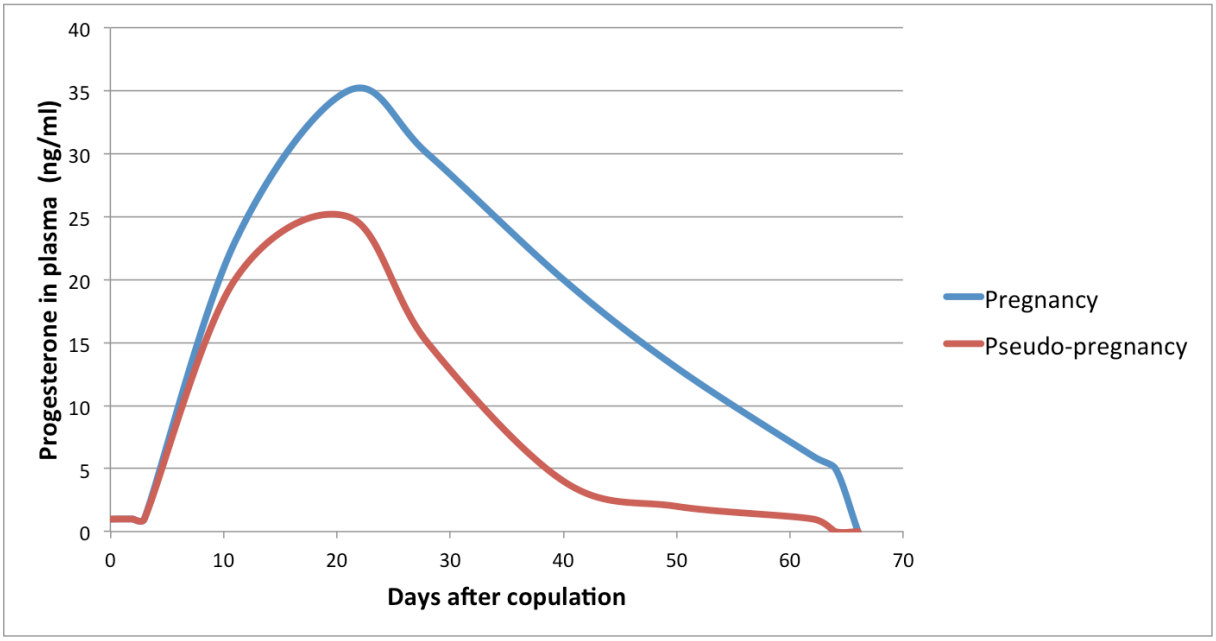

Figure 4. The concentrations of progesterone in plasma during pregnancy and pseudo-pregnancy. Data from Verhage et al. (1976).

Does the placenta produce progesterone during pregnancy?

It has been suggested that the placenta in the female cat produces the progesterone responsible for the plasma concentrations of that steroid after day 40 of gestation (Tsutsui *et al.,* 2009). This could explain the longer duration of elevated plasma levels of progesterone during real pregnancy compared to during pseudo-pregnancy (fig. 4). However, in a study done by Tsutsui *et al.* (2009), 50% of the queens that went through an ovariectomy after day 40 aborted the fetuses, and no significant levels of circulating progesterone could be detected afterwards. Since 50% of the females successfully delivered a litter even after the ovaries had been removed and the levels of progesterone were low, the authors suggest that either the gestation after day 40 is not dependent on high levels of progesterone, or the placenta synthesizes and secretes this hormone locally, and it could therefore not be detected in plasma. In a study done by Braun *et al.* (2012), a large gene expression of enzymes catalyzing the last step of steroid hormone synthesis was found in placentas of ovariohysterectomized cats. Progesterone and estradiol were also extracted from placental tissue. Both findings indicate that the hormones had been synthesized locally. However, the researchers found only very low gene expression of enzymes catalyzing the middle step of the synthesis of progesterone and estradiol. The authors suggested that these intermediates might be synthesized in other organs, such as fetal glands or ovaries, and then delivered to the placenta where the final step of progesterone synthesis would take place. Based on their findings, the researchers concluded that the placenta in the cat is capable of synthesizing steroid hormones.

