

Pyometra in a Bengal Cat

This report describes the clinical course of pyometra in a valuable queen and the diagnostics that were performed to identify the problem and monitor the response to treatment.

A one year, 10 month-old Bengal queen was presented with purulent vaginal discharge and a history of atypical irritability. The queen was observed to show signs of estrus approximately 1 month prior to the onset of the vaginal discharge. The cat was otherwise bright and alert and, aside from the vaginal discharge and a moderately irritable disposition, had an unremarkable physical exam. Cytology followed by culture and sensitivity of the vaginal discharge, ultrasound examination, and blood work, including a progesterone level, were all consistent with pyometra. The cat was treated medically for an open-cervix pyometra with antibiotics, prostaglandin and bromocriptine. The response to treatment was monitored by serial ultrasound examination of the uterus, repeat blood work including progesterone levels, and by observing the cat's behaviour. When the queen showed signs of estrus two weeks following treatment, the owner was advised to breed her. However, as the tom was inexperienced, the queen was not bred. The queen was monitored for development of a second pyometra following this heat. Although progesterone levels indicated the queen was in diestrus, the uterus did not become fluid-filled. Bromocriptine was re-initiated to lower serum progesterone levels but concurrent prostaglandin therapy was unnecessary due to the absence of uterine fluid. The queen did not develop pyometra a second time.

Introduction:

Female cats (queens) are one of the more reproductively prolific species known to man. They are seasonally polyestrous and capable of bearing 50 to 100 kittens in a breeding life when allowed to mate naturally.¹ Certain characteristics of their reproductive cycle set them apart from other species;

nevertheless, there are many aspects of their reproductive physiology and endocrinology that are poorly understood and require further investigation.

There are five phases to the estrous cycle. The course of the estrous cycle is largely dictated by events such as ovulation, coitus, and pregnancy or pseudopregnancy. See Figure 1 for a schematic of reproductive cycle possibilities.

The first phase of the estrous cycle described is proestrus, which may last from 12 hours to 3 days. During proestrus, toms may be attracted to the queen but she will not be receptive. Queens will typically act very friendly during this phase. They will be affectionate towards humans, other objects, or other cats. This act of affection may progress to rolling and stretching in lateral recumbency or even to the lordosis posture.¹ In the lordosis stance, the queen's ventral chest and abdomen touch the floor, the perineum is slightly raised, and the tail is deviated to one side in anticipation of the tom. Although the queen may behave in a friendly manner, she will not accept advances made by the tom and may even become aggressive towards him.¹ Proestrus may be quite subtle and not observed in all queens. The initiation of proestrus is thought to be triggered by the release of follicle stimulating hormone (FSH) from the pituitary gland, which stimulates the development of ovarian follicles and the synthesis of estradiol.¹ Unfortunately, there is little data available on FSH levels during the estrous cycle.

Estrus follows proestrus and is defined as behavioural receptivity to mating. It lasts an average of 4 to 7 days but may range from 1 to 21 days and is associated with maximum follicular production and secretion of estrogen.^{2,3} Queens will rub their head and neck against objects or roll around on the floor. They may even vocalize to attract the tom then posture in the lordosis stance, treading with their hindlimbs.¹⁰ Serum estradiol rises rapidly during this phase and is important for producing the overt estrus behaviour and for priming the gonadotropin surge that will cause ovulation.⁴ These hormonal changes cause the labia to become slightly edematous and hyperemic. Vulvar discharge is scant and

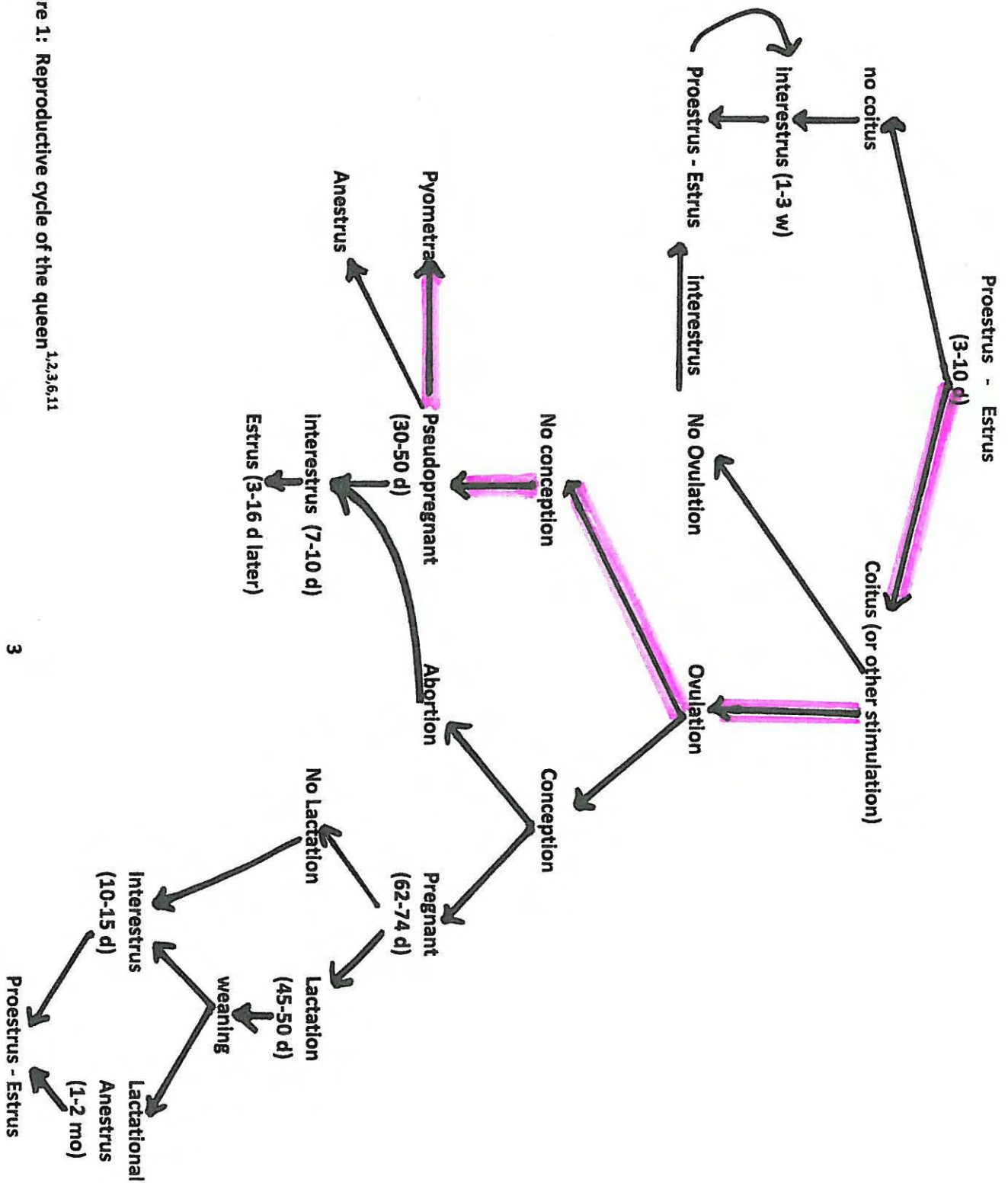


Figure 1: Reproductive cycle of the queen^{1,2,3,6,11}

rarely noticeable because of the fastidious grooming habits of most queens.¹ If discharge is observed, a small amount of whitish fluid may be seen at the vulva.⁵ The signs of estrus may be more exaggerated in long-haired breeds versus short-haired breeds.⁵ If copulation occurs during estrus, this phase will end on average 4 to 5 days later when ovulation occurs.⁵ In the absence of mating or spontaneous ovulation, heat periods may be observed every 10-14 days during the reproductive season.³

Interestrus occurs during the breeding season and is the period between one estrus and the next in queens that have not ovulated. It is the interval between waves of ovarian follicular activity. During this time, the estradiol and progesterone concentrations return to basal levels and breeding behaviour stops. Queens usually return to proestrus within 1 to 3 weeks but this may vary from 3 days to 7 weeks.¹

Anestrus occurs between October and January, when daylight hours are short. This is the period of sexual rest when queens are non-receptive to breeding and may hiss or strike when approached by toms. Both estradiol and progesterone concentrations are at basal levels.²

The luteal phase, or diestrus, is the period after ovulation when the dominant hormone is progesterone. The queen does not experience a pre-ovulatory rise in progesterone as does the bitch.² The act of mating, more specifically the distension of the posterior vagina by the penis, causes a reflex release of gonadotropin releasing hormone (GnRH) from the mid-ventral hypothalamus via neuroendocrine reflexes.^{2,3} Within minutes, GnRH release causes a luteinizing hormone (LH) surge from the anterior pituitary gland. The LH release must be preceded by several days of estradiol priming.⁶ Luteinizing hormone peaks within 2 hours and returns to basal levels in approximately 8 hours.⁵ If the LH release is sufficient, ovulation will occur. Studies have shown that multiple matings stimulate a higher, longer lasting surge, which increases the chance of successful ovulation compared to one mating.⁷ Typically, the LH threshold is reached by the fourth or fifth day of estrus,^{3,4} or after 4 or more matings.⁸ Ovulation

occurs approximately 48 hours after the LH surge.⁹ All oocytes are ovulated at one time so all kittens in one litter will be the same age. Queens are capable of superfecundation which means siblings from the same litter may be sired by different toms.¹⁰ This is more common in stray cat populations than in breeding facilities.

