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STANDARDS of CARE
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Canine Pyometra

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The cystic endometrial hyperplasia (CEH)/pyometra complex may present as either an acute or chronic disease that occurs as a result of chronic and repeated exposure of the endometrium to progesterone. The underlying uterine pathology is CEH, which predisposes the uterus to an ascending bacterial infection causing pyometra. Generally, the diagnosis of open-cervix pyometra is based on physical examination findings of enlarged uterine structures and the presence of a purulent vaginal discharge. Closed-cervix pyometra is more insidious, with early clinical signs of general malaise that may escalate to clinical signs compatible with a life-threatening disease in later stages. Rapid recognition and intervention in fulminant cases of pyometra is important because these patients may be profoundly dehydrated and demonstrating signs of septicemia or shock secondary to systemic infection.

Ovariohysterectomy is the treatment of choice for canine pyometra. The use of natural prostaglandin $F_{2\alpha}$ (Lutalyse, Pharmacia Animal Health) for medical management may be advocated in young females that are part of a valuable breeding program. Owners must be aware that the potential for successful pregnancy and parturition is variable following medical management.

DIAGNOSTIC CRITERIA

Historical Information

Gender Predisposition

Sexually intact females are predisposed to pyometra.

Age Predisposition

Pyometra may develop in any intact female. The CEH/pyometra syndrome predominantly occurs in middle-aged females.

Breed Predisposition

None.

Owner Observations

Chief complaints include signs of general malaise, lethargy, depression, and anorexia. Vomiting and diarrhea may also be seen. Mucopurulent or seropurulent vaginal discharge is noted in open-cervix presentations. Polyuria and polydipsia may be

reported. These observations are associated with *Escherichia coli* endotoxin-induced antagonism of antidiuretic hormone (ADH) receptors in the renal tubules.

Other Historical Considerations/Predispositions

- CEH occurs in older females (>6 years of age) as a result of repeated exposure of the endometrium to estrogen and progesterone.
- The cervix is relaxed during estrus, and normal vaginal flora ascends into the uterus. In the diestrus phase, progesterone promotes endometrial growth, glandular secretions, and reduced myometrial contractions and closes the cervix. This provides an excellent medium for bacterial growth.
- The distinction between CEH/pyometra and metritis is made based on the stage of the reproductive cycle. Metritis is a uterine infection that develops postpartum, when serum progesterone levels are low. In contrast, pyometra usually develops during diestrus, when progesterone levels are high.
- Clinical signs occur within 1 to 2 months after estrus or estrogen therapy.
- There is an increased risk associated with estrogen therapy ("mismate" injections) in younger females (<6 years of age) and bitches that never carried a pregnancy.
- CEH and exogenous estrogen therapy must compromise the normal uterine immune defense mechanisms because bacterial contamination of the uterus occurs without developing pyometra.

Physical Examination Findings

- General malaise
- Dogs may appear dehydrated from vomiting, diarrhea, and polyuria.
- Approximately 41% of bitches are febrile; however, they may be normothermic or hypothermic if shocky at the time of presentation.
- The hindquarters may be wet from purulent vaginal discharge in bitches presenting with an open cervix.
- Abdominal distention may be seen in bitches presenting with a closed cervix.
- Abdominal palpation elicits resistance and pain behavior. The uterus may be palpably enlarged; gentle palpation techniques should be employed because the uterus may be friable.

Laboratory Findings

- **Complete blood count (CBC) abnormalities** include a neutrophilia with or without a left shift. Septic cases may have a neutropenia, a degenerative left shift, and toxic changes to the cells. Nonregenerative anemias are seen in 26% of pyometra cases. However, the CBC and differential counts may be normal.
- **Azotemia** occurs in 18% to 26% of cases, usually from prerenal causes. However, renal failure is rare.
- **Hyperproteinemia and hyperglobulinemia** may present due to dehydration and chronic antigenic stimulation.
- **Unguided cystocentesis** is not recommended if a gravid uterus or pyometra is suspected.
- **Urinalysis** may show isosthenuria from ADH antagonism. Bacteriuria may be present because the urinary tract is often infected with the same organisms found in the uterus.
- **Proteinuria without pyuria or hematuria** may occur due to immune complex deposition along the glomerular basement membrane. The glomerulonephropathy allows leakage of plasma proteins into the glomerular filtrate. Protein loss corrects with pyometra resolution.
- **The most commonly cultured bacteria** from the uterus of CEH/pyometra dogs include *E. coli, Streptococcus* sp, and *Staphylococcus* sp.

