

# Reproductive Oncology

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The actual incidence of reproductive tract tumors is difficult to ascertain, presumably because a significant percentage of dogs and cats are neutered, particularly in the United States. Data from European countries, where elective neutering is less common, provides insights. Several studies document the relative frequency of reproductive tumors. Larger studies of the more common tumors, eg, testicular tumors, provide a substantial amount of information on the clinical presentation and response to treatment of dogs, but overall there is less information available on cats. Numerous case reports document the less commonly reported tumors and will be included in the following discussion.

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Cases of female and male reproductive tract tumors are reviewed. The studies investigated include cat and dog.

## Female Reproductive Tract Tumors

### Ovarian Tumors

Tumors of the ovary are uncommon in dogs and cats. In a pathology survey over a 1-year period, 12 of 2,350 dogs (0.5%) had primary ovarian tumors.<sup>1</sup> In another report documenting the frequency of ovarian tumors in dogs also based on surgical and postmortem submissions, 51 of 4187 tumors (1.2%) were of ovarian origin.<sup>2</sup> In a study of 2,917 tumor bearing dogs there were 24 ovarian tumors (0.8%).<sup>3</sup> The actual frequency of ovarian tumors may be underestimated as ovaries are not routinely sectioned at necropsy and are more commonly examined only if there is a gross lesion. In a study of 400 bitches that included sectioning of all ovaries, 25 (6.3%) ovarian tumors were identified.<sup>4</sup> Additionally, the frequency of ovarian tumors is affected by the fact that many companion animals are neutered. Ovarian tumors typically occur in intact females; although ovarian tumors can arise from incompletely resected ovarian tissue.<sup>5-8</sup> Ovarian remnant syndrome with return to estrus after ovariohysterectomy due to residual tissue, or accessory ovaries, has been recognized and reported in dogs and cats.<sup>9</sup> Feline ovarian tumors are rare, but this likely is due to the fact that a high percentage of cats are neutered. Of 571 feline neoplasms, there was only one ovarian tumor.<sup>2</sup> In a study of 395 feline tumors, three (0.8%) were ovarian in origin.<sup>3</sup>

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There are three main categories of ovarian tumors including epithelial, germ cell, and sex cord-stromal tumors. In addition, there are several other miscellaneous neoplastic diseases of the ovaries. The reported relative frequency of the different categories of canine ovarian tumors varies between studies, with epithelial tumors most common in some studies,<sup>10-12</sup> and sex cord-stromal tumors in others.<sup>4,13-15</sup> In a study of 94 canine ovarian tumors over a 12-year period, 60% were epithelial, and 27% were granulosa-theca cell tumors.<sup>10</sup> In a retrospective study of 71 canine ovarian tumors, 46% were epithelial tumors, 34% sex cord stromal tumors, and 20% germ cell tumors. The majority of ovarian tumors are unilateral; 84% in one study.<sup>16</sup> The left ovary is more commonly affected,<sup>13</sup> although bilateral involvement is relatively common with epithelial tumors, and sertoli-leydig cell tumors.<sup>13,16-17</sup> The relative risk of epithelial tumors increases with age.<sup>10</sup> There is no apparent breed predilection.<sup>18</sup> In cats the most common ovarian tumors are of sex cord-stromal origin; typically granulosa cell tumors.<sup>19</sup> Epithelial tumors are rare in cats, with a report of an adenocarcinoma with spindle cell transformation in a 5-year-old cat; and bilateral cystadenomas in a 10-year-old cat.<sup>19-20</sup>

The metastatic rate of ovarian tumors is variable depending on the primary. Metastasis of ovarian tumors is typically recognized as peritoneal dissemination or implantation; although distant metastasis and organ involvement can also occur.<sup>16</sup>

### Pathology

**Epithelial tumors.** Epithelial tumors include papillary adenoma, papillary carcinoma, cystadenoma, cystadenocarcinomas, and undifferentiated carcinomas. In a report on a compilation of 71 canine ovarian neoplasms, 33 (46%) were of epithelial origin, and 21 of the 33 (64%) epithelial tumors were malignant.<sup>16</sup> Of the malignant epithelial tumors 10/21 (48%) had metastasized.<sup>16</sup> In cats, ovarian epithelial tumors arise from the coelomic epithelium on the surface of the ovary and from the rete ovarii. In the bitch there are subsurface epithelial structures (SES) which may be a potential origin for epithelial tumors.<sup>19</sup> In the dog papillary adenomas may arise from the surface epithelium, subsurface epithelial structures or the rete ovarii; but the majority arise from the subsurface epithelial structures, they are frequently bilateral and multicentric.<sup>21</sup> Papillary carcinomas in the dog are usually of SES origin and are similar in appearance to adenomas (smooth nodular, or cauliflower-like surface) but are typically larger and can have areas of necrosis and hemorrhage; metastasis is common and occurs by implantation, lymphatic or vascular invasion.<sup>21</sup> An 11-year-old female Pekinese presented for vomiting and listlessness and was subsequently diagnosed with an ovarian papillary carcinoma with metastasis to the sternal lymph node and hemorrhagic carcinomatous pleural effusion.<sup>22</sup> Cystadenomas arise from the epoophoron and/or rete ovarii. Serosus cystadenomas are uncommon, but have been reported and were detected in 8

of 25 dogs with ovarian tumors, from a group of 400 bitches.<sup>4,23</sup> One of 22 feline and 14 of 276 canine ovarian tumors were cystadenomas.<sup>21</sup> There is one report of an ovarian fibroadenoma in a 7-year-old female cocker spaniel.<sup>21</sup>

**Germ cell tumors.** Germ cell tumors include dysgerminoma (counterpart of the testicular seminoma), teratoma, and malignant teratoma or teratocarcinoma. Dysgerminomas and teratomas are of primordial germ cell origin; dysgerminomas represent a less-differentiated tumor than the mature teratoma. Based on one report, 17% of ovarian tumors were germ cell tumors in the canine, and 15% in the feline.<sup>24</sup> Dysgerminomas represent 6%-12% of ovarian tumors in dogs.<sup>24</sup> Dysgerminomas are recognized most frequently in the dog,<sup>13-14,24,25</sup> but they have also been reported in cats.<sup>21,24,26</sup> Six of 22 feline ovarian tumors were dysgerminomas.<sup>21</sup> Dysgerminomas on histopathology are composed of a uniform population of polyhedral cells that are arranged in sheets, cords, or alveoli; scant fibrous stroma; highly vascularized; mitoses are numerous and sometimes have an aberrant appearance; and there may be regions of necrosis and hemorrhage within the tumor. Despite the presence of a high mitotic rate, necrosis, and hemorrhage (all suggestive of a more malignant tumor), the majority of dysgerminomas are clinically benign. The histologic appearance of benign and malignant dysgerminomas is similar; in the canine 10%-20% of dysgerminomas are malignant.<sup>21</sup> Metastases (3 of 14 cases in one report) have been identified in the regional, mesenteric, and mediastinal lymph nodes, abdominal organs (liver, kidney, adrenal), omentum, serosal surface of the intestinal tract, and lung.<sup>21,24</sup>

Teratomas are tumors that are composed of tissue from more than one primary embryonic germ layer. Based on a compilation of 344 canine ovarian tumors; 2.7% (9 tumors) were teratomas.<sup>18</sup> They arise from at least two and usually all three germinal layers (endoderm, mesoderm, ectoderm) and have been reported to occur in both dogs and cats. Tissue representing any organ (eg, hair, bone, cartilage, teeth, nerve tissue, adipose tissue, hepatic tissue, adnexal glands, respiratory tract and intestinal epithelium, smooth or skeletal muscle), except ovary or testis, may be present.<sup>18,21,27-29</sup> Teratomas are unilateral tumors; more commonly arising from the left ovary. Canine teratomas range in size from 2-10 cm.<sup>21</sup> Teratomas often have multiple cysts lined by squamous epithelium that contain hair, keratin, and sebaceous material (termed dermoid cysts). Immature partially differentiated to mature and fully differentiated teratomas have been observed in dogs and cats. Teratomas are less common in cats than dogs.<sup>20,28</sup> Malignant teratomas (teratocarcinomas) are less common than teratomas in dogs.<sup>30</sup> Of 17 teratomas in dogs, 5 (29%) were malignant in one case series.<sup>21</sup> In a compilation of 71 canine ovarian tumors, there were 7 teratomas, 6 of which were malignant and 3 of the dogs with malignant teratomas had metastasis.<sup>16</sup> Any component of a teratoma may become malignant and potentially result in metastasis.<sup>28,31</sup> Sites of metastasis include abdominal viscera, lymph nodes, bone and lung.<sup>18,21,30</sup>

**Sex cord-stromal tumors.** Sex cord-stromal tumors include granulosa cell tumor, theca cell tumor, interstitial cell tumor (luteoma, lipid cell tumor), and sertoli-leydig cell tumor.

Granulosa cell tumors can have multiple histologic patterns including follicular, sertoli cell, and sarcomatous; areas of luteinization may be present; and Call-Exner bodies are evident in a subset of tumors.<sup>19</sup> Thirty of 69 canine ovarian tumors were granulosa cell tumors; 23 (77%) were functional based on clin-

ical signs of hyperestrogenism, and 2 (7%) were malignant.<sup>21</sup> In a series of 22 feline ovarian tumors, 9 were granulosa cell tumors and 5 were interstitial gland tumors.<sup>21</sup> Three of 5 cats in one report had multiple metastases to the pelvic and abdominal peritoneum, and 1 had pulmonary metastasis.<sup>20</sup>

Interstitial cell tumors reported in 6 dogs, 5-14 years of age, 3 of 6 dogs had vaginal discharge and/or a swollen vulva, unilateral, relatively small benign tumors.<sup>21</sup> Interstitial cell tumors in cats are solid, orange-yellow to brown on gross examination.<sup>19</sup> They are described as lipid-cell or Leydig-like tumors. All 5 cats in one report had lipid-cell type tumors,<sup>19</sup> and in another report one cat had an androgenic tumor.<sup>20</sup> On histopathology there is a homogeneous population of large distinctly bordered polyhedral cells with variable sized round central nuclei; a variable number and size of intracytoplasmic vacuoles; and a fine fibrovascular stroma separating the cells into lobules.<sup>19</sup>

Theca cell tumors or thecoma are infrequently diagnosed in the dog.<sup>21,32</sup> There is one report of a 6-year-old spayed female cat that was diagnosed with a testosterone producing thecoma at the left ovarian stump.<sup>33</sup>

