

Compendium

Canine Prostatic Carcinoma

Sandra M. Axiak, DVM, DACVIM (Oncology)
University of Missouri

Astrid Bigio, DVM
Louisiana State University

Abstract: Canine prostatic carcinoma is locally aggressive with a high rate of metastasis. Common metastatic sites include lymph nodes, lungs, liver, spleen, and bone. Staging relies on chest radiography, abdominal radiography, and abdominal ultrasonography, in addition to radiography of any painful regions. An enlarged, mineralized prostate is a frequent finding; in a castrated male dog, it is predictive of prostatic carcinoma. NSAIDs are an important component of treatment, although additional local and systemic therapies should be considered to improve the quality of life of these patients.

Canine prostatic carcinomas have a low incidence (0.43%), with Shetland sheepdogs and Scottish terriers having an increased risk.¹ Due to rapid growth and metastasis,¹⁻⁴ dogs may be presented late in the course of the disease, when clinical signs are representative of metastatic disease rather than a primary urogenital ailment.¹⁻⁴ For example, dogs with metastasis to the brain, lumbar spine, or pelvis may present with clinical signs that are primarily neurologic. Dogs diagnosed with prostatic cancer have a median age of 10 years.^{4,5} Castration at an early age is controversial as a risk factor for development.¹⁻⁶ Most canine prostate cancers do not express androgen receptors^{2,4}; as a result, dogs are refractory to the hormone ablation therapy commonly used in men.¹⁻⁶

Clinical Signs

Stranguria, pollakiuria, and hematuria occur due to compression or invasion of the urethra by the prostatic tumor, invasion of cancer into the bladder, or concurrent prostatitis. Secondary infection is frequently reported (36% of affected dogs) and can exacerbate lower urinary tract signs.³ Dyschezia, tenesmus, and constipation are related to obstruction of the descending colon by the enlarged prostate and/or enlarged lymph nodes in the sublumbar region.^{3,4} Metastasis to bone can also lead to lameness and neurologic signs such as ataxia and paresis or paralysis of the hindlimbs.²⁻⁴ Systemic signs such as lethargy, anorexia, weight loss, coughing, and exercise intolerance may also be present in late disease stages.²⁻⁴

Diagnosis

The most common examination finding is a firm and irregular prostate palpated on rectal examination; enlarged lymph nodes in the sublumbar region may also be present. A mass may be palpated just caudal to the bladder if the prostate tumor has extended into the abdomen. If urethral obstruction has occurred, the bladder will be firm, painful, and enlarged. Additional abnormalities reported

are a dull demeanor, dehydration, pyrexia, dyspnea, cachexia, and dehydration.²⁻⁴

Other prostatic conditions that result in prostatomegaly are chronic prostatitis, prostatic abscessation, benign prostatic hyperplasia (BPH), and prostatic cysts, which are all more common in intact male dogs.⁷ In castrated dogs, prostatic carcinoma is the most common cause of prostatomegaly.⁷

A complete blood count, chemistry panel, and urinalysis should be conducted for a patient with suspected neoplasia or infection. Non-regenerative anemia (anemia of chronic disease) and leukocytosis (mature neutrophilia) are common. Azotemia can indicate postrenal obstruction, primary renal disease, or prerenal azotemia from dehydration. Prostate-specific antigen, a serum screening test historically used to detect early prostate cancer in men, is not useful as a screening tool in dogs.² A urinalysis may show pyuria, hematuria, and bacteriuria; in addition, neoplastic cells may be seen in urine sediment, although differentiation between reactive and neoplastic epithelial cells may not be possible.⁴

Key Points

- Neutered dogs with prostatic mineralization are likely to have prostatic neoplasia.
- NSAIDs improve survival times and may improve quality of life in dogs with prostatic carcinoma.
- In all cases of suspected prostatic carcinoma, a minimum database (consisting of a complete blood count, chemistry panel, and urinalysis), chest radiography, abdominal radiography, and abdominal ultrasonography are recommended to detect metastasis in the lungs, lymph nodes, liver, and spleen.
- An additional site of metastasis is the skeleton, and any areas of pain or lameness should be investigated with radiography. CT and bone scintigraphy are additional diagnostics to consider.