Other Diagnostic Findings

- Abdominal radiographs may identify an enlarged, fluid-dense uterus that displaces the distal colon dorsally and gastrointestinal tract rostrally. However, if the cervix is open enough, fluid may have drained, resulting in unremarkable radiographic findings.
- Abdominal ultrasound will show an enlarged, fluid-filled, tubular structure. Uterine wall thickness may be variable. The uterus may be distinguished from loops of bowel by the increased wall thickness and absence of peristaltic activity.
- In some cases, fluid characteristics may be helpful in differentiating pyometra (hyperechoic) from hydrometra (less echoic).
- Both abdominal radiographs and ultrasound may identify free abdominal fluid and loss of serosal detail in cases of uterine rupture.
- The uterus will become enlarged early in gestation, requiring diagnostic pregnancy tests to differentiate it from pyometra.

Summary of Diagnostic Criteria

- Pyometra should be suspected in sexually intact, middle-aged females with general malaise and vaginal discharge that have recently experienced a heat cycle or estrogen therapy.
  Common clinical signs of CEH/pyometra include:
  — Lethargy
  — Inappetence
  — Vomiting
  — Diarrhea
  — Purulent vaginal discharge
  — Polyuria and polydipsia
- Physical exam findings commonly include:
  — Dehydration
  — Depression
  — Body temperature change
  — Vaginal discharge
  — Distended and/or painful abdomen
- Abdominal radiographs and ultrasound may identify an enlarged, tubular, fluid-filled uterus.
- A CBC may be normal or may demonstrate an inflammatory leukogram with or without a left shift.
- Azotemia may be observed.

Differential Diagnoses

- Other causes for an enlarged uterus include:
  — Pregnancy
  — Hydrometra/mucometra
  — Hematometra
- The water content within the mucin determines the description of hydrometra or mucometra. These are difficult to diagnose unless uterine infection develops.
- Hematometra has been reported in one dog with anticoagulant rodenticide toxicity and in two dogs with uterine torsion.
- Mineralization of fetal skeletons occurs 42 to 52 days after mating. Prior to this, the enlarged uterus may be confused with the radiographic appearance of pyometra.

TREATMENT RECOMMENDATIONS

Initial Treatment

Emergency management is centered on resolving shock, dehydration, metabolic derangements, and bacteria-induced septicemia.

- Choice of IV fluid type (crystalloid, colloid, plasma) and administration rate should be based on the degree of patient dehydration and electrolyte and acid–base abnormalities.
- Patients experiencing shock and/or that may be septic may require aggressive IV crystalloid and colloid therapy for circulatory support prior to surgery. However, removal of the infected uterus may necessitate emergency surgery prior to full patient stabilization.
- Antibiotic therapy should be directed at *E. coli.* Primary antimicrobial choices include ampicillin (10 to 20 mg/kg IV q6h), amoxicillin/clavulanic acid (10 to 20 mg/kg PO q12h), enrofloxacin (5 to 10 mg/kg IV q24h), or second-generation cephalosporins (cefoxitin, 10 to 30 mg/kg IV q8h).
- Ideally, a culture and sensitivity should be performed on uterine or vulvar fluid. Broad-spectrum antibiotics should be started empirically and modified pending bacteriology results. Some authors recommend ampicillin as a first choice, although *E. coli* may be resistant.
- Due to their nephrotoxicity, aminoglycosides should be used with caution in dehydrated, azotemic patients.
- Ovariohysterectomy is the treatment of choice for both open- and closed-cervix pyometras in females that are not intended for breeding or are no longer contributing to a breeding program.

Alternative/Optional Treatments/Therapy

- Medical management in pyometra involves administration of prostaglandin $F_{2\alpha}$. Medical management should be restricted to dogs under 6 years of age, with an open cervix, that are not critically ill and have owners who are adamant about their ongoing contribution to a breeding program.
- Administration of prostaglandin $F_{2\alpha}$ causes myometrial contraction and inhibition of progesterone synthesis due to lysis of the corpus luteum.

CHECKPOINT

Different authors report variable percentages for successful return to fertility after medical treatment for pyometra, in part reflecting a relatively small percentage of dogs that are bred again. Regardless, the underlying CEH persists and recurrence rates for pyometra are high, suggesting that the infection remains subclinical and is not totally cleared from the uterus.

