

Case Report

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Case report

Clinical Efficacy of hCG for Ovulation Induction in Maine Coon Queens: A Case Series from a Breeding Cattery in Uruguay

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Simple Summary

Domestic cats, including the Maine Coon breed, have seasonal reproductive cycles and are generally considered induced ovulating animals, but ovulations may also occur in the absence of mating. However, breeders often need to plan pregnancies to optimize litter size and kitten survival. This study aimed to evaluate whether human chorionic gonadotropin (hCG) can reliably induce ovulation in Maine Coon queens, leading to successful pregnancies and healthy litters. Seven female cats were selected during their fertile phase and given a single injection of the hormone. All seven cats ovulated, became pregnant, and gave birth within a short time frame. The average litter contained six kittens, larger than the typical litter size for this cattery, and very few kittens died at birth. The treatment was well tolerated, and no side effects were observed. These results show that hCG-induced ovulation is a safe and effective method to help breeders manage reproduction in Maine Coons, ensuring more predictable pregnancies, larger litter sizes, and higher survival of kittens. This approach can improve the efficiency of breeding programs, reducing queen stress and supporting the health and welfare of both mothers and kittens.

Abstract

The present study evaluated the efficacy of human chorionic gonadotropin (hCG)-induced ovulation in Maine Coon queens under subtropical conditions, with catteries managed outdoors or indoors under controlled photoperiods. Seven queens in proestrus or estrus were selected based on vaginal cytology and received a single intramuscular injection of 100 IU hCG to induce ovulation. Serum progesterone levels were measured 24 hours post-treatment, and fertile toms were introduced for mating. All queens ovulated, became pregnant, and delivered within a 4-day window, with a mean gestation length of 67.9 ± 2.1 days. The mean litter size was 6.2 ± 3.2 kittens, significantly larger than historical records for the cattery ($p \leq 0.05$), while neonatal mortality at birth was low (4.5%). These outcomes indicate that the applied protocol reliably induces ovulation, enhances fertility, and improves perinatal survival. The study also highlights breed-specific reproductive traits of Maine Coons, including late sexual maturity, large litter size, and susceptibility to spontaneous ovulation. Exogenous hCG administration was well tolerated, with no adverse effects observed. Overall, the findings support the use of hCG-induced ovulation as a practical and effective strategy for reproductive management in Maine Coon breeding programs, particularly under controlled environmental conditions, enabling optimization of litter timing, size, and neonatal survival.

Keywords: human chorionic gonadotropin; ovulation synchronization; pregnancy; cat

1. Introduction

In recent years, the breeding of domestic cats (*Felis catus*) has increased considerably [1]. The queen is a seasonally polyestrous, induced ovulator and long-day breeder. At the onset of the breeding season—initiated by the natural extension of the photoperiod—queens typically exhibit recurrent estrous cycles lasting 5–7 days, separated by interestrous intervals averaging 9 days (range: 2–19 days) in the absence of ovulation [2–4]. In queens that do not undergo mating and/or spontaneous ovulation, estrous periods recur at average intervals of 10–14 days (range: 0–20 days) throughout the breeding season. The interval devoid of overt behavioral or clinical signs of estrus is termed interestrous [5]. Although this stage is characterized by apparent ovarian quiescence, follicular recruitment and development toward the subsequent estrous cycle are already underway. During interestrous, circulating estrogen concentrations typically decline to basal values; however, in some queens, successive follicular waves may overlap [6].

During estrus, serum estradiol concentrations reach their maximum [5,6]. Ovulation may occur spontaneously, though more commonly as a consequence of repeated copulations, and generally ensues approximately 24–48 hours thereafter [7,8]. A serum progesterone (P4) concentration exceeding 1.0–2.0 ng/ml [3.2–6.4 nmol/L] is considered indicative of luteal activity in the queen and, therefore, confirmatory of ovulation [2,9]. Plasma P4 concentrations peak between days 25 (d25) and 30 of gestation before gradually declining. In the second half of pregnancy, the feline placenta becomes the primary source of progestins until parturition, which typically occurs around d65 [5,10].

