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Infertility in the Queen June 2006

Record Keeping

- ◆ Health and breeding records are very important; breeders of pedigreed cats need a simple but complete system to record data for each breeding cat
- ◆ Individual record for each cat:
 - a. Call name and registered name; registration number; microchip number
 - b. Complete description and photo
 - c. Birth date
 - d. Sire and dam
 - e. Vaccination and deworming record
 - f. Record of major health problems and their treatment
 - g. Record of elective procedures (i.e. dental cleanings, spay, neuter, etc.)
- ◆ Additional records for breeding cats should include at a minimum:
 - a. Age at first heat
 - b. Record of each heat and the breeding plans
 - c. Record of any health problems during the pregnancy and of any medications administered
 - d. Record of each breeding (name of tom, dates bred, number of breedings, whether breeding was witnessed, any problems) and its outcome (i.e. pregnancy or date of return to heat)
 - e. Record of each pregnancy (projected due date, actual due date, number of kittens born live/dead, any congenital defects or other problems)
 - f. Description of each delivery (length of time, interventions needed, etc.)
 - g. Dates/results of any x-rays/ultrasounds done for reproductive reasons
 - h. Birth weights of kittens, health problems in the neonatal period
 - i. Health status of each kitten at 1 and 5 years of age, if known

Infertility

- ◆ Infertility may mean one of the following in female cats:
 - Inability to be bred by a male
 - Inability to conceive after successful breeding
 - Inability to carry a pregnancy to term
- ◆ **Cats that are difficult to breed may produce other cats who are difficult to breed!**
- ◆ Investigation of infertility in the queen requires:
 1. A complete physical exam and thorough medical history (including drugs or herbal products administered and vaccination history)
 2. Blood chemistries, complete blood count, urinalysis, retrovirus testing
 3. Vaginal cytology, serum progesterone to establish phase of estrous cycle
 4. Evaluation of diet, housing, show/travel stresses

5. Evaluation of social interactions with other cats in cattery
6. Evaluation of breeding behaviour when with male
7. Evaluation of cattery environment: temperature, ventilation, available light, population density, cage design, etc.

Resources for healthy indoor feline environments:

<http://www.cfainc.org/articles/cattery-planning.html>

<http://www.nssvet.org/ici/index.php>

Although this website is geared toward cats in research settings, there is valuable information for catteries:

<http://www.awionline.org/pubs/cq02/Cq-cats.html>

Failure to Cycle

- ◆ Immaturity: First estrus may occur any time between 4 and 21 months of age
- ◆ Senility: Queens over 8 years old may have absent or infrequent estrus cycles
- ◆ Previous ovariohysterectomy/ovariectomy: Serum luteinizing hormone (LH) will be over 1 ng/ml in OHE/ovariectomized females due to loss of negative feedback from ovaries
- ◆ True primary anestrus: Queens that fail show first estrus by 24 months of age (uncommon); evaluate karyotype for chromosomal abnormalities
- ◆ Secondary anestrus: failure to cycle, or infrequent cycles
 1. **Silent estrus:** Normal hormonal events without behavioral estrus
 - Queens that are timid, low on social scale in cattery; crowded conditions
 - Must differentiate from pseudopregnancy due to spontaneous ovulation
 - House queen with different cats (smaller group) or separately; expose to tom
 2. **Inadequate daylight:** Indoor housing may not ensure enough hours daylight
 - 14-16 hours artificial light necessary; equivalent to 100-watt light bulb per 13 x 13 foot space; if you can read a newspaper, it is enough light
 3. **Spontaneous ovulation/pseudopregnancy:** Noncopulatory ovulation may be a cause of long interestrus intervals (40-50 days)
 - Detect with vaginal cytology and elevated serum progesterone in the absence of confirmed pregnancy
 4. **Intercurrent diseases/stressors:** Conditions causing debilitation or prolonged ill health may affect estrous cycles; stressors such as frequent exhibition/travel, crowding, antagonistic interactions with other cats may also suppress cycles
 5. **Medications:** Some medications may interfere with estrous cycles by suppressing gonadotropin secretion, such as corticosteroids, progestins, anabolic steroids, androgens; some antifungals such as ketoconazole can lower testosterone levels, griseofulvin could inhibit spermatogenesis
- ◆ Cabergoline (*Galastop*[®], Boehringer Ingelheim) may be useful in inducing estrus, not well studied in the queen
- ◆ FSH can be used to induce estrus in the queen, but prolonged usage has been associated with cystic ovaries:
 - Day 1: 2.0 mg, IM; Days 2 and 3: 1.0 mg, IM; Days 4 and 5: 0.5 mg, IM

