

Theriogenology Question of the Month

This feature is sponsored by the American College of Theriogenologists. Readers of the *JAVMA* are invited to submit contributions. Contributions should provide a learning exercise about theriogenology. A specific question should be posed for the readers. The author's answer to the question and a brief discussion should be presented. Possible topics include commonly seen problems in domestic or exotic animals. Herd problems in dairy and beef cattle, sheep, goats, horses, and exotic hoofstock, problems in kennels or catteries, or flock problems in domestic and exotic fowl also are appropriate. Please contact Dr. Craig A. Smith, Associate Editor (800/248-2862, ext 259, or FAX 847/925-1329), for further details.

History

A 4-year-old sexually intact female Gordon Setter was referred to the veterinary medical teaching hospital because of possible pyometra. She had been mated by a fertile male 17 and 19 days before examination. In a sample obtained at the time of breeding, results of serologic tests for *Brucella canis* were negative.

Prior to examination, the bitch had been anorectic with intermittent vomiting for 5 days and had been lethargic with polyuria and polydipsia for 4 days. She had been treated by another veterinarian 3 days previously. Results of serum biochemical analysis performed at that time were within reference ranges, although neutrophilia was detected (WBC count of 16,700 to 19,000 cells/ μ l; differential counts were not performed). At that time, urinalysis revealed hematuria, and urine specific gravity was 1.020. Abdominal radiographs were unremarkable. The dog had been treated by IV administration of fluids and cephalexin. The dog had been discharged to the owner with instructions for oral administration of amoxicillin.

At the time of examination, the bitch had consistently vomited after administration of amoxicillin. She was still vomiting after drinking water but was not apparently vomiting after eating food. Her attitude had improved, but she was still slightly inappetent. The owner remarked that the bitch's hindquarters were wet but could not define whether it was attributable to urine or vulvar discharge.

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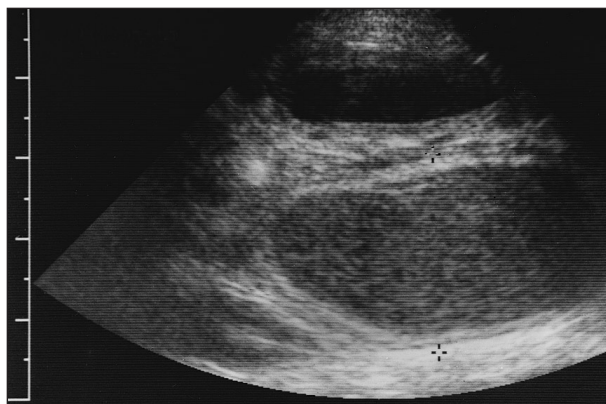


Figure 1—Ultrasonogram of the uterus of a 4-year-old sexually intact female Gordon Setter that had been mated 17 and 19 days preceding the examination. Marks on scale on left side are at intervals of 5 mm. Distance between asterisks is 24.6 mm.

During physical examination, the bitch's rectal temperature, pulse rate, and respiratory rate were within reference ranges. She was slightly dehydrated (approx 5%) and appeared to be underweight. The perivulvar area was encrusted with odorless serous discharge. The uterus was palpable as a tubular structure in the caudoventral portion of the abdomen.

A swab specimen was collected from the area of the vagina immediately cranial to the urethral papilla. Cytologic evaluation revealed that numerous polymorphonuclear leukocytes (some of them degenerative), bacteria, and normal noncornified epithelial cells were evident. Results of a CBC revealed immature neutrophilia (WBC count, 20,500 cells/ μ l [reference range, 4,100 to 13,300 cells/ μ l]; 620 band neutrophils/ μ l [reference range, 0 to 130 cells/ μ l]) and mild normocytic normochromic anemia (Hct, 37.6%; reference range, 38.5 to 56.7%). Results of serum biochemical analyses were within reference ranges. Urinalysis was not performed, because a urine sample collected during natural voiding could have been contaminated with inflammatory vaginal discharge, and unguided cystocentesis is contraindicated when palpable uterine enlargement is evident.

Abdominal ultrasonography was performed (Fig 1).

