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Clinical management of pregnancy in cats

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Abstract

Average gestation length in domestic cats is 65.6 days, with a range of 52–74 days. Average reported litter size is 4.0 kittens per litter; litter size is not correlated with number of matings in a given estrus. Superfecundation is common in domestic cats; superfetation never has been definitively proven to occur. Eclampsia may occur during pregnancy in queens, with non-specific clinical signs. Ectopic pregnancy and uterine torsion have been reported. Pregnancy loss may be due to infectious causes, including bacteria, viruses or protozoa, or non-infectious causes, such as hypoluteoidism and chromosome errors.

Keywords: Pregnancy; Cats; Hormones; Viruses; Litter size; Abortion

1. Introduction

Normal pregnancy and abnormalities of pregnancy are studied in domestic cats both for their value to veterinarians working with cat breeders and as models for studying reproductive physiology of non-domestic cats. This manuscript is a review of normal pregnancy endocrinology and physiology and reported abnormalities of pregnancy in domestic cats.

2. Endocrinology of pregnancy

The three principal hormones of pregnancy, estradiol-17β, luteinizing hormone and progesterone, are secreted to varying extents throughout the gestation period in queens.

2.1. Estrogen

During the first half of gestation, serum concentrations of estradiol-17β fluctuate around baseline, with one-half of queens showing a significant rise approximately 1 week before parturition [1]. Serum luteinizing hormone concentrations also fluctuate around baseline in the first half of gestation but remain low until the time of parturition [1].

2.2. Progesterone

The concentration of progesterone in serum rises after either spontaneous or induced ovulation and it must be present throughout gestation for pregnancy to be maintained. Identification of the source of progesterone secretion in cats differs among studies. In one study, in which pregnant queens were ovariecтомized at days 45–49 of gestation, none of the queens aborted, suggesting an extra-ovarian source of progesterone [2]. It also has been demonstrated that the enzymes necessary for production of progesterone exist in the feline placenta, suggesting that the feto-placental unit could be a source of gestational progesterone [3]. On the other hand, a recent study demonstrated that pregnant queens ovariecтомized at day 30 or 45 of gestation exhibited a decline in serum progesterone concentration and subsequently aborted; however, pregnancy was maintained by supplementation of the queens with synthetic progesterone after ovariecotomy [4]. Prolactin is considered a luteotropic...
hormone [5]. Administration of a prolactin-inhibiting
drug, cabergoline, in the latter half of gestation caused a
decrease in serum progesterone concentration and from
88% to 100% of treated queens subsequently aborted
[4,6], suggesting that corpora lutea are the primary source
of progesterone during pregnancy in cats. Knowledge of
the source of gestational progesterone alters diagnostic
methods used for assessment of pregnancy loss and
affects the choice of drugs and regimens to be used for
pregnancy termination in cats.

Progesterone, from whatever source, varies in extent
of secretion during gestation, with peak serum values of
11–60 ng/ml reported after the first mating [1]. Serum
progesterone concentrations fall to a nadir in most
queens prior to parturition; however, unlike the bitch,
queens can progress into active labor with serum
progesterone concentrations >1 ng/ml [1].

3. Characteristics of normal pregnancy

3.1. Litter size

The average litter size in cats is 4.0 kittens per litter
[1,7–9], but varies among breeds. Number of matings is
not correlated with litter size [8]. A litter of 18 kittens
was reported in one queen undergoing pregnancy
termination via ovariohysterectomy [10]. The cervix of
queens is not patent during diestrus and pregnancy; no
vulvar discharge is observed during pregnancy in
normal queens [11]. In late gestation, normocytic,
normochromic anemia with reticulocytosis commonly
develops [12]. Total and differential white blood cell
counts have not been demonstrated to vary with
pregnancy in cats [12].

3.2. Gestation length

Gestation length in domestic cats, from date of first
or last mating until onset of parturition, averages 65.6
days, with a range of 52–74 days [1,7,9,13]. Gestation
lengths of less than 60 days are associated with
decreased viability of offspring. A variation in gestation
length by breed may exist; one study documented a
mean gestation length of 63 days for Siamese queens
and of 65 days for Persian queens [8]. Gestation length
varies by species as well; generally, gestation length is
correlated with body size in felids.

3.3. Diet during pregnancy

During pregnancy, dietary demand for protein
increases, especially for the amino acids—arginine,
lysine and tryptophan [9,14]. Pregnant queens seek out
higher protein diets, in preference to carbohydrate-rich
diets [15]. At a minimum, diets for pregnant queens
should contain 32% protein and 18% fat [9]. By the time
of parturition, queens should have gained 12–38% of
their pre-pregnancy body weight [7].

