

“Lady Bug is Bugging Out”

Jessica N. Saunders

Mississippi State University

College of Veterinary Medicine

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Advisor:

Darcie Sidelinger, DVM

## **Introduction**

Pyometra is a common reproductive disease of canines that is defined as an accumulation of purulent material within the uterus that occurs following estrus.<sup>2</sup> Approximately 19% of intact female canines younger than the age of 10 have pyometra. The etiology and pathogenesis of pyometra are not entirely understood; however, it is known to be influenced by hormonal and bacterial factors.<sup>7</sup> Pyometra typically occurs in the bitch within 4-8 weeks of her last estrus and there are two different types of pyometra, open cervix and closed cervix pyometra.<sup>2, 11</sup> Bitches affected by closed cervix pyometra are more systemically ill than those affected by open cervix pyometra. Diagnosis is best made primarily by diagnostic imaging.<sup>2</sup> Other diagnostics such as vaginal cytology, complete blood count and serum chemistry, and urinalysis can be helpful.<sup>2, 5</sup> The treatment of choice is surgery because it is curative and prevents reoccurrence. However, medical treatment is an option for females of reproductive age that are valuable breeding dogs and for females who are stable in the disease process.<sup>2</sup> Even though pyometra is a potentially life-threatening disease, the prognosis is favorable.<sup>8</sup>

## **History and Presentation**

Lady Bug, an approximately 3-year-old, intact female, Boston Terrier, who presented to MSU-CVM Animal Health Center on January 7, 2019 for bloody vaginal discharge. Lady Bug's last heat cycle was on December 4, 2018. She was naturally bred on December 17th, 19th, and 21st. Lady Bug was bred previously and delivered 5 puppies in October of 2017. There were no complications during the pregnancy or birth. She was bred by the same male on both occasions.

On January 4, 2019, Lady Bug began to have bloody vaginal discharge. The owner reported that it was a large amount of discharge and it was more than she had during her heat

cycle. She also had an episode of loose stool on the same day, but the owner believed this was due to her eating a ham bone. On January 5, 2019, Lady Bug became lethargic and inappetent. On the evening of January 6, 2019, the owner was able to get Lady Bug to eat a bowl of chicken and rice.

On initial presentation, Lady Bug was bright, alert, and responsive. However, as the day progressed, she became dull and depressed. Her vital parameters consisted of a heart rate of 144 beats per minute, respiratory rate of 24 breaths per minute, and temperature of 102.9°F. She was thin and given a 4/9 body condition score (4-5/9 is ideal). On oral examination, her capillary refill time was less than 2 seconds and her mucous membranes were moist and pink, indicating a normal hydration status. No harsh lung sounds, murmurs, or arrhythmias were appreciated during cardiopulmonary auscultation. All peripheral lymph nodes palpated within normal limits. The abdomen was tense on palpation, but no abnormalities were noted. The rectal examination was within normal limits. No pain was elicited during palpation on the cervical, thoracic, or lumbar spine. Lady Bug's vulva was swollen, and she had a moderate amount of sanguineous vaginal discharge. The vaginal discharge appeared dark red and contained blood clots. At this time, based on the signalment, history, and physical examination, the differential diagnoses were abortion, subinvolution of placental sites (SIPS), vaginitis, or vaginal trauma.

On January 22, 2019, Lady Bug returned to MSU-CVM for re-evaluation. She was still lethargic and had a decreased appetite. The owner offered her a variety of canned dog food and chicken tenders. She ate about 3 times per day but only in small amounts. The owners reported that she was weak and reluctant to walk or move. Her stool was loose, and her defecation decreased in frequency. The owner believed the discharge decreased in frequency to about once every hour. The owner also reported that Lady Bug developed an ear twitch around the same

time as the lethargy began. The ear twitching became significantly more noticeable and more frequent than at her last visit with MSU-CVM. The owner saw the twitching when Lady Bug was relaxed, but not while sleeping or concentrating.