In comparison, it is commonly known that the placenta in humans is responsible for producing the progesterone that maintains pregnancy after the luteal regression takes place (Tuckey, 2005).

However, in the bitch, sow and cattle, it is the corpora lutea that secretes sufficient levels of the hormone until the end of gestation (Meyer, 1994).

Distinguishing pregnancy from pseudo-pregnancy

One way to distinguish a real pregnancy from a pseudo-pregnancy would be to measure the levels of prolactin and relaxin in plasma (Brown, 2011). In a study done by Banks *et al.* (1983) it was seen that the plasma concentration of prolactin was constant during pseudo-pregnancy but increased during real pregnancy. The increase was slow for the first 5 weeks but after that the concentrations got marginally higher. Similarly, a study done by Stewart & Stabenfeldt (1985) showed that plasma levels of relaxin were elevated during pregnancy but not during pseudo-pregnancy. The elevated concentrations during pregnancy could be detected at day 25 and rapidly increased up to a peak value at day 30-35. The concentrations then remained constant at high levels until day 50-60 when they started to decline, reaching basal levels at the time of parturition.

In a study done by Brown *et al.* (1994), progesterone concentrations in feces were measured, and it was concluded that steroid hormones are excreted in feces in concentrations comparable to those in plasma, thereby useful for detection of pregnancy.

DISCUSSION

The different phases of the estrous cycle

The behavioral phases of the estrous cycle are described differently by different authors, something that can make the subject confusing. Interestrus seem to be the most debated phase and can be used synonymously to anestrus, the anovulatory phase after estrus, or the whole period between two estrus phases, including diestrus. The behavior of the cat during interestrus and anestrus are very similar, something that could suggest that they should go under the same name, as these periods are defined as the behavior of the queen and not the hormonal phases (follicular phase, luteal phase). However, since the duration of those periods are very different it might make it easier to refer to them separately. The duration of the estrous periods can have a wide range in different queens or even in the same queen during separate cycles. For example, the estrus phase has been observed to last between 2-19 days in the female cat. This wide variation can probably be due to several reasons, such as individual hormone release, environmental effects and differences in display of estrus behavior. It could also be due to a variation in the definitions of estrus behavior between researchers, resulting in very different findings.

The induced ovulation in the female cat

It has been shown that the number of matings and the interval between them had an impact on whether the queen ovulates or not. Concannon *et al.*, (1980) showed that only 50% of the females

ovulated after a single copulation and 100% after four, but no studies could be found where they compared that to two or three copulations. Since some of the females ovulated after only one mating, it was suggested that there are individual differences in the LH surge she can produce after coital stimuli. While this sounds like a reasonable suggestion, several other factors have been seen to play a role in the induced ovulation of the queen. Banks & Stabenfeldt (1982) showed that the day of estrus that the queens were mated had an impact on the LH surge they produced. On the first day of estrus less then half of the queens (6/14) managed to produce a high enough LH peak to ovulate, while 64% (9/14) were capable of ovulating the second day. It has been shown that estrus and the follicular phase do not always coincide perfectly (Shille *et al.*, 1979), something that could account for these results. However, in another study it was observed that 10/12 queens were capable of ovulation on the first day of estrus (Wildt *et al.,* 1981). These different results might be due to the different numbers of copulations (two compared to three), the interval between copulations (6 hours compared to 1 hour), estrus and the follicular phase not overlapping perfectly or individual variations in capability to produce a high enough LH surge. It should be noted that both of these studies were conducted with a relatively low number of cats, which makes any conclusions drawn from the results questionable. A study including more cats would be needed to get a more reliable result.