True ovarian quiescence is observed only during anestrus, which, unlike interestrous, represents a prolonged period of reproductive inactivity. Anestrus arises in response to markedly short natural photoperiods (winter months) or under conditions of artificially reduced daylight exposure (4–6 hours/day). Conversely, it may be absent in queens continuously exposed to long-day photoperiods, particularly indoor cats or those maintained in breeding colonies under constant artificial lighting [11].

The feline reproductive cycle can be artificially modulated by photoperiod, as daylight exposure influences melatonin secretion during autumn, thereby attenuating gonadotrophin release via the pineal gland. This neuroendocrine organ regulates several physiological processes, including reproduction, in accordance with circadian rhythms by modulating the hypothalamic–pituitary–gonadal axis [12,13].

Because many cats now live predominantly indoors, artificial lighting may alter reproductive seasonality. As a result, some queens may display estrous cycles year-round, although most indoor cats still exhibit a degree of seasonal anestrus [4,14]. Certain breeds, particularly Oriental breeds, appear less sensitive to photoperiodic cues and may continue to cycle throughout the year [15].

Ovulation in queens can be induced either mechanically, through vaginal stimulation (e.g., with a glass rod or cotton swab), or pharmacologically, via administration of luteinizing hormone (LH); LH-like agents, such as human chorionic gonadotrophin (hCG); or LH-releasing compounds such as gonadotropin-releasing hormone (GnRH), of which gonadorelin is a synthetic agonist [16–21]. From an endocrine perspective, hCG acts directly on the ovary, thereby bypassing the hypothalamic–pituitary axis [16].

Maine Coons are regarded as a late-maturing breed, largely due to their large body size, and typically reach sexual maturity only after attaining approximately 80% of their target adult body weight. Among their distinctive characteristics, this breed exhibits comparatively protracted pubertal development, with puberty occurring between 9 and 16 months of age, and one study reporting a mean age at puberty of 9.6 months [22].

In addition, Maine Coons are reported to display breed-specific physiological features, including variations in gestational parameters as well as hematological and biochemical reference values [23]. The mean litter size (5.5) in Maine Coons has been shown to be significantly larger than that of other breeds [22–24].

Induction of estrus in queens may be undertaken for several reasons, primarily related to reproductive management and the optimization of cattery efficiency. Estrus synchronization

facilitates breeding planning, enabling breeders to schedule parturitions at convenient times and to avoid overlapping litters during periods of reduced staff availability or limited demand for kittens [11]. In catteries that employ artificial insemination, synchronization of estrus and ovulation is essential to ensure that it occurs at the optimal stage of the cycle, thereby maximizing conception rates [25]. Moreover, synchronization supports genetic selection by permitting multiple litters within a shorter timeframe, facilitating the identification of desirable individuals for future breeding programs. From a husbandry standpoint, concentrating parturitions within a defined period enhances maternal and neonatal care efficiency, allowing work routines to be planned in advance [26]. Finally, synchronization may reduce stress in queens by limiting repeated, unwanted estrous cycles, which may otherwise predispose them to uterine or mammary pathologies associated with prolonged P4 exposure [15,27].

It is worth noting that much of the current knowledge on feline reproduction derives from studies conducted in North America, Australia, and Northern Europe, under climatic and photoperiodic conditions typical of continental regions [28–37]. Therefore, this study, conducted in a subtropical zone, may provide new insights in this reproductive area.

2. Case Description

Uruguay has a humid subtropical climate, located between 30° and 35° south latitude. In the present study, catteries were managed as outdoor facilities with cat runs, under natural light conditions and maintained at ambient room temperature. Animals were fed commercial feline diets with ad libitum access to water.

2.1. Breeder Characteristics

At the breeder's discretion, each queen produced one litter per year, in accordance with the breed's seasonal reproductive pattern in this region. International guidelines recommend a maximum of three litters per queen over a two-year period, although four litters are permitted under the regulations of the World Cat Federation (WCF) [38]. Births were consistently recorded between mid-September and late April, corresponding to spring and early autumn at this latitude.