Of 71 dogs with primary ovarian neoplasms, 12 (17%) had sertoli-leydig cell tumors, one had metastasized to the peritoneum, and of the seven dogs in which the uterus was examined 6 (87%) had endometrial hyperplasia.<sup>34</sup> A report exists of an androblastoma with sertoli-leydig cell pattern in a cat.<sup>35</sup> Three other cases have been reported in cats.<sup>21</sup>

**Miscellaneous ovarian tumors.** Other mesenchymal ovarian tumors include hemangioma, leiomyoma, and lipoma.<sup>2,21</sup> Metastatic tumors that have been observed in the canine ovary include malignant melanoma, mammary gland carcinoma, transmissible venereal tumor, and lymphoma.<sup>12,21,36</sup> A 3-year-old cat with lymphoma at multiple sites, including the liver, spleen, omentum, kidneys, and lung, also had evidence of lymphoma in the ovaries.<sup>37</sup>

### Clinical Presentation

The clinical signs observed in dogs and cats with ovarian tumors are variable (Table 1). Ovarian tumors may be detected incidentally during ovariohysterectomy or on postmortem examination in dogs that do not have any clinical signs referable to the tumor. Most commonly, clinical signs are observed secondary to a space occupying mass, or secondary to peritoneal (abdominal distention) and/or pleural effusion due to tumor dissemination.<sup>38</sup> Ascites can be due to fluid production by tumor cells, lymphatic obstruction and/or irritation, and inflammation of the serosal surfaces. It is also possible, particularly with functional sex cord stromal tumors, to have clinical signs secondary to excessive estrogen and/or progesterone production. Persistent proestrus/estrus of more than 30 days duration may be associated with functional ovarian tumors. Of 58 dogs with ovarian tumors that had histopathologic evaluation of the uterus, cystic endometrial hyperplasia was seen in 67%, including in the majority of dogs with sex cord-stromal tumors (18/19; 95%), all of the granulosa cell tumors (7/7; 100%), 55% (17/33) of dogs with epithelial tumors, and none of the dogs with malignant teratomas (6/6).<sup>16</sup> Additional uterine changes reported in dogs with ovarian tumors include endometritis, and/or squamous metaplasia.<sup>16</sup>

Dysgerminomas occur primarily in older age animals with a mean age of 10.5-13 years,<sup>13,18,24</sup> the youngest 2 years of

**TABLE 1. Clinical Summary of Canine Ovarian Tumors**

Clinical presentation	Incidental finding at time of ovariohysterectomy or necropsy; majority are unilateral tumors. Clinical signs typically occur secondary to a space occupying mass or effusion due to metastasis. Clinical signs in dogs with functional tumors secondary to excessive estrogen and/or progesterone production include signs of persistent estrus, pyometra, and bone marrow toxicity are all possible.
Diagnostics	Abdominal ultrasound to identify the primary and evaluate for metastasis. Abdominocentesis and cytology in dogs with effusion. Complete blood work and thoracic radiographs.
Treatment	Ovariohysterectomy is curative for benign tumors. Adjuvant chemotherapy for malignant or metastatic tumors; intracavitary cisplatin versus intravenous chemotherapy.
Prognosis	Good prognosis for benign tumors. Relatively high metastatic rate in malignant epithelial tumors. Chemotherapy may prolong survival but little data is available.

age,<sup>21,39</sup> and oldest 20 years old.<sup>40</sup> Dysgerminomas in the canine tend to be large; the reported size ranges from 2 to 30 cm, ovoid, with a smooth or nodular surface. A 2-year-old intact female rottweiler was diagnosed with an ovarian dysgerminoma and, within 2 weeks of exploratory laparotomy, was diagnosed with intracranial metastasis.<sup>39</sup> The age of cats that have been reported to have dysgerminomas ranges from 1 to 17 years of age; with a median of 5 years in a group of 6 cats.<sup>21</sup> Tumors have been bilateral in some cases and metastases have been identified.<sup>18,21,26</sup> Two of 6 feline dysgerminomas in one report had metastasized.<sup>19</sup> There are reports of mixed tumors (dysgerminoma and teratoma) in cats.<sup>20,24</sup> Clinical signs in patients with dysgerminomas may include a palpable abdominal mass, bloody vaginal discharge, polyuria, polydipsia, emesis, weight loss, diarrhea and lethargy. Cystic endometrial hyperplasia, and signs of persistent proestrus/estrus are seen in some patients compatible with hormone production. Some dogs will have a concurrent pyometra (5 of 7 in one study), which may be the underlying cause of some of the clinical signs.<sup>18</sup>

Teratomas are typically identified in younger animals (range, 2-8 years of age; median, 4 years; canine) than the age of dogs with dysgerminomas.<sup>18</sup> Teratomas have been diagnosed in dogs ranging in age from 1 to 17 years.<sup>21</sup> The size of teratomas usually ranges from 2 to 10 cm, but masses up to 31 cm have been identified.<sup>41</sup> The youngest reported cat with a 15 × 11 × 10 cm ovarian teratoma was 5 months old at the time of diagnosis.<sup>42</sup> There is a report of a 10-month-old cat with an ovarian teratoma that presented for regular cyclic signs of estrus 4 months after ovariohysterectomy.<sup>43</sup> Sudden death was the presentation for a cat with a ruptured teratoma (or due to rupture of an adjacent ovarian blood vessel).<sup>24</sup> Clinical signs in dogs with teratomas are primarily due to the effects of a space-occupying mass and include depression, weight loss, palpable abdominal mass, distended abdomen, as well as intermittent episodes of intestinal obstruction in 1 dog.<sup>24,31</sup> Other signs include abdominal pain, hemoperitoneum, and sudden death due to massive hemorrhage.<sup>21</sup> Calcified abdominal masses are typically seen in dogs with teratomas; with mineralization/ossification observed on abdominal radiographs.<sup>18,24,29,31,44-46</sup> Mineralization although common is not always identified in canine teratomas.<sup>47</sup> Malignant teratomas (teratocarcinoma) have been recognized with metastasis within the abdominal cavity primarily but also to the lung.<sup>29-31</sup>

In one report, 20 of 69 dogs with ovarian neoplasms had ovarian adenomas; 6 of the 20 dogs had clinical signs of hormonal disturbance with either pyometra or cystic endometrial

hyperplasia.<sup>13</sup> The youngest reported cat with an ovarian interstitial gland tumor was a 2-month-old kitten.<sup>19</sup>

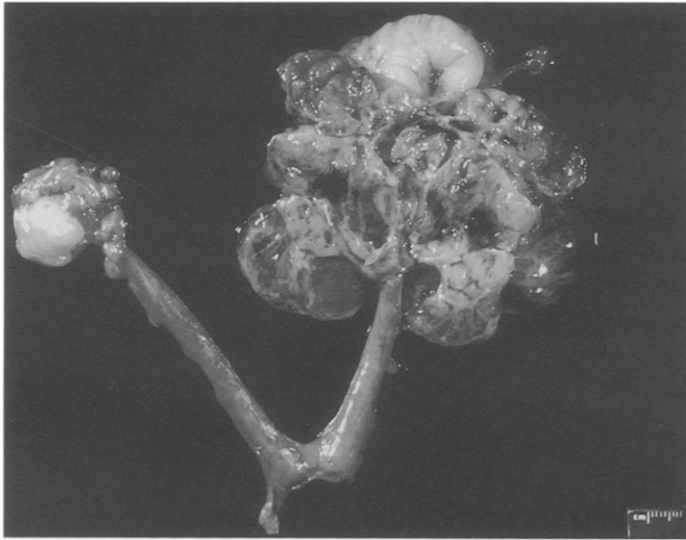
In a series of 276 canine ovarian tumors, 101 were granulosa cell tumors, and there were 8 thecomas and 5 luteomas.<sup>21</sup> The mean age of dogs with granulosa cell tumors is 10 years, range of 8-16 years.<sup>16</sup> Tumors have been reported in dogs as young as 14,<sup>48</sup> and 29 months of age.<sup>49</sup> Granulosa cell tumors may be functional and produce estrogen and/or progesterone with resultant clinical signs.<sup>50</sup> Bone marrow failure and severe hemorrhagic diathesis were reported in a dog with an estrogen secreting granulosa cell tumor.<sup>50</sup> Nineteen of thirty (63%) dogs with granulosa cell tumors had pyometra.<sup>13</sup> The majority, although not all, granulosa cell tumors are palpable at the time of presentation in small to medium sized dogs.<sup>8</sup> Granulosa cell tumors are typically benign but malignant tumors have been reported.<sup>13,51-53</sup> In one group of 30 dogs with granulosa cell tumors, 2 (6.7%) had evidence of metastasis.<sup>13</sup> Metastasis most commonly occurs to the peritoneal surfaces, but spread can be to multiple organs and sites including lymph nodes, liver, pancreas, spleen, kidneys, gastrointestinal tract, and meninges.<sup>51-52</sup>

Four of 9 (44%) cats with granulosa cell tumors had metastasis; and four of the cats had clinical signs of abnormal estrus.<sup>19</sup> Two other studies have indicated that over half of granulosa cell tumors in cats are malignant.<sup>20,54</sup> Metastasis is most commonly to the abdominal organs<sup>55</sup> and peritoneum but pulmonary metastasis can occur as well.<sup>20,56,57</sup> All five cats in one study showed signs of abnormal estrogen production (prolonged estrus; or cystic or adenomatous hyperplasia of the endometrium).<sup>20</sup> Additionally all 5 cats had a palpable abdominal mass.<sup>20</sup> Age of cats with granulosa cell tumors ranges from 3-16 years of age (unknown, 3, 10, 14, 16 years old).<sup>20</sup>

There is one reported case of a dog with an ovarian steroid cell tumor resembling a luteoma that was causing hyperadrenocorticism.<sup>58</sup> The signs resolved after ovariohysterectomy.

### Diagnostics

The ultrasonographic appearance and identification of ovarian tumors in dogs has been well described.<sup>7,49,58-62</sup> Ultrasound most commonly will identify an abdominal mass as ovarian in origin, or at least it will be included in the list of differentials.<sup>59</sup> Ovarian masses on ultrasound are classified as solid, solid with a cystic component or cystic.<sup>59</sup> Abnormalities in the uterus consistent with pyometra or cystic endometrial hyperplasia were identified on ultrasound in 5 of 10 dogs with confirmed ovarian tumors.<sup>59</sup> Abdominocentesis and/or thoracocentesis



**Fig 1. Unilateral ovarian adenocarcinoma. Ovariohysterectomy is recommended for ovarian tumors.**

and cytology are indicated in dogs with effusion. Additional diagnostics should include complete blood work and thoracic radiographs.