3.4. Multiple sires and multiple ages within litters

Super-fecundation, the presence of offspring from
more than one sire in a single litter, is reported to
commonly occur in cats. Superfetation, the simulta-
neous presence of offspring of greatly differing
gestational age in the uterus, never has been definitively
demonstrated to occur in domestic cats despite case
reports purporting to show kittens of different ages in
the uterus of pregnant queens [10,16,17]. True super-
fetation cannot be differentiated from arrested devel-
opment unless all kittens are normal at term delivery on
two or more widely divergent dates. For superfetation to
happen, conception must occur after tertiary follicles
have been induced to ovulate by copulatory behavior in
a pregnant female. Periods of follicular growth do occur
during the luteal phase in cats [18] and the ovary can
respond to exogenous gonadotropins at mid-gestation
[19]. Conversely, it also [is] known that queens may
show estrous-like copulatory behavior during preg-
nancy with no significant elevations in concentrations of
estradiol or luteinizing hormone in serum, suggesting
that such activity may not be associated with the
endocrinology or physiology of fertility [20].

4. Abnormalities of pregnancy

4.1. Eclampsia

Eclampsia is hypocalcaemia. Although thought to
occur most commonly at peak lactation in queens
nursing large litters, eclampsia also has been reported to
occur in queens from 3 to 17 days before parturition
[21]. No correlation was shown between diet and
likelihood of onset of eclampsia. Clinical signs were
non-specific and included acute onset of lethargy and
anorexia, trembling and muscle fasciculations, dehy-
dration, weakness, pallor, hypothermia, dyspnea and/or
tachypnea and bradycardia. Diagnosis can be made by
demonstration of abnormally low concentrations of
calcium in serum. All affected cats responded to
intravenous and/or subcutaneous calcium administra-
tion with subsequent oral calcium supplements until one
month after parturition. All queens gave birth and
lactated normally. Veterinarians are encouraged to
consider eclampsia as a rule-out for non-specific signs of illness in queens during late gestation.

4.2. Ectopic pregnancy

Ectopic pregnancy refers to the extra-uterine development of one or more fetuses. In a primary ectopic pregnancy, development of the zygote through both the embryonic and fetal stages occurs outside of the uterine body. A secondary ectopic pregnancy is defined as continuing development of a fetus in the abdominal cavity after rupture of the uterine wall, which may be associated with a history of trauma. Of the case reports describing ectopic pregnancy in queens, none of them describes the presence of viable kittens outside of the uterus. Instead, most report the occurrence of mummified or macerated fetuses in the abdominal cavity, with or without apparent supporting membranes, at some period of time after routine ovariohysterectomy or parturition [22–26]. Most ectopic fetuses are aseptic, although affected cats may be symptomatic. Clinical symptoms include gastrointestinal (vomiting anorexia), urinary (hematuria, pollakiuria, urination outside of the litter box) and such non-specific signs as depression and lethargy. Diagnosis is made by abdominal radiography or ultrasonography. Surgical removal of the fetal tissues and supporting structures is the usual treatment.

4.3. Torsion of uterus

Torsion of one or both uterine horns occurs rarely in queens, but onset most frequently occurs in the latter half of pregnancy, from the fifth week to parturition. Unilateral torsion is more common, occurring in 93% of cases [27]. Suggested reasons for its occurrence include fetal activity or movement of the queen that causes the uterine horn to rotate around its long axis to produce excessive laxity of the broad ligament [27,28]. The degree of torsion can vary from 180° to 900° and less severe clinical signs are associated with a lesser degree of torsion [29]. The clinical presentation includes acute onset of mucoid, serosanguineous or hemorrhagic vulvar discharge; abdominal pain and/or distension; hypothermia; tachycardia and pallor; and dystocia [27,29,30]. The condition is diagnosed by abdominal ultrasonography. Diagnosis can be enhanced by color flow Doppler ultrasonography or by exploratory laparotomy. The latter option often is chosen because surgery is the preferred treatment. Detorsion can be attempted if the uterine tissue appears viable, but clinical signs of reperfusion injury must be anticipated. Most often, en bloc ovariohysterectomy is the preferred treatment. In one survey of 14 queens with uterine torsion, three of them died despite prompt surgical intervention [27].

