Reproductive disorders of the spayed bitch
Cheryl Lopate
Reproductive Revolutions, Wilsonville, OR

Abstract
Ovariectomized bitches will often present to veterinarians for signs of vaginal discharge, recurrent or returning signs of estrus, or for vaginal masses. These may be due to presence of remnant ovarian tissue or other sources of estrogen exposure, vaginitis, vaginal foreign bodies, anatomic defects of the vaginal canal, or from other metabolic conditions. This paper reviews causes of vulvar discharge, ovarian remnant syndrome, stump pyometra or granuloma, and the different types of vaginal masses that may be seen in the ovariectomized bitch. It provides insight into the clinical signs, diagnostic workup and therapies that can be utilized to diagnose and treat these disorders.

Keywords: Ovarian remnant syndrome, vulvar discharge, vaginitis, vaginal mass, spayed

Introduction
Veterinarians are frequently presented spayed bitches with reproductive disease. The most common complaints are vulvar discharge, recurrent or returning signs of estrus, or vaginal masses. Diagnosis of these disorders may be straightforward in some cases, but they are often complicated and confusing. A step-wise approach to their diagnosis begins with a good history paying careful attention paid to nutrition (type of food being fed) along with any supplements or medications the bitch may be administered purposefully or that she may be exposed to via the owner’s personal use. A complete physical examination, followed by a minimum database of bloodwork and a urinalysis should follow. Ancillary diagnostics may include endocrinology, diagnostic imaging consisting of ultrasonography, radiography with or without contrast medium, magnetic resonance imaging, endoscopy and possibly laparoscopy or laparotomy depending on the situation. Each complaint will be reviewed separately although there is some overlap amongst them. A list of potentially estrogenic foods has been included in Table 1.

Vulvar discharge
A common presenting complaint of spayed bitches is the presence of vulvar discharge with or without perivulvar dermatitis. This discharge may be mucoid, mucopurulent, purulent or bloody and it may be chronic or intermittent. Causes of vulvar discharge in the bitch typically originate somewhere in the genitourinary system and can be due to infection (bacterial or viral; chronic or acute), chemical irritation from urine or other instilled substances, foreign bodies, neoplasia (vaginal, cervical or uterine), stump pyometra or granuloma, ovarian remnant syndrome (with or without ovarian cysts or neoplasia), congenital anatomic defects or trauma. There are two reports of vaginal discharge associated with non-reproductive tract neoplasia. It has also been reported that endocrine disease such as diabetes mellitus or chronic pyoderma may also have vaginitis as a presenting sign. Vascular anomalies (hamartoma and vascular ectasia) have been described in two case reports presenting with bloody vulvar discharge. Coagulopathies may also present with vulvar bleeding.

Clinical signs may include excessive licking or pruritus, stranguria, hematuria, dysuria, pollakiuria, incontinence, polyuria, and polydipsia. Discharge may accumulate on the perineum or haircoat. Vaginal discharge has been reported to be mucoid in about a third of the cases (33%), mucopurulent in 20% of the cases, and purulent in just over a quarter of the cases (27%). Discharge is typically blood tinged in cases of ovarian remnant syndrome or coagulopathy.

The initial diagnostic plan following physical examination should start with a diagnostic vaginal cytology to characterize the discharge. This cytology should be obtained using some type of guarded technique to avoid vulvar, clitoral or vestibular contamination. Sedation may be necessary in some spayed bitches to obtain vaginal samples. Particular attention should be paid to the types of vaginal cell present to determine if there is any estrogenic influence present (superficial cells should not be
Further attention should be paid to the types and number of bacteria as well as the presence of neutrophils (degenerate or non-degenerate) and whether there is phagocytosis of bacteria present. Normal, spayed bitches will have predominantly basal and parabasal cells with low to moderate amounts of mucus, low numbers of neutrophils and low numbers of bacteria (rods and cocci) with none intracellularly. Cultures should be obtained with a long, guarded culture swab. Cultures should be submitted for aerobes, Mycoplasma and Ureaplasma. A urinalysis (sterilely obtained, preferably by cystocentesis to avoid vaginal and vestibular contamination) should be performed to rule out the urinary tract as the source of infection in any bitch with signs of vaginitis. Urine culture may also be necessary to rule out a subclinical cystitis. When lymphocytes predominate, an immunologic etiology may be present. Eosinophilia may also be present in these bitches. A complete blood count and serum chemistry should be performed to identify inflammation, anemia, or signs of endocrine disorder and a prothrombin time, partial thromboplastin time and buccal mucosal bleeding time should be performed to rule out coagulopathy.

