The term Pyometra describes a pus-filled uterus and the associated ovarian and systemic changes. It is associated with the diestral phase of the ovarian cycle, at which time, the corpus luteum is actively secreting progesterone which increases secretion of the uterine glands, inhibits myometrial contraction and maintains closure of the cervix (Stone, 2003). It has been suggested that pyometra is a condition of middle aged and older dogs. However, pyometra has been reported in dogs as young as 4 months old and as old as 16 years (Niskanen and Thrusfield, 1998; Fukuda, 2001; Egenvall et al., 2001; Johnston et al., 2001). In yet another survey, the mean age of dogs presenting with pyometra was 2.4 years (Egenvall et al., 2001). The younger age was attributed to the frequent administration of estrogens for mismating in this population (Feldman and Nelson, 2004).

The canine pyometra is one of four stages of the cyclic hyperplasia-pyometra complex (Dow, 1957) and is clinically characterized by varying degrees of inappetence, vaginal discharge, in open pyometra cases, polydypsia, polyuria, and in severe cases, distension of abdomen. Closed pyometra is a more serious condition than open pyometra not only because there is no outlet for the infection, but also because a diagnosis of closed pyometra can easily be missed due to its insidious nature (Ettinger and Feldman, 1995). Pyometra shows polysystemic involvement and nulliparous or primiparous bitches have a moderately higher risk of pyometra as compared to multiparous bitches (Niskanen and Thrusfield, 1998).

Pyometra is an important disease in the canine species as up to 24% of intact bitches develop a pyometra before they are ten years of age. Uropathogenic E. coli is the most commonly isolated pathogen from canine uteri affected by pyometra (> 90% of cases). Under these circumstances, bacteria (especially E. coli) that have migrated from the vagina into the uterus find the environment favorable to growth, especially since progesterone also causes mucus secretion, closes the cervix (preventing uterine drainage), and decreases uterine contractility. The condition of the cervix is a major factor in the severity of the condition (Romagnoli, 2002). Originally cystic endometrial hyperplasia (CEH) and pyometra were defined as one disease entity. It was believed that bitches were first affected by CEH, which predisposed the uterus to a secondary bacterial infection, which then resulted in a pyometra. More recently the question has been raised if pyometra and cystic endometrial hyperplasia are two separate disease entities. Although, both diseases bear many similarities with each other and can be found as subsequent events, the conditions have the potential to derive de novo. Any stimulus in a progesterone-influenced uterus can lead to CEH and therefore the presence of CEH in pyometra could merely be the result of a uterine reaction to the bacterial infection. The pathogenesis of pyometra is not thoroughly understood. Many factors, such as the influence of age, ovarian hormones, breed, parity, treatment with exogenous hormones but also bacterial factors have been shown to play a role in the development of the disease.

Pyometra has initially been described as a condition of older, ovary-intact bitches that still undergo oestrous cycles. The mean age is reported to be between 7 to 8.5 years, although a range from 4 months to 18 years has been reported. A breed predisposition has been described for the Golden Retriever, Cavalier King Charles Spaniel, Miniature Schnauzer, Irish Terrier, rough Saint Bernard, Leonberger, Airedale Terrier, rough Collie and Rottweiler. On the other hand, Dachshunds and Fox Terriers were underrepresented. Pyometra is believed to be
facilitated by the unique canine oestrous cycle, during which an oestrogen phase is followed by a relatively long progesterone dominated phase (dioestrus). The length of the dioestrous phase in a non-pregnant bitch is not significantly shorter than that of a pregnant bitch. This is suggesting that a luteolytic mechanism, as present in other domestic species, is missing in the dog. Studies show that the overwhelming proportion of affected bitches present within 8-12 weeks of their last heat. It is known that bitches harbour the pyometra-causing bacterial strains within their rectum and the bacteria end in the uterus during oestrus when the cervix is open. If the bitch cannot rid herself of the bacteria before diestrus, the risk for pyometra is greatly increased. Leukocytic inhibition and decreased myometrial contractions, in the progesterone influenced uterus facilitate bacterial growth. The progesterone influence in dioestrus also results in uterine stromal and glandular epithelial proliferation and increased glandular secretion. These effects are cumulative. Therefore, the risk of uterine disease increases with each oestrous cycle. Although there is no evidence of abnormal ovarian hormone concentrations in the pathogenesis of pyometra it has been shown that progesterone is necessary to initiate a CEH reaction and oestrogen potentiates the effect by upregulating the expression of progesterone receptors. Exogenous hormone administration, especially of oestradiol early in diestrus (“mismatching shot”), can be linked to an increased risk in developing the disease. In dioestrus, the most common time for the diagnosis of pyometra, the uterus of healthy bitches has been found to be free of bacterial growth.

The diagnosis of endometritis in the bitch, which has been reported recently, has emphasized the role of the bitch’s immune response. Previously it was believed that endometritis does not exist in bitches and a bacterial infection would each time result in pyometra. However, latest studies show that bacteria can be isolated from subfertile bitches that do not show the characteristic signs of pyometra. Interestingly, the mean age of these bitches diagnosed with endometritis was lower than in bitches with pyometra. It is hypothesized that bitches might contain bacteria in the form of subclinical endometritis for some time before, as of yet, unknown factors allow bacterial proliferation and subsequent pyometra. The role of bacteria in the disease process has also recently been further elucidated. There is evidence that differences in the profile of uropathogenic virulence factors between E. coli strains contribute to the disease. The latest research suggests that both, the varying virulence of the bacterial strains and the state of the bitch’s immune system, are critical aspects in the pathogenesis of canine pyometra.