Question

Is the uterine enlargement attributable to pregnancy or to pyometra? *Please turn the page.*

Answer

Pyometra.

Results

The uterine horns were diffusely enlarged and filled with complex fluid. Amniotic vesicles were not seen. There was a small amount of free anechoic fluid in the abdomen, and the left renal pelvis was dilated, probably secondary to diuresis. The diagnosis was open-cervix pyometra.

Discussion

Pyometra is a chronic condition with acute onset. Repeated exposure of the endometrium to estrogen followed by progesterone, as happens in bitches during every estrous cycle, leads to development of **cystic endometrial hyperplasia (CEH)**, which appears grossly as irregular cystic thickening of the endometrial surface.^{1,2} During proestrus and estrus, the cervix is open, and bacteria that normally inhabit the vagina ascend into the uterus.³ During diestrus, the reproductive tract is under the influence of progesterone. Thus, the cervix is functionally closed, secretory activity of the endometrial glands is stimulated, and myometrial contractility is inhibited, which can lead to bacterial colonization and secondary infection of the uterus.¹

The organism most commonly isolated from the uterus of bitches with pyometra is *Escherichia coli*.¹⁻⁶ The large surface area of the infected uterus provides continual antigen exposure, allowing formation of large numbers of antibodies against *E coli*. When the gram-negative organisms die, endotoxins are released from the cell wall. Deposition of antigen-antibody complexes in the renal glomeruli, decreased glomerular perfusion as a result of dehydration or hypovolemic shock, and a direct negative effect of endotoxins on the concentrating ability of the renal tubules combine to cause development of secondary renal disease.^{1,6} Azotemia is evident in 18 to 26% of dogs with pyometra,^{1,6} and endotoxemia is evident in 8%.⁴

Age of dogs at the time of diagnosis of pyometra ranges from 6 months to 15 years (mean, 5.0 years).^{1,5-7} Clinical signs of pyometra usually become evident during diestrus, with onset detected 1 to 50 weeks (mean, 5.4 weeks) after estrus.¹ Clinical signs reported, in order of prevalence, include anorexia, lethargy, polyuria and polydipsia, vomiting, and diarrhea.^{1,7} When the cervix is open, purulent vaginal discharge may be detected. When the cervix is closed, abdominal distention is often evident. Approximately 41% of dogs are febrile at the time of admission, but dogs that are in hypovolemic shock at the time of admission may be hypothermic.¹ The uterus may be palpably enlarged. Caution should be employed during abdominal palpation of dogs with suspected pyometra, because it is possible to rupture a distended friable uterus. In dogs with abdominal distention or those that are obese, have a tense abdominal wall, or have signs of pain during palpation, radiography or ultrasonography of the abdomen may be necessary to determine whether there is uterine enlargement.

In dogs with pyometra, total WBC count ranges from 2,500 to 94,000 cells/ μ l (mean, 37,300 cells/ μ l).^{1,5}

Band neutrophil counts reportedly range from 0 to 4,300 cells/ μ l (mean, 520 cells/ μ l).¹ However, dogs with pyometra may have values for WBC and differential cell counts that are within reference ranges. In a study⁵ of 40 dogs with open-cervix pyometra, only 30 (75%) had immature neutrophilia. Mild-to-severe normochromic normocytic anemia, defined as PCV < 36%, was reported in 26/101 (26%) dogs with pyometra.¹

Definitive diagnosis of pyometra requires documentation of uterine distention attributable to purulent discharge. Uterine enlargement may be palpable or may be detected during abdominal radiography or ultrasonography. Because clinical signs of pyometra develop at the same stage of the estrous cycle that corresponds to pregnancy, accurate pregnancy diagnostic tests are required to differentiate the 2 conditions, because medical or surgical treatment for pyometra will terminate pregnancy.

Patency of the cervix is inferred by evidence (open cervix) or lack of evidence (closed cervix) of purulent vaginal discharge. Visual examination of the cervix of dogs requires specialized equipment, and an open cervix is not visibly patent in dogs, even with the use of endoscopy.