The bacterial flora of the vagina has been well documented and it is not abnormal to culture a variety of bacteria from the bitch’s vaginal canal (Table 2). It can be difficult at times to determine if a pathologic bacterial population is present versus normal vaginal flora, so the use of cytology in conjunction with culture to provide clear evidence of inflammation (phagocytosis of bacteria) is imperative. Bacterial growth is considered more likely to be significant when there is growth of a single, or possibly two organisms, with moderate to heavy growth. Infectious vaginitis has been shown to result in isolation of heavy growth of a single organism in 27-40% of cases. Mycoplasmas have been isolated from 88% and Ureaplasmas from 50% of normal bitches; while more bitches with infertility present with Ureaplasmas (75%), compared to those with no signs of reproductive disorders (40%). Brucellosis may cause vaginal discharge.

Viral infection with herpesvirus may cause vesicular vaginitis which can be diagnosed on endoscopic examination. These bitches may present with excessive licking, dysuria, or pollakiuria, with a serosanguinous or sanguinous vulvar discharge. Visual inspection of the mucosal surface of the vagina and vestibule, as well as the mucocutaneous junctions of the vulvar lips, will reveal either vesicular lesions or round, ulcerated lesions that have already ruptured. Lymphofollicular hyperplasia may be seen in the vagina or vestibule and may be either pathologic or a normal finding. Viral inclusion bodies may be seen on cytologic examination. Treatment with topical antiseptics have been advocated, but most of these cases will resolve on their own in a few weeks if left untreated. Herpesvirus may recrudesce and cause similar signs in the future particularly during times of physical or physiologic stress.

Vaginoscopy is very helpful to assess the appearance of the mucosa as well as to obtain biopsy samples where appropriate. The use of an otoscope speculum allows visualization of the caudal vagina and vestibule only. A pediatric proctoscope or endoscope (cystoscope or ureteroscope) is needed to evaluate the vaginal canal proximal to the vestibule-vaginal junction. Digital examination of the vagina is also necessary, as strictures and septa may easily be missed during vaginoscopic examination as the endoscope is small and easily slips past any narrowings. Sedation may be necessary for these examinations in spayed bitches.

Anatomic defects of the vulva, vestibule and vagina can cause vaginitis. Vestibulovaginal strictures or stenosis, vaginal septa, hymenal remnants and juvenile or hooded vulvas can cause pooling of mucus or urine in the vaginal canal resulting in infection, inflammation or chemical irritation, incontinence or urinary tract infection. Endoscopy and/or radiography with contrast medium are necessary for diagnosis. Adult onset clitoral enlargement is likely due to exposure to either endogenous (adrenal or ovarian remnant origin) or exogenous androgens (either via direct administration, nutritional supplement or exposure to an owner’s medicated cream or patch).

Treatment of vaginitis should include appropriate antibiotic therapy, based on culture and sensitivity, only if clear evidence of infection is present. Many cases of vaginitis will resolve without any treatment within a few months of presentation. If phagocytosis of bacteria is not evident, the use of antibiotics may disturb the normal vaginal flora and worsen the condition. Douching is an effective treatment for non-infectious vaginitis. This author uses a sterile physiologic saline solution for large

Clinical Theriogenology • Volume 6, Number 3 • September 2014  • 206
volume douching and then follows with a 1% acetic acid rinse in the last one or two rinses. Initially
douching may need to be performed more frequently to clear the tenacious mucoid secretions from the
walls, but then typically can be performed with less frequency as the discharge resolves. The author has
also found that the use of probiotics, particularly those with *Enterococcus faecium*, can help re-establish
normal vaginal flora. In the author’s experience, in cases of chronic vaginitis due to vaginal or vulvar
anatomic defects, douching may be needed intermittently for the patient’s entire life and probiotics may
be needed daily. Resolution of signs may take months to years, or may remain for the remainder of the
pet’s life and need to be treated intermittently. In some cases, administration of glucocorticoids may
help resolve chronic, non-infectious vaginitis. Bitches with incontinence may respond to treatment with
phenylpropanolamine, estriol or diethylstilbestrol.

Surgical treatment of anatomic defects may result in resolution of signs. Bitches that are over-conditioned with a hooded or juvenile vulva, should be encouraged to lose weight prior to
surgery and if signs do not resolve with weight loss alone, episioplasty can be performed. Surgical
removal of hymenal remnants may be beneficial. Surgical removal of strictures or septa has been
described. Surgical removal of strictures via vaginectomy or vaginal anastomosis and resection have
been described but the owners should be warned that healing may result in worsening of the stricture as
well, so may not provide a cure. Clitorectomy may also be beneficial in cases where a persistent
clitoritis is confirmed.

**Ovarian remnant syndrome**

Ovarian remnant syndrome is a condition where functional ovarian tissue remains in a previously
spayed female. Bitches may have signs of estrus return within weeks to months of spay surgery or it may be many years before signs present. Bitches with ovarian neoplasia in the remnant
tissue have a tendency to take longer to display signs of estrus compared to bitches with normal ovarian
architecture. It has been reported to have an incidence of up to 17-43% of all complications of
ovariohysterectomy. Most reports indicate that cats are overrepresented compared to dogs but one report showed a higher number of canine cases compared to feline. This may be due to the caseload of the clinic or the types of cases referred to this particular institution during the time frame studied.