Non-copulatory means can also stimulate the release of LH from the pituitary gland. Ovulation may occur in response to stroking the back, mounting but no intromission, and stimulation of the vagina or cervix with a thermometer or cotton-tipped swab.¹¹ Visual, auditory, or olfactory cues may also stimulate ovulation,^{12,13,14} or it may be induced medically with human chorionic gonadotropin (hCG) or gonadotropin-releasing hormone (GnRH).^{10,15} Since the queen may ovulate without intromission, she is more accurately called an induced *and* spontaneous ovulator.² Non-copulatory ovulation occurs in 35-70% of queens.¹⁰

Corpora lutea form from ruptured follicles approximately 1 to 2 days following ovulation and begin secreting progesterone within 24-48 hours.¹⁶ The progesterone levels may reach up to 100 to 200 nmol/L by 15 to 25 days after ovulation, although these values are highly variable between queens.^{3,6,17,18} The progesterone levels reach similar values in pseudopregnant and pregnant queens or just slightly higher in pregnant queens.^{3,11,18} High concentrations of progesterone are maintained by centrally mediated blockage of GnRH release, which prevents the cat from returning to estrus.^{3,6} The length of time that these progesterone values are maintained differs between pregnancy and pseudopregnancy. If the oocytes are not fertilized after ovulation (or if embryonic loss occur), a pseudopregnancy will take place that lasts about 30 to 50 days.⁸ Progesterone concentrations will start to decline by about Day 25 to Day 30 and will be less than 3.2 nmol/L (or basal levels) by Day 30 to 40.³ The mechanism for the decrease in progesterone was first postulated by Paape and colleagues. They suggested that the decrease in progesterone levels in pseudopregnancy may be pre-programmed at the

time of ovulation.¹⁶ If fertilization does not occur, the lack of gestational luteotropic factors may cause the corpus luteum to atrophy.¹⁶

During pseudopregnancy, the queen will cease mating behaviour. This period of non-sexual activity is indistinguishable from anestrus and interestrus. Pseudopregnancy in cats differs from dogs in that it is generally only half as long as the normal gestation length and is very rarely associated with clinical signs. The only sign is lack of estrus activity. If clinical signs do occur, they are usually mild but may include lactation and nesting behaviour.⁸ New ovarian follicular activity usually resumes within 10 days following the regression of the corpus luteum, which allows the queen to rapidly return to a fertile state.⁵ A queen may have 4 to 5 pseudopregnancies during the course of one polyestrous season.¹⁶

If fertilization of the oocytes occurs, the embryos enter the uterine horn by Day 5 after copulation.⁵ Implantation occurs about 12 to 13 days after breeding.² Gestation length is approximately 66 days, but varies from 62 to 74 days.² Progesterone is maintained at a high concentration throughout pregnancy and for a longer time period than is seen with pseudopregnancy. Concentrations of progesterone initially decrease around Day 25-35 but then remain stable at approximately 15-30 nmol/L and do not decrease below 3-5 nmol/L until Day 60, near the end of gestation.^{6,18} As the progesterone levels decline, the main source of progesterone is most likely the corpus luteum and not the placenta as was previously postulated.¹⁸ Although the literature is somewhat unclear on the subject, the placenta appears to be of little importance in maintaining pregnancy and either does not secrete progesterone at all, or does so in very small quantities.¹⁸ A minimum of 3 nmol/L is needed to maintain pregnancy.³ Other hormones secreted during pregnancy are relaxin, prostaglandin, and prolactin. Relaxin is produced by the fetoplacental unit and is important for softening the tissues that surround the pelvis. It is produced by Day 20 of gestation and continues until parturition.^{3,19} Pregnancy can be differentiated from pseudopregnancy by a test measuring the hormone, relaxin at 35 days post-breeding.¹⁰

Prostaglandin (PGF_{2α}), produced both by the fetoplacental unit and the endometrium at Day 30, plateaus at Day 45, surges just before parturition, then abruptly falls a few days after delivery.⁵ Prolactin, important for development of mammary glands and the initiation and maintenance of lactation, increases starting at about Day 25-35, plateaus at Day 50, then increases suddenly just before parturition.^{3,20} It appears that prolactin is a major luteotrophic factor in cats after Day 20-25 when implantation has occurred.²¹ It inhibits regression of the corpus luteum and stimulates progesterone production in quantities adequate to maintain pregnancy.²¹ Relaxin may also be a luteotrophic factor.³ Together, the hormones relaxin and prolactin may be responsible for preventing the corpus luteum from atrophying around Day 25 to 30.⁶

Proestrus and estrus may resume about 10 days after the end of diestrus, although nursing queens may experience a lactational anestrus that can last up to 8 weeks after weaning. Most queens return to estrus 4 weeks after weaning. It is possible for a queen to return to estrus while still nursing.³

Contrary to belief, pregnant cats may show signs of estrus, including acceptance of advances by the tom. Although increases in estradiol do not occur, nor does an LH surge after copulation, the pregnant cat behaves identically to a non-pregnant cat during estrus.⁵ Superfetation, which is different gestational ages of fetuses does not occur in the queen because she always ovulates all her mature eggs for one particular cycle at one time.¹⁰

Pathophysiology of Pyometra

Pyometra is a well-recognized disease in bitches but significantly less information is available on pyometra in cats.

Cystic endometrial hyperplasia (CEH), endometritis, and pyometra in bitches and queens occur as a progression of disease in the uterus.²² These diseases of the uterus are usually associated with the

luteal phase of the estrous cycle, but there are exceptions. Cystic endometrial hyperplasia occurs when high progesterone levels induce cystic dilation of the uterine glands and hyperplasia of the superficial glandular epithelium.²³ In addition, elevated levels of progesterone may increase uterine glandular secretions, inhibit local leukocyte function, and decrease myometrial contractility.²⁴ Chronic exposure of the endometrium to estrogen, as may occur from repeated estrous cycles that do not result in pregnancy, may compound the severity of endometrial hyperplasia.²³ Queens with uncomplicated CEH usually show no clinical signs of illness. The only indication that there is uterine pathology may be failure of implantation, small litter size, or infertility.²⁵ There is no effective treatment for CEH.²

Both endometritis and pyometra are associated with bacterial infections. Endometritis may occur after ascending bacteria from the vagina gain access to the lining of the uterine walls and cause inflammation of the endometrium. This is most likely to occur during estrus, when estrogens dilate the cervix and decreased contractility of the myometrium allows the infection to become established.² Less commonly, the bacterial infection that establishes itself in the endometrium may be of hematogenous origin.²⁶ The only sign that endometritis is present may be infertility although, on occasion, thickening of the uterine wall may be observed with ultrasonography.² Blood work is usually normal and there may be little to no vaginal discharge. The diagnosis can be confirmed with a uterine biopsy and culture.²²

Endometritis often progresses to pyometra. Pyometra may be defined as a significant accumulation of purulent exudate in the uterine lumen. The most common bacterial pathogen is *Escherichia coli*. Other pathogens that have been reported are *Streptococcus*, *Staphylococcus*, *Klebsiella*, *Pseudomonas*, *Proteus*, *Moraxella*, and *Pasteurella* spp.²⁷ Cystic endometrial hyperplasia and pyometra can be diagnosed at any age, and in multiparous queens,⁸ although it is more common in older queens and unbred queens that are greater than 3 years old.²³ Pyometra or metritis has also been reported to develop secondary to a retained fetus, retained fetal membranes, or trauma during parturition.¹¹

Another factor that plays a role in the development of CEH is spontaneous ovulation. Breeding catteries tend to have more frequent spontaneous ovulation, and because the timing of pregnancies is often planned to accommodate show schedules, queens do not get bred on every heat cycle. Pregnancy is known to protect the uterus against pathologic changes.²⁸ If breeders wish to postpone estrus or suppress estrus temporarily, there are no safely reliable products for this purpose. Synthetic progesterone analogues are used essentially to induce pseudopregnancy in the cat. Examples of exogenous progesterones (or progestins) for preventing estrus (or for contraception) are megestrol acetate and medroxyprogesterone acetate (MPA). Both of these drugs may induce pyometra, especially in young queens, by causing irreversible endometrial hyperplasia.²⁷ The safest approach to discontinuing the estrous cycle would be to reduce daylight hours to less than 10 per day to induce anestrus.²⁸ In addition to causing pyometra, these drugs can cause lethargy, depression, weight gain, polyuria, polydipsia, skin changes, mammary hyperplasia, mammary cancer, adrenal suppression, and diabetes mellitus.¹⁰

Many cases of pyometra are associated with the luteal phase of the estrous cycle and retained corpora lutea, as determined by progesterone assays or histopathology after ovariohysterectomy.²⁷ This is not always the case, however, as 30 to 60% of pyometra cases occur in the follicular phase of the ovarian cycle.²⁹ During the follicular phase, progesterone levels are low and estradiol levels are high as a result of follicular secretion. This suggests that pyometra may also be influenced by estrogens. It has been accepted that CEH/pyometra may develop and progress slowly or may progress and regress over successive estrous cycles.²⁹ Estrogens increase progesterone receptors in the endometrium, dilate the cervix, and may exacerbate endometrial changes.²⁷ In essence, estrogens enhance the progesterone effects on the endometrium, but by themselves do not induce pyometra.²⁹ Exogenous estrogens have a similar effect in older cats by causing the cervix to stay open longer, allowing bacteria access to the already hyperplastic endometrium.

There is speculation that some queens are at higher risk of uterine disease in the immediate post-weaning period. Shortly after weaning, or during lactation, a queen may experience an estrous cycle, ovulate, and develop a corpus luteum. Inappropriate retention of the corpus luteum may increase the chances of pyometra post-partum.²⁹ This theory still requires further investigation.

A correlation between feline leukemia (FeLV) positive cats and pyometra has not been established. Three out of 13 queens with feline infectious virus (FIV) developed pyometra subsequent to pregnancy or complications of pregnancy, but a direct cause and effect relationship has not been established.²⁷

Typical findings in cases of CEH, endometritis and pyometra:

Any queen that presents with vaginal discharge should be suspected of having pyometra until proven otherwise.³⁰ Queens that are unbred and greater than 3 years old or queens that repeatedly ovulate when bred but do not conceive are especially at risk. The average age of cats with pyometra is seven years according to one author,²⁷ but other investigators report a slightly younger age of incidence (over 5 years of age)¹¹ or (an average of 5 years of age).³¹ Elderly, nulliparous queens are more likely to develop the disease due to the endometrial changes that occur over the years. There is no correlation between the development of pyometra and the age of the first coitus, or the number of litters queened.²⁷

Diagnosis of CEH may be challenging. In cases of CEH and endometritis, the complete blood count and chemistry profile are normal.⁸ Vaginal discharge with CEH and endometritis may be so minimal or so rapidly removed by the queen that it goes unnoticed.²⁵ In cases of endometritis, thickening of the uterine wall or fluid in the uterus can sometimes be observed with ultrasonography. If pathology is not obvious with ultrasonography, the diagnosis of endometritis may be confirmed with a uterine biopsy and culture. If the queen with endometritis is valuable, an attempt may be made to breed her while

concurrently administering a broad spectrum antibiotic.²² However, since endometritis often progresses to pyometra, most affected queens should be removed from the breeding program.

