Pyometra is an acute or chronic suppurrative inflammation of the uterine wall in ovary-intact queens. It is characterized by endometrial hyperplasia with cystic dilation of endometrial glands and accumulation of a neutrophil-rich exudate in the uterine lumen.

The incidence of feline pyometra is not well documented and probably under-estimated because queens often don’t present with clinical signs\(^1\). The disease is most often observed in dioestral animals (=mated, spontaneously ovulated or induced to ovulate) most commonly 4 weeks after the last onset of estrous. So called ‘stump pyometras’ can occur if uterine tissue was left behind during ovariohysterectomy. Increased incidence seen with age with the mean age at presentation being 7.6 years\(^1\).

**Pathogenesis**

The pathogenesis of pyometra is incompletely understood in both the bitch and the queen but probably more so in the queen. In the bitch it is currently believed to be of multifactorial origin. This is most likely a similar scenario for the queen.

It has been shown that progesterone exposure alone without prior oestrogen priming can lead to cystic endometrial hyperplasia (CEH) in the queen\(^2\). This is attributed to the effects progesterone has on the uterus, such as uterine stromal and glandular proliferation, leukocyte inhibition, decreased myometrial contractions and keeping the cervix closed. However, an influence of estrogen has also been demonstrated in another study as uterine oestrogen receptor expression has been shown to be reduced in cats with milder forms of CEH compared with cats with more severe forms\(^3\).

The use of exogenous steroid hormones (progestagens such as megestrol acetate) for contraceptive purposes has been shown to induce the disease in both bitches and queens.

Although queens are by definition induced ovulators, there are reports that some individuals repeatedly undergo spontaneous ovulation\(^4\) and subsequently a phase of progesterone dominance that lasts 40 to 50 days (pseudopregnancy). The incidence of spontaneous ovulation and ensuing pseudopregnancy in queens is probably much higher than originally thought\(^1\). There have been reports of up to 30% of queens spontaneously ovulating but this may be even higher and also may be affected by breed, age and parity. The relatively long progesterone-dominated diestrous phase in queens that undergo ovulation seems to predispose them to cystic endometrial hyperplasia and subsequent pyometra by ascending infection of bacteria.

The age queens present with uterine lesions is commonly more than 5 years, with the average being 7.5 years and a range from 1 to 20 years\(^4,6\).

In cats, no breed predisposition has been reported but it has been observed by the authors that oriental breeds of cats which can call all year round and also tend to have short inter-estrous/call intervals (associated with overlapping follicular waves) are more prone to developing pyometra than domestic short haired cats. It is possible that the uterus of these queens may be exposed to greater periods of estrogen priming and this coupled also with spontaneous ovulation and ensuing period of progesterone dominance may predispose oriental breeds to a higher incidence of the development of pyometra.

Bacteria isolated from pyometra cases are uropathogenic *E. coli* in the overwhelming majority of cases in queens and bitches. Other bacteria, mostly vaginal commensals such as coagulase positive, *Staphylococcus* spp., *Klebsiella*, *Proteus* and *Streptococcus* spp., have sometimes been recovered. One study in dogs reported the recovery of the same *E. coli* strains, as determined by biochemical fingerprinting, from the faeces and the uterus of bitches with pyometra\(^7\). The uterus is presumed to become infected via ascent of fecally-derived bacteria from the vagina during estrus, when the cervix is relaxed. Similar studies have not been reported in cats. Pathogenic *E. coli* strains carry different uropathogenic virulence factors (UVF), which facilitate infection in the urogenital tract in many species. Adhesive proteins, at the tip of bacterial pili (fimbriae), bind to receptors on epithelial cells of the urogenital tract. Three different types of adhesins (FimH, PapGIII and Sfa) have been identified in *E. coli* strains\(^9\). However, other strains even retained their binding ability if all 3 known adhesins (FimH, PapGIII and Sfa) were disabled\(^10\). This suggests that factors, other than bacterial factors, are involved. This is further strengthened by the observations made in a disease model that intrauterine inoculation of *E. coli* in estrus or anestrus did not result in pyometra but inoculation of the same strain in diestrus did\(^11\). No comparable studies have yet been undertaken in the queen.