**Etiology**

Failure to identify the ovary in its entirety may occur due to the fatty bursa surrounding the ovary in the bitch, particularly in anestrous bitches where the ovary can be very small. Improper placement
of clamps, ligatures or Ligaclips during surgery may result in a portion or the entire ovary to be left
behind. Inadequate exposure of the ovary may occur due to failure to break down the suspensory
ligament of the ovary or an abdominal incision that is too small or located too posteriorly. Accessory
ovarian tissue has been reported in queens, women and cows, but not in bitches. There is no known
breed or age predilection. In cats, it has been shown that a piece of ovarian tissue may re-establish a
blood supply and become functional again if the ovarian tissue is loosely attached to the intestinal
mesentery. It took only six months to re-establish follicular activity in these animals. So it is possible
that if a portion of an ovary is dropped into the abdomen of a dog it may re-establish a blood supply and
become a functional ovarian remnant.

There are five case reports of ovarian tumors in previously spayed bitches with ovarian remnant
syndrome: four report granulosa cell tumors (GCT) and the other was combination of a luteoma and
Sertoli cell tumor. There is typically a long period of time (2.5-10 years range but 6-9 is average) from
ovariectomy to initiation of signs of estrogenization in bitches that develop GCT in their ovarian remnant
tissue. Similarly, the luteoma/Sertoli cell tumor did not show clinical signs for ten years. Persistently elevated levels of gonadotropins may contribute to tumorigenesis. Granulosa cell tumors can produce both estrogens and progesterone. The estrogen secreted by the tumor may result in the
typical signs of estrogen expression (vulvar swelling and discharge, attraction of males, etc) and this may
be intermittent or persistent. If progesterone is also produced by the tumor, cystic endometrial
hyperplasia may develop and if there is uterine body left, may eventually develop into pyometra. This
elevation in progesterone may be due to partial luteinization of granulosa cells due to the persistent estrogen secretion by the tumor. In humans, GCTs express gonadotropin receptors and respond to gonadotropins.

Clinical signs

Clinical signs will vary depending on how much of the reproductive tract was left behind at the time of ovariohysterectomy. Vulvar edema, flagging and receptive behavior, and attraction of male dogs will be noted in the majority of cases, while bloody vulvar discharge will be seen only in those which have uterine tissue remaining. Some bitches will display mammary development and lactation associated with pseudocyesis. Cyclic behavior will be typical of an intact animal (four to 14 months between cyclic behaviors). Some studies showed the right ovary is more commonly left behind compared to the left ovary and this may be due to its more cranial location and thus greater difficulty in exteriorizing it fully. Other studies did not have this finding which may be due to the population of animals examined. It has been reported that ovarian remnants are not more common in deep-chested or obese individuals and this may be due to additional efforts made by the surgeon to obtain good exposure in these patients. It has also been reported that ovarian remnants are not more common in bitches with pyometra or that are spayed at the time of a cesarean section and this may be due to the stretch on the suspensory ligaments with these conditions allowing better ovarian exposure. Indeed, most remnants occur after elective ovariohysterectomy, often in pre- or peri-pubertal individuals, probably due to small ovarian size and the desire to use as small an incision as possible, thus making exposure more difficult and identification of the ovary proper more challenging.

Endocrinology of intact versus neutered animals

Estradiol concentrations are too variable to use to classify a bitch as intact or gonadectomized. Estradiol is produced via aromatization of androstenedione and testosterone in peripheral tissues. Estradiol is not produced by the adrenal glands. Progesterone concentrations rise more significantly in intact anestrous bitches following cosyntropin injection, than in gonadectomized bitches (Table 3). Progesterone can be produced by the adrenal glands so an ovariectomized animal can have a low level of progesterone present. Because there may or may not be a significant response to gonadotropin releasing hormone (GnRH) to stimulate release of progesterone or testosterone, these hormones are not recommended for testing purposes. Gonadotropin releasing hormone causes an increase in estradiol concentrations in intact bitches but not in ovariectomized bitches. Concentrations of luteinizing hormone (LH) and follicle stimulating hormone (FSH) are significantly higher in ovariectomized vs. intact bitches due to lack of negative feedback on the hypothalamus and pituitary via the ovaries. In one study, concentrations of LH were typically >8 ng/ml in ovariectomized bitches. In the same study, FSH concentrations in intact (mean 98±49 ng/ml) and ovariectomized (mean 1219±763 ng/ml) were significantly different. Gonadotropin releasing hormone stimulation results in a significant increase in LH in ovariectomized and anestrous bitches; whereas GnRH stimulation does not cause a significant increase in FSH in ovariectomized bitches while it does in anestrous bitches. This is most likely due to alterations in intracellular storage of FSH compared to LH. Gonadotropin releasing hormone stimulation testing of FSH may provide a diagnostic tool for distinguishing ovariectomized from intact bitches by the lack of response in ovariectomized bitches. While FSH may be valuable for determination of spay/neuter status, few laboratories have assays available commercially, so it is very difficult to use on a routine basis. It is extremely important that if FSH testing will be used that the laboratory’s assay be validated for canine serum.