Diagnosis of pyometra is usually more straight forward. The patient is an intact queen with estrus observed in the last 4³² to 8 weeks.²⁷ If the cervix is open, clinical signs usually include a vaginal discharge ranging from creamy tan-pink to dark brown.¹¹ Other clinical findings are lethargy, anorexia, a palpably enlarged uterus or abdominal distension, dehydration, pyrexia, and less commonly, polyuria and polydipsia.^{25,28,30,32,33} If the queen has a closed pyometra, the abdomen is distended, there is no vaginal discharge, and signs of septicemia such as shock may be present. Cats with closed-cervix pyometra may be profoundly ill from endotoxemia and have sub-normal temperatures, tachycardia, tachypnea and poor peripheral perfusion.^{8,25,27,30,34} Careful abdominal palpation is needed to avoid iatrogenic rupture of the uterus and subsequent peritonitis.²⁷ The complete blood count and serum chemistry findings usually show elevated white blood cells with a neutrophilia. Profound leukocytosis exceeding $30 \times 10^9/L$ with a degenerative left shift is more common in closed-cervix pyometra compared to open-cervix pyometra.^{31,33} Leukocytosis is also affected by endometrial necrosis, degree of bacterial growth, and duration of inflammation.³² Some cases of open-cervix pyometra may have normal leukocyte counts.³¹ There may be a non-regenerative, normocytic, normochromic anemia due to chronic inflammation and suppression of erythropoiesis in the bone marrow.²⁷ Hyperglobulinemia from chronic inflammation occurs in 30-60% of cases.²⁷ Hyperproteinemia and pre-renal azotemia (elevations in blood urea nitrogen and creatinine) may result from dehydration or circulatory collapse. An elevated creatinine was found in 12% of cats with pyometra in one study.³² Urine specific gravity is variable early in the disease process, but may exceed 1.030.³¹ Hypokalemia may be non-specific or due to anorexia or vomiting. Hypoglycemia may be present due to increased consumption of glucose and decreased gluconeogenesis, but is much less common in cats compared to dogs.^{27,32} Pyometra can cause changes in liver and kidney function when hepatic perfusion decreases or septicemia occurs. Septicemia may

lead to hepatocellular damage and decreased hepatic circulation with cellular hypoxia in dehydrated cats. This may result in increased alkaline phosphatase (ALKP) and hyperbilirubinemia, and has been observed in 12% of cases.²⁷ Increased alanine aminotransferase (ALT) has been observed in 7% of cases.³² Most of these liver changes are self-limiting and resolve after supportive therapy is initiated. Renal damage has also been reported, most likely due to bacterial endotoxin.³¹ In addition to elevated blood urea nitrogen and creatinine, proteinuria and isosthenuria may be seen in the urinalysis when the kidneys are affected.²⁷ Unlike bitches, polyuria and polydipsia is not commonly observed in feline pyometra. In dogs, *E. coli* endotoxins interfere with sodium and chloride ion absorption in the loop of Henle and reduce medullary hypertonicity, causing impaired water absorption. *E. coli* endotoxins also antagonize antidiuretic hormone's (ADH) effect on collecting ducts, causing increased urine production.³⁵

Vaginal cytology typically shows abundant neutrophils and erythrocytes. Endometrial cells may also be present. Bacteria are rarely observed on the smear.²⁷

Progesterone levels are usually greater than 15 nmol/L, although this is not a consistent finding, as progesterone is not required to induce or maintain pyometra.²⁷

Diagnosis is made by abdominal ultrasound or radiographs. Ultrasound allows determination of uterine size and wall thickness and the presence of fluid or other structures within the lumen. The uterine enlargement is usually symmetrical with homogenous luminal contents that may be anechoic or echogenic with a slow swirling pattern.³⁷ Radiography may show uterine enlargement that appears homogenous and sometimes sacculiform, with craniodorsal displacement of the small intestine.²⁷ A distended uterus may be difficult to diagnose if organs, specifically the bladder, are overlapping the uterus or if the uterine enlargement is mild, as may be the case in open-cervix pyometra.

Histopathology

Uterine fluid may be collected after performing an ovariohysterectomy or by swabbing the anterior vagina. The fluid is typically thick, opaque, and mucopurulent. Histopathology of the uterus after surgical removal may show irregularly thick, ulcerated or necrotic mucosa. The most remarkable finding is endometrial hyperplasia. There may also be visible cysts in hyperplastic areas of the uterus. Changes observed due to infection vary depending on the bacteria colonizing the uterus and the chronicity of the infection.³⁶

Differential Diagnosis:

There are several differential diagnoses for pyometra. The list includes conditions that cause uterine enlargement such as pregnancy, abortion, endometritis, mucometra, hydrometra, neoplasia, and recent parturition. Conditions that cause a vulvar discharge should also be considered. These are proestrus, vaginal foreign body, vaginal mass or infection, vaginal trauma, vaginal hematoma, or urinary tract infection. Finally, diseases that cause abdominal enlargement such as obesity, abdominal mass, peritonitis, hemoabdomen, or ascites may also be considered differentials for closed-cervix pyometra.

Pregnancy is the most important differential for pyometra. Calcification of fetal skeletons can occur by Day 38 of gestation, but is not reliably observed on a radiograph until Day 43.⁸ Prior to Day 43, pregnancy and pyometra both appear as an enlarged uterus on an abdominal radiograph. Palpation of the uterus at or near Day 25 in a pregnant queen can reliably detect firm, 'walnut-sized' isolated structures in the uterus, but would only be useful if the cat was presented at this stage of gestation. After Day 35, the individual structures are not palpably distinct.¹¹ Ultrasound is a more useful tool to differentiate between pregnancy and pyometra. It can be used to detect pregnancies 22 days after the last breeding date and is 99% accurate after day 28.¹⁰ Fetal heart beats can be observed as early as Day 22 to 24 of gestation by ultrasonography.⁸

Embryonic death that occurs before Day 25 after ovulation usually results in complete embryonic resorption and absent clinical signs in the queen.³⁷ Resorption may be recognized by a reduction in embryo size, a change in embryonic fluid from anechoic to hypoechoic, the presence of particles in the fluid, or an absent heart beat.³⁷ Fetal death after 35 days usually results in abortion that may or may not affect the entire litter.³⁷ Fetal death that occurs later in gestation with retention of mummified or macerated fetuses may result in a serosanguinous or purulent vaginal discharge that resembles pyometra.³⁰ Usually a confirmed pregnancy has been previously documented. An ultrasound may show non-viable (absent heart beat) or mummified fetuses.³⁰ Recognition of fetal structures rapidly diminishes after death with only mineralized structures identified after 24 hours.³⁷ Intrauterine or intrafetal gas may also be identified.³⁷ The queen may be systemically ill, or remain asymptomatic. If spontaneous abortion occurs, the queen may consume the material before it is observed and the abortion may go unnoticed.³⁰ The later in gestation that fetal death occurs, the more likely it is to see expelled fetal parts.

Endometritis may be detected by ultrasound but is dependent on the degree of uterine wall pathology. A biopsy (and culture) is the best method to confirm this diagnosis. Other diseases that appear similar to pyometra on ultrasound are hydrometra and mucometra, which are the accumulations of sterile fluid in the uterus secondary to cystic hyperplasia of the endometrium.¹¹ The vaginal discharge of these diseases resembles mucous rather than purulent discharge. On ultrasound examination, the luminal contents may be anechoic when hydrometra is present, or echogenic if mucometra is present.³⁷ The end result of uterine wall pathology and fluid accumulations is eventually pyometra and differentiation between these conditions becomes academic unless the breeder is determined to obtain a litter from the cat.

Ultrasound examination may also differentiate pyometra from uterine neoplasia, which is rare in the cat. Uterine neoplasia may be nodular and project into the lumen of the uterus or it may appear cystic.³⁷ In contrast, uterine walls in cats with pyometra are generally thickened and smooth, but could be thin or irregular.³⁷ Some examples of uterine neoplasia are adenomas, adenocarcinomas, leiomyomas, and leiomyosarcomas.^{37,38} Uterine neoplasia may be found concurrently with pyometra.³⁸

Post-partum lochia may be difficult to differentiate from pyometra, particularly if the owner is not aware that recent parturition occurred. Occasionally it contains a dark green heme pigment known as uteroverdin that comes from the placenta. A post-partum uterus may be palpably larger than a normal uterus, as normal involution of the uterus in cats takes approximately 24 days.³⁷ During the first 2 weeks after delivery, 3 distinct layers of the uterus may be visualized by ultrasound examination.³⁷ The walls become thinner and the layers less distinct as involution progresses. This is unlike pyometra, where uterine walls appear thickened, unless the uterus is massively dilated.³⁷ In addition, a queen that has just delivered usually has well-developed mammary glands and is lactating.

A queen that is in proestrus may rarely be observed to have a vaginal discharge. Vaginal cytology would be helpful in differentiating pyometra from proestrus.

Conditions that cause a vulvar discharge such as a foreign body, mass, vaginal infection, or trauma may be differentiated by careful inspection of the vulva and vagina, or by vaginoscopy. Finding vulvitis or vaginitis does not exclude the possibility of concurrent uterine pathology.

A severe urinary infection would be a consideration for vulvar discharge if the vaginal vestibule was visualized by vaginoscopy and the discharge was only observed distal to the urethral orifice. The other indication would be flocculent, sludge-like material observed in the bladder, or increased bladder wall thickness on ultrasound examination. Typical clinical signs of a lower urinary tract infection would be dysuria, stanguria and pollakiuria. A cystocentesis and, if necessary, an aspirate of the kidneys could be

obtained, followed by a culture to rule out a bladder and/or renal infection if the uterus was unremarkable on ultrasound exam. Pyelonephritis, especially if chronic, can appear as increased renal echogenicity and reduced corticomedullary definition on ultrasound examination.³⁹

Finally, cats that present with an enlarged abdomen when the status of the uterus is unknown could be differentiated from pyometra with abdominal x-rays and/or abdominal ultrasound. Ultrasound (and to a lesser degree, radiographs) could locate abnormal fluid accumulation in the case of hemoabdomen, ascites, or peritonitis, and determine if the source of enlargement was abdominal fat. An X-ray or ultrasound could also determine if a mass was present. Abdominocentesis and cytology could then be performed to differentiate hemoabdomen from ascites and peritonitis.

Treatment:

The goals of treatment are to stabilize the queen, commence antibiotics, and then determine if the queen will be treated medically or surgically. The choice of medical versus surgical intervention is based on the severity of the clinical symptoms of the queen and her value to remain in the breeding program. Initially, a clinically ill queen with pyometra should be stabilized with intravenous fluids to correct dehydration and electrolyte imbalances such as potassium and chloride. Intravenous dextrose is recommended if the cat is hypoglycemic. A broad-spectrum antibiotic should be initiated, such as enrofloxacin, amoxicillin clavulanic acid, cephalosporin or trimethoprim sulfonamide, or preferably chosen based on results of culture and sensitivity of the vaginal discharge.

The treatment of choice following stabilization is ovariohysterectomy because it eliminates the site of infection. It should be the only choice if the queen has a closed-cervix pyometra or is severely ill due to septicemia, shock, or azotemia, and especially if there is evidence of uterine rupture. Although it offers the best chance for cure, surgery has been associated with some mortality and morbidity.