In this cattery, the mean litter size was 4.1 ± 1.9 kittens, with females representing 42.9% of births, consistent with previous reports [23,24,39]. At birth, female kittens weighed 94.72 ± 11.04 g, compared with 116.39 ± 11.09 g for males, for a total of 132 kittens born.

In litters comprising five or more kittens (37.9%), the proportion of female kittens increased to 47.7% ($p \leq 0.05$).

The incidence of stillbirths was 0.52 ± 0.32 per litter, while pre-weaning mortality averaged 0.71 ± 0.53 per litter, predominantly attributable to aspiration pneumonia, as previously documented [22]. This condition is frequently observed in kittens, particularly in the Maine Coon breed [12]. When stillbirths were evaluated in relation to litter size, 43.1% of litters containing three or more kittens were affected [24].

2.2. Animal Selection

Diagnostic colposcopy was performed on the day of hormone treatment using serum-moistened swabs to determine the stage of the reproductive cycle. Seven queens identified as being in proestrus or estrus were subsequently selected for the study.

Selected animals weighed 5.5 ± 0.8 kg, with a mean age of 3.6 ± 1.1 years [40].

2.3. Laboratory Methodologies

Vaginal cytology was performed using cotton swabs moistened with distilled water. The swab tip was inserted into the vulva at an upward angle to access the vagina, then advanced cranially. Sampling was achieved by rotating the swab 2–3 times clockwise before withdrawal. The collected material was rolled onto glass slides in three rows and air-dried. Samples were stained with Diff-

Quick and examined under light microscopy at 10× magnification. Digital images were obtained using a mobile phone camera, and the proportions of epithelial cell types (parabasal, intermediate, superficial) and neutrophils were quantified per 10 fields of view (Figure 1).

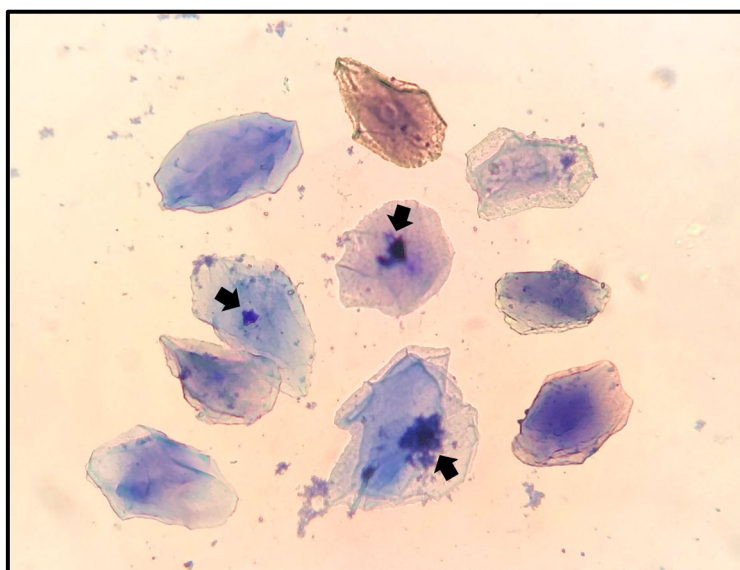


Figure 1. Vaginal cytology from a queen on d3 of estrus (Diff-Quik stain). The epithelial cell population shows partial cornification, with flattened cells exhibiting irregular, angular borders. Approximately 40% of the cells retain their nuclei, which appear shrunken and hyperchromatic, indicative of pyknosis (arrows). In queens during estrus, over 75% of vaginal epithelial cells are typically cornified; intermediate cells may persist, and complete cornification is not always observed [4].

On the following day, jugular blood samples were collected from all selected queens for serum P4 measurement, using a solid-phase competitive chemiluminescent enzyme immunoassay (Siemens IMMULITE™ 1000) with commercial test kits (Siemens Diagnostic Product Corporation™, Los Angeles, CA, USA). The assay sensitivity was 0.2 ng/mL (0.6 nmol/L), with intra- and inter-assay coefficients of variation of 3.9% and 7.2%, respectively.

