

Common Lesions in the Female Reproductive Tract of Dogs and Cats

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KEYWORDS

• Bitch • Pathology • Queen • Reproductive

Our knowledge and understanding of female reproductive physiology and endocrinology in dogs and cats have grown exponentially. In turn, this has helped us gain a better understanding of fertility problems in these species that may originate from pathologic changes throughout the reproductive tract. Private practitioners working on small animal species are commonly confronted with lesions in the female reproductive tract. Many of these lesions may appear at any time during the reproductive life of the patients. In order to avoid unnecessary therapy or treatment delay, it is important for the clinician to quickly recognize and understand the pathology of the most common reproductive lesions to achieve a rapid and effective diagnosis. Epidemiological investigations into small animal reproductive health demonstrate that certain reproductive lesions may occur more frequently in the bitch and queen, so the clinician must be aware of the range of differential diagnosis and the clinical approach. This article gives an overview of the pathology, clinical and therapy signs of the most common lesions that affect the ovaries, uterus, cervix and vagina in the bitch and queen that may be encountered in practice.

COMMON LESIONS IN THE OVARY

Ovarian Remnant Syndrome

Retention of active ovarian tissue, or “remnant ovarian tissue” (ROT), due to improper clamping of the ovarian pedicle during an ovariectomy or ovariohysterectomy (OVH)

The authors have nothing to disclose.

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Vet Clin Small Anim 42 (2012) 547–559

doi:10.1016/j.cvsm.2012.01.011

0195-5616/12/\$ – see front matter © 2012 Published by Elsevier Inc.

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Fig. 1. A 2.2×1.8 cm follicular cyst in a queen with persistent estrual activity. (Courtesy of Rita López, UADY, School of Veterinary Medicine.)

is an iatrogenic condition commonly seen in the bitch and queen.¹ The presence of an accessory ovary or losing the ovary in the abdomen during surgery can produce similar clinical signs. Under experimental conditions, autografted hemiovaries in the abdominal cavity in dogs have demonstrated good implantation and further ovarian activity.²

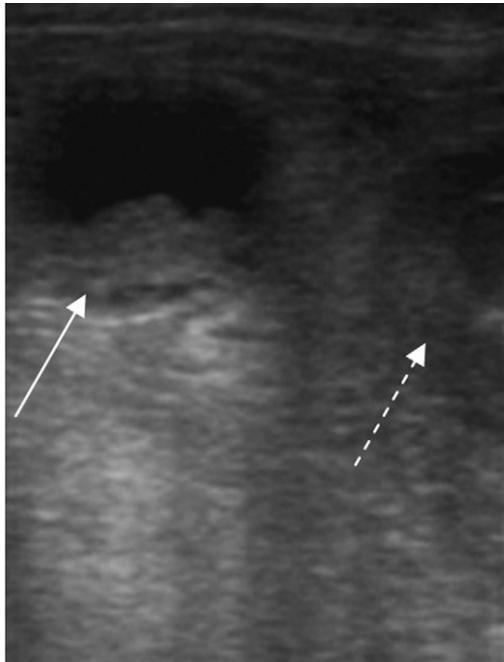


Fig. 2. Ultrasound image of a 2.5-cm follicular cyst in a bitch with history of irregular heats. Ovary (*continuous arrow*) is localized at the caudal pole of the left kidney (*broken arrow*). A process of luteinization can be observed inside the follicle. Small follicles are also present in the ovary. (Courtesy of Enrique Pasos, UADY, School of Veterinary Medicine.)

In the bitch, remnant ovarian tissue can develop follicles and corpora lutea, and follicles may become cystic. Because of this, common clinical signs of ROT include periods of vaginal bleeding for several weeks, swelling of the vulva, licking of the vulvar lips, and attraction to males.³ Occasionally, multifocal areas of erythema are noted on the ventral aspect of the abdomen.³ Less frequent clinical signs include mammary gland enlargement due to progesterone activity, pollakiuria and stranguria, dermal hyperpigmentation and alopecia, polyuria and polydypsia, poor coat, weight loss, and recurrent urinary tract infections.⁴