For valuable queens that are not systemically ill, have an open cervix pyometra, and no evidence of retained fetal tissue or fetuses, medical therapy may be attempted. Medical treatment includes prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) and antibiotics. The main goal of $PGF_{2\alpha}$ is to stimulate myometrial contraction and expulsion of uterine contents. The recommended dose of $PGF_{2\alpha}$ for cats with pyometra is 0.1 to 0.25 mg/kg SQ q 8 to 12 h for up to 5 days.²² The European trend has been to give lower doses more frequently (0.05 mg/kg q 5 to 8 h).²² In general, higher doses have not proved to be more beneficial. Side effects of the drug may occur in up to 76% of queens and may include vocalization, panting, restlessness, intense grooming, tenesmus, salivation, vomiting, diarrhea, kneading, mydriasis, urination and lordosis.^{8,26,33} These side effects may last for up to 60 minutes after injection, but are rarely severe enough to warrant discontinuing the drug. Usually the most dramatic reactions are seen after the first few injections and then they diminish with further treatments. Lower doses such as 0.02 to 0.05 mg/kg may decrease side effects. These adverse side effects of $PGF_{2\alpha}$ reflect the physiologic effects of endogenous prostaglandins, which include regulation of intracellular production of cyclic AMP to induce changes in cellular function.³³ Prostaglandins normally mediate processes such as vasodilation, hemostasis, pulmonary vasoconstriction and bronchodilation, gastrointestinal tract secretions, renal blood flow and glomerular filtration rate, inflammation, and fever. The most serious potential side effect of $PGF_{2\alpha}$ therapy is peritonitis from uterine rupture or leakage of the oviducts. This side effect is rare if the cervix is open.³³ However, it may occur more often in cats than in dogs, especially if the uterus is contracting against a closed cervix, a uterine torsion is present, or the uterine exudate is viscous and hard to expel.³⁴ The contractile effect on the myometrial, gastrointestinal, tracheobronchial and bladder smooth muscles accounts for the clinical responses and potential adverse effects observed with administration.³³ If $PGF_{2\alpha}$ is given at 10 to 20 times the recommended dose, ataxia and severe respiratory distress may occur.³⁴ Hospitalization of the queen during prostaglandin therapy is at the discretion of the veterinarian and based on the clinical status of the queen. The queen may be required

to be hospitalized for a day or two to see how she will react to the prostaglandin treatment even if she is not ill enough to receive intravenous fluids.

The side effects of prostaglandins in humans from contact on the skin or accidental injection are contraction of the uterus and possible abortion if pregnant. Constriction of the airways causing respiratory distress may also occur, especially in individuals with bronchial disease or asthma. It is very important that people handling this drug are aware of these side effects and protect themselves appropriately or avoid using them altogether.

Prostaglandins are not licensed for use in the cat so informed owner consent is important. Unlike the natural $\text{PGF}_{2\alpha}$, dinoprost tromethamine (lutalyse)⁹, synthetic prostaglandins, such as cloprostenol (Estrumate), and fluprostenole (Equimate) are not recommended for use in cats because they are more potent than natural prostaglandins and their dose and efficacy has not been evaluated in this species.²⁷

The success of using $\text{PGF}_{2\alpha}$ in open-cervix pyometra is largely attributable to the myometrial contraction effects. It does not reliably induce luteolysis or inhibit synthesis of progesterone in the cat.³³ In some cases where queens with pyometra in the luteal phase have been treated with $\text{PGF}_{2\alpha}$ partial luteolysis probably occurred, as the progesterone levels did decrease.³³ Unfortunately, treatment of pyometra with $\text{PGF}_{2\alpha}$ does nothing for the underlying CEH pathology, and for this reason, pyometra can recur. Since most queens have an elevated progesterone level when they have pyometra, luteolysis may improve recovery by removing the deleterious effects of progesterone. Consequently, if progesterone is elevated, another drug should be given to achieve luteolysis. Either bromocriptine or cabergoline may be used for this purpose. Both drugs are dopamine agonists and prolactin inhibitors. They reduce progesterone indirectly by failing to promote longevity of the corpus luteum. Both drugs must also be compounded. A third drug that is available in Europe is Aglepristone (Alizine), made by the Virbac Corporation. Its mechanism of action is to bind with high affinity to progesterone receptors, blocking

progesterone from exerting its biological effects.⁴⁰ Again, informed consent by the owner is important, as these drugs are not licensed for use in cats. The recommended dosage of bromocriptine is 0.25 mg/cat q 24 h PO for 5 to 7 d.²² The dose for cabergoline is 5 ug/kg q 24 h PO for 5 to 7 d.²² Cabergoline can terminate pregnancy in the cat by causing progesterone levels to drop to basal levels within 4 to 8 days following administration.¹⁸ Bromocriptine may also cause abortion by dropping progesterone levels. Both bromocriptine and cabergoline may cause anorexia, vomiting, salivation and incoordination.^{18,41} These side effects are minimal compared to those that may be observed with PGF_{2α} therapy.

Most protocols involving the use of dopamine agonists and anti-progestins have been reported in bitches.⁴⁰ In two separate studies, bitches with pyometra were treated successfully with cabergoline, cloprostenol, and antibiotics over a 2 week period. The success rate was 83% and 95%, respectively.^{42,43} In another study, the use of aglepristone, given alone or with cloprostenol, was compared in the treatment of metritis, and open and closed-cervix pyometra in 67 bitches. The combination of aglepristone and cloprostenol was more effective in the treatment of open and closed pyometra than aglepristone alone.⁴⁴ Aglepristone was also found to be effective in inducing cervical opening within 48 hours in cases of closed-cervix pyometra.⁴⁴ Information obtained from these studies in bitches may be extrapolated and used in the development of treatment protocols for queens with pyometra.

Queens should be re-evaluated weekly for two weeks after prostaglandin therapy. Usually the complete blood count normalizes by this time. The vaginal discharge, if present, should be clear but may persist for up to 10 days after treatment.⁸ Less purulent and more mucoid discharge is usually a sign of improvement. The uterus should return to its normal size by two weeks. If leukocytosis is present, the vaginal discharge is mucopurulent, the uterus is enlarged, or the queen is febrile after two weeks of treatment, a second round of prostaglandin can be initiated.⁸ Cats may return to estrus within 1 to 6

weeks of PGF_{2α} therapy.⁸ Low progesterone levels (less than 2 nmol/L), following treatment with either bromocriptine or cabergoline, will bring the queen back into heat sooner. It is very important that queens are bred on the following estrus to obtain a litter and reduce the likelihood of recurring pyometra.^{8,26,33} The duration of antibiotics for the course of treatment of pyometra should be at least four weeks and may be continued for at least 4 weeks into pregnancy if the queen gets bred on her next estrus.²²

Prognosis:

The prognosis if ovariectomy is chosen as the means of treatment is excellent. A retrospective study of 183 cases of pyometra in cats showed that 8% of the cats died or were euthanized after surgery. Twenty percent of the cats had post-operative complications such as anorexia, lethargy, anemia, pyrexia, vomiting, icterus, subcutaneous emphysema and in one case, a sponge foreign body.³² If a cat is diagnosed with a ruptured uterus prior to surgery, the prognosis for surgical therapy carries a very poor prognosis. Less than 50% of cats may survive due to sepsis and peritonitis.³²

The prognosis for medical treatment is also good and may be excellent as long as candidates are selected carefully based on having an open-cervix and lack of systemic involvement. The response to long term PGF_{2α} therapy largely depends on the degree of underlying uterine pathology. Ninety-five percent of treated queens return to normal estrous cycles.³³ Successful mating of those that returned to estrus resulted in pregnancy in nearly 85%.²⁷ Although most queens are able to conceive and deliver litters after treatment, pyometra is likely to recur in up to 14% of treated queens.³³

If queens are affected by a second occurrence of pyometra, they may still be treated successfully and can carry pregnancies to term.^{8,26,33} However, the progressive and recurrent nature of CEH and pyometra warrant ovariectomy at the earliest opportunity.

Clinical Report:

A one year, 10 month old Bengal queen was presented with a history of vaginal discharge for 3 days. She was housed strictly indoors and was current on vaccinations against feline viral rhinotracheitis, calicivirus, panleukopenia, and feline leukemia virus.^b She had successfully delivered one litter consisting of 4 kittens, 13 weeks (91 days) previously, and had returned to estrus approximately 4 weeks (30 to 35 days) previously. Historically, the owner had observed this queen's length of estrus to be rather short in duration; lasting approximately 24 hours on the cycle in which she conceived, and 48 hours in length on the cycle that was one month prior to presentation. Besides the vaginal discharge, the owner had noted that she was more cantankerous than usual. She had not been placed with the male when she showed signs of estrus 1 month prior.

On physical exam, the cat appeared to be bright and alert and nervous. She was in good body condition (body score 3/9) and weighed 3.9 kg. Hydration was normal; mucous membranes were pink with a capillary refill time of less than 2 seconds. Her heart rate was approximately 160 beats per minute (bpm) and her lungs auscultated normally with a respiratory rate of 25 breaths per minute (bpm). Her rectal temperature was 38.7°C. Abdominal palpation revealed a tense abdomen with a moderate-sized bladder but no abdominal pain. A uterus could not be palpated at the time but the cat was slightly uncooperative for this part of the exam and intent on escaping. A hemorrhagic purulent vaginal discharge was noted.

Based on the physical examination findings of a purulent vaginal discharge, the differential diagnoses were open-cervix pyometra, abortion, pregnancy, and uterine neoplasia. Other differentials for vaginal discharge are a vaginal foreign body, vaginal mass, trauma to the vagina, vaginitis, or a severe urinary tract infection.

Blood was collected for a complete blood count, serum chemistry, FeLV and FIV status, and progesterone levels, and sent to an external laboratory. A vaginal swab was collected for cytology and routine culture. An ultrasound-guided cystocentesis was also performed and the urine sent to an outside lab for culture. The collection of urine with the assistance of the ultrasound was necessary to avoid aspirating the contents of the uterus and contaminating the urine sample, and to avoid peritoneal contamination or even perforation of the uterus. A urine specific gravity was performed in house. The abdominal ultrasound showed enlarged uterine horns craniodorsal to the bladder that contained anechoic material, most likely fluid (Figure 2). These tubular structures measured 1.26 cm across the diameter of uterine horn in cross section. The wall of the uterus appeared thickened and measured 0.24 cm. There were no retained fetal membranes observed in either horn. The observation of the fluid-containing uterine horns is significant, as normal uterine horns in healthy cats cannot be imaged by ultrasound due to the lack of fluid contents. Figure 3 is a view of the distended uterus in the alternate sagittal plane. Then diameter of the horn including the walls measured 1.34 cm.

The cytology of the vaginal swab was stained in house using Diff-Quick^c stains and examined under the microscope. The cytology showed a majority of neutrophils and a few red blood cells. In addition to the neutrophils, there appears to be one macrophage and one degenerating cell (see Figure 4). Cats with pyometra have been shown to have increased parabasal cells in their vaginal cytology,³¹ but this was not obvious because of the overwhelming number of neutrophils observed.