#### Treatment

Treatment for ovarian tumors most commonly entails surgical resection either ovariectomy or more commonly ovariohysterectomy (Fig 1). Ovariohysterectomy is indicated particularly in dogs with pyometra secondary to altered hormonal function due to the ovarian tumor. Dogs that are diagnosed with estrous cycle abnormalities or pyometra and have ovariohysterectomy performed should have histologic examination of the ovaries performed, even if the ovaries appear normal at surgery. Ovarian tumors can be present and only detected upon histopathologic sectioning.<sup>63</sup> Ovariectomy alone or ovariectomy in conjunction with removal of the ipsilateral uterine horn has been reported, with subsequent successful breeding.<sup>49</sup> Dysgerminomas are typically treated by surgical resection alone. It is thought that, because dysgerminomas are similar histologically to seminomas, they might be amenable to radiation therapy if alternate nonsurgical treatment is indicated.<sup>25</sup>

Dogs with functional granulosa cell tumors may require additional supportive treatment in conjunction with surgical resection to remove the estrogen source. Blood products and antibiotics may be indicated to support dogs in the perioperative and postoperative period. Depending upon the status of the bone marrow other supportive measures may include the use of granulocyte colony stimulating factor and erythropoietin to stimulate production of neutrophils and red blood cells, respectively. Granulosa cell tumors can appear benign on histologic examination with no evidence of metastasis at the time of surgery; however, metastasis a short time after surgical resection can occur.<sup>53</sup>

There are a limited number of reports on other approaches to the management of ovarian tumors and, specifically, metastatic ovarian tumors. Intracavitary cisplatin is one potential option for the management of dogs with diffuse abdominal disease.<sup>38,64</sup> There is one report on the combination of cytoreductive surgery and a 6-month course of intraperitoneal cisplatin for a dog with metastatic papillary adenocarcinoma with serosal implantation of tumor and peritoneal effusion.<sup>38</sup> The dog did well with

no evidence of tumor at the time of a second-look laparotomy at 6 months; but at 8 months after therapy, the dog had hemoperitoneum, but no necropsy was performed. Intraperitoneal drug administration is used to achieve a higher drug concentration in the peritoneal cavity. A 5½-year-old dog with metastatic bilateral papillary cystadenocarcinoma and bicavity malignant effusion was treated with ovariohysterectomy and a combination of cyclophosphamide, chlorambucil, CCNU, and bleomycin.<sup>65</sup> The dog was alive and free of apparent disease 10 months after the initial diagnosis.<sup>65</sup> Treatment should include cytoreductive surgery and potentially combination chemotherapy using an alkylating agent in conjunction with a platinum compound. A dog with ascites secondary to a metastatic adenocarcinoma of the ovary that was causing an extra-hepatic obstruction of the portal vein had resolution of signs and fluid after surgery alone with approximately 1-year follow-up after surgery.<sup>66</sup> Another dog with bilateral ovarian adenocarcinoma, mesenteric and peritoneal metastasis, and ascites had resolution of the abdominal fluid that persisted even 8 months after ovariohysterectomy alone.<sup>60</sup> A dog with metastatic granulosa cell tumor was treated with a combination of surgery and immunotherapy (mixed bacterial toxins) and was alive and apparently free of disease 2 years after diagnosis.<sup>1</sup> A 17-month-old cairn terrier with a granulosa cell tumor, and second retroperitoneal mass that extended into the left kidney capsule was managed with a combination of ovariohysterectomy and a course of oral cyclophosphamide.<sup>67</sup> Eleven weeks after surgery, the dog presented for signs compatible with tumor recurrence and was euthanized.<sup>67</sup>

#### Uterine Tumors

Uterine tumors occur infrequently. In a total population of 75,000 dogs, 3,073 tumor bearing dogs were identified of which 11 had uterine tumors; 10 leiomyomas, and 1 leiomyosarcoma.<sup>68</sup> In another study of 2,361 dogs with neoplasms, 9 dogs were identified that had tumors of the uterus/cervix.<sup>69</sup> In a study of 2,917 tumor bearing dogs, 9 (0.3%) had uterine tumors.<sup>3</sup> In general epithelial tumors of the uterus are malignant and the majority of mesenchymal tumors of the uterus are benign. In the dog uterine leiomyomas are reported most commonly, and leiomyosarcomas are comparatively rare.<sup>21,68,70</sup> There is a report of an extraluminal uterine leiomyoma in a 10-year-old intact female German shepherd that had parovarian and follicular cysts and elevated estrogen level.<sup>71</sup> Ultrasound was useful in identifying an intraluminal uterine mass (3 × 5 cm) that was subsequently identified as a uterine leiomyoma.<sup>62</sup> There is a neoplastic syndrome in German shepherd dogs that is characterized by multifocal renal cystadenocarcinomas, nodular dermatofibrosis, and multiple leiomyomas in the uterus in the majority (~80%-90%) of bitches diagnosed with this disease.<sup>72,73</sup> There is one report of an 11-year-old mixed breed dog with a large intramural uterine mass that was diagnosed as an angiolipoleiomyoma; a benign tumor reported to occur in humans.<sup>74</sup> There is one report of diffuse bilateral hemangiosarcoma of the uterus with invasion of the ovaries and broad ligament in a 15-year-old mixed breed dog.<sup>75</sup> Uterine carcinomas are rare. In 6000 canine tumors, there were no uterine carcinomas.<sup>76</sup> There are sporadic case reports. A 3-year-old mixed breed dog was diagnosed with an endometrial carcinoma that was speculated to be iatrogenic secondary to hormonal therapy (estrogenic and progestational steroids).<sup>77</sup> A

10-year-old beagle was diagnosed with a uterine carcinoma that may have been secondary to whole body radiation exposure when less than a year of age.<sup>51</sup> A 7-year-old mixed breed dog was diagnosed with a poorly differentiated carcinoma of the uterus with metastasis to the myocardium.<sup>78</sup> An adult Terrier was diagnosed with a large (25 × 16 × 7 cm) lipoma of the uterine broad ligament.<sup>21</sup> Lipomas of the broad ligament in dogs occur occasionally, and are typically pedunculated 2-4 cm oval or spherical masses.<sup>36</sup> Both dogs and cats with lymphoma can have secondary involvement of the uterus rarely.<sup>36</sup>

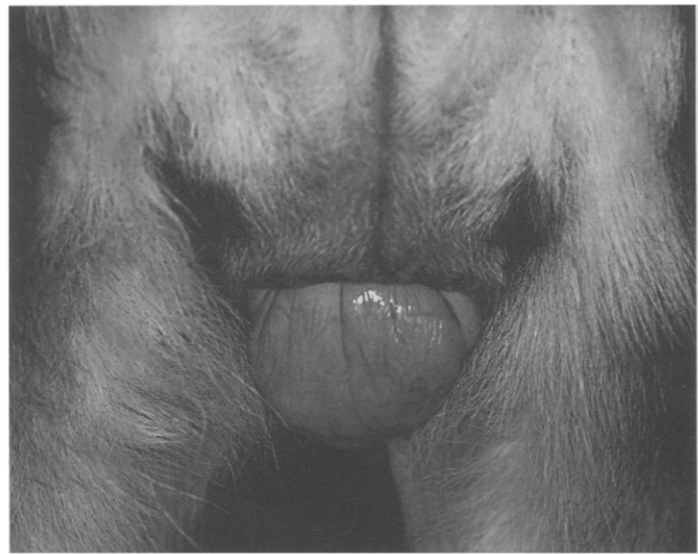
In a survey of 256 cats with tumors, one uterine adenocarcinoma and one uterine adenoma were identified, both in 4-year-old cats.<sup>79</sup> In a survey of 464 tumors from cats there were a total of 42 tumors of the genital system with one uterine lymphosarcoma.<sup>80</sup> Uterine leiomyomas in cats are often multiple and are observed less frequently than in the dog but are relatively common.<sup>21</sup> Uterine adenocarcinoma was reported in a 15-year-old Siamese with an 8 cm invasive tumor with metastasis to the visceral and parietal peritoneum, omentum, diaphragm, and lungs.<sup>81</sup> A 10-year-old Persian with a large endometrial adenocarcinoma with metastasis to the pelvic and abdominal peritoneum, and small metastases in both ovaries.<sup>20</sup> Other tumors reported to occur in the feline uterus include a carcinosarcoma, fibroma, and papillary adenocarcinoma.<sup>82</sup> A 12-year-old female cat presented with signs of decreased vision, and on fundic examination had areas of retinal hemorrhage and detachment. The cat was euthanized and the diagnosis was uterine adenocarcinoma with ocular metastasis.<sup>83</sup> One report of a cat with a metastatic uterine squamous cell carcinoma raises the question of tumor origin as squamous cell carcinoma would more likely arise from the cervix than the uterus.<sup>84</sup>

### Clinical Presentation

Clinical signs are typically not evident until a uterine tumor reaches a large size. Presenting signs may include an alteration in estrus cycle, vaginal discharge (purulent to hemorrhagic), polydipsia, polyuria, vomiting, weight loss, and abdominal distension.<sup>37</sup> A secondary pyometra may develop secondary to an estrogenic effect on the uterus. Radiographic evaluation of the abdomen may be suggestive of a mass but localization to the uterus may be difficult before exploratory laparotomy. Ultrasonographic examination is commonly performed and is likely to provide localization of a mass lesion to the uterus. It should be remembered that it is possible for tumors to arise in normal tissue that can remain after an incomplete hysterectomy. For example, an endometrial adenocarcinoma developed in a spayed cat in the remaining 2 cm of uterine tissue, with subsequent death due to multiple abdominal metastases.<sup>84</sup> Other clinical signs on presentation may depend on the site of metastasis with partial blindness and neurologic signs occurring in cats with metastasis to the eyes, and brain, respectively.<sup>85</sup> Metastasis from uterine tumors in cats have been reported in the eyes, cerebrum, ovaries, adrenal glands, lung, liver, kidneys, bladder, colon, diaphragm, and regional lymph nodes.<sup>83,85</sup>

### Treatment

Treatment entails ovariohysterectomy. It should be noted that any patient with estrous cycle abnormalities or pyometra could potentially have an underlying neoplastic process so close inspection and histopathology is indicated for any patient undergoing surgery for a pyometra.



