# Bouvier Health Foundation Education Series

This edition of the Health Education Series centers on a serious condition affecting the intact bitch – Pyometra. The article comes to us from reproductive specialist, Cheryl Lopate, DVM, MS, Dipl ACT. Dr. Lopate co-owns and operates a reproductive specialty practice in Aurora, Oregon providing services to companion animals and horses; in addition, is also a member of a multi-vet small animal practice in Wilsonville, OR.

For those not familiar with the condition, Pyometra affects intact bitches, causing a variety of clinical signs and symptoms. Pyometra is typically pre-empted by pathologic changes in the uterus. The Greek derivation of pyometra is: pyo = pus and metra = uterus, so pyometra = an accumulation of pus in the uterus. We hope this article will help you identify potential problems early, but veterinary intervention is essential for the health of the bitch and her future ability to conceive.

## Pyometra in the Bitch

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As the bitch goes through the normal estrous cycle, the glands in the uterus produce secretions. As the bitch ages (with or without repeated pregnancy), these glands may fail to empty either due to scarring around the opening of the glands which occludes them or due to failure of the muscles of the uterine wall to contract regularly. This failed emptying causes cyst development within the lumen (center opening) of the uterus (called cystic endometrial hyperplasia or CEH).

With each estrous cycle, as the cervix relaxes, the bacteria that normally reside in the vagina, or are introduced during mating, can enter the uterus. Ordinarily, estrogen provides protection against infection by promoting immune function and by stimulating uterine contractions. So, in the normal bitch, the bacteria that contaminate the uterus during estrus and mating can be cleared from the uterus before the cervix closes and as progesterone rises. In the bitch with cystic endometrial hyperplasia (CEH), uterine contractions may not be as efficient, and bacteria may remain in the uterine lumen and subsequently invade the uterine wall.

Following ovulation, progesterone concentrations rise and remain elevated for 45 – 60 days. Progesterone is a hormone that promotes both uterine glandular secretion (for pregnancy maintenance) and bacterial growth while it suppresses uterine contractions, thereby creating an environment in the uterus conducive to bacterial overgrowth. In bitches with CEH, the bacteria that are retained in or around the glands and surrounding tissues proliferate during the phase of progesterone production.

In the early stages of this disease, there is only inflammation in the wall of the uterus (called subacute endometritis). At this point, there are no outward signs of disease in the bitch. With repeated cycles, this inflammation gets worse and worse until finally there are enough bacteria and inflammation retained in the uterus that pus begins to be produced in significant quantities inside the uterine lumen.

In some bitches, there may be a stage of accumulation of mucus in the uterus prior to pus formation. In these bitches, there is glandular or lymphatic dysfunction, resulting in fluid buildup, but there is no overgrowth of bacteria in this fluid. This condition is called mucometra. It is commonly undiagnosed because the bitch has no outward signs of disease and any discharge present is clear to milky in color, so

it either goes unnoticed or the owners are not concerned about it. Mucometra typically resolves on its own, without treatment, either during anestrous or at the onset of the ensuing cycle.

While CEH is present in the majority of the bitches that develop pyometra, in some cases, bitches may develop pyometra without any evidence of CEH. It is unclear at this time, why some of these bitches develop pyometra and this variant of the disease is actively being researched. In some cases, there may be physical or anatomic defects that predispose to bacterial contamination of the uterus such as vaginal strictures or physical defects of the cervix or uterus. It is also proposed that bacteria may be introduced into the uterus through the bloodstream, especially when the blood supply to the uterus is increased (during estrus).

Pyometra typically occurs 4 – 6 weeks following ovulation; however, it can occur earlier if the infection is severe enough, if bacterial numbers are very high or if the source of the infection is the bloodstream rather than the vagina. Pyometra can also occur during anestrus or estrus in the occasional bitch. It can also occur in a portion of the uterus during pregnancy, while the rest of the uterus in unaffected.

When pus is present and the cervix is closed the disease is termed a closed pyometra. When the cervix has opened and the uterus is draining, the disease is called an open pyometra. The severity of the signs the bitch will show is highly dependent on whether the cervix is opened or closed.