A discussion with the owner followed the tentative diagnosis of open-cervix pyometra. The owner was concerned for the cat but also intended to continue breeding her. She was informed of the risks of treating pyometra medically versus performing an ovariohysterectomy. Because the cat was bright and

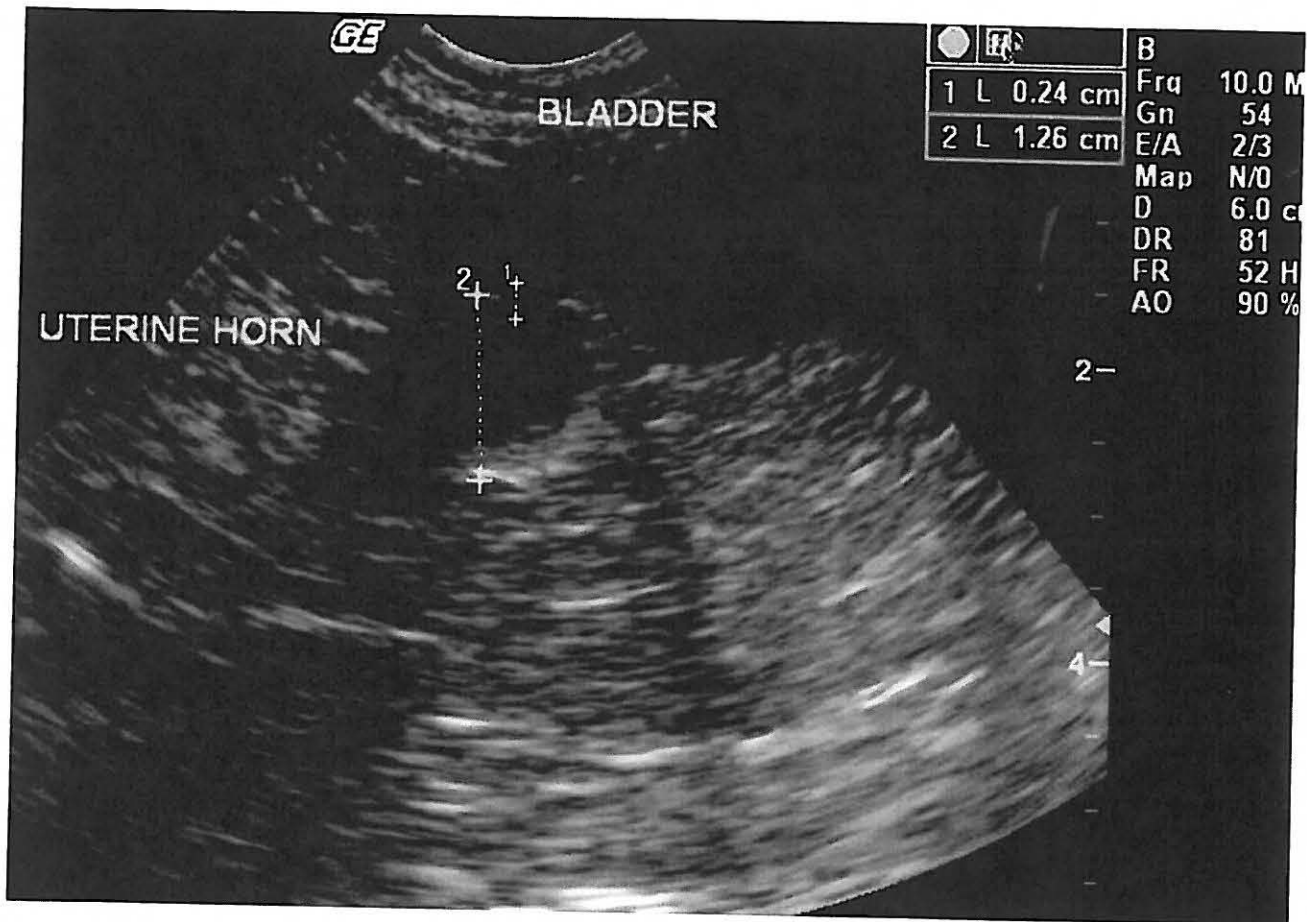


Figure 2: Transverse view of the uterus located craniodorsal to the bladder on Day 1.

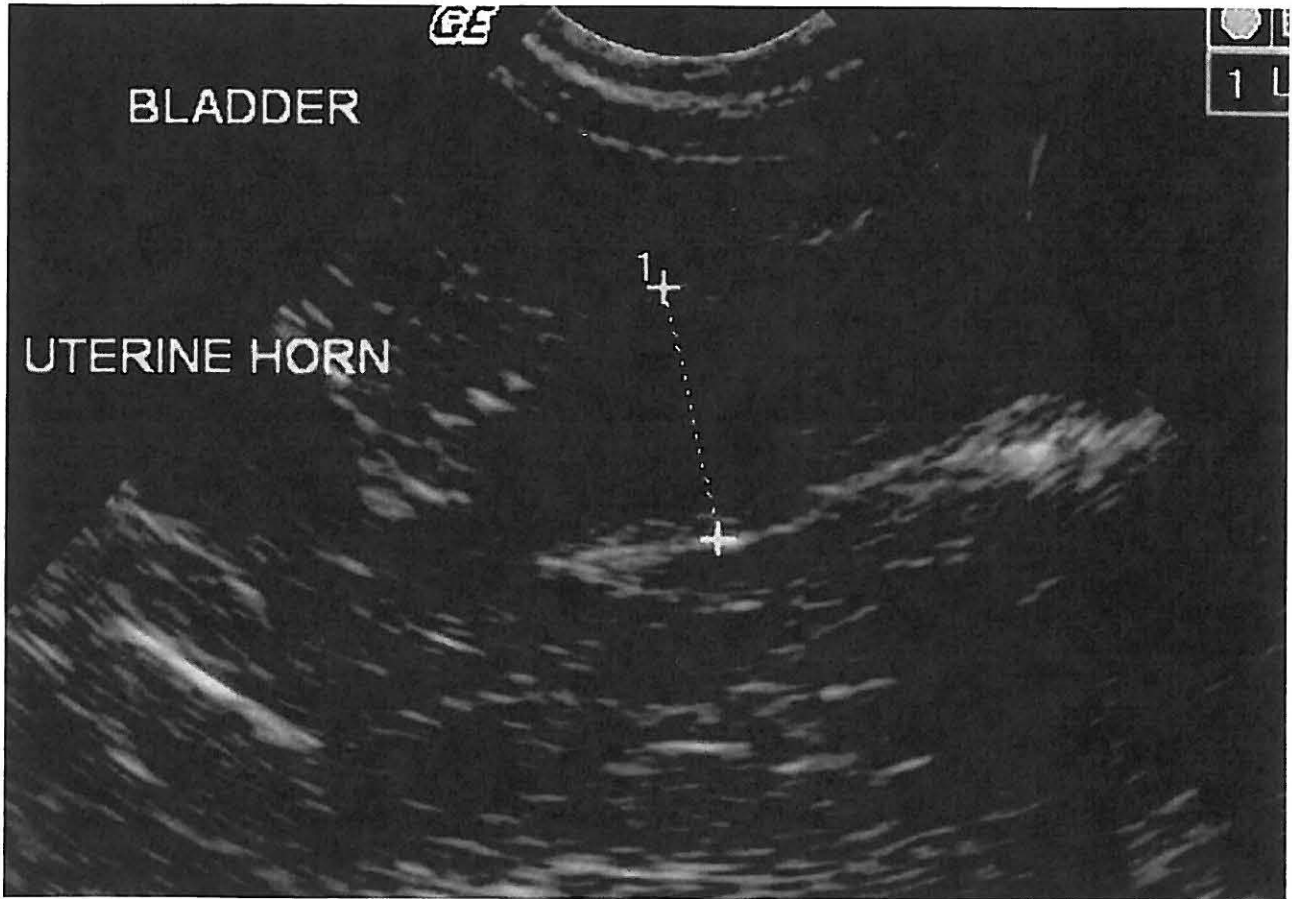


Figure 3: Sagittal view of the uterine horn dorsal to the bladder on Day 1.

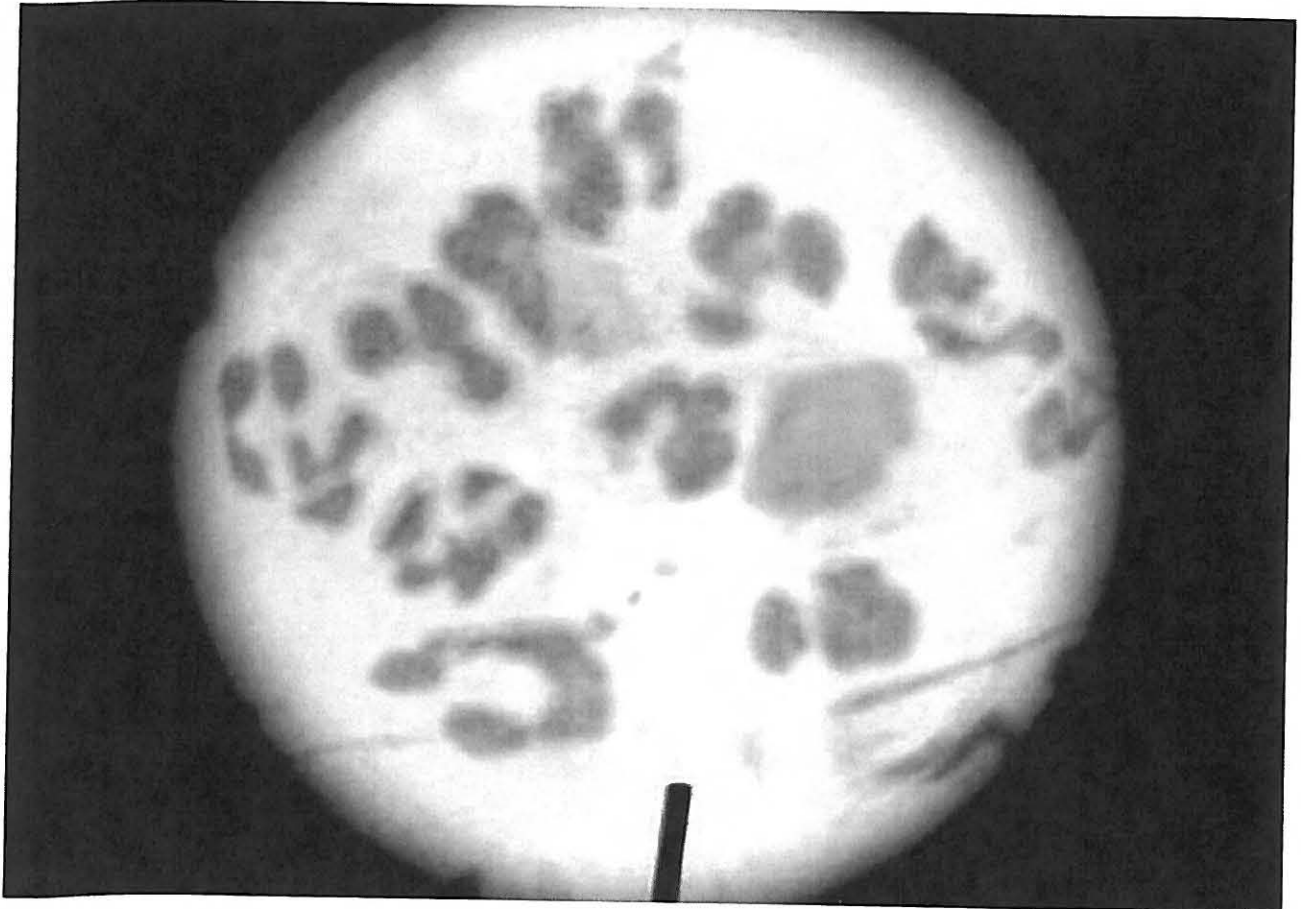


Figure 4: Vaginal cytology demonstrating abundant neutrophils on Day 1.