Figure 1. Mineralized prostatic mass caudal to the bladder (circle).

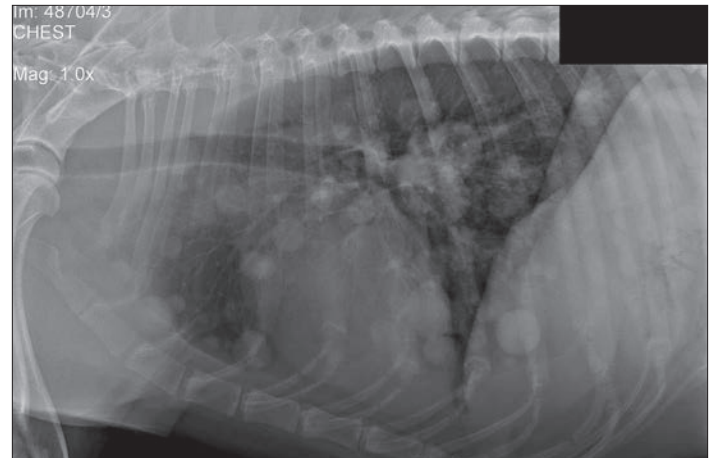


Figure 2. Metastasis of prostatic cancer to lung parenchyma.

Abdominal radiography may reveal ventral displacement of the descending colon due to lymph node enlargement in the sublumbar region. The prostate may appear as an enlarged, mineralized soft tissue mass just caudal to the bladder (**FIGURE 1**). The presence of mineralization in a prostatic mass is predictive of prostatic neoplasia in castrated male dogs, with an overall sensitivity of 84% and specificity of 100%.⁸ In intact dogs, mineralization can occur with prostatic neoplasia, paraprostatic cysts, BPH, or prostatitis.⁸ Tumor metastasis to the lumbar spine and pelvis may also be detected.

Metastasis to the lung parenchyma, found on chest radiography, is present in 44% of dogs at diagnosis³ (**FIGURE 2**). On abdominal ultrasonography, the prostate appears enlarged, irregular, heterogeneous, and, in many cases, mineralized.⁸ The lymph nodes of the sublumbar region, liver, and spleen may appear enlarged with irregular hyperechoic nodules. Additional findings are invasion of the bladder, hydronephrosis, and hydroureter (**FIGURE 3**); less common findings are evidence of metastasis to the kidneys, adrenal glands, or colon.

Bone metastasis appears as lytic, proliferative, or mixed lesions on radiography, most commonly in the lumbar vertebrae,

pelvis, and femur. Because metastasis can occur in any bone, reported lameness or pain should be thoroughly investigated with radiography. Cytology or biopsy with histopathology may be used to confirm metastatic disease. Nuclear scintigraphy can also be utilized to further pinpoint areas of skeletal metastasis, although this diagnostic test is very sensitive but not specific for cancerous bone lesions.²

Computed tomography (CT) is a sensitive tool to detect local invasion and metastasis of prostatic carcinoma (**FIGURE 4**). CT of the lungs can detect nodules as small as 1 mm in diameter.⁹ In