Once pyometra develops, the amount of pus may vary from just a few milliliters, to liters of fluid, depending on the size of the bitch's uterus, the rate of proliferation and the species of bacteria present. Generally speaking, bitches with more pus are sicker than those with lesser amounts (often related to whether the cervix is open or not). In some cases, the bacteria may be more virulent so that the bitch may be quite ill with very little fluid present. The inflammation that results from the buildup of pus normally causes the release of low levels of prostaglandin F2-alpha (PGF2α). This hormone begins to cause a natural decrease in progesterone production, and promotes cervical relaxation and uterine contraction. Until progesterone begins to drop off, the cervix of the bitch will remain closed holding the pus within the uterus. Once the cervix opens, it allows the pus to drain out of uterus, into the vagina, and out the vulva. In some cases, significant PGF2α release may not occur, and then progesterone will remain elevated and the cervix will remain closed. This may be due to pathology in the uterine wall and the resultant lack of normal response to inflammation. In certain cases of open pyometra, progesterone may already be very low or at baseline at the time of diagnosis.

With closed pyometra the bitch is often very depressed, with a high fever, and she quickly becomes dehydrated. Severe vomiting and diarrhea are common very early in the disease and the bitch may be drinking excessively and urinating frequently. These bitches are usually not eating well (if at all) and quickly become weak and may collapse or die. They become sick due to the toxins produced by the bacteria in the uterus. These toxins are excreted into the bloodstream and will quickly affect other organ systems. The most severe signs in pyometra result from the effects of these toxins on other body systems, a condition called the systemic inflammatory response syndrome (SIRS). Overwhelming bacterial infection will result in sepsis, shock and coagulation disorders (DIC). Kidney and liver disease (acute failure) are commonly seen in patients with SIRS. These bitches must be treated quickly and aggressively, because the toxins can rapidly overwhelm the body's immune system resulting in collapse and death.

Bitches with open pyometra are generally not as sick as those with closed pyometra. They are usually minimally depressed, often only with low grade fever and minimal dehydration. There may be some vomiting and increased thirst (and accompanying increase in urination) but signs are usually not as severe as with closed pyometra. Damage to the kidney and liver is usually minimal to non-existent. These

bitches may still be eating relatively normally. The degree of illness is typically proportional both to the amount of pus in the uterus and the toxicity of the bacteria present.

E. coli is the most common bacteria isolated from the uterus of bitches with pyometra. There are many different strains of E. coli, some more toxic than others. E. coli may have a predisposition to bind to receptors in the uterus primed with progesterone and thereby may overgrow other bacteria that may be present.

Diagnosis of pyometra is based on clinical signs in the bitch along with some typical laboratory abnormalities. Microscopic examination of the vulvar discharge (when present) will reveal many degenerate white blood cells and bacteria. Culture of the discharge is highly recommended to ensure that the antibiotics chosen will be effective. Elevations in the peripheral white blood count are common (in bitches with closed pyometra levels may be 10x or more higher than normal, while with open pyometra elevations are not as severe 0.5 – 2x higher). There may also be elevations in kidney and liver enzymes depending on the amount of insult to these organs by the bacterial toxins.

Ultrasound examination of the uterus provides the definitive diagnosis and allows assessment of how much pus is actually in the uterus. The uterus may be mildly (1 - 2 cm) to markedly (6 – 8 cm, or more) distended. In advanced cases, ultrasound may reveal uterine rupture or leakage of fluid across the uterine wall resulting in peritonitis. Ultrasound also allows assessment of areas of thinning in the uterine wall that may indicate impending uterine rupture. If ultrasound is not available, x-rays of the abdomen may reveal an enlarged tubular structure in the abdomen (this must be differentiated from intestinal abnormalities or pregnancy, prior to mineralization of the fetuses).

Treatment of pyometra will depend on the type of pyometra the bitch has and the clinical signs the bitch is displaying. The treatment of choice for any pyometra is ovariohysterectomy (spaying). Ovariohysterectomy is curative in that it removes the offending organ from the body and prevents recurrence. In bitches that are severely ill or dehydrated, stabilization with fluids and antibiotics may be required prior to surgery. Care must be taken during surgery to gently manipulate the fluid filled uterus as it may be predisposed to rupture. Surgery is not without risk however, and possible complications include hemorrhage, peritonitis, uterine rupture, wound infection and anesthetic complications.

In cases where the affected bitch is a valuable breeding animal, medical therapy may be selected over surgical therapy. In order for medical therapy to be a viable option, the bitch must be clinically stable. It is preferable to have an open cervix when choosing medical therapy, but some bitches with closed cervix pyometra may also be successfully treated. Medical treatment involves fluid and antibiotic administration and uterine evacuation. Fluids may be given intravenously or under the skin. In some bitches, there may be little to no dehydration and they are drinking adequately so that fluids are either minimally necessary or not required at all. Broad spectrum antibiotics should be administered. Antibiotics will generally be continued long term after resolution of the pyometra on ultrasound (typically 4 – 8 weeks after the uterus is evacuated).