The diagnosis of ROT can be made based on clinical history, clinical symptoms, and routine vaginal cytologic examination (80%–90% superficial cells will indicate an increasing circulating levels of estradiol). When vaginal cytology does not offer satisfactory results or there are still doubts, the levels of 2 ovarian hormones, estradiol and progesterone, can be measured to determine the presence of an ovarian tissue. The use of ultrasonography to diagnose ROT in the dog and cat is limited due to the small size of the remnant tissue. However, it may be useful in medium-sized to large dogs.⁵

The treatment of choice is surgical excision of the remnant tissue. When surgery is not an option or no tissue is found but the problem persists, lifelong therapies are available. Megestrol acetate or mibolerone has been mentioned for use in medical treatment.^{6,7} However, several side effects such as mammary gland tumors, acromegaly, clitoral enlargement, and suppression of adrenocortical function may be induced with medical options and caution should be used. The use of a gonadotropin-releasing hormone (GnRH) agonist such as deslorelin is also proposed for medical treatment of ROT but there is not enough medical evidence supporting its efficiency.

In queens, ROT occurs more frequently than in bitches. In this species, revitalization and follicular activity of an ovarian remnant left in the abdominal cavity were shown to occur in the absence of surgical implantation.⁸ Clinical signs in the queen can occur several months or years after OVH and include estrus periods with interestrus intervals from 3 weeks to 6 months. Although cats are considered induced

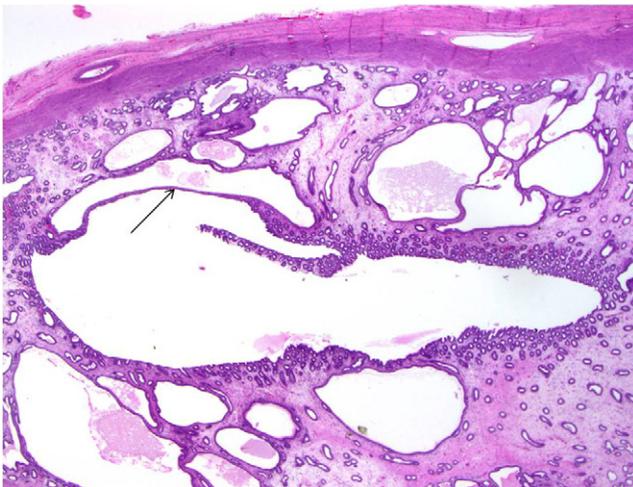


Fig. 3. Photomicrograph of a bitch with cystic endometrial hyperplasia. Endometrial glands are variably dilated and lined by attenuated epithelium (arrow). (Courtesy of Dr Catherine Lamm, University of Glasgow, School of Veterinary Medicine.)

ovulators, spontaneous ovulations may also occur⁹ and prevent queens from entering estrus; cats may show seasonal ovarian activity and seasonal anestrus during late autumn and early winter. Thus, clinical signs of ROT in queens vary year round. Vaginal cytology in a queen with ROT, as in the bitch, reveals many superficial cells indicating estrogenic influence. Stimulation tests using GnRH or human chorionic gonadotropin (hCG) and measuring progesterone concentrations provide a reliable method to diagnose ROT in queens.^{10,11} The treatment of choice is surgical. Medical management includes synthetic progestagens,¹² but side effects such as cystic endometrial hyperplasia, pyometra, diabetes, bone marrow toxicity, thyroid dysfunction, and mammary adenoma/fibrosarcoma within others can occur.

Cystic Ovaries

Anovulatory ovarian functional follicular cysts are common incidental findings in older bitches and queens, particularly in those that have never had a litter or may have been single or multiple (**Fig. 1**). Follicular ovarian cysts originate due to failure to ovulate and should be differentiated from other cysts developing from or within the ovaries or the ductal remnants adjacent to them such as cystic rete ovarii, paraovarian cysts, and subsurface epithelial structures (SESS) and from ovarian neoplasias.