- Clinical response may not be evident for 48 hours after initiating therapy; therefore, it is not an appropriate choice for critically ill patients.
- Treatment protocol includes progressively increasing the dose of prostaglandin $F_{2\alpha}$:
  — **Day 1:** 0.1 mg/kg SQ once daily
  — **Day 2**: 0.2 mg/kg SQ once daily
  — **Days 3 to 7:** 0.3 mg/kg SQ once daily
- One author recommends measuring serum progesterone concentrations prior to initiating therapy:
  — If progesterone levels are >1 ng/mL, a luteolytic dose of prostaglandin $F_{2\alpha}$ should be given on days 1 and 2, 100 µg/kg SQ three times daily; days 2 through 7, 200 µg/kg SQ once daily.
  — If progesterone levels are <1 ng/mL, <250 µg/kg SQ once to twice daily until the uterine size is normal.
- Duration of therapy depends on improving uterine size and discharge.
- There is a narrow margin of safety with this drug, and total doses >250 µg/kg/day are associated with more severe side effects.
- Dogs may experience restlessness, hypersalivation, vomiting, and diarrhea shortly after injection. Some dogs experience abdominal pain, tachycardia, and shock-like symptoms including pallor, weakness, and poor pulse quality. Side effects generally resolve within 60 minutes.
- Prostaglandin $F_{2\alpha}$ should be administered in the morning and dogs monitored throughout the day.
- Prostaglandin $F_{2\alpha}$ may be given to patients with a closed cervix; however, salpingitis, uterine rupture, and peritonitis may occur. One source cites only 34% of closed-cervix pyometra patients responded favorably to therapy. Dogs with a closed cervix should be hospitalized throughout the treatment period.
- A second course of prostaglandin $F_{2\alpha}$ therapy may be required for complete resolution of clinical signs.
- Synthetic prostaglandins (cloprostenol [Estrumate, Schering-Plough Animal Health] and fluprostenol [Equimate, Bayer]) are more potent than natural prostaglandins. Adverse side effects, including shock, are more likely at recommended doses.
- Other medical therapies that have been reported include antiprolactins (bromocriptine, cabergoline), antiprogestins (RU46534, aglepristone), and ecbolic agents (oxytocin). There are few published studies using these drugs, and currently none are recommended for treatment of canine pyometra.

RESOURCE LIST

- **Prostaglandin $F_{2\alpha}$ (Lutalyse, Pharmacia)**—Day 1: 0.1 mg/kg SQ once daily; Day 2: 0.2 mg/kg SQ once daily; Days 3–7: 0.3 mg/kg SQ once daily.
- **Prostaglandin $F_{2\alpha}$ (Lutalyse)**—*If progesterone levels are >1 ng/mL:* Days 1–2: 100 µg/kg SQ three times daily; Days 2–7, 200 µg/kg SQ once daily. *If progesterone levels are <1 ng/mL:* <250 µg/kg SQ once to twice daily until the uterine size is normal.
- **Ampicillin**—10–20 mg/kg IV q6h.
- **Amoxicillin/clavulanic acid (Clavamox, Pfizer)**—10–20 mg/kg PO q12h for 14 days.
- **Enrofloxacin (Baytril, Bayer)**— 5–10 mg/kg, dilute 1:3 with sterile water, give slowly IV once daily or PO q12h for 14 days.
- **Cephalosporins, second generation (cefoxitin)**—10–30 mg/kg IV q8h.
- **Metoclopramide (Reglan, Wyeth)**—0.2–0.4 mg/kg PO SQ IM q6h. Alternately as a constant rate infusion 0.01–0.02 mg/kg/hr.
- **Chlorpromazine**—0.2–0.4 mg/kg SQ q8h.

Supportive Treatment

- IV fluids should be continued until vomiting has resolved and normal eating and drinking behavior is resumed.
- Antiemetics may be given in cases of protracted vomiting or patients receiving prostaglandin $F_{2\alpha}$.
- Antibiotic therapy may be modified once culture and sensitivity results are received. Bacteria cultured from vaginal swabs do not necessarily identify the organisms within the uterus unless the cervix is open and the culture was taken near the cervix with a guarded swab.