Oil immersion lens (x 1000)

alert, appeared to be behaving quite normally and the cervix was open, it was agreed that medical management could be initiated, as long as the cat continued to do well. The queen was started on amoxicillin-clavulanate trihydrate-potassium^d at 16 mg/kg PO q 12 h and subcutaneous injections of dinoprost tromethamine^a at 0.15 mg/kg q 8 h. Since she had a nervous disposition, but appeared unaffected by her medical situation, it was agreed that she could be treated by the owner at home. The owner was informed that the prostaglandin was to be used in an off-label manner and was warned of the serious side effects of the drug in humans with accidental exposure. The owner was no longer of child-bearing age, had no history of asthma, and agreed to use gloves when handling the medication. The subcutaneous technique for administering the medication was demonstrated. The owner was also briefed on the side effects in cats and was to monitor for them. The plan was to discontinue the drug if it appeared to be causing excessive discomfort or nausea. Both the PGF_{2α} injections and oral antibiotics were to be continued until there was no fluid in the uterus, as observed by ultrasound. The owner was warned that the treatment would only continue as long as the cat seemed to be bright, alert, eating and drinking normally, and behaving normally. The owner was also told that a cat with pyometra had a 14% chance of recurring pyometra when she came back into heat³³ and that she must breed her on the next heat for the best assurance of fertility. She was aware that the queen should have an ovariohysterectomy if her condition worsened, if she was not going to be bred on every subsequent heat, or if she was to be removed from the breeding colony.

The results of the CBC on Day 1 supported pyometra. The complete blood count showed normal red blood cell numbers and indices, except for a mildly elevated mean corpuscule hemoglobin concentration (MCHC), which was artefact likely due to *in vitro* hemolysis (Table 1). A true increase in MCHC does not normally occur, as an increased amount of hemoglobin cannot be produced in the red cell. The leukogram showed a mild inflammatory response. Neutrophil numbers were elevated, without a left shift, and there were occasional Doehle bodies observed. Doehle bodies indicate toxic change in the

leukocyte. The pathologist reported some poikilocytes present but this was likely artefact as there was no indication of azotemia or other metabolic disturbances to explain it.

The results of the serum chemistry panel are summarized in Table 2. The low glucose and creatinine were artefact. The glucose concentration measured from the gray top tube showed that the true value for serum glucose was normal. The slight elevation in anion gap was also likely due to artefact, but may be explained by the increase in phosphorus. Total phosphorus was slightly elevated and could be due to an increase in dietary intake or just due to the young age of this cat. Since phosphorus is usually measured as an anion, it could explain the increase in the anion gap (anion gap = unmeasured anions minus unmeasured cations). The urine specific gravity was 1.045, which is adequate and is consistent with the absence of endotoxic effects at the level of the loop of Henle or ADH antagonism. A negative urine culture together with a heavy growth of *Escherichia coli* from the vaginal swab made it clear that the purulent discharge containing bacteria was originating from the uterus or the vaginal rather than the bladder (see Table 3).

The cat was negative for *Mycoplasma hemofelis/hemominutum*, FeLV and FIV (see Table 2). The progesterone level was 61.5 nmol/L, which is consistent with the luteal phase of the ovarian cycle (Table 2). A value greater than 15 nmol/L seems typical of most pyometra cases, although not the rule.²⁷ Since prostaglandin does not reliably lyse the corpus luteum in cats, bromocriptine^e was added to the treatment regime to lower the serum progesterone level. The dose administered was 0.06 mg/kg (0.25 mg/cat) PO q 24 h for 5 days. It was started three days after the initiation of PGF_{2α} therapy, immediately after obtaining the progesterone result. An oral formulation of this drug was compounded at a local pharmacy.

Urine Specific Gravity

USG	Normal USG
1.040	>1.035

Urine culture

gram stain reveals only debris, no organisms identified
Bacti Organisms no growth of organisms after 72 hours

Vaginal swab culture

gram stain reveals gram negative rods	
bacti organism: heavy growth of <i>Escherichia coli</i>	
sensitive to:	chloramphenicol
	amoxicillin/clavulanic acid
	doxycycline
	enrofloxacin
	ceftiofur
	piperacillin
	sulfa trimethoprim
	tobramycin
	ticarcillin/clavulanic acid
	marbifloxacin
gentamicin	
intermediate:	cephalothin
resistant to:	amoxicillin
	clindamycin
	azithromycin
	cloxacillin

Table 3: Urine Specific Gravity
Culture results of urine and vaginal swab, Day 1

Results reported by an external laboratory (except USG)

Reference ranges supplied by an external laboratory

On Day 8 a second ultrasound was performed to monitor the response to PGF_{2α} and bromocriptine. The owner had reported that the cat was still doing well. She was eating, drinking and acting normally. The cat was not suffering from any ill effects of the medication. The owner reported minimal pink-tinged mucoid vaginal discharge. The ultrasound showed scant fluid in the uterus (see Figure 5). At this time the diameter of the uterine horn measured 0.51 cm. Although improved, the uterus could still be observed to contain some fluid, which was not considered normal, so treatment was continued. The amoxicillin clavulanic acid was continued for an additional 3 weeks and the PGF_{2α} treatment was also extended for an additional week, administered SQ q 8 h. Blood was drawn for another complete blood count and serum chemistry panel.

The blood work results on Day 8 (Table 1 and 2) showed a persistent inflammatory leukogram with elevated neutrophils and basophils. The increase in basophils was likely due to the increase in the inflammatory response from the uterine infection. It is not uncommon to see the inflammatory cells increase during the course of treatment, but after the second week of treatment the values usually return to normal.¹⁰ Although the white blood cell count had increased from Day 1, no Doehle bodies were reported this time. The chemistry appeared very similar to Day 1, with a low creatinine, again due to artefact. The progesterone level following bromocriptine treatment had fallen to 1.7 nmol/L, indicating significant regression of the corpus luteum in response to this drug. Progesterone values less than 1.6 nmol/L indicate absent corpora lutea.¹¹ This result may have indicated that only remnant corpora lutea remained.

On Day 14 the owner reported that the queen was showing signs of estrus. The cat was throwing herself at the tom and trying to position her body beneath him. The owner's concern was that the queen's "heat" was typically short in duration and she wanted to breed the cat, based on the information that pregnancy may protect the cat from a subsequent pyometra. The owner was

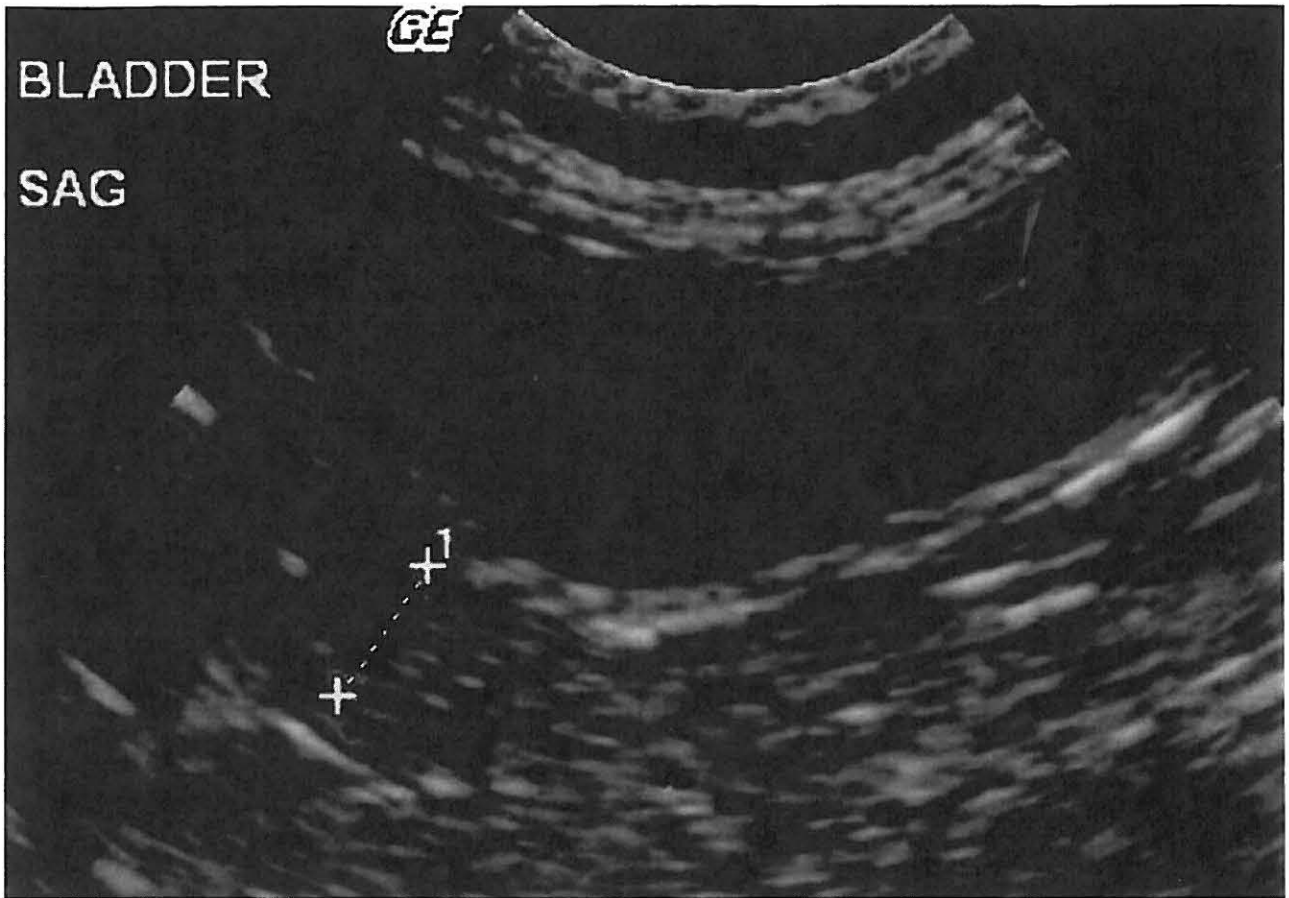


Figure 5: Sagittal view of the bladder with uterine horn located dorsally on Day 8.

instructed to discontinue the $\text{PGF}_{2\alpha}$ injections and return with the cat for an ultrasound the following day. The owner was to supervise the queen and tom together that day, but remove the female if she showed any signs of aggression.