Prolonged or Persistent Estrus

1. **Normal phenomena:**

- May be due to very short interestrus intervals or receptivity to mating during the nonfollicular phase of the estrous cycle
- Investigate using vaginal cytology, serum estradiol levels every 2-3 days over a 3-4 week period
- Breed queen to an experienced male, or induce ovulation with GnRH (25 µg intramuscularly)
- Try to induce anestrus by maintaining queen in less than 8-10 hours of daylight

2. **Ovarian cysts and tumours:**

- Cats can have both functional and non-functional ovarian and parovarian cysts; tumours most common in older queens
- Evaluate with ultrasonography, serum estradiol levels

Failure to Conceive with a Normal Cycle

1. **Maternal abnormalities:**

- Congenital defects: persistent hymen, vaginal strictures
- Inbreeding depression: intensive inbreeding can cause subfertility, loss of vigor and reproductive capacity
- Uterine disease: cystic endometrial hyperplasia (CEH)/pyometra
 - a. Ultrasound uterus (uterine wall thickness, fluid accumulation)
 - b. Laparoscopy or laparotomy to visualize reproductive tract, biopsy/culture uterus (for valuable queens)
 - c. Queens with repeated pseudopregnancies may have CEH
 - d. Ultrasound 18-21 days after breeding to differentiate failure to conceive from early fetal death

2. **Male infertility:** breed queen to a proven sire (sired kittens within previous 6 months); check male for presence of hair ring around base of penis that can prevent intromission

3. **Breeding management issues:**

- Review breeding management, videotape breedings if necessary
- Fearful queen may not breed, fear impairs hormonal events; dominant queens may require sedation to allow male to breed (best medication to use not known)
- Partner preferences and aversions are known to occur
- If queen returns to estrus less than 21 days after breeding, she did not ovulate, probably due to inadequate breedings (incomplete breedings, too few breedings)
- Check timing of breeding (too early, too late); best to breed days 2-4
- Check serum progesterone 1-2 weeks after breeding to see if ovulation occurred; ovulation is associated with serum progesterone > 2 ng/ml

4. **Failure to ovulate:** If breeding management issues have been ruled out as a cause, ovulation can be induced with GnRH or hCG

- Repeated treatments have been associated with immune-mediated decreases in fertility

5. **Fetal resorption/abortion:** Queen returns to estrus 60+ days after breeding

Cystic Endometrial Hyperplasia (CEH)

- ◆ Disorder of proliferative and degenerative changes in endometrium associated with aging; chronic subclinical condition; common in queens over 5 years and maiden queens over 3 years, but can be seen at any age
- ◆ Progesterone induces hyperplasia of the surface or glandular epithelium and cystic dilatation of the uterine glands; fluid in the cystic structures is usually uncontaminated, but if free in the uterus, it will support bacterial growth; progesterone also inhibits the local immune response and decreases myometrial contractility
- ◆ Repeated pseudopregnancies may predispose some queens to CEH; progestins used to control estrus also a risk factor
- ◆ Diagnosis: queen is not ill but fails to conceive or has small litters; ultrasound may detect thickening of uterus; definitive diagnosis only with uterine biopsy
- ◆ No treatment for uncomplicated CEH; endometritis (CEH plus bacterial infection) may respond to prolonged antibiotic treatment but can progress to pyometra