Diagnosis

Vaginal cytology will confirm the presence of estrogen during the follicular phase of the cycle or if the bitch has steroidogenically active follicular cysts or neoplasia of the ovarian remnant. The presence of nucleated or anucleated superficial cells is consistent with estrogenic stimulation. Exposure
to or administration of exogenous estrogens, either intentionally (diethylstilbestrol or estriol for incontinence) or unintentionally (exposure to the owner’s estrogen supplements, creams or patches or supplementation of estrogen containing foodstuffs) may result in signs of estrus without a remnant being present and this must be differentiated during diagnostic testing.30,32

Other causes of bloody vulvar discharge need to be ruled out including supernumerary or accessory ovaries, neoplasia, vaginal foreign bodies, vaginitis, stump pyometra, trauma, and coagulopathy.30,31

**Ultrasound examination.** Ultrasonography may be used before or after stimulation tests to detect ovarian tissue, cysts, or neoplastic ovarian tissue.31,32 Very small remnants may be missed with ultrasonography and the lack of finding tissue compatible with ovarian tissue, does not rule out the diagnosis. Suture granulomas may be confused with an ovarian remnant. A diagnosis may be made by ultrasonography only a portion of the time (50-75%).32,45

**Baseline endocrine testing.** Estradiol concentrations can be determined when the bitch shows signs of bloody discharge, vulvar edema, or receptive behavior.30-32 It should be remembered that estrogen concentrations are highest during the follicular phase of the cycle and that once the LH surge happens, estrogen concentrations drop quickly. If samples are not obtained during the follicular phase of the cycle, they may not be diagnostic.30 There is considerable overlap of normal ranges between intact and ovariecotomized animals, so in some cases, estradiol concentrations may be low enough that a diagnosis cannot be confirmed. Keep in mind that exogenous estrogen exposure may result in elevated estradiol concentrations and may mislead the veterinarian to believe there is a remnant present when there is not.30 For this reason, stimulation testing is usually recommend over a single baseline estradiol concentration. Adrenal production of estrogens is also possible and may be seen with adrenal neoplasia or adrenal disease. Estradiol concentrations fluctuate throughout the day, so a single sample may be misleading if it is at a nadir.30 Basal estradiol concentrations are detectable in bitches with remnant ovarian tissue but not in ovariecotomized bitches.45 Basal estradiol levels are higher in bitches with remnant tissue than in intact anestrus bitches.45

Progesterone concentrations will be elevated (>2 ng/ml or 6.28 nmol/L) after ovulation occurs.30-32 Depending on the size of the remnant, concentrations of progesterone may be much higher or may remain in this low range during the luteal phase of the cycle, which may last from 45 to 75 days after ovulation.30,45 Low levels of progestagens can come from the adrenals but levels over 2 ng/ml can only be produced by functional ovarian tissue or by exogenous progestagen exposure.

Both estrogen and progesterone may be affected by lipemia and hemolysis, so samples should be taken following a six to eight hour fast and should be drawn atraumatically, placed in plain red top tubes, centrifuged within 30 minutes of sampling and the serum removed from the red blood cells and then either refrigerated or frozen depending on length of time until testing (<24 hours or >24 hours, respectively).

Luteinizing hormone is secreted episodically at lower concentrations in intact bitches throughout the estrous cycle and then in a very high pulse at the time of LH surge during late proestrus.44,46 Secretion of LH increases after gonadectomy as a result of diminished negative feedback, but it still remains pulsatile in its release pattern.46 Basal LH concentrations are significantly higher in ovariecotomized bitches than in anestrus bitches.42,46,47 A single positive LH test provides a positive predictive value that a bitch is ovariecotomized only 22% of the time.47 It may take up to four serial tests to accurately determine spay vs. intact status of a given individual.47 If a test result is high, repeat sampling another two to three times at two week intervals should help to determine if it is consistently high (ovariectomized) or intermittent (intact).44 A single negative test following any positive tests is consistent with an intact animal.47 Serial testing can also be done hourly as episodic pulses of LH are known to occur frequently but do not last more than about an hour, except for the pre-ovulatory LH surge which may last up to 36 hours.47 Secretion of LH follows a similar pattern in bitches ovariecotomized prior to puberty.47
Basal LH concentrations are higher in bitches with remnant tissue than in intact bitches in anestrus, but lower than ovariectomized bitches. Basal LH concentrations are higher in bitches with an interval from ovariectomy to appearance of the first estrous cycle after surgery of more than three years, compared to those who display signs in under three years. The higher LH concentrations in bitches with remnant tissue may be due to lower sensitivity to negative feedback hormones as a result of disruption of the blood supply to the remnant by the initial surgical procedure or by partial removal of the ovaries. The diminished blood supply may reduce or ablate ovarian activity for long periods of time, possibly accounting for the delay in resumption of signs in many individuals. The chronic secretion of GnRH because of lack of negative feedback by inhibin from the ovaries, may in turn result in hypertrophy and/or hyperplasia of pituitary cells. These gonadotroph cells may lose some of their normal characteristics of sensitivity to negative feedback, such that when the remnant tissue becomes active again, LH may not be suppressed to the extent it is in a normal intact bitch, thus resulting in higher basal LH concentrations compared to intact bitches.