**Fig 2. Vaginal hyperplasia and prolapse in a young intact female mixed breed dog.**

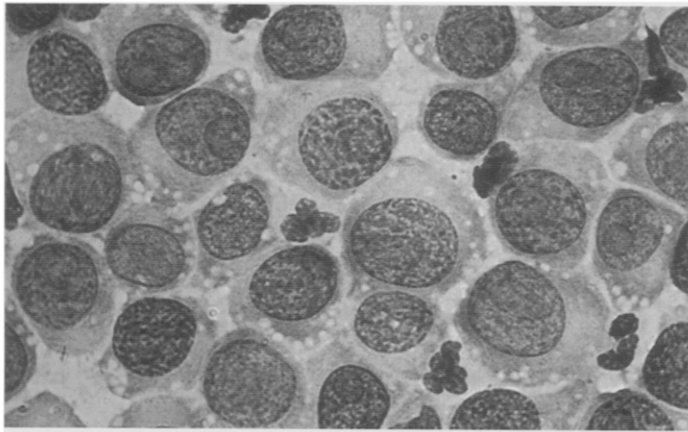
### Vaginal and Vulvar Tumors

Vaginal and vulvar tumors are reported to represent 2.4-3% of tumors in tumor-bearing dogs.<sup>68,69</sup> In a study of 2,917 tumor-bearing dogs, 56 (1.9 %) had tumors of the vagina and/or vulva.<sup>3</sup> Reproductive tract tumors in female dogs most commonly involve the vagina/vulva presumably to the number of dogs that are neutered with removal of the other parts of the reproductive tract. In one survey of 2,361 canine neoplasms there were 70 tumors of the vagina and vulva, 25 ovarian tumors, and 9 tumors involving the uterus/cervix.<sup>69</sup> The majority of the tumors at this site are benign.<sup>86</sup> In a survey of a total of 3,073 tumor-bearing dogs there were 85 (2.8%) dogs with tumors of the vagina or vulva with the majority (78%) of the tumors diagnosed as leiomyoma.<sup>68</sup> Leiomyomas are benign tumors of smooth muscle origin. The other tumors included 9 transmissible venereal tumors, 5 lipomas, 3 leiomyosarcomas, 1 mast cell tumor, and 1 epidermoid carcinoma.<sup>68</sup> In a review of 99 dogs with vulvar or vaginal tumors there were 72 benign, 17 malignant and 10 TVTs.<sup>86</sup>

It should be noted that intact female dogs more commonly present with an apparent mass that is actually a vaginal prolapse secondary to focal vaginal hyperplasia during proestrus (Fig 2).<sup>87</sup> In a report of 44 dogs with vaginal or vestibular masses, 18 of 44 (41%) had a vaginal prolapse; and the majority were large breed young (mean age of 2 years) intact dogs.<sup>87</sup>

### Diagnostics

Evaluation of a suspected vaginal mass should include vaginal and rectal palpation, evaluation of the stage of the estrous cycle (vaginal cytology, serum progesterone level), vaginoscopy, and biopsy prior to definitive surgical resection to determine the nature of the mass. Aspiration cytology may be diagnostic and is particularly useful for TVTs, which are readily diagnosed based on cytology (Fig 3) and which may then obviate the need for further diagnostics such as biopsy. Additional diagnostics can be performed based on the initial assessment of the mass and may include abdominal ultrasound and thoracic radiographs to assess for regional and pulmonary metastasis. Specific staging tests may be indicated depending on the diagnosis of the primary tumor. For instance, for mast cell tumors in this loca-



**Fig 3. Cytology from a vaginal transmissible venereal tumor. Relatively homogeneous population of ovoid cells with large nuclei, and multiple intracytoplasmic vacuoles.**

tion full staging is warranted and may include abdominal ultrasound, regional lymph node aspiration if feasible, bone marrow aspirate, and buffy coat smear; to assess the patient for evidence of local and distant metastasis of the mast cell tumor.

### Pathology

In a report of 99 dogs with vaginal or vulvar tumors, 73% (72 of 99) were benign and 83% (60 of 72) of the benign tumors were leiomyomas, fibromas, or polyps.<sup>86</sup> Clinically and histologically this group of benign tumors are classified together and other authors have classified all of these under the heading of leiomyomas because of the similarity.<sup>68</sup> The histopathologic diagnosis for a series of 72 dogs with benign tumors of the vulva/vagina included fibroma (27), leiomyoma (26), polyp (7), lipoma (4), nerve sheath tumor (3), fibrous histiocytoma (2), benign melanoma (1), myxoma (1), and myxofibroma (1).<sup>86</sup> The histopathologic diagnosis for a group of 17 dogs with malignant tumors included leiomyosarcoma (10), squamous cell carcinoma (4), hemangiosarcoma (1), osteosarcoma (1), and adenocarcinoma (1).<sup>86</sup> There is a case report of a 9-year-old German shepherd with an infiltrative vulvar and vestibulovaginal hemangiosarcoma.<sup>88</sup> Mast cell tumors can occur on the vulva and in the perineal region. Tissue biopsy is required to determine tumor grade; but it is important to remember that mast cell tumors in this location are associated with more aggressive behavior and are more likely to metastasize regardless of grade.

Urinary tract carcinomas may secondarily involve the vagina and vestibule and should be included in the list of differentials for tumors occurring in this region; and for dogs presenting for vaginal discharge.<sup>89-93</sup> Metastasis to this site is rare but has been reported. Vaginal smears in 5 dogs with mammary carcinoma

(all of the inguinal gland, and with regional lymph node metastasis) contained cells that were similar to those of the mammary tumor.<sup>94</sup> Necropsy of 3 of the dogs revealed micrometastasis of the mammary gland tumor in the submucosa of the vagina.<sup>94</sup>

### Clinical Presentation

The age of a group of 66 dogs with vulvar/vaginal leiomyomas ranged from 5 to 16 years with a mean of 10.8 years.<sup>68</sup> There is a report of a 2.5-year-old intact female Labrador retriever with a vaginal leiomyoma.<sup>95</sup> Dogs with TVTs tend to be younger with a reported range of 2-7 years and mean of 4.1 or 4.4 years.<sup>68,86</sup> Most dogs with vaginal leiomyomas are intact females; supportive of the supposition that these tumors are estrogen dependent.<sup>90</sup> The duration of clinical signs prior to diagnosis varies based on whether the growth is intraluminal or extraluminal; shorter duration expected with intraluminal growth.<sup>68</sup> Clinical signs are typically vulvar discharge and mass protruding from the vulva (Table 2).<sup>86</sup> Other signs include perineal swelling, stranguria, hematuria, tenesmus, and excessive licking of the vulvar region.<sup>68,86</sup> Dogs with vaginal TVTs will typically present for bleeding and often a mass will be visible. TVTs are red, proliferative, friable tumors that bleed easily. In a report of 99 dogs with vulvar/vaginal tumors 49% were characterized as pedunculated or polypoid and all of these were benign.<sup>86</sup> In the same study, 27% were sessile, broad based, or irregular and 7 of these were malignant and 10 were TVTs, with all of the TVTs characterized as friable and hemorrhagic.<sup>86</sup> There is a report of two cats that presented for chronic constipation (ages, 8 years and 14 years, respectively) that were both diagnosed with vaginal leiomyoma as the cause of the obstruction.<sup>96</sup>

Vaginal and vulvar lipomas grow slowly over a long time period, and dogs typically do not present until the tumors are quite large (n = 5 dogs; range, 5-20 cm diameter).<sup>68</sup> Leiomyosarcoma has the potential to metastasize; in a group of three dogs with vaginal leiomyosarcoma 1 dog had metastasis to the spleen.<sup>68</sup> Although leiomyosarcoma is associated with potentially more aggressive behavior it is of interest to note that one 15-year-old dog with a vaginal leiomyosarcoma underwent local tumor resection four times over a 2.5 year period, and died with recurrent disease and no evidence of metastasis.<sup>68</sup>

### Treatment

Treatment is surgical resection; and is likely curative for benign tumors.<sup>90,97</sup> The majority of vaginal tumors can be easily resected by episiotomy and local resection, but some tumors may require a more aggressive resection.<sup>86,90</sup> A technique that allows resection of more extensive tumors uses a combination of

**TABLE 2. Clinical Summary of Canine Vaginal and Vulvar Tumors**

Clinical presentation	Mass protruding from the vulva and vaginal discharge are the most common clinical signs. Other signs include perineal swelling, stranguria, hematuria, tenesmus and excessive licking of the vulvar region.
Diagnostics	Vaginal and rectal palpation. Evaluation of stage of the estrous cycle (vaginal cytology, serum progesterone level). Vaginoscopy. Biopsy and histopathology. Other diagnostics as indicated to potentially include complete blood work, abdominal ultrasound and thoracic radiographs.
Treatment	Surgical resection. Vincristine intravenous chemotherapy for transmissible venereal tumors.
Prognosis	Majority of tumors at this location are benign and surgery is curative.

vulvovaginectomy and perineal urethrostomy.<sup>88,89</sup> This technique allows resection of the distal urethra if necessary and dogs maintain urinary continence. In a report of 99 dogs the mean survival of dogs with benign tumors was 18 months; and 11.6 months for 9 dogs with malignant tumors.<sup>86</sup> It should be noted that there were no tumor related deaths among the 43 dogs with benign tumors; and only 1 tumor related death in the group of dogs with malignant tumors.<sup>86</sup> Based on follow up information in 58 dogs: 14% (n = 8 dogs) had tumor recurrence, 4 dogs with benign tumors.<sup>86</sup> Furthermore of the 4 dogs with recurrent benign tumors, 3 were sexually intact, and with surgery on the primary combined with OVH have remained tumor free.<sup>86</sup> Benign tumors at this site are thought to be hormonally (estrogen) related, while malignant tumors are more common in spayed females.

There is one report of a dog with a recurrent anaplastic sarcoma (probable rhabdomyosarcoma) of the vagina that was unresponsive to a combination of doxorubicin and cyclophosphamide.<sup>89</sup> The vaginal tumor recurred 7 months after surgery, and by 10 months after surgery the dog was dead.