Two studies regarding the time from copulation to ovulation was found, with two different results. Shille *et al.* (1983) reached the conclusion that ovulation occurred 23-32 hours following copulation while Wildt *et al.* (1981) observed that the interval was 48-64 hours. The studies were conducted with differences in the number of copulations, time interval between copulations and on different days of estrus, making it very difficult to draw conclusions of the exact period of time. However, since the queens were mated on the first day of estrus in the second study (Wildt *et al.,* 1981), it is possible that an LH surge occurred that was mistakenly assumed to be enough to cause ovulation, but in fact did not. According to some other authors (Banks & Stabenfeldt, 1982), an earlier study (Shille, 1979) got the same results as the first study mentioned, suggesting that the most usual time interval ranges between 23-32 hours.

Since there are so many deciding factors, it would be difficult to conduct a study focused on one of them while not being biased by the others. However, more studies would be needed to determine the exact mechanisms of the induced ovulation in the queen.

Pregnancy and pseudo-pregnancy

The duration of pregnancy and pseudo-pregnancy has been observed in many studies, and while the gestation period has been shown to be uniform and only differ with a few days between individuals, the duration of the pseudo-pregnancy has a wide range. Paape *et al.* (1975) observed that the pseudo-pregnant period lasted between 30-73 days and calculated a mean of 40.7 days. It is to be noted that the duration of pseudo-pregnancy for most females in the study was in the lower third of that interval, and in only one queen the period lasted as long as 73 days, making

that average a little higher than it possibly should be. However, other studies made on the subject (Verhage *et al.,* 1976; Wildt *et al.,* 1981) had similar results, showing that the duration of pseudo-pregnancy in the queen is highly variable.

The plasma levels of estradiol and progesterone during pregnancy and pseudo-pregnancy are well documented and many studies have been conducted with the same results. The concentrations of the hormones follow an almost completely opposite pattern but only small differences in concentrations could be seen between pregnancy and pseudo-pregnancy before luteal regression takes place in the latter. While the plasma levels of both estradiol and progesterone was observed to be slightly higher during pregnancy, it is doubtful if this could be used to determine if the queen is pregnant or not, due to individual variations of the hormone levels.

Whether the placenta in the female cat produces progesterone to maintain pregnancy or not seems to be unclear (Tsutsui *et al.*, 2009; Braun *et al.*, 2012). No elevated blood levels could be found after ovariectomy but just like the researchers suggested, the placenta might synthesize and secrete it locally (Tsutsui *et al.*, 2009). This theory was supported by the second study (Braun *et al.*, 2012) where progesterone and estradiol were found in placental tissue. As there seem to be a great variety between species regarding this matter (Tuckey, 2005; Meyer, 1994), more research is needed to determine the hormonal role of the placenta in the queen. A possible explanation might be that the small concentrations of progesterone found in the placentas are an evolutionary remnant of producing progesterone, and not actually needed to maintain pregnancy.

Measuring progesterone, relaxin and prolactin has been suggested as methods to distinguish pregnancy from pseudo-pregnancy, as already mentioned (Banks *et al.,* 1983; Stewart & Stabenfeldt, 1985; Brown *et al.,* 1994; Brown, 2011). Prolactin was shown to be elevated during pregnancy, but the difference from pseudo-pregnancy could be detected first after 6 weeks and at that time it is likely that the corpora lutea would already have begun regression. Measuring declining progesterone levels in feces 40 days after copulation would therefore be an easier way to detect pseudo-pregnancy at that time, as it is a noninvasive method and would cause less stress for the cat. However, relaxin had elevated levels in plasma after only 25 days during gestation and could be used to detect pregnancy earlier then the other two substances. But since both relaxin and prolactin need blood tests, the owner would have to take the cat to a veterinarian, while a feces test could be sent to the lab via mail.

Conclusions

The reproductive processes in the female cat are not completely mapped out yet. The mechanisms of the induced ovulation and the hormonal role of the placenta are some of the fields yet to be fully understood, and more research would be needed for a more complete understanding of the reproductive physiology of the queen.

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