Bitches that develop GCT in their ovarian remnant have high circulating estradiol and/or progesterone concentrations. These bitches tend to take longer to begin to show clinical signs of ovarian remnants. Basal LH in bitches with ovarian remnants is higher than in anestrous bitches. This high basal LH may be due to loss of sensitivity to the negative feedback from estradiol resulting from partial ovarian removal or partial to complete disruption of the blood supply to the ovaries at the time of ovariectomy or ovariohysterectomy. The resultant lack of ovarian activity for long periods of time results in hypersecretion of gonadotrophs and hypertrophy/hyperplasia of pituitary gonadotrophs cells. As these cells transform, they may lose their sensitivity to negative feedback to the ovarian hormones that are beginning to be secreted from the remnant tissue as its blood supply is gradually re-established. Thus the ovarian hormones cannot suppress LH secretion to the levels typically seen in anestrous bitches. So, in bitches with remnant GCT tissue, estradiol and LH concentrations will be higher than those present in anestrous bitches. It has been hypothesized that another possible reason for increased LH concentrations in bitches with GCT is that there is a positive feedback of estradiol 17-β on LH release, as seen in late proestrus in intact bitches. This hypothesis may be less likely since in the bitch it has been demonstrated that estradiol 17-β exerts negative feedback until its secretion stops (at the end of proestrus) and this is when LH increases.

Anti-Müllerian hormone (AMH), also known as Müllerian inhibitory substance, is a protein hormone, produced by the granulosa cells of primary, secondary and early antral follicles. When used in bitches over six months of age, the sensitivity of this assay was 93.9% and the specificity was 93.8%. The advantages of AMH over other types of tests are that it requires only a single basal sample and is not subject to the stage of the estrous cycle. The ability of this test to diagnose ovarian remnant syndrome successfully has not yet been extensively studied, but holds some promise and research is presently ongoing.

**Stimulation testing.** Administration of GnRH (2 µg/kg) or human chorionic gonadotropin (hCG, 44 IU/kg) will cause luteinization if there is functional mature follicular tissue present. If the medication is given too early in proestrus, luteinization may not occur, so it is important to assess vaginal cytology first and to wait until at least 70% of the superficial cells are anucleated before this type of stimulation testing. Progesterone concentrations should be measured two to three weeks after stimulation testing. Elevated progesterone at this time indicates functional ovarian tissue. Not all remnants will respond to stimulation testing, so a negative result does not rule out a remnant.

Human chorionic gonadotropin (1500 IU IV) or GnRH stimulation testing (10 µg/kg IV) can be used to determine if an animal has functional ovarian tissue. Baseline samples and samples taken at 10, 60 and 120 minutes after injection are recommended. Ovariectomized animals have no change in estradiol or progesterone concentrations following stimulation while intact animals should have a two- to four-fold increase, depending on stage of the cycle. Stimulation testing with GnRH will result in increased LH concentrations at ten and 60 minutes after administration in both intact and remnant bitches, but not in ovariectomized bitches; however, there is overlap between ovariectomized and anestrous
bitches though making this an unreliable test. The increase in progesterone and estradiol is lower in remnant than intact bitches. This lowered response again may be due to changes in the gonadotrophs due to altered function from the negative feedback being decreased from altered blood supply to the remnant tissue. It is possible that higher LH concentrations may be found if the animal is tested after 60 minutes, since the response could simply be delayed. Stimulation with GnRH results in an increase in estradiol concentrations at 60 minutes after injection. The increase in estradiol after stimulation is higher in anestrus bitches than those with remnant ovarian tissue. Some bitches with remnant tissue may have a lower estradiol concentration 60 minutes after GnRH stimulation. This may be due to cystic changes in some remnant tissue, changes in vascularization of the remnant or be a response to the follicular phase of follicle development in the remnant, since testing is usually performed after the bitch begins showing clinical signs indicating activity in the remnant tissue. Gonadotropin releasing hormone stimulation of bitches with GCT affecting the ovarian remnant results in a significant increase in LH at both 10 and 60 minutes after injection and of estradiol at 60 minutes after injection. In intact bitches with GCT, GnRH stimulation results in no significant elevation of LH or estradiol compared to anestrous or ovarioectomized bitches.