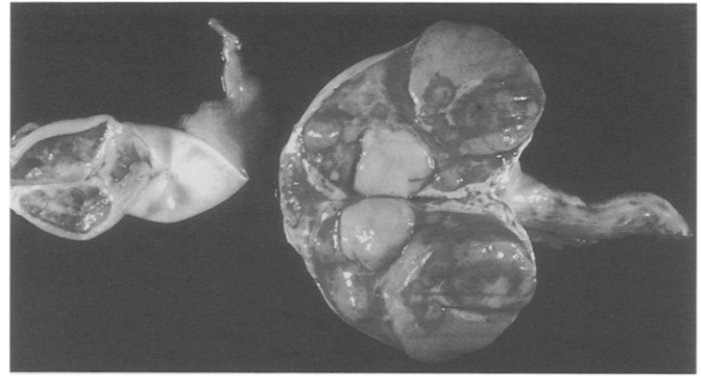
Chemotherapy is warranted in the management of mast cell tumors that occur on the vulva and in the perineal region. A number of different protocols are in use, including lomustine (CCNU) or combination intravenous vinblastine and oral prednisone.<sup>98,99</sup>

TVT is a chemoresponsive tumor most commonly treated with weekly intravenous vincristine at a dose of 0.7 mg/m<sup>2</sup>.<sup>100,101</sup> Chemotherapy treatments are continued until 1-2 treatments beyond full clinical remission of the tumor. There are reports of surgical management of TVTs but recurrence is more likely with surgery.<sup>102</sup> One dog that underwent surgical resection of a vaginal TVT had an OVH performed 5 weeks later due to suspected pyometra. On histopathology there was evidence of metastasis to the uterus as well as chronic purulent endometritis.<sup>68</sup> TVTs can metastasize; and will most commonly go to the regional lymph node. Chemotherapy is still effective in this setting. Another alternative treatment option for localized disease is external beam radiation therapy.<sup>100,103</sup> A relatively low total dose of radiation (10-30 Gy) can be curative; and is effective in patients that have failed previous surgery and chemotherapy.<sup>103</sup>

## Male Reproductive Tract Tumors

### Testicular Tumors

In male dogs, the testicle is the second most common site of tumor development.<sup>104</sup> In a 12-year hospital-based cancer survey, there were a total of 178 testicular tumors (7%) in 2,550 dogs with cancer from a total population of 60,000.<sup>105</sup> A survey included 580 unselected male dogs that were submitted for routine necropsy with sectioning and histopathology performed on all testicles<sup>106</sup>: 94/580 (16%) had testicular tumors, and 39/94 (41%) had more than one type of testicular tumor. In this survey, there were 56 interstitial cell tumors, 45 seminomas and 36 sertoli cell tumors.<sup>106</sup> These three most common types of testicular tumors overall occur at approximately equal frequency.<sup>107</sup> In a survey of 410 dogs with testicular tumors there were 137 sertoli cell tumors, 127 seminomas, and 96 interstitial cell tumors.<sup>104</sup> In a study of lifetime occurrence of neoplasia in a combined total of 241 German shepherds and Belgian Malinois, seminoma was the malignancy that occurred



**Fig 4. Gross appearance of a testicle with both an interstitial cell tumor and a functional seminoma. Contralateral testicle is atrophied.**

most frequently.<sup>108</sup> Sertoli cell tumors arise from the sustentacular cells of seminiferous tubules. Seminomas arise from the germinal epithelium of seminiferous tubules. Interstitial cell tumors arise from Leydig cells between seminiferous tubules. The three most common testicular tumors have relatively distinct gross appearances, but histopathology is required to make a definitive diagnosis. Sertoli cell tumors are typically firm, lobulated, white or gray surface, and are greasy on palpation. Seminomas typically are homogeneous, soft and bulging, may be lobulated, and are cream colored on the cut surface. Interstitial cell tumors are soft, bulging, and bright yellow or orange on the cut surface, and often contain cysts with clear or bloody fluid. Multiple as well as bilateral testicular tumors are common particularly in older dogs. In a study of 198 dogs with testicular tumors, the age range was 3-19 years with a mean of 10.2 years and 38 of 198 (19%) had more than one type of testicular tumor.<sup>109</sup> In a study of 410 dogs with testicular tumors; 45 (11%) had two different types of testicular tumors (Fig 4) and 1 dog had three different types of testicular tumors.<sup>104</sup> Metastasis to or involvement of the testicles has been reported to occur with canine lymphoma, and rarely in dogs with hemangiosarcoma.<sup>21</sup> In general interstitial cell tumors are small and may not be detectable on clinical examination. Sertoli cell tumors and seminomas are frequently large palpable tumors, and particularly sertoli cell tumors may be associated with clinical signs of feminization syndrome.<sup>3</sup> In a study of 207 cases of testicular tumors over a period of 3+ years diagnosed by surgical biopsy or necropsy examination, there were 60 sertoli cell tumors, 62 seminomas, and 87 interstitial cell tumors; 10/207 dogs demonstrated hematologic abnormalities (eg, anemia, leukopenia, pancytopenia) associated with the testicular tumors.<sup>110</sup> Blood dyscrasias associated with hyperestrogenism are most commonly associated with sertoli cell tumors, but has been reported to occur with seminomas and interstitial cell tumors.<sup>110</sup> In a group of 10 dogs with blood dyscrasias associated with a testicular tumor, 8 were sertoli cell tumors, and there was 1 seminoma and 1 interstitial cell tumor.<sup>110</sup> Boxers have been reported to be over-represented based on several studies.<sup>3,104,109,111</sup> In dogs with undescended testicles tumors develop more frequently in the right testicle; but this is likely due to the fact that the right testicle is twice as likely to not descend.<sup>112</sup>

Testicular torsion is uncommon but dogs that present due to torsion of the spermatic cord most commonly have a testicular tumor; and the majority are intra-abdominal.<sup>113</sup> Dogs with retained testicles may develop tumors at an earlier age. In one study, the cryptorchid dogs with sertoli cell tumors were on

**TABLE 3. Clinical Summary of Canine Testicular Tumors**

Clinical presentation	Majority of dogs are asymptomatic; and a testicular mass is detected on physical examination. There may be contralateral testicular atrophy in dogs with functional testicular tumors. Signs of feminization syndrome most commonly seen with sertoli cell tumors including gynecomastia, galactorrhea, attraction of males, symmetrical alopecia, pendulous prepuce, change in semen quality, and signs of bone marrow suppression. Dogs with interstitial cell tumors and increased testosterone may present with perineal hernia, tail gland and perianal gland hyperplasia and adenomas.
Diagnostics	Physical examination and palpation of the testicles. Ultrasound examination of the testicles and abdomen. Complete blood work particularly in dogs with clinical signs of hyperestrogenism.
Treatment	Orchiectomy is the treatment of choice. Cisplatin chemotherapy for metastatic sertoli cell tumors or seminomas. Limited information available on efficacy. Radiation therapy effective in treatment of metastatic seminomas based on a small series of cases.
Prognosis	Majority of dogs are cured with surgery alone. Guarded prognosis in dogs with hyperestrogenism and bone marrow failure. Treatment should include supportive measures such as antibiotic therapy, and blood products.

average 1.7 years younger than dogs with scrotal testes with tumors.<sup>114</sup> The mean age of dogs based on tumor location was 7.8 years (abdominal), 8.8 years (inguinal) and 11 years (scrotal) in a series of dogs with sertoli cell tumors.<sup>111</sup> There is a significant association between cryptorchidism and sertoli cell tumors and seminomas; but not interstitial cell tumors.<sup>3</sup> Additionally, there is a significant association between cryptorchidism and the development of sertoli cell tumors in dogs at an earlier age.<sup>3</sup> One study investigated the prevalence of cryptorchidism in a group of 176 dogs with testicular tumors and a group of breed-matched controls; 58 of 108 (54%) dogs with sertoli cell tumors and 23 of 68 (34%) dogs with seminomas were in cryptorchid testes compared with 10% prevalence of cryptorchidism in the control group.<sup>111</sup>

Testicular tumors are rare in cats. In a review of 395 feline tumors there were no testicular tumors identified.<sup>3</sup> There are only isolated case reports of testicular tumors in cats. There is one report of a 2-year-old cat with a teratoma that developed in a unilateral cryptorchid testis with metastasis to the omentum; the cat died secondary to metastasis a little over one month after surgery.<sup>115</sup>

### Clinical Presentation

The majority of dogs with testicular tumors are asymptomatic; and a testicular mass is an incidental finding (Table 3). Breeding dogs may present with a change in fertility.

**Seminoma.** In one study of 45 dogs with seminomas, approximately 1 in 9 dogs over 4 years of age had a seminoma; and in less than one-third of the dogs was the tumor detectable on physical examination.<sup>106</sup> Of the dogs with seminomas 8 of 45 (18%) had bilateral tumors. The seminomas ranged from 1 mm to 10 cm in diameter, but 75% were less than 2 cm. Seminomas were discrete masses that were pale cream to grayish in color, firm and homogeneous tissue. Gross metastases were identified in 3 of the 4 dogs that were ultimately determined to have metastases. The overall metastatic rate was 9%, with metastasis to the iliac lymph nodes in 3 dogs, and iliac and para-aortic lymph nodes involved as well as multiple pulmonary metastases in 1 dog.<sup>106</sup> Three of 47 (6%) dogs, all with retained tumorous testicle, had metastasis to the sublumbar lymph nodes in all 3 dogs, and in 2 dogs to the mesenteric lymph nodes and spleen as well.<sup>109</sup> Metastasis of seminomas is relatively uncommon but is reported.<sup>106,116-118</sup> One study reports a 7-year-old male coonhound with a seminoma that metastasized widely to the thoracic and abdominal viscera, internal and peripheral lymph nodes, meninges of the brain, and both eyes.<sup>116</sup> In a 9-year-old

male Scottish terrier, a seminoma of the right testicle had spread to the epididymis and adjacent lymphatics as well as to the regional lymph nodes and omentum.<sup>118</sup> In a report of 47 dogs with 55 seminomas, 62% (34) were scrotal, 24% (13) were abdominal, and 7.5% (4) were inguinal in location.<sup>109</sup> Signs of feminization syndrome can occur with seminomas, although it is far less common than with sertoli cell tumors. In a group of 47 dogs with seminomas, 1 dog had a pendulous penile sheath and 2 had evidence of alopecia.<sup>109</sup> In another report, an 11-year-old male toy poodle with alopecia was diagnosed with a seminoma at the time of castration; the alopecia subsequently resolved.<sup>119</sup>

A 3.6-year-old intact female collie was diagnosed with lateral hermaphroditism, and seminoma.<sup>120</sup> There are three forms of hermaphroditism. In unilateral hermaphroditism one gonad is an ovotestis, and the other is a testis or an ovary. Bilateral hermaphrodites have two ovotestes. In lateral hermaphroditism, one gonad is a testis and one is an ovary.