5. Pregnancy loss

Pregnancy loss can be due either to infectious or non-infectious causes. Infectious agents include bacteria, viruses and protozoa.

5.1. Bacterial

Bacterial infection as a cause of pregnancy loss rarely is reported in cats. For example, one case of dystocia and birth of dead kittens was associated with environmental contamination by Salmonella typhimurium, apparently from raw food fed to all the cats in the facility [31]. Then, in another case, experimental infection with Bartonella henselae was associated with sub-fertility in the queens, but the bacteria was not transmitted venereally, transplacentally or through colostrum or milk [32]. Catteries with adequate hygiene are unlikely to develop a problem with pregnancy loss due to bacterial infection.

5.2. Viral

5.2.1. Feline leukemia virus

Feline leukemia virus is a retrovirus with horizontal transmission that is most commonly found in cats from multi-cat households and in cats allowed outside exposure to other cats. While feline leukemia virus infection has been associated with epidemics of abortions in catteries [33], improved understanding and management of the disease have decreased the number of cases reported. Management for control of feline leukemia virus includes testing of all cats in a facility and removal of all animals with positive tests and testing of all cats before introduction into a facility [34]. Cats with a history of exposure to feline leukemia virus that successfully fight off infection and become non-viremic still appear to be more susceptible to infectious disease, stressing the importance of avoidance over vaccination or treatment [35].

5.2.2. Feline immunodeficiency virus

Feline immunodeficiency virus (FIV) is another cause of pregnancy loss in queens. One study reported that no transplacental transfer of FIV occurred in seropositive queens [36], but a recent study demonstrated the occurrence of decreased litter size and presence of placental infection in seropositive queens.
In the latter study, control queens produced litters averaging 3.8 kittens and only one of 31 concepti was non-viable. By contrast, the average litter size in queens experimentally infected with FIV prior to breeding was 2.7 kittens and 15 of 25 conceptuses were non-viable. FIV was present in 14 of 15 placentas. FIV also has been reported to be transmitted horizontally by direct contact (biting) and indirect contact (excreted in milk or semen) [38]. The effect of vaccination as a control measure to prevent pregnancy loss from FIV infection in catteries has not been reported.

5.2.3. Feline enteric corona virus

Feline enteric corona virus (FCoV) is a ubiquitous virus that causes feline infectious peritonitis (FIP) in some cats [39,40]. FCoV is endemic in most multi-cat households, with a sero-prevalence of 75–100% [40]. After initial exposure to FCoV, about 10% of cats develop FIP, 13% become healthy carriers and the remaining 77% become infected, shed virus in feces for several months and then clear the virus, leaving them susceptible to reinfection [41]. Facilities containing queens with high titers for FCoV are more likely to report reproductive failure, abortion and dead fetuses at birth [33]. Because the virus is ubiquitous, preventive management is preferred to test-and-removal or treatment programs. All cats in a facility should be tested every 3–6 months and seropositive animals housed separately from sero-negative animals. Only sero-negative animals should be introduced into sero-negative facilities. Seropositive queens should be bred only to seropositive toms and sero-negative queens to sero-negative toms. An on-line registry exists that allows cat breeders to find animals in their breed that match the serologic status in their cattery (http://www.catbreeder.com/). To prevent transmission of FCoV, provide one litter box for every one or two cats; clean litter boxes at least once daily and disinfect them once weekly; keep litter boxes away from food; and, vacuum around litter boxes regularly [41]. Some lines of cats have a genetic predisposition to development of FIP. In one study, the heritability for development of FIP after exposure to FCoV in Persian cats and Birmans cats was 54% and 52%, respectively [42]. Parents and offspring of cats that develop FIP should be removed from the breeding program.

5.2.4. Feline herpes virus

Feline herpes virus infection causes viral rhinotracheitis. Queens infected experimentally via intranasal exposure, mimicking natural exposure, aborted secondarily to severe, debilitating upper respiratory disease; no placental lesions were identified [43]. Control by vaccination of queens before breeding is recommended.

5.2.5. Panleukopenia

Panleukopenia, or feline distemper, is caused by a parvovirus. Infection or vaccination with a modified-live virus vaccine can cause either abortion or birth of kittens with cerebellar hypoplasia, depending on the stage of gestation during which the viral exposure occurs [33,44]. Control by vaccination of queens at a sufficient interval before breeding is recommended.