Treatment
Once a remnant is confirmed, exploratory laparatomy can be performed to remove the remnant tissue. Surgery is best performed during diestrus because luteal tissue is more prominent in fat than is follicular tissue, but surgery can also be performed during estrus. If the remnant is not grossly visible, ovarian pedicle granulomas should be removed and submitted for histopathology. Increased vascularity of the pedicle tissue may indicate remnant tissues. Any tissue left along the broad ligament should be removed and submitted as well. The abdomen should be explored carefully from the caudal pole of the kidney to the uterine stump on both sides and then the rest of the abdomen should be explored for the presence of ectopic ovarian tissue, since a dropped ovarian fragment may revascularize anyplace in the abdomen. Historically, in some countries, a piece of ovarian tissue was allografted into the gastric mucosa near the portal vein drainage area to act as a source of gonadal steroids after ovariohysterectomy to prevent the complications of alopecia and coat changes as well as incontinence issues; thus, it is easy to see how a dropped ovary may revascularize. Any remnants of the uterus or oviducts should also be removed during the exploratory whenever possible.

Other options for treatment include estrus suppression using mibolerone, megestrol acetate, medroxyprogesterone acetate or Suprelorin® (deslorelin) implants. If uterine tissue remains and megestrol acetate is used to suppress estrus, cystic endometrial hyperplasia may develop and result in pyometra or stump pyometra. Long term use of progestagens may also result in adrenocortical suppression and insulin resistance.

Stump pyometra or granuloma
Stump pyometra occurs as a result of incomplete ovariohysterectomy. Pyometra occurs as a result of the priming of estrogen receptors followed by progesterone production. Estrogens and progesterone may be either endogenous or exogenous in origin. Endogenous hormones are more common and typically result from ovarian remnant syndrome. Regardless of the source of the hormones, the effect on the uterus is the same. Cystic endometrial hyperplasia, with or without and endometritis, initially develops. Bacteria from the vagina or via hematogenous infection then invade the uterine lumen and proliferate resulting in pyometra. A uterus previously primed with cystic endometrial hyperplasia and/or endometritis may develop pyometra weeks to years later even without additional hormone exposure, although in many cases of stump pyometra, there is either an endogenous (ovarian remnant or adrenal) or exogenous progestagen exposure. Abscessation may also occur as a result of stump reaction, use of non- absorbable suture in the uterine body ligatures, excess tissue manipulation causing tissue trauma, prior endometritis or pyometritis at the time of ovariohysterectomy, or failure to use aseptic surgical technique. In some cases, suture reaction will occur resulting in
granuloma formation. Use of non-absorbable suture in particular, will cause more suture reaction than absorbable suture material. Suture material can also be carcinogenic and initiate sarcomas.56

It is common practice, particularly in young patients, to leave all or part of the uterine body and often part of the uterine horns during a spay because the surgeon tries to use as small an incision as possible. Leaving all or part of the uterus predisposes the patient to stump pyometra later in life if an ovarian remnant is present or the animal is exposed to exogenous steroids. While the main concern about leaving uterine tissue at the time of spay is stump pyometra or stump granuloma, neoplasia can also develop in the uterine stump. While leiomyoma, leiomyosarcoma and lymphosarcoma are common neoplasms of the canine uterus, hemangiosarcoma may also develop in the uterus and present as bloody vulvar discharge.57,58

Clinical signs include all those typically associated with pyometra, including depression, anorexia, fever, inappetance, vomiting, abdominal pain or distension, polyuria, polydipsia, with or without vaginal discharge.50,51,53 There may be leukocytosis with a left shift, monocytosis, azotemia, elevation of hepatic enzymes, hypoalbuminemia, hyperglobulinemia, non-regenerative anemia.50,51,53 Stump granuloma may present with urinary signs (stranguria, pollakiuria, hematuria, dysuria, incontinence), digestive signs (dyschezia, constipation, incontinence), signs of bloody vulvar discharge, or the lesion may be palpable as an abdominal mass in the caudal abdomen on physical examination.

Surgical treatment is necessary. The affected stump tissue should be removed whenever possible. Adhesions may involve the urinary tract, body wall or pelvic canal. Surgical complications include septic peritonitis, septicemia, ureteral or bladder trauma, incontinence, suture reaction and dehiscence.50-53 Both ovarian pedicles should be examined and any granulation tissue or ovarian tissue at these sites should be removed and examined histologically.50-53 If the stump tissue cannot be completely removed because of extensive adhesions, options include suctioning or aspiration of infected contents, drain placement, marsupialization or omentalization.51,53 Aspiration should not be used if the patient is septic or has peritonitis or has a source of continued infection.51,53

This disease can be completely prevented by complete removal of the entire uterus, ligating the uterine body at the level of the cervix.50