Patient Monitoring

- Hydration status, serum electrolyte values, acid–base status, and coagulation parameters should be monitored at least daily in critically ill patients.
- In medically managed cases, a thorough physical examination should be performed prior to each prostaglandin $F_{2\alpha}$ injection.
- Serial abdominal ultrasounds should be performed every 2 to 3 days after initiation of prostaglandin $F_{2\alpha}$ therapy. Progress is measured by decreasing uterine size toward normal without evidence of peritonitis. Abdominal radiography may also be performed, but exact uterine measurements may not be achieved.
- Vaginal discharge may continue for approximately 2 weeks, gradually becoming serous before stopping.
- Some cases may require a second course of prostaglandin $F_{2\alpha}$ therapy for complete resolution of clinical signs.
- Dogs treated during diestrus may cycle sooner than expected if treated with prostaglandin $F_{2\alpha}$ due to a shortening of the luteal phase.
- Evidence of clinical deterioration warrants an ovariohysterectomy.

Milestones/Recovery Time Frames

- Clinical response may not be seen for up to 48 hours after initiating prostaglandin $F_{2\alpha}$ therapy.
- White blood cell (WBC) count should decline to normal as the infection resolves with medical management. In postoperative patients, there may be a transient increase in WBC count due to recent tissue manipulation and bone marrow response to infection.
- Vaginal discharge may continue for approximately 2 weeks, gradually shifting from purulent to serous before stopping. This may be difficult to monitor in meticulous females.
- Approximately one-third of open-cervix pyometra cases require a second course of prostaglandin $F_{2\alpha}$ therapy. Approximately 25% to 40% of closed-cervix pyometra cases similarly require a second course of therapy.
- Recurrence of pyometra may be as high as 77% following medical management. CEH persists after medical management that predisposes the bitch to another ascending infection.
- Success rates for pregnancy and whelping following medical therapy are variable (40% to 82%).
- All sources strongly recommend breeding on the next estrus cycle because pregnancy may decrease the risk of a subsequent infection.

Treatment Contraindications

- Prostaglandin $F_{2\alpha}$ therapy is contraindicated in patients with known respiratory or cardiac disease.
- Medical management is contraindicated in critically ill patients due to a delayed response to prostaglandin $F_{2\alpha}$ therapy.
- Continued prostaglandin $F_{2\alpha}$ therapy is not recommended in deteriorating patients despite aggressive supportive care.

PROGNOSIS

Favorable Criteria

- Ovariohysterectomy is the treatment of choice.
- Medical therapy may be used in the following cases:
  - — Less than 6 years of age
  - — Open cervix
  - — Owners who are adamant about the dog's future breeding
  - — Not systemically ill with evidence of shock or sepsis

Unfavorable Criteria

Medical therapy should not be used in the following cases:

- Older than 6 years of age
- Closed cervix
- Critically ill with evidence of shock or sepsis

RECOMMENDED READING

Breitkopf M, Hoffmann B, Bostedt H: Treatment of pyometra (cystic endometrial hyperplasia) in bitches with an antiprogestin. *J Reprod Fertil* 51(Suppl):327–331, 1997.

Feldman EC: The cystic endometrial hyperplasia/pyometra complex and infertility in female dogs, in Ettinger SJ, Feldman EC (eds): *Textbook of Veterinary Internal Medicine*. Philadelphia, WB Saunders, 2000, pp 1549–1554.

Feldman EC, Nelson RW: Cystic endometrial hyperplasia/pyometra complex, in Feldman EC, Nelson RW (eds): *Canine and Feline Endocrinology and Reproduction*, ed 2. Philadelphia, WB Saunders, 1996, pp 605–618.

Franson B, Lagerstedt AS, Hellmen E, Jonsson P: Bacteriological findings, blood chemistry profile and plasma endotoxin levels in bitches with pyometra or other uterine diseases. *Zentralbl Veterinarmed* 44(7):417–426, 1997.

Hoffman B, Schuler G: Receptor blockers: General aspects with respect to their use in domestic animal reproduction. *Anim Reprod Sci* 60–61:295–312, 2000.

Kustritz MV: Theriogenology question of the month. *JAVMA* 220(2):175–177, 2002.

Noakes DE, Dhaliwal GK, England GC: Cystic endometrial hyperplasia/pyometra in dogs: A review of the causes and pathogenesis. *J Reprod Fertil* 57:395–406, 2001.

Root-Kustritz MV: Disorders of the canine uterus and uterine tubes (oviducts), in Johnson SD, Root-Kustritz MV, Olson PN (eds): *Canine and Feline Theriogenology*. Philadelphia, WB Saunders, 2001, pp 206–224.