At the second presentation, Lady Bug was bright, alert, and responsive but as the day progressed, she became dull and depressed like her last visit. She was tachycardic (heart rate of 174 beats per minute), normothermic (temperature of 101.7°F), and had a normal respiratory rate (respiratory rate of 30 breaths per minute). She lost approximately 2 pounds since her last visit (14 to 12 lbs.). On oral examination, her capillary refill time was 2 seconds and her mucous membranes were tacky and pale, indicating a 5% dehydration. Lady Bug's vulva was still swollen, but she had a mild amount of serosanguineous to mucopurulent vaginal discharge. The vaginal discharge appeared light pink and contained a mild amount of mucous. She exhibited bilateral ear twitching while relaxed. Based on signalment, history, and physical examination findings at this subsequent visit, the primary differential diagnosis was open cervix pyometra.

### **Diagnostic Approach/Considerations**

On January 7, 2019, a complete blood count and small animal profile were performed. Neither of these laboratory tests revealed abnormalities. A coagulation profile was performed due to the amount of blood loss. The prothrombin time (PT) was normal (8.5 seconds) and the partial thromboplastin time (PTT) was normal (11.3 seconds). The Theriogenology service was then consulted. A vaginal cytology was obtained. This revealed a large amount of red blood cells and nucleated, cornified cells, which is typically seen during proestrus. A progesterone level was obtained and resulted in 12.9 ng/ml. When progesterone is >10.0 ng/ml, this indicates the fertile period began. However, this value may not have been high enough to maintain a pregnancy.

Based on these results, it was too early in Lady Bug's cycle (approximately day 20) to determine if she was pregnant or aborting. It was recommended that she return in two weeks (approximately day 35 of her cycle) for better results.

On January 22, 2019, a packed cell volume and total protein were obtained to ensure Lady Bug was not anemic. The packed cell volume was mildly decreased at 34% and the total protein was within normal limits at 7.2 g/dL. An abdominal Focused Assessment with Sonography for Trauma (FAST) scan was then performed. This revealed a thickened uterine wall, a distended uterus, and fluid accumulation within the uterus. Based on these results, Lady Bug was diagnosed with an open pyometra. The Neurology service was then consulted to assess Lady Bug's ear twitch. No pain was elicited during palpation on the cervical, thoracic or lumbar spine. No conscious proprioception or cranial nerve deficits were present.

### **Pathophysiology**

The etiology of pyometra is still unknown despite extensive research. However, the hormonal component of the disease plays a large role in the pathogenesis. Pyometra most commonly occurs during diestrus, when progesterone is the dominant hormone.<sup>7</sup> When the endometrium is continually and repeatedly exposed to progesterone from many estrous cycles, it creates a disorder termed cystic endometrial hyperplasia (CEH). This results in endometrial gland proliferation, endometrial gland secretion, a decrease in myometrial contractions, and closure of the cervix. Decreased immune function within the uterus has also been seen with the presence of progesterone. These changes create an ideal environment for bacteria to proliferate, leading to a condition termed cystic endometrial hyperplasia-pyometra complex. However, recent research has discovered that pyometra does not necessarily occur due to CEH and they

may occur independently of each other. Other contributing factors may be involved, such as exogenous estrogen. Studies have shown that exogenous estrogen administration increases the uterus' response to endogenous progesterone, leading to pyometra.<sup>5</sup> Currently, no definitive evidence exists that pyometra is caused by the uterus' response to hormones or by disruption in the production of these hormones.<sup>7</sup>

The most common organism isolated in pyometra cases is *Escherichia coli*.<sup>2, 7, 8, 11</sup> Rarely, other bacteria are isolated, such as *Klebsiella*, *Streptococcus*, *Staphylococcus*, and *Pseudomonas*.<sup>4, 7</sup> Many of these bacteria are normal flora of the canine vagina, indicating that an ascending infection into the uterus is a likely cause of pyometra.<sup>4, 8</sup> According to epidemiologic studies performed, the fecal strain of *E. coli* has been found to be identical to the uterine strain of *E. coli* in females with pyometra. Therefore, an ascending infection from the anus into the uterus is a likely cause of pyometra.<sup>7</sup> Pyometra has also been linked to bacterial isolates in the urinary tract. However, it is still debated whether the bacterial isolates in the urinary tract ascend into the uterus, or if the vaginal discharge ascends into the urinary tract due to the anatomical position of the urethra.<sup>7, 8</sup> To conclude, despite the unknown mechanism of infection, the uterus is infected during estrus because the cervix is open to bacteria, and once the cervix closes in diestrus, the uterus becomes filled with purulent material.<sup>11</sup>