2.4. Treatment

Queens identified as being in proestrus or estrus based on colpocytology received a single intramuscular injection of 100 IU hCG (Chorulon™, MSD Animal Health, Boxmeer, Netherlands) on day 0 to induce ovulation [25,26]. This was the first use of hCG in this cattery, either for ovulation induction or any other purpose. All treated queens responded to induction, and no adverse reactions were observed at the injection site. Fertile toms were introduced for three consecutive days.

2.5. Response to Ovulation Induction

Serum P4 concentrations, measured 24 hours after hCG administration (coinciding with male introduction), averaged 3.0 ± 0.7 ng/mL [range: 2.0–4.1 ng/mL] (9.5 ± 2.2 nmol/L [range: 6.4–13.0 nmol/L]). Concurrent vaginal cytology confirmed ovulation.

All queens conceived, as verified by ultrasound (Esaote Mylab Delta Vet™ with 4–9 MHz micro-convex linear probe, Italy) performed on d25 post-mating, which demonstrated fetal membranes surrounding embryos and mobile embryos measuring 1.71 ± 0.33 cm (Figure 2) [10]. The seven parturitions occurred within a four-day window, with natural deliveries at 67.87 ± 2.05 days following gonadotropin administration. The mean litter size was 6.2 ± 3.2 kittens, significantly larger than the historical mean for this cattery ($p \leq 0.05$). Neonatal mortality at birth was 4.5%, markedly lower than both previous cattery records and international reports for this breed ($p \leq 0.01$) [22,24].

2.6. Statistical Analysis

Statistical analysis was conducted using SAS 9.0 software for Windows (SAS Institute Inc.TM, Cary, NC, USA). The results are presented as means \pm SD. Obstetric and newborn parameters were analyzed by one-way ANOVA. A significance level of $p < 0.05$ was used.



Figure 2. Ultrasound image of longitudinal section of the fetus, d25.

3. Discussion

It is noteworthy that, although domestic cats are seasonal breeders and ovulation has traditionally been considered coitus-induced through cervical stimulation by penile spicules, recent evidence indicates that spontaneous ovulation may occur in at least 30% of estrous cycles [8,12,22,41]. Factors such as body weight, age, social environment, and breed may influence this phenomenon, with Maine Coons appearing to exhibit a higher prevalence of spontaneous ovulation than other breeds [42]. This predisposition could increase susceptibility to P4-dependent conditions [12,15,43], among which the cystic endometrial hyperplasia–pyometra complex (CEH–pyometra) is particularly common. CEH–pyometra is characterized by endometrial gland proliferation, cyst formation, and uterine dilation, followed by bacterial colonization and purulent fluid accumulation under conditions of cervical closure [15,27]. P4 plays a central pathogenic role by stimulating endometrial hyperplasia, enhancing glandular secretions, suppressing leukocyte activity, reducing myometrial contractility, and maintaining cervical closure [15,27].

With respect to gestation length, studies report conflicting results: one study reported no breed-related differences [34], while another demonstrated significant breed effects, with longer gestations (> 66 days) in Siamese and Oriental Shorthair cats, and shorter ones (63 days) in Korats [44]. Moreover, 95% of births in Maine Coons were reported to occur between days 65 and 68 post-mating [24], in agreement with the present study, thereby confirming that pregnancy duration in this breed is relatively stable.

Perinatal mortality in the studied cattery was comparatively high, consistent with earlier reports, highlighting elevated mortality rates in Maine Coons [22,24]. In a retrospective study of neonatal kittens submitted to a diagnostic laboratory, aspiration pneumonia and septicemia each accounted for approximately 15% of deaths [45]. These outcomes reflect the physiological immaturity of neonates, including pulmonary insufficiency, impaired thermoregulation, and an underdeveloped

immune system, all of which compromise suckling ability. If kittens are too weak to nurse or maternal care is inadequate, tube feeding may be required to ensure survival.

Although mean birth weight in the present cohort was higher than values reported in some studies [44,46–48]—likely reflecting the large body size of both queens and litters—low relative birth weight (10–15% below surviving littermates) likely contributed to perinatal losses. Conversely, Socha et al. [24] reported birth weights in Maine Coons similar to those observed here. These findings emphasize the importance of systematic neonatal monitoring and timely supportive care to enhance survival in this breed.