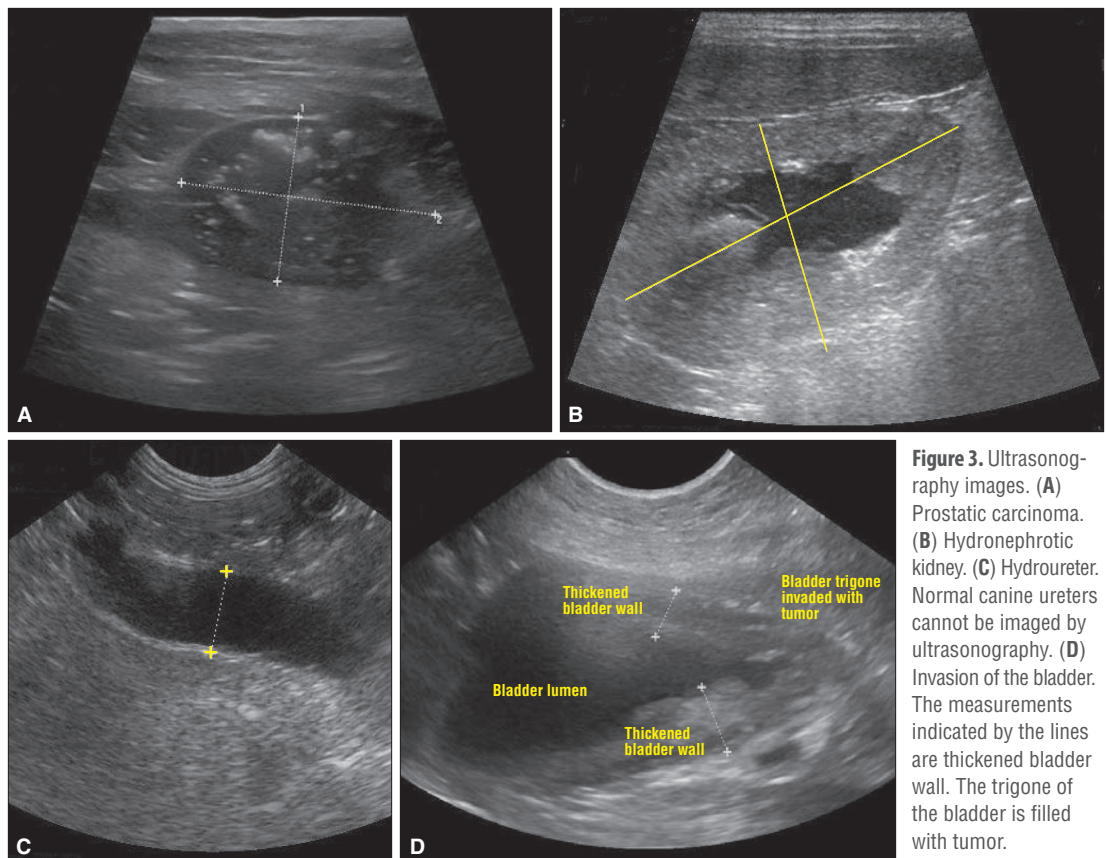


Figure 3. Ultrasonography images. (A) Prostatic carcinoma. (B) Hydronephrotic kidney. (C) Hydroureter. Normal canine ureters cannot be imaged by ultrasonography. (D) Invasion of the bladder. The measurements indicated by the lines are thickened bladder wall. The trigone of the bladder is filled with tumor.