In the bitch and queen, clinical signs include persistent or irregular proestrus/estrus manifestations due to hyperestrogenism, anestrus, and infertility. In chronic cases, symmetrical bilateral alopecia and bone marrow suppression may occur; it also predisposes both species to cystic endometrial hyperplasia (CEH)-pyometra complex. In the queen, signs include persistent estrus and aggression even during the

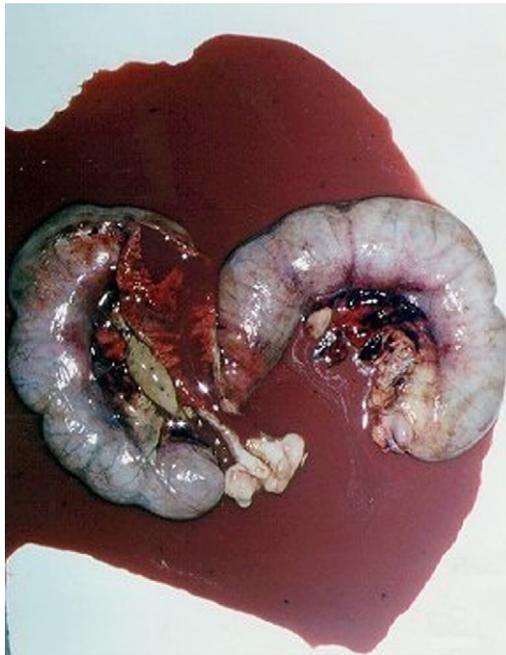


Fig. 4. Recovered uterus of a bitch suffering from pyometra. A bloody to mucopurulent exudate can be appreciated.

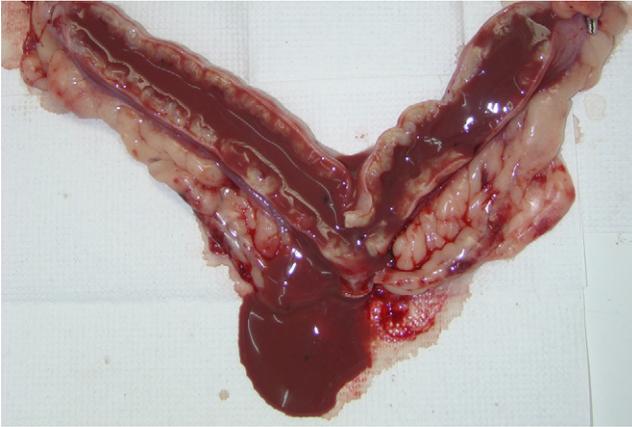


Fig. 5. Recovered uterus of a queen suffering from pyometra. A bloody exudate can be appreciated.

nonseasonal periods of the year; persistent anestrus due to an increase in progesterone secretion does not develop as in bitches since no luteinization of preovulatory follicles occur in this species. The diagnosis is based on vaginal cytology, hormone assays, and ultrasonography. Ovarian ultrasonography will reveal one or more large follicles (1–5 cm in diameter) as hypoechoic to anechoic structures depending on the



Fig. 6. Dystocia in a bitch predisposing to metritis. Note the thick, dark-brown vaginal discharge and a trapped decomposed pup and placenta.

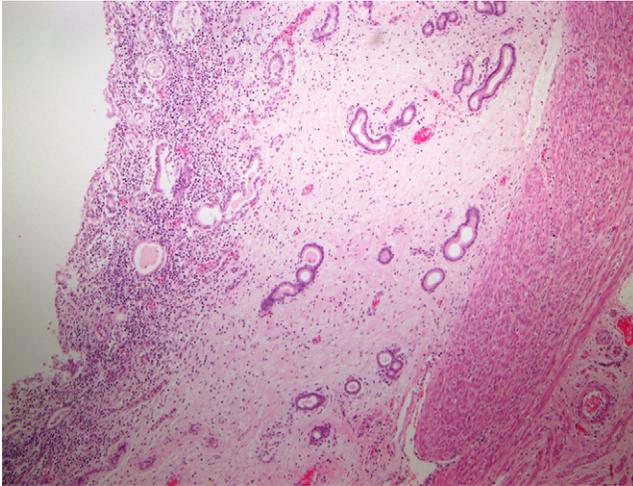


Fig. 7. Photomicrograph of the canine uterus showing a leukocyte infiltration in the endometrium (endometritis). (Courtesy of Dr Catherine Lamm, University of Glasgow, School of Veterinary Medicine.)