The breeds predisposed to developing pyometra are rottweilers, rough-coated collies, chow chows, golden retrievers, miniature schnauzers, Bernese mountain dogs, Cavalier King Charles spaniels, and English springer spaniels but any breed can be affected.<sup>1, 2, 4</sup> Pyometra typically occurs in middle to older aged bitches.<sup>1, 2, 4, 8, 11</sup> Pyometra is also seen in cows, small ruminants, swine, horses, cats, and pocket pets (such as rabbits, hamsters, ferrets, rats and guinea pigs).<sup>11</sup>

Pyometra can be classified as closed (closed cervix) or open (open cervix) pyometra. Closed cervix pyometra is when the cervix remains closed in the disease. The purulent fluid accumulation solely depends on the uterine lumen. If it is late in the course of the disease, the endometrium is generally atrophied.<sup>6</sup> A closed cervix does not allow for elimination of the infectious material within the uterus.<sup>4</sup> Bitches often present much more systemically ill with closed pyometra, showing signs including pyrexia, shock, and dehydration.<sup>2, 4, 11</sup> Uterine rupture often results in peritonitis and endotoxemia, and death may ensue.<sup>2, 4</sup> Pyrexia is more commonly observed in bitches with closed cervix pyometra.<sup>2</sup> Open cervix pyometra is when the cervix remains open in the disease. The inflammation is much more significant with open pyometra.<sup>6</sup> Significant vulvar discharge is present and often appears as serosanguineous or mucopurulent.<sup>4, 6, 11</sup> The clinical presentation for both open and closed pyometra is often non-specific and includes lethargy, depression, anorexia, vomiting or diarrhea, polydipsia, and polyuria.<sup>2, 4, 11</sup> Often, the vulva will be enlarged. The vulva may appear discolored or scalded in some cases. Uterine enlargement may be palpated on physical examination, but it is often difficult.<sup>2</sup>

The most common complication associated with pyometra is peritonitis. Leukopenia observed on bloodwork, abnormal body temperature, moderate to severe depression, and pale mucous membranes all represent increased risk for complication. The total mortality rate of patients with pyometra was reported as 10%, including euthanized patients.<sup>9</sup>

## **Treatment and Management**

The treatment of choice for pyometra in canines is ovariohysterectomy.<sup>2, 5, 6, 7, 11</sup> Ovariohysterectomy is curative, results in a quicker recovery, and eliminates reoccurrence. Complications associated with surgery include anesthetic complications, hemorrhage, and

rupture of the uterus leading to peritonitis. Complications that occur after surgery are infection of the incision site, local swelling, or fistulous tracts.<sup>5,7</sup>

Medical treatment is another successful option for pyometra.<sup>5</sup> However, case selection is made based on certain criteria. Medical management is best used in animals of a young age that are still considered valuable breeding bitches. It is well suited for animals in good health, animals predisposed to side effects associated with anesthesia and/or surgery, females with open cervix pyometra, and for females who lack cystic endometrial hyperplasia.<sup>1,6</sup> The most commonly used medication is prostaglandin F<sub>2</sub>-alpha. Prostaglandins cause luteolysis, which results in a decrease in progesterone concentration, allowing the cervix to relax and uterine contents to escape.<sup>2,5,6,7,10</sup> Prostaglandins also promote myometrial contractions, which further encourages uterine contents to expel.<sup>2</sup> One subcutaneous injection per day for 5-7 days is the recommended treatment and the success of treatment should be evaluated 10-14 days after initial injection.<sup>6</sup> Side effects associated with prostaglandins include vomiting, defecation, urination, tachycardia, restlessness, anxiety, fever, hypersalivation, dyspnea, and/or panting.<sup>2,5,6,7,10</sup> The side effects will typically begin within minutes of administration and will persist for an hour or more after administration. Repeated prostaglandin treatments have shown to decrease the severity and frequency of side effects. Walking the animal for approximately 20-60 minutes immediately after treatment has shown to decrease the severity of side effects.<sup>5</sup> Recurrence after treatment with prostaglandins is variable, ranging from 5% in bitches who were pregnant after the cure to 70% over a 27-month period.<sup>6</sup> Therefore, the recommendation is to breed the bitch at the first heat cycle following treatment or to spay before the next heat cycle.<sup>6,11</sup> Other medications that can be used are dopamine agonists, such as cabergoline and bromocriptine. These act by inhibiting the production of prolactin, a luteotroph, from the pituitary gland. This