Vaginal masses

Vaginal masses include vaginal prolapse, neoplasms of the vagina and urethra, clitoral hypertrophy, abscesses, hematomas or cystic structures59-67 Vaginal prolapse, also called vaginal hyperplasia/hypertrophy, is typically a disease of intact bitches, but spayed bitches may develop vaginal prolapse if they have an ovarian remnant; are exposed to exogenous estrogens via foods or supplements; ingest estrogenic medications (for urinary incontinence or a human medication) or are exposed to a estrogen cream or patch used by their owner. Vaginal prolapse occurs due to edema of the submucosa and hypertrophy of the stratified squamous epithelium resulting in a protrusion of a mass of round tissue from the floor of the vagina or doughnut shaped tissue protruding circumferentially from the walls of the vagina.59 Bitches may lick excessively at the prolapsed tissue or show signs of stranguria or dysuria.59 Spontaneous regression occurs with removal of the source of estrogen.59 Surgical removal is typically not necessary in spayed bitches if the source of estrogen can be identified and removed.

Vaginal tumors account for 2.4-3% of tumors in dogs.66,68,69 Excluding transmissible venereal tumors (TVT), 81-83% are reported to be benign.68-70 The most common benign tumors are leiomyomas, fibromas, polyps and lipomas.62,63,65,66,68-71 Extraluminal leiomyomas usually arise from the roof of the vestibule, while intraluminal leiomyomas typically arise from the vestibular wall and can become quite large (10-12 cm).59,70 The most common malignant tumors are leiomyosarcoma and squamous cell carcinoma.66,68 Botryoid rhabdomyosarcoma,72 hemangioma,67 hemangiosarcoma,73 lymphangiosarcoma,74 neurofibroma, histiocytoma, mxyoma, myxofibroma, and mast cell tumors75 have also been described. The mean age of occurrence is 10+ years.59,69,70 Malignant tumors have been reported with higher frequency in spayed bitches.69 Some of these tumors may be hormone responsive, so the owners should always be queried about exogenous hormone exposure if the patient has been ovariectomized.62,65,68-70,76
Clinical signs usually include excessive licking, protrusion of the mass through the vulvar lips or perineal swelling, hemorrhagic or mucopurulent vulvar discharge, stranguria, dysuria, hematuria, pollakiuria, incontinence, tenesmus or dyschezia. Benign tumors tend to be more pedunculated, while malignant tumors tend to more invasive and are therefore more difficult to excise. Treatment includes surgical resection, laser ablation, chemotherapy, or radiation therapy depending on location. Vaginal cysts may be marsupialized into the vaginal canal to allow continued drainage or they can be surgically removed. Some masses may require episiotomy, vulvovaginectomy and perineal urethrostomy for removal. Tumors arising from the anterior vagina may require vaginectomy with pubic and ischial osteotomy. Use of aplepristone, a progesterone receptor antagonist, may be beneficial to reduce the size of hormone responsive tumors, prior to surgical excision.

Urethral neoplasia may be epithelial (transitional cell carcinoma and squamous cell carcinoma) or mesenchymal (leiomyoma, leiomyosarcoma). Most of these tumors are malignant. The mean age of occurrence is 10.2 years. Clinical signs include stranguria, hematuria, dysuria and bloody vulvar discharge.

Transmissible venereal tumor is typically a neoplasm of intact animals, but if an animal with a small tumor was spayed, it may not be diagnosed until vaginal discharge developed days to months later. Since this tumor is spread during coitus it is typically acquired when the bitch is intact, however, on occasion, spayed bitches will stand to be mated by a male dog. Bitches with ovarian remnants may also acquire TVT when the remnant becomes steroidogenically active and estrus behavior returns. Clinical signs with TVT usually include serosanguinous vulvar discharge. The mass may have multiple nodules and is typically proliferative in appearance (cauliflower-like) with a friable surface. Either vincristine alone or combined with surgical excision is the treatment of choice; while radiation therapy may also be effective.

Clitoral enlargement may occur in spayed animals as a result of endogenous steroid production from the adrenal glands, exogenous androgen or anabolic steroid administration, accidental exposure or exposure to an owner’s testosterone cream or patch. Clitoritis or vaginitis may result from exposure or from trauma caused by licking. Removal of the source of steroid may result in resolution of signs with no further treatment. Typically, if there is no os clitoris, the hypertrophy will resolve with cessation of hormone exposure. Surgical removal is possible if hypertrophy persists.