An important consideration is that repeated administration of exogenous gonadotropins, such as equine chorionic gonadotropin or hCG, may induce antibody production against FSH and LH. Such antibodies may cross-react with endogenous hormones, thereby attenuating ovarian responses to subsequent stimulation or, in some cases, leading to infertility through neutralization of gonadotropins [11,49]. Consequently, permanent or frequent repetition of such treatments is discouraged.

Previous studies have demonstrated that continuous induction of estrus and ovulation every 44–50 days promotes the development of anti-gonadotropic antibodies. However, the effects of annual or strategically timed protocols remain less clear [49]. One study evaluating hCG doses from 0 to 500 IU, administered either as a single dose or repeated after 24 hours, reported a 100% ovulatory response only with 500 IU, while 100 IU induced ovulation in merely 25% of queens [16]. In contrast, the protocol applied in the present study (100 IU single dose) successfully induced ovulation in all queens. This suggests that timing, dosage, and environmental context may critically influence outcomes.

It should also be acknowledged that queens in cattery environments are subject to additional stimuli, such as the presence of toms or human handling, which can promote hypothalamic GnRH release, thereby triggering LH surges and ovulation even in the absence of copulation [7,12,41].

The pharmacokinetic profile of hCG, which exhibits a prolonged half-life of up to four days, may elicit secondary follicular waves and accessory ovulations in treated queens, potentially modifying the oviductal endocrine milieu and impairing implantation [50,51]. Despite these considerations, the treated queens in this study exhibited larger litters and reduced neonatal mortality, supporting the efficacy of the applied protocol under subtropical and controlled indoor conditions.

Maine Coons are recognized as a late-maturing breed due to their prolonged somatic growth [23], leading to the assumption that breeding should be delayed to optimize reproductive performance. However, the present findings do not support this assumption. Despite the breeder's practice of limiting each queen to one litter annually, extended inter-litter intervals were not observed, and litter sizes exceeded those reported for other domestic breeds [23,24,52]. These results suggest that prolonged recovery intervals may not be required in Maine Coons. Nevertheless, the influence of body condition must be considered, as both excessive adiposity and underweight status can negatively impact fertility in cats [53–55] and other mammals, including mice [56].

The sex ratio observed in this study did not conform to the predictions of the Trivers–Willard hypothesis [57], which posits that smaller litters are more likely to produce female offspring, whereas larger litters favor a higher proportion of males. Interestingly, larger litters in this cohort exhibited a significantly greater proportion of females ($p \leq 0.05$), though still below parity. This deviation may reflect adaptive strategies of domestic cats, which are largely solitary, with males enjoying broader reproductive opportunities by mating with multiple females across extensive territories [57,58]. According to the Trivers–Willard model, in polygynous species where male reproductive success varies widely, mothers in favorable condition are predicted to invest preferentially in male offspring [58,59]. In the present study, deviations from this model may be attributable to evolutionary adaptations of domestic cats or the presence of sex-linked lethal alleles, which are more prevalent in inbred populations and may skew sex ratios through recessive X-linked embryonic lethality or resorption.

4. Conclusions

These findings indicate that hCG-induced ovulation is highly effective in Maine Coon queens, achieving both consistently high fertility rates and low perinatal mortality. The applied protocol proved reliable under indoor housing and controlled photoperiod conditions, suggesting its suitability for systematic reproductive management in breeding catteries. Moreover, the results highlight the potential to optimize litter size and neonatal survival while minimizing reproductive stress, providing practical guidance for breeders aiming to enhance reproductive efficiency and overall kitten welfare.

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Data Availability Statement: The original contributions presented in this study are included in the article. Further inquiries can be directed to the corresponding author(s).

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Abbreviations

The following abbreviations are used in this manuscript:

hCG	Human chorionic gonadotropin
P4	Progesterone
LH	Luteinizing hormone
FSH	Follicle-Stimulating Hormone

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