**Diagnosis**

Classically, a queen with pyometra presents with a history of having been in heat within the last 4 weeks\(^5\). Presenting complaints most commonly include, but are not limited to purulent vaginal discharge, anorexia, abdominal distension, dehydration, pyrexia and vomiting\(^5\). Pyometra should be ruled out in any ill, ovary-intact queen. Polyuria and polydipsia are not commonly seen and importantly, in contrast to bitches, clinical signs can be few or very mild in queens with a pyometra (and personal experience). Care should be taken during abdominal palpation as it can result in uterine rupture.
The presence of vaginal discharge is also dependent on the patency of the cervix. In ‘open-cervix pyometra’ a blood stained, purulent vaginal discharge may be the only clinical sign. Animals with ‘closed-cervix pyometra’ may not show any vaginal discharge and are more commonly systemically ill because resorption of bacterial toxins from the uterine lumen into the circulation can result in endotoxaemia. Bacteraemia may also occur.

The leukogram frequently of a queen with pyometra usually shows a marked neutrophilia (> 35 x 10^9/L) with a left shift (±toxic change) but can be variable and, in rare cases, even be normal. It is not uncommon to have no other hematological disturbances in queens with pyometra. Hyperproteinemia, hypokalemia and azotemia can all occur in queens but it is not uncommon to see only mild or even biochemical changes.

Progesterone concentration will commonly be elevated above 2ng/mL or below baseline.

Changes observed in an abdominal radiograph are commonly a distended uterus, which can lead to displacement of the small intestine. It has to be noted that these changes are very similar to an early pregnancy prior to fetal skeletal ossification (starting at approximately 40 days after the luteinizing hormone peak). The limitation of a radiographic exam is that it is often difficult to differentiate from other causes of uterine enlargement, such as mucometra, hydrometra, hemometra, leiomyoma.

Therefore abdominal ultrasound is the most important diagnostic tool in a pyometra case. The uterine horns typically appear distended with hypo-/ to hyperechoic fluid with or without flocculation. The uterine wall often appears thinned with irregular edges and small hypoechoic areas consistent with cystic changes of the endometrial glands. However, the uterine wall can appear thinner than normal if the uterus is severely extended. The pyometra can be diffuse or segmental.

Cytology of the uterine or vaginal discharge is likely to reveal degenerative neutrophils and phagocytized bacteria. Collection of a guarded swab from the cranial vagina is recommended for culture.

**Treatment**

Ovariectomy with resection of the entire cervix is the treatment of choice in all animals not intended for breeding. Owners of breeding animals should also be informed about the likelihood of recurrence. Patients are often in poor condition for surgery and potential acidosis, arrhythmias and dehydration need to be corrected before the patient undergoes anesthesia. Intravenous fluids should be given and intravenous antibiotics should be administered. It must be noted that great care should be taken in handling the uterus as it is often very friable. The cervix should be removed in its entirety in order to avoid leakage of pus into the abdomen. Postoperative monitoring for signs of shock, dehydration, sepsis, electrolyte/acid-base imbalances, hyperproteinemia, hypoglycemia and anemia is required for at 24-48 hours following surgery.

Medical treatment is a valid choice in young and healthy breeding animals.

The rationale behind medical treatment for pyometra is 3-fold:

- removal of progesterone allowing opening of the cervix and improving local immune status
- drainage of pus and elimination of bacteria through an open cervix aided by uterine contractions
- prevent further bacterial proliferation

1. Prostaglandin F2α (PGF2α): is not registered for the use in companion animals. It can be used off-label. It has a desired luteolytic effect and ecbolic effect.

Especially in the case of closed-cervix pyometra, it is paramount to start with low doses of PGF2α in order to not only minimize the ecbolic effect of the drug and reduce the risk of uterine rupture but reduce the side effects associated with high doses of PGF2α. Once luteolysis has occured and the cervix opens the dose can be increased and evacuation of the uterus is a desired effect of treatment.

**Side effects:** Side effects are dose-dependent and rarely seen with the new low dose protocol and usually only a transient hypersalivation is seen. Tolerance of the PGF2α and reduction of side effects is seen after subsequent injections. They include: tachypnoea, vomiting, diarrhea, urination, anxiety; they usually start about 20 min after treatment. Animals should therefore be hospitalized for at least 1 hour after treatment to observe side effects.

In systemically well queens, they can be managed as ‘in hospital day patients’ – receiving injections throughout the day while under veterinary supervision but able to go home overnight when no medication is given.