Summary

Reproductive disorders in previously spayed bitches are common. They can be very frustrating cases for the veterinarian and the owner alike. A step-wise approach to diagnosis is necessary and may require time and a variety of testing to arrive at a concrete diagnosis. Once a diagnosis is made, treatments are relatively straightforward. Chronic vaginitis cases are the most frustrating as they may never completely resolve and may require lifelong therapy.
Table 1. Foods with potentially high estrogen content

<table>
<thead>
<tr>
<th>Alfalfa</th>
<th>Eggplant</th>
<th>Pumpkin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animal Flesh</td>
<td>Fennel</td>
<td>Red beans</td>
</tr>
<tr>
<td>Anise Seed</td>
<td>Flaxseeds</td>
<td>Red clover</td>
</tr>
<tr>
<td>Apples</td>
<td>Garlic</td>
<td>Rhubarb</td>
</tr>
<tr>
<td>Baker’s yeast</td>
<td>Hops</td>
<td>Rice</td>
</tr>
<tr>
<td>Barley</td>
<td>Licorice</td>
<td>Sage</td>
</tr>
<tr>
<td>Beets</td>
<td>Oats</td>
<td>Sesame seeds</td>
</tr>
<tr>
<td>Carrots</td>
<td>Olive oil</td>
<td>Soybean sprouts</td>
</tr>
<tr>
<td>Cherries</td>
<td>Olives</td>
<td>Soybeans</td>
</tr>
<tr>
<td>Chickpeas</td>
<td>Papaya</td>
<td>Split peas</td>
</tr>
<tr>
<td>Cowpeas</td>
<td>Parsley</td>
<td>Sunflower seeds</td>
</tr>
<tr>
<td>Cucumbers</td>
<td>Peppers</td>
<td>Tomatoes</td>
</tr>
<tr>
<td>Dairy foods</td>
<td>Plums</td>
<td>Yams</td>
</tr>
<tr>
<td>Dates</td>
<td>Pomegranates</td>
<td></td>
</tr>
<tr>
<td>Eggs</td>
<td>Potatoes</td>
<td></td>
</tr>
</tbody>
</table>


Lignans (most fruits and vegetables) are weak estrogens that block the action of other estrogens and isoflavones (soy, dairy, gluten grains and legumes) stimulate estrogen receptors.

Table 2. Bacterial isolates from the vaginal canal of healthy and diseased, intact and ovariectomized bitches

<table>
<thead>
<tr>
<th></th>
<th>Hirsh 19</th>
<th>Bjurström 20</th>
<th>Olson 23</th>
<th>Doig 24</th>
<th>Bjurström 26</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Mycoplasma spp</em></td>
<td>59.3%</td>
<td></td>
<td></td>
<td>88-95%</td>
<td></td>
</tr>
<tr>
<td><em>Ureaplasma spp</em></td>
<td></td>
<td></td>
<td></td>
<td>37-50%</td>
<td></td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>31-45%</td>
<td>84.7%</td>
<td>38-45%</td>
<td>32.1%</td>
<td></td>
</tr>
<tr>
<td><em>Staphylococci spp</em></td>
<td>13-27%</td>
<td>33.9%</td>
<td>23.8 - 66.7%</td>
<td>12.8%</td>
<td></td>
</tr>
<tr>
<td><em>Streptococci spp</em></td>
<td>43-61%</td>
<td>47.5-55.9%</td>
<td>9.5-28%</td>
<td>19.2%</td>
<td></td>
</tr>
<tr>
<td><em>Proteus spp</em></td>
<td>7-13%</td>
<td>25.4%</td>
<td>4.8-15%</td>
<td>6.4%</td>
<td></td>
</tr>
<tr>
<td><em>Bacillus spp</em></td>
<td>2-3%</td>
<td>14.3-15%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Corynebacterium spp</em></td>
<td>7-11%</td>
<td>40.7%</td>
<td>9.5-10%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Pseudomonas spp</em></td>
<td>4-9%</td>
<td>10.2%</td>
<td>5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Micrococcus spp</em></td>
<td></td>
<td></td>
<td>14.3%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Neisseria spp</em></td>
<td></td>
<td></td>
<td>4.8%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Klebsiella spp</em></td>
<td>1%</td>
<td></td>
<td>4.8%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Hemophilus spp</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Pasteurella spp</em></td>
<td>5-26%</td>
<td>98.3%</td>
<td></td>
<td>6.4%</td>
<td></td>
</tr>
<tr>
<td><em>Enterococcus spp</em></td>
<td>2%</td>
<td>44.1%</td>
<td></td>
<td>1.3%</td>
<td></td>
</tr>
<tr>
<td><em>Moraxilla spp</em></td>
<td>2%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Flavobacterium</em></td>
<td>3%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Percentages indicate the percentage of individuals where the organism was recovered.

Table 3. Progesterone concentrations in intact anestrus bitch and ovariectomized bitches before and after stimulation with cosyntropin

<table>
<thead>
<tr>
<th></th>
<th>Range</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intact basal</td>
<td>0.01 – 0.65 ng/ml</td>
<td>0.21 ng/ml</td>
</tr>
<tr>
<td>Intact post-stimulation</td>
<td>0.3 – 3.7 ng/ml</td>
<td>1.7 ng/ml</td>
</tr>
<tr>
<td>Spayed basal</td>
<td>0.01 – 0.14 ng/ml</td>
<td>0.04 ng/ml</td>
</tr>
<tr>
<td>Spayed post-stimulation</td>
<td>0.3 – 1.3 ng/ml</td>
<td>0.8 ng/ml</td>
</tr>
</tbody>
</table>
References