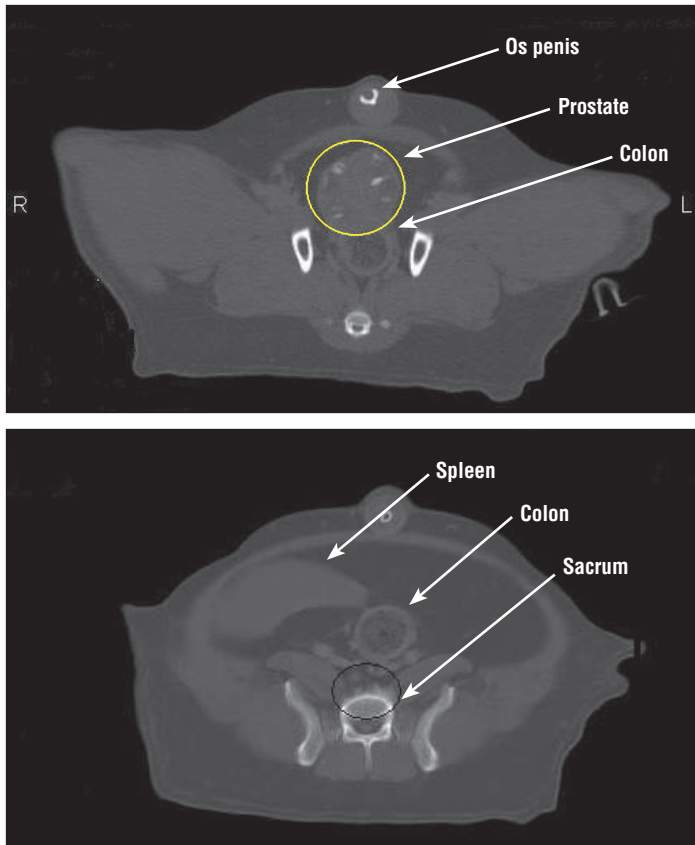


Figure 4. CT images. (A) Prostatic carcinoma (circle). (B) Sacral metastasis not evident on radiographs (circle).

addition, CT or magnetic resonance imaging of the spine or brain might be useful in dogs with neurologic signs to define metastatic sites.

Samples for cytology of the prostate can be obtained by evaluation of prostatic wash fluid, traumatic catheterization of areas with bladder involvement, or ultrasound-guided fine-needle aspiration. As a precautionary note, although not reported with prostatic adenocarcinomas, transitional cell carcinoma of the bladder can seed into the abdomen after fine-needle aspiration.¹⁰ The reported agreement between cytologic and histologic findings is 80% for prostatic carcinoma.¹¹ Secondary infection and inflammation can interfere with interpretation of cytology.³ Cytology of the lymph nodes, liver, and spleen is recommended if these structures appear abnormal on ultrasonography.

Histopathologically, canine prostate tumors show considerable heterogeneity. Grading is not routinely performed for prostatic tumors as it is in men because all canine prostatic carcinoma subtypes are considered malignant with a high metastatic potential. No difference in survival has been found for the different histologic subtypes. Adenocarcinomas are more common in intact males than castrated males,⁴ and 53% of canine prostatic carcinomas show mixed morphologic features.⁴ Immunohistochemistry can be performed to further delineate the cell of origin; however, canine prostatic carcinomas express markers of both urothelial and ductal

origin, making the differentiation between adenocarcinoma and other carcinoma subtypes, especially transitional cell carcinoma, problematic.²⁻⁴ Other types of neoplasia found in the prostate include transitional cell carcinoma and, less commonly, fibrosarcoma, leiomyosarcoma, hemangiosarcoma, and lymphoma.²

Treatment

Obstruction of the urethra is a medical emergency. Appropriate supportive care and relief of obstruction by placement of a urinary catheter are imperative to prevent bladder rupture. Treatment of secondary bacterial prostatitis should be based on culture and susceptibility testing results, in addition to using antibiotics that penetrate the prostate. Examples of such drugs are fluoroquinolones, chloramphenicol, and trimethoprim-sulfamethoxazole.⁷

Complete prostatectomy is not often used in the treatment of canine prostatic cancer.² Dogs that undergo complete excision of the prostate are at risk of becoming incontinent.¹² Other possible complications are colonic necrosis and urinary tract infection.¹²⁻¹⁴ Because complete excision of a prostatic tumor is not usually possible due to location and invasiveness, disease recurrence and metastasis are almost inevitable.¹⁴ In one study,¹⁴ the median survival time after total prostatectomy was 17 days, with death or euthanasia due to complications of surgery or tumor progression; however, this surgery may be considered for dogs with early-stage disease.