amount of luteal tissue (**Fig. 2**). Histologic examination of ovarian cysts greatly facilitates distinction between follicular cysts and cysts arising in the rete ovarii, paraovarian cysts, or SESs. However, their functional significance is minimal unless they destroy the adjacent ovarian architecture. Usually, these animals lack clinical signs and ovarian cysts are found incidentally during ultrasound or surgery. The treatment of choice for ovarian follicular cysts is OVH. However, when a single cyst is suspected, laparotomy and cyst rupture may be attempted. Medical treatment includes the induction of ovulation by allowing breeding (in queens) or hormonal therapies with a GnRH and/or hCG.

Differential diagnoses include ovarian tumors, particularly sex-cord stromal tumors such as the granulosa-theca cell tumor, which may be hormone active and produce estrogens. By using medical treatment, the response may allow differentiation of follicular cysts with granulosa-theca cell tumor or other tumors. Other ovarian tumors such as papillary cystadenoma and cystadenocarcinoma occurs commonly in the bitch and may occasionally stimulate the production of ovarian steroids and be involved in CEH.¹³

COMMON LESIONS IN THE UTERUS

Cystic Endometrial Hyperplasia-Pyometra Complex

Pyometra is one of the most common diseases of the uterus in small domestic animals. Literature regarding the cystic endometrial hyperplasia-pyometra complex in dogs and cats is vast and its etiology and pathogenesis have been extensively described.^{14–18} The disease is hormone mediated and involves cystic dilatation of endometrial glands; there is accumulation of noninflammatory, watery to viscid, aseptic fluid within the uterine lumen with posterior bacterial contamination, endometrial inflammation, and presence of blood and pus. Pyometra develops in most cases as a consequence of CEH.¹⁷ However, not all cases of CEH will end in pyometra.¹⁴ A second pathologic form of endometrial hyperplasia in the bitch (pseudo-placental endometrial hyperplasia [PEH]) must be distinguished from



Fig. 8. Vaginal prolapse type I in the bitch.

CEH by the pathologists and clinicians. It also occurs during the luteal phase of the cycle but endometrial proliferation does not involve cystic distention of endometrial glands and is very similar to the normal histology of the endometrium at placentation sites in normal pregnancy.¹⁸ Because of the alteration of the endometrial surface associated with CEH, infertility due to implantation failure after conception can occur¹⁹ (**Fig. 3**). Clinical signs may vary widely depending on the stage of the disease and patency of the cervix; when bacterial replication produce endotoxins, moderate to severe signs of systemic inflammatory response syndrome may be evident.²⁰ Characteristics of the odorous vaginal discharge may vary from bloody (**Fig. 4**) to bloody mucopurulent depending on whether damage to the endometrial blood vessels has occurred. Ultrasonography is the most efficient way to confirm CEH-pyometra cases. The treatment of choice is OVH with prior rehydration and antibiotic therapy. The latest protocols for medical treatment include inhibitors of progesterone receptors such as aglepristone alone^{21,22} or in combination with prostaglandin (PG)F₂ α .^{22,23} Aglepristone therapy is also recommended as a preoperative measure to reduce the risk of side effects.

Pyometra is also quite common in the queen, although CEH is not. In the queen, pyometra may occur when cycling at the age of 1 to 10 years or older (mean, 7 years) after a nonfertile breeding. Pathogenicity is similar to that of the bitch but its development is faster (1–4 weeks after estrus) and can also be induced by exogenous administration of progestagens. The frequency of pyometra in queens is lower than that in the bitch because of their special reproductive cycle; queens are seasonal