One day later (Day 15), the owner brought the cat back for another ultrasound exam. A vaginal swab was also performed and cytology showed cornified epithelial cells with a fairly clear background. These findings were consistent with estrus. The ultrasound exam showed no fluid in the uterus (Figure 6). There was no vaginal discharge observed, indicating that the pyometra had resolved. The owner reported that her new and only tom, approximately 1 year old and inexperienced, was not able to breed the queen. He seemed reluctant to try, even though she appeared quite receptive. It was suggested that the owner monitor the queen for signs of returning pyometra.

On Day 32 the owner returned with the cat. She was concerned that the progesterone levels were elevated as the cat was behaving cantankerously again. The owner reported that the cat had only shown signs of estrus once, on Day 14. Physical exam findings were unremarkable. The cat's body condition and weight, 3.9 kg, were unchanged. There was no abdominal pain or distension and there was no vaginal discharge or fever. Blood was collected for serum progesterone. Ultrasound of the uterus was normal, in that the uterus could not be observed.

The progesterone result was reported to be greater than 63.6 nmol/L, higher than when it had been measured before the initial bromocriptine treatment. The elevated progesterone level supported the prediction made by the breeder that this cat was once again in the luteal phase of her cycle and had ovulated regardless of whether intromission was achieved. Her concerns for the queen developing another pyometra were valid. Bromocriptine treatment at 0.06 mg/kg was initiated again PO q 24 h for 5 days but without the $\text{PGF}_{2\alpha}$ as there did not appear to be any need to evacuate the uterus. The cat

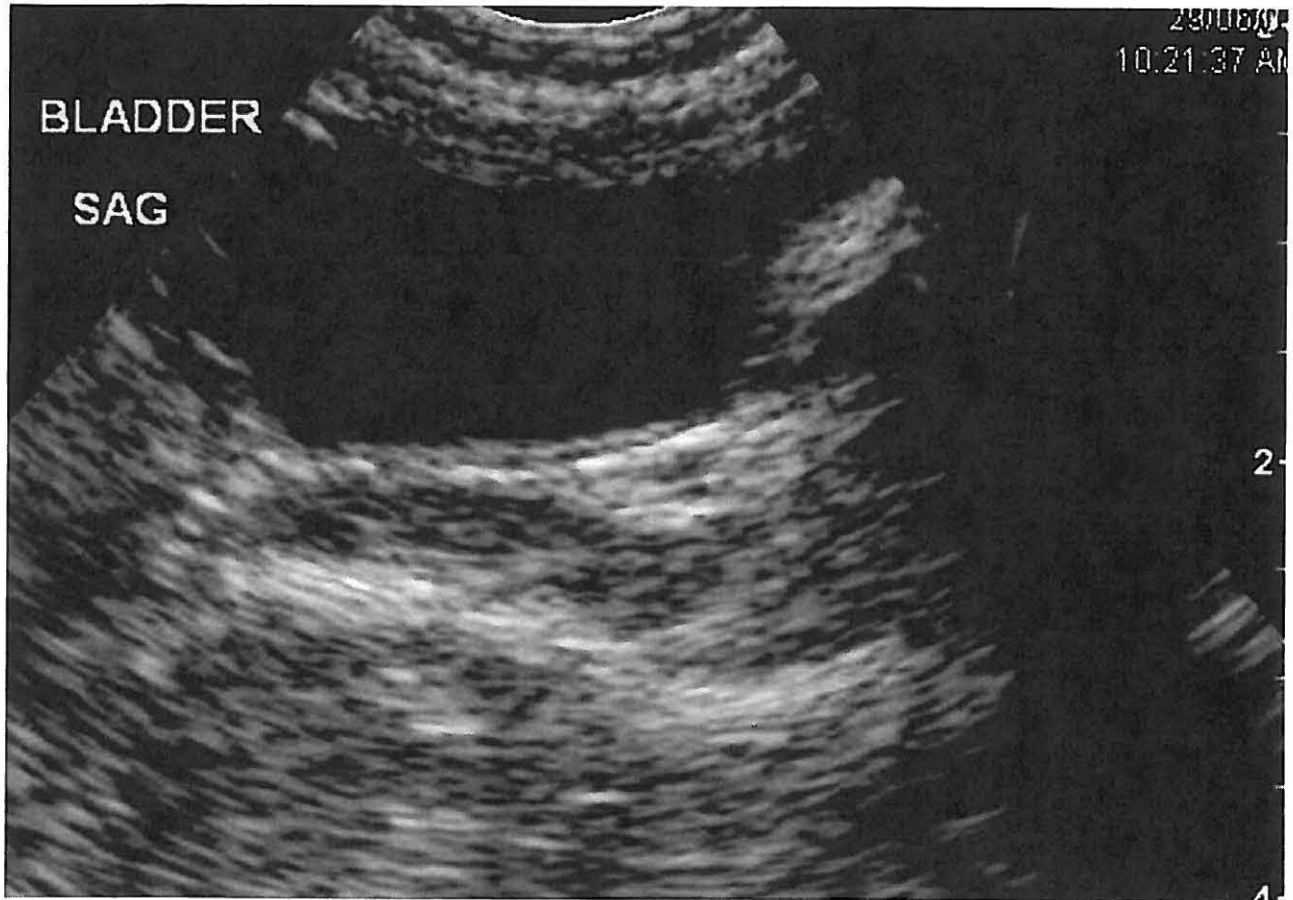


Figure 6: Sagittal view of the bladder on Day 15

(Colon located caudal to bladder)

was still on amoxicillin clavulanic acid at this point and was to continue on this antibiotic for another 3 weeks q 12 h.

On Day 37 a follow-up ultrasound was performed. The cat was still in good spirits and no vaginal discharge was observed. The ultrasound showed possibly a very minimal amount of fluid in the caudal uterus (body). The owner was instructed to try to breed the cat again when she came into heat, and to consider a different tom. Alternatively, the breeder could have an ovariohysterectomy, ensuring the queen would not develop pyometra again. The breeder claimed this queen's kittens were valuable and intended to continue to breed her to obtain two more litters. Since the owner did not have an alternate Bengal tom, she planned to breed the queen with the inexperienced young male if she showed signs of estrus again, or until she could import another Bengal tom.

Since this report was written, the cat has not been observed to show estrus again. This is expected as fall had arrived and the daylight hours were becoming shorter. Most likely the cat is now in anestrus. The owner has since had the young tom castrated. She is importing a new Bengal tom in January, 2008.

Discussion/Critique of the case:

An intact queen with a vaginal discharge is considered to have a pyometra unless it can be proven otherwise. Although this queen did not appear sick (she was still active, eating, drinking, and grooming herself), and the uterus could not be palpated due to a tense, uncooperative patient, a pyometra was considered the primary differential based on the observation of the vaginal discharge and the fact that this cat was reproductively intact. The time from the last observed estrus (30-35 d) was also appropriate for pyometra.

The goal of the diagnostic approach for vulvar discharge should be to locate the source of the discharge and determine the underlying cause. The possibilities include diseases that are either uterine, vaginal, or urinary in origin, or a combination of these diseases.

Differentials for uterine diseases include pregnancy and embryonic loss or abortion in the event that the queen had contact with the tom. Ultrasound would be useful to determine if the queen was pregnant, as the embryo in the gestational sac and a heart beat could be observed at 1 month gestation.³⁷ If the owner observed estrus approximately 1 month ago, ovulation probably occurred 4 to 5 days after estrus, which makes the length of gestation about 25 to 30 days. If early pregnancy loss had occurred at this time, it would be too early to see mummified fetuses (skeletons). Early pregnancy loss (before Day 25) is more often associated with fetal resorption, which usually does not cause any symptoms.³⁷ Fetal death after 35 days usually results in abortion of live or dead fetuses. It is unlikely that this queen would have been more than 35 days along in gestation. Furthermore, this queen was not known to have contact with the tom, which made pregnancy and pregnancy loss less likely.

For the same reason, post-partum lochia or metritis, retained placentas, and subinvolution of placental sites were also very unlikely causes of vulvar discharge. If the queen did become pregnant, 25-30 days gestation is less than half the normal length of pregnancy, so parturition and the conditions associated with the post-partum uterus were even more unlikely.

Other differentials for uterine pathology are mucometra, hydrometra, endometritis and uterine neoplasia. The cytology of the purulent, hemorrhagic vaginal discharge contained predominantly neutrophils and red blood cells, ruling out proestrus, hydrometra and mucometra. Proestrus vaginal cytology usually contains intermediate epithelial cells, and some cornified cells, not the overwhelming number of neutrophils and red blood cells that were seen. The cytology of discharge from hydrometra and mucometra would be mucous with very few cells. Endometritis was less likely because it rarely

causes vaginal discharge. An abdominal ultrasound revealing the tubular structures that measured approximately 1.3 cm in diameter, consistent with fluid-filled uterine horns, supported the diagnosis of pyometra and ruled out endometritis, which usually only causes a thickening of the walls. Although the walls were thickened, the thickening was uniform along the length of the horns, which made neoplasia less likely. There were no other abnormalities seen on abdominal ultrasound examination such as abnormal abdominal fluid or hyperechoic fat to suggest peritonitis from uterine rupture. The kidneys did not show any evidence of pyelonephritis such as renal pelvic dilation, increased echogenicity, or poor corticomedullary definition,³⁹ and there was no evidence of renal calculi, which could contribute to a pyelonephritis. The bladder also appeared normal. Thickened walls, often observed in cases of cystitis, were not seen. The ultrasound and negative urine culture results obtained by cystocentesis eliminated the bladder (and kidneys) as a possible source of infection. Furthermore, there was no history of dysuria, stranguria, or pollakiuria, as one would expect for a severe lower urinary tract infection. Although this case did not have a concurrent cystitis/bladder infection, it is not unusual for this to occur with pyometra.