Subtotal intracapsular prostatectomy can immediately palliate clinical signs and is associated with a lower rate of postoperative complications than total prostatectomy.¹⁴ The reported median survival time is 130 days, with most dogs euthanized due to tumor progression or metastasis; in the study mentioned above,¹⁴ two dogs were euthanized within 3 days after surgery due to surgical complications. In another study,¹⁵ eight dogs that underwent partial prostatectomy using a neodymium:yttrium-aluminum-garnet (Nd:YAG) laser had a median survival time of 103 days; however, three of these dogs died of surgical complications within 16 days of the procedure. Partial subcapsular prostatectomy followed by intraoperative photodynamic therapy provides disappointing results, with a median survival time of 41 days.¹⁶ One dog has been treated with photodynamic therapy alone, with stable disease 34 weeks after treatment.¹⁷ Transurethral resection of prostatic tumors has also been attempted, with rapid palliation of clinical signs; complications include iatrogenic urethral perforation and biochemical abnormalities resulting from prolonged exposure to lavage fluid.¹⁸ Other options for palliation of clinical signs are placement of a cystostomy tube, an indwelling urethral catheter, or a urethral stent. Placement of a urethral stent is rapid, and relief of obstruction is immediate. Uncommon complications are urinary incontinence or reobstruction if the stent is dislodged; survival after stenting for dogs with prostatic cancer is not reported.¹⁹ Obstruction of ureters can also be relieved with ureteral stenting.

Radiation therapy is often used, although not well studied, in dogs with prostate cancer. Intraoperative radiation therapy using orthovoltage was performed in 10 dogs²⁰; two dogs died of complications related to biopsy performed at the same time, and the remaining eight dogs survived for a median of 114 days. The total

dose and dose per fraction must be carefully considered to avoid the complications of chronic colitis and urethral stricture.²¹ Examples of irradiation currently used but not studied for prostatic carcinoma include stereotactic radiosurgery; brachytherapy seed, bead, or straw implantation; and intensity-modulated radiation therapy.

Cyclooxygenase-2 (COX-2) is expressed in prostatic carcinomas but not the normal canine prostate,²² so treatment with COX-2 inhibitors may have an antitumor effect. The antiinflammatory effects may also be helpful in improving the patient's quality of life. In a retrospective study,²² dogs treated with piroxicam or carprofen had a median survival time of 6.9 months, compared with less than 1 month in untreated dogs. Possible adverse effects of NSAIDs are gastrointestinal ulceration and kidney damage. It is important to monitor for these effects. It is unknown at this time which NSAIDs are more or less effective based on selectivity.

Chemotherapy has not been studied for the treatment of canine prostatic carcinoma, but should be considered based on the high rate of metastasis. Commonly used drugs are those studied and used in treating transitional cell carcinoma of the bladder, including carboplatin or mitoxantrone in combination with an NSAID. Potential adverse effects include bone marrow suppression, nausea, vomiting, and diarrhea. Although the role of chemotherapy has not been well defined for dogs with prostate cancer, men with advanced refractory prostate cancer treated with a combination of prednisone and mitoxantrone have an improvement in health-related quality of life.²³

Bone metastasis may cause a decline of quality of life in canine patients with prostatic carcinoma. Bisphosphonates (e.g., pamidronate) inhibit bone resorption by osteoclasts and therefore may relieve pain and reduce the risk of pathologic fracture.²⁴ Samarium-153 ethylenediamine-tetramethylene-phosphonic acid (¹⁵³Sm-EDTMP) is an injectable radiopharmaceutical that has been used in dogs and people for metastatic lesions in bone and primary bone tumors.²⁵ An additional treatment option is external beam radiation therapy to palliate pain associated with bone metastases.

Conclusions

A digital rectal examination should be performed on routine physical examinations. Prostatic carcinoma is more common in castrated dogs than in intact males, and secondary prostatic and bladder infection can occur. Definitive diagnosis of carcinoma can often be obtained with cytology if infection is not present, and histopathology can be used when cytology is not diagnostic. NSAIDs are an important component to any treatment protocol and have been shown to improve overall median survival times compared with no cancer therapy. There is no current standard of care for the treatment of dogs with prostatic carcinoma, but in considering treatment, both local and systemic disease control should be considered. Research is ongoing to investigate both local and systemic means of control.