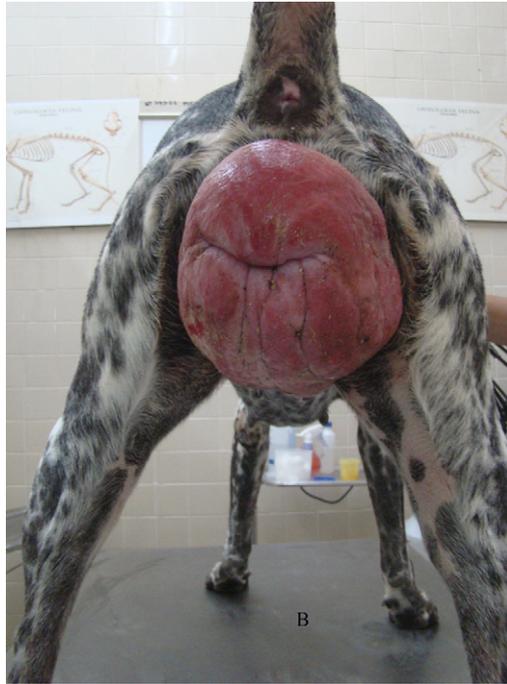


Fig. 9. Vaginal prolapse type III in the bitch.

species and are induced ovulators so there is no prolonged exposure to progesterone as in the dogs. The whole period of progesterone influence over the uterus is shorter (40–50 days) compared to the bitch (over 60 days). Although there is evidence of spontaneous ovulations in queens even in the absence of males,^{9,24} the frequency of this event is low. Vaginal discharge may be difficult to detect because of the grooming habits of cats; the discharge is generally purulent and fetid but may vary from bloody to mucoid, to yellow pus or a mixture (Fig. 5). Clinical signs associated with pyometra should be differentiated from feline infectious peritonitis. Ultrasound and radiography may indicate a uterine enlargement and may be useful to rule out pregnancy. Treatment of choice is OVH. The progesterone antagonist aglepristone is a new promising approach for the medical treatment of pyometra in this species alone or combined with PGF₂ α therapy.

Metritis and Endometritis

Metritis is an inflammation of the uterus involving the mucosa and myometrium layers. Unlike pyometra, this is an acute problem generally occurring during the first week postpartum as consequence of bacterial invasion through a dilated cervix to a susceptible uterus. Dogs can have chronic lymphoplasmatic endometritis, not unlike horses, which can result in infertility. It is associated in most cases with dystocia and obstetric manipulation (Fig. 6), abortion, retained placenta, or retained dead fetuses. However, in some cases it is produced after natural mating or artificial insemination. In queens, it may also occur in any type of birth. Common isolated bacteria from metritis cases are *Escherichia coli* and *Proteus*, but *Streptococcus* and *Staphylococcus* may also be involved. The infection is limited to the uterus but in unattended



Fig. 10. A case of vulvar canine transmissible venereal tumor in a bitch.

complicated cases can cause a systemic illness leading to septicemia. Acute metritis should be considered in any postpartum animal with signs of systemic illness or with an abnormal vaginal discharge.

Postpartum metritis in the bitch and queen is characterized by a foul-smelling vaginal discharge from purulent to sanguine-purulent. Clinical signs develop very quickly especially when associated with retained fetal membranes; signs include lethargy, anorexia, pyrexia, dehydration, decreased milk production, and abandonment of newborn. Abdominal palpation may reveal a flaccid uterus, and if the presence of a retained fetus or placenta is suspected, an ultrasound and radiology should confirm the diagnosis. Systemic therapies alone or associated with $\text{PGF}_{2\alpha}$ have shown consistent positive results. OVH is the last resort when cases become complicated or in animals with refractory cases.

Endometritis (inflammation of the endometrium) is present in many cases of infertile bitches and queens. This is generally chronic and subclinical and must be differentiated from an acute postpartum infection. The histology after recovering the uterus from an OVH (**Fig. 7**) will show an infiltration of polymorphonuclear cells in the endometrium. In the queen with normal ovarian activity, it is associated with infertility and may be more complicated to diagnose than in the bitch, especially when low-grade metritis or a mild infection is present.²⁵ In the queen, the history of infertility (mating at least 3 times with a fertile male without giving birth) may indicate a uterine infection.^{25,26} Therapy using a broad-spectrum antibiotic should be started. Aglepristone together with 15 days of antibiotics has been successfully used in the treatment of endometritis.²⁷



Fig. 11. A case of intersex in a bitch. Note the clitoromegaly.