**Recommended treatment protocol:**

Naturally occurring PGF2α, e.g. dinoprost tomethamine: (Lutalyse®)

a. Start with 10-15 µg/kg 3 times a day (TID) for 1 day subcutaneously (SC).

b. Then increase to 25 µg/kg TID for 1 day SC.

c. Finally, 50 µg/kg TID for up to 10 days SC or until vaginal discharge is no longer observed. The corpus luteum (CL) in the queen is more resistant to the luteolytic effects of PGF2α than in bitches. Furthermore, if treatment is started soon after ovulation the CLs can be refractory to the effects of PGF2α. Often higher doses of PGF2α for longer durations are required to obtain resolution (personal communication Karin Onclin)

This protocol can be used on its own or in combination with dopamine agonists (e.g. cabergoline) or progesterone receptor antagonists (e.g. aglepristone).

2. Dopamine agonists (used off-label), which act as prolactin agonists, can be used as early as 15-20 days after mating1. If used in combination with PGF2α, they potentiate the luteolytic effect. More rapid luteolysis leading to cervical opening within 24 to 48 hours can be achieved. The recommended dose for the dopamine agonists cabergoline and bromocriptine is 5µg/kg and 10-25 µg/kg, respectively, per os 3 times a day for 7 days when used in combination with PGF2α.

3. Progesterone receptor antagonists, such as aglepristone competitively bind to the progesterone receptor with a greater affinity than natural progesterone. Aglepristone has minimal side effects and is a good choice to treat closed-cervix pyometra as it results in cervical opening with minimal uterine contractions. However, queens that present with poor liver and/or kidney function should not be treated with aglepristone.

The recommended dose of aglepristone in the queen is:
10 mg/kg twice 24 h apart and again on Day 7 and Day 14 post diagnosis if resolution of the pyometra has not occurred. In chronic cases, treatment with aglepristone every week for 2 months has been reported (Karin Onclin personal communication). However, as the queen is more resistant to a drop of progesterone, aglepristone is less effective in queens than in bitches. It is therefore recommended, in our personal experience, to combine aglepristone treatment with 5-10 days of PGF2α.

This protocol in combination with treatment with trimethoprim/sulfadiazine for 7 days (15mg/Kg subcutaneously once a day) resulted in a success rate of 90% (9 out of 10 cats)\(^2\). The authors did not note any recurrences for 2 years after treatment.

4. Antimicrobial therapy: should be initiated immediately with a wide-spectrum antibiotic. Culture and susceptibility testing should be performed but therapy has to be started at the time of diagnosis on the assumption that an E. coli infection is present. Excellent results have been achieved with amoxicillin/ clavulanic acid (12.5-25 mg/kg p.o. 2 or 3 times a day) or cephalosporins (e.g. cefazolin; 22 mg/kg i.v./i.m. TID) and potentiated sulfonamides. (Care should be taken in using cephalosporins or sulphonamides if renal function is impaired.) If oral antibiotics are given, care must be taken to give the drugs at a different time as the prostaglandin, which will often lead to vomiting. Antimicrobial therapy should be continued for at least 14 days after resolution of vulvar discharge and removal of all fluid from the uterine lumen as determined by ultrasound.

Monitoring

The recommendations for monitoring treatment success are:

- Vaginal discharge should greatly increase in volume within 24 hours of treatment and usually ceases about 7 to 10 days. However, in contrast to dogs, pyometra in cats is often slower to resolve.
- Weekly blood cell counts should be performed to demonstrate decreasing neutrophilias; usually normally 10-15 days after commencement of medical therapy
- It is essential to follow these queens closely with vaginal cytologies and ultrasound examinations in order to detect recurrence of pyometra early. A pregnancy exam about 25 to 30 days after the peak of the luteinizing hormone should be scheduled after the subsequent oestrus.

Prognosis

The prognosis for survival is good with medical and surgical treatment if uterine rupture has not occurred. The mortality rate of queens has been reported to be 8%\(^4\).

Prevention

Animals not intended for breeding should be neutered by ovarioectomy (especially if a pre-pubertal animal) or ovariohysterectomy. Safe, long-term, reversible contraceptives that can be used in breeding queens include GnRH analogues such as a deslorelin implant (Suprelorin®)\(^{13}\) which inhibits oestrous by downregulation of the hypo-pituitary-ovarian axis. Recently, use of melatonin implants has been implicated as a way to safely prevent calling for up to 4 months\(^{14}\). Use of anabolic steroids such as mibolerone or progestagens (megestrol acteate) for estrous prevention are contraindicated in cats.

References

10. Kekerke, N., et al., The role of Type 1, P and S fimbriae in binding of Escherichia coli to the canine endometrium. Veterinary Microbiology, 2013.

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