References

1. Bryan JN, Keeler MR, Henry CJ, et al. A population study of neutering as a risk factor for canine prostate cancer. *Prostate* 2007;67:1174-1181.
2. LeRoy BE, Northrup N. Prostate cancer in dogs: comparative and clinical aspects. *Vet J* 2009;180:149-162.
3. Bell FW, Klausner JS, Hayden DW, et al. Clinical and pathologic features of prostatic adenocarcinoma in sexually intact and castrated dogs: 31 cases (1970-1987). *J Am Vet Med Assoc* 1991;199(11):1623-1630.
4. Cornell KK, Bostwick DG, Cooley DM. Clinical and pathologic aspects of spontaneous canine prostate carcinoma: a retrospective analysis of 76 cases. *Prostate* 2000;45:173-183.
5. Teske E, Naan EC, vanDijk EM, et al. Canine prostate carcinoma: epidemiological evidence of an increased risk in castrated dogs. *Mol Cell Endocrinol* 2002;197:251-255.
6. Obradovich J, Walshaw R, Goullaud E. The influence of castration on the development of prostatic carcinoma in the dog. *J Vet Intern Med* 1987;1:183-187.
7. Smith J. Canine prostatic disease: a review of anatomy, pathology, diagnosis, and treatment. *Theriogenology* 2008;70:375-383.
8. Bradbury CA, Westropp JL, Pollard RE. Relationship between prostatomegaly, prostatic mineralization, and cytologic diagnosis. *Vet Radiol Ultrasound* 2009;50(2):167-171.
9. Nemanic S, London CA, Wisner ER. Comparison of thoracic radiographs and single breath-hold helical CT for detection of pulmonary nodules in dogs with metastatic neoplasia. *J Vet Intern Med* 2006;20:508-515.
10. Vignoli M, Rossi F, Chierici C, et al. Needle tract implantation after fine needle aspiration biopsy (FNAB) of transitional cell carcinoma of the urinary bladder and adenocarcinoma of the lung. *Schweiz Arch Tierheilkd* 2007;149(7):314-318.
11. Powe JR, Canfield PJ, Martin PA. Evaluation of the cytologic diagnosis of canine prostatic disorders. *Vet Clin Pathol* 2004;33(3):150-154.
12. Basinger RR, Rawlings CA, Barsanti JA, et al. Urodynamic alterations associated with clinical prostatic diseases and prostatic surgery in 23 dogs. *J Am Anim Hosp Assoc* 1989;25:385-392.
13. Hardie EM, Barsanti JA, Rawlings CA. Complications of prostatic surgery. *J Am Anim Hosp Assoc* 1984;20:50-56.
14. Vlasin M, Rauser P, Fichtel T, et al. Subtotal intracapsular prostatectomy as a useful treatment for advanced stage prostatic malignancies. *J Small Anim Pract* 2006;47:512-516.
15. L'Eplattenier HF, van Nimwegen SA, van Sluijs FJ, et al. Partial prostatectomy using Nd:YAG laser for management of canine prostate carcinoma. *Vet Surg* 2006;35:406-411.
16. L'Eplattenier HF, Klem B, Teske E, et al. Preliminary results of intraoperative photodynamic therapy with 5-aminolevulinic acid in dogs with prostate carcinoma. *Vet J* 2008;178:202-207.
17. Lucroy MD, Bowles MH, Higbee RG, et al. Photodynamic therapy for prostatic carcinoma in a dog. *J Vet Intern Med* 2003;17:235-237.
18. Liptak JM, Brutscher SP, Monnet E, et al. Transurethral resection in the management of urethral and prostatic neoplasia in 6 dogs. *Vet Surg* 2004;33:505-516.
19. Weisse C, Berent A, Todd K, et al. Evaluation of palliative stenting for management of malignant urethral obstructions in dogs. *J Am Vet Med Assoc* 2006;229(2):226-234.
20. Turrel JM. Intraoperative radiotherapy of carcinoma of the prostate gland in ten dogs. *J Am Vet Med Assoc* 1987;190(1):48-52.
21. Anderson CR, McNiel EA, Gillette EL, et al. Late complications of pelvic irradiation in 16 dogs. *Vet Radiol Ultrasound* 2002;43(2):187-192.
22. Sorenmo KU, Goldschmidt MH, Shofer FS, et al. Evaluation of cyclooxygenase-1 and cyclooxygenase-2 expression and the effect of cyclooxygenase inhibitors in canine prostate carcinoma. *Vet Comp Oncol* 2004;2(1):13-21.
23. Osoba D, Tannock IF, Ernst DS, et al. Health related quality of life in men with metastatic prostate cancer treated with prednisone alone or mitoxantrone and prednisone. *J Clin Oncol* 1999;17(6):1654-1663.
24. Fan TM, de Lorimer LP, Charney SC, et al. Evaluation of intravenous pamidronate administration in 33 cancer-bearing dogs with primary or secondary bone involvement. *J Vet Intern Med* 2005;19:74-80.
25. Barnard SM, Zuber RM, Moore AS. Samarium Sm 153 lexidronam for the palliative treatment of dogs with primary bone tumors: 35 cases (1999-2005). *J Am Vet Med Assoc* 2007;230(12):1877-1881.