Clinical signs
Vary with patency of the cervix; in open-cervix pyometra, bitches present with vulvar discharge and are often less clinically ill; bitches with closed-cervix pyometra are almost always systemically ill; polyuria/polydipsia are often presenting complaints along with fever, vomiting, abdominal distention and lethargy mediated by septicaemia, bacteraeemia and/or endotoxaemia; Clinical signs are not definitive! therefore pyometra should be suspected in any intact bitch presenting 4 to 12 weeks after having been in heat with any of the following signs: vaginal discharge, depression, Polyuria/polydipsia, vomiting, and/or pyrexia.

Diagnosis
In patients with uterine rupture, free fluid may be identified within the abdominal cavity, and the omentum may be hemorrhagic secondary to bacterial peritonitis (Bigliardi et al., 2004). Fluid in the uterus (ultrasonography) and systemic inflammatory response; haematology: neutrophilia (> 35 x 109/L) with left shift, ± toxic change; however, sometimes the leukogram can even be within normal limits. Leukocytosis, anemia hypoalbuminemia, hypergлобulinémia increased alkaline phosphatase levels, azotemia, and acidosis can all occur to various degrees (De Schepper, 1985).

Differential Diagnosis
Uterine enlargement:
mucometra, hemometra (not associated with systemic clinical signs and neutrophilia)
• pregnancy (can be ruled out by ultrasonography 25 d post the LH peak)

Systemic clinical signs: diabetes mellitus, hyperadrenocorticism, renal disease, diabetes insipidus (not usually associated with leukocytosis). Vaginitis: not associated with systemic clinical signs and neutrophilia, ultrasonography won’t show fluid filled uterus.

Treatment
The most important aspect of treatment of pyometra is quick action to provide supportive care. Female dogs are often septic and in shock (see septic shock). Intravenous fluids and antibiotics should be given immediately (“Pyometra” -2004). Once the female dog has been stabilized, then the treatment of choice is an emergency spay (“Pyometra” -2006).

Surgical treatment:
Ovariohysterectomy is the treatment of choice for non-breeding animals; patients are often in poor condition for surgery and should be stabilized with intravenous fluids and antibiotics before the procedure; in breeding bitches medical management of the disease is possible; however, it should be noted that the disease will likely recur and it is strongly recommended to breed the bitch in the next cycle and have her ultrasonographically examined for pregnancy 28 days after the LH surge; it is possible that she will have a new infection at that stage and in that case ovariohysterectomy should be strongly recommended.

Medical treatment:
The rationale behind medical treatment serves two purposes:
1) removal of progesterone
• Prostaglandin F2α (PGF2α)
Not approved for the use in dogs! Can be used off-label.
• dinoprost: non-synthetic, inexpensive
dose: 10 μg/kg three times a day (TID) for 1 day subcutaneously (SC)
25 μg/kg TID for 1 day SC
50 μg/kg TID for 3-4 days SC
The dose can be adjusted to sensitivity of the bitch; some dogs are more sensitive and react with more side effects; others might need dose up to 100 μg/kg for 2 to 3 days.
Side effects: side effects are dose dependent and diminish after several injections; they include: tachypnoea, vomiting, diarrhea, urination, anxiety; start about 20 min after treatment; walking the dog for 15 min after administration seems to alleviate the side effects; dog should be hospitalized for at least one hour after treatment to observe side effects.

Especially in the case of pyometra it is paramount to start with low doses in order to minimize the ecobic effect of the drug as long as the cervix is closed (! risk of uterine rupture!); once the cervix opens the dose can be increased and evacuation of the uterus is a desired effect of treatment.
• Aglepristone
Progestosterone-antagonist; competitively prevents progesterone binding to its receptor; more expensive than prostaglandin; causes luteolysis but poor uterine contractions; works well in combination with prostaglandins in closed-cervix pyometra; aglepristone is given first and prostaglandin treatment can be started 24 to 48 hours later; cervix will open 26 hours (+/- 13 hours) after first aglepristone injection;
dose: 10 mg/kg given twice 24 hours apart; can follow with an injection 8 days later.
2) Elimination of bacteria from the uterus
Antimicrobial therapy should be initiated immediately with a wide-spectrum antibiotic; excellent results have been achieved with amoxicillin/clavulanic acid (12.5-25 mg/kg per os, twice a day), cephalosporins (e.g. cephalozin; 22 mg/kg intravenously, three times a day) and potentiated sulfonamides; if oral antibiotics are given, care must be taken to give the drugs at a different time as the prostaglandin, which can lead to vomiting; antimicrobial therapy should be continued for at least 14 days after resolution of the vulval discharge.
**Prognosis**

The prognosis for survival is good with surgical and medical treatment if uterine rupture has not occurred (4% mortality rate). Recurrence is relatively common (20% within 12 to 14 months of initial treatment) but is dependent on age, parity and presence of uterine pathologies. If CEH is still observed 4 weeks after cessation of treatment the prognosis for future fertility is greatly reduced.

**Follow-up care**

- weekly blood cell counts should be performed to demonstrate decreasing neutrophilia (left shift should be no longer present).
- ultrasonography is recommended; visible reduction in lumen size after 5 to 7 days
- serum progesterone levels usually decline within 48 hours if prostaglandins are used; although levels can be hard to interpret if aglepristone is used;
- breeding management in next cycle and early pregnancy diagnosis by ultrasonography to exclude recurrence of the disease; note that treatment will often lead to shortened interoestrous interval; can be lengthened with mibolerone (androgen-receptor agonist) in order to allow for sufficient interoestrous interval; start one month after end of medical treatment and keep administering it for 2 to 3 months.

**Prevention of Pyometra**

The best way to prevent pyometra is to have all female animals spayed at or before six months of age. If the animal is used for breeding, then spaying the animal after she is past her breeding years is highly recommended. Pyometra is a fairly common and serious problem and is just one of many compelling reasons to have your female pet spayed at an early age.

**References**