An excess of seminomas was observed in Vietnam service U.S. military working dogs, the majority of which were German shepherd dogs.<sup>121</sup> The potential risk factors included exposure to zoonotic infections, chemical pesticides, phenoxy herbicides and extensive use of therapeutic drugs such as tetracycline.<sup>121</sup>

There is a report of a bilateral cryptorchid 2-year-old cat with a seminoma that was euthanized one year after surgery due to metastasis to the sublumbar lymph nodes causing obstipation.<sup>5</sup>

**Sertoli cell tumor.** In a survey of 67 dogs with testicular sertoli cell tumors, the mean age was 9.5 years, the majority were unilateral but were bilateral in 4/67 (6%), 20 (30%) were abdominal, 7 (10%) were inguinal and the rest were scrotal in location.<sup>114</sup> In a group of 8 dogs with sertoli cell tumors and bone marrow hypoplasia the age ranged from 2.5 to 13 years (mean of 7 years).<sup>122</sup> In a group of 58 cryptorchid dogs with sertoli cell tumors, 34 (59%) were located in the abdominal cavity, and 24 (41%) were in the inguinal region.<sup>111</sup> Clinical signs of feminization with alopecia was noted in 21 dogs, and symmetrical alopecia alone in 17 dogs for a total of 57% of the dogs showing signs of estrogen production. Additionally, feminization is more frequently observed in dogs with retained testicles.<sup>109,111,114,123</sup> In a group of 108 dogs with sertoli cell tumors; signs of feminization occurred in 16.7% of dogs with scrotal tumors, 50% of dogs with inguinal tumors, and 70.4% of dogs with abdominal tumors.<sup>111</sup> Signs associated with feminization syndrome include: gynecomastia (Fig 5), galactorrhea, attraction of males, atrophy of the scrotal non-neoplastic testicle, symmetrical alopecia (Fig 6), cutaneous hyperpigmenta-





**Fig 5. Evidence of gynecomastia in an intact dog with a functional intra-abdominal retained tumorous testicle and hyperestrogenism.**

tion, epidermal thinning, squamous metaplasia of the prostatic epithelium, atrophy of the prepuce or pendulous prepuce, change in semen quality, and signs of bone marrow suppression.<sup>109,122-124</sup> In dogs that have prostatic hyperplasia due to squamous metaplasia, prostatic cysts and or abscesses are often observed as well.<sup>125-127</sup> The effect of estrogen on the bone marrow is a transient increase in granulocytopoiesis and neutrophilic leukocytosis which is followed by progressive leukopenia, thrombocytopenia and nonregenerative anemia.<sup>110,122</sup> The clinical signs in a group of 8 dogs that had bone marrow hypoplasia secondary to sertoli cell tumors included hemorrhage secondary to thrombocytopenia, anemia secondary to blood loss or decreased erythrocyte production, and infection with fever due to neutropenia.<sup>122</sup> In a group of 37 dogs with sertoli cell tumors, 20 (54%) had symmetrical alopecia, gynecomastia in 16 (43%), and attraction of other male dogs was identified in 5 (14%).<sup>123</sup> Hyperprogesteronemia was determined to be the cause of alopecia in an 11-year-old Airedale terrier.<sup>128</sup> Of 17 dogs with sertoli cell tumors, 4 had non-regenerative anemia; bone marrow aspiration was done in 2 dogs and 1 had pancytopenia and 1 had erythroid aplasia.<sup>124</sup> Lethargy is another sign reported with sertoli cell tumors. This may be due to the effect of estrogen on the thyroid gland; have identified atrophied thyroid glands in dogs at necropsy.<sup>123</sup> Of 67 dogs with sertoli cell tumors six (9%) had confirmed or suspected metastasis.<sup>114</sup> In another report 4 of 37 (11%) dogs developed metastasis to the iliac lymph nodes primarily, but also to other lymph nodes, spleen, liver and kidney.<sup>123</sup> A 15-year-old mixed breed dog with metastasis of a sertoli cell tumor to the lung and kidneys had hypertrophic osteoarthropathy.<sup>129</sup>

In one study of 36 dogs with sertoli cell tumors clinical signs of estrogen production by the tumor was identified in only 6/36 (17%); and included bilaterally symmetrical alopecia (6 dogs), gynecomastia (6 dogs), and mammary hypertrophy (2 dogs).<sup>106</sup> All 6 of these dogs had gross enlargement of the affected testicle and atrophy of the other testicle. The other 30 dogs in the study did not have any clinical signs of estrogen activity and only 9/30 (30%) had testicular enlargement. Bilateral involvement was noted in 4/36 (11%). Metastases were detected in 5 of 36 dogs (14%) with metastasis to the iliac lymph nodes in 5, lung in 3, liver in 1, kidney in 2, and spleen in 1 dog.<sup>106</sup> There is a report of two dogs that had massive scrotal swelling that was partially reducible into the abdominal cavity but in each case was due to a sertoli cell tumor; and there was metastasis in both dogs.<sup>130</sup>

There is a syndrome reported in middle-aged miniature schnauzers of sertoli cell tumors in cryptorchid male pseudohermaphrodites.<sup>131,132</sup> In compiling several reports there have been a total of 6 dogs with this syndrome.<sup>131-134</sup> In these dogs the uteri have undergone endometrial cystic hyperplasia, or have developed mucometra or pyometra.<sup>131-132,135</sup>

There is a report of 2 cats with sertoli cell tumors; with metastasis to the liver and spleen in one cat that was a bilateral cryptorchid.<sup>136</sup>

*Interstitial cell tumor.* Interstitial cell proliferations are diagnosed as hyperplasia, adenoma and carcinoma, but can be difficult to differentiate. Interstitial cell tumors are typically small nonpalpable discrete masses, and are often an incidental finding.<sup>137</sup> In a series of 56 dogs with interstitial cell tumors, 9 of 56 (16%) had testicular enlargement, 24 of 56 (43%) had bilateral tumors, and none of the dogs had any signs of hormonal imbalance. The majority of the tumors were less than 2 cm in diameter<sup>106</sup>; and none of the dogs had evidence of metastasis.<sup>106,109</sup> Interstitial cell tumors metastasize very rarely.<sup>106</sup> It has been stated that interstitial cell tumors are always reported to occur in the scrotum.<sup>109</sup>

Interstitial cell tumors have been associated with increased production of testosterone and a high prevalence of prostatic disease and perianal gland neoplasms. Interstitial cell tumors



**Fig 6. Symmetrical alopecia in a dog with a sertoli cell tumor and hyperestrogenism.**

may contribute to an increase in perineal hernia, tail gland and perianal gland hyperplasia and adenomas.<sup>104,109,138</sup> Perianal gland hyperplasia can present as multiple discrete nodules or a diffuse bulging perianal ring.<sup>138</sup> These changes will regress after castration.<sup>138,139</sup> There are only isolated case reports of dogs with interstitial cell tumors with bone marrow hypoplasia and signs of feminization.<sup>110,140</sup>

There is one report of a 13-year-old cat with a testicular interstitial cell tumor that was an incidental finding at necropsy.<sup>21</sup> There is another report of two adult older cats with interstitial cell tumors.<sup>141</sup>

### Other Testicular Tumors

Testicular tumors arising from the stroma are rare. There are two reports of leiomyoma of the testicle, involving the testicular tunic in an 11-year-old beagle, and a 13-year-old miniature poodle.<sup>21,142</sup> There is one 11-year-old Labrador retriever with an enlarged right testicle that was castrated, and histopathology revealed it was a schwannoma.<sup>143</sup> There is one report of a dog with a testicular hemangioma but no other details were provided.<sup>104</sup>

Metastasis to the testes is rare but can occur. Three dogs that presented for testicular enlargement were ultimately diagnosed with primary gastrointestinal adenocarcinomas with metastasis to the testes.<sup>144</sup>

### Diagnostics

Due to the high incidence of testicular tumors in dogs, physical examination of intact male dogs, particularly older dogs, should include palpation of the testicles and assessment for both mass lesions and contralateral testicular atrophy. In dogs with clinical signs of hormone imbalance, serum testosterone, estrogen and/or progesterone levels can be measured.<sup>128,140,145,146</sup> A full evaluation may include complete blood work, urinalysis with culture if indicated, thoracic radiographs, and abdominal and testicular ultrasound. Abdominal radiographs may reveal a mass effect with a retained tumorous testicle.<sup>147</sup> A coagulation panel may be warranted in dogs that present with evidence of anemia, petechiae, ecchymoses, or hemorrhage. Abdominal ultrasound is done to evaluate patients for evidence of metastasis to the regional lymph nodes and/or abdominal organs. Ultrasound can assist in evaluating scrotal, inguinal as well as retained abdominal testicles; although the ultrasonographic changes in dogs with testicular tumors are not typically specific enough to predict the tumor type.<sup>137,148-150</sup> Ultrasonographic examination may be necessary to identify non-palpable testicular tumors that occur in dogs that present for infertility.<sup>151</sup> Altered spermatogenesis is commonly identified in dogs with testicular tumors.<sup>152</sup> Ultrasound guided aspiration biopsy of testicular masses may be indicated in valuable breeding animals.<sup>149</sup> Aspiration cytology can be done to rule out other causes of testicular disease.<sup>153</sup> Definitive diagnosis of testicular tumors is typically based on histopathologic examination after castration. A number of other diagnostics on testicular tumors have been evaluated, including measures of proliferative activity.<sup>154-159</sup> Immunohistochemistry may be necessary in a subset of tumors and can be useful in identifying the cell of origin.<sup>155,160</sup> The overexpression of p53 and p21 proteins have been identified in canine testicular tumors using immunohistochemistry.<sup>156</sup> AgNOR counts, an indirect measure of proliferation, in seminomas that ultimately

metastasized were significantly higher than the counts in behaviorally benign seminomas.<sup>157</sup>

### Treatment

Orchiectomy is the treatment of choice for testicular tumors, and is usually curative. Bilateral castration is recommended as based on one report 50% of the dogs had bilateral tumors, whereas only 12% of the tumors in the opposite testicle were clinically detected.<sup>112</sup> Unilateral castration is done in select instances.<sup>137,151</sup> Ultrasonographic evaluation of the opposite testis is advised. Exploratory laparotomy may be necessary in dogs with retained abdominal testicles. Laparoscopic surgery has been described in a cryptorchid dog for treatment of a seminoma.<sup>161</sup> In dogs with prostatic cysts additional surgery may be necessary such as marsupialization of the cyst.<sup>162</sup> In dogs with signs of feminization due to estrogen production by the testicular tumor; these signs are expected to resolve 2-6 weeks after castration unless metastases are present and there is a persistent source of estrogen.<sup>114</sup> Full regrowth of the hair coat is compatible with resolution of the hormonal imbalance.<sup>163</sup> Serum hormone levels can be documented to return to normal after castration.<sup>128,146</sup> For retained testicles requiring an exploratory laparotomy, the iliac lymph nodes should be assessed at surgery and biopsied if indicated to stage the tumor. Of 15 dogs with sertoli cell tumors showing feminization, follow up of 12 of the dogs indicated that all 12 had resolution of the clinical signs within 2-3 months.<sup>123</sup> Recurrence of signs of feminization after surgery has been associated with the development of regional lymph node metastasis.<sup>123</sup> Dogs with bone marrow hypoplasia secondary to estrogen toxicity require close monitoring after surgery to monitor for return of bone marrow function, and supportive care as necessary.<sup>164</sup> Of a group of 8 dogs with bone marrow hypoplasia secondary to sertoli cell tumors 1 was euthanized, 2 recovered after castration with supportive care, while the remaining 5 treated similarly died due to bone marrow failure.<sup>122</sup> Treatment of dogs with bone marrow hypoplasia includes: antibiotics as necessary, platelet rich plasma infusion for thrombocytopenia, fresh whole blood for anemia and thrombocytopenia, and close monitoring of clinical condition to monitor for response to therapy. Aplastic anemia in dogs with estrogen toxicity warrants a poor prognosis.<sup>110</sup>