Pyometra

- ◆ Severe endometrial infection with accumulation of pus in uterus
- ◆ Typically occurs following an estrus, when bacteria from vagina invade uterus through open cervix; usually associated with CEH
- ◆ Vagina normally has bacteria present; vaginal cultures therefore hard to interpret; most common bacteria are *E. coli* and *Streptococcus*, *Staphylococcus*, etc.
- ◆ Clinical signs: Vulvar discharge (if cervix open), depression, dehydration, anorexia, fever, weight loss, distended abdomen
- ◆ Diagnosis: Increased white blood cell count, enlarged uterus on x-rays or ultrasound
- ◆ Treatment: IV fluids may be needed, antibiotics (fluoroquinolones, amoxicillin-clavulanate) plus ovariohysterectomy (OHE) or prostaglandin therapy for valuable breeding queens
- ◆ Antibiotics alone, vaginal douches not very effective
- ◆ Prostaglandin therapy: best for open-cervix; complication rate is low!
 - Candidate queens are under 6 years, in good health (no asthma), no retained fetal material or live fetuses, no complications (i.e. uterine torsion)
 - Prostaglandin F2 α , dinoprost (*Lutalyse*[®], Pharmacia & Upjohn) treatment: queen may or may not be hospitalized; different dosing options:
 - High dose: 0.1 to 0.25 mg/kg SC twice daily for 5 to 7 days
 - Low dose: 0.02 to 0.05 mg/kg SC 4-6 times daily for 5 to 10 days
 - Treatment may cause cervix to open, uterus to contract, may cause lysis of CL
 - Monitor for: rising fever, abdominal pain, systemic illness, uterine rupture
 - Assess success of treatment by monitoring white blood cell counts, ultrasound
 - Side effects common at higher doses, especially first day: restlessness, vocalizing, panting, vomiting, diarrhea, salivation, intense grooming of flanks and vulva; lasts 15-20 min; side effects uncommon at low doses (often only a bit of salivation)
 - Re-examine cat 1 and 2 weeks post-treatment: clear vulvar discharge by day 7, normal by 14 days; if bloody or purulent discharge persists, treat again

- Breed at next heat! Fertility rates after treatment are good (80% or better)
- Adjunctive therapy:
 - Prolonged oral antibiotic therapy (4-6 weeks)
 - Cabergoline (*Galastop*[®], Boehringer Ingelheim): 5 µg/kg, PO, 5 days; prolactin inhibitor, luteolytic, no side effects
 - Aglepristone (*Alizine*[®], Virbac): progesterone receptor antagonist, 10-15 mg/kg, SC, 2 days in a row

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DRUG FORMULARY for Feline Reproduction

Drug	Manufacturer	Indication	Indication/Dose
Aglepristone: <i>Alizine</i> ®	Virbac	Mammary hyperplasia, pyometra	10-15 mg/kg, SQ, 2 days
Bromocriptine: <i>Parlodel</i> ®	Sandoz	Mammary hyperplasia, pyometra	0.25 mg/cat, PO, 5 to 7 days
Cabergoline: <i>Galastop</i> ® <i>Dostinex</i> ®	Boehringer Ingelheim, Pharmacia & Upjohn	Mammary hyperplasia, pyometra, abortion (after 25 days)	5 µg/kg, PO, SID, 5 to 7 days (combine with cloprostenol for abortion)
Cloprostenol: <i>Estrumate</i> ®	Schering Plough	Abortion (after 25 days, with cabergoline)	5 µg/kg, SC, every 48 hours
FSH: <i>FSH-P</i> ®	Schering Plough	Induce estrus	2 mg/cat, IM, SID first day, then reduce dose to 1.0 or 0.5 mg SID for 4 more days (max. of 5 days)
GnRH (gonadorelin): <i>Cystorelin</i> ®	Merial	Induce ovulation when in estrus	25 µg/cat, IM, once
HCG: <i>Chorulon</i> ®	Intervet	Induce ovulation when in estrus	250 µg/cat, IM, daily on first 3 days of estrus
MPA: <i>Provera</i> ®, <i>Depo-Provera</i> ®	Pharmacia & Upjohn	Postpone estrus (start in anestrus)	2.5 mg/cat, PO, weekly; 2.0 mg/kg, IM, every 5 months
Megestrol acetate: <i>Ovaban</i> ®	Schering Plough	Postpone estrus (start in anestrus)	2.5 mg/cat, PO, weekly
Metoclopramide: <i>Reglan</i> ® and generics	Ayerst	Stimulate milk production	0.2-0.4 mg/kg, PO, TID
Oxytocin	Various generics	Uterine inertia	2.5-5.0 units/cat, IM every 20-30 minutes, max 3 doses
Proligestone: <i>Delvosteron</i> ®	Intervet	Postpone estrus (start in anestrus)	100 mg/cat, SC, every 5 months
Prostaglandin F2α <i>Lutalyse</i> ®	Pharmacia & Upjohn	Pyometra, induce abortion after 35 days	0.1-0.25 mg/kg, SQ, BID to TID
Terbutaline: <i>Bricanyl</i> ®, <i>Brethine</i> ®	AstraZeneca, Geigy	Stop premature labor	0.03-0.08 mg/kg, BID to TID

Note: Many of these drugs are not licensed for use in the cat in all countries, or may not be licensed for these indications. Not all medications are available in all countries or may not be available in veterinary formulations. Drugs may be available under different brand names from different manufacturers. Always consult your veterinarian about any medication for your cat.