3 CE Credits

This article qualifies for 3 contact hours of continuing education credit from the Auburn University College of Veterinary Medicine. CE tests must be taken online at Vetlearn.com; test results and CE certificates are available immediately. Those who wish to apply this credit to fulfill state relicensure requirements should consult their respective state authorities regarding the applicability of this program.

1. Which statement regarding prostatic carcinoma in dogs is true?

- a. Intact males are more likely than castrated dogs to develop prostatic carcinoma.
- b. Clinical signs at presentation may be representative of metastatic disease rather than a primary urogenital ailment.
- c. Mineralization of a prostatic mass is not predictive of diagnosis in castrated males.
- d. The median age at diagnosis is 3 to 4 years.

2. Which screening test is always recommended in healthy dogs?

- a. chest radiography
- b. abdominal ultrasonography
- c. CT
- d. digital rectal examination

3. Which location is a common site of metastasis of prostatic carcinoma?

- a. heart
- b. skin
- c. bone
- d. intestines

4. Which disease(s) can cause mineralization of the prostate in intact male dogs?

- a. chronic prostatitis
- b. BPH
- c. paraprostatic cysts
- d. all of the above

5. Which treatment method is known to be associated with the highest risk of postoperative incontinence?

- a. intracapsular subtotal prostatectomy
- b. total prostatectomy
- c. NSAID administration
- d. radiation therapy

6. A 10-year-old castrated beagle presents for stranguria and hematuria. Rectal examination reveals an irregular, enlarged prostate, and abdominal radiography reveals that the prostate is mineralized. Which of the following is the most likely diagnosis?

- a. BPH
- b. prostatic abscess
- c. prostatic neoplasia
- d. paraprostatic cysts

7. Which treatment is most likely to palliate pain associated with bone metastasis?

- a. urethral stent
- b. chemotherapy
- c. bisphosphonates
- d. subtotal prostatectomy

8. Which antibiotic is known to effectively penetrate the prostate?

- a. amoxicillin
- b. enrofloxacin
- c. cefpodoxime
- d. cephalixin

9. Which treatment has been proven to improve median survival times in dogs with prostatic carcinoma compared with no treatment?

- a. cisplatin
- b. carboplatin
- c. NSAIDs
- d. mitoxantrone

10. Which statement regarding prostatic neoplasia in dogs is true?

- a. Grading should be performed for all canine prostatic tumors to determine treatment.
- b. Sarcomas are the most common type of prostatic tumor.
- c. Prostatic carcinomas are often mixed in morphology.
- d. The presence of inflammation does not affect interpretation of cytology.