Cisplatin had apparent efficacy in the treatment of 2 of 3 dogs that were treated for aggressive testicular tumors.<sup>165</sup> One dog underwent abdominal exploratory, resection of an intra-abdominal metastatic sertoli cell tumor then 5 cycles of cisplatin at 60 mg/m<sup>2</sup> IV every 3 weeks and was alive and doing well 31 months after surgery. A second dog with metastatic sertoli cell tumor with involvement of the liver and spleen was treated with 2 cycles of cisplatin and died 7 months after surgery. A third dog with metastatic seminoma diagnosed at the time of initial presentation received 3 cycles of cisplatin and died 5 months later of progressive disease.<sup>165</sup> One dog with a metastatic seminoma was treated with actinomycin-D, chlorambucil, and mithramycin with no effect.<sup>118</sup> Several dogs exhibited more than 50% reduction in measurable disease in dogs with metastatic sertoli cell tumors treated with chemotherapeutic agents including vinblastine, cyclophosphamide, and methotrexate.<sup>166</sup>

Radiation therapy has been used successfully to treat 4 dogs with metastatic seminoma that involved the sublumbar lymph

nodes; a total dose of 17-40 Gy.<sup>167</sup> Survival times ranged from 6-57 months, and none of the dogs died or were euthanized due to the seminoma.<sup>167</sup>

### Prostatic Tumors

Prostatic tumors are relatively uncommon in dogs and are rarely reported in cats.<sup>168,169</sup> In an 11-year study of nearly 4,500 dogs at necropsy the incidence of prostatic neoplasia was 0.35%.<sup>170</sup> In a retrospective study of 140 dogs with prostatic disease 22 (16%) had prostatic adenocarcinoma.<sup>171</sup> In a study of 177 dogs with prostatic disease 7.3% had prostatic adenocarcinoma but it was the most common disease identified in neutered dogs; and bacterial prostatitis and prostatic cysts were more frequently reported in intact male dogs.<sup>172</sup> In one study the average age of dogs with prostatic adenocarcinoma was 9.3 years with a range of 5-13 years.<sup>171</sup> The median age of 168 pet dogs with prostatic cancer was 10 years.<sup>173</sup> The majority of prostatic tumors are adenocarcinomas. In a report of 14 dogs with prostate cancer, 10 were diagnosed as adenocarcinoma and 4 were undifferentiated carcinomas on histopathology.<sup>174</sup> Other tumor types that have been identified in the prostate include undifferentiated carcinoma, transitional cell carcinoma, leiomyosarcoma, and squamous cell carcinoma.<sup>175-178</sup> Transitional cell carcinoma of the prostatic urethra frequently will invade the prostate; and it can be difficult to distinguish primary from secondary prostatic cancer. The most common sites of metastasis of prostatic carcinomas are the regional lymph nodes, lung, urinary bladder and bone.<sup>179</sup> Additional sites of metastasis include mesentery, rectum, pelvic musculature, heart, adrenal gland, kidney, spleen, and liver.<sup>179</sup> Metastasis of prostatic tumors can be via lymphatics as well as hematogenous with metastasis to the regional lymph nodes and bone respectively. In one study 5 of 12 (42%) of the dogs had evidence of bone metastasis.<sup>180</sup> In a necropsy study of 76 dogs with prostatic carcinoma, 80% had gross metastases with skeletal metastases identified in 22%.<sup>178</sup> Additionally, the youngest dogs were more likely to have skeletal metastases than the oldest dogs.<sup>178</sup> Metastatic sites included lymph node (39), lung (38), bone (17), liver (7), colon (6), kidney (5), heart (4), adrenal (4), brain (4), and spleen (1).<sup>178</sup> The 17 dogs with skeletal metastases had 29 axial and 9 appendicular skeletal lesions. Lumbar vertebrae (12), pelvis (5), and femur (5) were most commonly affected; and 36 of 38 (95%) of the lesions were proximal to the elbow or stifle.<sup>178</sup>

A 10-year-old intact male Boxer was diagnosed with a prostatic leiomyosarcoma that, on necropsy examination, was determined to have metastasized to the regional lymph nodes, mesentery, kidneys, and lung.<sup>176</sup> This prompted a search of the Veterinary Medical Data Base for mesenchymal tumors of the prostate. A total of 1,397 prostatic tumors were diagnosed over a 20-year period (1977-1997). Mesenchymal tumors accounted for 27 of 1,397 (1.9%) of all prostatic tumors. Hemangiosarcoma was the most common mesenchymal tumor of the prostate accounting for 18/27 (67%), there were no cases of leiomyosarcoma identified, but there were 3 cases of prostatic leiomyoma.<sup>176</sup> There is one report of a 9-year old mixed breed dog with primary lymphoma of the prostate.<sup>181</sup> Lymphoma of the prostate is uncommon but is more commonly associated with multicentric disease rather than as a primary site of involvement.<sup>36</sup> Metastasis to the prostate is rare.<sup>182</sup> A 10-year old mixed breed dog with medullary thyroid carcinoma had docu-

mented metastasis to the prostate as well as the regional lymph nodes, liver and spleen.<sup>183</sup>

There is no breed predilection but most dogs are medium to large breeds.<sup>170,178</sup> Tumors develop both in intact and castrated male dogs. It had been thought that prostatic carcinoma infrequently developed in castrated males,<sup>184</sup> but it has been shown that prostatic neoplasia develops in both castrated and intact male dogs.<sup>174,178,185</sup> Furthermore, two studies have suggested that there is actually an increased risk of prostatic adenocarcinoma in castrated male dogs compared to intact male dogs.<sup>185,186</sup> Prostatic carcinoma develops in dogs castrated both before and after the onset of puberty.<sup>185</sup> It is possible that the development of canine prostatic carcinoma is not hormonally mediated or nontesticular hormones arising from the adrenal glands may influence the development of prostatic cancer. The tumor in dogs does not appear to require androgens for the initiation or progression of cancer,<sup>187</sup> and does not appear to respond to androgen deprivation (antiandrogens or castration). It has been suggested that perhaps canine prostatic cancer represents end-stage disease that is androgen-independent.<sup>173</sup> There is one report of a dog with prostatic adenocarcinoma with concurrent sertoli cell tumor, and elevated estrogen levels secondary to the testicular tumor.<sup>126</sup> Based on a retrospective study of 76 dogs it was determined that prostatic carcinoma most frequently affected sexually intact dogs or dogs castrated after sexual maturity.<sup>178</sup> Further investigations will be necessary to determine the potential benefit, if any, of early castration.

### Clinical Presentation

Clinical signs in dogs with prostate cancer may include urinary tract signs, difficult or abnormal defecation, a range of systemic signs of illness, or lameness and pain secondary to bone metastasis.<sup>179</sup> A normal sized prostate on rectal in a neutered dog should be considered abnormal and may be compatible with prostatic neoplasia or other prostatic disease. Dogs may present due to signs of pain due to the bone metastasis and may have no direct signs that relate to the prostate gland.<sup>175,188</sup> In one study dogs with bone metastasis had a higher frequency of weight loss or emaciation, and lumbar pain compared to dogs without bone metastasis.<sup>180</sup> In a retrospective study of 76 dogs with prostatic carcinoma clinical signs were referable to the urinary tract (hematuria, stranguria, incontinence) in 62%, tenesmus due to prostatic enlargement was noted in 30%, signs referable to skeletal involvement was seen in 36%, and signs of systemic disease (weight loss, anorexia) occurred in 42% of the dogs.<sup>178</sup> 9/17 dogs with skeletal metastases first presented for clinical signs referable to these metastases, including myelopathic signs with vertebral metastasis (5), and lameness due to pelvic or long bone metastasis (4).<sup>178</sup> Hypertrophic osteopathy was diagnosed in a 7-year-old male beagle that presented for straining to defecate and was diagnosed with prostatic adenocarcinoma with metastases to the iliac and left renal lymph nodes but no evidence of pulmonary metastasis.<sup>189</sup> There was non-painful swelling of all four limbs secondary to the hypertrophic osteopathy, with classic radiographic changes detected.<sup>189</sup>

Cats with prostatic carcinoma have similar signs on initial presentation. Although infrequently reported, feline prostatic carcinoma is typically locally advanced at the time of diagnosis with evidence of metastasis.<sup>168,169</sup>