Closed-cervix pyometra is virtually always treated by ovariohysterectomy. Although medical treatment can cure bacterial infections, it does not alter the underlying CEH, and the bitch is predisposed to pyometra after each subsequent estrous cycle. Dogs with closed-cervix pyometra can be successfully treated, using **prostaglandin F_{2 α} (PGF_{2 α})**. Reported complications for administration of PGF_{2 α} to dogs with closed-cervix pyometra include salpingitis as a result of movement of purulent fluid into the uterine tubes and resistance to treatment necessitating 2 or 3 courses of administration before resolution of the pyometra.⁶

Open-cervix pyometra also is treated most often by ovariohysterectomy. Administration of PGF_{2 α} also can be used to treat dogs with open-cervix pyometra.

Several criteria should be met before instituting medical treatment for pyometra. Optimally, the cervix should be open; however, this is not a mandatory requirement. The bitch should be of breeding age and a valuable part of a planned breeding program. Because CEH persists after medical treatment and presumably contributes to decreased fertility in the bitch, medical treatment is best reserved for bitches with extraordinary genetic value. Bitches that receive PGF_{2 α} should not be azotemic. Clinical response may not be evident for up to 48 hours after institution of medical treatment, suggesting that medical treatment of azotemic bitches unnecessarily exposes them to prolonged and potentially worsening renal disease.⁶

Dosages of PGF_{2 α} used for treatment of dogs with pyometra vary from 27 to 500 μ g/kg (12 to 227 μ g/lb) of body weight, SC, once or twice daily for 1 to 10 days.⁶⁻⁸ Adverse effects of PGF_{2 α} administration are dose-dependent and include vomiting, diarrhea, and hypersalivation. Once-daily treatment causes predominantly uterine contractions, whereas twice-daily treatment causes uterine contractions and luteolysis. Luteolysis and the subsequent decrease in serum pro-

gestosterone concentration abrogate progesterone's uterine effects. Treatment with PGF_{2α} should be continued until the uterus has nearly returned to its anticipated normal size, as assessed by serial palpation, abdominal radiography, or abdominal ultrasonography.

In addition to PGF_{2α}, medical treatment should include administration of an appropriate antimicrobial as determined on the basis of bacterial culture and antimicrobial susceptibility testing of a specimen obtained from the cranial vagina. Treatment with antibiotics should be continued for 1 month.

Prognosis for future fertility is guarded. In 3 studies⁶⁻⁸ in which injection of PGF_{2α} was evaluated as medical treatment for dogs with pyometra, overall mean pregnancy rate after treatment was 51%. Reported recurrence rates for pyometra were 10, 15, and 77% in those studies. In 1 of those studies,⁸ pyometra recurred in 4 of 9 bitches within 1 year after treatment (2 of them after they had whelped a litter and the other 2 after they had been mated and pregnancy had been diagnosed), and pyometra recurred in 3 of the remaining bitches within 27 months after treatment. Because CEH persists in bitches with pyometra after medical treatment, potentially predisposing them to infection with bacteria ascending from the vagina, bacterial culture of a specimen obtained from the cranial vagina and appropriate antibiotic treatment may be required during subsequent estrous cycles. Bitches with a history of pyometra should be ovariohysterectomized as soon as their use in a breeding program is completed.

Outcome

The bitch reported here was young, was valuable as a breeding animal, had an open cervix, and was non-azotemic. She was treated with lactated Ringer's solution (IV), amoxicillin-clavulanate (PO), and PGF_{2α} (250 μg/kg [114 μg/lb], SC, q 12 h). By the time the third

dose of PGF_{2α} was administered, a substantial volume of sanguinopurulent discharge was expelled through the vagina, the uterus was palpably less turgid, and the bitch had great improvement in attitude and appetite, especially when the owner was present. Lateral radiographic views of the abdomen were obtained after the fifth injection of PGF_{2α}; the uterus was not visible as a discrete organ. Also, the uterus was palpably reduced in size at that time. The dog was discharged to the owner with instructions to continue oral administration of amoxicillin-clavulanate for a total of 4 weeks. Vaginal discharge was evident more than 30 days after treatment with PGF_{2α}, but it resolved before the subsequent estrus. The bitch was treated with antibiotics during that estrus, was bred, and gave birth to 3 healthy puppies.

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