results in a decrease in progesterone concentrations and promotes regression of the corpus luteum<sup>2, 5</sup>. Dopamine agonists are often used in combination with prostaglandins.<sup>2, 5, 10</sup> The protocol for combination therapy is 5µg/kg of cabergoline orally and 1µg/kg of cloprostenol subcutaneously every day for a total of 7-14 days.<sup>3</sup> Lastly, progesterone receptor antagonists, such as aglepristone, are used in the treatment of pyometra. These bind competitively to the progesterone receptors located in the uterus, which inhibits endogenous progesterone from exhibiting its effects.<sup>2, 5, 6, 10</sup> The protocol for aglepristone is one injection subcutaneously on days 1, 2, and 8.<sup>6</sup> The success of treatment is evaluated based on discontinuation of discharge and normal uterine diameter. On day 15 and sometimes day 30, additional treatment may be needed if these changes have not occurred.<sup>6</sup> Side effects of progesterone receptor antagonists include pain and inflammation at injection site, anorexia, excitation, vomiting, and diarrhea; however, these are uncommon.<sup>10</sup> This medication functions best in combination rather than as a stand-alone agent for treating pyometra.<sup>5, 6, 10</sup> According to a study, the success rate increased with additional cloprostenol (90%) compared to aglepristone used alone (60%). Recurrence of pyometra with aglepristone has been shown in 18.9% of cases at the following heat cycle.<sup>6</sup> Regardless of the type of treatment, antibiotics, such as amoxicillin/clavulanic acid, should be administered. Fluid therapy may also be needed depending on the hydration status.<sup>1, 2, 5, 6, 7, 10</sup>

Due to Lady Bug's age, good health, potential for breeding again, and having an open pyometra without evidence of cystic endometrial hyperplasia, she was a good candidate for medical management. The owners decided on medical management due to financial constraints. On January 22, 2019, Lady Bug was given her first dose of Lutalyse (dinoprost tromethamine), which is a prostaglandin. She was given one dose at 0.01 mg/kg subcutaneously on this day. On January 23, 2019, she received her second dose at 0.01 mg/kg, third dose at 0.02 mg/kg, and

fourth dose at 0.03 mg/kg. On January 24, 2019, Lady Bug received her fifth dose at 0.03 mg/kg, sixth dose at 0.04 mg/kg, and seventh dose at 0.04 mg/kg. On January 25, 2019, she received her eighth and ninth doses at 0.05 mg/kg. Every day during treatment, Lady Bug received Cerenia (Maropitant citrate) subcutaneously at 1 mg/kg to prevent vomiting associated with the prostaglandin injections. Lady Bug was walked following each injection of prostaglandins for 20-30 minutes. She experienced few side effects associated with prostaglandin administration, such as hypersalivation, urination, and defecation. On January 7<sup>th</sup>, Lady Bug was started on Clavamox (amoxicillin/clavulanic acid) at 20 mg/kg. Because she developed a bilateral ear twitch of unknown cause, the antibiotic treatment was changed to Baytril (enrofloxacin) at 11.7 mg/kg on January 22<sup>nd</sup>. After Lady Bug's eighth dose of prostaglandin, a progesterone level was performed and resulted in 0.33 ng/ml. This revealed that Lady Bug's treatment was successful.

### **Case Outcome**

Lady Bug presented to MSU-CVM Animal Health Center on January 30, 2019 for re-evaluation after treatment of pyometra. An abdominal FAST Scan was performed and revealed mild fluid accumulation within the uterus. The uterus was one fourth to one eighth the previous size. The bilateral ear twitching resolved. It was recommended to complete the antibiotic and return for a recheck in about 2 weeks. Lady Bug's final recheck was on February 12, 2019. Another abdominal FAST Scan was performed, and the uterus was no longer distended nor was there accumulated fluid present. It was recommended that Lady Bug be spayed as soon as possible to prevent reoccurrence.

Today, Lady Bug is healthy and doing well at home. She went into heat in July and has not had any complications. The owners do not wish to breed her again but plan to have her spayed in the future.

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