## Diagnostics

A systematic approach to the evaluation of dogs with suspected prostatic carcinoma is recommended to rule out other causes of prostatic disease such as benign prostatic hypertrophy, prostatitis, and prostatic cysts or abscesses.<sup>171,190-193</sup> Physical examination of the prostate gland is best achieved by a combination of rectal and abdominal palpation. The prostate on rectal palpation in dogs with prostatic cancer is typically large, firm, irregular, nodular, and/or asymmetric. It may be possible to palpate enlarged sublumbar lymph nodes in dogs with regional lymph node metastasis. Radiographic examination of the prostate and correlation to specific disease processes has been described.<sup>194,195</sup> Imaging should include evaluation of the prostate as well as the regional lymph nodes and lung for evidence of regional and distant metastasis. Radiographic examination of the prostate will frequently reveal an enlarged prostate and there may be evidence of mineralization within the prostate.<sup>186</sup> Multifocal, irregularly shaped, parenchymal mineral densities are most commonly seen with prostatic neoplasia, but this change has also been identified in chronic prostatitis.<sup>195</sup> Additionally, a 9-year-old male Labrador retriever with a 25 cm diameter prostatic mass with evidence of mineralization on ultrasound was ultimately diagnosed with nodular hyperplasia of the prostate and treated successfully with surgery.<sup>196</sup> Radiographic assessment of the sublumbar lymph nodes may reveal enlarged lymph nodes and in some cases reactive new bone along the lumbar vertebrae (typically the 4<sup>th</sup> – 7<sup>th</sup> lumbar vertebrae) and pelvis. Sites of bone metastasis include pelvis, lumbar vertebrae, as well as scapula, ribs and digits.<sup>180</sup> Metastatic bone lesions may be osteoblastic and/or osteolytic. The radiographic appearance of bone metastases in one study included osteoproliferative (3), osteodestructive (3), and mixed lesions (6).<sup>178</sup> The lumbar vertebrae are most frequently involved but it is also possible to see radiographic changes in the sacral and/or coccygeal vertebrae.<sup>180</sup> Bone scintigraphy may facilitate identification of bone metastasis sites in dogs with prostatic adenocarcinoma and should be considered in dogs that are to undergo prostatectomy.<sup>188</sup> Bone proliferation and/or lysis may occur due to direct extension or metastasis of prostatic carcinoma. There may be mineralization in the lumbar lymph nodes in dogs that have regional lymph node metastasis.<sup>180</sup> Contrast studies such as retrograde urethrography may show irregularities in the prostatic urethra, and reflux of contrast material may occur into the mass.<sup>197</sup> However, presence of contrast medium reflux is not specific for prostatic neoplasia. In a radiographic study of 30 dogs with various prostatic diseases, destruction or distortion of the prostatic urethra was seen only in dogs with neoplasia, but the appearance was not sufficient for differentiation of prostatic versus nonprostatic neoplasia.<sup>195</sup> The majority of cases currently are imaged using ultrasonography. Ultrasound allows visualization of the prostate and assessment of the regional lymph nodes for evidence of metastasis. There have been a number of reports on the ultrasonographic evaluation of the prostate.<sup>198-201</sup> It has been recommended that distension of the urinary bladder aids in visualization and evaluation of the prostate gland using a combination of ultrasonography and distention retrograde urethrography.<sup>200</sup> Cytologic evaluation of material from the prostate can be useful in the differentiation of neoplasia of the prostate from other prostatic diseases. In one report transitional cell carcinoma of the prostatic urethra in 2 dogs appeared cytologically similar to prostatic adenocarci-

noma cells.<sup>202</sup> Techniques that have been evaluated for the diagnosis of prostatic disease include ejaculation, prostatic massage, prostatic aspiration biopsy and punch biopsy.<sup>203-205</sup> A perineal punch biopsy technique using a needle biopsy has been reported to be an accurate method for diagnosing canine prostatic diseases, although in a report of 14 dogs where this procedure was used only one dog had a prostatic tumor.<sup>205</sup> A transperineal approach for aspiration and biopsy of the prostate has been used as opposed to a transrectal approach to avoid the possibility of infection secondary to bacterial contamination.<sup>203</sup> Cells from the prostate can be obtained by a prostatic massage.<sup>202,206</sup> Another method that has been shown to be useful in the diagnosis of prostatic neoplasia is a urethral brush technique done in conjunction with prostatic massage.<sup>207</sup> Although direct percutaneous aspirates of the prostate may be diagnostic, it is possible to seed tumor cells along the needle tract and this has been documented to occur.<sup>208</sup> Needle biopsies can be performed either peri-rectally or trans-abdominally. There is some risk of hemorrhage, trauma to the urethra, as well as tumor seeding using this technique. The other diagnostic approach is to perform an abdominal exploratory and biopsy of the prostate; with biopsy of the regional lymph nodes if indicated. Complete blood work, including urinalysis, is indicated but rarely contributes to the definitive diagnosis of prostatic neoplasia. Urinary tract infection may be present concurrently and urine culture should be done if there is evidence of an infection.<sup>186</sup> There is one report of a dog with prostatic carcinoma that had neoplastic cells in the peripheral circulation.<sup>209</sup> Serum and seminal plasma concentrations of acid phosphatase, prostate specific antigen, and canine prostate specific esterase have not been shown to be useful in the definitive diagnosis of canine prostatic adenocarcinoma.<sup>210,211</sup>

## Treatment

In reviewing a group of 21 dogs with prostatic carcinoma that received only palliative or supportive care (eg, castration, estrogen therapy, antibiotics) the dogs were all euthanized within 2 months after diagnosis.<sup>212</sup> It is not uncommon for dogs to be euthanized at the time of diagnosis due to the advanced stage of disease.<sup>170,178</sup> Median survival for 72 dogs with prostatic carcinoma was 0 days, with 58 dogs euthanized at the time of diagnosis, and a median survival of 30 days for 12 dogs that lived longer than one week.<sup>178</sup> Castration of dogs with prostatic carcinoma can result in involution of the non-neoplastic portion of the prostate but does not alter the progression of the tumor. Initial improvement in the size of the prostate of a 7-year old male English Bulldog with prostatic carcinoma was accompanied by continued weight loss and difficult urination.<sup>213</sup>

There are reports of dogs initially treated for prostatic cysts and/or abscesses that subsequently months to years later were diagnosed with prostatic carcinoma.<sup>170,214</sup>

There are a number of reports on the various surgical techniques used in performing prostatectomy and the potential complications in both normal dogs and dogs with prostatic disease.<sup>177,215-219</sup> Prostatectomy in 14 dogs (one had prostatic adenocarcinoma) resulted in urinary incontinence in 13 of 14 (93%).<sup>220</sup> Prostatectomy is rarely considered in the management of canine prostatic cancer for several reasons. The incidence of postoperative urinary incontinence is high, particularly in dogs with prostatic neoplasia. Secondly, the local disease is usually advanced and metastasis is present in many



**Fig 7. Male dog with a penile transmissible venereal tumor.**

dogs at the time of initial diagnosis such that prostatectomy is not warranted.

A 10-year-old weimaraner that underwent prostatectomy for prostatic adenocarcinoma was urinary incontinent after surgery but survived for 9 months; death was attributed to metastatic disease.<sup>216</sup> In another report of 3 dogs that underwent prostatectomy the histopathologic diagnosis was prostatic adenocarcinoma (1), prostatic leiomyosarcoma (1), and transitional cell carcinoma of the bladder with involvement of the prostate (1). Survival times were 2.5, 7 and 6 months respectively after surgery.<sup>177</sup>

Intraoperative orthovoltage radiotherapy in 10 dogs with either localized prostatic carcinoma ( $n = 7$ ) or prostatic carcinoma with metastasis to the regional lymph nodes ( $n = 3$ ) resulted in a median survival time of 180 and 80 days, respectively (not a statistically significant difference).<sup>212</sup> Survival time in this study ranged from 41-750 days.<sup>212</sup> Treatment of dogs with prostatic adenocarcinoma with Cobalt 60 external beam radiation therapy has been of some benefit with reduction in tumor size, relief of urinary outflow obstruction, and/or obstipation, but the maximum survival reported from one institution was only 5 months.<sup>186,221</sup>

Research is being done to investigate the role of photodynamic therapy in the canine prostate but information based on clinical cases is lacking.<sup>222</sup>

There is one report of an 11-year-old castrated male cat with a prostatic adenocarcinoma that was treated by prostatectomy combined with postoperative chemotherapy (combination of 4 cycles of doxorubicin and cyclophosphamide). Ten months after surgery, the cat was seen for dyschezia and it was determined based on necropsy that there was recurrence of the prostatic adenocarcinoma with metastasis to the pancreas and lungs.<sup>223</sup>

## Penile and Preputial Tumors

### Clinical Presentation

Urethral and penile neoplasms are relatively rare. TVTs and squamous cell carcinomas are the most common neoplasms of the canine penis.<sup>182</sup> TVT is the most common tumor in male dogs at this location; and typically involves the glans penis and prepuce so careful and full examination is important (Fig 7). TVT commonly occurs in younger dogs; 58% of the tumors in

one study occurred in dogs 4 years of age and younger.<sup>224</sup> TVT is transmitted from one dog to another by exfoliation and implantation of tumor cells into vaginal or penile epithelium that is traumatized during coitus. In a report of 86 tumors involving the canine penis or prepuce there were 84 TVTs (78 involved the penis, 6 involved the prepuce), 1 preputial papilloma, and 1 preputial carcinoma.<sup>224</sup> Of 160 tumors of the male genital system, there were 9 that involved the penis, including 8 transmissible venereal tumors, and one angioma.<sup>69</sup> Any cutaneous tumor can potentially involve the prepuce, but the most frequently observed tumors of the preputial skin include papilloma, hemangioma, fibroma, sebaceous gland adenoma, lymphangioma, mast cell tumor, fibrosarcoma, and squamous cell carcinoma.<sup>36</sup> Papillomas occur most frequently on the glans penis and are typically single, may be multiple, pedunculated or wide-based irregular or cauliflower shaped tumors.<sup>36</sup> There is one report of a dog with a chondrosarcoma of the os penis.<sup>225</sup>

### Treatment

As for vaginal TVT, tumors of the male genitalia are most commonly treated using vincristine chemotherapy.<sup>100</sup> TVT is a very radioresponsive tumor and a relatively low dose can be curative.<sup>100,103</sup> Other tumors in this region are typically treated surgically and may require partial or complete penile amputation combined with scrotal urethrostomy.<sup>226</sup> A 9-year-old male Shetland sheepdog was reported to have a squamous cell carcinoma of the penile glans treated by penile amputation and urethrostomy.<sup>227</sup> A 5-year old Chihuahua that presented for dysuria and penile prolapse underwent penile resection and scrotal urethrostomy; the histopathologic diagnosis was primary lymphosarcoma of the penis.<sup>228</sup>

## Scrotal Tumors

Essentially any tumor that involves the skin can potentially arise in the scrotum but the most common tumors are mast cell tumors, and melanomas.<sup>36</sup> In a series of 100 dogs with scrotal tumors there were 88 mast cell tumors, 5 hemangiomas, 3 melanomas, 3 histiocytomas, and one neurofibroma.<sup>21</sup> Other tumors that have been reported to occur on the scrotum of the dog include papilloma, sebaceous adenoma, fibroma, angioma, apocrine gland tumors, fibrosarcoma and squamous cell carcinoma.<sup>36</sup> There is a report of a 12-year old Scottish terrier with a scrotal mass that was diagnosed as malignant mesothelioma of the tunica vaginalis; death occurred three months after surgery with evidence of multiple metastases to the peritoneal cavity.<sup>229</sup> There is another report of a dog with a mesothelioma of the spermatic cord although no other details were provided.<sup>21</sup> There is one report of a fibroma of the scrotum in a cat.<sup>230</sup>

### Clinical Presentation

Dogs with scrotal tumors typically present for a mass that has been identified involving the scrotum.

### Treatment

Castration and scrotal ablation is recommended for dogs with mast cell tumors and other potentially malignant tumors. Additional systemic therapy is warranted in dogs with scrotal mast cell tumors as regardless of tumor grade, mast cell tumors in this location are associated with more aggressive behavior and are more likely to metastasize.<sup>98,99</sup>

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