Diseases of the vagina, such as vaginal foreign body, vaginal mass, vaginitis, and vaginal trauma or hematoma may have been discovered when the sample was collected from the vaginal vault with a swab or if vaginoscopy had been carried out. These conditions were ruled out early even without vaginoscopy because there were no localizing signs such as hyperemia or edema of the vulva or vaginal vestibule. Often the history for vaginal abnormalities includes increased vulvar licking or pollakiuria. None of this was mentioned in the history. Furthermore, general anesthesia would have been necessary to perform vaginoscopy in this cat and this was deemed unnecessary after the ultrasound exam was performed and the origin of the discharge located.

Ultrasound is the most sensitive tool for determining whether pyometra is present and may result in earlier treatment and improved success or outcome. Radiographs could have been carried out as a diagnostic aid in determining if this cat had pyometra, but it was felt that ultrasound would be a superior choice, as it could readily distinguish between early pregnancy and pyometra. Occasionally it is difficult to diagnose pyometra based on radiography alone, especially in cases of open-cervix pyometra when the uterus is draining and the horns may not be as distended. In addition, pyometra with viable fetuses in the contralateral horn can be diagnosed and differentiated from other conditions by ultrasonography.

Treatment consisting of prostaglandin therapy and antibiotics were instituted immediately after samples were collected for lab analysis, without waiting for culture results. Antibiotics were chosen based on the assumption that *E. coli* was a likely pathogen. *Escherichia coli* seems to be the most common pathogen isolated from uterine contents in the queen due to the proximity of the anus to the vulva. Since the queen was not septic or showing signs of shock, intravenous fluid therapy was not necessary.

The blood work results were unremarkable but were important to establish the degree of severity of the pyometra in this queen, especially because she was quite nervous and would not be a good candidate for hospitalization. Had there been a left shift on the inflammatory leukogram, azotemia, elevated liver enzymes, or hypoglycemia, the cat would have been hospitalized and treated with intravenous fluids and other required medication (glucose, electrolytes) in addition to the antibiotics, prior to initiating the prostaglandin therapy. Fortunately, the owner of this cat was quite astute and capable of doing treatments at home. Due to the diligence of this owner monitoring for vaginal discharge, this queen was probably presented early in the course of pyometra. The mild symptoms and lack of a non-regenerative anemia supported this reflection.

The recommendation for open-cervix medical treatment of pyometra is somewhat of a contentious issue. There are some veterinarians who feel that medical intervention that promotes continued breeding of these queens may perpetuate the susceptibility of future generations of queens to CEH, endometritis and pyometra. Publications looking at the incidence of infertility in offspring from CEH-pyometra cases could not be found. However, this kind of information may be needed to convince some breeders that the long term risks of pyometra in future generations may outweigh the desire to rebreed affected queens. As stated previously, medical treatment does not cure CEH and it appears inevitable that, as the queen ages, her susceptibility to pyometra will remain, if not increase. Furthermore, a disease that can be solved surgically should not be treated medically if it places the queen at risk of developing septicemia or peritonitis from uterine rupture.

The other risk with medical therapy comes from implementing off label drugs for the treatment of this disease in the cat. Neither bromocriptine nor dinoprost tromethamine are licensed for use in the cat. The off-label use implies that there has not been any extensive testing for safety and efficacy in the species in which it is to be used. The patient is, therefore, more at risk of side effects. If informed consent is given by the owner, the off-label use of dinoprost tromethamine and bromocriptine is acceptable because there are no other approved substitutes for use in the cat. The concern with prostaglandin is that the potential side effects in both cats and dogs are numerous and could be substantial enough to warrant discontinuation of the drug. Most of the time these side effects can be eliminated by lowering the dose (to 0.05 mg/kg) and giving it more frequently (4-6 times per day). The second issue is the risk to the owner himself/herself if they wish to treat the pyometra at home. Prostaglandin must be handled very carefully, and preferably not by people with asthma, respiratory disease or those who may be pregnant. There may be repercussions to the veterinary prescribing the drug if there is inadvertent human exposure that results in deleterious side effects.

In retrospect, a further complete blood count should have been performed on Day 14 to see if the neutrophilia resolved. However, the queen was in estrus at that point and had remained on the antibiotics so it was unlikely that the course of therapy would have been altered. The plan was to stay on the antibiotics for a total of 7 weeks if the queen was responding to treatment adequately, and apparently she was, according to the ultrasound and lack of vaginal discharge and the fact that she returned to estrus.

This queen appeared to have a short estrus (1 day) but the length of estrus in cats can vary and this is still considered normal. Experienced breeders become quite attentive to how long estrus lasts in their queens, as breeding opportunities may be missed if they do not pay attention. Although the return to estrus on Day 14 seemed abrupt, it was physiologically possible. Decreasing progesterone to basal levels with bromocriptine therapy brings the queen back into estrus sooner because the follicles in the ovaries can resume normal activity and begin to produce estradiol again. The recommencement of the estrous cycle just two weeks following treatment is an example of how well cats can return to a fertile state. Estrus at Day 14 was confirmed in this queen with vaginal cytology. Cats typically display a phenomenon called "clearing" on their vaginal cytology when they are in estrus. Estrogen thins the vaginal mucosa so cornified epithelial cells, without any white or red blood cells in the background should be seen.⁶

The owner was advised to discontinue the prostaglandin therapy when the queen showed signs of estrus so that there would not be any detrimental effects on implantation from myometrial contractions in the event that she was successfully bred.

Unfortunately, the tom was not successful at breeding the queen when she returned to estrus. His inexperience could have cost this queen her breeding career if she developed pyometra for a second time, which would have prompted the owner to remove her from the breeding program. However, the

owner was intent on carrying on by monitoring the queen closely for signs of returning pyometra. When the progesterone levels climbed a second time, indicating the luteal phase, bromocriptine therapy was immediately recommenced in hopes that this phase and the effects of progesterone on the endometrium would be short-lived. An ultrasound exam 5 days later showed a small amount of fluid near the body of the uterus, which was not unexpected, since there was probably some glandular fluid production as a response to former elevated progesterone levels. Since the volume of fluid was very minimal and the cat was on antibiotics, the owner elected to continue monitoring the queen for signs of pyometra and try to breed her on the subsequent estrus rather than spaying her. Following the second treatment with bromocriptine, the queen has not shown estrus again and most likely is in anestrus. Since it is now winter and photoperiods are shorter, increased circulating melatonin and prolactin levels have inhibited ovarian activity.⁴⁵ Hopefully, the cat will remain in anestrus until the breeder acquires a new, experienced tom. Further serial ultrasound monitoring of the uterus would be more imperative if the breeder used artificial daylight hours in her colony to maintain cycling all year round or if, under natural photoperiods, the time of year was between February and August. Anestrus may have been confirmed by vaginal cytology and differentiated from interestrus, the period between estrous cycles, which would look the same to the breeder.

The sequence of events in this queen's reproductive cycle is outlined in pink in Figure 1.

When pyometra developed following pseudopregnancy, the queen returned to estrus after treatment, ovulated, became pseudopregnant again, and then went into anestrus.

Most cases reported in the literature have used only $\text{PGF}_{2\alpha}$ and antibiotics to treat pyometra in cats and have been successful. The reported recurrence rate of 14% followed the use of $\text{PGF}_{2\alpha}$ and antibiotics in open-cervix pyometra cases.³³ This recurrence rate may be improved when bromocriptine or cabergoline are added to the therapy. In this case of pyometra, bromocriptine appeared to work

exceptionally well at reducing the progesterone values and was the only treatment needed (besides antibiotics) when there was risk of recurring pyometra (based on high progesterone values) but absent fluid in the uterus. Bomocriptine appeared to have no side effects at the dose recommended in this queen. It appears to be a reasonable adjunctive therapy for use in medical treatment of pyometra and works well when given with antibiotics to high-risk queens that have minimal fluid in their uterus and are in the luteal phase of their cycle.

The prognosis is not as good for this queen, as reported in the literature because she is under 2 years old and already has pyometra. Usually this disease is associated with proliferation and degeneration of the endometrium that is associated with hormonal stimulation and aging. As this queen ages, her endometrium will be more susceptible to the hormonal influence of repeated progesterone (and estrogen) each time she cycles and ovulates. It is not uncommon to see pyometra in very young queens, and theoretically the condition could occur any time after the onset of puberty. Pyometra has also been artificially stimulated with progestin use in pre-pubertal kittens.⁴⁶ Many reproductive specialists believe that pyometra tends to be familial when seen at such a young age. In these cats, the reproductive history of the queen's relatives should be questioned. As far as the breeder knew, there was no history of pyometra in this queen's relatives. If pyometra is common in related cats, an ovariohysterectomy should be recommended as the primary choice of treatment, even if the queen has an open cervix and is not systemically ill.

Client education is extremely important in successfully treated cases of pyometra so that owners know that the non-gravid uterus could potentially be susceptible to infection with every subsequent estrous cycle. These queens should be bred every time they show estrus to reduce this risk. Once the breeder has retired the queen from their breeding program, an ovariohysterectomy should be performed.

There is no one breed that is more susceptible to pyometra than another. Bengals cats have not been reported to have a higher incidence of CEH/pyometra. However, more veterinary advice on medical treatment of pyometra is sought by purebred cat breeders because the reproductive status of these queens is of greater concern.

Summary:

This report describes the diagnosis and clinical management of a young queen with pyometra. The diagnosis was based on clinical signs, abdominal ultrasound examination, vaginal culture, and blood work. Treatment was monitored by serial ultrasound examinations and blood work. Successful treatment consisted of antibiotics, prostaglandin, and bromocriptine. The queen returned to estrus during the course of treatment; however, breeding was unsuccessful. High progesterone levels indicated the queen returned to the luteal phase of her cycle. Bromocriptine was prescribed for a second time, while remaining on the antibiotics to prevent the recurrence of pyometra. The bromocriptine, by itself, was successful in reducing the progesterone levels. It appears to be an important adjunctive therapy in the treatment of pyometra when progesterone levels are elevated. Ovariohysterectomy remains the treatment of choice for pyometra. Medical therapy should only be attempted after careful consideration of the risks to the queen and her future offspring.

Endnotes:

- a. Lutalyse (dinoprost tromethamine) Pharmacia & Upjohn. Kalamazoo, MI 49001-0199
- b. LVK iv (rhinotracheitis, calicivirus, panleukopenia, and feline leukemia) virus killed vaccine. Fort Dodge Laboratories, Inc. Fort Dodge, Iowa 50501.
- c. Diff Quick stains. EMR Chemicals, Inc. Gibbstown, NJ 08027-1297
- d. Clavamox (amoxicillin 50 mg/12.5 mg clavulanic acid) Pfizer, Kirkland, QC H9J 2M5
- e. Parlodel (bromocriptine mesylate) Pharmascience, Montreal, Quebec H4P 2T4

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