Uterine Neoplasias and Cysts

Uterine neoplasia occurs infrequently. The majority of uterine tumors in dogs are of mesenchymal origin; they lack a glandular component and are benign. Leiomyomas account for 85% to 90% of all canine uterine tumors and are commonly associated with ovarian follicular cysts, CEH, mammary neoplasia, and hyperplasia.²⁸ Clinical signs are typically not evident until a uterine tumor reaches a large size. In queens, it may present alterations in the estrus cycle, vaginal discharge, and secondary pyometra.²⁹ Other less frequent uterine but malignant neoplasms are leiomyosarcoma and carcinoma. Treatment entails OVH.

Endometrial polyps are also seen in old bitches and queens but normally only one develops and they are frequently small and of little consequence unless their growth compromise the uterine lumen.¹⁸ Serosal inclusion cysts may develop in the uterus of the bitch during post partum uterine involution and are incidentally found during OVH or laparotomy.³⁰ These are frequently submitted as a “lesion of concern,” and, except when the structures are of considerable size, they are of minimal clinical significance.

COMMON LESIONS IN THE VAGINA

Vaginal Prolapse

There are several forms of vaginal prolapsed, and the terminology in the literature is often confused. A true vaginal prolapse occurs when the entire vaginal wall extends through the vulvar opening. This condition is rare in the bitch and queen.³¹ True vaginal prolapse occurs around parturition, when concentration of serum progesterone declines and the concentration of serum estrogen increase. True vaginal prolapse is graded I through III. Swelling and elevation of the vaginal folds may develop immediately cranial to the urethral orifice (**Fig. 8**) and are categorized as type I. As the



Fig. 12. An extreme case of canine transmissible venereal tumor in the vagina of a dog. (Courtesy of Ms Jamie Scott, Private Practice.)

edema progresses, the vagina fold becomes large enough to protrude outside the vulva (type II) until there is a full protrusion of the vaginal circumference through the vulva “donut shaped” (**Fig. 9**) that can cause abrasion of the mucosa and urethral twist (type III). In a type III vaginal prolapse, the urethra may be displaced and twisted and dysuria may occur. The prolapsed vagina is very vulnerable to trauma, ulceration, necrosis, and self-mutilation and may interfere with normal mating. In the queen, vaginal prolapse is very rare and is reported to occur during estrus or anestrus.³²

Often confused with true vaginal prolapse is the physiologic vaginal protrusion associated with estrogen stimulus during proestrus-estrus. In this case, the tissue is extremely edematous and the vaginal tissue protrudes in thick folds.³³ Vaginal protrusion can be distinguished from a true vaginal prolapse by careful physical examination, clinical history, and knowledge of the stage of cycle.

Vaginal Neoplasia

Vaginal and vulvar neoplasm represents 2.4% to 3% of all tumors in tumor-bearing dogs³⁴ and the majority of them are benign. Vaginal leiomyomas are among the most common benign tumors in bitches together with fibromas and fibroleiomyomas.³⁵ Other tumors reported include lipomas, polyps, melanomas, myxomas, and myxofibromas, but these are much less frequent. Canine transmissible venereal tumor (**Fig. 10**) is the most common tumor in the vagina in tropical developing countries,³⁶ but it is relatively uncommon in the United States and Canada. Clinically, these neoplasms can look similar. Diagnosis is made by physical examination and is confirmed with cytology or histopathology. A prolapsed vagina (see **Fig. 8**) and intersex lesions resulting in clitoromegaly (**Fig. 11**) can be mistaken with tumors. Most vaginal neoplasms behave in a benign fashion and complete surgical resection is usually curative. In the case of transmissible venereal tumor when tumors are too

large (Fig. 12), chemotherapy is compulsory. In queens, vaginal tumors are uncommon and may be found in healthy animals; benign leiomyomas are the most commonly reported.^{37,38}

SUMMARY

Lesions on the reproductive tract are common findings in small animal practice. Some of these lesions, such as pyometra and metritis, can seriously affect the reproductive capacity of the bitch and queen and, if not recognized and treated early, can lead to mortality. Clinicians must be aware of the different reproductive lesions and be prepared to differentiate those of concern and identify which require treatment.

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