5.3. Protozoan

Toxoplasma gondii is a protozoan parasite for which cats are the definitive hosts. Infected cats shed non-sporulated (non-infective) oocysts in feces. Cysts undergo sporulation outside the cat and are ingested by intermediate hosts. Cats become infected by ingesting animal tissues containing tissue cysts. Reproductive effects of toxoplasmosis in cats are most common in pregnant queens that develop neurologic disease and subsequently abort and in kittens infected transplacentally that die shortly before or after birth [33,45,46]. Adult cats may be more likely to be infected with T. gondii as they age [47] or if they have a concurrent viral infection [48]. Prevention of exposure to toxoplasmosis is preferred to treatment. Domestic cats should not be allowed to hunt and should not be fed raw meat. Big cats are less likely to be exposed to tissue cysts of Toxoplasma if fed frozen beef rather than pork or horsemeat [45].

5.4. Non-infectious causes

Non-infectious causes of feline pregnancy loss include hypoluteoidism, chromosomal errors, improper diet and administration of embryotoxic drugs or nutrients to the queen. The first three causes are discussed in the following section. Also, pregnancy loss may be idiopathic.

5.4.1. Hypoluteoidism

Hypoluteoidism is defined as premature cessation of function of corpora lutea resulting in a decline in serum progesterone concentration and subsequent pregnancy loss. Corpus luteum are the primary, if not the sole, source of progesterone during pregnancy, although there may be other origins as well. Underlying causes of spontaneous decreases in luteal function are unknown. It has been demonstrated that secretory products of the uterus do not appear to have an effect on luteal function.
Accordingly, cystic endometrial hyperplasia or other sources of uterine inflammation that result in subsequent release of endometrial prostaglandin do not appear to be involved in hypoluteoidism.

5.4.2. Chromosomal errors

Chromosome abnormalities in kittens causing lethal developmental errors have been reported as a cause of sub-fertility in queens [33]. Karyotyping of aborted offspring is required for diagnosis. Dams and sires producing offspring with chromosomal abnormalities should not be bred to each other again, but they may safely be bred to other, unrelated individuals.

5.4.3. Diet

Dietary causes of poor reproductive performance in the cat include severe malnutrition and taurine deficiency. Cats have a limited ability to synthesize taurine; therefore, a dietary source is required. Cats on a taurine-deficient diet exhibit resorption or abortion of fetuses, an increased incidence of near-term fetal death and kittens with low birth weights [50,51]. Commercial diets that are certified by the American association of feed control officials (AAFCO) contain adequate amounts of taurine.

5.4.4. Idiopathic

Queens can occasionally experience pregnancy loss with no known reason. A study of five cats with a history of pregnancy loss during mid-gestation demonstrated multifocal placental necrosis followed by fetal death and autolysis, but no infectious organism or underlying pathologic process was identified [52]. It is difficult to differentiate early pregnancy loss from lack of conception in queens. Abnormalities of established pregnancy appear to be uncommon. Complete physical examination and a thorough diagnostic work-up are required (Table 1). Definitive diagnosis of problems promotes changes in cattery management or alterations in care for individual queens to enhance future fertility.

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Table 1
Key for abnormalities of pregnancy in queens

| Assumption: the queen is in good body condition and is being fed a commercial diet for adult cats that contains sufficient levels of protein and fat |
|-----------------------------------------------|
| 1. The queen is aborting or fetal resorption has been documented using ultrasonography but the queen is not systemically ill |
| 1'. The queen is aborting or fetal resorption has been documented using ultrasonography and the queen is systemically ill |
| 2. Abdominal pain and signs of shock are not present |
| 2'. Abdominal pain and signs of shock are present |
| 3. Serum calcium concentrations are normal |
| 3'. Serum calcium concentrations are low |
| 4. Possibilities include infection with feline leukemia virus, FIV, panleukopenia, chromosome errors and possibly hypoluteoidism—test for FeLV and FIV, check vaccination status for panleukopenia and necropsy abortuses if possible, karyotype abortuses, consider monitoring serum progesterone concentrations throughout pregnancy at a subsequent breeding |
| 5. Possibilities include infection with bacteria, feline viral rhinotracheitis or toxoplasmosis. Bacterial infection is non-specific in clinical signs; necropsy and culture the abortuses. Treat the queen and any surviving kittens with an appropriate antibiotic and consider prophylactic antibiotic therapy at subsequent breeding. Look for an environmental source of bacterial contamination. Feline viral rhinotracheitis is associated with severe upper respiratory infection; check vaccination status of the queen. Toxoplasmosis is associated with severe neurologic disease of the queen; toxoplasmosis titers may be evaluated in serum |