Uterine evacuation is the mainstay of medical therapy and is accomplished through the administration of PGF2α (the same hormone that the bitch naturally produces in the face of inflammation in the uterus). Administration of this hormone results in smooth muscle contraction and cervical relaxation, both of which promote uterine evacuation. The uterus is made of smooth muscle (as is the GI tract and parts of the respiratory system). Because the drug will affect all smooth muscle, side effects include GI cramping, drooling, nausea, vomiting and diarrhea. These side effects are transient, lasting only about 30 minutes after each injection. The bitch develops tolerance to the drug as repeated doses are given, so the side effects diminish as treatment progresses. In order to minimize the side effects, very low doses are given

early in the treatment course and as the bitch adapts to the drug the dose is slowly increased. The drug is given 2 – 3 times daily.

In addition to causing uterine contraction, PGF2α also causes regression of the structures on the ovaries producing progesterone (the corpora lutea) which is important to prevent further proliferation of the bacteria in the uterus. Treatment with PGF2α will be continued until the uterus is completely evacuated (from 5 – 10 days in most cases, but up to 30 (or more) days in refractory or recurrent cases). Prior to conclusion of prostaglandin therapy, it is important to ensure that the progesterone concentration is basal and that it remains basal – as it has a tendency to rebound; and if it does the infection may return.

In cases of closed pyometra, cabergoline or bromocriptine may also be administered at the onset of treatment. These medications are dopamine agonists and result in decreased prolactin production. Prolactin is a hormone produced by the bitch to help support the corpora lutea, so that progesterone production can be maintained for an extended period of time. By stopping the production of prolactin, cabergoline acts in concert with PGF2α to lower the progesterone concentration and thereby assist in cervical relaxation and uterine evacuation.

The bitch must be hospitalized while being treated with PGF2α so she can be monitored for adverse side effects and deterioration in her condition. Monitoring of the white blood count is performed as uterine evacuation occurs and the count should drop back to normal once the infection is effectively cleared. Sequential ultrasound examinations are performed to monitor the progression of uterine evacuation and help determine when prostaglandin therapy may be concluded.

Any deterioration in the bitch's condition requires reassessment of the treatment plan and in some cases surgical intervention may be required if medical therapy is inadequate.

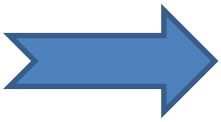
Breeding bitches with a history of pyometra should be mated on the cycle following treatment using appropriate antibiotic therapy and surgical insemination (whenever possible) to minimize the contamination brought into the uterus. The interval between estrous cycles is usually shortened (by 4 - 6 weeks) following medical treatment because of the shortening of the luteal phase (progesterone secretion) resulting from prostaglandin therapy. Bitches treated medically will be predisposed to recurrence on subsequent cycles, so should be spayed as soon as their reproductive careers are concluded. Mated bitches must be monitored carefully after breeding for any signs of recurrence of the pyometra prior to (and after) diagnosis of pregnancy. Pyometra and pregnancy can occur simultaneously. Approximately 30 – 50% of bitches medically treated for pyometra can be successfully bred on subsequent cycles. The prognosis depends on the amount of damage to the endometrium. This is dependent on the amount of pathology in the uterus, the length of time the pyometra was present prior to diagnosis, the response to treatment and the incidence of relapse.

Prevention of pyometra is difficult, but the normal aging changes in the uterus can be slowed by placing bitches not actively being bred on mibolerone to stop cyclicity and thereby prevent the effects of prolonged periods of progesterone dominance from acting on the endometrium and causing pathology from occurring. The greater the number of estrous cycles the uterus is exposed to the greater the chances of pyometra occurrence. In other words, intact bitches with short interestrous intervals and aged bitches are more predisposed to pyometra because of the number of times the endometrium is exposed to prolonged progesterone production.

The changes that lead up to pyometra are normal aging changes in the uterus and therefore most intact bitches, if they were to live long enough, would eventually develop pyometra. For this reason, it is

recommended that any bitch not being actively used for breeding or planned future breedings should be spayed to prevent occurrence of this disease.

BHF sincerely thanks Dr. Lopate for allowing us to share this informative article. Additional information regarding the doctor and her practices can be found at www.reproductiverevolutions.com and always remember it's through the sharing of knowledge that the lives of our canine companions will be enhanced.



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